Tobacco smoking cessation management: integrating varenicline in current practice

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Abstract: Tobacco smoking is widespread and is one of the world's most prevalent modifiable risk factors for morbidity and mortality. It is important to facilitate smoking cessation better in order to reduce the health consequences of tobacco use. The most effective approach assisting smokers in their quit attempts combines both pharmacotherapy and nonpharmacological interventions. This review summarizes the latest international epidemiological data available on tobacco use, considers the associated effects on health, and reviews existing policies against tobacco use. Among the interventions for smoking cessation, the three major pharmacotherapies (which have demonstrated efficacy when combined with behavioral support) are discussed: nicotine replacement therapy (NRT), bupropion, and varenicline. As the newest pharmacotherapy made available in this area, particular consideration is given to varenicline, and a review of our clinical experience is offered.

Keywords: tobacco smoking cessation, nicotinic substitution, nicotine replacement therapy (NRT), bupropion, varenicline

Introduction

Approximately 1.3 billion people worldwide currently smoke cigarettes or other products. Yet the prevalence of smoking varies greatly among nations, with many industrialized countries having seen a reduction in tobacco use, and there has been a growing shift in use from developed to developing countries in recent years. Approximately a third (35%) of men in developed countries smoke compared with almost half of the male population in developing nations (Shafey et al 2008). In the US in 2005, 45.1 million (20.8%) adults were classified as current cigarette smokers. Within that population, the highest prevalence by age group was found in those aged 18–24 years (23.9%) and those aged 25–44 years (23.5%). In Canada the prevalence of current smokers over the age of 15 years is slightly lower at 19%, 20% among men and 17% among women (Health Canada 2007). At 28.6%, the prevalence of current smokers in Europe at the end of 2005 was higher than that recorded in North America (40% for European men and 18.2% for women). Within regions, however, prevalence varies widely, particularly among countries in Western and Eastern Europe (World Health Organization [WHO] 2007). There is also a socioeconomic variation in smoking prevalence. A higher proportion of adult smokers live below the federal poverty level than in higher socioeconomic groups. Variations in tobacco smoking prevalence have also been reported according to race, ethnicity, and education level.

The financial costs of cigarette smoking are manifold. The cost to the economy alone in the US is estimated to be US$167 billion annually as a result of lost productivity and premature death (US$92 billion), and health-care expenditure (US$75.5 billion) (Centers for Disease Control and Prevention 2006). Across Europe, the economic burden associated with smoking in 2000 was estimated to range from €97.7 billion to €130.3 billion (WHO 2007).

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Active smoking: health implications

Approximately 50% of all long-term smokers die prematurely as a result of the adverse effects of their habit. Cigarette smoking is estimated to be responsible for nearly 44,000 deaths in the US every year (18.3% of the annual national total of 2.4 million). As such, the American Heart Association considers cigarette smoking to be the country's leading preventable cause of premature death (American Heart Association 2008). Similarly, the *World Health Report 2002* estimated that tobacco was the leading risk factor for premature mortality in Europe, causing about 1.6 million deaths that year (WHO 2002).

In particular, tobacco use increases risk of cancer and respiratory and cardiovascular diseases. With 16 million cases of coronary heart disease (CHD) diagnosed in 2005, CHD is the major cause of death in the American population. It is estimated that more than 90% of cardiovascular events will occur in individuals with at least one elevated cardiovascular risk factor (Greenland et al 2003), and around 8% in people with only borderline levels of multiple factors (Vasan et al 2005). Myocardial infarction (MI) risk factors include: hypertension; diabetes; abdominal obesity; dietary patterns; physical activity; alcohol consumption; psychosocial factors; and, in particular, abnormal lipids and smoking. The relative risk (RR) of acute MI as a result of smoking, or an adverse lipid profile, hypertension or diabetes is greater among younger (rather than older) individuals. Overall, current smokers face an almost 3-fold increase in nonfatal MI risk compared with that of never-smokers, irrespective of sex, geography, and variety of tobacco products or the type of cigarettes smoked. The risk has been shown to be directly proportional to the number of cigarettes smoked, with an odds ratio (OR) of 9.16 (99% CI 6.18–13.58) calculated for those who smoke more than 40 cigarettes a day, and no threshold or plateau in the dose-response curve indicating that there is a level of smoking that could be considered to be safe (Yusuf et al 2004). Cigarette smokers are also 10 times more likely to develop peripheral vascular disease and twice as likely to suffer a stroke than individuals who have never smoked (Centers for Disease Control and Prevention 2005).

Smoking cessation, however, can successfully and substantially reduce the number of premature deaths related to the adverse effects of tobacco smoking. Although the benefits of smoking cessation as a health intervention are greater the earlier they are introduced, smoking cessation is beneficial at any stage as it improves prognosis and quality of life, even after disease onset.

Public policies against tobacco smoking

Smoking is becoming increasingly less socially acceptable, and an increasing number of tobacco control policies have been introduced in the US and Europe in recent years. The implementation of anti-tobacco legislation is designed to minimize tobacco consumption and to create a more supportive environment for those smokers who would like to quit. The policies address multiple aspects of tobacco use and the tobacco industry, including: increased prices and taxes on tobacco products; tobacco advertising and sponsorship bans; regulation of tobacco products; inclusion of stronger health warnings on labels; restricting the sale of tobacco products to minors; smoking bans on public transport and in public areas, such as workplaces and also restaurants, bars, and pubs (Hu et al 1995; Fichtenberg et al 2002).

Public health campaigns have increased the public's awareness and understanding of the harmful health effects of both active and passive smoking. As a result, people's attitudes towards smoking are less tolerant, and there has been an increase in motivation and education for smokers to quit. There is increasing pressure from the public towards smoke-free environments, creating a need to provide effective support for those smokers attempting to quit. As smoking cessation is becoming an important component of national and international tobacco control policies and programs, and is an effective health intervention, programs that focus on prevention, diagnosis, and treatment of tobacco dependence must be a key part of primary care (WHO 2007).

Managing smoking cessation

In a survey of 4 countries, it was found that most smokers would like to quit (Hyland et al 2006). It is important to motivate smokers to act upon these desires and to encourage patients to stop as quickly and as early as possible. The essential features of smoking cessation treatment have been encapsulated in the "five As" (Fiore et al 2000):

1. Ask about smoking at every opportunity.
2. Advise all smokers to stop.
3. Assess their willingness to stop.
4. Assist the smoker to stop.
5. Arrange follow-up.

However, a simpler and more patient-centered approach to smoking cessation treatment may be to ask the patient about their previous attempts to quit and to evaluate the best options for future attempts. This can be effective even if the smoker is early in the motivational cycle, as many smokers

will express an interest in quitting if they are offered help (Pisinger et al 2005). Healthcare practitioners should also be mindful that most smoking cessation attempts fail and that patients dependent on tobacco, like those with other chronic diseases, need long-term support to achieve the ultimate goal of abstinence and to reduce tobacco-related health risks. The most effective methods of helping smokers to quit smoking combine pharmacotherapy and nonpharmacologic interventions (Fiore et al 2000; Lancaster et al 2000a; West et al 2000).

Nonpharmacologic interventions

Behavioral support is essential for the treatment of tobacco dependence. Health professionals should (minimally) be able to provide simple, brief advice (1–2 minutes) routinely to all smokers who use their services. Provision of more intensive advice (more than 20 minutes) is also useful for smokers who are motivated to quit, and additional reinforcement methods such as self-help manuals, videos or CD Roms can also be used. Smokers can seek support through a wide range of available channels, including the Internet, the telephone, and one-on-one or group counseling sessions.

Intensive behavioral support provided outside routine clinical care by appropriately trained smoking cessation counsellors is the most effective nonpharmacological intervention for smokers strongly motivated to stop smoking. Various psychological models can be used, most of which comprise a review of the patient's smoking history and their motivation to quit, identification of those situations that led to relapse during previous quit attempts, and advice on strategies for dealing with such situations should they occur during future quit attempts (Coleman 2004). In addition, general motivational techniques or motivational enhancement therapy can be used to instigate behavioral changes. These techniques aim to change the smoker's normal ambivalence to their habit by evaluating the importance of change and by reinforcing self-efficacy. Behavioral and cognitive therapy can be useful to help smokers recognize, avoid, and cope with difficult situations in which they are most likely to smoke (Fiore et al 2000; Le Foll et al 2002; Lancaster et al 2000b).

Smokers tend to consider health risks less than nonsmokers (Weinstein 1998), but pregnancy or severe health problems (eg, an MI) can lead to increased motivation to stop and can improve abstinence rates, especially when a specific tobacco-dependence intervention is provided. It is important for the clinician to tailor treatment to the individual patient and to offer them a personalized understanding of their health risks by explaining the connection between their symptoms of disease and their smoking, and by identifying the benefits that will be afforded should they stop smoking.

Pharmacotherapy

Three types of available pharmacological interventions for smoking cessation have demonstrated efficacy when used in conjunction with behavioral support: nicotine replacement therapy (NRT), bupropion, and varenicline (Fiore et al 2000; West et al 2000). Because no criteria are available to assess which pharmacotherapy will prove most effective in a given patient, treatment decisions are made at the discretion of the clinician and should take into account contraindications and the smoker's history and preference.

Other medications, especially nortryptiline and clonidine, are considered to be effective adjunct therapy in smoking cessation, but they remain second-line options at this time (Le Foll et al 2007).

Nicotine replacement therapy

NRT aims to alleviate nicotine withdrawal symptoms and to reduce smokers' desire to smoke. A variety of products are available (see Table 1). Those products with a shorter duration of action, in which blood-nicotine levels reach a peak within 20 minutes, allow patients to tailor better their nicotine intake via NRT according to their needs (Silagy et al 2004; Gries et al 1998; Gourlay et al 1997; Benowitz et al 1997).

To optimize the efficacy of NRT, it must be used sufficiently and correctly. Clinicians can improve efficacy if they provide patients with practical advice on how to adjust their nicotine substitution level depending on the clinical signs of toxic effects or persistence of withdrawal symptoms (eg, depressed mood, irritability, anxiety, craving, nervousness, impaired concentration). Clinicians can also calculate the optimal substitution dose of nicotine more precisely on the basis of the level of cotinine (inhaled nicotine per 24 hours = urinary cotinine [μg/L] x 0.013) in order to reach full replacement of their usual nicotine concentration (Lagrue et al 1994; Benowitz 1996; Larramendy et al 2004). Accurate calculation is particularly useful when titrating the correct dose in more severely addicted smokers and for pregnant women, adolescents, and cardiovascular patients in whom NRT can now be prescribed (Joseph et al 1996; Dempsey et al 2001; McRobbie et al 2001; Meine et al 2005; Moolchan et al 2005).

Use of patches (for background nicotine replacement) and gums or tablets (for urges) seems to improve the chance

Table 1 Summary of some key information relating to a selection of pharmacotherapies available for smoking cessation

Pharmacotherapy	Strength	Pharmacokinetic	Dosage
Nicotine patch	7, 14, 21 mg 5, 10, 15 mg	C_{max}: 4–9 hours	According to nicotine absorption
Nicotine gum/tablets	2, 4 mg	C_{max}: 20–30 min	9–12 to 23–30/day
Nicotine inhaler	10 mg/cartridge	C_{max}: 20–30 min	6–16 cartridge/day
Nicotine nasal spray	10 mg/ml	C_{max}: 10 min	8–40 doses/day
Bupropion hydrochloride	150 mg/tab	C_{max}: 2.5–3 hours $T_{1/2}$: 20 hours Steady-state: 5–8 days	150 mg every morning for 6 days, then 150 mg twice daily Delay of 8 hours between pills
Varenicline tartrate	0.5, 1 mg/tab	C_{max}: 3–4 hours $T_{1/2}$:24 hours Steady-state: 4 days	0.5 mg once daily for 3 days, then 0.5 mg twice daily for 4 days and then 1 mg twice daily

of quitting successfully. Several patches can be used simultaneously on the skin of patients with a high level of physical dependence. Local skin irritation and contact sensitization can be reduced by moving the application site daily, and sleep disturbance can be decreased by removing the patch before bed. There are no significant differences between 24-hour and 16-hour patches in terms of quit rates and withdrawal symptoms.

In addition to providing nicotine replacement, the NRT inhaler acts as a substitute for the behavioral aspect of cigarette smoking, but it requires deep and frequent inhalation in order to replace nicotine concentrations in the blood significantly (Corelli et al 2006; Frishman et al 2006).

NRT should be prescribed as monotherapy initially, with subsequent combination therapy (consisting of various combinations of NRT products) if monotherapy proves unsuccessful.

The RR of abstinence when using any form of NRT product is 1.58 (95% CI 1.50–1.66) relative to control. The RR for each product varies from 1.43 (CI 1.33–1.53) for nicotine gum and 1.66 (CI 1.53–1.81) for the patch, to 1.90 (CI 1.36–2.67) for the inhaler and 2.00 (CI 1.63–2.45) for oral tablets. NRT products, therefore, increase the probability of successful cessation by 50%–70% depending on the exact product used (Stead et al 2008).

Bupropion

Bupropion was originally licensed as an atypical anti-depressant, but has been proven to be an effective non-nicotine medication for use in smoking cessation (Nomikis et al 1989; Hurt et al 1997; Jorenby 2002). It inhibits the reuptake of both dopamine and norepinephrine in the central nervous system (Nomikos et al 1989). Its dopaminergic activity on the pleasure and reward pathways in the mesolimbic system and the nucleus accumbens could explain its success in reducing nicotine craving and the symptoms of withdrawal. It may also function as a nicotine acetylcholine receptor antagonist, which may be critical for smoking cessation (Slemmer et al 2000).

Bupropion's effect on nicotine dependence appears to be quite separate from its antidepressant effect, as it has been shown to be effective in patients who have no depressive symptoms.

Insomnia, which has been reported in 30–40% of patients taking bupropion, can be reduced by taking the evening dose more than 4 hours before bed. There are also suggestions that bupropion increases risk of suicide, but this remains unproven at this time.

As treatment-emergent hypertension has been reported, especially when bupropion is used in combination with the NRT patch, it may be prudent to take into consideration blood pressure measurements. Bupropion is useful either as monotherapy or in combination with NRT products. Combination therapy can be particularly relevant when dealing with smokers who have high levels of nicotine dependence and in those with a history of psychiatric problems. It can also be used to prevent relapse in patients who have failed on prior therapy (Hays et al 2001). Attenuation of weight

Duration	Adverse effects (not exhaustive)	Contraindications/Precautions (not exhaustive)
3 months Maintenance up to 12 months	Local skin reaction, insomnia	Hairless, clean, dry, low friction skin areas
Up to 12 weeks	Mouth soreness, dyspepsia, jaw ache, hiccups,	Intermittently, slowly chewed To avoid acidic drink for 15 min before use
Up to 6 months	Mouth and throat irritation	
3–6 months	Nasal irritation	
7–9 weeks Maintenance up to 6 months	Insomnia, dry mouth, seizure (0.1%)	History of seizure, eating disorders, serious head trauma, adolescents below 18 years and pregnant women, concomitant intake of monoamine oxidase inhibitors
12 weeks Maintenance up to a further 12 weeks (if required)	Nausea (30%), insomnia, abnormal dreams, headache	Adolescents below 18 years and pregnant women

gain was observed in abstinent smokers during bupropion treatment, and the agent may also be offered to patients who are concerned about post-cessation weight gain.

A meta-analysis of several trials shows that bupropion nearly doubles cessation rates with an OR of 1.94 (95% CI 1.72–2.19), a similar efficacy to NRT (Hughes et al 2007).

Varenicline

Varenicline is the most recent drug developed for specific use in smoking cessation. It has a different mechanism of action to the other available smoking cessation products and appears to be an improvement on existing treatments for tobacco dependence.

Pharmacology

Chemically and pharmacologically related to cytisine, varenicline is a selective partial agonist of the $\alpha4\beta2$ nicotinic receptor and can act like an agonist or an antagonist, depending on the state of the receptor. Thus it is designed to work on the same receptor in the brain as nicotine to help relieve the craving and withdrawal symptoms associated with giving up smoking, while at the same time block the satisfying effects of nicotine.

As a partial agonist, varenicline stimulates a moderate and sustained release of dopamine in the shell of the nucleus accumbens, thereby counteracting the low dopamine levels and withdrawal symptoms observed during smoking cessation. Furthermore its competitive binding to the nicotinic receptor should prevent the nicotine-induced dopaminergic activation in the event that the patient smokes, making it useful to decrease the reinforcing effects of nicotine (Coe et al 2005). Varenicline has also been described as a full agonist of the monomeric $\alpha7$ receptor (Mihalak et al 2006), suggesting that the relationship between the binding affinity and the functional potency of varenicline at different receptors requires further examination.

A total treatment duration of 12 weeks is usually recommended (Nides et al 2006). If a patient who has managed to stop smoking at the end of the treatment period lacks confidence about remaining abstinent, it is worth considering treatment continuation, bearing in mind the high smoking relapse rates. Results of a long-term safety study indicate that varenicline is well tolerated and has a favorable safety profile for administration of up to 1 year (Williams et al 2007).

Varenicline is highly absorbed after oral administration; it is not affected by food intake and is not significantly bounded to protein. Less than 10% of the compound is metabolized in the liver and it is primarily excreted (unchanged) in the urine. However, precautions should be taken with patients who have severe renal impairment. It has a half-life of 17–30 hours (Faessel et al 2006a, b; Obach et al 2006). No significant drug-drug interactions have so far been identified with the use of varenicline, and there do not appear to be contraindications at this time.

Efficacy

Several double-blind, randomized, controlled clinical trials (RCT) of varenicline have been carried out involving almost

5,000 smoking cessation participants, 2,451 of whom received varenicline (Cahill et al 2007). One relapse prevention trial has been carried out, and while all cessation trials assessed varenicline against placebo, 3 also included a bupropion experimental arm. The period of follow-up in the cessation trials was 12, 24, and 52 weeks.

The RCTs demonstrated that varenicline has superior efficacy compared with placebo and bupropion. The pooled OR for validated continuous abstinence at 12 months for varenicline versus placebo was 3.22 (95% CI 2.43–4.27) and 1.66 (95% CI 1.28–2.16) for varenicline versus bupropion (Gonzales et al 2006; Jorenby et al 2006; Nides et al 2006; Oncken et al 2006). The relapse prevention trial concluded that varenicline offers significant benefit versus placebo with an OR for validated continuous abstinence of 1.34 (95% CI 1.06–1.69) (Tonstad et al 2006).

A recent study has also suggested that varenicline is more effective than NRT in short-term routine treatment of tobacco dependence, with a benefit similar to that seen for varenicline over bupropion in the previous RCTs. The study also demonstrated that the efficacy of varenicline was similar in both patients with and without mental illness (Stapleton et al 2008). The efficacy and safety of varenicline used in combination with bupropion or NRT is not recommended at this time as no trials in this area have yet been carried out.

Safety

In clinical trials, varenicline exhibited a favorable safety profile compared with placebo and was well tolerated at doses up to (and including) 2 mg/day in healthy adult smokers (see Table 1). The nausea was generally mild to moderate and often diminished over time or in response to a dose reduction, or administration with food (Gonzales et al 2006; Jorenby et al 2006). Although the side effects associated with treatment were relatively common, there was no difference in patients withdrawing from treatment between the varenicline and placebo study arms. No treatment-related deaths were reported in any of the RCTs (Cahill et al 2007).

Suicidal ideation and suicide attempts have recently been reported in patients who stopped smoking while taking varenicline. Although it is difficult to establish whether these events are attributable to varenicline or the smoking cessation attempt itself (which can be associated with depressed mood and sometimes suicidal thoughts) the European regulatory authority recommend that: "clinicians should be aware of the possible emergence of significant depressive symptomatology in patients undergoing a smoking cessation attempt, and should advise patients accordingly" (Pfizer 2008).

Local tobacco smoking cessation management

Tobacco smoking is a chronic, relapsing medical condition that requires long-term management. As there are numerous time constraints placed on physicians, patients should be offered the option of being referred to a specialist smoking cessation service. In our treatment program, behavioral support is given in combination with pharmacological therapy and clinical decisions are made with reference to published literature (for choice of therapy, optimum dose) and the patient's medical history. As reported in several recommendations, the initial counseling session is scheduled to be long enough to carry out a thorough interview of the patient and to develop a solid treatment plan. In our center, the first patient session requires 60 minutes. As follow-up is critical to the success of treatment, provision is made to ensure smokers who want to give up receive regular support sessions, which are either carried out face-to-face or over the phone.

Because there are no clear-cut criteria to identify whether a patient will benefit from a particular therapy, the medication is selected for each patient with full consideration of: their current medical conditions; contraindications and potential adverse effects of each medication; their individual preference for a given treatment; previous use of smoking cessation aids; level of tobacco dependence, and any concerns about weight gain. All smokers who have previously relapsed when attempting to quit are questioned about their prior use of pharmacotherapy and their perceptions of the treatment options. Even light smokers and those who smoke socially who have failed in previous attempts to quit can benefit from pharmacotherapy.

In patients who voice positive experiences with a given product, it may be appropriate to prescribe treatment with the same agent, but with consideration given to increasing the dose, frequency, or duration of therapy. However, in patients who report negative experiences with a particular agent, an alternative treatment choice should be selected. There is currently no evidence to indicate that one medication is the most effective for all the smokers attempting to quit.

NRT in its various formulations remains a well-tolerated and effective approach to aiding smoking cessation. It is the only drug treatment available for pregnant women and adolescents who wish to stop smoking but who have failed previously and who have experienced urges and withdrawal symptoms. By employing the concept of therapeutic drug

monitoring, urinary cotinine concentrations are used in these patients to tailor the nicotine replacement dose so that it approaches full replacement of the nicotine that would normally be inhaled through smoking. By achieving the correct target blood concentration, pharmacotherapy can be optimized.

It may be appropriate to use higher doses of nicotine replacement products in heavy smokers to relieve their nicotine withdrawal symptoms sufficiently (eg, use multiple patches at one time). In our clinic, one form of smoking cessation aid is seldom used alone; rather NRT patches tend to be used alongside self-administered forms of NRT, especially in patients who are unable to stop smoking using a single, first-line therapy. Use of any short-acting NRT product is recommended as often as is necessary in order to control intermittent withdrawal symptoms or cravings. Owing to the central nervous system tolerance that most smokers have to nicotine, over-replacement is rare.

As NRT requires frequent dosing, or non-traditional routes of administration, time is taken to explain the proper use of each product to patients. It is important to schedule follow-up office visits or phone calls to monitor response to treatment. Although several durations of treatment have been proposed, no optimal length of treatment has been clearly established and treatment should be continued as long as is determined necessary for each patient. Treatment duration, for example, may need to be longer in those who are heavily dependent on tobacco. In pregnant women who have previously failed to quit smoking with the support of behavioral therapy, NRT is proposed in the acute forms, eg, gums, tablets, or inhaler. If necessary a patch can be used, but it is recommended that it is removed before sleep to minimize exposure of the fetus to nicotine. The same advice would apply to women who are breast-feeding.

Although NRT remains widely used for smoking cessation, some people prefer a treatment that does not use nicotine. Bupropion provides smokers with an alternative treatment option, especially if they are found to be intolerant to varenicline. For smokers concerned about potential weight gain, it might be preferable to use bupropion as it has been shown to offer the greatest attenuation of weight gain during treatment. Buproprion is combined with NRT on a patient-by-patient basis. For patients with more severe nicotine dependence, more than 2 products are often used simultaneously.

Varenicline offers a new option for smoking cessation and problems of relapse. It could be a first-line option for tobacco smoking cessation if the patient expresses a particular preference, and it is particularly useful in smokers who cannot tolerate adverse events related to bupropion or NRT, in those in whom these medications are contraindicated, and in patients who have already tried and failed on other smoking cessation pharmacotherapies. Furthermore, the mixed agonist-antagonist effects of varenicline appear to reduce the psychogenic rewards associated with smoking, while also relieving nicotine craving and withdrawal symptoms during abstinence.

As successful smoking cessation is improved with adequate support, smokers prescribed varenicline receive a patient support plan that they can customize as they try to quit to help identify and address their individual behavioral triggers. Varenicline should not be prescribed in addition to other smoking cessation medications. The treatment is easy for patients who have difficulty adhering to multiple doses of medications throughout the day, and is also attractive to patients who desire a simplified regimen. Apart from the nausea, which tends to pass or can be minimized through dose reduction and advice on eating, varenicline is usually well tolerated. Patients at our clinic are advised to take varenicline with a glass of water and after, or during, a meal to reduce such side effects. It is also recommended that the second pill is taken at dinner rather than before bed in order to reduce insomnia and avoid disturbed dreams. At the end of the treatment period, therapy tends to be extended in patients who have only recently managed to quit, in whom the quit attempt has not stabilized, or in those who have experienced minor relapses.

Conclusion

Tobacco smoking is highly prevalent throughout the world and is, perhaps, the greatest modifiable risk factor for increased morbidity and mortality. Smoking cessation is associated with immediate and long-term health benefits, resulting in improved general health and a reduced risk of smoking-related diseases. As physicians tend to deal with most smokers fairly regularly, they have substantial opportunity to influence their smoking behavior, and are in a unique position to be able to help with treatment. The likelihood that a smoker will be successful in their quit attempt depends on several factors, at the core of which is their motivation. If they are not motivated to quit, an important step is to devise strategies to increase their willingness to give up and education should be given on the impacts smoking can have on health. As such, health professionals should be familiar with smoking cessation strategies and should promote cessation as an effective health intervention to patients who smoke. All physicians should ensure that they are aware of the different treatment options available, and they should offer

these regularly to their patients. Although medications can be effective in reducing withdrawal symptoms and improving treatment outcomes, a combination of pharmacotherapy and behavioral counseling is more likely to increase abstinence rates. Several medications are available with demonstrated efficacy is helping smokers to quit: NRT, bupropion, and varenicline. As reported in the literature, varenicline seems to be the most effective treatment option currently available, and could be prescribed according to the patient's preference and medical history.

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