

REVIEW ARTICLE

PHARMACOLOGICAL TREATMENT OF SMOKING CESSATION

By

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INTRODUCTION

Tobacco is a unique product. It is the only product that kills its consumers when used as recommended by the manufacturer. It is addictive, deadly yet legal. Smoking is a known cause of multiple cancers, heart disease, stroke, complications of pregnancy, chronic obstructive pulmonary disease (COPD), and many other diseases. In addition, recent research has documented the substantial health dangers of involuntary exposure to tobacco smoke. Despite these health dangers and the public's awareness of those dangers, tobacco use remains surprisingly prevalent.⁽¹⁾

Tobacco dependence displays many features of a chronic disease. Only a minority of tobacco users achieve permanent abstinence in an initial quit attempt. The majorities of users persist in tobacco use for many years and typically cycle through multiple periods of remission and relapse. A failure to appreciate the chronic nature of tobacco dependence impedes clinicians' consistent assessment and treatment of the tobacco user over time.⁽²⁾

Modern approaches to treating tobacco use and dependence should reflect the chronicity of tobacco dependence. A chronic disease model recognizes the long-term nature of the disorder with an expectation that patients may have periods of relapse and remission. If tobacco dependence is recognized as a chronic disease, clinicians will better understand the relapsing nature of the condition and the requirement for ongoing, rather than just acute care. The existence of numerous effective treatments gives the clinician and patient many options should repeated quit attempts be needed.⁽²⁾

A chronic disease model emphasizes for clinicians the importance of continued patient education, counseling, and advice over time. Although most clinicians are comfortable in counseling their patients about other chronic diseases such as diabetes, hypertension, or hyperlipidemia, many believe that they are less effective in providing counseling to patients who use tobacco.⁽³⁾ As with these other chronic disorders, clinicians should be encouraged to provide tobacco-dependent patients with brief advice, counseling, and appropriate medication. It is important for clinicians to know that assessing and treating tobacco use generally leads to greater patient satisfaction with health care.⁽⁴⁾ Moreover, policy changes (e.g., tax increases, smoke-free ordinances) often lead smokers to seek treatment for this chronic disease.

Although this should aid clinicians in the assessment and treatment of tobacco users, clinicians should remain cognizant that relapse is likely and that it reflects the chronic nature of dependence. Most smokers who ultimately quit smoking experience episodes of relapse on the way to success. Relapse should not discourage the clinicians or the tobacco user from renewed quit attempts.

Treatment – Pharmacologic Therapies:

Nicotine replacement therapy, bupropion hydrochloride and varenicline have been shown to significantly improve cessation rates. Therefore, pharmacologic therapy should be recommended to all patients except in the presence of specific contraindications.

The following section discusses choosing among the various forms of nicotine replacement therapy, burpropion, varenicline and other agent.

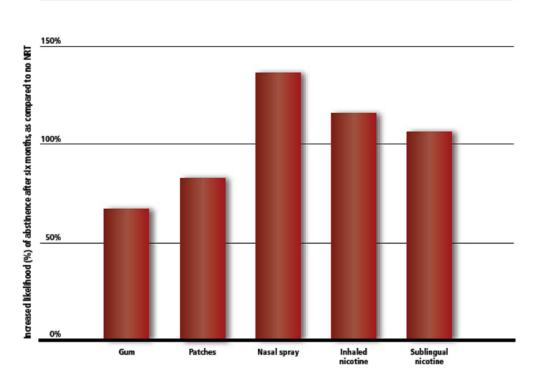
Nicotine replacement therapies (NRT): has been used for many years, but alternative methods of delivery continue to be developed and new combinations are being tried.

Nicotine replacement therapy has been shown to help people stop smoking. It is extremely safe and highly cost effective. Its main mechanism of action is to reduce the severity of withdrawal symptoms associated with smoking cessation. Although NRT does not completely relieve withdrawal symptoms, it makes the experience of stopping less unpleasant.

All types of NRT available deliver nicotine in different ways, but there is no evidence of any difference in effectiveness between them. Also there is no evidence that matching particular products with particular types of people who smoke makes any difference in outcome. Product selection should be guided by the client preference.⁽⁵⁾ NRT can be safely used by people with cardiovascular diseases.⁽⁶⁾

The use of NRT in pregnancy carries a small potential risk to the fetus, but NRT is far safer than smoking. Expert opinion suggests that NRT can be used by women who are pregnant once they have been advised of and have assessed the potential risks and benefits.⁽⁷⁾

There is insufficient evidence that the use of NRT by young people who smoke improves continuous 6-month abstinence rates. Nevertheless, expert opinion is that NRT may be considered for use by dependent adolescents who want to stop smoking.⁽⁸⁾



NICOTINE REPLACEMENT THERAPY (NRT) CAN DOUBLE QUIT RATES

Source: Silagy C, Lancaster T, Stead L, Mant D, Fowler G. Nicotine replacement therapy for smoking cessation. Cochrane Database System Review 2004;(3):CD000146.

NRT is safe to use repeatedly with other attempts to stop smoking by people who have tried to stop but have not succeeded in the past.⁽⁹⁾

Pharmacologic properties of nicotine: a smoker absorbs 1-3 mg nicotine per cigarette regardless of nicotine-yield ratings on the box. Nicotine results in increased release of catecholamines, vasopressin, endorphins, cortisol, and ACTH. These biochemical changes lead to addiction as smokers experience pleasure, increased arousal, decreased anxiety and decreased hunger with increased metabolic rate. Within hours of cessation of smoking, smokers begin to experience the nicotine withdrawal syndrome that peaks at 48 hours. Symptoms of nicotine withdrawal include: craving, anxiety, restlessness, irritability, depressed mood, increased appetite, and difficulty concentrating.

Nicotine replacement therapy:

- The different formulation of nicotine replacement therapy provide alternate methods for delivery and have slightly different onset of action and duration.
- Nicotine replacement therapy works by making it easier to abstain from tobacco by partially replacing the nicotine previously obtained from tobacco. At least 3 mechanisms by which NRT could be effective include:
 - 1. Reducing either general withdrawal symptom, thus allowing people to learn without cigarettes.
 - 2. Reducing the reinforcing effects of tobaccodelivered nicotine.
 - 3. Providing some psychological effects on mood and attention states.
- Nicotine replacement medications should not be viewed as stand-alone medications that make people stop smoking. Reassurance and guidance from health professionals can be critical to achieve and sustain abstinence.
- Contraindications to NRT: may include hypersensitivity to nicotine, recent myocardial infarction (within three months), unstable or progressive angina pectoris, prinzmetal's variant angina, severe cardiac arrhythmias or stroke in acute phase.
- Use of NRT in pregnant and breastfeeding women: manufacturers' information states that nicotine passes to the fetus and affects its breathing movements and circulation, and that nicotine passes freely into breast milk in quantities that may affect the child even with therapeutic doses and that ideally nicotine should be

avoided during breast-feeding. However, NRT should be considered when pregnant or breastfeeding woman is unable to quit, and when the likelihood of quitting, with its potential benefits, outweighs the risks of NRT and potential continued smoking.

• Suggested criteria for prescribing NRT:

The smokers:

- Is motivated to quit.
- Agree to 100 percent cessation, quit date, and followup.
 - Smoking more than 10 cigarettes per day.
 - Understands the benefits and risks and agree to use NRT.

• Steps for providing NRT:

- 1. Assess level of addiction/ motivation.
- 2. Discuss different types of NRT.
- 3. Consider contraindications/factors altering dosing.
- 4. Prescribe appropriate dose of NRT, reviewing use and common side-effects.
- Underscore absolutely no smoking while on NRT both to avoid overdose symptoms and because studies have shown that smoking while using NRT markedly decreases likelihood of successful quit attempt.
- 6. Ensure follow-up within three to five days to assess correct dosing and possible effects.
- 7. Ensure person receive further follow-up to increase likelihood of success.
- 8. More than eight weeks treatment with NRT is not recommended, as there is no evidence that treatment beyond eight to twelve weeks increase the success rate.^(10,11)
- **Overdose symptoms of NRT:** upset stomach/ abdominal pain, nausea/vomiting, diarrhea, dizziness, tachycardia (racing heart), change in hearing/vision, bad headache, flushing, confusion, hypotension.

• Suggested NRT dose for different daily smoking level:

Type of NRT	<10 cig/day	10-20 cig/day	>20 cig/day
Patch	None	14mg (Nicotinell) 10 mg (Nicorette)	21mg (Nicotinell) 15 mg (Nicorette)
Gum	None	2mg gum, 8-12/day	4mg gum, 8-12/day
Nasal Spray	None	1mg (2sprays)each hour 8-12 times per day	1-4mg (2-6 sprays)each hour 8-12 times per day
Inhaler	none	6-12cartridges/day	Not recommended

Source: The National Advisory Committee on Health and Disability Wellington, New Zealand: Guidelines for smoking cessation March 2004, Page 18.

- *Withdrawal symptoms of NRT:* Craving, irritability, anxiety, sleep disturbance, impaired concentration, hunger, weight gain and depression.
- **Recommendation:** start with a higher dose for two to four weeks, and then decrease to next dose for two weeks and so on. No studies have shown that treatment beyond eight to 12 weeks increases treatment effectiveness.

Transdermal nicotine patches:

- Nicotine patches deliver nicotine through the skin at a relatively steady rate. Currently, 4 patch formulations are on the market; they vary widely in their design, pharmacokinetics, and duration of wear (ie, 24- and 16-h wear). For some products, progressively lower doses can be used to provide weaning over a period of several weeks or longer to enable gradual adjustment to lower nicotine levels and ultimately to a nicotine-free state. Smokers who use more than 10 cigarettes per day should use the 21-mg/day patch for the first 6 weeks, move to the 14-mg/day strength for 2 weeks, and then use the 7-mg dose for the final 2 weeks. Nicotine patches have higher compliance than other NRT products but may not adequately protect against craving provoked by smoking-related stimuli. For breakthrough cravings not adequately controlled by trans-dermal nicotine alone, acute therapies may be added.
- The patch should be applied at the same time each day, usually at the beginning of the day. The patch should be applied to a non-hair, clean and dry area above the waist front or back or upper part of arm. Don't put the patch on a burned, broken, cut or irritated skin in any way.

- The 16 hour patch is recommended for pregnant women where the use of a patch is judged appropriate.
- There is no evidence that "weaning" patches are necessary people can stop from a full strength patch straight away. However, some people may prefer to "wean' themselves off.
- Important side-effects of nicotine patch include skin irritation, itching, abnormal dreams or difficulty sleeping, diarrhea and indigestion. These often are reduced over time. It is normal for the patch to cause some tingling or mild burning when first applied. This should go away in an hour. The skin under the patch may be red for a day after removal. If this persists or becomes swollen, discontinuation or dose adjustment can be done. Undesirable effects are headache, gastro-intestinal discomfort, nausea, vomiting, erythema and reversible atrial fibrillation.

Nicotine gum:

• First available in the 1980s, nicotine polacrilex (nicotine gum) is available without a prescription. The gum is available in doses: 2 mg and 4 mg, delivering approximately 1 mg and 2 mg of nicotine. Users are instructed to use a piece of gum every 1-2 hours for the first 6 weeks, then to reduce use to one piece every 2-4 hours for 3 weeks, and one piece every 4-8 hours for 3 weeks. In highly dependent smokers, the 4-mg gum is superior to the 2-mg gum. Since about 50% of the nicotine in gum is absorbed, a fixed schedule of 10 pieces per day, a smoker receives about 10 mg or 20 mg of nicotine per day using the 2-mg gum, respectively.

- The slow absorption of nicotine from the gum doses does not produce the extremely high levels of nicotine. Acidic beverages interfere with buccal absorption of nicotine; patients should avoid acidic beverages (eg, soda, coffee) for 15 minutes before and during chewing gum except water. Nicotine gum chewing may cause jaw soreness; therefore, the smoker should chew the gum to release nicotine, and then move the gum between the cheek and gum. The gum can also cause a mild burning sensation in the mouth and throat, which may be undesirable.
- The gum is placed in the mouth, moisten and bite down once or twice to release the peppery taste, then "parked" between the cheek and gum. The gum should be slowly and intermittently chewed and parked for about 30 minutes on fixed schedule (one piece every one to two hours) for eight weeks. This medicine should not be chewed like regular chewing gum

Lozenge: Available in 2- and 4-mg formulations since 2002, nicotine from the lozenge is absorbed slowly through the buccal mucosa. Generally, patients should use 1 lozenge every 1-2 hours during the first 6 weeks of treatment, using a minimum of 9 lozenges/day, then decrease lozenge use to 1 lozenge every 2-4 hours during weeks 7-9, and then decrease to 1 lozenge every 4-8 hours during weeks 10-12. The lozenge should not be chewed, and the amount of nicotine absorbed per lozenge is somewhat higher than that delivered by gum.

Inhaler:

- The inhaler is a small plastic tube containing a replaceable nicotine cartridge.
- Currently marketed as a prescription medication in the United States, the inhaler consists of a mouthpiece and a plastic cartridge containing nicotine. When the inhaler is "puffed," nicotine is drawn into the mouth of the smoker and satisfies the behavioral aspects of smoking, namely, the hand-to-mouth ritual.
- Each inhaler cartridge contains 10 mg nicotine, of which 4 mg can be delivered and 2 mg are absorbed. Nicotine is not delivered to the bronchi or lungs, but rather it is deposited and absorbed in the mouth, like nicotine gum. Most people use between 6 and 16 cartridges a day, the recommended duration of treatment is 3 months, after which patients may be weaned by gradual reduction over the following 6-12 weeks.
- The user should puff on the inhaler every 20 minutes. After four 20-minutes puffing sessions, the cartridge should be changed.

• In cold weather, it is advisable to keep the inhaler warm to help the nicotine vapor be released from the cartridge.

Nasal spray: Marketed as a prescription medication, the nasal spray delivers nicotine more rapidly than other NRTs and relieves acute craving. The multidose bottle with a pump delivers 0.5 mg of nicotine per $50-\mu$ L squirt. Each dose consists of 2 squirts, one to each nostril. The dose of nasal spray should be individualized for each patient based on the patient's level of nicotine dependence. Most patients start with 1 or 2 doses per hour, which may be increased up to the maximum of 40 doses per day.

Sublingual tablet: A small nicotine tablet has been developed. The product is designed to be held under the tongue, where the nicotine in the tablet is absorbed sublingually. The levels of nicotine obtained by use of the 2-mg tablet and 2-mg nicotine gum are similar. It is recommended that smokers use the product for at least 12 weeks, after that the number of tablets used is gradually tapered. The tablet is designed to dissolve completely.

Bupropion (Zyban):

- Bupropion is an antidepressant medication that almost doubles the chances of long-term abstinence from smoking. Its action in helping people to stop smoking is independent of its antidepressant effects, so it works even in people without a history of depression. Like NRT, it acts to reduce the severity of withdrawal symptoms, but it may also have other actions that help people stop. Evidence that bupropion is more or less effective than NRT or nortriptyline is limited.
- Bupropion acts by alleviating some of the symptoms of nicotine withdrawal, which includes depression. One clinical trial demonstrated that highly nicotinedependent smokers who receive bupropion are more likely to experience a decrease in depressive symptoms during active treatment. Like NRT products, bupropion has been endorsed by the US Clinical Practice Guideline as a first-line therapy.⁽¹²⁾
- It has a number of action that are thought to contribute to its ability to help smokers quit. These include inhibition of neuronal re-uptake of dopamine and noradrenalin, non-competitive inhibition of the nicotinic acetylcholine receptor and effects on serotonin re-uptake.⁽¹³⁾ From a clinical perspective, it help smokers by reducing the severity of withdrawal symptoms, including the desire or urge to smoke, thereby making the quit attempt easier and success more likely.

- Combining the results of over twenty studies it showed that compared to placebo, bupropion approximately double the chances of remaining abstinent for a year.⁽¹⁴⁾
- Bupropion has been shown to approximately double rates of cessation compared with placebo, and the medication is equally effective for men and women. It has also been shown that bupropion combined with nicotine replacement medications may increase cessation rates relative to bupropion alone. The recommended and maximum dose of bupropion is 300 mg/day, given as 150 mg twice daily, keeping at least 8 hours between each dose. The quit date should be set between the 8th and 14th day. The person continues to smoke as up to their quit date and then stop completely, aiming not to have a single puff after that.
- **Older people:** 150mg once daily dose is recommended, similar to hepatic and renal insufficiency patients.
- **Side effects:** Dry mouth and insomnia are the most common adverse events associated with use. A very small risk of seizure exists.
- Contraindication: seizure disorder or history, CNS tumors, abrupt alcohol or sedative withdrawal, anorexia nervosa, monoamine oxidase inhibitors within 14 days and lactation.
- **Precautions:** hepatic, renal impairment, hepatic cirrhosis, predisposition to seizures, including a history of head trauma, diabetes, history of psychiatric illness, especially bipolar disorder, autoimmunity, Epstein Barr virus, HIV, older people, pregnancy and children under 18 years.

Varenicline (Champix) is a partial agonist selective for alpha4, beta2 nicotinic acetylcholine receptors. Action is thought to result from activity at a nicotinic receptor subtype, where its binding produces agonist activity while simultaneously preventing nicotine binding. Agonistic activity is significantly lower than nicotine. Also elicits moderate affinity for 5-HT3 receptors. Maximum plasma concentrations occur within 3-4 h after oral administration. Following regular dosing, steady state is reached within 4 days. Initiate one week before date chosen to stop smokingDays 1-3: 0.5 mg after meal.Days 4-7: 0.5 mg twice daily after meal.Day to end of treatment: 1 mg twice daily after meal. Continue treatment for 12 w; take tablet with full glass of water

For patients who have successfully stopped smoking at the end of 12 weeks an additional course of 12 weeks treatment with varenicline at 1 mg twice daily may be considered.

In two randomized controlled trial to compare the effect of varenicline versus sustained-release Burpropion and placebo for smoking cessation, Varenicline was significantly more efficacious than bupropion SR at the end of 12 weeks of drug treatment and at 24 weeks followup.^(15,16)

Other medications: Besides NRT products and bupropion, nortriptyline and clonidine are endorsed by the US Clinical Practice Guideline as second-line therapies.

Nortriptyline: It is a tricyclic antidepressant that has been shown to be as effective as bupropion and NRT in adding smoking cessation. Its action in helping people to stop smoking is independent of its antidepressant effects, and it works in those without a history of depression. Nortriptyline in combination with transdermal nicotine was also shown to enhance the cessation rates above levels seen with transdermal nicotine alone. The tricyclic antidepressant doxepin has also been shown in a small human study to improve cessation rates.

The most commonly encountered side effects associated with nortriptyline include fast heart rate, blurred vision, urinary retention, dry mouth, constipation, weight gain or loss, and low blood pressure on standing, GI upset, bone marrow depression, confusion, delusion, hallucination, anxiety, extrapyramidal symptoms

Its main advantages are its low cost and the ability to monitor therapeutic blood levels.

Dose: initially 25mg/day, begin 10-28 days before quit date; increase gradually to 75-100mg/day over 10 days – 5 weeks; continue for total of 12 week. The dose should be tapered at the end of treatment to avoid withdrawal symptoms that may occur if it is stopped abruptly. There is limited evidence of any benefits of extending treatment past 3 months.

Clonidine: An alpha-2-noradrenergic agonist used to treat hypertension, clonidine has been shown to diminish symptoms of both opiate and alcohol withdrawal symptoms. In one study of heavy smokers who had failed in previous quit attempts it showed that those treated with clonidine had twice the rate of abstinence as those treated with placebo at the end of the 4-week treatment, and the effect persisted for the 6-month follow-up period. Although clonidine may be efficacious in the treatment of nicotine addiction, the conditions under which it is most appropriately used are not well defined. The most common side effects of clonidine are constipation, dizziness, drowsiness, dryness of mouth, and unusual tiredness or weakness.

Pharmacotherapy selection NRT: patch, gum, Varenicline **Bupropion** inhaler, lozenge, nasal spray Choose monotherapy or combination pharmacotherapy Choose type based on: Choose combination of pharmacotherapy based Evidence 1. on: 2. Patient preference Failed attempt with monotherapy 1. 3. Patient experience breakthrough cravings 2. Patient needs 4. Level of dependence 3. 5. Patient history Multiple failed attempts 4. Patient clinical suitability 6. 5. Experiencing nicotine withdrawal. 7. Potential drug interaction/side effect **Caution:** Patient with dual diagnosis What specific combinations (medical, psychiatric,...) of pharmacotherapy should consider: I use? For all the above: monitor carefully Contraindications 1. Frequency of monitoring determined by: 2 or more form of 1. 2. Specific NRT Patient needs 1. pharmacotherapy Bupropion + NRT 2. Type of pharmacotherapy 2. 3. Dual purpose medications Figure: 1 See the following guide on using this algorithm

Algorithm for Pharmacotherapy selection

Guide for using the algorithm in (Fig. 1)

Factors to consider in prescribing pharmacotherapy

Three distinct types of pharmacotherapy have demonstrated efficacy for smoking cessation: (a) nicotine replacement therapy (including patch, gum, inhaler, lozenge, nasal spray), (b) bupropion and (c) varenicline (for a description of these pharmacotherapy, including dose and side effects/drug interactions.) Selecting a particular type of pharmacotherapy should be guided by the following seven factors:

1. Evidence

The importance of evidence-based medicine is the top priority in considering which form of pharmacotherapy to prescribe or recommend to a patient. The decision to prescribe smoking cessation medications needs to be based on evidence of effectiveness and safety.

2. Patient preference

Patient preference is an important priority in facilitating adherence to the treatment protocol. There is no value in prescribing or recommending a medication that a patient will not take. "It is essential that the patient be comfortable with the decision, have reasonable expectations for product efficacy, and have confidence in their ability to use the medication appropriately". Preference is particularly important if a patient does not want to use a specific product. However, patient preference can be modified through an informed and shared decisionmaking process between the clinician and patient.

3. Patient experience

The patient's expectation of success is exceedingly important in determining actual success. Expectations are often informed by experience. Therefore, a patient's experience with smoking cessation attempts and use of pharmacotherapy needs to be a significant factor in influencing choice of pharmacotherapy. "A clinician must understand what the patient has tried and why the patient did not succeed". If the patient was successful with a particular medication for a period of time, it may be prudent to try the same medication again; if unsuccessful with a particular medication, then probably should not use again.

4. Patient needs

Because there is little evidence-based information to guide tailoring of specific pharmacotherapy to specific patients, patient needs are vital. Consideration of patient needs is important in determining their willingness to use medications, the ease of use of various smoking cessation products and likelihood of compliance. Other patient needs to take into account before prescribing or recommending a particular pharmacotherapy include: extent and severity of cravings, situations or times when cravings are strongest, triggers for smoking, specific hurdles to overcome, etc.

5. Patient history

"Patient history provides the framework within which I can prescribe". Many patients have comorbidities (medical, psychiatric, alcohol/drug abuse) which need to be taken into account. For example, a patient with a history of alcohol abuse or seizures would be excluded from bupropion use. Smoking history, past quit attempts and experience with pharmacotherapy are all factors influencing the decision of pharmacotherapy choice.

6. Patient clinical suitability for pharmacotherapy

Some patients may not be suitable for pharmacotherapy interventions and potential contraindications need to be considered. Generally, pharmacotherapy would not be recommended for patients having a low level of nicotine dependence. In addition, a patient may prefer a nonpharmacological approach to treatment.

7. Potential drug interactions/side effects

Issues of safety are fundamental in determining choice of pharmacotherapy. Contraindications, use of other medications, and the side effect profile all need to be considered. However, this is generally a minor problem with cessation drugs. "Potential drug interactions are a show-stopper when it is relevant, but it is rarely an issue, so it is important but infrequent".

Combinations of pharmacotherapy

For some patients, choosing a combination of pharmacotherapy will increase their ability to stop smoking. Combination pharmacotherapy is indicated for patients based on five factors:

1. Failed attempt with monotherapy

Use of monotherapy which resulted in a failure to quit smoking is the top priority when considering use of combination pharmacotherapy. The general principle is that intensity of medications should be increased when monotherapy has resulted in relapse. A caveat is that the medication was used appropriately and that there was "a 'true' attempt to quit".

2. Patients with breakthrough cravings

Breakthrough cravings may be an indication that more treatment is needed. An additional form of NRT or an addition of NRT (as needed) to a non-NRT oral medication may be helpful. Combinations of NRT can be used for steady-state delivery (patch) and as needed (gum/lozenge).

3. Level of dependence

Highly dependent smokers are more likely to benefit from combination pharmacotherapy. It may be important to begin with combination pharmacotherapy for these individuals. Because this group has a difficult time in quitting smoking, combination therapy may facilitate increased success.

4. Multiple failed attempts

Multiple failed attempts may be an indication that more intensive therapy is needed. "Careful assessment of previous attempts usually reveals complex situations which are more likely to be addressed with combination pharmacotherapy." However, it is important to keep in mind that failed attempts may also be based on patient lack of commitment rather than insufficient medication.

5. Patients with nicotine withdrawal

Patients experiencing nicotine withdrawal can be a trigger for their relapse to smoking. The combination of pharmacotherapies (for example, addition of NRT to another pharmacotherapy) can be a helpful response for managing nicotine withdrawal symptoms.

Specific combinations of pharmacotherapy

When prescribing or recommending combinations of pharmacotherapy, first select combinations of NRT. Then, prescribe a combination of bupropion and NRT for more heavily dependent patients.

1. Two more forms of NRT

The use of two or more forms of NRT has the strongest evidence base and is the most commonly used form of combination therapy. There is a high level of confidence that this combination can be used safely and effectively. "This approach permits optimal titration of NRT to meet nicotine needs and can be achieved easily and cheaply".

2. Bupropion + form of NRT

Bupropion plus a form of NRT can be effective for some patients. This combination is generally used in more heavily dependent patients.

Impact of comorbidities on selection of pharmacotherapy

When prescribing pharmacotherapy to patients having a dual diagnosis (that is, medical, psychiatric or other substance use in addition to smoking), specific attention should be given to:

1. Contraindications

Attention to contraindications is the top priority in the selection of type of pharmacotherapy in patients with comorbidities. Ensuring the safety of a patient is always of primary importance in prescribing or recommending medications. Contraindications are primarily an issue with use of bupropion (that is, history of seizures, alcohol problems) and with patients who are already taking other medications.

2. Specific pharmacotherapy useful for certain comorbidities

Specific pharmacotherapy may be useful for treatment of certain comorbidities in addition to smoking cessation. For example, bupropion may be a good choice for depressed patients who want to quit smoking. However, for patients with anxiety disorders or eating disorders, bupropion would not be a good choice.

3. Dual purpose medications

"It's nice to treat two things with one med so if I can do that I will". Most common is use of bupropion for depressed patients who want to quit smoking. Bupropion can also be useful for patients who do not want to gain weight. Dual purpose medications may have added value in enhancing compliance.

Frequency of monitoring

All patients taking pharmacotherapy should be monitored carefully. The frequency of monitoring should be determined by:

1. Patient need

The top priority for frequency of monitoring should be determined by patient needs. For example, patients with multiple or difficult quit attempts will likely require more support.

2. Type of pharmacotherapy

Some types of pharmacotherapy may require more frequent monitoring, particularly if there is potential for adverse events (for example, drug interaction, side effects).

Source: P Bader, P McDonald and P Selby: An algorithm for tailoring pharmacotherapy for smoking cessation: results from a Delphi panel of international experts. Tob Control 2009 18: 34-42 originally published online October 9, 2008, doi: 10.1136/tc.2008.025635

REFERENCES

 U.S. Department of Health and Human Services. The health consequences of smoking: a report of the Surgeon General. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. 2004.

- 2. U.S. Departement of Health and Human Services:Treating Tobacco use and Dependence 2008 update: Page:15.
- Owen L. Impact of a telephone helpline for smokers who called during a mass media campaign. Tobacco Control. 2000;9:148–54.
- Fichtenberg CM, Glantz SA. Effect of smoke-free workplaces on smoking behaviour: systematic review. British Medical Journal. 2002;325:188.
- West R, McNeill A, Raw M. Smoking cessation guidelines for health professionals: an update. Health Education Authority. Thorax. 2000;55:987–99.
- McRobbie H, Hajek P. Nicotine replacement therapy in patients with cardiovascular disease: guidelines for health professionals. Addiction. 2001;96:1547–51.
- Benowitz N, Dempsey D. Pharmacotherapy for smoking cessation during pregnancy. Nicotine & Tobacco Research. 2004;6:S189–202.
- MHRA. 2005. Report of the committee on safety of medicines working group on nicotine replacement therapy: Medicines and Healthcare products Regulatory Agency, Committee on Safety of Medicines. Available online at: http://www.mhra.gov.uk/home/idcplg?ldcService=GET_F ILE&dDocName=CON2 023239&RevisionSelectionMethod=LatestReleased Accessed: 3 July 2006.
- Silagy C, Lancaster T, Stead L, Mant D, Fowler G. 2006. Nicotine replacement therapy for smoking cessation. Cochrane Database of Systematic Reviews (2).

- 10. Silagy C, Mant D, Fowler G, Lancaster T. Nicotine replacement therapy for smoking cessation. In: The Cochrance Library.
- 11. Tonnesen P, Paolctii P, Gustavsson G, et al. Higher dosage nicotine patches increase one year smoking cessation rates: result from European CEASE trial. Collaborative European Anti-smoking. Evaluation. Eur Respir J. 1999.
- 12. Fiore MC. Treating tobacco use and dependence: an introduction to the US Public Health Service Clinical Practice Guideline. Respir Care. 2000;45:1196-9.
- 13. Hughes, Jr, Stead LF, Lancaster, T. (2004). Antidepressants for smoking cessation. Cochrane Database of Systematic Review, (4), CD000031. PUB2.
- 14. Richmond, R. & Zwar, N. Review of bupropion for smoking cessation. Drug Alcohol Review. 2003;22:203–20.
- David G, Stephen I, Mitchell N, Cheryl O, Salomon A, Clare. B, et al. an α4β2 Nicotinic Acetylcholine receptor partial agonist, versus sustained release burpropion and placebo for smoking cessation. The Journal of the American Medical Association. 296:47-55.
- Douglas E, Taylor H, Rigotti N, Azouly S, Watsky E, Billing C. Varenicline, an α4β2 Nicotinic Acetylcholine receptor partial agonist, versus sustained release burpropion and placebo for smoking cessation. The Journal of the American Medical Association. 296:56-63.