

SMOKING AND SMOKING CESSATION



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- › Introduction to the Behaviour of Smoking
 - › Psychopharmacology- Pharmacokinetics of Nicotine
 - › The physiology and psychology of addiction to tobacco
 - › Nicotine Withdrawal Syndrome
 - › Behavioural Psychology
-

Nicotine Dependence: A Medical Condition



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ICD-10 Code

(W.H.O. *I*nternational *C*lassification of *D*iseases)

Current Tobacco Use Z 72.0

Harmful Tobacco Use – non dependent F17.1

Tobacco Dependence Syndrome –

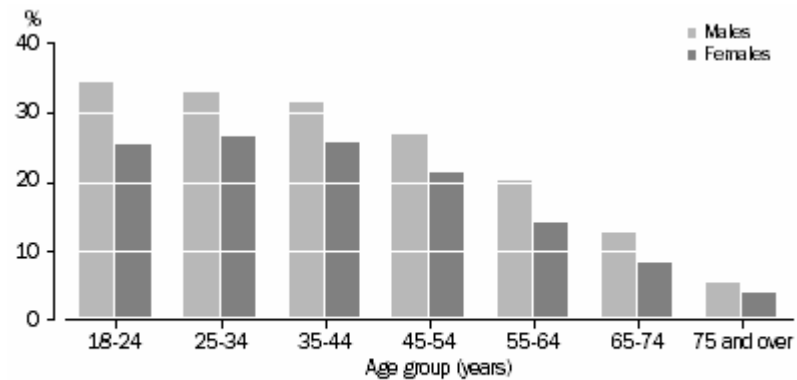
Mental and Behavioural Disorders due to Tobacco use F17.2

DSM IV

(Diagnostic and Statistical Manual of Mental Disorders –
American Psychiatric Association)

Nicotine Dependence 305.10





(a) Includes current daily smokers and other current smokers

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

17.8% of Australians smoke. Note the age and gender differences

- › Most Australian smokers want to quit
 - › Very few do not (about 6% in Australia)
 - › Many/most fail at quit attempts with or without pharmacotherapies
 - › The average age of quitting is 42
 - › 66% > 40 years of age
 - › 60% have secondary education
 - › Slightly more males than females
 - › People with children in the home

 - › Tobacco Facts, AHWS
-

- › To feel healthier
 - › Cost too high
 - › Pressure from family/friends/doctor
-

- › Withdrawals too hard
 - › Cost of treatment
 - › Fear of weight gain
-

Those who continue to smoke and are *our target* are the:

- › Lower socio-economic groups
 - › Particularly very high prevalence in indigenous population
 - › Poorer educated
 - › Single
 - › Younger (male = female)
 - › ***Unwell***
-

No nicotine in cigarettes = no smoking

NICOTINE

- › **Is colourless and odourless**
 - › **Is short acting (\cong 40 mins $\frac{1}{2}$ life \therefore 25/day)**
 - › **Is quickly eliminated (whole life \pm 20Hrs)**
 - › **Low levels in cigarettes \rightarrow compensatory smoking**
 - › **Fewer cigarettes/day \rightarrow compensatory smoking**
 - › **Smokers titrate plasma nicotine v. accurately**
-

- › **Most nicotine from smoking is blown into the air**
- › **Nicotine enters the lungs and arterial blood very quickly**
- › **Nicotine is not eaten but can be chewed (buccal absorption)**
- › **Smokers titrate their blood levels of nicotine very accurately**

Inhaling nicotine is very fast

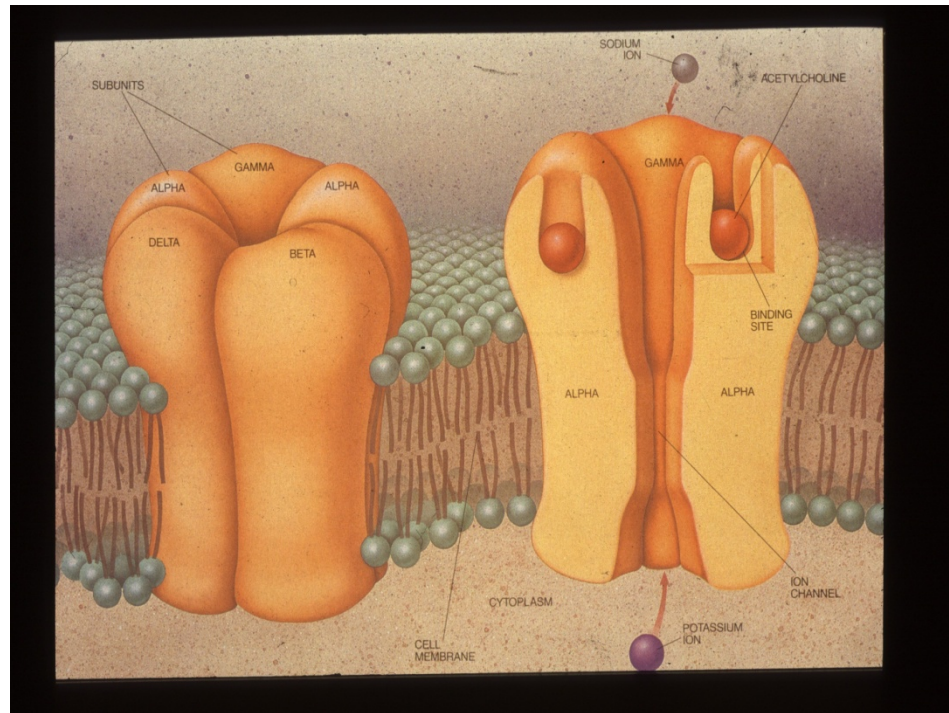
Transdermal nicotine is very slow

Speed of Delivery makes all the difference to addictions! (No nicotine patch addicts)

∴ behaviour 2nd to biology

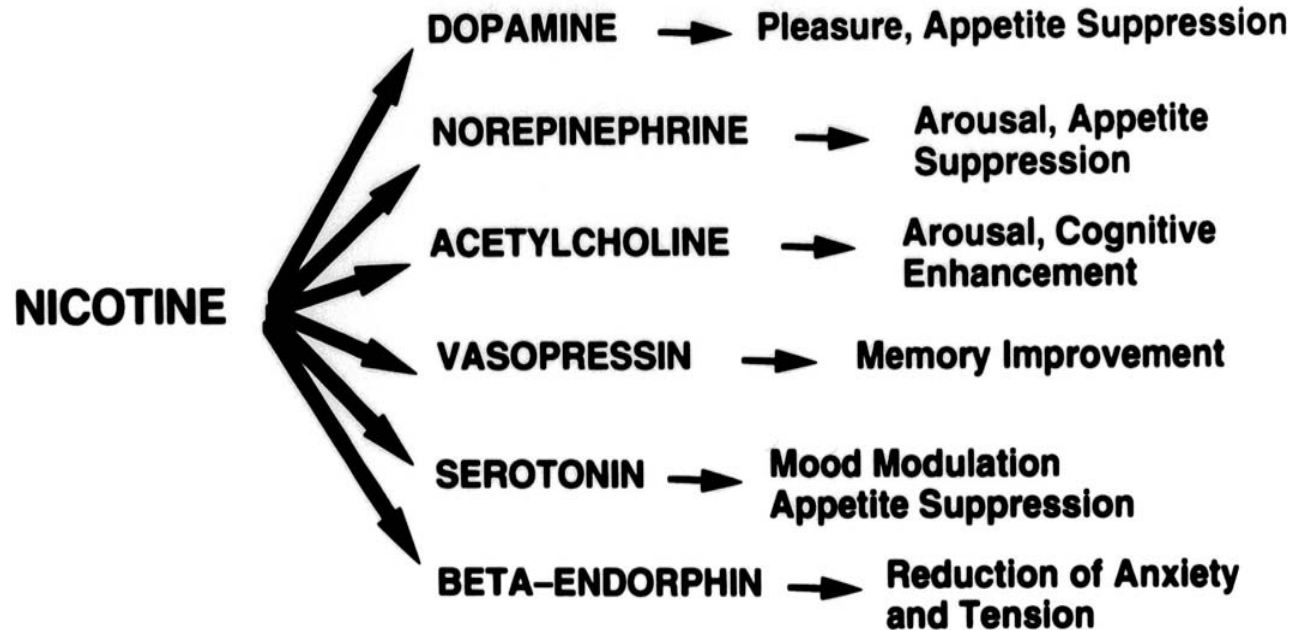
so numbers per day is less important in nicotine dependence

Nicotine (Nicotinic) Acetylcholine Receptor



Changeux, Scientific American, 1990s

Nicotine elicits the instant release of many “rewarding” neurotransmitter substances

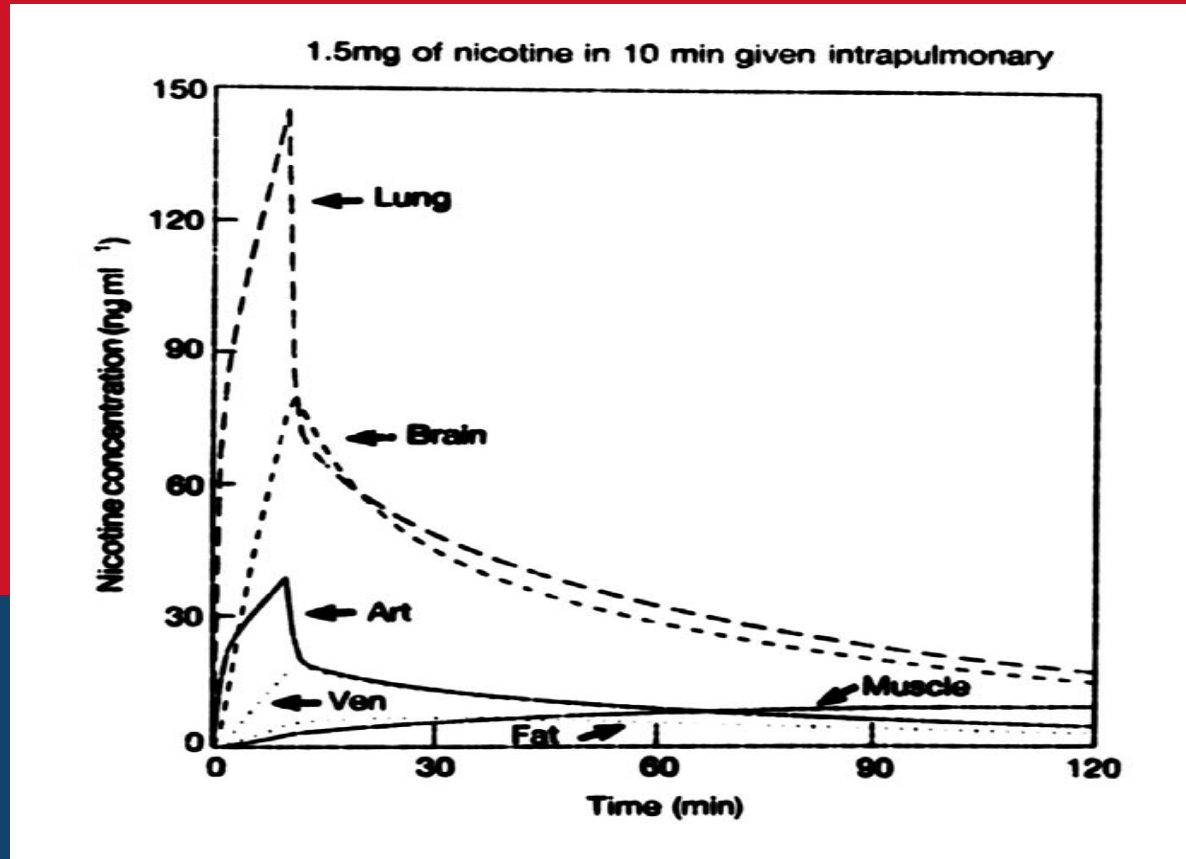


NICOTINE PHARMACOKINETICS

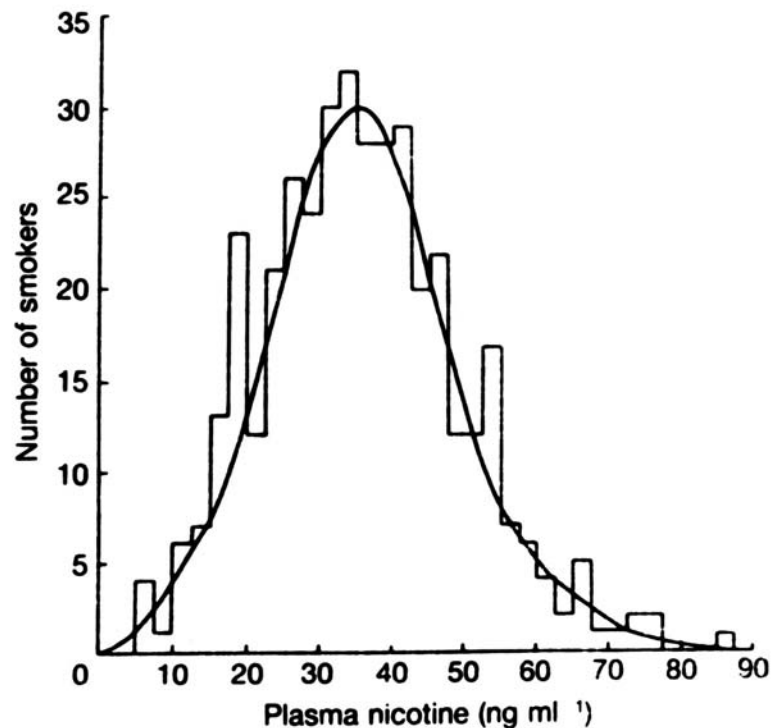
SHORT HALF-LIFE ~ 40 MINS

WHOLE LIFE ~ 12-20 Hrs

Benowitz, 1995



Plasma levels of Nicotine 2 mins post cigarette (unrelated to numbers or strength of cigarettes)



Russell, Benowitz (1980s)

Levels are higher in schizophrenics,
Olinicy et al, Biol Psych 1997

Smokers are not an homogenous group

Nicotine Dependence:-

- › Varies in intensity (e.g. like Alcohol Dependence) (Benowitz, 2007)
- › Is highly heritable >50% (Ho,2007)
- › Is lifelong (Tyndale,2009)

Nicotine blood levels:-

- › Range (10-80ng/ml) (Russell, Fagerstrom 1980s)
- › Schizophrenic patients have higher blood levels (Olincy, 1997)

Treatment (Rx):-

- › Responses to Rx vary (Hajek,Tyndale 2009)
 - › Response to Rx may be heritable (David, 2007)
-

› *Poorer Trial Outcomes*

Irvin, Nicotin Tob Research, 2000

› *Higher Dependency Scores*

Fagerstrom, Tob Control, 1996

› *Concomitant Mental Illness (Depression)*

Lasser, JAMA, 2000

› *Concomitant Drug Use*

Degenhardt, Nicotin Tob Research, 2001

› *Reduced impact of OTC NRT*

Pierce et al JAMA 2002

Better outcomes of NRT in Asia (higher prevalence-dilution effect, SRNT Bangkok,2008)

Most smokers in Australia want to quit.....those who could have quit-have (?).

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
- › Slow are less addicted
- › Fast at risk of Ca of the Lung
- › Fast do not do well on NRT
(Benowitz, Tyndale, et al 2000s)
- › Fast inhale deeper→higher CO readings (Bittoun, 2008)

NCI Phenotypes and Endophenotypes: Foundation for Genetic Studies of Nicotine Use and Dependence, Nov. 2009

Smoking (anything) → Polychromatic Aromatic Hydrocarbons (PAHs)

which greatly effect other liver enzyme activity → CYP1A2 →

so

- › Caffeine intake is double in smokers
- › Caffeine toxicity is common in withdrawals
- › Alcohol intake is double in smokers
- › Tolerance to alcohol drops in withdrawal

and

Smokers need more Insulin, Pain relievers, Anti-psychotics, Anti-coagulants, Caffeine, Alcohol etc etc

Quitters need less Insulin, Pain relievers, Anti-psychotics, Anti-coagulants *and must be monitored*

(Benowitz, Zevin, et al 1990s)

More Genetic Influences of Smoking

- › Genetic vulnerability to initiation to smoking, nicotine dependence, failure to quit, DSM1V (withdrawals)
- › Reinforcement value of nicotine may be due to endophenotype (dopamine D2 receptor, $\alpha 4$ $\beta 2$ Achr types)
- › Variations in responses to Rx are genetic (eg Bupropion)
- › LTUQ (Lifetime Tobacco Use Questionnaire)
- › Genetic pleitropy, eg serotonin transporter gene 5HTT associated with anxiety-alcohol consumption-smoking

NCI Phenotypes and Endophenotypes: Foundation for Genetic Studies of Nicotine Use and Dependence, Nov. 2009

- › Psychiatric Illness (Hughes, 1986)
 - › Familial traits in the above (Hughes, 1988)
 - › Depression → smoking → depression (Breslau, 1991)
 - › Smoking and Depression (Glassman, 1993)
 - › Adolescents and mood disorders (Kendler, 1993)
 - › ½ of all cigarettes smoked in US are smoked by depressed people -- same in Australia (Jorm, 2008)
-

In Australia

- › Only 22.5% of smokers have no mental illness.
- › 34.8% have a life-time mental illness
- › 41% have mental illness in the past month
- › OR (Odds ratio) of current smoking and mental illness is 2.7
- › Australia smokers have OR 5.5 of sedative, stimulant or opiate use disorder

Dengenhardt, 2001

- › Smokers had more depression and anxiety symptoms, more stressors and lower socioeconomic status compared with non-smokers.
- › The association between smoking and psychiatric symptoms persisted even when stressors, socioeconomic characteristics and other factors were statistically controlled.
- › Smoking is associated with poorer mental health.
- › In helping patients to give up smoking, doctors need to be aware that some may have underlying mental health problems that require attention.

Smoking and mental health: results from a community survey.

Jorm AF. Rodgers B. Jacomb PA. Christensen H. Henderson S. Korten AE.

Medical Journal of Australia. 170(2):74-7, 1999 Jan 18

NICOTINE WITHDRAWALS



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Can begin within hours of the last cigarette:-

- › 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***

(toxicity and overdose are EXTREMELY rare)

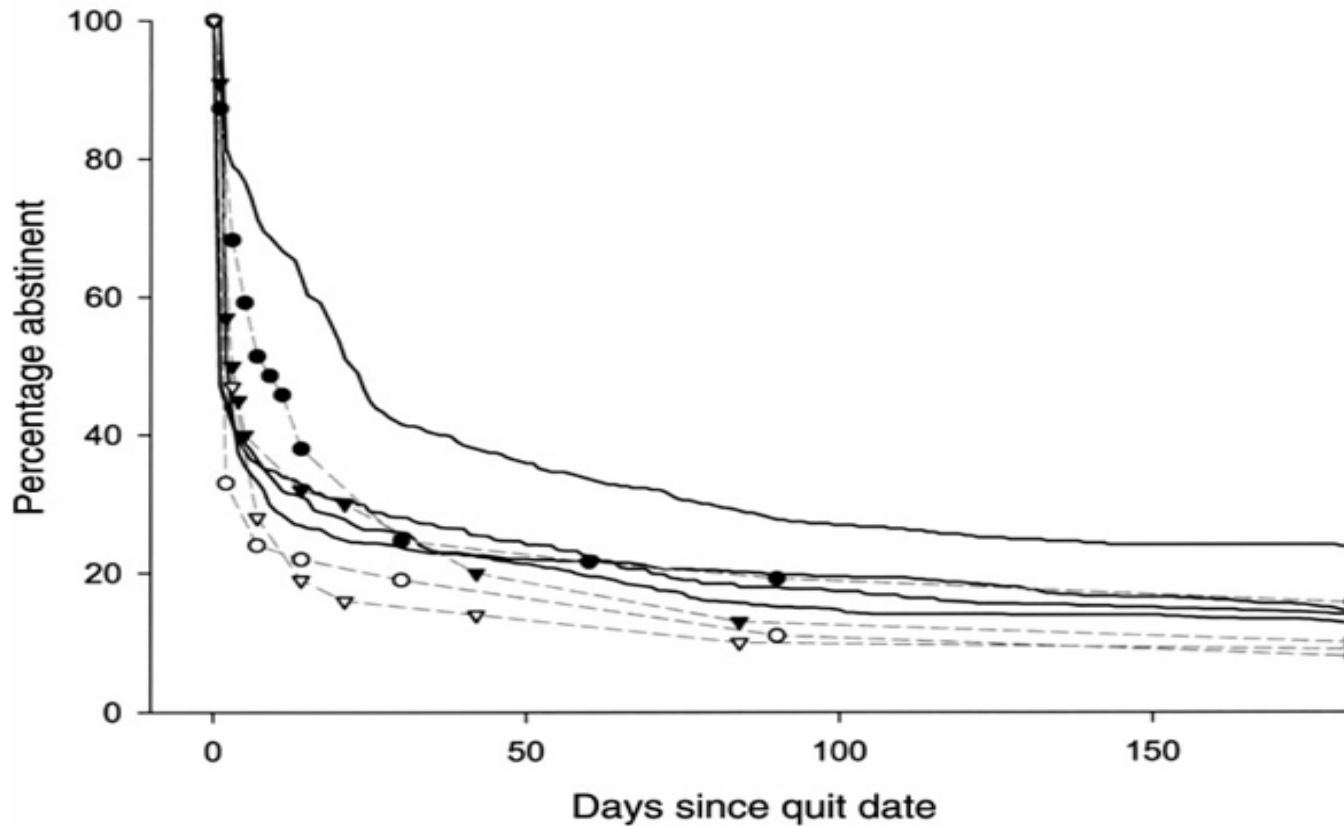


Figure 1 True survival curves (solid lines) and line-graph relapse curves (dotted lines) in self-quitters (open circles and triangles) and those in control groups (solid circles and triangles) from studies.

- › Daily smoking (number and type irrelevant)
 - › 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)
 - › Factor in:-
 - › Gender (women slower nicotine metabolisers)
 - › Ethnicity (faster or slower metabolisers)
 - › Co-morbidities (especially mental health and pregnancy)
 - › Concomitant Medications (caffeine, alcohol, insulin, antipsychotics etc, etc)
 - › Expired CO (deep vs shallow inhalations)
-

- › Smoke within ½ hour of waking or **time to first cigarette (TTFC)**
- › Multiple short previous attempts to quit/severity of withdrawals
- › Smoking or withdrawals on past use of Nicotine Replacement Therapies (NRT)

Of little relevance:

- › Numbers of cigarettes smoked/day
 - › History of smoking
 - › Brand or strength of cigarette
-

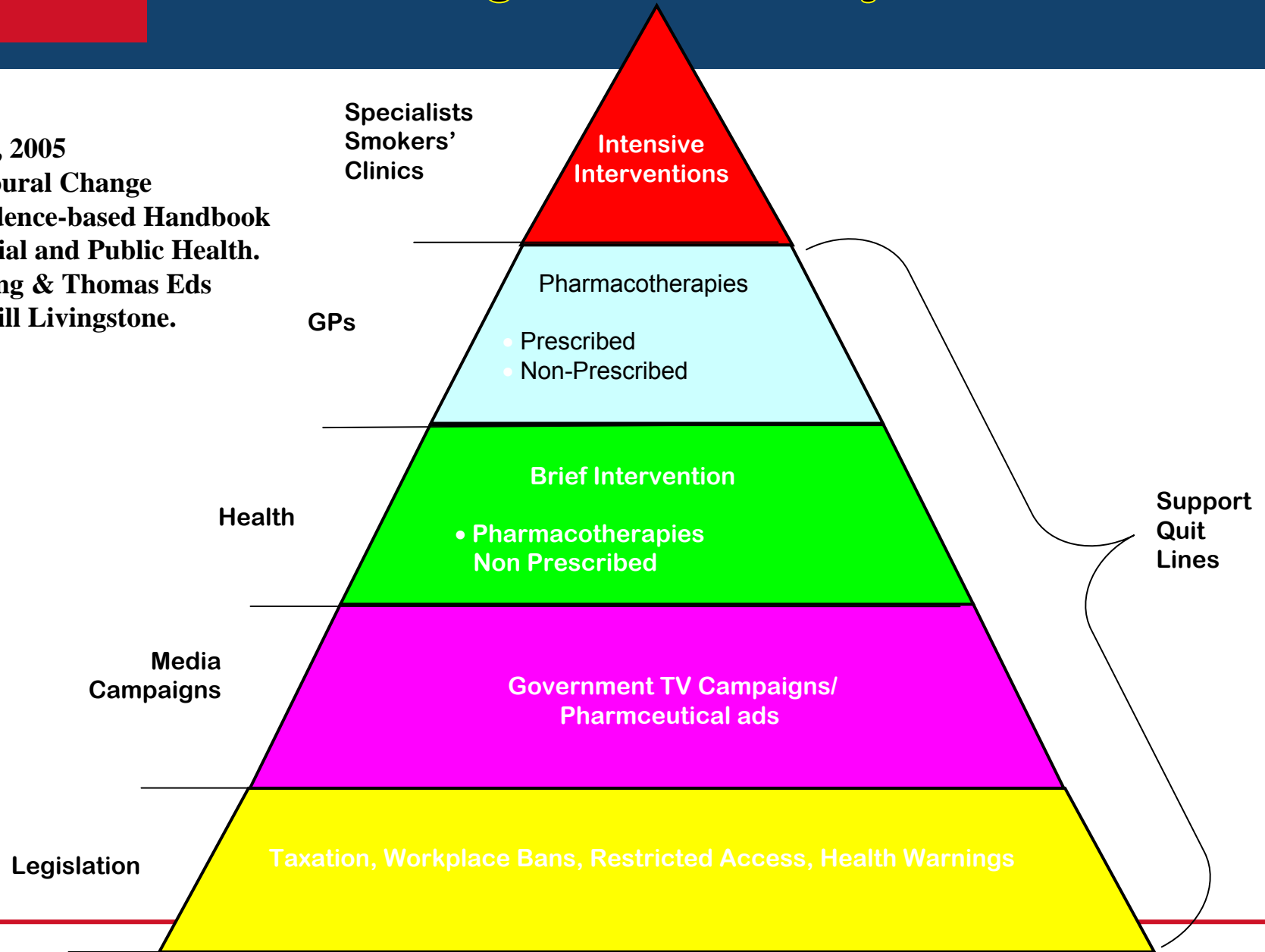
Nicotine Dependence: A Treatable Condition



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Smoking Cessation Pyramid

Bittoun, 2005
Behavioural Change
An Evidence-based Handbook
For Social and Public Health.
Browning & Thomas Eds
Churchill Livingstone.



- › What is best practice?
 - › Clinical Judgments
 - › The Carbon Monoxide Meter- a vital clinical tool
-

- › 1. The biology
 - › 2. The behaviour and
 - › 3. The social and environmental contexts.
-

There is to date no evidence for :-

- › Hypnotherapy
 - › Acupuncture/laser acupuncture
 - › Weaning off by reduction in nicotine content of cigarettes
 - › Weaning off by reduction in numbers of cigarettes
 - › Psychotherapy
 - › Negative affect counseling
 - › Stress management
 - › Constructed formal exercise programmes
 - › The 4 D's
 - › Lotions, creams and potions that are sold purporting smoking cessation
-

- › Nicotine Replacement Therapy (*NRT*) of all types
- › Bupropion (Zyban)
- › Varenicline (Champix)
- › Nortryptiline (Allegron)
- › Combination of all NRTs
- › Combination of NRT and Bupropion
- › Combination of Varenicline and NRT
- › Combinations of all of the above

see Cochrane Reviews

- › 1 CIGARETTE = ~ 40ng/ml (range 10-80) N.B. unrelated to brand concentration or numbers smoked.
 - › 1 x 2mg nicotine gum/lozenge/sublingual tab = 7ng/ml
 - › 1 x 4mg nicotine/lozenge gum = 15ng/ml
 - › 1 x 21(or16Hr)mg nicotine patch = 10ng/ml
-

What has been learnt about NRT?

- › NRT-as blood levels vary MANY smokers are underdosed with single form (1 x 21mg patch =10ng/ml)
 - › Patches may take hours to peak
 - › No evidence that weaning off is required (Garvey, 1998)
 - › No evidence to start on lower doses
 - › Evidence that combination is better (Bittoun, 2007, Shiffman, 2008 etc)
 - › Smoking while using NRT is safe and is a gateway to quitting (Fagerstrom,2000)
 - › Safe (except patch in pregnancy)
-

How do we take advantage of this?

- › Increase and combine nicotine replacement therapies where required (Bittoun, 2006)
 - › Apply 24hr 21mg patches last thing at night to peak in the morning (Bittoun, 2006)
 - › Assess “*Topography*” of smoking: Use Carbon Monoxide (CO) meter to titrate NRT (Bittoun, 2008)
 - › Alternate pulsatile NRT and Smoking (CDTQ)
 - › Use patches to start with and continue to smoke (PreQuit) (Fagerstrom, Shiffman, 2000s)
 - › Pulsatile nicotine in pregnancy → patch post natal (Bittoun, Femia, 2010 in press)
-

- › Do not confuse nicotine withdrawals with nicotine toxicity (eg NRT underdose) OR caffeine toxicity
 - › Nicotine toxicity and overdose are **EXTREMELY** rare
 - › TTFC (Time To First Cigarette) most important feature of tobacco dependence (Fagerstrom,2003)
-



Bittoun Combination Nicotine Replacement Therapy Algorithm[#]

If suitable * → 1 x 21mg nicotine transdermal patch
Baseline CO reading (commence just before sleep, change each night¹)
If within 4 days this ...

A
Eliminates both smoking and urges to smoke completely
CO reading 0-5ppm

B
Reduces smoking >5 but <10/day
CO reading reduced >1/2
↓
Add either 4mg nicotine gum / lozenge / inhaler / sublingual tablet² for “breakout” smoking
↓ If smoking & urges to smoke eliminated (if not go to C)

C
Reduces smoking but to >10/day
CO reading reduced <1/2
↓
Add a second 21 mg patch for daytime only (one patch at night – two in daytime)³
↓ If smoking persists got to B (ie 2 patches + B)

D
Eliminates smoking however urges /symptoms of withdrawal persists.
Either treat behaviour cues or go to B
CO reading 0-5ppm

Continue for 2 weeks then reduce added “breakout” NRT CO reading

Continue 1 x 21mg nicotine patch for a minimum of 7-8 weeks, then either spontaneously stop or alternate patch wearing days (one day on/one day off) for a further week, then off⁴ CO reading

* KEEP IN MIND CONTRAINDICATIONS: 1) PREGNANCY OR LIKELIHOOD (all NRT OK but not Patch)
2) RECENT CARDIOVASCULAR EVENT (48hrs)

1 Applying patch last thing before sleep allows the slow rise of nicotine overnight - the likelihood of 1st cigarette of the day “urge” is strongly diminished.

2 Either 4mg nicotine gum or lozenge depending on patient choice. Inhaler or sublingual tablet recommended over the others if patient needs faster reinforcement.

3 No evidence in our experience of toxicity. Consider reducing concentrations if nausea occurs.

4 There is no evidence for weaning (or reduction) of patch strengths

- › Cigarette
- › Nasal Spray
- › Inhaler
- › Sublingual Tablet
- › Lozenge
- › Gum
- › Patch

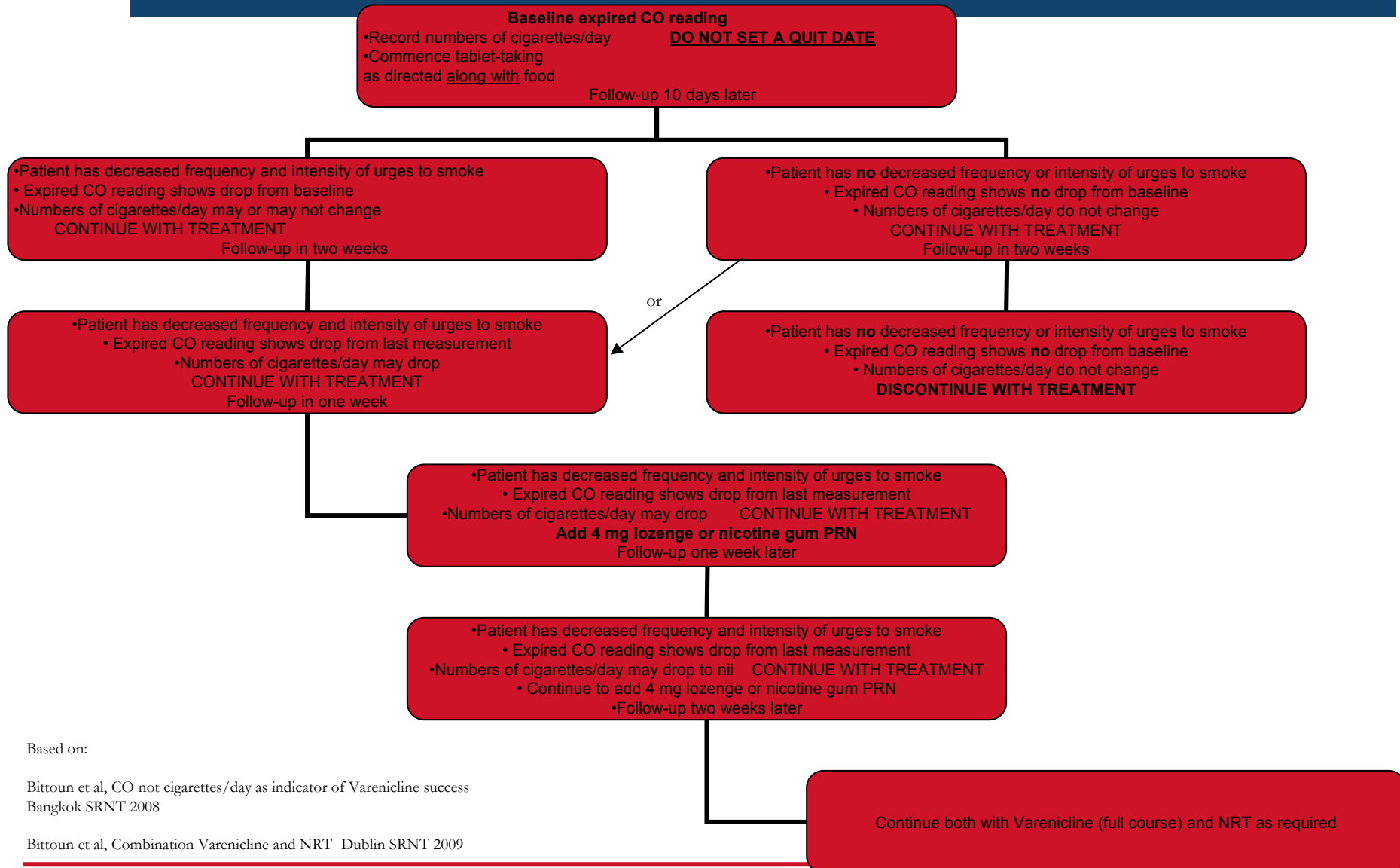


- › Best OR of all Rx
 - › Delayed responses > 2 weeks
 - › Longer = better
 - › 30% nausea as side-effect
 - › Reports of suicide ideation and aggression
 - ? Side-effects of the drug or withdrawals
-

What have we learnt about Varenicline?

- › Do not confuse nicotine withdrawals with medication side-effects
 - › There are more than one type of nACh receptor subtype ($\alpha 4\beta 2$) responding to nicotine—eg $\alpha 7$ increasingly more important (Rose, 2009)
 - › Not *all* patients do well on Varenicline
 - › Not *all* patients do well on Varenicline alone
-

- › Combining Varenicline and NRT is valid (Ebbert, 2009)
 - › Combining Varenicline and NRT is effective (Bittoun, 2009)
 - › Combining Varenicline and bupropion is valid and effective (Ebbert, 2009)
-



Based on:

Bittoun et al, CO not cigarettes/day as indicator of Varenicline success
Bangkok SRNT 2008

Bittoun et al, Combination Varenicline and NRT Dublin SRNT 2009

- › Head to head validated abstinence each of the above show 30% to 40% long-term (12 months) abstinence. These treatments double the chances of quitting compared to “cold-turkey”.
 - › As in other medications, there is a substantial placebo effect in smoking cessation treatments ranging from 15% to 20% abstinence.
 - › However combinations along with counselling can show 50% or more long-term validated abstinence.
-

Validated abstinence

- › Is defined as the persistent lack of an independent biochemical marker of tobacco smoking such as carbon monoxide, plasma nicotine (or its metabolite urine cotinine), thiocyanate or other products found in tobacco smoking. Note that nicotine and urine cotinine will be positive in non-smokers using NRT.
 - › *Absolute quitting may not always be the agenda, see below for harm-reduction and temporary abstinence using NRT*
-

- › Carbon Monoxide is a gas created from combustion or burning.
 - › This gas is very toxic and in high enough levels can cause death. Smokers inhale considerable amounts of carbon monoxide when they drag on a cigarette.
 - › Often when reducing the numbers of cigarettes smoked, they drag harder and produce MORE carbon monoxide.
 - › If the cigarette is loosely packed (roll your own) or is “milder” then MORE carbon monoxide is created.
-

- › All daily smokers will show an *abnormal* reading
 - › All smokers who quit will become normal within days.
 - › Non-smokers have little to no carbon monoxide in their expired air unless they are subject to intense passive smoking (usually in a small confined space such as a car).
-

Carbon Monoxide meters can help diagnose highly dependent smokers as high readings

- › Have been shown to correlate with nicotine blood levels, which have in turn been correlated with symptoms of withdrawal in a quit attempt.
- › As carbon monoxide changes with time and depth of inhalation and background plasma nicotine levels determine depth of inhalation, this measurement can indicate the amount of NRT that may be required when a smoker is using NRT and still smoking.
- › “Top-up” NRT can be added as carbon monoxide levels drop.
- › As quitting smokers’ Carbon Monoxide drops there will be an increase in oxygen carrying capacity. This happens to every single smoker—independent of age or history of smoking or disease.

This means that every single smoker will improve their health.



Counselling in Smoking Cessation

Counselling is dose-related.

Better outcomes occur if counseling is

- › intensive
- › personalized
- › frequent

Cochrane Reviews

- › No evidence for 4 Ds
- › No evidence that MOTIVATION is king
- › No evidence that pamphletering helps
- › No evidence that social support helps
- › No evidence that stress management helps

NO EVIDENCE FOR
“STAGES OF CHANGE” model
Cochrane Review

Some Evidence-based Behavioural Tips

- Smoke outside (Gilpin, 1999)
- Smoke outside car (Gilpin, 1999)
- Reduce caffeine intake by half (Swanson, 1994)
- Reduce Alcohol (Garvey,1992)
- For weight control, urges to smoke and sweet tooth- Glucose (West, 2001)
- Urges to smoke - short exercises (Taylor, 2007)
- Do not quit with PMT –Premenstrual tension (O’Hara, 1989)
- Buddying might not help (May, 2006)
- Separate activities-smoke outside/coffee inside (Femia, 2009 unpublished)

Cue Extinguishment!

Relapse

- › endemic
- › 50% occur within 1st week of quitting
- › ~ 10% in 2nd week of quitting
- › After 3 months of abstinence and no lapses the quit is likely permanent

Lapse

- › 95% of lapses become relapses
- › 85% lapses are *just one puff* within 1 to 4 days of a quit attempt
- › Second lapse is most frequently on the same day as the first

Shiffman, 2000

- › *8% still abstinent at 12 months in Australia today (Cold turkey).*
-

Increased risk if:

- › Living with a smoker
- › More than half of friends smoke
- › Use alcohol in excess
- › Use other drugs

Garvey, 1992

Ask:

About where smoking takes place-in the home/car/workplace

Do you live with a smoker?

Are >50% of friends smokers?

Advise:

- › Smoke outside → gateway to quitting (Gilpin, 1999)
 - › Smoke outside car → gateway to quitting (Gilpin, 1999)
 - › Don't avoid cues (Thewissen, 2008)
 - › Everyone smoke outside (Gilpin, 1999)
 - › Avoid proximal smoking (Garvey, 1992)
-

- › **Ask** (about smoking and interest in quitting)
 - › **Advise** (talk about the many ways that are valid to either quit or are a gateway to quitting). Measure and explain expired CO to engage and motivate.
 - › **Assess** smoker's level of dependency, psychosocial and pharmacological influences.
 - › **Assist** (recommend treatments and behavioural changes)
 - › **Arrange Follow-up** (within the first week) (assess and explain expired CO, levels of smoking, effects of medication) arrange further follow-ups.
 - › Keep notes on each client
-

Treatment advice is no longer a “one-size-fits-all” regimen, eg clinical practice guidelines

- › Use a medical model of individual treatments
- › Consider harm-reduction
- › Base “tips” on evidence
- › Incorporate environmental cues
- › Consider drug interactions
- › Enforce policies

The Hard to treat smoker: Brief Interventions, individualised treatments and harm-reduction strategies

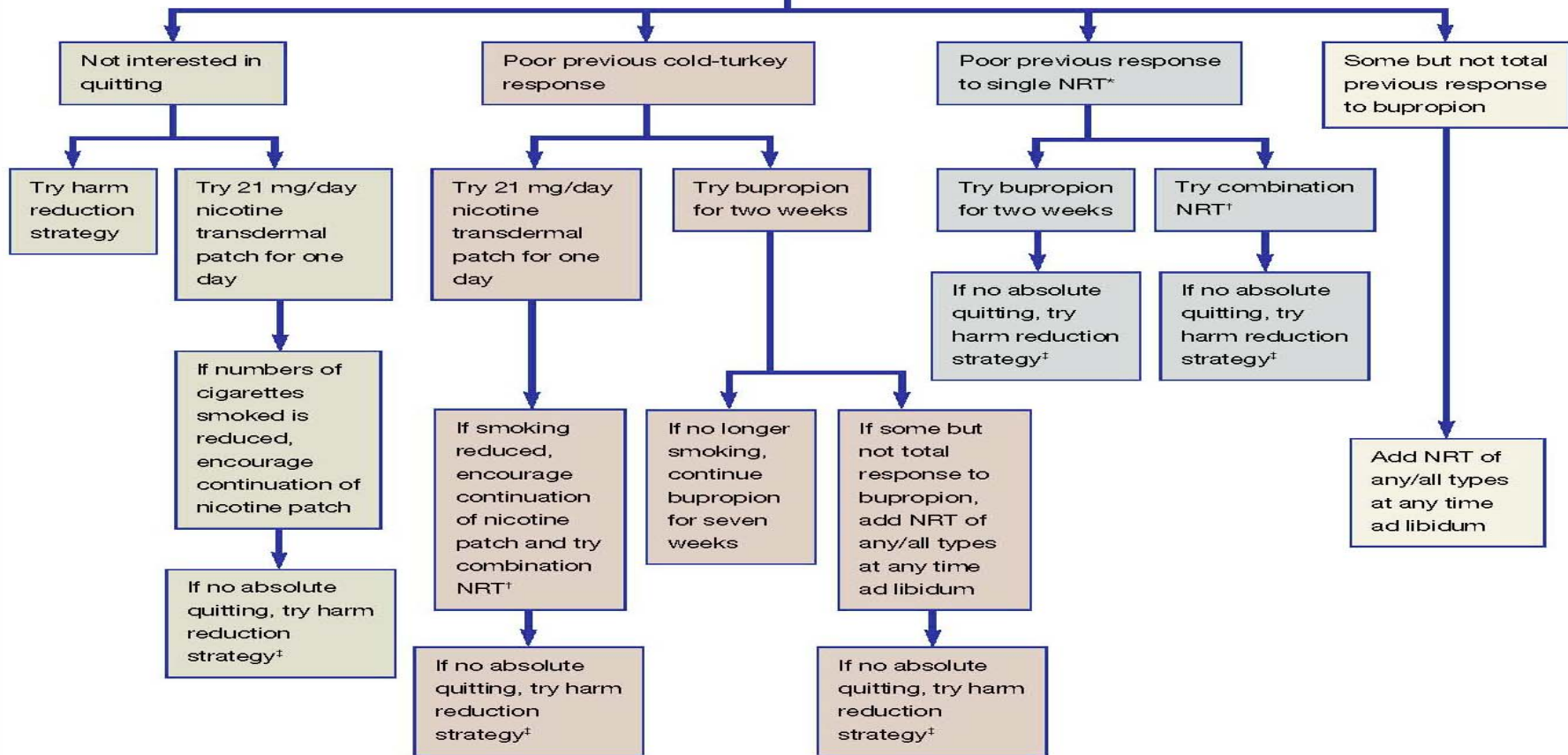


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- › 25% Smoke while on NRT.
 - › Nicotine intake is suppressed when on NRT.
 - › Reducing can be a gateway to quitting.
-

- › Relief of craving and other withdrawal symptoms
 - › Reduced cigarette consumption and prevention of compensatory smoking
 - › Smokers may learn that they can manage without tobacco for several hours leading to an increased motivation to quit
-

The treatment-resistant smoker



* NRT = nicotine replacement therapy.

† Combination NRT = transdermal nicotine patch plus nicotine gum, lozenge, inhaler or sublingual tablet.

‡ Harm reduction strategy = using NRT periodically to reduce smoking or achieve temporary abstinence.

Note contraindications and that new drugs will be available soon.

TYPICAL CHRONIC COPD/DIABETIC/CARDIAC PATIENT

- › NEEDS TO QUIT
- › MULTIPLE QUIT ATTEMPTS
- › DEPRESSED (?) BUT NOT CLINICALLY
- › BEEN THERE /DONE THAT WITH MOST Rx

HOW TO START:

- › Describe new science behind addiction (varying levels)
- › Describe genetic factors (brain and liver responses)
- › Discuss new treatment options (safety and efficacy of ↑ doses of NRT-combinations, varenicline)
- › DESCRIBE “NO NEED TO ABRUPTLY QUIT!
- › ENCOURAGE: Give it a go—see what happens philosophy.

THEN:

1) Pharmacotherapies

- › If smoked in past on NRT (very common)→ go to Bittoun algorithm
- › If past Varenicline success but relapsed→ discuss re-use
- › If past Varenicline failure →go to Bittoun algorithm

2) Implement immediate psychosocial changes (whether ready to quit or not) on NRT or Varenicline

- › Every one smoke outside (includes the patient, friends, relatives)
- › No smoking in the car (stop and get out to smoke)
- › Separate behavioural triggers – coffee inside—cigarette outside
Alcohol inside—cigarette outside
Newspaper/book inside --- cigarette outside

FOLLOW-UP: On Varenicline *no* earlier than 10 days from commencement

On NRT (as per algorithm)

- › Develop a hierarchy of strategies for smokers that begins with permanent cessation but----
 - › Consider harm-reduction for resistant smokers
 - › ?? Unethical to exclude recommending harm reduction behaviours to resistant smokers as an alternative to the
“Quit or You’ll Die” Dogma.
-

- › Smoking greatly affects the reproductive lives of both men and women.
- › Not smoking increases the likelihood of becoming pregnant-so it is important to quit if planning a pregnancy.
- › Pregnant women who smoke should quit as soon as possible without any pharmacotherapy.
- › If unable to do so it is **safer** to use NRT (excluding the patch) than to smoke in pregnancy.
- › Pulsatile nicotine in pregnancy—no patch
- › Patch and all other forms of NRT post-partum if lactating