Government of **Western Australia**
WA Country Health Service

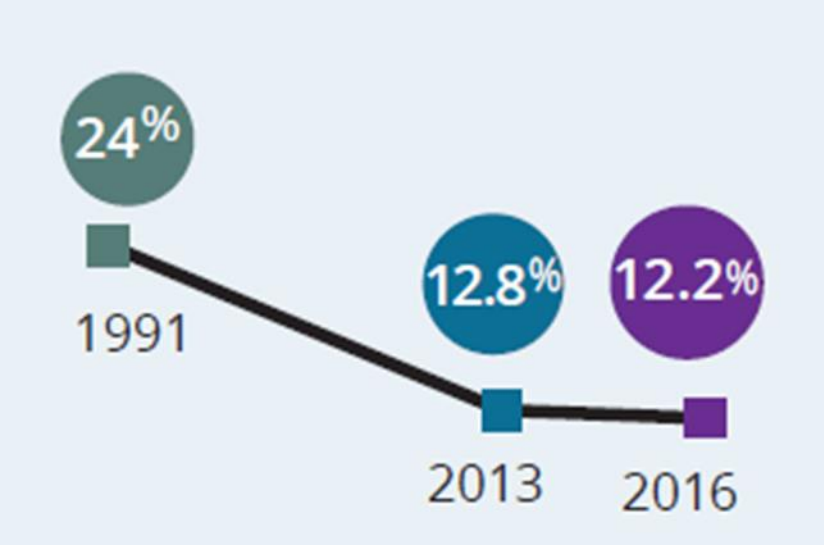
SMOKING CESSATION AND NICOTINE DEPENDENCE IN PATIENTS WITH MENTAL ILLNESS

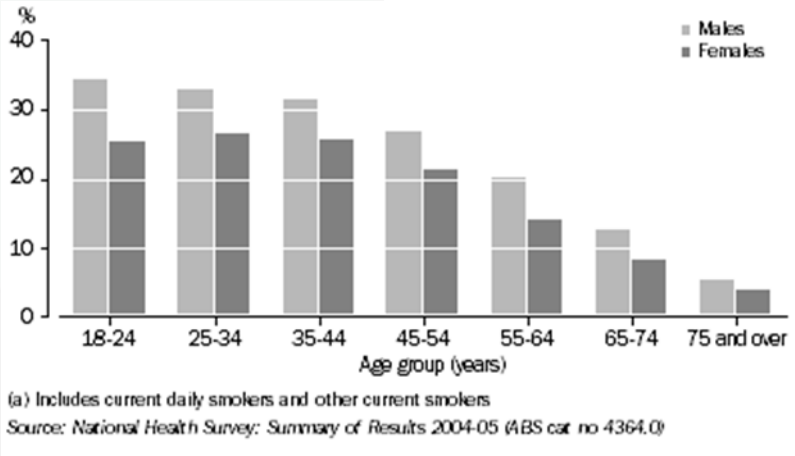
DRS KELLY RIDLEY AND MATHEW COLEMAN

GREAT SOUTHERN MENTAL HEALTH SERVICE

AUSTRALIA - DAILY TOBACCO SMOKING

- 12.2% daily smokers[1]
- Kills 15,000 p.a
- Up to 2/3 die from smoking
- Leading cause of preventable death in Australia





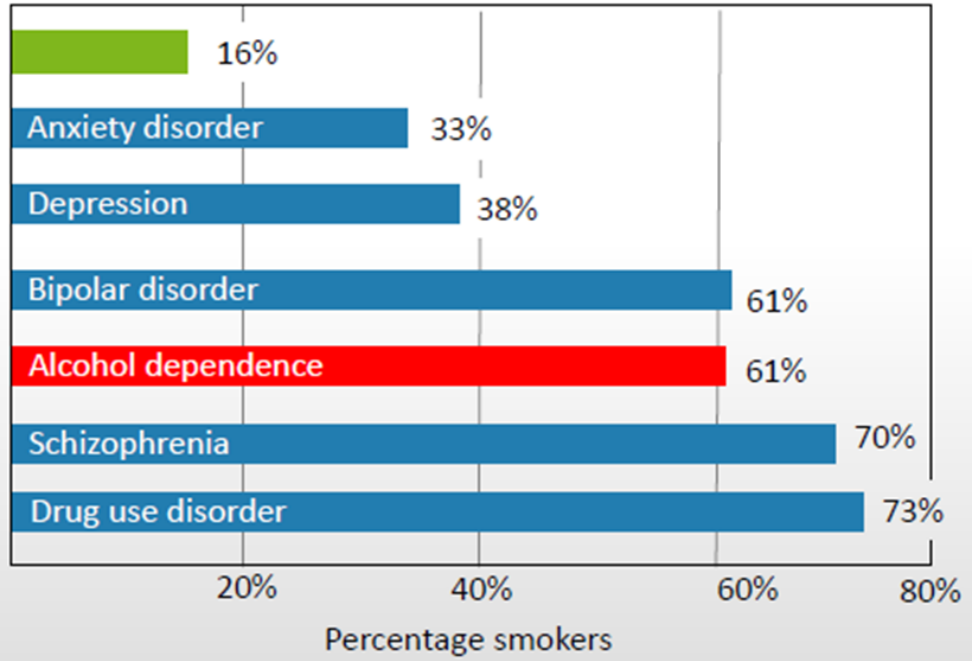
(a) Includes current daily smokers and other current smokers

Source: National Health Survey: Summary of Results 2004-05 (ABS cat no 4364.0)

Smoking Rates in Mental Illness

- Twice as likely to smoke (32%) as those without mental illness (16%) [1]
- Smoking rates increase with severity of mental illness [2,3]
  - Depression: 36%
  - Bipolar disorder: 61%
  - Schizophrenia: 70%

In Australia OR 5.5 of sedative, stimulant or opiate disorder if smoking (Dengenhardt, 2001)



1. Australian National Survey of Mental Health and Wellbeing. ABS 2008 2. Cooper J. Aust NZ J Psych 2012 3. AIHW. National Drug Strategy Household Surveys 3. Bowden J. ANZJ Psych 2011

MH Smoking Patterns

- Smoke more heavily [1,2]
- Have higher levels of nicotine dependence [1,2]
- Less likely to be offered Rx[3]

- Have more difficulty quitting [2]

1. Bowden JA. ANZ J Psych 2011 2. Lasser K. JAMA 2000 3. Campion J. Adv Psychiatr Treat 2008
Levels are higher in schizophrenics,Olincy etal, Biol Psych 1997
Depression, Benowitz 2012
P.H of Alcohol Abuse, Hurt, 2012

REASONS FOR HIGH SMOKING RATES IN MH

- Shared genetic predisposition
  - Depression[1]
  - Schizophrenia [2]
  - Alcohol dependence
- Common environmental factors
- Self-medication [3-6]
- To reduce side-effects of medication [6]
- Culture of smoking in mental health facilities, group homes
- Less likely to be offered treatment [7]

1. Kendler K. Arch Gen Psych 1993. 2. Ferguson D. Psych Med 2003 3. Ziedonis D. Nic Tob Res 2008
4. Barr R. Neuropsychopharm 2008 5. Kalman D. Am J Addict 2000 6. Matthews A. CNS Drugs 2011
7. Campion J. Adv Psychiatr Treat 2008

ARE SMOKERS OFFERED TREATMENT?

- GPs
  - Offered Medication [1]
    - Smoking 4.4%
    - Hypertension 57.4%
    - Diabetes 46.2%
    - Hyperlipideamia 47.1%
- Psychiatrists[2]
  - Screening rates falling → 60%
  - Treatment rates – 1-12%

1. Bernstein, 2013 AJPH
2. Rogers and Sherman, 2014 AJPH

BARRIERS FOR DOCTORS

- Is it a chronic illness? A lifestyle choice?
- Lack of time
- Fear of alienating smokers
- Lack of skills
- Despondency re: efficacy
- Fear of adverse events
- Persistent myths
- Someone else's job

Mendelsohn, 2013 Aust Medicine

Government of **Western Australia**
WA Country Health Service

CIGARETTES 101

Background to Quitting

- 70% Australian smokers want to quit
- 50% attempt each year
- Average age of quitting is 43 -> so many unsuccessful attempts -> danger of the ‘q’ word.

(AIHW 2016)

NICOTINE EFFECT

Stimulant
Calmative
Increased concentration
Euphoria
Appetite suppressant

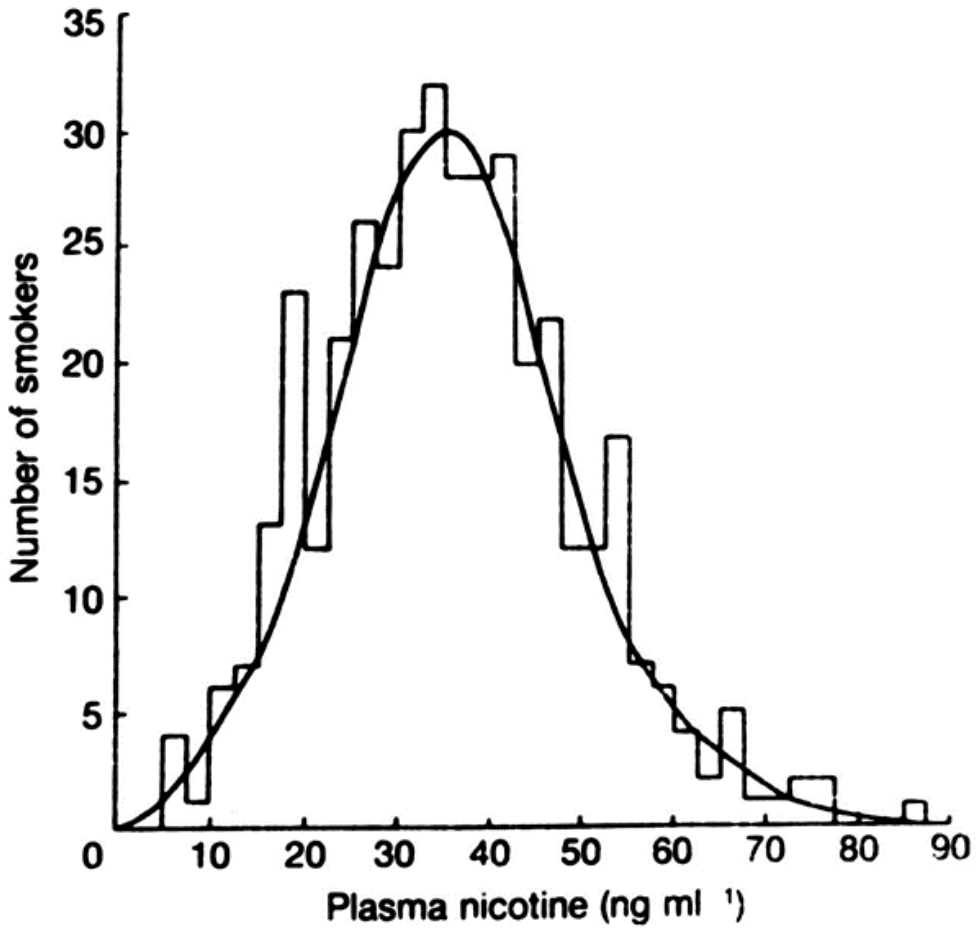
WITHDRAWAL SX

Agitation/ irritability
Anxiety
sleep disturbance
Appetite changes
Low mood
Poor concentration

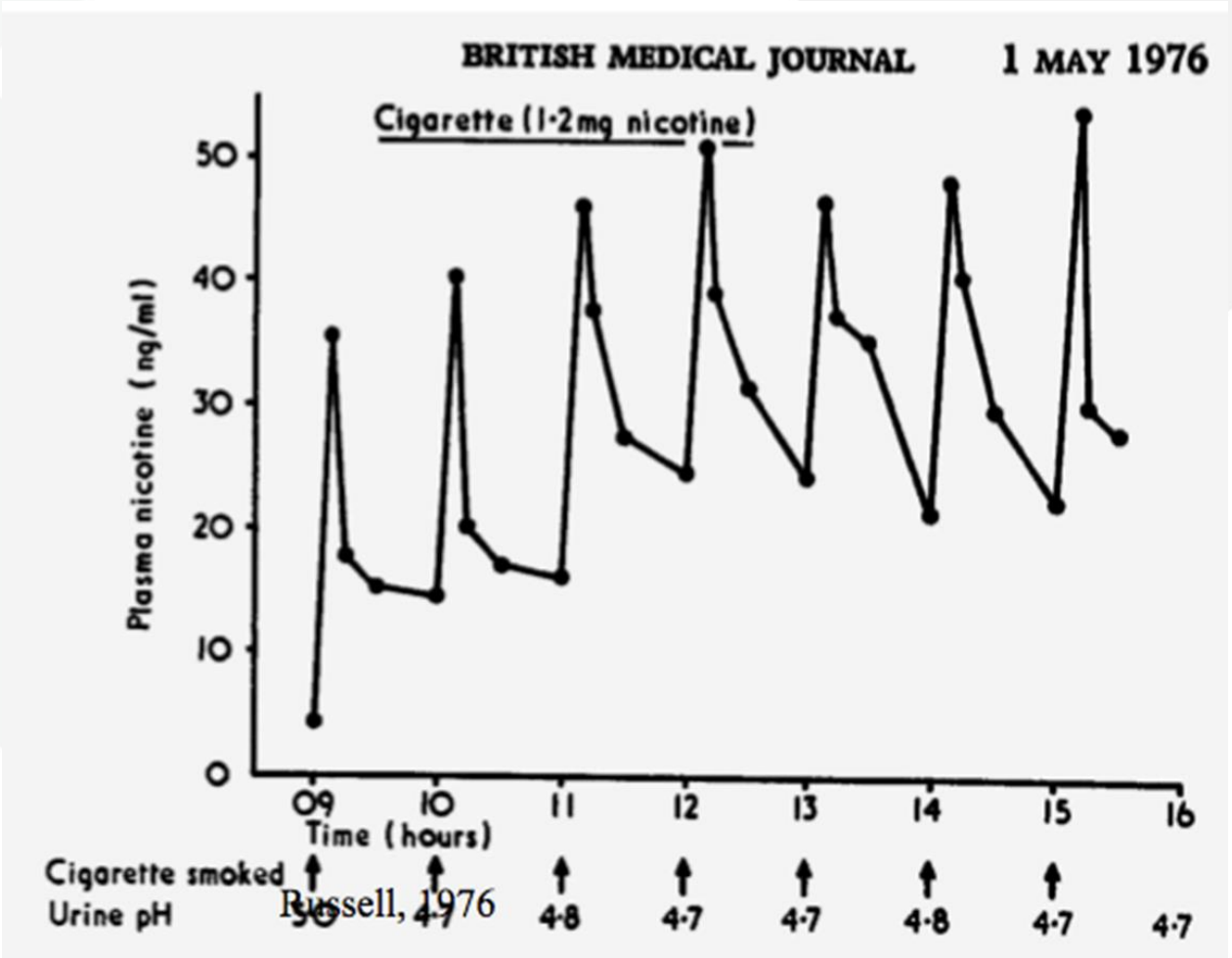
Polycyclic Aromatic Hydrocarbons

- Produced by smoking organic material
- Induces CYP 1A2, therefore need more
  - Insulin
  - Antipsychotics eg olanzapine, clozapine, haloperidol
  - Antidepressants eg fluoxetine, fluvoxamine
  - Diazepam
  - Analgesia, eg methadone,
  - Caffeine
  - Alcohol

This is NOT a nicotine effect.
Important to think about during inpatient admissions/discharge


35
30
25
20
15
10
5
0
Number of smokers
10
20
30
40
50
60
70
80
90
Plasma nicotine (ng ml 1)

"Controlled Smoking"



Russell, 1976

WHY ME?

- Regular appointments
- Motivation to quit present
- Pharmacological, psychological and behavioural strategies used to address smoking similar to other drugs.
- Maximising the effect of prescribed medication
- Preventable causes of death

- Because otherwise no one else might.

Cookson C et al. Smoking and its Treatment in Addiction Services: Clients' and staff behaviours and attitudes. BMC Health Serv Res. 2014:14; 304

The Effects of Quitting on Mental Health

- Meta-analysis of 26 studies found that stopping smoking is associated with improvements in:
  - Depression
  - Anxiety
  - Stress
  - Psychological quality of life
  - Positive affect
- Smoking is also a predictor of suicide even after controlling for mental illness, and the risk falls after cessation

OK, HOW

OPEN THE CONVERSATION

- Find the motivation:
- Cost
- Maximise medications
- Other substance dependence
- Physical
- Effects on others eg kids.

- “Can I help you save some money by making some changes to smoking” vs “do you want to quit”

ASSESSMENT OF A SMOKER

- **TTFC < 30min (number and type irrelevant)**
- Carboxymeter
- Medical History (psychiatric in particular)
- Quitting History (previous short-lived attempts, pharmacological failures)
- Family History (heritability)
- Environmental Contexts (others smoke at home and/or at work)
- Cravings if using NRT

- Not important= “readiness to change”.

Evidence-Based Pharmacotherapies for Withdrawals

1ST Line

- NRT of all types
- Combination of all NRTs
- Varenicline (Champix)
- Combination of Varenicline and NRT
- Bupropion (Zyban)
- Combination of NRT and Bupropion

2nd Line

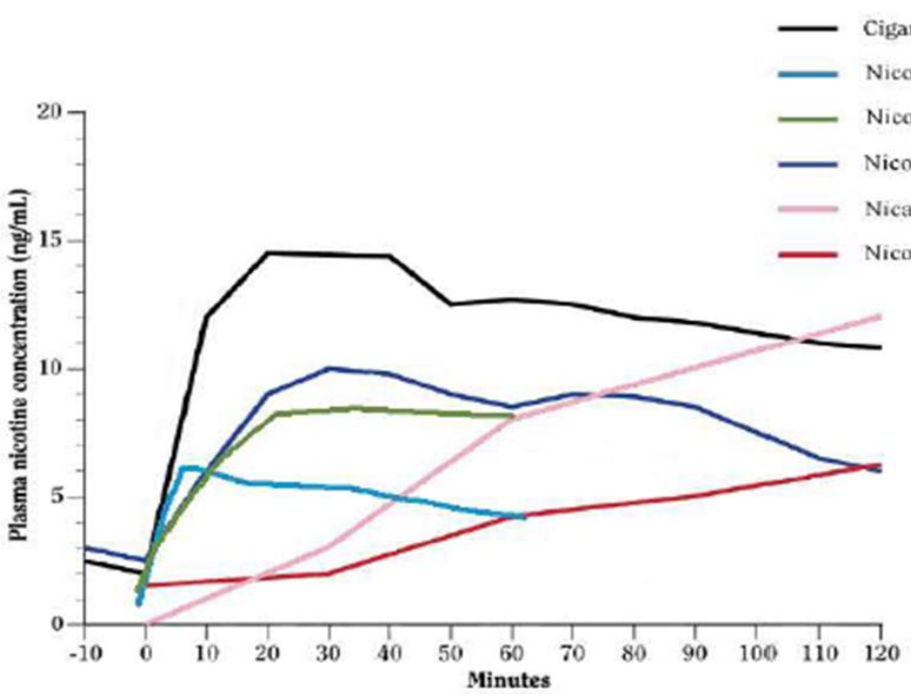
Nortiptyline, Naltrexone

>outcomes by 50% with combined behavioural/lifestyle interventions

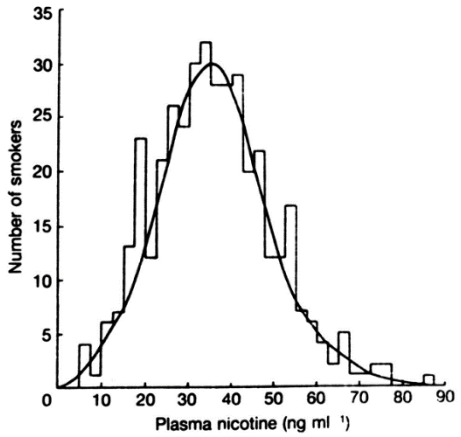
Speed of action	Product	Time to peak	Use
Slow		Nicabate 3-7 h Nicotinell 9-12 h	Continuous application
		Nicorette 6-9 h	16 hour application
Medium		30-60 minutes	Regular or prn use
Fast		10 minutes	Spray: Rescue cravings **TTFC <30mins**
			Strips: Rescue cravings **TTFC >30mins**

1. Hansson A. BMJ Open 2012 2. Kraiczi H. Nic Tob Res 2011 3. Hukkanen J. Pharmacol Rev 2005
4. Du D. JOSC 2014

Nicotine Blood levels: cigarettes vs NRTs



Source: Adapted from Fant et al. 1999 with permission from Elsevier, ©1999.
Note: **mg** = milligrams; **ng/mL** = nanograms per milliliter.



The Health Consequences of Smoking—50 Years of Progress. A Report of the Surgeon General, 2014

NRT Patch Correct Use

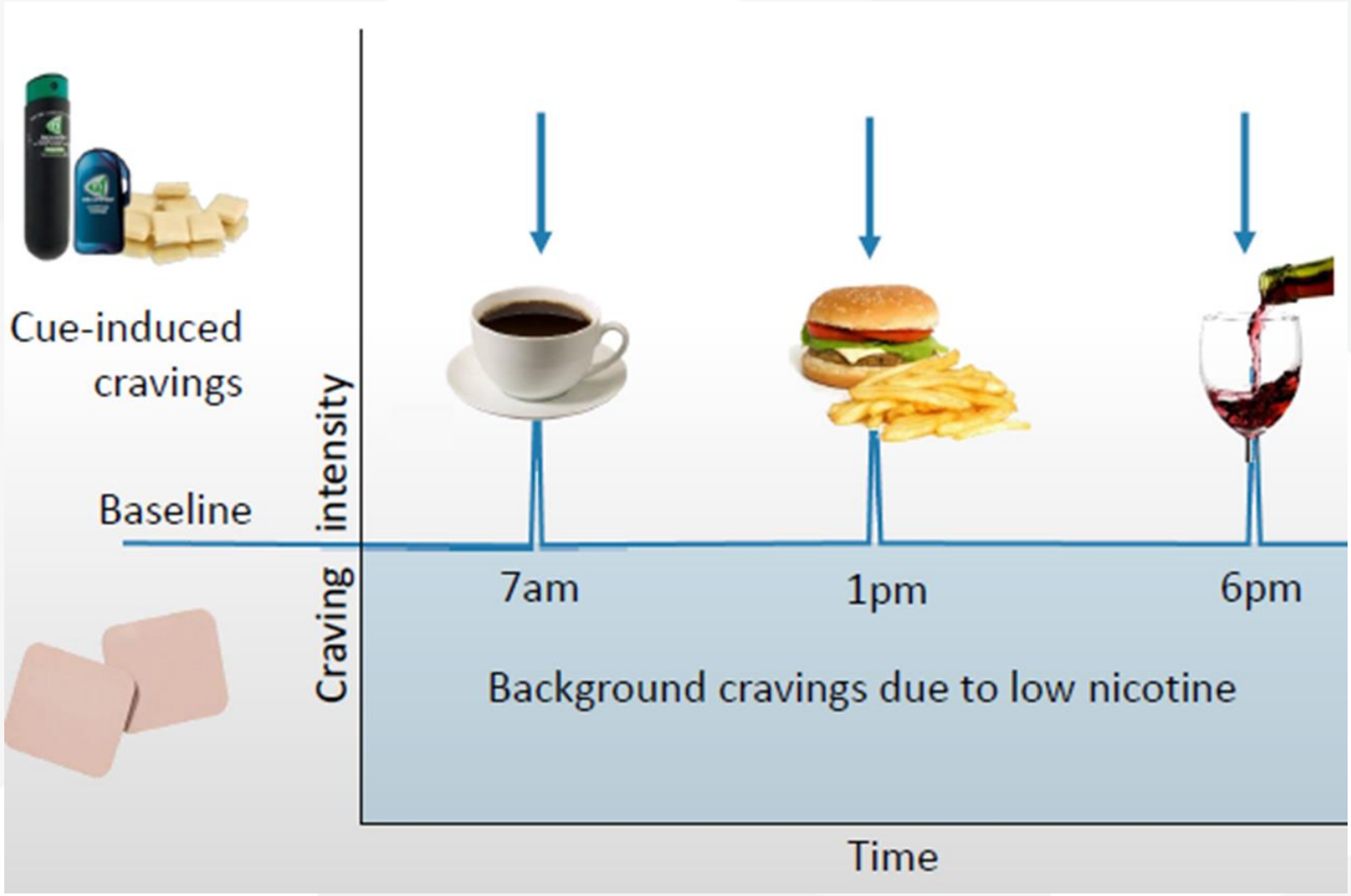
- Full Strength Patch
  - 21mg/24hr
  - 25mg/16hr
- Apply to clean, dry, hairless skin on upper back, chest or arm
- Rotate site daily
- Applied at night if morning cravings
- Can be applied in morning TTFC > 1hr

Medium-Acting NRT

- Lozenges
  - Don’t swallow, dissolve over 20mins
- Chewing gum
  - Chew and park, avoid excess swallowing
  - 4mg>2mg, should last 30mins
  - Reflux, hiccups, nausea, jaw pain
- Inhalers
  - Sensory smoker
  - Freq shallow or 4 deep puffs for 20-40min

Fast-Acting NRT

- Mouth Spray
  - Rapid absorption ~ Max at 10mins
  - Spray under tongue or into cheek
  - Don’t inhale or swallow
  - Doubles quit rate (RR 2.48)
  - Hiccups, inc saliva, mouth/throat irritation


Cue-induced cravings
Baseline
Craving intensity
7am
1pm
6pm
Background cravings due to low nicotine
Time

PRECAUTION WITH NRT

- Pregnancy
- Recent AMI
- <45kgs
- <12 years of age

VARENICLINE

- Champix or Chantix
- A selective $\alpha 4\beta 2$ receptor partial antagonist

Reduce withdrawal symptoms

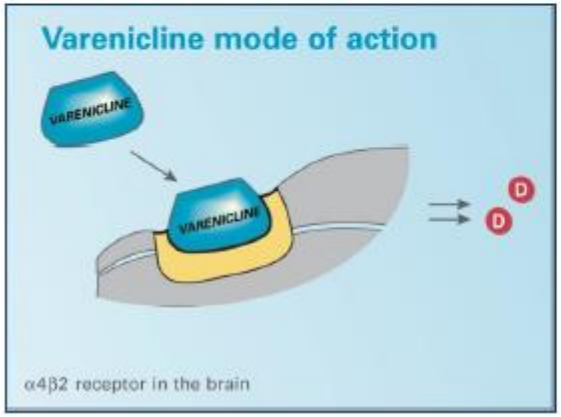
› Partial agonist

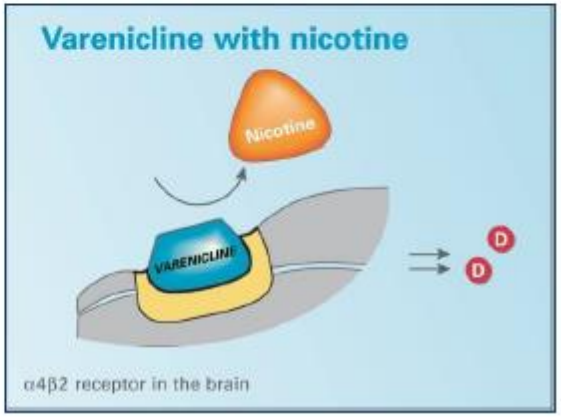
› Binds to α4β2 nicotine receptors partially stimulating dopamine release

Reduces smoking satisfaction

› Antagonist

› Prevents stimulation of receptor by nicotine, reducing pleasurable effects of smoking





VARENICLINE

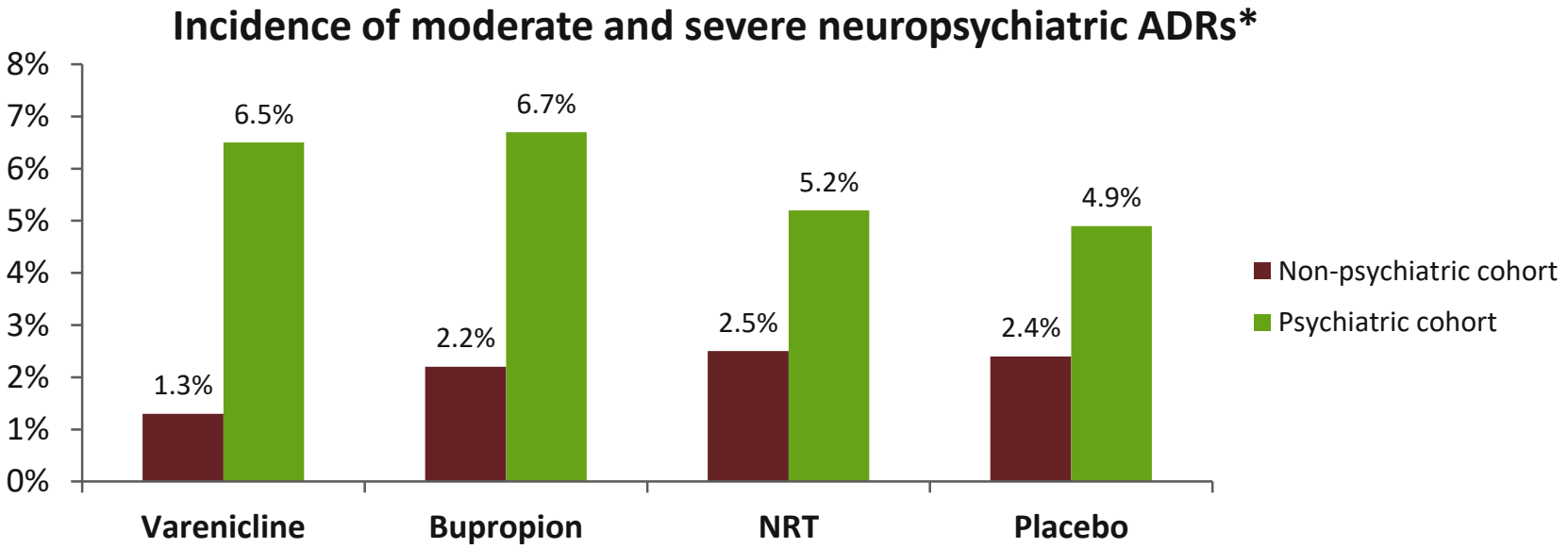
- Response to varenicline determined by variations in nicotine receptors
- Women do better
- Longer is better
- Nausea and insomnia (not genetically linked)
- Tolerability usually evident at 0.5mg bd (day 4)
- Methamphetamine and alcohol

J Foulds 2007

King DP. Smoking cessation pharmacogenetics. Analysis of varenicline and bupropion. Neuropsychopharm. 2012

EAGLES Study

- 4-arm RCT of 8144 people (4116 with a stable mental illness)



*Data presented were analyzed from weeks 9-12.

- Quit rates vs. placebo: **Varenicline OR: 3.61 (3.07-4.24)**; Bupropion OR: 1.75 (1.52-2.01); NRT OR: 1.68 (1.46-1.93)
- No significant increase in risk of neuopsychiatric AEs when varenicline or buproprion were compared with placebo (primary comparison) or NRT patch in both the non-psychiatric and psychiatric cohorts

Anthenelli RM, et al. *Lancet.* 2016;387:2507-2520.

BUPROPION (ZYBAN)

- Increases DA and NA in reward pathway, and antagonist at nACHR
- Antidepressant
- P450 CYP2B6 metabolizes Bupropion to hydroxybupropion.
- This enzyme is genetically determined
- Poor metabolizers do not do well
- Effectiveness RR=1.62

BUPROPION

- Side effects
  - Insomnia, headache, nausea, anxiety, dizziness, ?DSH and seizures
- Contraindicated
  - Seizures
  - Alcohol, benzos, MAOIs, pregnancy,

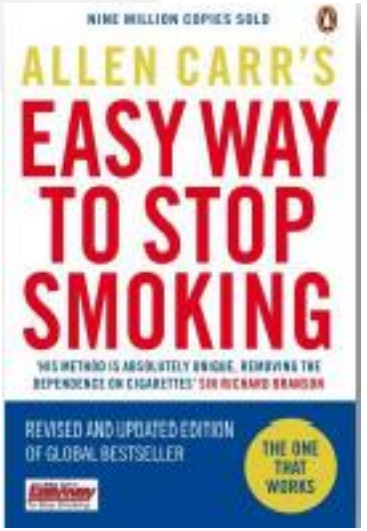
Behavioural / Lifestyle Interventions

these are evidence based

- Reduce caffeine intake by ½ (coke)
- Lead normal life—avoiding cues is not the Rx
- Short forms of exercise
- Quick sugar hit
- Eat breakfast
- Encouragement, revisiting information and motivation
- Distraction techniques
- Urge surfing

OTHER INTERVENTIONS – NO EVIDENCE

- Hypnotherapy
- CBT
- Lobeline (Indian Tobacco)
- Nicobloc
- Accupuncture
- Alan Carr (UK)
- Smokenders (USA)



PITFALLS AND TRAPS

- Consider tobacco with cannabis
- Partners who smoke
- Not treating assertively enough initially
- Not treating for long enough
- Not considering medication dosages
- Demonising nicotine

SMOKERS CLINIC MODEL

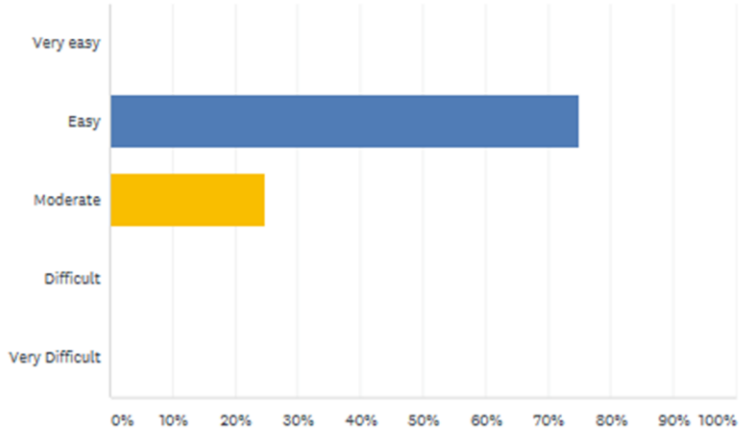
- 15/44 achieved abstinence
- Mean reduction in exp CO >43% (based on ITT)
- F>M (3.4 times more likely)
- Trend towards better outcomes for serious mental illness
- Varenicline safe to use
- Number of sessions perhaps not important

- Limitations
- Sample size (but results trending the same)
- Endpoint data (FTND and missing exp CO)
- VC trial unsuccessful
- Staff engagement as patients

Q4

Difficulty learning nicotine dependence/smoking cessation subject matter?

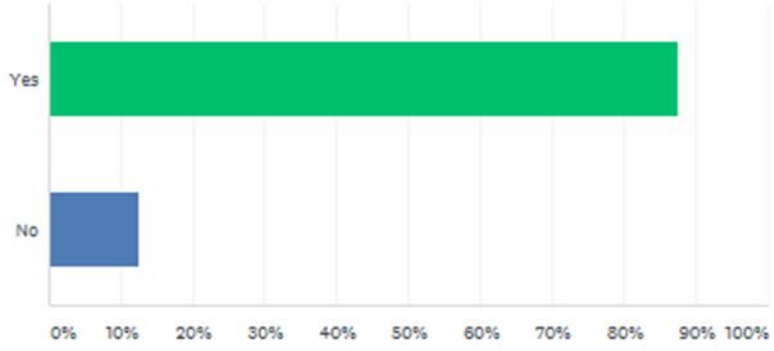
Answered: 8 Skipped: 0



Q8

Have you continued to use this information for clinical work outside your time allocated to "Smokers Clinic"?

Answered: 8 Skipped: 0



KEY PRINCIPLES

- Same strategies for general population
- Nicotine is your best friend
- More frequent follow up, reviews and support
- Optimise pharmacotherapy
  - Combination NRT
  - Higher doses and longer
- Attention to MH and SUD
- Consider interactions and medication
- This is everyones' problem, a chance to have a win and make a change

QUESTIONS OR COMMENTS

"WHAT ABOUT E-CIGARETTES?"

- Long term safety and efficacy unknown
- Quality concerns on e-cig units and juice: particulate metal, nicotine concentration, flavouring
- 54 calls to poisons NSW in 2013
- Burns from faulty batteries
- Vaporised nicotine, propylene glycol and glycerol all safe. No PAH, no ETS
- Harm minimisation= must stop smoking
- Legal implications

E-CIGARETTE GUIDELINES

- RANZCP 2018: lack of long term studies, but good harm minimisation when other strategies don't work. Lack of legal opportunities to purchase= exposure to unregulated units.
- RACP 2019: Nicotine highly addictive and a poison. Lack of long term evidence lacking. Cautious in recommending, but total smoking abstinence is the goal. "careful clinical judgement"
- Royal College of GPs 2017: not a first line smoking cessation aid, but may be recommended to an individual as part of treatment plan.