WeMeReC
Welsh Medicines Resource Centre
Canolfan Adnoddau Moddion Cymru

Bulletin
"Independent prescribing information for NHS Wales"

Smoking cessation

Few interventions are associated with greater health gains than those that support smoking cessation. They are a cost-effective means of preventing ill health and premature death from a wide range of diseases.[1]

The effects of tobacco smoking impact both the individuals who smoke and those people exposed to second-hand smoke. In pregnancy, smoking poses specific health risks to both mother and baby. Government policy to combat smoking aims to prevent people, especially children, from starting to smoke; to raise awareness of the dangers associated with passive smoking; and to help smokers to stop, particularly pregnant women and those in lower socio-economic groups. Smoking is the primary reason for the gap in healthy life expectancy between the rich and poor.[1]

Stop smoking messages have been the subject of sustained public health campaigns and numerous guidelines produced by the National Institute for Health and Clinical Excellence (NICE) (see page 2 of the Supplement). A ban on smoking in enclosed public spaces came into force in Wales in April 2007. In the Welsh Health Survey of that year, 24% of adults reported that they were smokers and 29% reported they were ex-smokers.[2]

Effective interventions

The serious harm associated with smoking tobacco is caused by the tar, gases (oxidant gases and carbon monoxide), and other substances produced, but it is an addiction to nicotine that drives the desire to smoke. Overcoming nicotine addiction is the key to smoking cessation. In addition to the use of self-help materials, effective interventions that can be provided include:

- brief interventions (level 1)
- intensive behavioural support: individual counselling (level 2) and group therapy (level 3)
- pharmacotherapy (in addition to advice and support – some level of support for behavioural change was offered in all clinical trials).[1]

Health professionals across all specialties should be prepared to offer advice about quitting to any person who smokes. Simple advice can have a significant effect on smoking cessation.[3] The 3As approach (adapted from the 5As framework)[4] for providing advice is advocated.[5]

1. **Ask**
   Identify and document smoking status.
2. **Advise**
   Provide a clear, positive message to stop.
3. **Act**
   Assess interest in and barriers to stopping; the level of nicotine dependence, and smoking history, e.g. previous quit attempts.
   Assist by offering support, including higher level behavioural interventions and pharmacotherapy.
   Arrange follow-up and enlist others' support.

Recognising the time constraints for many consultations, at which smoking may be only one aspect of discussion, a "very brief" intervention would aim to provide confidence-boosting advice and to direct individuals to NHS stop smoking services. A "brief" but more comprehensive intervention would be expected to last 5 to 10 minutes. Anyone providing advice about smoking cessation should be aware that success rates are improved when more intensive support is provided.[1,3] Points are awarded towards the Quality and Outcomes Framework (of the General Medical Services contract) for recording the smoking status of patients and for offering advice on the benefits of stopping smoking and/or referring to more intensive support services.[6] Patients reluctant or unable to stop smoking should be offered drug treatment and/or additional support by suitably trained practitioners.

Stop Smoking Wales 0800 085 2219

An NHS service that provides support for smoking cessation. (Launched in November 2007; formerly the All Wales Smoking Cessation Service).

www.stopsmokingwales.com

Behavioural interventions, other than referral to NHS stop smoking services (and hospital-based services), that are available to support cessation include telephone counselling via "quitlines", and sessions based in the work place.[1] Further ways of providing support remotely, such as via the internet and mobile phones, are being explored.[6] Incentivised options are also the subject of clinical studies.[6]

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Regardless of the type of support provided, it is still very difficult to stop smoking. The improvements achieved with behavioural interventions on six month abstinence rates are relatively small. Typically, success rates of 2-3% for unassisted attempts[7] are raised to no more than 10%.[3,8] Using the medicines available for smoking cessation (see below) alongside support for behavioural change can further improve quit rates, raising them to above 20% in some cases.[3,7,8]

Individuals trying to stop smoking should be advised that relapse is common. Several attempts may be required for long-term success. At present there is no particular intervention that can be recommended for preventing relapse in smokers who have quit for a short period.[6] Current practice around relapse prevention is the focus of ongoing research. There is no evidence of any long-term benefit from simply reducing smoking in an individual.[6]

Pharmacotherapy

Pharmacotherapy for smoking cessation aims to control and reduce addiction to nicotine. The therapies used are: nicotine replacement therapy (NRT) (available in various formulations on prescription, over the counter in pharmacies, and on general sale), and varenicline and bupropion (both available as tablets on prescription). These therapies should not be used in combination with each other.[1] Any recommendation or prescription for these medicines should be offered alongside advice, and encouragement to help an individual to quit smoking.

In selecting a medicine to support smoking cessation, no particular agent should be favoured – the agreed choice should be the one considered most likely to succeed.[1] People trained in supporting smoking cessation can provide patients with information about these medicines; however, were applicable, clinicians need to assess patients appropriately before prescribing therapy.

Factors to take into account when deciding which treatment/s to use and in which order include: whether a referral to Stop Smoking Wales has been made and the availability of appropriate counselling or support; contraindications and potential adverse effects; a patient's personal preferences and previous experience of smoking cessation aids; the likelihood that they will follow the course of treatment; and their level of dependence. The most widely used measure of nicotine dependence is the Fagerström test; however, of the six component questions (see page 2 of the Supplement), the two considered most indicative relate to the number of cigarettes smoked per day, and how soon after waking the person smokes.[5]

Medication should normally be part of abstinent-contingent treatment, in which the smoker commits to stop on or before a particular date.[1] The quantity supplied should be sufficient to last until two weeks after the "target stop date". Typically, this will be two weeks of NRT, and three to four weeks of varenicline or bupropion (because of different modes of action). Subsequent prescriptions should be given only to people who have demonstrated, on re-assessment (e.g. by CO testing),[5] that their quit attempt is continuing.[1]

NRT

The delivery of nicotine from replacement therapies is at a lower dose and at a slower rate than that with smoking. Because of the risks associated with tobacco smoking, **NRT can be considered for all people attempting to stop**, including pregnant and breastfeeding women, and young people aged from 12 to 17 (in whom other treatments are not licensed).[1] It can also be considered for patients with underlying cardiovascular or respiratory disease.[1,9] The number needed to treat (NNT) for NRT, calculated from placebo-controlled trials of six months or longer, is 16 (95% CI 14-17).[8]

Adverse effects associated with use of NRT are not generally serious, and are predictably similar to some of those caused by smoking. They usually improve with time, but should be reported if they continue or become troublesome. Effects include nausea, indigestion, dizziness, headache, cold and flu-like symptoms, dry mouth, rash and, less frequently, palpitations. Specific effects have been observed with different formulations, e.g. sleep disturbance and skin reactions with the use of 24 hour patches, and throat irritation with oral agents.

NRT is considered a safer alternative to tobacco use in virtually all circumstances, however, the potential for adverse effects is noted in patients with:

- diabetes – potential alterations in blood-sugar concentrations necessitate closer monitoring.[9]
- severe renal impairment, and moderate to severe hepatic impairment – a reduction in nicotine clearance can increase the risk of adverse events.[9]
- hospitalisation for recent MI, stroke, severe dysrythmia and/or unstable disease – use NRT under medical supervision when non-pharmacological methods fail.[9]

Any impact of NRT on the effect of other medicines is most likely to be caused indirectly by smoking cessation rather than the product itself. For example, the metabolism of theophylline is increased with tobacco smoking and so may alter on cessation.

There are many different **NRT preparations** available in varying strengths. These include: patches, gums, lozenges, a sublingual tablet, a nasal spray, and an inhalator. (See the accompanying supplement for information about the products and their use.)

The range of NRT formulations offers a variety of approaches for tailoring therapy. The oral and nasal preparations provide fast release of nicotine whereas patches provide slower, sustained-release delivery. For this reason, intermittently-dosed products are preferred to patches for pregnant or breastfeeding patients. If patches are used, these women should be advised to remove them before going to bed and, where applicable, to avoid using them at least one hour before breastfeeding.[1]

NRT should be used regularly at first, and at an adequate dose. People who show a high level of dependence on nicotine and/or are finding their NRT treatment insufficient may require higher doses. For those in whom single forms of NRT are inadequate, a combination of nicotine patches and another form of NRT can be considered.[1] The quantity of the second product prescribed should reflect "prn" use.[10]

Unless otherwise stated, treatment is recommended for two to three months for the best chance of success; it can then be withdrawn gradually. If continued for longer and abstinence is not achieved after six to nine months, treatment should be reviewed. In adolescents, therapy should be reviewed by a doctor, pharmacist, or nurse when continued beyond 12 weeks.[9]

Hospitalised and pre-operative patients

Smokers have an increased risk of intra-operative and postoperative complications. These vary with disease and type of surgery, but include pulmonary and circulatory events, infections, reduced bone fusion, and impaired wound healing.[11] Evidence relating to smoking cessation and the timing of interventions is limited. However, there is some support for benefit (both short- and long-term) from clinical trials of intensive interventions, including individual counselling and NRT, when initiated at least four weeks before surgery.[11] In all but exceptional circumstances, patients admitted to hospital who use tobacco (in any form) should be offered advice about stopping and, if appropriate, NRT to help them to abstain temporarily. These patients should also be offered a referral for cessation support and, where acceptable, follow-up appointments should be booked before discharge.[1]

Nicotine-assisted reduction to stop (NARS)

Using NRT to help reduce the frequency of smoking as a prelude to quitting ("cutting down to quit") has been studied with conflicting results. A recent systematic review suggests that such use can improve abstinence rates by approximately 3%; however, the importance of the behavioural support provided in the relevant trials is unknown.[12] Supplying NRT for this purpose is, therefore, recommended by NICE only in research programmes for individuals who have repeatedly tried and failed to stop smoking or who are adamant they do not want to quit abruptly and would otherwise not attempt to stop.[1] Adolescents should consult a health professional about using NRT this way.

Varenicline

Varenicline (*Champix*®)▼ is a nicotinic receptor ($\alpha_4\beta_2$) partial agonist. Studies of varenicline taken for 12 weeks have been conducted in adults who smoked at least 10 cigarettes per day. The NNT for six months' abstinence with varenicline, calculated from placebo-controlled trials, is 7 (95% CI 6-10).[8] Varenicline improves continuous abstinence rates at one year, and is superior to bupropion.[13] One study has shown a small additional benefit when therapy was extended to 24 weeks (but only after success at 12 weeks).[14] Comparisons with NRT are limited to one open-label study using an NRT patch: significant improvements in abstinence rates were only observed at the end of the treatment period and not at later follow-up points.[15]

Varenicline should be started one to two weeks before the "target stop date" at 500 micrograms daily for three days, then 500 micrograms twice daily for four days, then 1 mg twice daily for 11 weeks (reduced to 500 micrograms twice daily if not tolerated). The 12 week course can be repeated in abstinent individuals to reduce the risk of relapse. The lower dose of varenicline should be used in patients with severe renal impairment. The lower dose is also recommended in patients with moderate impairment who experience intolerable adverse events. Varenicline is still subject to intensive post-marketing surveillance (including Yellow Card reporting). The most frequent adverse event (reported in about a third of patients) is nausea. It is generally mild to moderate in severity and occurs early in treatment. Headache is also commonly reported, as are abnormal dreams, and insomnia.

Depression, suicidal ideation and behaviour, and suicide attempts have been reported with varenicline. Clinicians should be aware of the possible emergence of such symptoms in patients attempting to stop smoking. Varenicline should be stopped immediately if agitation, depressed mood, or changes in behaviour are observed. Varenicline has not been studied in patients with psychiatric illness and care should be taken in patients with a history of such illness.

Stopping varenicline is associated with an increase in irritability, urge to smoke, depression, and/or insomnia in up to 3% of patients. To prevent this, and relapse in the period immediately following treatment, tapering the dose should be considered.

Bupropion

The effects of nicotine on neurotransmitters and links with depression have prompted research into the use of antidepressants for smoking cessation. Bupropion (*Zyban*®) is an atypical antidepressant with dopaminergic and noradrenergic effects that can aid smoking cessation.

Studies of bupropion taken for seven to nine weeks have been conducted in adults who smoked at least 15 cigarettes per day and were motivated to stop. Subjects had no depression. The NNT for six months' abstinence with bupropion, calculated from placebo-controlled trials of six months or longer, is 11 (95% CI 9-12).[8] Bupropion improved abstinence rates when compared with an NRT patch.[13]

Bupropion should be started one to two weeks before the "target stop date" at 150 mg daily for six days then 150 mg twice daily, with a minimum of eight hours between doses. Treatment can be continued for up to nine weeks but should be discontinued if abstinence is not achieved at seven weeks. It should be used with caution in patients with hepatic impairment or renal insufficiency and in the elderly. The lower 150 mg daily dose is recommended in these groups of patients.

Bupropion is associated with a dose-related risk of seizures: the incidence with use of 150 mg twice daily is approximately 1 in 1000. Bupropion is contraindicated in patients with: a current seizure disorder or a history of or predisposition to seizures, CNS tumour, withdrawal from alcohol or a medicine associated with seizures on withdrawal (e.g. benzodiazepines); an eating disorder; severe hepatic cirrhosis; a history of bipolar disorder, or use of MAOIs.

Bupropion commonly causes insomnia. This can be reduced by avoiding bedtime doses (provided there is at least eight hours between doses). Hypertension (in some cases severe) has been reported in patients taking bupropion. A baseline blood pressure measurement should be obtained at the start of treatment and monitoring undertaken.

Use of bupropion has been associated with reports of depression, including suicide attempts. Depressed mood may be a symptom of nicotine withdrawal; clinicians should be aware of the possible emergence of these symptoms with a smoking cessation attempt.

Because bupropion inhibits the cytochrome P450 CYP2D6 enzyme pathway, certain antidepressants, antipsycotics, beta-blockers, and anti-arrythmics should be prescribed at the lower end of the recommended dosage ranges in patients taking bupropion. If bupropion is to be started in a patient already taking such a medicine, the need to reduce the dose of that medicine should be considered. The expected benefits must be weighed against potential risks.

Furthermore, as bupropion is metabolised by CYP2B6, co-administering drugs that affect this enzyme (e.g. substrates such as cyclophosphamide and inhibitors such as orphenadrine or clopidogrel) may result in altered levels of bupropion and its metabolites. The clinical effect of this is not known but monitoring is advised. Because bupropion is extensively metabolised, medicines that inhibit metabolism (e.g. valproate) or those that induce metabolism (e.g. carbamazepine, phenytoin) may alter its clinical effects.

The Summaries of Product Characteristics should be consulted for full prescribing information.

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