

Nicotine Addiction & Nicotine Replacement

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declaration of competing interests

- Dr Hayden McRobbie has undertaken research and consultancy for, and received honoraria for speaking at meetings from the manufacturers of smoking cessation medications



Giving up smoking is difficult for some

- The majority of smokers want to quit¹
- Most people try to quit without any assistance²
- Only 2-3% of those who stop smoking unassisted remain abstinent after a year³



The cigarette

- "The cigarette should be conceived not as a product but as a package. The product is nicotine. Think of the cigarette pack as a storage container for a day's supply of nicotine.... Think of the cigarette as the dispenser for a dose unit of nicotine..... Smoke is beyond question the most optimised vehicle of nicotine and the cigarette the most optimised dispenser of smoke." (Philip Morris 1972)



What's in a cigarette?

• Tobacco smoke contains over 4,000 identified compounds, including:

- 2-nitropropane
- Acetaldehyde
- Acrolein
- Acrylonitrile
- Ammonia
- Aromatic amines
- Arsenic
- Aza-arenes
- Benzo (a) pyrenes
- Carbon monoxide
- Carboxylic acids
- Dimethylnitrosamine
- Formaldehyde
- Hydrazine
- Hydrogen cyanide
- Insecticide residues
- Isoprenoids
- Naphthalenes
- Nickel
- Nicotine
- Nitrogen oxides
- Non-volatile nitrosamines
- Phenols
- Polonium-210
- Polynuclear aromatic hydrocarbons
- Pyridine
- Urethane
- Vinyl chloride



Measurement of tar & nicotine

- Machine smoking
- Fixed to ISO standards
 - 2 sec
 - 35ml puff
 - once a minute
 - To a predetermined butt length



...but they're not made for machines

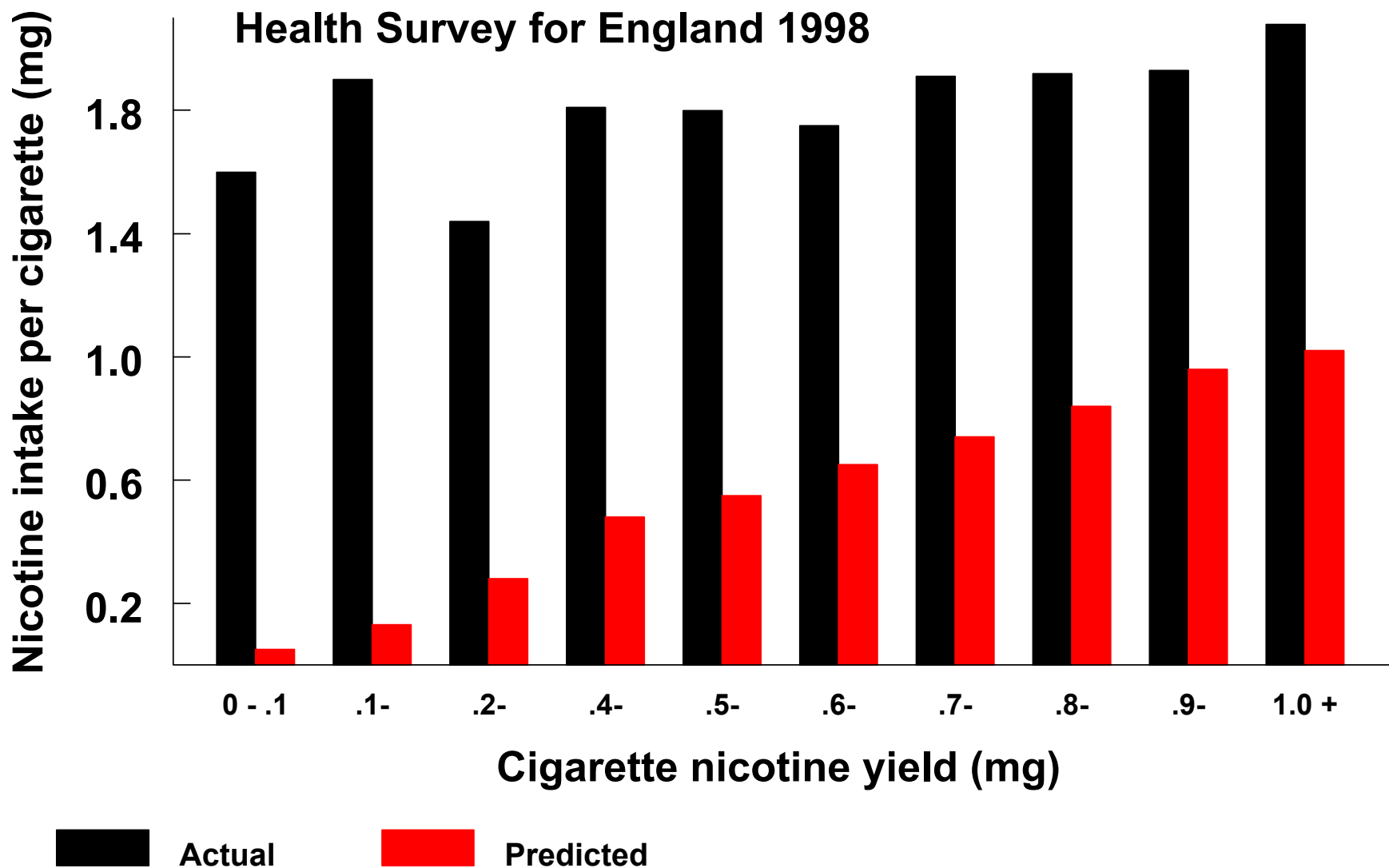
Human smoking

- Compensates to achieve desired nicotine dose
 - Longer, deeper, more puffs
 - More of the rod smoked
 - Ventilation holes blocked by fingers, lips or saliva



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Predicted and actual nicotine intake





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Reasons for smoking

Self-reported smoking motives

- stress relief
- boredom relief
- concentration aid
- aid to socialising
- enjoyment
- weight control



Are all smokers addicted?

- Most are, but not all

Addiction is:

- A loss of control over behaviour
- Behaviour is no longer a matter of considered choice
- A function of
 - the drug (e.g. it's reinforcing properties)
 - the person (e.g. mental health, biochemistry)
 - the situation (e.g. stress, lack of alternatives)



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How does nicotine do it?



Tobacco withdrawal syndrome

Signs & symptoms

Irritability

Depression

Restlessness

Poor concentration

Increased appetite

Sleep disturbance

Urges to smoke

↓ Heart rate

↓ Tremor

↑ Skin temperature

Mouth Ulcers

Constipation

Duration

< 4 weeks

< 4 weeks

< 4 weeks

< 2 weeks

> 10 weeks

< 1 week

> 2 weeks

Long-term

Long-term

Long-term

> 4 weeks

>4 weeks

Prevalence

50%

60%

60%

60%

70%

25%

70%

> 80%

> 80%

> 80%

40%

17%



A question...

- If smokers smoke just for nicotine then shouldn't NRT help cease tobacco use?



Answer – YES it does

- BUT – its not a magic cure
- Long-term quit rates are typically less than 20%



Is it because of different delivery?

- IV nicotine
 - Faster than NRT, but relief of craving is still about the same as NRT
- Little difference between nasal spray (fast) and patch (slow) in reducing craving
- Differences in nicotine delivery do not provide the whole solution



A puff on a cigarette

- Repeated hundreds of times a day
- Individual puffs are felt as pleasurable
- Each puff delivers nicotine plus the sensations associated with inhaling smoke



De-nicotinised cigarette research

- Gives similar sensory impact without nicotine
- Gives feeling of satisfaction
- Reduces urges to smoke



Sensorimotor cues

- Sensory components
 - Taste
 - Aroma
 - Sensations in airways
- Nicotine may have sensory effects
- Motor components
 - Handling
 - Puffing
 - Inhaling



Methanol

- Sensory cue
- ‘Mild local anaesthetic’ – may reduce local irritant effects of nicotine
- Increases permeability of membranes possibly leading to increases nicotine absorption
- These were known to the tobacco industry and identified in their documents (Ferris et al 2004)



Other things in tobacco smoke

- Monoamine oxidase inhibitors
 - May act with nicotine to reinforce smoking behaviour
- Acetaldehyde
 - May enhance rewarding properties of nicotine
- Ammonia
 - Added by tobacco companies to increase nicotine absorption



rationale for using nrt

- Nicotine deprivation in smokers causes withdrawal discomfort
- Nicotine via alternative routes provides relief and assists with transition to complete abstinence
- NRT provides temporary nicotine substitution (weaning)
- NRT contains nicotine only, and slower delivery



how does it work?

- Reduces the severity of withdrawal symptoms
- Reduces urges to smoke
- Delays weight gain
- Reduces relapse



how effective is NRT?

- Doubles success rates
- Products are equally effective
- Efficacy is independent of the intensity of additional support
- Effect still seen at 1-year



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effectiveness

Product	Odds ratio	95% confidence interval
Gum	1.66	1.51-1.81
Patch	1.84	1.65-2.06
Nasal Spray	2.35	1.63-3.38
Inhaler	2.14	1.44-3.18
Sublingual tablet or lozenge	2.05	1.62-2.59
Overall	1.77	1.66-1.88



i've tried it and it doesn't work

- Unrealistic expectations
 - 'magic cure'
 - waiting for the drug to 'make the user stop smoking'
- Insufficient and incorrect use
 - fear of nicotine, using only when desperate)
- Lack of preparation for the fact that oral products may be unpleasant initially



can they cause dependence?

- NRT cannot cause new dependence as users are already dependent on nicotine
- The chances of long-term use are related to speed of nicotine absorption
- Long-term users are mostly smokers whose chance of success would be otherwise small



is it safe?

- Media scares
 - Could it cause cancer?
- Years of population use with no adverse effects
- NRT is safe, particularly compared to smoking

speed of
nicotine
delivery



how do NRT products differ?

- Ease of use
- Frequency of use
- Speed of absorption
- Degree of behavioural replacement
- Sensory effects
- Ability for user to titrate dose



how much nicotine?

- Most current NRT products provide similar nicotine delivery in average users, about 50% of their daily intake from smoking
- Nicotine in these doses is considered harmless (the dangers of smoking are mainly due to combustion products and other chemicals)



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nrt products

Currently available

Gum

Patch

Lozenge

Sublingual tablet

Inhaler

Nasal spray

In development

Pouch

Mouthspray

Faster acting gum

Faster acting lozenge

Nicotine canon



nicotine chewing gum

- 2mg and 4mg
- Takes some 20 minutes to reach peak concentration
- Recommend 10-15 pieces a day, hourly
- Use for 8 weeks
- Start chewing slowly, takes a few days to get used to
- Each piece lasts 30 minutes (can be chewed longer)



transdermal patch

- 16 hour and 24 hour patches
- Most smokers should start on full strength (21mg/24 hr or 15mg/16 hr)
- Smaller patches for weaning-off period (these are not necessary)
- Takes hours to reach peak concentration
- Use for 8 weeks (at least)



inhaler

- Despite its name nicotine is not inhaled into the lungs - like other oral products it is absorbed through the oral mucosa
- Takes some 30 minutes to reach plateau
- Recommend puffing for some 10-20 minutes every hour
- 10 puffs equals one puff from cigarette (1 cartridge = 4 cigs)
- Aim to use 6 cartridges per day



sublingual tablet (microtab)

- 2 mg tablets
- Takes some 20 minutes to reach peak concentration
- Recommend 10-15 tablets a day, hourly (can use up to 40/day)
- Use for 8 weeks
- Tablets dissolve under tongue in approximately 30 minutes



lozenge

- Novartis '1mg' lozenge, delivery as for 2mg products, no outcome data
- GSK new 2mg and 4mg lozenges
- Both reach peak plasma concentration in approximately 20-30 minutes
- Use 12-15 lozenges per day



nicotine nasal spray

- Takes only minutes to reach plateau
- Recommend one shot in each nostril hourly
- Recommend use for up to 3 months
- Warn of initial aversive effects and supervise the first trial



advantages of patch

- Easy to use, not aversive
- No social acceptability problem
- Better compliance
- No long-term use



advantages of oral products

- Faster nicotine absorption
 - Control over nicotine dose
 - Some behavioural replacement
 - Can be used opportunistically for relapse prevention
-



nrt combinations

- Provide an increase in long-term quit rates (42%)
- How?
 - Increase in nicotine dose
 - More control / behavioural replacement
- No safety concerns
- Which combinations?
 - Patch + patch
 - Patch + oral product
 - ? Oral product + oral product



side effects

- Most side effects are 'local'
- Patches can cause skin irritation (common to experience redness under the patch)
- Oral products - adverse taste is often the main complaint
- Swallowed nicotine can cause a 'burning' sensation in the throat and hiccups
- Mouth ulcers are probably not related to the oral products (nicotine withdrawal symptom)



contraindications

- None genuine, users take more nicotine from their cigarettes in addition to other dangerous chemicals
- According to labelling, not for pregnant women, people with heart problem or indigestion should consult doctor or pharmacist
- Change product if side effects strong - primarily skin reaction to patch



drug interactions

- Are there any drug interactions with NRT?
- Smoking cessation, not NRT may cause alterations in some circulating drug levels, but not normally enough to cause therapeutic problems. E.g.
 - Theophylline
 - Insulin
 - Clozapine
 - Imipramine
 - Chlomipramine



information for clients

- Not a magic cure, effort needed
- Provides nicotine smokers miss, but more slowly and less of it than cigs
- Does not mimic cigs effects, but takes the edge off the discomfort
- Oral product can be unpleasant initially, must persevere to benefit
- Instruct on product specific use issues



Four key points

- Take pride;
- Be professional;
- Be a revolving door;
- Be proactive.



Take pride

- Psychiatrist treating social phobia;
 - No premature deaths avoided
- GP treating high blood pressure
 - 1 premature death avoided for every 40 people seen
- AKP coaches 1 in 20 people you see and who quits will be saved!



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Individual treatment



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