What we know about smoking today: What, who and particularly why

Webinar

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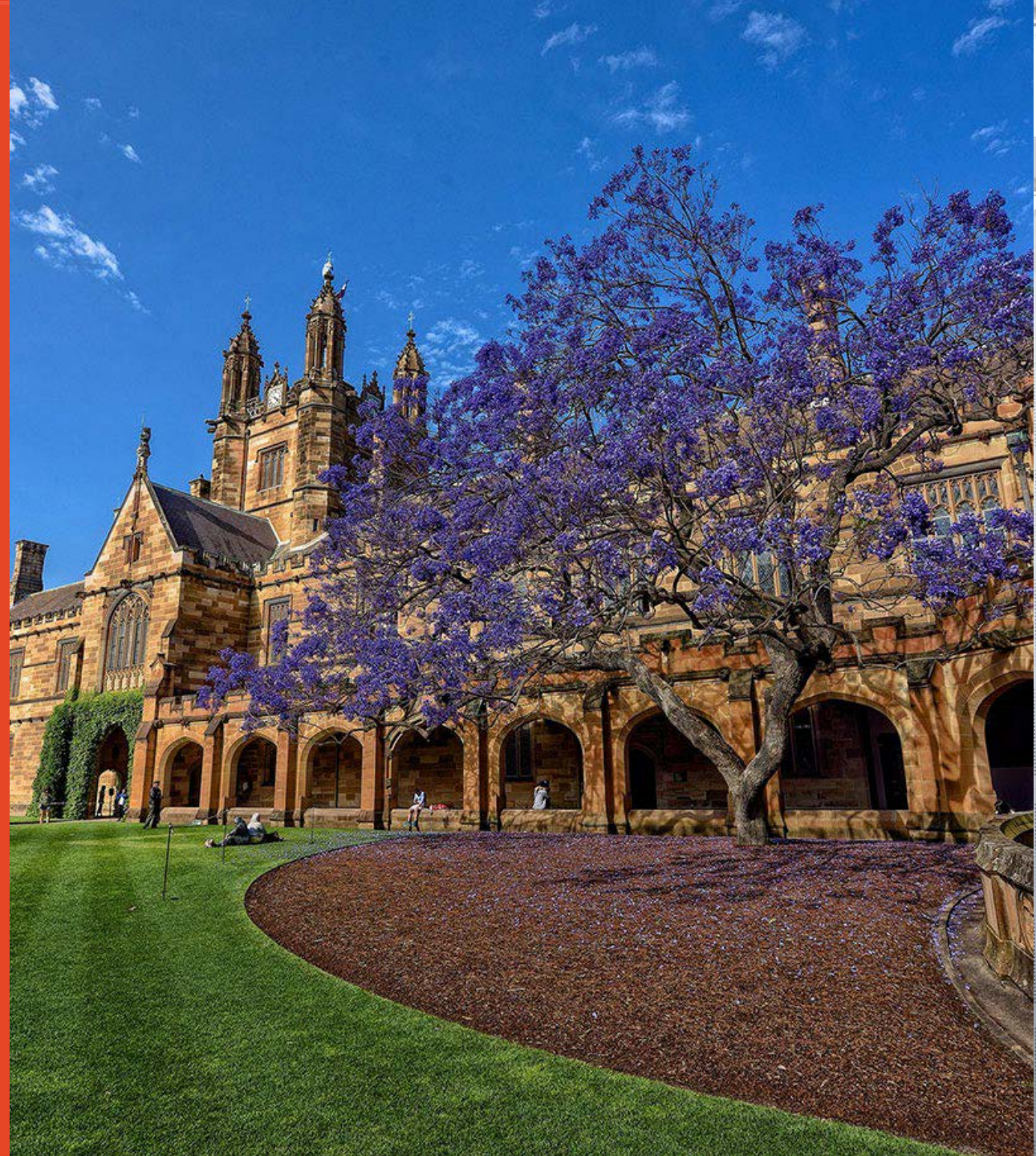

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WHAT WE KNOW ABOUT SMOKING TODAY: WHO, WHAT AND PARTICULARLY WHY

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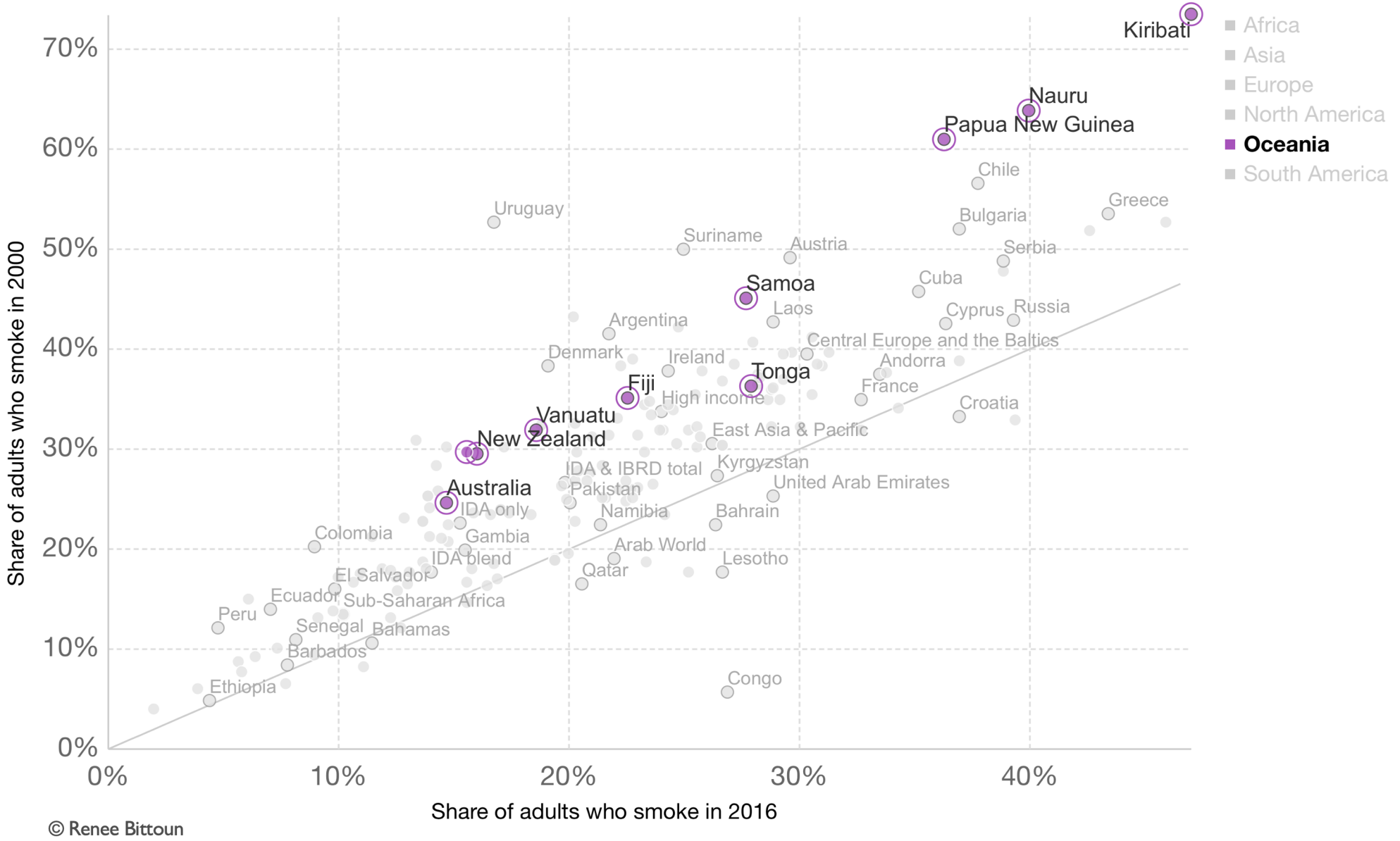
NO CONFLICTS OF INTERESTS

Share of adults who smoke in 2000 vs. 2016

The share of adults, aged 15 years and older, who smoke any tobacco product on a daily or non-daily basis.

Our World in Data



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Source: World Health Organization (WHO)

OurWorldInData.org/smoking • CC BY

WHAT HAS HELPED TO DRIVE DOWN SMOKING PREVALENCE?

- High taxes: Do you know how much?
- Fewer venues to smoke
- Graphic warnings on packaging
- Social marketing campaigns
- Restriction of sales to minors
- Moving tobacco products out of sight
- Heavily subsidised pharmacotherapies for **ALL**
- Increasingly smoking socially unacceptable

WHO IS STILL SMOKING IN AUSTRALIA TODAY?

Smokers with:

- High dependence
- Mental health concerns- nicotine negative effects
- Drug and alcohol comorbidities
- Diseases related to their smoking
  e.g. COPD
- Multiple unsuccessful attempts
- Multiple life stressors
- Aboriginal and Torres Strait Islanders
- Indigenous pregnant women

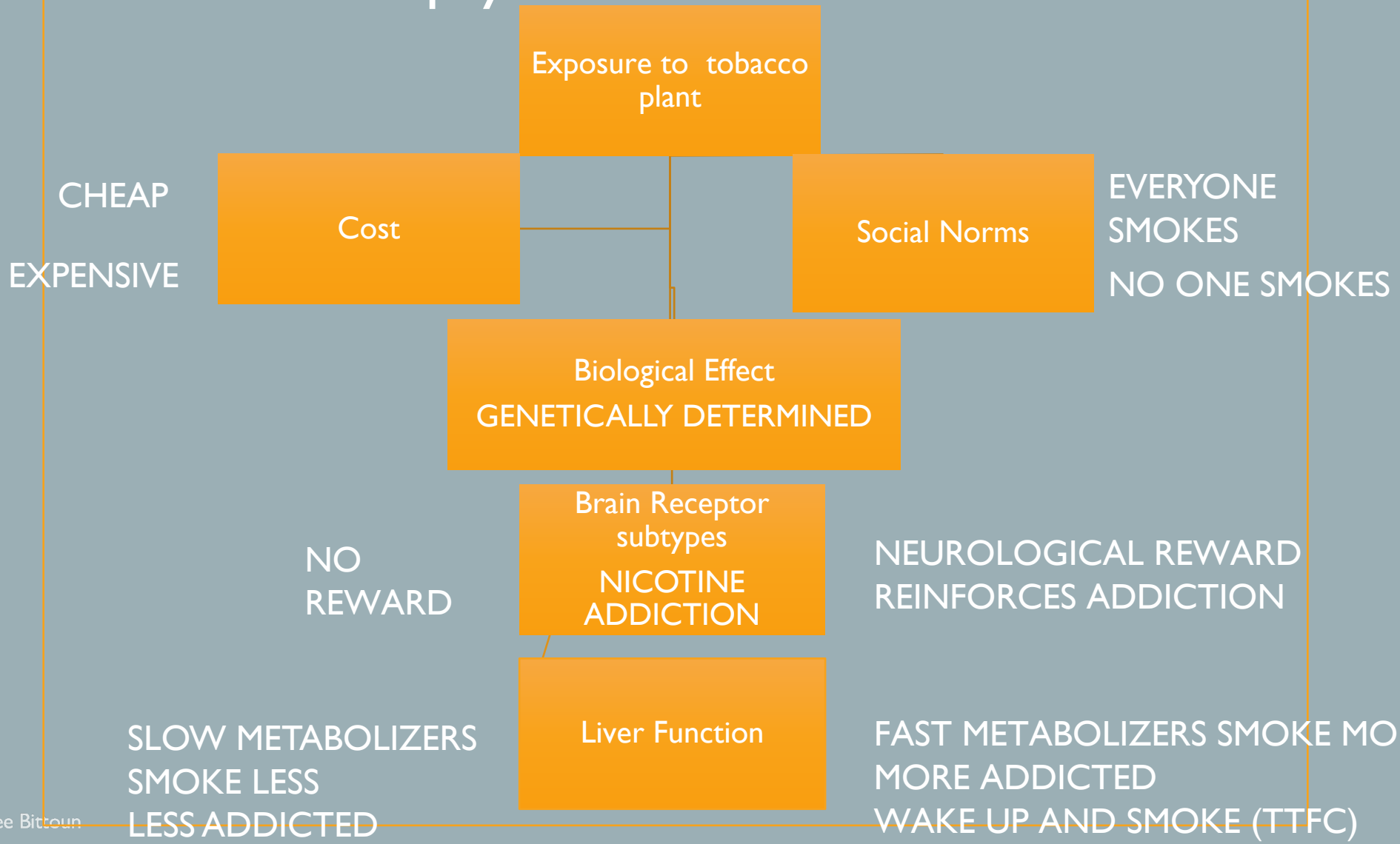
Low socio-economic status is common amongst these groups

MEDICAL CONSEQUENCES OF SMOKING- OVERVIEW

- *Lung cancer* - smoking causes 90% of lung cancers
- *Liver cancer* - smoking causes 70% of liver cancers in patients with Hepatitis C
- *Prostate cancer* - increased deaths in smokers
- *Colorectal cancer* - increased risk after 20 years of smoking
- *Breast cancer* - 10% increased risk in both active and passive smokers
- *Emphysema* – half of all smokers are diagnosed with emphysema, and there is now a female predominance
- *Asthma* - increased rates of asthma in smoking adolescents and adults
- *Stroke* - 20% - 30% increased risk in passive smokers
- *Coronary heart disease* – smoking increases the risk by 4 times
- *Diabetes* – 30% – 40% increased risk in smokers
- *Blindness* – increased risk of macular degeneration
- *Fetal health* – increased risk of ectopic pregnancy, miscarriage, prematurity and low birth weight
- *Neonatal health* – increased risk of *cot death*, cleft palate and neurological behavioral and cognitive disorders
- *DVT* Deep Vein Thrombosis

AND POOR MENTAL HEALTH

SMOKING BEHAVIOUR
Biopsychosocial influences



NICOTINE-SOME BASICS

- Nicotine is critical to smoking and is the primary addictive component of tobacco
- Nicotine is NOT yellow. It is colourless and odourless
- Nicotine is a constituent of tobacco smoke that exerts its psychoactive effects via binding to nicotinic acetylcholine receptors (nAChRs) in brain.
- It is *VERY* short acting, quickly eliminated and plasma levels are in nanograms *NOT* milligrams – all NRTs (Nicotine Replacement Therapies) deliver NGs
- Smokers titrate or compensate to the Nanogram. If cigarette is too weak drag harder/too strong puff lighter. Not enough cigarettes drag harder/too many puff lighter
- All this is in order to fill receptors in the brain

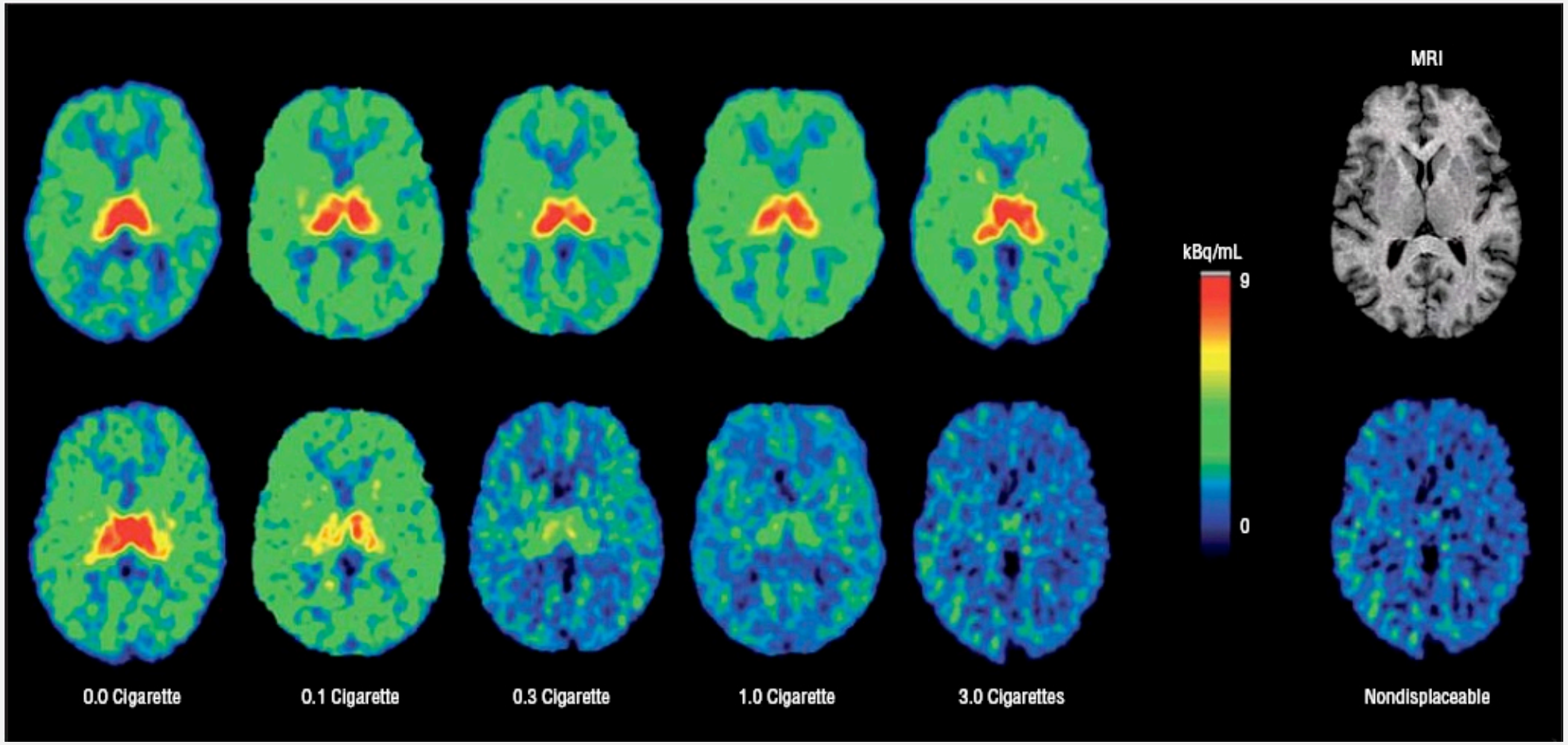
NICOTINE AND THE BRAIN

NICOTINIC ACETYLCHOLINE RECEPTORS-NACHRS

- nAChRs are expressed in brain areas that regulate a variety of behaviours.
- β2*nAChRs (including two major subclasses α4β2*- and α6β2*nAChRs) and α7 nAChRs are the most common nAChR subtypes in the CNS with complementary expression in the dorsal striatum, thalamus and amygdala but with neuroanatomical overlap in the ventral tegmental area (VTA), cortex, hippocampus and basal ganglia.
- These brain areas regulate sensory transmission, learning and memory, emotion, and reward.
- The levels of Physical Dependence correlate with changes in neural organization and volumes of upregulated receptors

Nicotine usurps Acetylcholine very well in these receptors IN SOME PEOPLE

Nicotine dynamics during smoking



Gradual increase BLUE rather than green in these brain scans of smokers indicates increasing activity levels of β2*-nACh receptors during a day of smoking

BRAIN RESPONSES AND HERITABILITY

- There is now convincing evidence for β2 subunit polymorphisms that predict risk for tobacco dependence both in animals and humans
- Candidate gene studies show that polymorphisms in CHRNB2 are associated with the subjective effects of nicotine and Fagerstrōm Test for Nicotine Dependence (FTND) scores
- There are heritable responses to varenicline, bupropion, and nicotine replacement therapy outcomes
- Nicotine addiction is not a matter of liking something too much, or a lack of will power, it results from changes in the anatomy and function of the brain.

MEDICAL CONSEQUENCES IN PREGNANCY

- Nicotine is extremely harmful to the developing fetus through many different mechanisms, and the harms increase with later gestational age at exposure.
- Pregnancies complicated by maternal nicotine use are more likely to have significant adverse outcomes.

<u>Nicotine-exposed children tend to have several health problems throughout their lives including</u>

- Impaired function of the endocrine, reproductive, respiratory, cardiovascular, and neurologic systems.
- Poor academic performance
- significant behavioral disruptions, including ADHD, aggressive behaviors, and future substance abuse
- Links to schizophrenia and suicide in the future adult

Smokers Demonstrate Excess Nicotinic Receptors During First Month of Abstinence: The predominance of green rather than blue in these brain scans of abstinent smokers indicates higher than normal levels of β2*-nACh receptors. Smokers continue to show elevated amounts of the receptors through 4 weeks of abstinence, but levels normalize by 6 to 12 weeks.

STRESS, STRESSORS, DISTRESS AND SMOKING

- Nicotine has an acute anxiolytic effect
- Nicotine has an acute antidepressant effect
- Nicotine has a very short half-life (40 mins→2 hrs) and wears off (think of how many are in a packet of cigarettes!)
- Nicotine wearing off → acute anxiety and depression (withdrawals)
- Smokers "manage" stressors better when on NRT
- After cessation smokers are "calmer", less volatile, less "reactive" to stressor.
- This is a learned process and takes time→ 3 months to adapt/neuroadapt

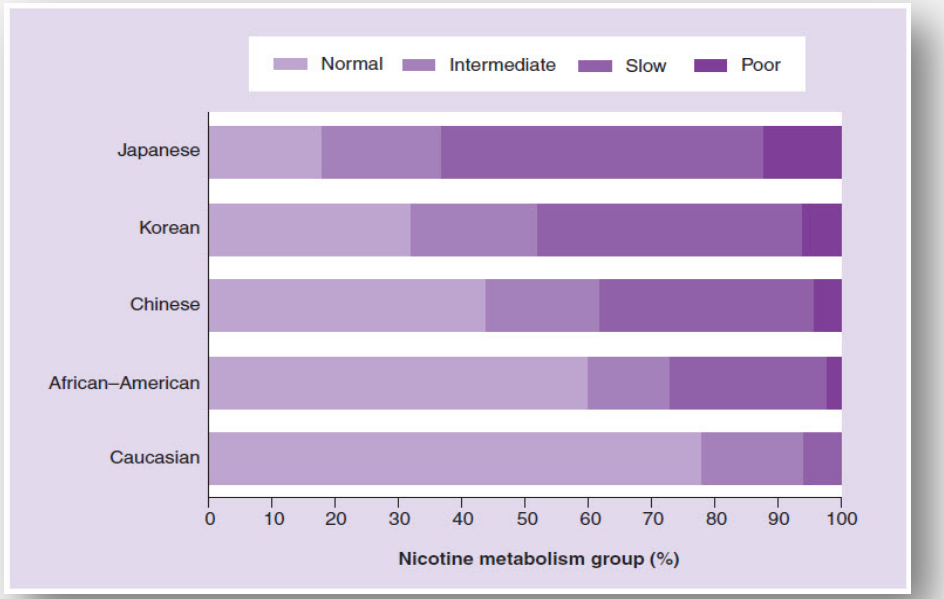
SMOKING AND LIVER FUNCTION

WHAT HAS BEEN LEARNT ABOUT METABOLIZING NICOTINE?

Genetic (racial) variations of the liver enzyme P450 CYP2A6 * ranging from fast to slow:

- Fast metabolizers smoke more/slow smoke less
- Fast are more addicted need to smoke straight away on waking
- Slow are less addicted
- Fast at risk of Ca of the Lung
- Fast do not do well on one form of NRT
- Fast inhale deeper → higher expired CO readings

RACIAL VARIATIONS



Mediterranean rim (Turks well studied) and Caucasians have higher levels of the normal (faster) CYP2A6 variants compared to Asians

FACTORS AFFECTING NICOTINE METABOLISM

P450 CYP 2A6 (*1 to *17 alleles)

- Diet and Meals: induce hepatic function.

  Nicotine clearance increases 40% after a meal.

  Grapefruit juice inhibits CYP2A6
- Age. Clearance decreases with age (23%).
- Neonates have reduced metabolism of nicotine → longer ½ life.
- Chronopharmacokinetics. Hepatic flow declines at night → reduced nicotine clearance.
- Gender differences. Women metabolise faster than men.
- Oral contraception increases it again by 30%.
- Liver disease impairs nicotine metabolism.

OTHER LIVER ENZYME EFFECTS

Smoking (anything) → Polycyclic Aromatic Hydrocarbons (PAHs) which greatly effect enzyme induction. PAHs occur in E cigarettes.

Smoking accelerates the metabolism of:

- caffeine – smokers tend to drink more coffee/caffeinated than non-smokers
- alcohol - tend to drink 3 times more than non-smokers
- some medications – anti-psychotics, anti-coagulants, pain relievers
- Insulin

This is not a nicotine effect

Caution when patients are hospitalised

TOOL 7

Quick guide to drug interactions with smoking cessation

NSW GOVERNMENT

Medication levels can vary if someone starts or stops smoking, or if they change how much they smoke.

- Cigarette smoking induces the activity of certain cytochrome P450 enzymes, particularly CYP1A2. These enzymes are involved in the metabolism of a number of medications.
- These effects are caused by components of tobacco smoke other than nicotine. **Therefore nicotine replacement therapy does NOT affect medication levels.**
- Decreased CYP1A2 activity after smoking cessation increases the risk of adverse drug reactions thus requiring adjustment to the dosage of some medications.
- CYP1A2 enzyme has a half-life of 36 hours, so dose adjustment to medications needs to be made within 2-3 days of smoking cessation.
- The change in metabolism/drug dose can occur with anyone who is reducing smoking. People considered light smokers may still need dose adjustment depending on the way they smoke (eg. compensatory smoking – inhaling more deeply).
- Predicting the required adjustment to medication can be challenging – the table below is a guide only. Therapeutic drug monitoring should be used where possible.

If unsure, access MIMS to establish smoking cessation effects on patient's medications.

Drugs affected by smoking cessation

Drug	Effect of smoking cessation	Impact on dosage required when client stops smoking	Clinical importance
Benzodiazepines	Possible increased sedation due to loss of CNS stimulation by nicotine.	May need lower dose. May be more sedated if dose remains the same	+
Beta blockers	Serum levels may rise and effects enhanced.	May need lower dose.	+
Caffeine and alcohol	Caffeine levels rise Alcohol levels rise	Reduce caffeine and alcohol levels by half within a week	+++
Chlorpromazine	Serum levels rise	May need lower dose	++
Clopidogrel	Effectiveness is significantly reduced when smoker stops smoking	Prasugrel or ticagrelor may be better choices for non-smokers	+++
Clozapine	Serum levels rise significantly	An average 50% dose reduction may be required	+++
Flecainide	Serum levels may rise	May need lower dose	+
Fluvoxamine	Serum levels may rise	May need lower dose	++
Haloperidol	Serum levels may rise	May need lower dose	+
Heparin	Serum levels may rise	May need lower dose	+
Imipramine	Serum levels may rise – monitor for side effects	May need lower dose	+
Insulin	Increased subcutaneous absorption due to vasodilation after quitting	May need lower dose	++
Olanzapine	Serum levels rise significantly	An average 30% dose reduction may be required	+++
Theophylline	Serum levels rise	May need lower dose	++
Warfarin	Serum levels increase by 15% on average	May need lower dose. Close monitoring of INR advised.	++
Methadone	Serum level may rise	May need lower dose	++

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Healthhttps://www.health.nsw.gov.au/tobacco/Pages/tools-for-health-professionals.aspx

SMOKING AND DRINKING

LIVER ENZYMES/METABOLIC EFFECTS

- Smokers drink at least twice as much alcohol as non-smokers
- PAHs and Nicotine induce alcohol dehydrogenase (ADH) AND CYP2E1 both metabolize alcohol in humans
- Alcohol alters the metabolism of Nicotine
- Nicotine may reverse cognition and in-coordination effects of alcohol

The effect of quitting/not smoking increases blood alcohol levels immediately → cheap drunk

NICOTINE WITHDRAWALS- ALL WELL DESCRIBED DECADES AGO

- Cravings or urges to smoke
- Anxiety
- Tension
- Aggression
- Increase in appetite
- Inability to concentrate
- Sleepiness/sleeplessness
- Depression
- Hunger
- Mouth ulcers
- Constipation

Withdrawals last from days to weeks. Withdrawals are most severe within the first week of quitting.

- Urges or cravings diminish in intensity and frequency over this period.
- 62% of smokers relapse due to withdrawals within the first two weeks of a quit attempt.

Do not confuse nicotine withdrawals with nicotine toxicity OR overdose or medication side-effects

(nicotine toxicity and overdose are EXTREMELY rare)

WHO FINDS IT HARDEST TO QUIT?

Characteristics:

- Highly dependant, so smoke within 30 minutes of waking (Time to First Cigarette-TTFC)
- Have multiple short previous attempts to quit, with high severity of withdrawal symptoms
- Smoking or withdrawals in the past while using Nicotine Replacement Therapies (NRT).
- Poor past experiences with quitting
- Likely to be a fast metabolizer of nicotine

Many smokers want to quit – some find it harder than others

WANTING TO QUIT AND ACTUALLY QUITTING

- Many smokers want to quit eventually
- Australian data: 383 participants answered an optional questionnaire while seeking financial assistance from Social and Community Service Organisations (AIHW)
- In any year 60% do not try and < 10% of smokers are planning to quit in the next 6 months.
- 53.5% reported they smoked on a daily basis (occasional smokers made up another 7.9%)
- 77% had tried to quit at some point, on average trying at least twice in the last 12 months
- 52.8% reported they would like help to quit smoking
- 77% of which preferred free access to NRT as a method of quitting
- Australian Institute of Health and Welfare figures : mean age was 43, and responses only came from people in the low SES bracket

<u>Committing to quit influenced by poor past experiences BUT decisions are corrupted by the addiction itself</u>

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https://ourworldindata.org/smoking

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Next Webinar

Part 2: Smoking Cessation

Date: 26th February 2020, 7.30pm

Register: https://zoom.us/webinar/register/WN_pkDOu75sSEGMPLj1xNxoWg