

Scientific Update™

Smoking Cessation and Strategies in Clinical Practice

Originally presented by: P. HAJEK, MD, K.O. FAGERSTROM, MD, AND U. KEIL, MD

A Report on a Presentation at the 24th Congress of the European Society of Cardiology

Berlin, Germany August 31- September 4, 2002

Reported and discussed by:
David Fitchett, MD

It is estimated that there are over 1 billion tobacco smokers in the world; this is approximately one-third of the population aged ≥ 15 years. There are large regional variations in smoking rates, with the highest rates in developing countries (eg, China, 61%) and the lowest in the developed nations (eg, Sweden, 17%).¹ In Canada, 24.8% of the population were current smokers in 1999, which was a substantial reduction compared to 1985, when 35.1% smoked.² Despite extensive health education, smoking rates in young people, aged 15 to 19, increased in Canada between 1991 and 1999. World-wide tobacco consumption also continues to rise, with a parallel increase in tobacco-related disease. It is estimated that smoking-related mortality will rise from a current 3 million, to 10 million in the next 30 years, with 70% of the deaths occurring in the developing world. Smoking is the single most significant cause of premature death in the developed world¹ and is responsible for 20% of deaths annually in the United States. Smokers who smoke more than 25 cigarettes per day are estimated to lose approximately 10 years of their life-span. Cigarette smoking is responsible for 80% of chronic lung disease and more than 30% of all deaths from heart disease and cancer.

Smoking and cardiovascular disease

Smoking is a powerful independent risk factor for coronary heart disease. Myocardial infarction (MI) is 4 times more frequent and occurs 8 to 10 years earlier in smokers as compared to non-smokers. Smokers with MI are more likely to be male, have an ST-segment elevation MI, and are less likely to have had a previous MI. Stroke also occurs approximately 3 times more frequently in smokers than in non-smokers of the same age. Although the relative risk of stroke, peripheral vascular disease, and cancer relate to the duration and intensity of smoking, it is unclear whether such a strong dose relationship exists for coronary vascular disease. Smoking 5 cigarettes daily may be as bad as smoking 25, in terms of risk for coronary disease.

Cardiovascular benefits of smoking cessation

The increased risk of MI is cut in half within 1 year of smoking cessation and returns to that of a nonsmoker by 15 years. A recent meta-analysis from McMaster University³ shows that smoking cessation after MI reduces mortality by 46% after an average follow-up of 4.8 years (Figure 1). In smokers who persisted to smoke after an MI, 20% had died by 4 years.³ Stopping smoking results in 1 life saved for every 13 patients who have successfully quit.

Cardiac patients are usually highly motivated to stop smoking. They are scared, yet highly addicted and dependent upon their habit. Consequently, cardiac patients are

Division of Cardiology

Duncan J. Stewart, MD (Head)

Gordon W. Moe, MD (Editor)

David H. Fitchett, MD (Assoc. Editor)

Juan C. Monge, MD (Assoc. Editor)

Beth L. Abramson, MD

Warren Cantor, MD

Luigi Casella, MD

Robert J. Chisholm, MD

Chi-Ming Chow, MD

Paul Dorian, MD

Michael R. Freeman, MD

Shaun Goodman, MD

Anthony F. Graham, MD

Robert J. Howard, MD

Stuart Hutchison, MD

Victoria Korley, MD

Michael Kutryk, MD

Anatoly Langer, MD

Howard Leong-Poi, MD

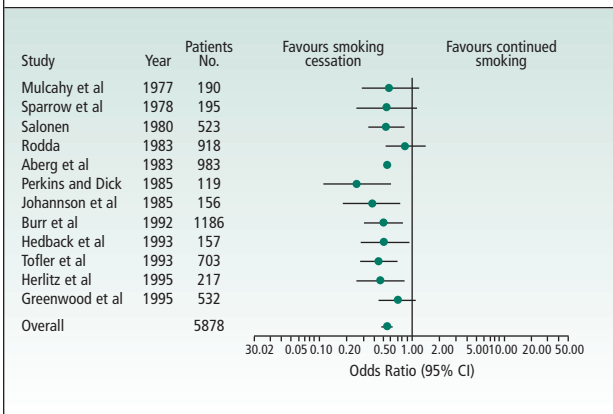
David Newman, MD

Trevor I. Robinson, MD

Bradley H. Strauss, MD

The opinions expressed in this publication do not necessarily represent those of the Division of Cardiology, St. Michael's Hospital, the University of Toronto, the educational sponsor, or the publisher, but rather are those of the author based on the available scientific literature. The author has been required to disclose any potential conflicts of interest relative to the content of this publication. *Cardiology Scientific Update* is made possible by an unrestricted educational grant.

Figure 1: Benefits (odds ratio for reduction of mortality) of smoking cessation after a MI³



very likely to misrepresent their smoking status at follow-up visits to their physician.

General principles of smoking cessation

Smoking cessation has a huge potential public health impact. However, the challenge of stopping such a highly addictive habit that has both behavioural and pharmacological dependence should not be underestimated. Many myths exist about quitting smoking (Table 1). Unassisted cessation attempts (ie, cold turkey) nearly always fail (3%-5% success). With a combination of behavioural therapy (motivation, support, and advice) and a pharmacological approach (nicotine replacement therapy or bupropion), long-term abstinence rates of 30% to 40% can be achieved. Successful smoking cessation requires both counselling and drug therapy. When available, the patient should be referred to an expert team of smoking cessation specialists. In the absence of such an expert team, the physician should initiate smoking cessation strategies as a part of standard medical practice.

Smoking cessation strategies

Behavioural interventions

Advising the patient to stop smoking as the sole intervention is usually inadequate. In addition, frequently urging a smoker to quit each time he/she visits the physician's office has only a small additional impact. Successful smoking cessation requires physician-initiated intervention. Subsequent success also depends on determining the patient's motivation to cease his habit. Setting a quit target date, explaining the benefits of medications to increase success, and arranging follow-up meetings are part of the initial interview. When available, individual and group counselling will improve success.

Table 1: Myths about smoking cessation

- Smoking is just a bad habit
- Quitting is just a matter of will-power
- If you can't quit the first time, you will never quit
- The best way to quit is cold turkey.
- Quitting smoking is expensive
- It's too late to quit smoking

Nicotine replacement therapy (NRT)

The extent to which many smokers are addicted to nicotine is comparable with addiction to hard drugs such as heroin or cocaine.⁴ Many of the initial problems encountered by the smoker who is trying to stop smoking result from acute nicotine withdrawal. The principle of NRT is to help the smoker learn to manage without smoking and its associated boluses of nicotine by providing a moderate level of nicotine that is then gradually withdrawn. Unfortunately, many smokers fail NRT because of inadequate dosing. The fact is, the most effective nicotine delivery system is cigarette smoking. Each cigarette provides 1.5 to 2 mg nicotine that reaches the brain in arterial blood in boluses at levels that are 4-fold higher than in venous blood. NRT can only partially compete with the nicotine levels generated by smoking a cigarette (Figure 2).⁴ In the case of the nicotine transdermal patch, plasma nicotine levels continue to rise for an average of 5 hours after application, and reach a plateau within 3 days. Maximal plasma levels of nicotine of 15-17 ng/ml may be achieved using the higher doses of the patch, which are usually lower than that measured in a one

Figure 2: Plasma nicotine levels after smoking 1 cigarette and taking various modes of nicotine replacement therapy.⁴

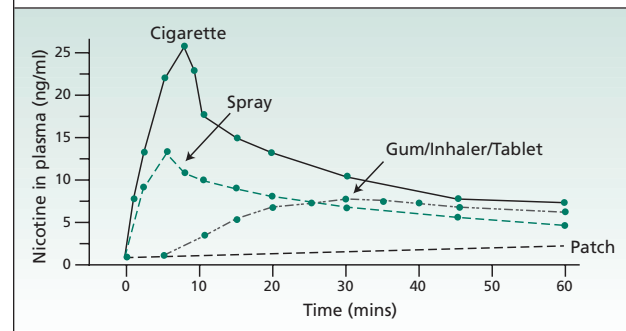


Table 2: Nicotine replacement therapy preparations

Available product	Doses	Usage	Comments
Nicotine chewing gum	2 and 4 mg	Up to 20/day	Usage of one piece when there is the desire to smoke (up to 20/day)
Nicotine transdermal patch	21, 14 and 7 mg patches	1 patch/day	Excellent compliance. Low blood levels
Nicotine inhaler*	10 mg/cartridge (4 mg delivered)	Up to 6-12 cartridges/day	Usage of 1 cartridge for 20 minutes of continuous puffing or an intermittent schedule totaling 20 minutes

*Not yet available in Canada

pack per day smoker (25-30 ng/ml). Despite the different availability profiles of the different NRT formulations (Table 2), similar odds ratios for abstinence at 1 year, compared to placebo, are observed for each product (overall odds ratio 1.73, 95% CI, 1.60-1.86). The choice of NRT delivery system depends largely on patient acceptability. Generally, however, gum and nicotine patches are most commonly used.

The dose of NRT is determined by the patient's dependency on cigarette smoking. A useful guide to the degree of nicotine addiction is daily cigarette consumption, and the time between waking and the first cigarette smoked. It is important to use a sufficiently high dose of NRT to reduce the craving for cigarettes. For those smoking more than 10 cigarettes/day, the highest dose of nicotine gum should be used. It is useful to estimate a patient's nicotine consumption based upon the 1.5 to 2 mg of nicotine inhaled/cigarette. To achieve adequate nicotine replacement, it may be necessary to use a combination of products.

Safety and adverse effects of NRT

The amounts of nicotine delivered by NRT are up to half that released by a cigarette when a person is smoking. Therefore, there are no contraindications to NRT as long as the alternative is smoking. In addition, studies suggest that NRT is safe and well tolerated.

The cardiovascular effects of transdermal nicotine was studied in normotensive and mildly hypertensive individuals in a study by Tanus-Santos et al.⁵ In the normotensive subjects, the 21 mg nicotine patch increased mean arterial pressure from 94 ± 4 to 117 ± 7 mm Hg ($P < 0.05$) and heart rate from 69 ± 3 to 83 ± 3 bpm ($P < 0.05$). However, there was no significant change in heart rate or blood pressure in the mildly hypertensive patients.

There is no evidence to indicate NRT induces acute coronary events. A population-based, case-controlled, study of

smokers included 653 cases admitted to hospital with their first MI and 2990 smoking controls. The study demonstrated that there was no increased risk of MI associated with the use of the nicotine patch.⁶ Transdermal nicotine also appears to be safe in patients with existing cardiac disease. In a double-blind placebo-controlled study, transdermal nicotine patch or placebo was given to 584 patients with at least one diagnosis of cardiovascular disease.⁷ During the treatment period of 10 weeks, and for a further 4 weeks, the patients were monitored for a range of cardiovascular complications including MI, cardiac arrest, arrhythmias, and congestive heart failure. A primary endpoint was achieved in 5.4% of patients in the treatment group and in 7.9% of those receiving placebo (difference not significant).

NRT is generally well-tolerated. The most common adverse effects relate to localized reactions to the delivery system such as skin irritation with the patch.

Bupropion

Bupropion is a monocyclic antidepressant with a structure similar to amphetamine, and has both dopaminergic and adrenergic actions. Whether its mechanism of action is related to relieving pre-existing depression, depression induced by smoking cessation, or preventing smoking relapse in individuals subject to depression, is controversial. Bupropion appears to reduce the craving for nicotine and diminishes the irritability, anxiety, hunger, and post-cessation weight gain. It is usually given for 1 week at a dose of 300 mg daily before smoking cessation and then continued for a further 7-12 weeks. Placebo-controlled trials have shown that bupropion doubles cessation rates. The smoking abstinence rates after 12 months were:

- placebo $5.6 \pm 0.02\%$
- nicotine-patch $9.8 \pm 0.02\%$
- bupropion $18.4 \pm 0.03\%$
- combined bupropion/nicotine patch $22.5 \pm 0.03\%$.⁸

The side effects from bupropion are mild, with nausea and insomnia being the most frequent. A warning was issued to all physicians by the Therapeutic Products Directorate of Health Canada in July 2001 stating that it had received 1127 reports of suspected adverse effects with bupropion.⁹ However, cause and effect relationships have not been established or speculated in the vast majority of reports submitted. Bupropion should not be used in patients with a history of seizures.

Choice of pharmacological agent

NRT is effective and should be the primary pharmacological aid to smoking cessation. It is simpler to use than bupropion and potentially safer. To be successful it is essential that adequate support be given to increase the smoker's commitment and adequate NRT dosing be used to attenuate the cravings of nicotine withdrawal. For heavily addicted smokers it may be necessary to use both NRT and bupropion to achieve success.

Outcomes of smoking cessation strategies

The success of smoking cessation strategies is closely related both to the motivation of the patient and the encouragement of the healthcare professional. Following an acute cardiac event or coronary artery bypass surgery, patients are highly motivated to quit smoking. Medium-term abstinence rates of up to 50% are observed in patients after bypass surgery. Unfortunately, for some, the motivation wears thin with time after surgery or the acute event. The EUROASPIRE report¹⁰ indicates that 21% of patients continue to smoke after an acute coronary event, a proportion that has not changed over the past 5 years.

Long-term abstinence from smoking depends on the program used. Self-quitting, without professional advice, has only a 3% to 5% chance of success. Physician advice alone may increase success to 10%. The addition of NRT to physician advice can double success rates. However, the best results (30%-40%) are achieved with combined group therapy and pharmacological support, although only 5% of smokers are willing to participate in such an intervention.

It is estimated that smoking cessation costs US \$3779 per quitter, which would result in a cost of US \$2587 per life-year saved.¹¹ These American figures for the cost of smoking cessation include various components, such as the cost of physician visits for screening, advising, motivating, and counselling, as well as the cost of direct interventions (ie, NRT pharmacotherapy). In comparison with other preventative

interventions, smoking cessation is extremely cost-effective. Interestingly, the more intensive the intervention, the lower the cost per quality-adjusted life-year saved.

Smoking cessation is a cost-effective life saving measure. Although it is difficult to achieve high initial rates of success, persistence is worthwhile. Male nonsmokers live 7.4 years longer than smokers, and 5.4 years longer, free of cardiovascular disease. Smoking cessation not only prolongs life expectancy, it also improves health. "It is better to be healthy than ill or dead."

References

1. Fagerstrom K. The epidemiology of smoking: health consequences and benefits of cessation. *Drugs* 2002;6 (Suppl 2):1-9.
2. Gilmore J. Report on Smoking Prevalence in Canada, 1985 to 1999. *Statistics Canada* 2001.
3. Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction. *Arch Intern Med* 2000;160:939-944.
4. The management of nicotine addiction. Royal College of Physicians of London. 1999. www.rcplondon.ac.uk/pubs/books/nicotine/7-management.htm
5. Tanus-Santos JE. Cardiovascular effects of transdermal nicotine in mildly hypertensive smokers. *Am J Hypertens* 2001;14:610-4.
6. Kimmel SE, Berlin JA, Miles C, Jaskowiak J, Carson JL, Strom BL. Risk of acute first myocardial infarction and use of nicotine patches in a general population. *J Am Coll Cardiol* 2001;37:1297-1302.
7. Joseph A, Norman SM, Ferry LH, et al. The safety of transdermal nicotine as an aid to smoking cessation in patients with cardiac disease. *N Engl J Med* 1996;335:1792-1798.
8. Joronby DE, Nides MA, Leischow SJ, et al. A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *N Engl J Med* 1999;340:685-691.
9. Health Canada Therapeutic Products Directorate http://www.hc-sc.gc/hpb-dgps/therapeut/zfiles/english/advisory/industry/zyban_e.html
10. EUROASPIRE II Study Group. Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries. *Euro Heart J* 2001;22:554-572.
11. Cromwell J, Bartosch WJ, Fiore MC, Hasselblad V, Baker T. Cost-effectiveness of the clinical practice recommendations in the AHCPR Guideline for smoking cessation. *JAMA* 1997;278:1759-1766.

Dr. Fitchett reports that he has no potential conflicts of interest in association with this article.

SNELL Medical Communication acknowledges that it has received an unrestricted educational grant from Pharmacia Canada to support the distribution of this issue of *Cardiology Scientific Update*. Acceptance of this grant was conditional upon the sponsors' acceptance of the policy established by the Division of Cardiology and SNELL Medical Communication guaranteeing the educational integrity of the publication. This policy ensures that the author and editor will at all times exercise unrestricted, rigorous, scientific independence free of interference from any other party.