The mechanisms of nicotine addiction and harm from tobacco smoke

Smoking tobacco is a pleasurable activity because one of the absorbed substances, nicotine, activates neurotransmitters that release dopamine, a hormone and neurotransmitter that is part of the human reward mechanism.\(^1\)\(^,\)\(^2\) Initial repeated use driven by societal factors is followed by habituated behaviour driven predominantly by a need for nicotine.\(^3\) Regular exposure to nicotine quickly results in addiction because the number of dopamine releasing nicotinic receptors in the brain increase to maintain an effective and pleasurable reward.\(^4\) The brain in essence changes its structure so that it can receive and process nicotine as effectively as possible. Any sudden cessation of supply will cause an acute nicotine withdrawal that is unpleasant, alters behaviour, physiology and mood so creating a manifest craving to reinstitute supply.\(^5\)

Tobacco contains more than 2,500 chemical constituents, many of which are known human carcinogens.\(^6\) These are rapidly absorbed through the lungs and delivered unmodified to the rest of the body having avoided first pass liver metabolism. These substances activate inflammatory pathways that cause cell damage and they activate oncogenesis.\(^6\) If the nicotine dependency and these neurophysiological changes are not reversed then harm to health will occur; the extent dependent on the amount of smoke inhaled, the length of exposure i.e. “pack years” and any underlying genetic predisposition e.g. alpha-1 antitrypsin deficiency and emphysema.\(^7\)\(^-\)\(^10\)

We know that habit and social cues also contribute to an individual’s impulse to smoke and so behaviour change interventions will enhance any quit attempt but as nicotine addiction is the most powerful of the three, this pharmacological aspect of therapy must be prioritised to increase the chance of a successful outcome.

Primary care professionals should assess nicotine dependency at every reasonable opportunity and when a treatment plan is agreed, to individualise and monitor their pharmacotherapy ensuring it is as much a part of any smoking cessation intervention as say drug therapy is currently in a hypertension control programme.

Know who your smokers are – practice and population approaches

There is some variation between the four countries both in collection of smoking statistics and prevalence. England currently samples a different cohort of 1800 people monthly and reports quarterly and in April 2014, 19.2% of the population in England was smoking tobacco regularly.\(^11\) In 2012 Northern Ireland’s smoking prevalence was 24% and in the Scottish and Welsh 2013 household surveys prevalence was 23.1% and 21%. The good news is that smoking rates are substantially lower than in the early 1970s when half the UK population smoked. However this dramatic fall in prevalence of tobacco smoking has slowed in the last decade despite a rise in tobacco control investment suggesting we need to work differently with those populations who are more resistant to current smoking cessation policy and offer.\(^12\) Measuring the
smoking prevalence between socioeconomic strata, ethnic groups and amongst our population with long-term conditions has helped us identify the greater need.

In 2012, 14% of adults in managerial and professional occupations smoked compared with 33% in routine and manual occupations. Smoking is common among lesbian (42-55%), gay (35% including 48% in those who were HIV-positive), bisexual and transgender people. The immigration of people to the UK from countries where smoking is more prevalent requires unique approaches and working with community leaders and influencers; an approach taken in Tower Hamlets in London with the Bangladeshi Tobacco Cessation Project. Cotinine determined tobacco use is as high as 60% in Bangladeshi men, and 35% in women. Recent figures from Crewe show that prevalence of current smoking in the migrant Polish community is 48% which is equivalent to the background rate of smokers here in the early 1970s. Though aligned and accurate data is not yet conclusive for Europe we can anticipate that from currently available figures that people from newer EU countries such as Croatia, Bulgaria and Romania have higher smoking prevalence and will likely need language and culture specific programmes to address this.

People who smoke and have long term conditions – ‘Sick smokers’

Up to 33% of people with mental health problems and more than two-thirds (70%) of patients in psychiatric units, smoke cigarettes. 42% of all the tobacco smoked in the UK is by people with a mental health problem. People in prison and the homeless have higher rates of both mental illness and smoking. People with severe mental illness are more likely to die prematurely and predominantly from physical diseases caused or made worse by tobacco smoking. Recent studies show that people with mental health problems are just as likely to want to stop smoking as the general population and are able to stop when offered evidence-based support. Medication adjustment is usually needed and close working with mental health teams is required when they decide to quit or reduce.

The annual QOF smoking returns suggests that up to 1:4 people with common long-term conditions continue to smoke. Whilst there is currently no national data set of smoking prevalence in people with respiratory disease there is evidence to suggest that at least as many people with asthma smoke as in the UK general population. The impact of tobacco smoking on children with asthma, either because they smoke themselves or they are exposed to others tobacco smoke is well described. Recent studies have suggested that smoke free legislation has resulted in a reduction in emergency presentations of children with asthma. The 2014 national report into asthma deaths (NRAD) showed that one of the ten asthma deaths in the under 10 year old group was a child who was a smoker and there was a 36% prevalence of smoking at home by family members in the group of children and young people who died from asthma. There are “Read Code” options available to add to asthma templates so that the potential impact of household smoking can be considered within an asthma management plan.

The prevalence of smoking in people with COPD is broadly between a third and a half using data from inhaler therapy trials over the last decade, with no apparent change over that time. In two boroughs of London, smoking prevalence in COPD has recently been recorded as 40% (Tower Hamlets - 2011) and 47% (Southwark -2013). People with COPD find it harder to quit and they do relapse but there is convincing evidence that they want to quit and can quit with evidence-based interventions regardless of severity.
Sometimes individual practice resources may not be sufficient to provide the level of intervention as recommended for these groups with high addiction and relapse so consideration of alternative models such as higher intensity services may need to be considered by Public Health and Clinical leaders responsible for commissioning tobacco cessation programmes.

**Smoking cessation as treatment – a life prolonging intervention for people with mild and moderate obstructive airways disease.**

Stopping smoking reduces all cause mortality in people with mild and moderate airways obstruction according to a 14.5-year cohort study that followed subjects in receipt of an intensive quit smoking intervention. Life was significantly lengthened in those who were sustained quitters. They received a treatment that included:

i) nicotine replacement,
ii) a strong physician message,
iii) a 10-week behavioural programme consisting of 12 sessions
iv) 5 years of reinforcement.

**FIGURE 1: Effect of sustained quitting when obstructive lung disease is mild or moderate**

A subsequent systematic review of RCTs for smoking cessation interventions in COPD has shown that the more time you spend with a patient the more cost effective the outcome and with the addition of drug therapy then the best results are seen for lives saved and years gained.
**TABLE 1: QALYs for smoking cessation in COPD**

Results of the base case: 1-year implementation of minimal counselling, intensive counselling or intensive counselling in combination with pharmacotherapy (‘pharmacotherapy’) compared with usual care, time horizon 25 years

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Life-years gained</th>
<th>QALYs gained</th>
<th>Reduction in mortality†</th>
<th>Cost per life year gained (€)</th>
<th>Cost per QALY gained (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal counselling</td>
<td>210</td>
<td>280</td>
<td>90</td>
<td>22400</td>
<td>16900</td>
</tr>
<tr>
<td>Intensive counselling</td>
<td>690</td>
<td>960</td>
<td>340</td>
<td>11600</td>
<td>8200</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>1590</td>
<td>2240</td>
<td>830</td>
<td>3300</td>
<td>2400</td>
</tr>
</tbody>
</table>

† Number of deaths avoided over the time horizon (25 years) of the analyses.

It is not currently known what proportion of people with COPD who smoke are receiving this level of intervention and it isn’t widely recorded or audited as an outcome measure for COPD services. Since the 2005 cohort study there is now widespread access to a wider range of nicotine replacement products as well as Varenicline and Bupropion.

**Tobacco smoking and its short or medium term impact – Health related motivators to support behaviour change**

Smoking kills an estimated 112,000 people each year and reducing the number of smokers and the amount they smoke in a lifetime would have a big impact on reducing preventable premature mortality, a key outcome for the NHS in the UK. However smoking tobacco also affects the lives of people that don’t yet have long-term problems but who sustain tobacco related morbidity in the short or medium term. The link may be less well understood by both patients and health professionals. Delayed recovery from illness and surgery through smoking is well described, as are the attendant increased costs to healthcare and the economy through disruption of education and industry.

Knowing where the health improving opportunities are, how to raise the subject and then how to treat is a fundamental knowledge and skill set for every health professional. We know that smokers are more motivated to receive messages and support to quit when they are experiencing a related health problem and that when they see their doctor they expect to be asked about tobacco smoking.

In general practice at least 1 in 5 of the people we see every day are smokers. Unfortunately only 8% of smokers who want to quit access a stop smoking service each year. 50% are estimated to try to quit with a poor 4% success rate. The addition of intensive support and pharmacotherapy results in quit rates in excess of 50% according to the Health and Social Care Information Centre [http://www.hscic.gov.uk](http://www.hscic.gov.uk).

There are opportunities through frequent contact with smokers to improve uptake of evidence-based interventions for tobacco addiction. The [NHS Making Every Contact Count (MECC) programme](http://www.hscic.gov.uk) has at its
core the principles of organisational and staff readiness to support empowered people to improve their health and wellbeing through behaviour change. In a GP surgery this could be realised with accessible information backed up with a well trained reception staff who facilitate access to the right stop smoking interventions and health professionals who are trained and confident to help quitters. There is no organ system that can’t be affected by tobacco smoke and being aware of those conditions and situations where smoking could be a relevant factor and using this situation for engaging people in behaviour change is a fundamental role of any health professionals.  

**What is the role of the GP?**

The GP’s role is not usually to deliver smoking cessation therapy but to explain that the best way to stop is with support and treatment, to direct smokers to a trained advisor, and to provide prescriptions as requested by the advisor. But this is not always achieved since time is a major factor. Ninety-three percent of GPs rate helping their patients to stop smoking as the single best thing they could do for their health, and smokers value GP’s smoking cessation advice. However, 91% of GPs feel deterred because of time pressures.  

This requires training and practice and a good way to start is by completing the “Very Brief Advice” (VBA) module available on the National Centre for Smoking Cessation Training (NCSCT - [http://www.ncsct.co.uk/](http://www.ncsct.co.uk/)) and then consider completing some of the other modules relevant to primary care. Also see the NCSCT Brief Intervention Video clip at [http://youtu.be/2MuNG9Txdkg](http://youtu.be/2MuNG9Txdkg)  

Dr Noel Baxter has provided a short training video on the role of primary healthcare professionals which can be viewed [HERE](http://www.ncsct.co.uk/). Also visit the PCRS-UK smoking cessation web page [HERE](http://www.ncsct.co.uk/) for more information.  

**Motivating change in behaviour**  
Of the 10 million smokers in the UK, 72% say they would like to give up. So, on the whole, smokers do not need to be told to stop – they need to be told how to stop.

The role of the smoking cessation advisor is crucial to this: advisors do not need medical training but they do need to have good knowledge of the subject, motivation, good communication skills, and to be sympathetic. Logistically they need to be accessible and to have enough time available for the job.

Group support is effective, but patients generally favour one-to-one intervention, and patient preference plays an important part in the success of a quit attempt. One-to-one advice gives privacy and means that meeting arrangements can be flexible. The importance of the bond between quitter and their smoking cessation advisor cannot be over-emphasised. Speaking to individuals with empathy and making it clear that they will be supported throughout the process of stopping smoking is pivotal. Keeping the same smoking advisor during the process is a great help to the patient.

Support should be offered over the 2- to 3-month period of nicotine withdrawal symptoms. 4-week quit targets are still used to monitor success of smoking cessation interventions with weekly meetings during
that time however for many this is too short an episode and facilitation of longer term follow up and review of relapse would be beneficial for those that have cravings for longer.

Pharmacotherapy
The smoking cessation advisor should go through all available treatments at the first meeting so that the patient can make a well-informed choice about which treatment they would prefer to use. All the treatments listed below have been recommended by the National Institute for Health and Clinical Excellence and should be used for nine to 12 weeks with longer use being safe and appropriate and still good value in some cases.

Nicotine Replacement Therapy (NRT)
NRT is available as chewing gum, nasal spray, mouth spray, patch, microtab, lozenge or inhalator. There is no evidence to suggest that any one form is more effective than any other, so patient preference should dictate which one or which combination is used. The degree of nicotine addiction and therefore the required dosage of NRT is best decided by asking how long after waking the first cigarette is smoked, the so called “Time To First Cigarette” (TTFC). If the TTFC is less than 30 minutes, the maximum dose should be used. NRT is available over the counter as well as by prescription, and like Bupropion it increases a smoker’s chances of quitting by 1.5 to 2 times.

Localised reactions can occur depending on the form taken; e.g. skin irritation with patches. NRT can be prescribed in pregnancy, breastfeeding and in children from the age of 12 years

Bupropion (Zyban®)
Originally developed as an anti-depressant, bupropion works as a dopamine re-uptake inhibitor, reducing the need for the next cigarette because of the fall in dopamine levels.

Side effects include insomnia, headache, dry mouth and nausea. It is reported to cause seizures in one per 1000 people. Some patients express a preference for bupropion if they have used it before or if it has been recommended by a friend.

Varenicline Tartrate (Champix®)
Varenicline tartrate is the most effective of the smoking cessation drugs. It is a first-in-class, non-nicotine drug, not related to bupropion. It has long-term quit rates of 22.5% compared with 15.7% on bupropion and 9.4% on placebo.

Varenicline tartrate has no known drug interactions. The main side effect is nausea which affects about a third of patients, so warning of this before prescribing is a good idea. It often occurs as the dose goes up on days 4 and 8, usually lasts for about an hour after taking the tablet for the first two or three weeks, and is mild to moderate with 97% of patients tolerating it. Taking treatment with drink or food can help, and if it becomes difficult to tolerate then anti-emetics such as prochlorperazine can be used for a short period or the dosage may be reduced from 1mg b.d. to 0.5mg b.d.

The smoking cessation treatment options, both pharmacological and advisory, are all inexpensive and are judged by NICE to be highly cost effective in terms of life years gained. The number needed to treat (NNT)
for successful cessation gives an indication of how effective this treatment is in reducing smoking-related mortality and morbidity. Behavioural support combined with therapy gives an average NNT of around 14. Compare this to another worthwhile intervention: an NNT of 1140 for a cervical smear preventing a death over 10 years. When we consider that one of two smokers die from long-term smoking, we see that properly-delivered smoking cessation is one of the most cost effective of all healthcare interventions.

Top tips for general practice

1. Making Every Contact Count (MECC). Patients expect to be asked about their smoking by a GP. 72% of smokers consider quitting and 30% try but only a tiny fraction (5-8%) of smokers use an evidence-based intervention each year.
2. Be objective and stratify - A high carbon monoxide and Fagerstrom test\(^{33}\) correlates with higher addiction and may need more resource for longer or to referral to a specialist team.
3. Have the tools you need on your desk and in your room
   a. A carbon monoxide monitor
   b. A microspirometer to assess lung age
   c. Examples of stop smoking medicines – show you know how to use them and that you consider them as treatments.
   d. A stop smoking prescribing ready reckoner\(^{34}\)
4. Tobacco smoke is more harmful than nicotine replacement, varenicline and bupropion and there are very few drug interactions. Start with a positive view that is that it is generally safe to use, well tolerated and then work with mental health experts and stop smoking specialists if you are supporting those with severe mental illness to quit.
5. Stop smoking medicines are essential treatments for tobacco addiction (93% of people who successfully quit at 4 weeks have used a stop smoking drug) and they work.\(^{35,36}\)
6. Even with optimal stop smoking cessation interventions 1 year quit rates may seem small when reflected on by individual practitioners but the effect in those who do quit is great and enduring. “An in-expensive intervention with a relatively low success rate can make an important difference if it has great potential and is applied early in the course of the diseases of interest.”\(^{28}\)

References:-


“Smoking in England statistics.”

“ASH Briefing: UK Tobacco Control Policy and Expenditure.”

ASH, “Smoking statistics who smokes and how much.”

“The Bangladeshi Stop Tobacco Project.”

ASH, “Tobacco and ethnic minorities.”


