Best Practice for Smoking Cessation: Pharmacotherapy

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Why is it so hard to quit?

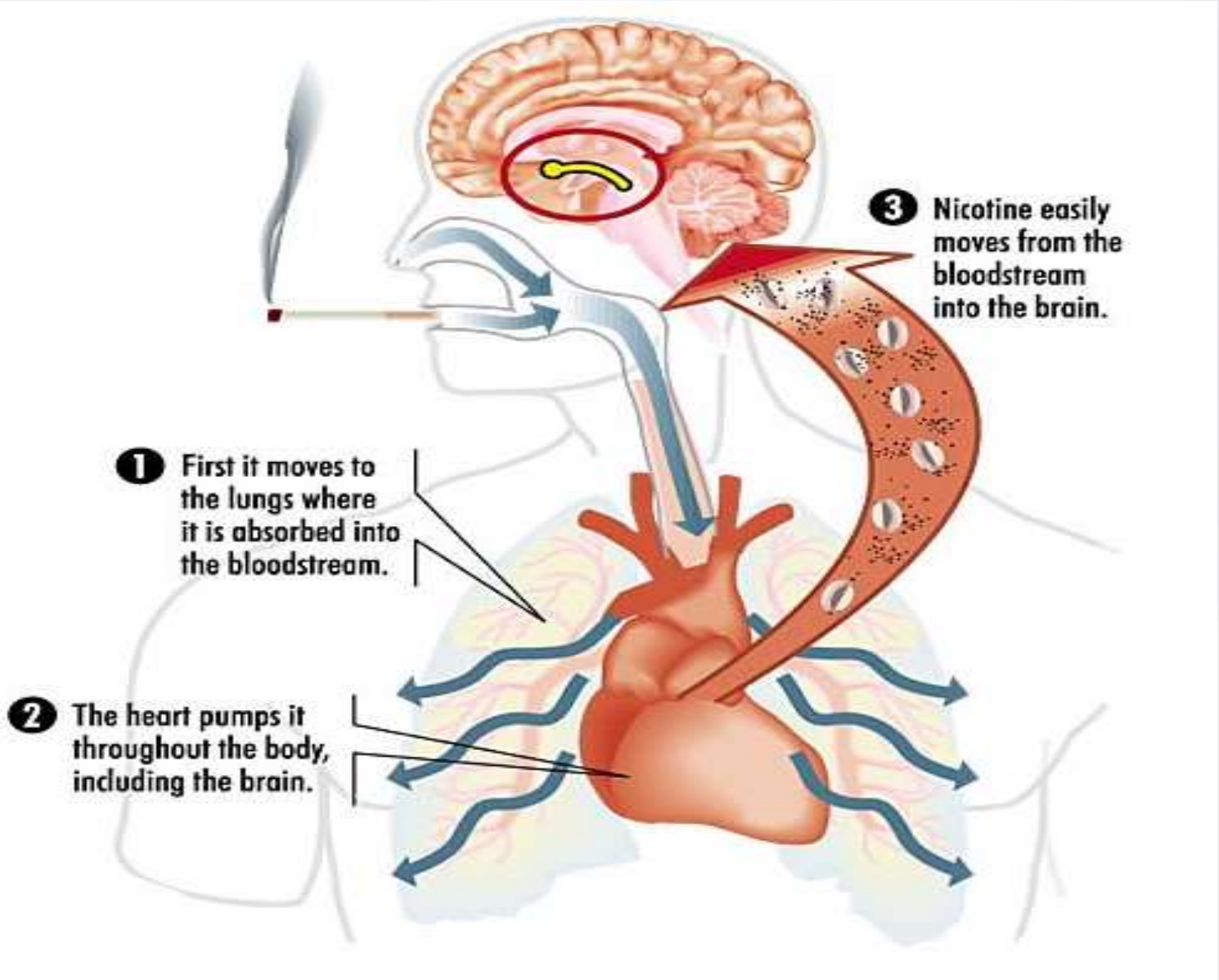
People who smoke aren't weak nor are they simply making a bad lifestyle choice.

Smoking is a complex process made up of:

- Nicotine dependence
- Behavioural connections
- Psychological connections

Nicotine

- **Short half-life (average 2 hours)**
  - In some individuals as short as 20-40minutes
- **What it does:**
  - Dependence, short term relief of anxiety and low mood, increased arousal and concentration
  - Minor haemodynamic effects: increased HR, transient increase in BP
- **What it doesn't do:**
  - Not classed as carcinogen by IARC
  - Does not cause cardiovascular disease
  - Does not cause lung damage
- **Plays a small role in human disease- 'people smoke for nicotine, but die from smoke'**



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http://www.tobaccofreedom.org/issues/addiction/index.html

Nicotine Dependence

- **Chronic medical condition with multiple cycles of relapse and remission**
  - Relapsed smokers need to be re-engaged and assisted through repeated quit attempts
- **Under recognised by health professionals**
- **Assessment is important**
- **Time to first cigarette a reliable indicator**

Questions	Response coding	Score	Dependence score
How soon after you wake do you smoke your first cigarette?	Within 5 minutes = 3 5 – 30 minutes = 2 31 – 60 minutes = 1 Over 60 minutes = 0		≤ 2 = very low 3 = low 4= moderate 5+ = high
How many cigarettes a day do you smoke?	10 or less = 0 11 – 20 = 1 21 – 30 = 2 31 or more = 3		
	Fagerstrom Score	/ 6	

Nicotine withdrawal syndrome

- **Symptoms begin within hours of quitting**
- **Duration and severity of symptoms are highly variable among individuals**
  - Generally worst in first 24-48 hours
- **Symptoms are usually alleviated in 2-4 weeks**
  - Dizziness, insomnia, restlessness, difficulty concentrating, irritability, increase appetite, mood changes

Other mechanisms underlying smoking

Psychological connection

- smoking is related to how clients feel, their moods and emotions
- commonly draw a connection between smoking and stress relief, feelings of comfort and relaxation

Behavioural connections

- behaviours that are closely linked to their smoking
- connections tend to be strong and have built up over many years

Okay so what can we do?

Importance of brief intervention

Brief advice from a healthcare professional prompts people to quit

NNT 1 in 33

Increases long-term abstinence rates by 1-3 percentage points (above unassisted quit rates, which are around 2-3%)

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Stead et al. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews 2013, Issue 5. Art. No.: CD000165.

Best practice for smoking cessation

- **3%- 5% people who smoke, successfully quit cold turkey**
- **Interventions that combine pharmacotherapy and behavioural support increase smoking cessation success in a wide range of settings and populations**
- **Need to encourage people who smoke to use both pharmacotherapy and behavioural support**

Pharmacotherapy

- **Nicotine replacement therapy (NRT)**
  - Transdermal- patches
  - Intermittent- lozenges, mouthspray, gum and inhalator
- **Bupropion (Zyban®)**
- **Varenicline (Champix®)**

Nicotine replacement therapy

- **Increases quit rates by 50-70% compared to placebo**
- **Reduces cravings and minimises withdrawal symptoms**
- **Safety and efficacy profile**
  - Does not produce dramatic surges in blood levels
  - Minimal addictive potential
  - No serious side effects, usually minor and formulation related
- **Best result = NRT (minimum 8/52) + behavioural advice + follow up**
- **No evidence for weaning the patch**

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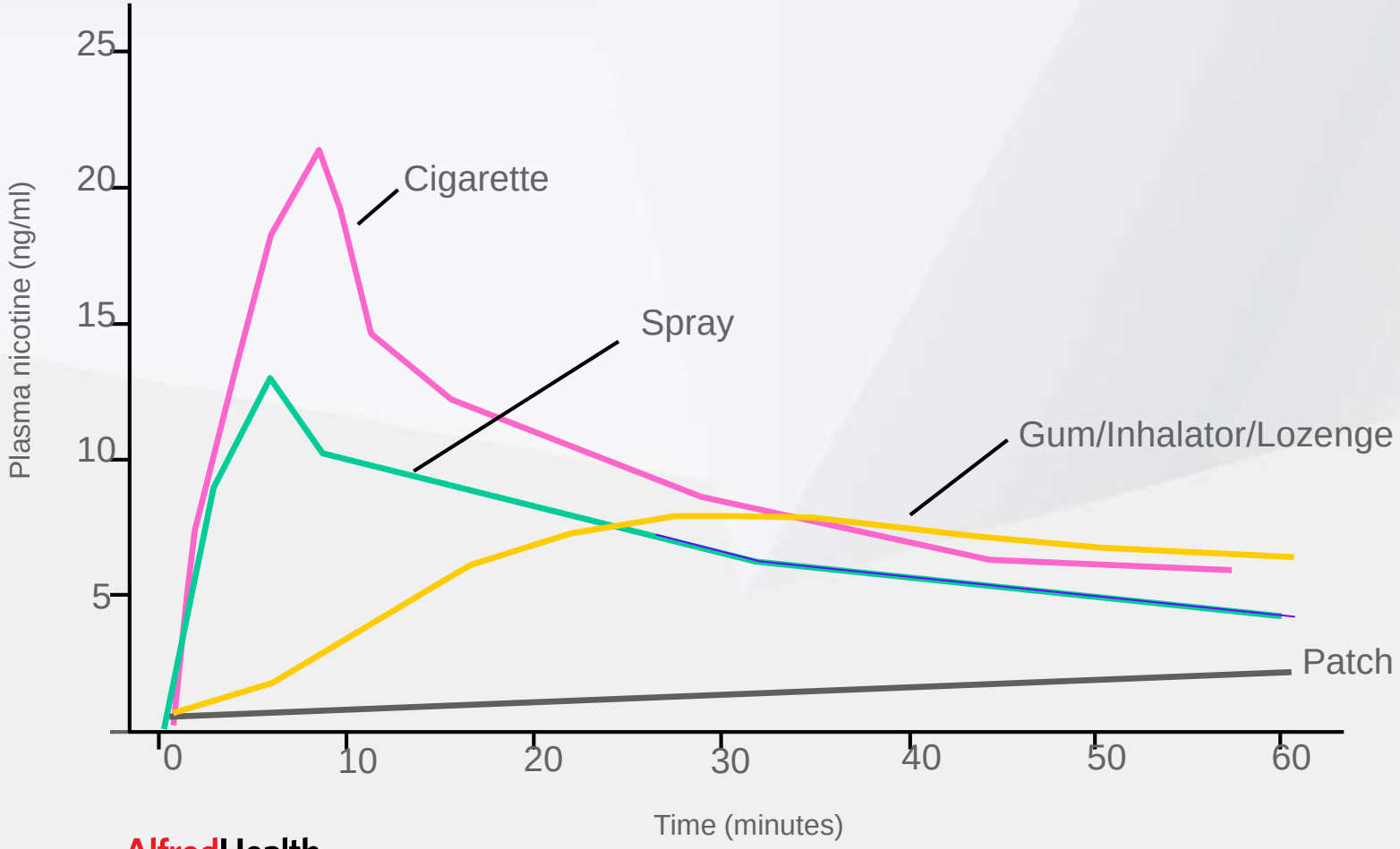
Stead 2012

Plasma nicotine levels- single dose



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Royal College of Physicians 2000

Combination Therapy

Patch + Intermittent

Patch: Steady protection (long acting and slow onset) to control baseline cravings

Intermittent: Quicker and more flexible relief
If possible use in anticipation of smoking trigger

- **Adverse effect profile similar to mono-therapy**

Nicotine patch

- **Slow skin absorption – takes several hours to reach steady state (depends on brand)**
  - If removed overnight, substantial nicotine levels are reached within 3 hours after a new patch is applied Fant 2000
- **Produces relatively constant withdrawal relief over 24 hours**
- **Can be started 2 weeks before setting ‘quit date’ - increases quit rates by 35% (compared to traditional quit day application)**
- **Continue to use patch after a lapse- 4-5 times more likely to be abstinent at end of treatment period** Mendelsohn 2013

Nicotine patch

- **Apply to clean, hairless skin**
- **Hold firmly in place for 20 seconds after application to assist adhesion**
- **Swimming & showering ok after an hour**
- **Tape around edges if lifting**
- **Rotate patch around body**
- **Sleep disturbance (vivid dreaming) common→ if disrupting daily activities, put patch on in AM and remove PM, could try lower dose patch; does decrease over time; consider caffeine reduction**
- **< 10% have skin irritation (usually due to adhesive) → cortisone cream may be helpful**
- **Different brands have different properties and deliver blood nicotine levels about half as those from smoking**

Nicotine gum

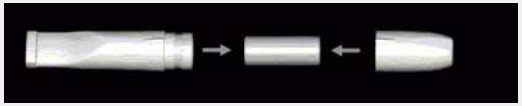
- **Nicotine is readily absorbed from oral mucosa membranes**
- **Two strengths- 2mg & 4mg gum**
- **Best to start immediately upon waking**
- **Use liberally (no greater than 1 piece/hour)**
- **‘Chew and park’ method – chew every 2 seconds for approximately 30minutes**
- **Adverse effects- nausea, hiccups, bloating**

Nicotine lozenge

- **Nicotine is readily absorbed from oral mucosa membranes**
- **Strengths**
  - 2mg & 4mg lozenge (Nicorette Cooldrops®)
  - 1.5mg & 4mg mini lozenge (Nicabate Mini lozenges®)
- **Use liberally to suppress cravings/urges to smoke**
- **Lozenge should be placed in the mouth and moved from one side to the other until completely dissolved**
  - Should not be chewed, sucked or swallowed whole
- **Adverse effects- hiccups, nausea, flatulence & sensitive mouth**

Nicotine inhalator

- **Nicotine is readily absorbed from oral mucosa membranes**
- **Strength- 15mg/cartridge**
- **When used as a cigarette, taking 8 times as many puffs as when smoking, delivers about 1 mg of nicotine**
- **A cartridge will deliver the same amount of nicotine (1 mg), at a uniform release rate, for the first seven consecutive uses**
- **Designed to combine pharmacological and behavioural substitution (hand to mouth ritual)**
- **Patients can self-titrate to the level of nicotine they require to relieve cravings**
- **Adverse effects- hiccups, sore throat, heartburn**



Nicotine spray

- **Nicotine is absorbed through oral mucosa membranes**
- **Oral spray form means that nicotine is administered instantaneously**
- **Strength- 1mg/dose (150 doses per device)**
- **Use liberally to suppress cravings/urges to smoke**
- **Priming is needed for first time use and if not used greater than 2 days**
- **Adverse effects- nausea, mouth irritation, taste disturbances, hiccups, indigestion**

Troubleshooting

- **Misconceptions can lead to inadequate dose**
- **Side effects of NRT can be nicotine withdrawal (or incorrect use)**
- **Common to underdose on NRT (overdosing is rare)**
- **Nicotine from all the intermittent products is absorbed through the buccal mucosa→ concurrent eating an drinking should be discouraged.**
- **Being nil oral is not a contraindication; avoid gum pre-op as can increase intra-gastric volumes**

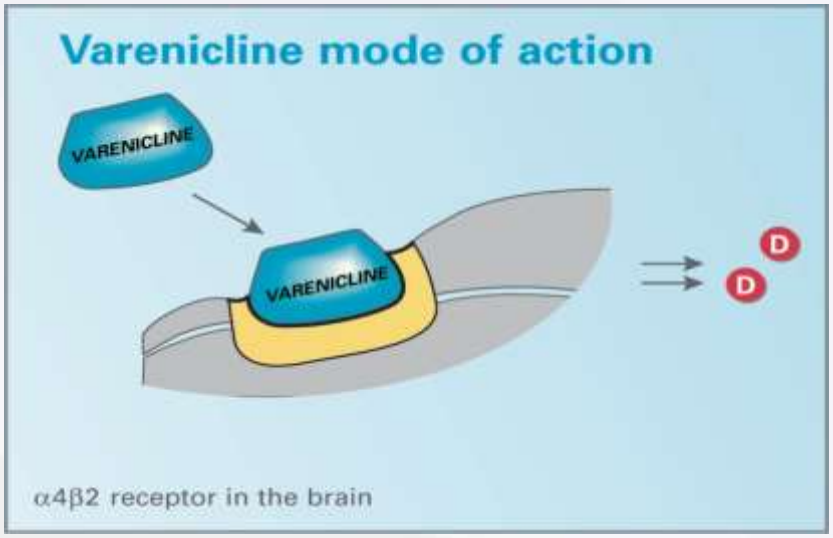
How to boost patient compliance…

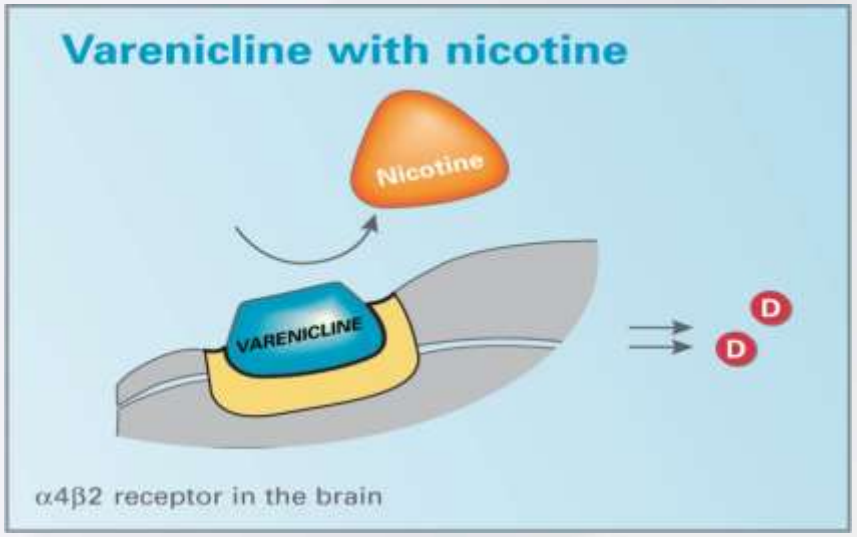
- **Concerns about safety**
  - NRT is always safer than smoking
  - Safety profile- does not cause cancer, lung disease, cardiovascular disease
- **Concerns about the addictiveness of NRT**
  - Minimal addictive potential
- **Lack of confidence in efficacy**
  - Proven effective (significant increases chances of quitting); minimises nicotine withdrawal symptoms
- **Not using enough**
  - More effective when dose titrated according to response
- **Stopping NRT too early**
  - Needs to be taken for long enough to start to address other drivers of smoking
  - Best not to cease until patient can resist cravings in situations

How to boost patient compliance….

- **NRT is not working**
  - May require increased dose (combination therapy, more doses of intermittent, second patch)
  - Are the products being used correctly/
  - Consider change to varenicline
- **Side effects**
  - Decrease over time
  - Are the products being used correctly?
- **Cost**
  - NRT cost vs. cigarettes (and ongoing smoking- financial & health)

Varenicline (Champix)





Varenicline- Troubleshooting

- **Nausea**
  - Always take with food
  - Increase fluid intake, 10 glasses water /day if clinically appropriate
- **Insomnia – bring evening dose forward**
- **Renal impairment – reduced dose 1mg per day**
- **If not tolerating for any reason consider reduced dose**

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

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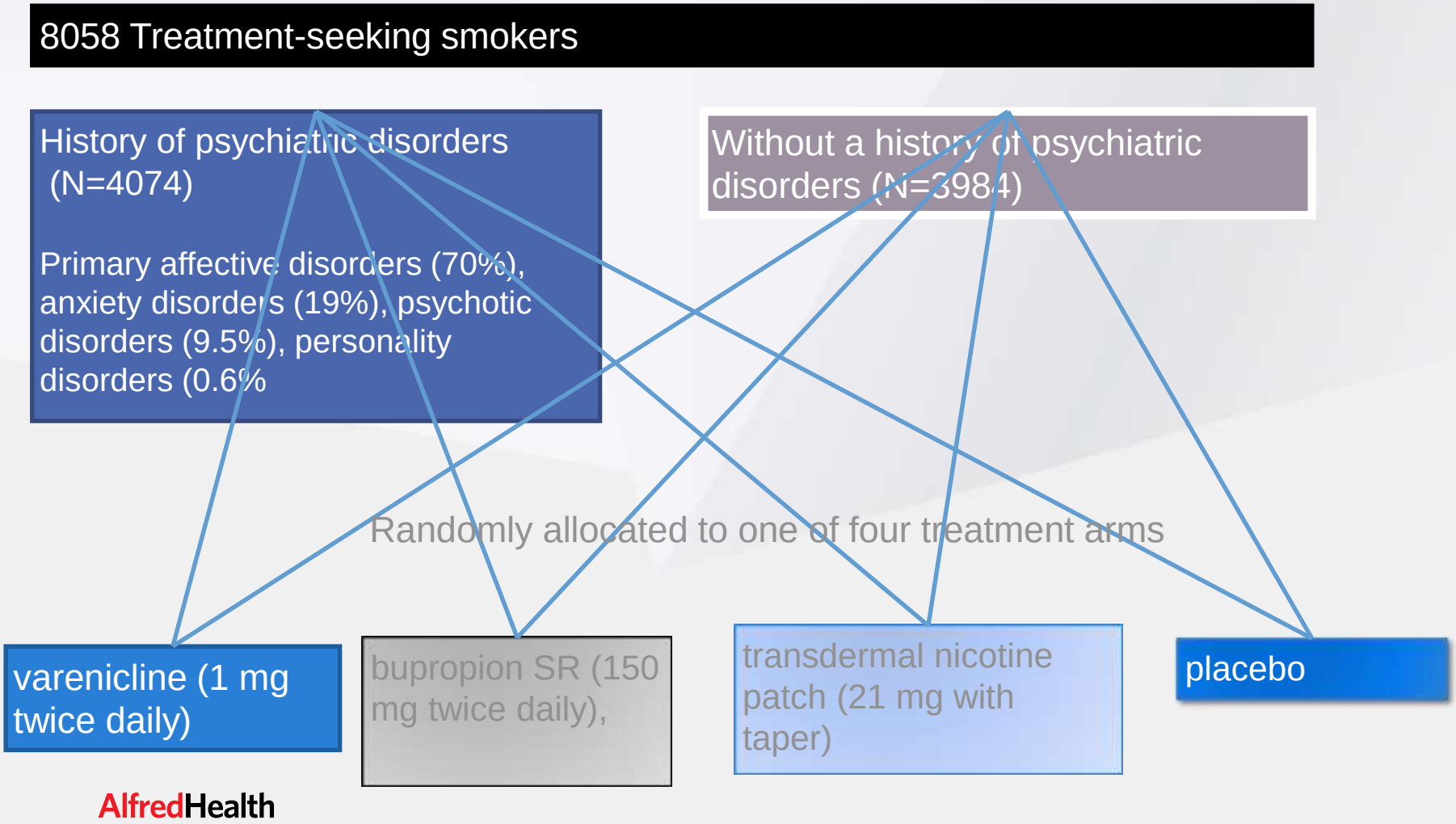
EAGLES Study



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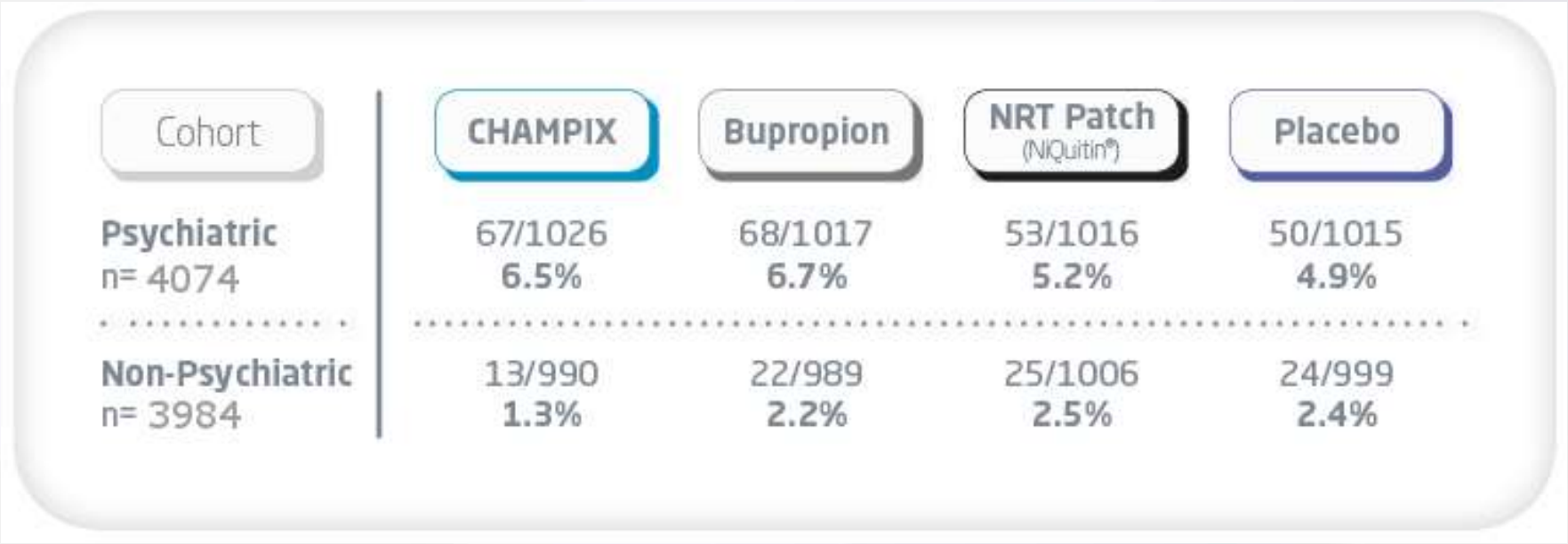
Anthenelli et al. 2016 Lancet 387 (10037): 2507-20



Cohort	CHAMPIX	Bupropion	NRT Patch (NiQuitin®)	Placebo
Psychiatric n= 4074	67/1026 **6.5%**	68/1017 **6.7%**	53/1016 **5.2%**	50/1015 **4.9%**
Non-Psychiatric n= 3984	13/990 **1.3%**	22/989 **2.2%**	25/1006 **2.5%**	24/999 **2.4%**

- **The rate of neuro-psychiatric adverse events (AEs) was similar (not significantly different) across the four treatment groups**
  (i.e. no indication that varenicline or bupropion are associated with these AEs anymore than nicotine patch or placebo)

- **More AEs in the psychiatric cohort compared with the non-psychiatric cohort**
  (i.e. people with mental illness were more likely to experience AEs, regardless of which medicine they were using)

Drug Interactions

Many interactions identified; varying clinical significance

Chemicals in tobacco smoke can interact by two mechanisms

- *Pharmacokinetic*- usually poly-carbons not nicotine
  stimulation of hepatic enzymes
  antipsychotics (clozapine, olanzapine), warfarin & caffeine

- *Pharmacodynamic*- largely due to nicotine
  alter the expected response or actions of other drugs
  beta-blockers, insulin

Dose adjustments may be required and based on clinical presentation and according to medical review

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