**An evidence-based guide to smoking cessation therapies**

**Faraz Siddiqui, Rumana Huque and Omara Dogar**

*Faraz Siddiqui is a Research Instructor at the Department of Medicine, The Aga Khan University, Pakistan. Rumana Huque is Executive Director at ARK Foundation, Bangladesh and Omara Dogar is a Research Fellow at the Department of Health Sciences, University of York, UK.*

*Email: omara.dogar@york.ac.uk*

Abstract

Despite a general decline in smoking rates in the UK, smoking prevalence remains high among young adults, pregnant women and those from socio-economically disadvantaged backgrounds. These three groups are also more likely to benefit from targeted smoking cessation interventions. Clinical contact between health professionals and patients who smoke creates an opportunity for offering cessation interventions and to reduce smoking-related harm. This article summarises evidence, based on high quality systematic reviews, on smoking cessation interventions that could be offered by health professionals coming in to contact with patients who smoke. The evidence presented here suggests that brief advice by a health professional is beneficial in achieving smoking cessation and so is intensive behavioural support alone or in combination with pharmacotherapies (nicotine replacement therapies (NRTs), bupropion and varenicline). Pharmacotherapies are also effective individually in promoting smoking cessation; a combination of NRTs (oral or skin patch) can be particularly helpful in promoting cessation among highly dependent smokers. Pharmacotherapies in combination with behavioural support delivered in health care settings are more effective than when used alone and delivered in community settings, respectively.

I

n the 1970s, about 50% of the UK’s population smoked tobacco in one form or another; the proportions dropped rapidly to one third by the 1990s and have since been declining at a slower rate (Office for National Statistics, 2009). Between 2001 and 2007, smoking rates have reduced from 28.4% to 22.4% (Simpson et al, 2010). However, more than twice as many people in socio-economically disadvantaged areas smoke compared to those in affluent areas (33.8% vs 14.1%) (Simpson et al, 2010), making it one of the principal causes of the health divide between rich and poor (Wanless, 2004). Among men, more than half of the excess risk of premature mortality between social classes is secondary to tobacco smoking (Jarvis and Wardle, 1999). Among women, two thirds of deaths among those who smoke are due to smoking itself; losing at least 10 years of average lifespan (Pirie et al, 2013). On the other hand, if people quit before the age of 40, 90% of excess deaths due to smoking can be avoided; and if before the age of 30, 97% of excess deaths can be avoided (Pirie et al, 2013).

Smoking cessation

Given that smoking is the single most preventable cause of premature mortality (Department of Health, 1998; Department of Health, 2000; Raw et al, 1998), the UK government has introduced a range of initiatives in recent decades to reduce smoking prevalence. Between 2001 and 2007, access to specialist advice on smoking cessation increased from 43.6% to 84.0% and referrals from general practices to Stop Smoking Services increased from 1.0% to 6.6%, leading to a significant reduction in the number of smokers (Simpson et al, 2010). However, comparatively higher rates of smoking are still found among younger adults, pregnant women and those who are the most socioeconomically disadvantaged, including ethnic minorities (Simpson et al, 2010; Owen et al, 1998). Nevertheless, if targeted appropriately, these groups are most likely to benefit from Stop Smoking Services. The highest quit rates in the UK were found among those from socio-economically deprived areas (7.2%) and young adults (16–25 years: 7.1%) (Simpson et al, 2010). Around 45% of women tend to stop smoking either just before or during their pregnancy (Woodby et al, 1999); however, only a third are able to maintain continuous abstinence after a year (Centers for Disease Control and Prevention (CDCP), 2002).

Smoking cessation by health care providers

The majority of smokers who wish to quit find it extremely difficult to give up on their own without proper professional support, leading them to several futile quit attempts (Fiore, 2000). Those attending Stop Smoking Services are four times more likely to give up their smoking habit successfully than those attempting to quit on their own (National Institute for Health and Care Excellence (NICE), 2008). Generally, 79–90% smokers are willing to quit (National Institutes of Health (NIH) State-of-the-Science Panel, 2006) and 70% of them visit a health professional seeking relevant support (Cherry et al, 2003). Nurses, being the largest group of health professionals and involved in the vast majority of clinical contacts, have an opportunity to influence the smoking behaviour of their patients and reduce smoking-related harm (Percival et al, 2003; Whyte and Kearney, 2003). A recent systematic review found a significantly profound effect of nurse-delivered interventions in increasing the likelihood of quitting among patients who smoked (RR 1.29, 95% CI 1.20-1.39) compared to control or usual care (Rice and Stead, 2013).

The NICE guidelines for health professionals recommend using a range of smoking cessation ‘interventions’ and activities, including pharmacological (nicotine replacement therapy (NRT), bupropion and varenicline) as well as non-pharmacological (behavioural therapies) options (NICE, 2008).

This article offers a practical, accessible and evidence-based guide on smoking cessation therapies for nurses providing health care in a variety of settings. It summarises evidence from a range of relevant Cochrane reviews on smoking cessation interventions, in line with the NICE recommendations (2008) and contemporary views on behavioural change theories and techniques (BCTs). *Table 1* summarises the evidence.

Defining quit

Smoking cessation experts have defined specific criteria as follows, referred to as the Russell standard, to confirm when a smoker is considered to have quitted (West, 2005):

A ‘self-reported 4-week quitter’ is a treated smoker assessed (face to face, by postal questionnaire or by telephone) 4 weeks after the assigned quit date who declares that s/he has not smoked even a single puff of a cigarette in the past 2 weeks

A ‘carbon-monoxide (CO) verified 4-week quitter’ is a self-reported 4-week quitter and his/her expired-air CO is assessed 4 weeks after the assigned quit date and found to be less than 10 ppm

A ‘52-week quitter’ is a treated smoker assessed (face to face, by postal questionnaire or by telephone) 52 weeks after the designated quit date and declares that s/he has not smoked more than 5 cigarettes in the past 50 weeks.

Smoking cessation therapies in health care practice

Brief interventions

Brief interventions by a health professional include opportunistic advice, discussion, negotiation or encouragement and, where necessary, referral to a specialist service, typically lasting less than 10 minutes (NICE, 2008).

Compared to no advice, brief advice by practitioners (physician or physician supported by other health care workers) to smokers increases the likelihood of successful quit attempts at six months (RR 1.66, 95% CI: 1.42–1.94). Assuming an unaided smoking cessation rate of 2-3%, brief advice can increase the cessation rate by a further 1-3% (Stead et al, 2013).

Behavioural support interventions/counselling (individual or group)

Behavioural support interventions are delivered through face-to-face consultations (‘individual behavioural therapy’) or consultations in groups (‘group behavioural therapy’) consisting of weekly appointments for the first 4 weeks of a quit attempt, where the smokers receive information, advice and encouragement and some form of behavioural change intervention (NICE, 2008). ‘Group behavioural therapy’, in addition to applying behavioural change techniques, offers an opportunity for social learning and mutual support (Stead and Lancaster, 2005). Telephone counselling and quit lines are also used to support those who are considering quitting, and those who have recently quitted (NICE, 2008).

Individual behavioural therapy

Individual behavioural therapy often takes the form of advice, discussion, encouragement and activities designed to help people stop smoking successfully. These activities are designed to change targeted behavioural patterns, involving three essential conditions: capability, opportunity and motivation—core to the framework of the ‘behavioural system’ (Michie et al, 2011b). The ‘active ingredients’ of behavioural support interventions are classified into four functions:

* Directly addressing motivation, e.g. by providing rewards dependent on abstinence
* Maximising self-regulatory capacity, e.g. facilitating barrier identification and problem solving
* Promoting adjuvant activities, e.g. advising on stop-smoking medication
* Supporting other behavioural change techniques (BCTs), e.g. building general rapport (Michie et al, 2011a).

In total, 43 such behavioural change techniques have been identified for this purpose (Michie et al, 2011a) and should form the core of behavioural support interventions delivered for smoking cessation.

Behavioural support interventions delivered via face-to-face sessions by a trained health care worker achieved higher success rates in quitting at 6 months (RR 1.39, 95% CI: 1.24–1.57) compared to brief interventions delivered by health workers other than nurses and doctors. The behavioural support interventions, typically involving intensive counselling for more than 10 minutes, included a review of the smoking history and their motivation to quit, identification of high-risk situations, and proposing problem-solving strategies to cope with such situations (Lancaster and Stead, 2005). On the other hand, when individual behavioural support interventions were compared to brief interventions, irrespective of who is delivering these, there was insufficient evidence to support any marginal benefit (five trials, RR 0.96, 95% CI: 0.74–1.25) (Lancaster and Stead, 2005).

Group behavioural therapy

Group therapies consist of information, advice and encouragement over several sessions. Such therapies are likely to double the chances of cessation among smokers compared to self-help materials alone (RR 1.98, 95% CI: 1.60–2.46) (Stead and Lancaster, 2005). However, there is limited evidence on whether adding group therapies to brief interventions received from health professionals produced any extra benefit (Stead and Lancaster, 2005).

There is also not enough evidence to suggest whether group behavioural therapies are more (or less) effective or cost-effective than individual behavioural therapies (Stead and Lancaster, 2005).

Nicotine replacement therapy

Among all tobacco ingredients, nicotine is the most addictive, but perhaps least harmful substance. Therefore, nicotine replacement therapy (NRT) is a highly attractive cessation tool, as it reduces motivation to smoke by countering the physiological and psychomotor effects of nicotine withdrawal, thus easing the transition to sustained abstinence (West and Shiffman, 2001). Commercially formulated NRTs are absorbed either through the skin in the form of transdermal patches or through oral mucosa in the form of chewing gum, nasal spray, inhalers and lozenges/tablets, all of which deliver nicotine more quickly than patches but less quickly than cigarettes.

All commercially available forms of NRT increase the likelihood of smoking cessation by about 50–70% (RR 1.60, 95% CI: 1.53–1.68) compared to placebo or non-NRT controls (Stead et al, 2012). The relative risks of smoking cessation for various forms of NRT are: nicotine gum 1.49 (95% CI: 1.40 – 1.60), nicotine skin patch 1.64 (95% CI: 1.52–1.78), nicotine inhaler 1.90 (95% CI: 1.36–2.67), tablets and lozenges 1.95 (95% CI: 1.61–2.36) and nicotine nasal spray 2.02 (95% CI: 1.49–2.73) independent of the duration of use, intensity of any additional behavioural support or the delivery settings (Stead et al, 2012).

Combinations of nicotine skin patches and oral NRTs can significantly increase the chances of successful cessation attempts among heavy smokers (RR 1.34, 95% CI: 1.18–1.51) compared to using a single type alone (Stead et al, 2012).

Initiating NRT use shortly before setting the quit date does not significantly increase the chances of successful cessation among smokers (RR 1.18, 95% CI: 0.98–1.51), compared to starting NRT on the quit date (Stead et al, 2012). Moreover, the evidence is limited on the usefulness of NRTs in increasing the chances of successful quitting among those who smoke less than 10–15 cigarettes in a day.

Skin patches of NRT are available in several different doses, and can deliver up to 44 mg of nicotine over a 16 or 24-hour period, with optimal results achieved for 25 mg patches (Stead et al, 2012). Application of NRT skin patches for extended durations does not suggest a difference in cessation rates, however both 16 vs 24 hour application methods are effective for smoking cessation when compared to a placebo. Nicotine lozenges and nicotine chewing gum are available in both 2 mg and 4 mg strengths. There is limited evidence on any remarkable difference between the various forms of NRT or its use beyond 8 weeks of therapy (Stead et al, 2012). Heavier smokers, highly dependent on nicotine, might benefit from a higher dose of nicotine gum (4 mg gum compared to 2 mg), but the evidence is weak in proposing the benefits of using higher doses of nicotine patch (Stead et al, 2012).

The use of NRT is considered relatively safe with minor adverse effects reported. These include skin sensitivity and irritation in patch users, which affects around 54% of users (Fiore et al, 1992), buccal mucosal irritation, hiccoughs, jaw pain and orodental problems from gum and tablets, and local irritation at the site of administration from nicotine inhalers and nasal sprays (Stead et al, 2012). There is lack of evidence to support that NRT increases the risk of cardiovascular events, cancers, stroke or reproductive/developmental effects (Lee and Fariss, 2016), however a significant association with heart palpitations and chest pain (RR 1.88 95% CI 1.37 - 2.57) has been observed with its use (Stead et al, 2012).

Other pharmacotherapies

Varenicline and bupropion are two popular forms of pharmacotherapies used to aid smoking cessation in practice. In addition, newer drugs like nortiptyline and cytisine have also been used recently. When smokers quit, they experience cravings to smoke and unpleasant mood changes due to the nicotine withdrawal. Varenicline is a nicotine receptor partial agonist that aims to reduce such symptoms. It counteracts the effects of nicotine on the neuronal acetylcholine receptors (nAChRs), based on the naturally occurring alkaloid compound cytisine (Papke and Heinemann, 1994; Slater et al, 2003). Nicotine withdrawal might precipitate depression, as nicotine appears to have anti-depressive properties. Bupropion (an anti-depressant) can substitute for this effect by influencing the neurotransmitters and receptors involved in nicotine addiction, thus aiding smokers in their efforts to quit (Benowitz and Peng, 2000; Kotlyar et al, 2001).

Nortiptyline (a tricyclic antidepressant) is believed to increase noradrenergic activity; it may be prescribed when first line treatments have been unsuccessful (Hughes et al, 2014).

Bupropion and nortriptyline both significantly increase the likelihood of smoking cessation (buproprion- RR 1.62, 95% CI: 1.49–1.76; nortriptyline- RR 2.03, 95 %CI: 1.48-2.78) compared to placebo (Hughes et al, 2014). Both the drugs are considered to be equally effective and of similar efficacy as NRT in achieving long term cessation, however their addition to NRT does not provide any additional benefit (Hughes et al, 2014).

Varenicline increases the chances of successful smoking cessation by more than two- to threefold (OR 2.88, 95% CI: 2.40–3.47) at six months relative to placebo (Cahill et al, 2013). Compared to a standard dosage, a reduced dosage is also effective (RR 1.25, 95% CI: 1.00-1.55) relative to the placebo for long-term smoking cessation, with reduced number and severity of side effects and achieving cessation rates roughly similar to NRT or bupropion (Cahill et al, 2016). When compared to bupropion, varenicline significantly increases the chances of successful smoking cessation (OR 1.59, 95% CI: 1.29-1.96) (Cahill et al, 2016). It is also more effective over single form of NRT (OR 1.57, 95% CI 1.29-1.91), but not more effective than combination NRT (OR 1.06, 95% CI 0.75-1.48) (Cahill et al, 2013). There is also limited evidence that varenicline might have a beneficial role in relapse prevention compared to placebo (RR 1.24, 95% CI 1.08–1.42) at 52 weeks (Cahill et al, 2016).

The adverse events with bupropion use include insomnia, dry mouth, nausea, and, rarely, seizures (1 in 1000) (Hughes et al, 2014). The adverse events reported with varenicline use mainly include mild to moderate levels of nausea. However, there is inconclusive evidence suggesting links with serious adverse events including depressed mood, agitation, suicidal thinking and cardiovascular problems (Cahill et al, 2016). Although, a  study from Thomas et al (2013) found that neither varenicline nor bupropion increased the risk of fatal or non-fatal self-harm, or increased the risk of depression treated with antidepressants compared with NRT alone.

The standard dosage of varenicline used in clinical trials is 1.0 mg twice a day (Cahill et al, 2016). The standard dosage of bupropion in practice is 150 mg once a day for 3-6 days, increased to 150 mg twice a day to be continued for 7 to 12 weeks, initiated a week before the quit date of the smoker (Hughes et al, 2014).

The use of cytisine is shown to have a beneficial effect in achieving smoking cessation compared to placebo (RR 3.98, 95% CI 2.07 - 7.87). Cytisine use also demonstrated benefit when compared to NRT (RR 1.43, 95% CI 1.13 - 1.80) with abstinence rates of 21.8% vs 15.3% at six months (Cahill et al, 2016). Adverse events with cytisine use include Gastro-Intestinal disorders, sleep disorders, nausea and vomiting; the rates for these adverse events are significantly higher than placebo (West et al, 2011) and NRT (Walker et al, 2015).

There is insufficient evidence to support the use of other antidepressive agents (Mono Amine Oxidase inhibitors, Selective Serotonin reuptake inhibitors, St. John's wort, venlafaxine, and dietary supplement S-Adenosyl-L-Methionine (SAMe) for smoking cessation (Hughes et al, 2014).

Electronic cigarettes

Electronic cigarettes (ECs) or electronic nicotine delivery systems (ENDs) are electronic devices that heat a liquid into an aerosol for inhalation. The liquid usually comprises propylene glycol and glycerol, with or without nicotine and flavours (Boyce et al, 2016). There is wide variation between different types of ECs; the more recent generations of ECs have a very similar nicotine delivery profile to combustible cigarettes.

There has been a steady growth in sales of ECs since it appeared on the market in 2006 (Boyce et al, 2016). ECs are considered a less harmful alternative to combustible cigarettes and promoted as a tool for harm reduction in the UK (Britton et al, 2016; McNeill et al, 2015). However, the role and impact of ECs remain a major public health debate (McNeill et al, 2015) as there is limited evidence on the long term health impact on active and passive use of e-cigarettes (Latif and Nair, 2016).

A recent Cochrane review showed that using EC containing nicotine increased the chances of stopping smoking in the long term compared to using an EC without nicotine (Boyce et al, 2016). Combined results from the two RCTs also suggest that use of a nicotine containing EC was associated with higher abstinence rates than placebo EC use (RR 2.29, 95%CI 1.05-4.96) (Boyce et al, 2016). However, authors could not determine if EC was better than a nicotine patch in helping people stop smoking, because the number of participants in the study was low. None of the studies found that smokers who used EC short- to mid-term (for two years or less) had an increased health risk compared to smokers who did not use ECs. The authors acknowledged that the quality of the evidence overall was low due to the small number of studies, although these studies were well conducted (Boyce et al, 2016).

Effective combinations

Behavioural support and pharmacotherapies individually aid smokers in successful attempts to stop smoking. Many guidelines recommend combining the two interventions to assist people in stopping smoking, but there are some combinations that are more effective than others, and some that work better in certain settings than in others.

A combination of behavioural support and pharmacotherapy can increase the chances of successful smoking cessation by 70–100% (RR 1.83, 95% CI 1.68–1.98) compared to controls receiving brief advice, usual care or less intensive behavioural support (Stead and Lancaster, 2016). Combination therapies demonstrate a greater benefit when delivered in health care settings (RR 1.97, 95% CI 1.79–2.18) than when used in community-based settings (RR 1.53, 95% CI 1.33–1.76) (Stead and Lancaster, 2016).

Using intensive behavioural support (face-to-face or via telephone) as an adjunct to pharmacotherapy increases the chances of successful smoking cessation by about 10-40% (face-to-face RR 1.12, 95% CI 1.04–1.20; via telephone RR 1.28, 95% CI 1.17–1.41) relative to controls using pharmacotherapy alone (Stead and Lancaster, 2015). Moreover, increasing the intensity of behavioural support in people attempting to stop smoking with pharmacotherapy increases the chances of successful smoking cessation by another 10-25% (RR 1.17, 95% CI 1.11–1.24) relative to less intensive behavioural support. However, there is insufficient evidence to support any beneficial effect of behavioural support when added to nortriptylin or varenicline (Stead and Lancaster, 2015).

Smoking in pregnancy

The addition of NRT to behavioural support may be an effective strategy to promote smoking cessation in pregnant women (RR 1.41, 95% CI 1.03 - 1.93), however, the interpretation should be made with caution, as the effect is lower in placebo RCTs (RR 1.28, 95% CI 0.99 - 1.66) compared to non-placebo RCTs (Coleman et al, 2015).

‘Smoking reduction’ vs ‘abrupt cessation’

A reduction in smoking before the quit date and stopping abruptly, with no prior reduction, produces comparable smoking cessation rates (Lindson‐Hawley et al, 2012). Trials using the nicotine assisted reduction to stop (NARS) strategy indicate that it is effective (RR 2.06, 95% CI: 1.34–3.15) in achieving sustained abstinence in smokers who are otherwise unable to attempt an abrupt quit (Moore et al, 2009). However, the majority of this evidence comes from studies using regular behavioural support and it is unclear whether NRT without the behavioural support component would remain as effective.

In smokers who are unwilling or unable to quit, using nicotine gum, inhaler or choice of product is effective in reducing the number of daily cigarettes smoked by 50% (RR 1.75 95%CI 1.44 -2.13), although smaller reduction was observed in carbon monoxide and cotinine levels. These methods also increase the likelihood of ultimately quitting smoking when compared to a placebo (RR 1.87, 95%CI 1.43-2.44). There is insufficient evidence at this time for the application of other methods (pharmacological intervention, electronic cigarettes, snus, nicotine patches and low tar cigarettes) in demonstrating a smoking reduction or complete cessation in such users (Lindson-Hawley et al, 2016).

Adjunct aids

There is insufficient evidence to suggest a possible beneficial role of smoking cessation and weight gain therapies in limiting post-cessation weight gain in people stopping smoking in the long term (Farley et al, 2012) and also of exercise interventions aiming to increase cessation rates among smokers (Ussher et al, 2014). The role of social support by peer or partner in improving smoking cessation rates among pregnant women or people attempting to quit remains inconclusive due to limited evidence (Park et al, 2012). Similarly, although there is evidence of a potential benefit from peer support provided to pregnant women for smoking cessation (RR 1.09, 95%CI 1.01-2.19), the evidence at this time is limited (Chamberlain et al, 2013).

Conclusions

The research on smoking cessation suggests that different therapies and their combinations work better in certain settings than in others, and need to be tailored according to the patient type and their preferences. Overall, even brief advice by a trained health professional is beneficial in achieving smoking cessation in a patient presenting to health services, but to a lesser extent than behavioural support alone or in combination with pharmacotherapies (nicotine replacement therapies (NRTs), bupropion and varenicline). Individual pharmacotherapies are effective for smoking cessation, however, these in combination with behavioural support are found to be more effective. These therapies are also seen to work better when delivered in health care settings relative to community settings. Combination NRTs (oral or skin patch) are observed to be particularly helpful in promoting cessation among heavy smokers compared to light smokers.

Acknowledgement

We are very grateful to Dr Kamran Siddiqi, a Senior Clinical Lecturer at the Department of Health Sciences, University of York and Hull York Medical School, for reviewing some sections of the manuscript.

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**Table 1: An evidence-based guide to smoking cessation therapies in practice**

|  |  |
| --- | --- |
| Sufficient evidence/ Definitely beneficial | * Brief advice by trained professionals in health care settings over no advice * Individual behavioural therapy by trained health workers over brief advice * Group behavioural therapy over self-help materials * NRTs over placebo in smokers motivated to quit * Combination of NRTs (skin patches and oral forms) among heavy smokers over single NRT * Varenicline (standard dose), Bupropion, Nortryptyline and cytisine over placebo * Varenicline (low dose) over placebo with fewer side effects. * Varenicline over buproprion and single NRT * Combinations of behavioural support and pharmacotherapies over brief advice or usual care * Combination therapy of behavioural support and pharmacotherapy in health care settings vs. community-based settings * Intensive behavioural support as an adjunct to pharmacotherapy * Increasing intensity of behavioural support in people using pharmacotherapies over same level of intensity |
| Insufficient evidence/ Probably beneficial | * Individual intensive behavioural support over less intense behavioural interventions * Group behavioural support interventions over brief advice * NRT use among lighter smokers (< 10-15 cigarettes per day) over placebo * NRT use pre-quit over NRT starting on quit day * NRT vs placebo in smokers who are not willing to quit * NRT for longer duration or in higher concentrations compared to standard use * Use of nicotine patches beyond 8 weeks of therapy * One form of NRT over another * NRT or partner support in pregnancy * Varenicline over placebo for relapse prevention * Combination of behavioural support with varenicline or nortriptyline * Nicotine assisted reduction to stop (NARS) vs. abrupt cessation * E-cigarettes vs non-nicotine placebo |
| Unknown evidence/ unknown benefit | * Group behavioural therapy over individual behavioural therapy * Varenicline or bupropion use in pregnancy |

**CONCLUSIONS/ KEY POINTS**

* Brief advice by a healthcare professional is beneficial in achieving smoking cessation
* Intensive behavioural support alone and in combination with pharmacotherapies is effective in promoting smoking cessation
* Pharmacotherapies (NRTs, bupropion, nortriptyline, varenicline and cytisine) are individually effective in promoting smoking cessation
* Combination of NRTs (slow and rapid release) are effective for promoting cessation among harder smokers
* Combination therapies of behavioural support and pharmacotherapy are more effective than pharmacotherapies alone in promoting cessation among smokers when delivered in health care settings
* Limited evidence of benefit from electronic cigarettes in smoking cessation

