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CLINICAL REVIEW

Managing smoking cessation

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Cross sectional studies show that most smokers in countries such as the United Kingdom and the United States report that they want to stop and intend to stop at some point.[1] The rate of attempts to stop is high—78 attempts per 100 smokers per year in the UK—with many smokers making several attempts in a year.[2] Nearly half of all smokers expect not to be smoking in a year's time,[3] but only 2-3% actually stop permanently each year.[3]

The most common reasons smokers give for smoking are stress relief and enjoyment,[4] but the main reason is nicotine dependence. Nicotine acts in the midbrain, creating impulses to smoke in the face of stimuli associated with smoking.[5] Consequent changes in brain chemistry also produce "nicotine hunger" when a smoker goes without nicotine. A third mechanism underlying nicotine dependence is nicotine withdrawal: unpleasant mood and physical symptoms that occur on abstinence and are relieved by smoking.[6,7] Nicotine dependence is the main reason that most unassisted quit attempts fail within a week.[8] We give evidence based recommendations and new treatment options for healthcare professionals to increase the success rate of these attempts. Most evidence for treatment comes from randomised controlled trials summarised in the Cochrane reviews for tobacco dependence.

Why should healthcare professionals help patients stop smoking?

Just over half of all smokers manage to stop before they die,[9] but in many cases it is too late. The British doctors study found that every year that smoking cessation is postponed after the age of 40 reduces life expectancy by three months.[10] It is vital, therefore, to encourage and support patients to stop as young as possible. Even with help, most attempts to stop eventually result in a return to smoking, and helping smokers stop can feel futile. But the evidence clearly shows that what doctors say and do about smoking in consultations makes a huge difference to their patients—it is a matter of life and death for many.

How should I broach the subject of smoking?

US and UK guidelines propose the "five A's": ask about smoking, advise patients to stop, assess motivation to stop and need for pharmacotherapy, assist with prescription or referral to a behavioural support programme, and arrange follow-up. This does not necessarily fit, though, with what doctors see as their role and as what patients need.[11] A simpler and more patient centred approach is to ask the patient about their smoking, acknowledging that they may have tried to stop many times in the past, and discuss the options that exist to support a quit attempt (fig 1). When faced with an offer of support, many patients (even those who were not thinking about making an immediate quit attempt) will respond positively.[12,13] It is crucial to offer help, not simply to instruct, nag, or even just advise patients to do something which most already know they should do and have tried to do many times.

Nicotine replacement therapy

A meta-analysis of more than 100 randomised controlled trials shows that all forms of nicotine replacement therapy are roughly equally effective in aiding long term cessation (odds ratio 1.77, 95% confidence interval 1.66 to 1.88), but the data are insufficient to exclude worthwhile differences in efficacy between some forms, particularly the nasal spray, and the others.[14] One option for patients who have previously used nicotine replacement but still failed to stop is to give the patch as well as another form of nicotine replacement, such as gum or lozenge. The patch provides background nicotine replacement and the gum deals with "breakthrough" urges. A meta-analysis of six trials shows that patch plus an acute form of nicotine replacement increases the likelihood of long term success (1.42, 1.14 to 1.76).[14]

A meta-analysis of seven trials showed that nicotine gum or inhaler used for 6-24 months by smokers aiming to reduce consumption but not stop led to greater carbon monoxide-confirmed reduction of smoke intake than placebo nicotine replacement.[15] We have no good evidence on whether sustained reduction assisted by nicotine replacement benefits health, though cohort studies of smokers who reduce consumption without nicotine replacement found no reduction in the incidence of smoking related disease

Methods

This review is based on a search of the Cochrane Library for Tobacco Addiction, reviews commissioned by the National Institute for Health and Clinical Excellence, and other papers in the authors' personal libraries.

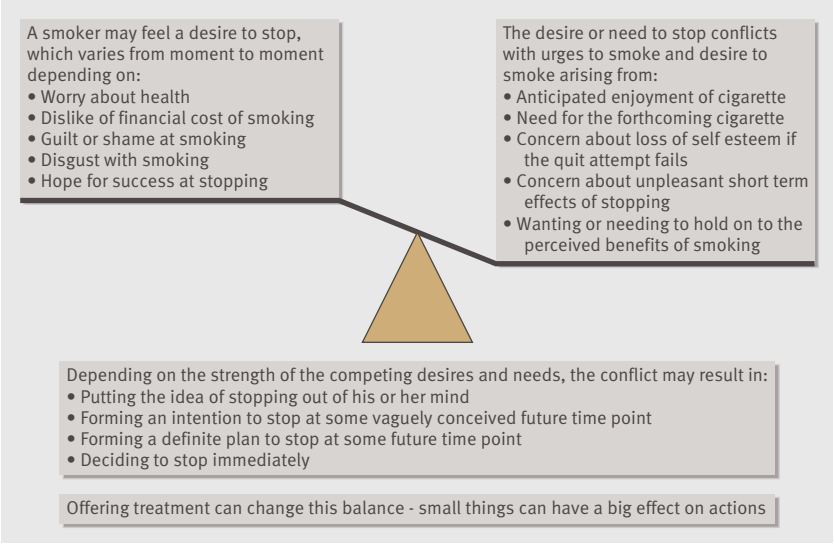

Fig 1 | **Motivational tension: inside the mind of a smoker—the desire to stop versus the need to smoke (adapted from West and Shiffman[44])**

and death.[16 17] However, the meta-analysis also found a relative risk 2.06 (1.34 to 3.15) in the likelihood of long term abstinence, and modelling showed it is cost effective.[15] Nicotine replacement therapy is licensed in the UK and elsewhere for reducing smoking before stopping.

Antidepressants

A systematic review showed that people who stop smoking experience depressed mood as a withdrawal symptom, so it is logical to use antidepressants as cessation treatment.[6 7] One antidepressant, bupropion, is licensed for use as a cessation aid and a meta-analysis of 31 trials shows that it approximately doubles cessation rates (odds ratio 1.94, 1.72 to 2.19).[18] Nortriptyline is not licensed for smoking cessation, but a meta-analysis of six trials shows that it is effective (2.34, 1.61 to 3.41).[18] Selective serotonin reuptake inhibitors are the first choice antidepressant in the UK and reduce withdrawal symptoms in smokers, but a meta-analysis shows they do not increase abstinence rates alone or in combination with nicotine replacement.[18] There is insufficient and conflicting evidence from meta-analyses on whether bupropion and nortriptyline when added to nicotine replacement have increased efficacy.[18]

A new drug

Varenicline is a newly licensed partial agonist acting on the $\alpha_4\beta_2$ nicotinic receptor. A meta-analysis of randomised controlled trials sponsored by the company that makes it showed that varenicline is both more effective than placebo (odds ratio 3.22, 2.43 to 4.27) and bupropion.[19] A meta-analysis comparing effect sizes in nicotine replacement studies with those in varenicline studies concluded that varenicline is more effective than nicotine replacement,[20] but definitive evidence will come from direct comparisons. The studies of varenicline all included frequent brief (<10 minutes) support. The pharmacology of varenicline and evidence from studies of other drugs for cessation[14 18] mean varenicline would probably work without frequent behavioural support, and we suggest using it if support is unavailable or unwanted. However, use of varenicline with behavioural support is much preferred.[21]

Choosing treatment

Bupropion, nicotine replacement therapy, and varenicline are reasonable first line choices, with nortriptyline used second line. Smokers have usually stopped several times and most have tried one or more drugs. Using a drug that previously suppressed urges to smoke is sensible. Using drugs that caused marked side effects, did not work well, or that the patient just does not believe in is inadvisable. Presenting the pros and cons and allowing a choice is the ideal.

How do I treat special groups?

Light and social smokers

Almost all trials of medication for smoking cessation include only moderate or heavier smokers, but a quarter of UK smokers smoke fewer than 10 cigarettes a day, and 12% of all smokers do not smoke daily.[2 3] Judging intake from cigarettes per day is unreliable—differences in puff frequency, depth, and volume play a bigger role in intake than number of cigarettes.[22] A review of observational studies showed that most light and social smokers experience urges to smoke and failure of attempts to stop,[23] so we believe it is reasonable to offer treatment. A subgroup analysis of one randomised controlled trial of a nicotine lozenge showed that the lozenge approximately doubled cessation rates and was as effective in light smokers as in heavier smokers.[24] A further randomised controlled trial enrolling only light smokers showed that nicotine gum was slightly but not significantly more effective than placebo,[25] but the odds ratio was consistent with the meta-analysis of all trials of nicotine replacement therapy.[14] Use any short acting form of nicotine replacement, and advise use as often as necessary to reduce urges to smoke and withdrawal symptoms.

Pregnant women

Programmes to help pregnant women stop smoking reduce the incidence of low birth weight and preterm delivery, a meta-analysis of randomised trials has shown.[26] Most women who stop in pregnancy in the UK do so without help from a health professional, and UK figures show nearly half of all women who smoke before pregnancy suspend their smoking during pregnancy.[27] Nicotine is a vasoconstrictor, and there is theoretical concern but no direct evidence that it could harm the fetus. Three trials of nicotine replacement in pregnant women showed no evidence of harm and no increase in cessation in pregnancy.[28] However, the trials were too small to exclude benefit of the size seen in non-pregnant women. The speed of

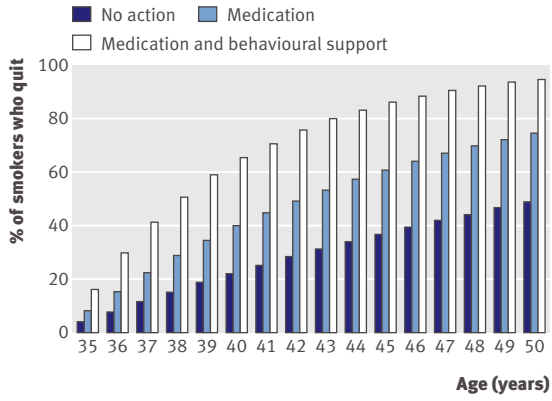

Fig 2 | **Effects on smoking prevalence of strategies to help smokers if all smokers made one attempt per year to stop, starting at age 35**

nicotine metabolism increases by about 30% in pregnant women,[29] which could impair the effectiveness of nicotine replacement. A reasonable position is to discuss use of nicotine replacement, ideally within the context of specialist support, and to use acute forms such as gum or inhaler or take nicotine patches off at night to minimise exposure to the fetus. The same advice would apply to women who are breast feeding.

Adolescents

For adolescents aged 12 years and over, nicotine replacement is the only drug treatment licensed in the UK. Systematic reviews of randomised controlled trials of nicotine replacement in adolescents have not found evidence of efficacy,[28 30] but interpretation is hampered by poor adherence and small sample sizes. Therefore, if adolescents report failed attempts to stop, urges to smoke, and withdrawal symptoms, treatment with nicotine replacement is reasonable. Most head teachers in the UK will not accept young people using oral nicotine replacement products, so patches are often preferred.

Is behavioural support or counselling effective?

If healthcare professionals specially trained to provide behavioural support are available, doctors should refer patients. Research with smoking cessation drugs has typically been tested in this context. Behavioural support itself improves success rates: meta-analyses of

Prescribing smoking cessation drugs

Bupropion

Start bupropion while smoking and quit smoking in the second week. Use 150 mg per day for six days, then 150 mg twice a day for eight weeks. Take the evening dose early to avoid wakefulness. Causes 1 in 1000 to have a seizure, which needs discussion with patient.

Nortriptyline

Start nortriptyline while smoking, increasing the dose from 25 mg to 75 mg. Quit while taking the maximum dose and continue for 8-12 weeks, tapering down at the end. Reassure patients that side effects abate in time and fewer than 1 in 10 patients stop because of side effects.

Varenicline

Start varenicline while smoking. Comes in a starter pack escalating the dose from 0.5 mg daily to 1 mg twice a day by the second week. Quit in the second week. Continue for 12 weeks. Most people experience mild to moderate nausea, which can be reduced by taking varenicline after food and with water. Take the evening dose early to avoid wakefulness. Side effects abate with time and fewer than 1 in 10 patients stop the drug.

Nicotine replacement patches

Put the patch on smooth, hairless skin. Avoid using the same site for all patches. Put the 24 hour patches on the night of the last cigarette. If it slides off, tape it on with micropore. Skin reactions are common: check site rotation, use an emollient or hydrocortisone cream, consider changing the make of patch or switching to another form of nicotine replacement.

A patient's story

My name is David, I am a smoker. I started smoking 53 years ago, at age 11. At the time there were no health warnings. My father tried to stop me, owing to my age, but if anything it made me more determined to smoke. The first time I was advised to stop smoking on health grounds was 1979, when I was 36 years old, and that was at my army discharge medical.

Then the warnings started to appear in the press, with the medical profession seeming to blame everything from in-growing toenails to heart disease on smoking. At the time I had few health problems. Then 18 years ago I had a minor operation at a private hospital and afterwards the surgeon told me I was wasting my money unless I stopped smoking, so I made the first attempt at stopping by undergoing a session of hypnotism. Alas it didn't work. The next attempt was a few years later when I tried acupuncture, which seemed to be working until the stud fell out. A year later I tried acupuncture again, but a lack of determination meant I was smoking again within three weeks.

The following years produced health problems, ranging from peripheral vascular disease to irregular heartbeat; I also had cancer of the bladder, all smoking related. Needless to say a number of consultants and my GP advised me to stop smoking, so I attended a couple of smoking cessation groups, tried patches, gum, and willpower, only for all to fail.

In March 2007 I had a chest infection, and after hearing my symptoms my GP sent me to my local hospital for further examination. This resulted in two days trying to convince a registrar through a junior house officer that I had a chest infection and not a heart attack. A succession of ECGs and a treadmill session convinced her it was not a heart problem but a chest problem, and I was discharged with a letter but no treatment.

The meeting with my GP gave me the chance to ask about a new drug that I had read about in the papers. My doctor said that to get the drug I had to attend a smoking cessation group. I enrolled along with my wife and was prescribed the drug, and as a result my wife and I smoked our last cigarette on 1 April 2007, appropriately All Fools day.

Now nearly nine weeks later I am almost ready to call myself a non-smoker. It hasn't been easy; there have been times when I have been dying for a nicotine intake, but thanks to the support of my wife, the no smoking group, and the medication I haven't smoked for almost nine weeks and I feel wonderful.

SUMMARY POINTS

Stopping smoking before the age of 40 is crucial to improve health—beyond 40, people lose three months of life expectancy for every further year smoking

The most important factor leading to failure of attempts to stop is nicotine dependence

Nicotine dependence is most effectively treated with a combination of drugs and specialist behavioural support, such as provided by the NHS Stop Smoking Service

Varenicline, bupropion, nortriptyline, and nicotine replacement are all effective

Relapse during or after treatment is common, and treatment is usually needed several times

trials of support versus brief advice found odds ratios of 1.56 (1.32 to 1.84) for individual support and 2.04 (1.60 to2.60) for group support.[31 32] Regular support on the telephone is also effective. A meta-analysis of 10 trials of telephone support for people stopping smoking gave an odds ratio of 1.64 (1.41 to 1.92).[33]

There is insufficient information to know which elements of behavioural support are effective or whether one approach, such as motivational interviewing or cognitive behavioural therapy, is more effective than another. There is some evidence to suggest that group support may be more effective in general than one-to-one support,[34] and that it should involve multiple sessions.[35] There is also evidence that such sessions can be effective even if conducted over the telephone. A meta-analysis of 10 trials of telephone support for people stopping smoking gave an odds ratio of 1.64 (1.41 to 1.92).[33] On the other hand, studies assessing the effectiveness of behavioural support provided by healthcare professionals in primary care with limited training who are providing the service in conjunction with other duties have not shown evidence of efficacy beyond brief advice.[35-37]

Of the many web based support packages available on the internet, only two have been evaluated in randomised controlled trials.[38 39] These trials of tailored programmes enrolled smokers who were using nicotine replacement. Both trials showed significant benefits 10-12 weeks after the quit date.

Other strategies

There are few adequate studies examining complementary therapies in smoking cessation. Meta-analysis of trials of acupuncture and hypnotherapy showed no benefit but could not exclude small effects.[40 41]

A systematic review found no randomised controlled trials of the Allen Carr Easyway method.[42] Two cohort studies with rigorous outcome assessments showed abstinence rates similar to those expected from behavioural support alone.[42] The method discourages use of medications such as nicotine replacement therapy and thus runs counter to NICE guidance about treatment for nicotine dependence.

How do I help my patients avoid relapse?

A systematic review of randomised controlled trials concluded that there are currently no effective psychological interventions to prevent relapse after the initial few weeks of abstinence. Extending use of bupropion for a year delays but does not prevent relapse, but for some smokers, extended use of nicotine replacement might be effective.[43] One randomised trial showed that giving an additional 12 week course of varenicline to people who were abstinent at the end of the first 12 week course reduced relapse to smoking by 30% up to six months after the end of all treatment, compared with placebo.[19]

Conclusions

Nicotine dependence is a life threatening disorder, most of the complications of which can be avoided if it is overcome before the age of 40. Now that there is strong evidence for the efficacy of several medications and specialist behavioural support, all doctors should ensure that they know about these treatment options and regularly offer these to their patients, as this can make a real difference (fig 2). At least half of all cessation attempts in the UK are made without any treatment, and only one in 20 are made with optimum treatment. Clinicians have a key role in improving on this.

Competing interests: PA receives a personal income from the UK National Health Service and the University of Birmingham. He has received research funds from the NHS, and various research charities and has received hospitality from various pharmaceutical companies, including those making products for smoking cessation. He has received free drugs for distribution to trial participants from King Pharmaceuticals and Novartis Consumer Health Care and has received consultancy income to him and his institution from Xenova Biotechnology and Pfizer for advice on smoking cessation. RW undertakes research and consultancy for, and has received hospitality and travel funds

Information resources for patients

- www.gosmokefree.co.uk—free UK NHS website with advice on stopping smoking and using medication, an email/text support programme that requires registration, and telephone helpline information
- www.quit.org—free information and telephone and other support for stopping smoking
- Drug companies offer free support programmes to people using their product. They give advice on how to stop and how to manage the medication and side-effects.
- Registration is required:
- www.click2quit.co.uk (Niquitin; GlaxoSmithKline)—internet support
- www.nicorette.co.uk (Nicorette; Pharmacia)—internet support
- www.zybannet.com (Zyban; GlaxoSmithKline)—telephone support from nurses.
- https://www.myliferewards.co.uk/PAGES/PxWelcome.aspx (Champix; Pfizer)—internet support

Ongoing research and unanswered questions

- Research is ongoing into other drugs to help in stopping smoking and more effective use of existing drugs
- Research is needed into why more smokers do not try to quit, why they often do not use the treatments that are available, and how best to reduce the risk of relapse after initial treatment
- Research is needed into how smokers who may never be able to overcome nicotine dependence could reduce their harm by switching to forms of nicotine intake that do not involve inhaling tobacco smoke

Additional educational resources

- Tips for doctors on how to help patients stop smoking are available at http://pcpoh.bham.ac.uk/primarycare/research/stopsmoking.htm
- The English national smoking cessation guidelines (1998) are available free and without registering at http://thorax.bmj.com/cgi/content/full/53/suppl_5/S1, with update (2000) at http://thorax.bmj.com/cgi/content/full/55/12/987
- www.treattobacco.net is an evidence based resource library of reviews, guidelines, slide shows, and other material summarising evidence about smoking cessation in several languages. Free and unregistered access
- www.dphpc.ox.ac.uk/cochrane_tobacco, the homepage of the Cochrane Tobacco Addiction Review Group, lists the reviews and invites new reviewers with ideas. Access to the Cochrane Library varies by country. In the UK, free unregistered access for all is available at www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME
- www.ash.org.uk is the website of a tobacco control campaign group with resources for health professionals to get involved in advocacy and information about giving up smoking.

from, manufacturers of smoking cessation drugs and has a share of a patent for a novel nicotine delivery device.

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