SMOKING CESSATION

The role of doctors in smoking cessation: evidence from the Cochrane Library

Tim Lancaster

Department of Primary Health Care, Oxford University, Oxford, UK

Address for correspondence:
Tim Lancaster
Co-ordinating editor
Cochrane Tobacco Addiction Review Group
Department of Primary Health Care
Oxford University
Old Road Campus
Oxford
United Kingdom
OX3 7LF

Email:
tim.lancaster@dphpc.ox.ac.uk

ABSTRACT

This article examines the role of doctors in assisting patients who smoke to quit, using evidence from Cochrane systematic reviews of randomised trials. Doctors may help such patients by providing advice, referring patients for counselling and support and by offering pharmacological therapy. Complementary therapies used for smoking cessation include hypnotherapy and acupuncture, but there is a lack of evidence that these interventions have a specific effect in aiding cessation. The number needed to treat (NNT) for simple advice to unselected smokers is 50 - 120. Based on a median no-treatment clinical trial quit rate of 7.5%, the NNT for nicotine replacement therapy is 23 (95% CI 20 to 27), for the antidepressant Bupropion 18 (95% CI 14 to 23), and for the nicotinic partial agonist Varenicline 10 (95% CI 7 to 14). These numbers compare favourably with other preventive healthcare interventions. There remains wide variations in the extent to which these interventions are available in different healthcare systems. SAHeart 2011; 8:24-27

BACKGROUND

Tobacco use remains the most significant modifiable contributor to the prevalence of cardiovascular and respiratory disease in high income countries. The success of tobacco control policies is reducing this prevalence in many of these countries, but the burden of tobacco related chronic disease is increasing in low and middle income countries as the prevalence of smoking rises. Smoking also increases mortality from tuberculosis and other diseases already more prevalent in middle and lower income countries.[1,2] For these reasons, if current patterns of consumption continue, it is estimated that by 2030, 70% of tobacco-related deaths worldwide will take place in developing countries.[3] To avert this public health catastrophe, robust tobacco control strategies are of central importance to all sectors of the world's population. In recognition of the importance of tackling this threat to health, over 160 countries are signatories to the World Health Organisation Framework Convention on Tobacco Control. The WHO FCTC emphasises the importance of multimodal approaches to tobacco control. Its mpower strategy highlights six key mechanisms to reduce demand for smoking: through monitoring, enforcement of smoke-free environments, provision of cessation programmes, and imposition of health warnings, advertising bans and taxation. In its 2009 report, WHO estimated that only 10% of the world's population was covered by any one of the measures, and identified wide variation in the implementation of mpower measures within Africa.[4]

Physicians can make contributions to all aspects of tobacco control, for example through advocacy, policy development, political engagement and role modelling. But for most doctors, the most direct opportunity to reduce smoking will be in the clinical setting, through encouraging individuals to stop smoking and developing services to support them in doing so. My objective here is to review the evidence for the effectiveness of smoking cessation interventions available to the physician advising patients how to stop smoking. The available interventions include behavioural interventions (brief advice, self-help materials, counselling), complementary therapies (hypnotherapy and acupuncture) and pharmacological therapy (nicotine replacement, antidepressants and the nicotine partial receptor agonist Varenicline).

METHODS

The principal data sources are reviews of interventions for smoking cessation from the Cochrane Database of Systematic Reviews. The

Cochrane Tobacco Addiction Review Group maintains a register of controlled trials in smoking cessation. Systematic reviews based on this register are published in the Cochrane Library, and are regularly updated. Detailed bibliographies of the included trials can be found within each review.

The aim of these reviews is to identify and synthesise the most reliable evidence evaluating interventions for smoking cessation. For individual patient interventions, the most reliable evidence comes from randomised controlled trials. In the Cochrane reviews, the principal outcome is sustained smoking cessation, defined as being at least six months after the intervention. Where appropriate, meta-analyses of individual trials provide a summary estimate of the effect of the interventions tested. This pooled estimate is expressed as a relative risk with 95% confidence intervals, where a relative risk greater than one indicates a higher likelihood of abstinence.

ADVICE FROM A DOCTOR

Physician advice to quit smoking is an inexpensive intervention, which can be offered in most healthcare settings. A Cochrane review of physician advice identified 41 trials, conducted between 1972 and 2007, including over 31 000 participants.[5] The most common setting for delivery of advice was primary care, but there were also studies in hospital wards, outpatient clinics, and workplace clinics. Meta-analysis of 17 trials of brief advice versus no advice (or usual care) detected a significant increase in the rate of quitting (relative risk [RR] 1.66; 95% confidence interval [CI] 1.42 to 1.94). There is little evidence as to whether giving the advice in different ways is more or less effective, though there is a small additional benefit from spending more time with the patient: Amongst 11 trials of more intensive advice the estimated effect was higher (RR 1.84; 95% CI 1.60 to 2.13) but there was no statistical difference between the intensive and minimal subgroups. Direct comparison of intensive versus minimal advice showed a small advantage of intensive advice (RR 1.37; 95% CI 1.20 to 1.56), and this effect may be greater in patients with medical conditions related to smoking, such as cardiac and respiratory disease, than in apparently healthy smokers. There was insufficient evidence to draw any conclusion about the effect of motivational as opposed to simple advice or between different advice-giving styles.

SELF-HELP MATERIALS

Self-help materials in various formats are a low cost option for supporting smoking cessation, but their effectiveness is low. In 12 trials involving 15 711 participants that compared self-help materials to no intervention, a Cochrane review (search date 2008) found a pooled effect that just reached statistical significance (RR 1.21; 95% CI 1.05 to 1.39).[6] The review did not detect a benefit from adding self-help materials to brief advice, or to nicotine replacement therapy. There were 25 trials using materials tailored for the characteristics of individual smokers, where meta-analysis supported a small benefit of tailored materials (RR 1.31; 95% CI 1.20 to 1.42). The evidence is strongest for tailored materials compared to no intervention, but also supports tailored materials as more helpful than standard materials. Part of this effect could be due to the additional contact or assessment required to obtain individual data.

COUNSELLING

Counselling can be provided to those seeking to quit smoking either through face to face contact with an individual healthcare worker or in group settings. A Cochrane review of individual counselling identified 30 trials with over 7 000 participants.[7] It found that individual counselling was more effective than a minimal intervention, with a relative risk for smoking cessation at long-term follow up of 1.39, 95% CI 1.24 to 1.57. Counselling provided additional benefit in patients receiving NRT. The review was unable to detect whether any specific form of counselling was more effective than another. A Cochrane review of group counselling (search date 2008) found similar effects in the group setting, but poor attendance at group counselling limits the usefulness of this approach.[8] Face to face intervention may not be crucial to the success of counselling. A Cochrane review of telephone counselling (search date 2008) found that both proactive and reactive quit lines improve quit rates to a similar degree.[9]

NICOTINE REPLACEMENT THERAPY

Nicotine replacement therapy (NRT) aims to aid smoking cessation by providing nicotine to reduce withdrawal symptoms and craving. It is appropriate for patients who show evidence of nicotine dependence, usually those who smoke more heavily, start early in the day and have withdrawals symptoms when they stop smoking. Nicotine is available as transdermal patches, chewing gum, nasal spray, as an inhaler and as sublingual lozenges. A Cochrane review of NRT (search date 2007) identified 132 trials.[10] Within these trials over 40 000 participants contributed to the primary comparison between any type of NRT and a placebo or non-NRT control group. The RR of abstinence for any form of NRT relative to control was 1.58 (95% CI 1.50 to 1.66). There were no significant

differences between the effects obtained using different nicotine products. The effects were largely independent of the duration of therapy, the intensity of additional support provided, or the setting in which the NRT was offered. There was some evidence of a small benefit from combining the nicotine patch with a form allowing ad lib dosing compared to use of a single form. Use of combination therapy may be considered for patients who have been unable to quit using a single type of NRT. There was borderline evidence that there is a small benefit from use of the nicotine patch at doses higher than 22mg (24 hours), or 15mg (16 hours) compared to the standard dose patch. Use of these may be considered for heavy smokers (i.e. smoking 30 or more cigarettes a day), or for patients relapsing because of persistent craving and withdrawal symptoms on standard dose therapy. There is limited evidence that a repeated course of NRT in patients who have relapsed after recent use of nicotine patches, will result in a small additional probability of quitting. One study directly compared NRT with Bupropin. Quit rates with Bupropion were higher than with nicotine patch or placebo.[11] Although there is an additional benefit when NRT is combined with behavioural support, NRT increases cessation rates whether behavioural support is provided or not, so it is still worth suggesting NRT if the resources are not available to provide such support.

ANTIDEPRESSANTS

There is increasing evidence that some antidepressants help smoking cessation. They may act by alleviating depressive symptoms associated with nicotine withdrawal, by substituting for antidepressant effects of nicotine that sustain smoking, or by acting on neural pathways that underlie nicotine addiction. A Cochrane review (search date 2009) identified 66 trials of antidepressants for smoking cessation, including 49 trials of Bupropion and nine trials of Nortriptyline.[12] Bupropion (RR 1.69; 95% CI 1.53 to 1.85) and Nortriptyline (RR 2.03; 95% CI 1.48 to 2.78) both significantly increased long term cessation, but selective serotonin reuptake inhibitors were not shown to help smoking cessation. Bupropion and Nortriptyline appear to be of similar efficacy to nicotine replacement therapy. Pooling three trials comparing Bupropion to the nicotine receptor agonist Varenicline, showed lower quitting with Bupropion (RR 0.66; 95% CI 0.53 to 0.82). There is a risk of about 1 in 1 000 of seizures associated with Bupropion use. Bupropion has been associated with suicide risk, but whether this is causal is unclear. Nortriptyline has the potential for serious side-effects, but none have been seen in the few small trials for smoking cessation.

NICOTINE RECEPTOR PARTIAL AGONISTS

Nicotine receptor partial agonists may help people to stop smoking by a combination of maintaining moderate levels of dopamine to counteract withdrawal symptoms (acting as an agonist) and reducing smoking satisfaction (acting as an antagonist). Varenicline was developed as a nicotine receptor partial agonist from Cytisine, a drug widely used in central and eastern Europe for smoking cessation. The first trial reports of Varenicline were released in 2006. A Cochrane review (search date March 2008) included 7 267 participants from nine randomised controlled trials of Varenicline.[13] Seven trials compared Varenicline with placebo for smoking cessation and three compared it with Bupropion. There was one trial of relapse prevention and one open-label trial that compared Varenicline with nicotine replacement therapy.

The pooled risk ratio for continuous abstinence for Varenicline versus placebo was 2.33 (95% CI 1.95 to 2.80). The pooled RR for Varenicline versus Bupropion at one year was 1.52 (95% CI 1.22 to 1.88). The RR for Varenicline versus NRT at one year was 1.31 (95% CI 1.01 to 1.71). The main adverse effect of Varenicline was nausea, which was usually not severe and reduced with time. Post marketing safety data suggest that Varenicline may be associated with depressed mood, agitation, and suicidal behaviour or ideation. Although it remains uncertain whether this represents a causal association, Varencline should be avoided or used with caution in patients with conditions or characteristics that could suggest an increased risk of suicide.

COMPLEMENTARY THERAPIES

Hypnotherapy and acupuncture continue to be used as smoking cessation interventions. There are methodological difficulties in conducting high quality trials of these interventions. The Cochrane reviews failed to detect a specific effect of either hypnotherapy or acupuncture on smoking cessation, but practitioner attention may provide a non-specific effect comparable to counselling.[14,15]

DISCUSSION

This review shows that there is evidence that a range of interventions potentially available to doctors may help their patients to quit smoking. What is the clinical significance of this evidence? Some idea of the potential impact can be gained from estimating the numbers needed to treat for different interventions. There are difficulties in estimating NNT's from meta-analysis of trials of smoking cessation, principally because the absolute quit rates vary depending on the population under study in each trial. For brief advice, which is generally given to smokers who are not specifi-

cally selected for motivation to quit, the background quit rate is low. Assuming an unassisted quit rate of 2 to 3% in this population, brief advice can increase quitting by a further 1 to 3%, giving a number needed to treat of 50 - 120. Although this may seem like a poor success rate for the individual doctor, advice is an inexpensive intervention which can be offered in settings where other resources may be limited and cumulatively the effects would be large if all doctors provided it.

Individuals taking up pharmacological treatment for smoking cessation are likely to be more motivated than the general population of smokers, so their unassisted quit rate may be assumed to be higher when calculating NNT's. Based on a median no-treatment (placebo) clinical trial quit rate of 7.5% the NNT for NRT is 23 (95% CI 20 to 27), for Bupropion 18 (95% CI 14 to 23), and for Varenicline 10 (95% CI 7 to 14). These numbers compare favourably with other preventive healthcare interventions.[4]

The ability of physicians to help their patients to quit smoking will of course vary depending on the resources available within their country and locality. In South Africa, Varenicline is not yet available, although it is likely that it will be licensed in the near future. As a measure of provision of treatment for tobacco dependence, the World Health Organisation tracks availability of eight evidence-based treatment resources described in this review: access to a national toll-free quit line, ability to purchase NRT, Bupropion and Varenicline, and smoking cessation support in primary care, in hospitals, in offices of health professionals and in the community. WHO's 2009 report on the global tobacco epidemic shows wide variation in availability of these resources. The report found that seventeen mainly high-income countries provide comprehensive smoking cessation services encompassing in full or in part all eight of these resources. About a third of middle-income countries and less than 15% of low-income countries provide coverage for NRT and/or cessation services.[4] Only four middle-income countries and no low-income countries provide a national toll-free quit line and coverage for both NRT and cessation services. In the majority of low- and middle-income countries, the cost of cessation assistance is not covered by government, and 8% of middle-income and 29% of low-income countries provide no assistance to smokers. Together with measures to control supply and demand for tobacco, identifying the resources to increase availability of tobacco dependence treatment is a major public health challenge for clinicians and for the global community.

REFERENCES

1. Liu BQ, Peto R, Chen ZM, et al. Emerging tobacco hazards in China: Retrospective proportional mortality study of one million deaths. BMJ. 1998 Nov 21;317(7170):1411-22.
2. Jha P, Jacob B, Gajalakshmi V, et al. A nationally representative case-control study of smoking and death in India. N Engl J Med. 2008 Mar 13;358(11):1137-47.
3. Peto R, Lopez AD. The future worldwide health effects of current smoking patterns. In: C Everett Koop, Clarence E Pearson, M Roy Schwarz, eds. Critical Issues in Global Health. New York: Jossey-Bass, 2000.
4. WHO Report on the Global Tobacco Epidemic, 2009: Implementing smoke-free environments/Available at: http://www.who.int/tobacco/mpower/2009/en/.
5. Stead LF, Bergson G, Lancaster T. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews 2008, Issue 2. Art. No.: CD000165. DOI: 10.1002/14651858.CD000165.pub3.
6. Lancaster T, Stead LF. Self-help interventions for smoking cessation. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD001118. DOI: 10.1002/14651858.CD001118.pub2.
7. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD001292. DOI: 10.1002/14651858.CD001292.pub2.
8. Stead LF, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD001007. DOI: 10.1002/14651858.CD001007.pub2.
9. Stead LF, Perera R, Lancaster T. Telephone counselling for smoking cessation. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD002850. DOI: 10.1002/14651858.CD002850.pub2.
10. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD000146. DOI: 10.1002/14651858.CD000146.pub3.
11. Jorenby DE, Leischow SJ, Nides MA, et al. A controlled trial of sustained-release Bupropion, a nicotine patch, or both for smoking cessation. N Engl J Med. 1999 Mar 4;340(9):685-91.
12. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD000031.
13. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews 2008, Issue 3. Art. No.: CD006103.
14. Barnes J, Dong CY, McRobbie H, et al. Hypnotherapy for smoking cessation. Cochrane Database of Systematic Reviews, 2010, Issue 3: Art. No.: CD001008.
15. White AR, Rampes H, Liu JP, et al. Acupuncture and related interventions for smoking cessation. Cochrane Database of Systematic Reviews, 2011, Issue 1: Art. No.: CD000009.