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An Overview On Nicotine Replacement Therapy For Smoking Cessation

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Abstract:

Smoking is currently the world's leading preventable cause of death. Cigarettes are one of the most polluted medication delivery systems, and smoking tobacco is a chronic illness. Many ailments are still caused by smoking. Diseases such as a wide variety of cancers, respiratory conditions, and cardiovascular disorders can result in death from tobacco use. It has been demonstrated that nicotine increases a smoker's dependence on tobacco. Since nicotine is the primary cause of dependence in smokers, it is beneficial for them to consume nicotine from a different, more dependable source to help their efforts to quit smoking. Nicotine Replacement Therapy is a common term used to indicate these alternative sources of nicotine. The most popular and initial products created under nicotine replacement treatment are nicotine chewing gums, nicotine transdermal patches, nicotine lozenges, nicotine oral inhalers, and nicotine nasal sprays. NRT products containing nicotine are readily available in the market as an over-the-counter medication. Cessation of smoking lowers morbidity and mortality. It is unclear, therefore, how much and how quickly quitting smoking reduces the current death rates from smoking-related diseases.

Keywords: Smoking, Smoking Cessation, Tobacco, Nicotine, NRT, Nicotine transdermal patch, Nicotine chewing gum, Nicotine lozenges, Nicotine oral inhaler, and Nicotine nasal spray.

Introduction:

The main aim of nicotine replacement therapy (NRT) is to help smokers stop smoking. By administering nicotine, NRT aims to reduce the desire to smoke as well as the physical and mental symptoms of withdrawal. By providing nicotine in dependable dosage forms such as nicotine gums, nicotine lozenges, nicotine patches, nicotine oral inhalers, and nicotine nasal spray, the nicotine found in cigarettes is replaced in this therapy. The medication prevents a need to smoke by lowering the withdrawal symptoms associated with quitting smoking. The majority of the carcinogens and poisons created during the burning and inhalation of tobacco products are responsible for the diseases associated with cigarette smoking, not nicotine. In that time, one of the main chemicals that contributes to tobacco product addiction is nicotine. Because it offers a pharmaceutical with a good risk-benefit ratio to replace the drug of abuse with nicotine medications, nicotine replacement therapy thus shows to be a beneficial treatment for tobacco dependency.

What is smoking?

Smoking is the process of inhaling and exhaling smoke from burning plant material, primarily tobacco, but it can also come from marijuana, cigars, pipes, or herbal cigarettes. The primary active ingredient of tobacco products is nicotine, an addictive alkaloid that releases dopamine, induces tolerance and physical dependency, and can have both calming and stimulating euphoric effects. Smoking has a major negative influence on oral health since it can lead to periodontal disease, oral cancer, halitosis, tooth discoloration, and poor wound healing.

Effects of smoking:

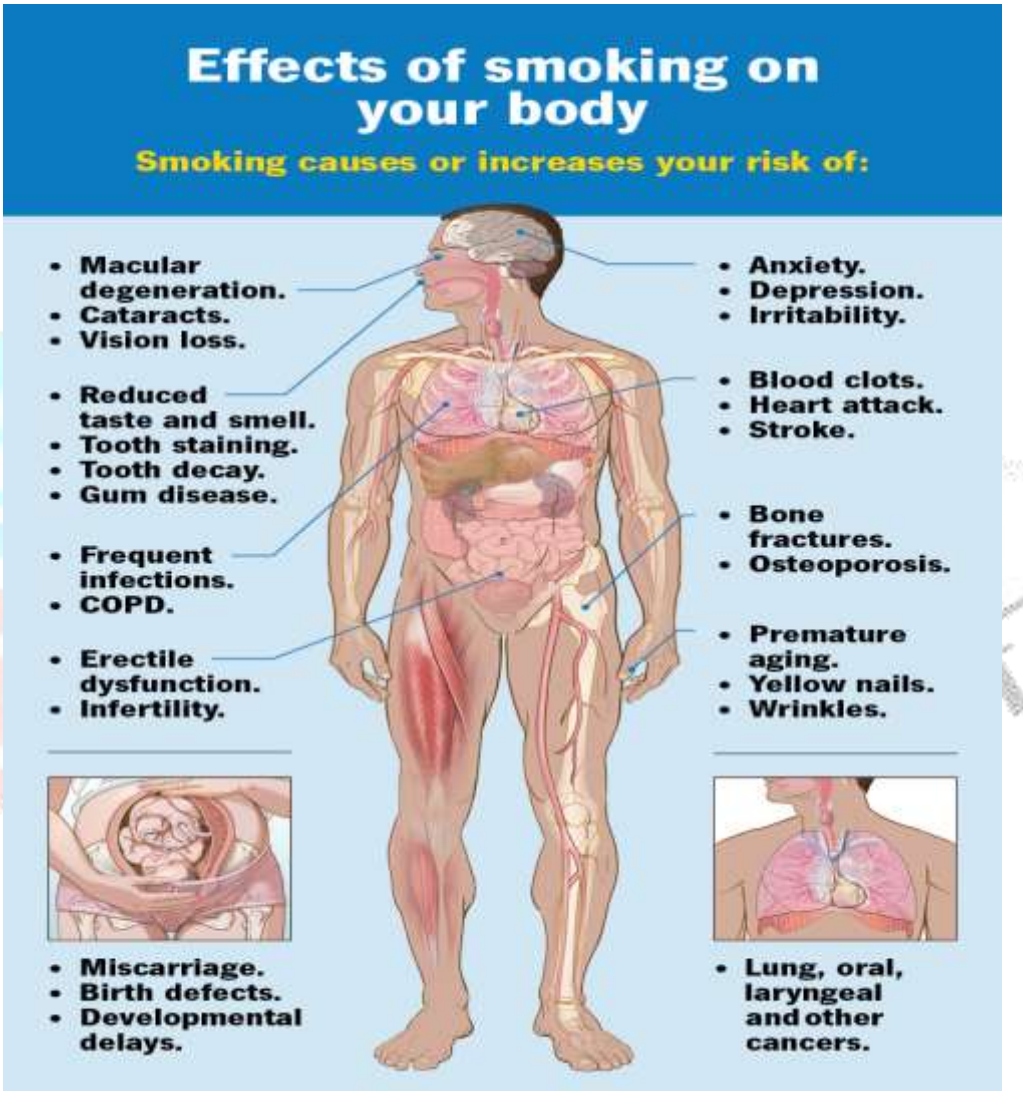

Fig. No.1 Effects of smoking on your body

1. Cancer:

Smoking can cause cancer almost anywhere on the body, including the majority of lung cancers. The mouth, nose, throat, oesophagus, liver, stomach, kidney, pancreas, ureter, colon, bladder, and blood cells are all included in this. The most common site for oral cancer is the tongue; additional cancer locations include the mouth, lips, throat, larynx, and parts of the nose.

2. Cardiovascular diseases:

Heart disease, stroke, and various other cardiovascular conditions are typically brought on by smoking. Blood clots, which stop blood flow to the heart, brain, or legs, are more likely to occur in smokers.

3. Diabetes:

Smoking causes type 2 diabetes. Active smokers have a 30–40% increased risk of diabetes compared to non-smokers.

4. Infections:

Smoking impairs immunity, increasing the risk of viruses and bacterial infections. Because smoking decreases blood flow, wounds may take longer to heal.

5. Dental issues:

Gum disease, tooth loss, and tooth sensitivity are all increased by smoking. Chewing and swallowing can be more difficult for people with dental disorders

What is Smoking Cessation?

The process of giving up tobacco use is known as smoking cessation, quitting smoking, or stopping smoking. The process of quitting smoking involves giving up tobacco, which contains the addition nicotine. It is reducing the chance of major health issues, including cancer. In general, the US Food and Drug Administration (FDA)-approved cessation drugs reduce physical withdrawal symptoms during the initial stages of stopping.

How to quit smoking:

1. Nicotine Replacement Therapy
2. Daily exercise
3. Behavioral therapy
4. Support groups
5. Drink fluids
6. Avoid triggers

Fig. No. 2 How to Quit Smoking

Nicotine Replacement Therapy:

NRT is a popular medication used to help people stop smoking. A key aspect in determining a drug's addictiveness is its rate of absorption. While nicotine replacement treatment (NRT) produces smaller and more gradual increases in plasma concentrations of nicotine without the tar, carbon monoxide, and other harmful substances found in tobacco smoke, cigarette smoking is the fastest way to deliver nicotine. It might lessen the unpleasant withdrawal symptoms that quitting smoking may cause, like cravings and low sensations. Nicotine patches, gum, nasal sprays, and inhalers are among the over-the-counter medications that are available.

Nicotine source:

TOBACCO

- Synonyms: Nicotiana, Tobacco plant
- Biological source: Nicotine is a volatile liquid alkaloid obtained from the dried leaves of Nicotiana tabacum.
- Family: Solanaceae
- Geographical origin:
  Originated from Australia, South Africa, America, and the South Pacific region. China is the largest tobacco producing country, followed by Brazil, India, and the United States.

Fig. No. 3 Tobacco plant as a source of Nicotine

- Chemical constituents:
- Alkaloid: Nicotine (0.6–9%) is an active principle; Anabasine, anatabine, cotinine, myosmine, and nornicotine
- Solanesol
- Polysaccharide: Raffinose, Glucose, Sucrose, Maltose, Xylose, and Fructose
- Polyphenol: simple phenol, flavonoids, non-flavonoids, phenolic acid, lignans
- Terpenoids
- Therapeutic uses:

1. Stimulant effect on heart and nervous system.
2. Insecticide and fungicide.

3. Used as antibacterial, anti-parasitic, anti-fungal, and antioxidant.
4. Used as anti-inflammatory and anti-tumor.
5. Applied for bronchitis, wounds, sore throats, and arthritis.
6. Effective for respiratory tract infection.
7. Dried tobacco stems and leaves are employed as analgesics and anti-rheumatic drugs.

Nicotine mechanism of action:

The main psychoactive ingredient in tobacco and tobacco products is nicotine, also known as 3-(methylpyrrolidin-2-yl) pyridine. Throughout the brain (CNS) and the peripheral nervous system, nicotine works as an agonist at nicotinic acetylcholine receptors (nAChRs) in the ventral tegmental area (VTA). AChRs are pentameric ion channels having acetylcholine (ACh) as the endogenous ligand. They are composed of combinations of α2-α7 and β2-β4 subunits. Through calcium-mediated second messenger systems, nAChR activation at postsynaptic membranes can result in action potential firing and subsequent gene expression modulation. Additionally, AChRs are found on presynaptic membranes, where they control the release of neurotransmitters.

Acetylcholine, a natural neurotransmitter for nicotinic acetylcholine receptors, possesses a chemical structure with nicotine. Nicotine produces pleasure, excitement, and mood regulation when it binds to nAChRs to promote the release of neurotransmitters (dopamine and others). Repeated exposure to nicotine causes neuroadaptation, which leads to tolerance to many of the effects of nicotine.

Forms of Nicotine Replacement Therapy:

1. Nicotine transdermal patch
2. Nicotine chewing gum
3. Nicotine lozenges
4. Nicotine nasal spray
5. Nicotine oral inhaler

1. Nicotine Transdermal Patches:

TNPs are widely utilized to treat nicotine addiction. For people with normal hearts (no irregular beats, high blood pressure, or recent cardiac problems), it is the main treatment for quitting smoking. When nicotine patches are applied topically, a prescribed quantity of nicotine is delivered via the skin and into the bloodstream in a somewhat constant state. The nicotine patch is a long-acting NRT that gives the user a steady dose of nicotine. Through the skin, patches deliver a precise dosage of nicotine. There are numerous patch types and strengths available, such as 16-hour and 24-hour patches. The number of cigarettes you smoke each day will impact which patch you should use.

How to use nicotine transdermal patches:

1. Select the appropriate patch strength: There are patches containing 7, 14, or 21 mg. The amount of smoke you now consume determines the strength you require. Lighter smokers may use 14 mg or 7 mg patches, but heavy smokers (more than 10 cigarettes per day) normally start with 21 mg patches.

2. Apply the Patch to Clean, Dry Skin: Choose a section of the upper body or upper outer arm that is hairless, clean, and dry. Do not apply to broken or irritated skin.

3. How to Apply the Patch: Take the patch out of the box, taking caution not to get it in contact with the sticky side. Make sure the patch adheres effectively, especially around the edges, by pressing it hard against your skin for ten or so seconds.

4. Leave the Patch On for 16–24 Hours: The majority of nicotine patches are made to be worn for a whole day in order to provide a consistent nicotine delivery.

5. Remove the patch and apply a new one every day. After taking off the previous patch, fold it in half, adhesive sides facing each other, and discard it properly. To prevent nicotine from getting into your mouth or eyes, wash your hands after putting the patch on and taking it off.

6. Avoid Using Certain Products on Patch Region: Lotions, oils, or powders should not be used on the patch region, as this may impair the patch's ability to adhere and release nicotine.

Marketed preparation:

Brand Name	Manufacturer	Doses strengths
Nicorette invisi	Pfizer	10 mg/16hrs,15 mg/16hrs, and 25 mg/16hrs
Nicotex	Cipla	7 mg/24hrs, 14 mg/24hrs, and 21 mg/24hrs
NicoDerm CQ	GlaxoSmithKline	10 mg/16hrs,15 mg/16hrs, and 25 mg/16hrs
Nicotrol	Johnson and Johnson	7 mg/24hrs, 14 mg/24hrs, and 21 mg/24hrs
Quit smoking	Teva	7 mg/24hrs, 14 mg/24hrs, and 21 mg/24hrs

2. Nicotine Chewing Gum:

Nicotine gum is a quick-acting substitute. Nicotine enters the body through the mouth's mucous membrane. The gum gradually releases nicotine, which is subsequently taken up by the oral buccal mucosa into the blood vessels. It is available without a prescription over the counter. Both 2 mg and 4 mg dosage forms are available. As you stop smoking, it lessens cravings and withdrawal symptoms.

How to use nicotine chewing gum:

1. Select the Correct Strength: There are two strengths of nicotine gum: 2 mg and 4 mg. If you smoke fewer than 25 cigarettes per day, 2 mg is suggested. If you smoke 25 or more cigarettes a day, 4 mg is suggested.

2. Use the Proper Chewing Method (Chew and Park): Chew gently until your mouth starts to tingle or taste peppery, which normally happens after 10-15 chews. To enable the absorption of nicotine, place the gum between your cheek and gum. After the tingling subsides, park the gum once more and chew till the feeling returns.

3. Avoid Chew Like Regular Gum: Avoid chewing the gum rapidly or continuously. This may result in an excessive release of nicotine, which could induce adverse effects including nausea or an upset stomach.

4. Avoid Eating or Drinking Right Before and After Using the Gum: Wait 15 minutes before eating or drinking, and refrain from doing so while chewing. Acidic foods and beverages, such as coffee, juice, and soda, can hinder the absorption of nicotine.

5. Reduce Use Gradually: To take yourself off of nicotine, gradually cut back on the quantity of pieces you chew each day.

Marketed Preparation:

Brand name	Manufacturer	Doses strength
Nicorette	Pfizer	2mg, 4mg
Nicogum	GlaxoSmithKline	2mg, 4mg, 6mg
Habitrol	Novartis	2mg, 4mg
Thrive	Johnson & Johnson	2mg, 4mg
Quit gum	Teva	2mg, 4mg

3. Nicotine Lozenges:

Nicotine lozenges are candy-sized, flavor-infused oral preparations that "dissolve slowly in the mouth" over the course of eight to ten minutes. They come in little, vibrant plastic vials. The buccal mucosa absorbs nicotine from the lozenge gradually, allowing it to enter the bloodstream. It must not chew. There are two strengths of the lozenge that are sold over the counter: formulations containing 2 mg and 4 mg. Additionally, the manufacturers of lozenges advise not eating or drinking for at least fifteen minutes either before or during the lozenge's use. (Some beverages can reduce the lotion's effectiveness.)

How to use nicotine lozenges:

1. Select the Appropriate Strength: If you smoke your first cigarette more than half an hour after waking up, 2 mg lozenges are advised. If you smoke your first cigarette within 30 minutes of waking up, 4 mg lozenges are advised.

2. How to use nicotine lozenges: place one in your mouth and let it dissolve gradually. Chewing or swallowing the lozenge whole will lessen its effectiveness and increase the risk of adverse effects, such as stomach pain. To prevent irritation, move the lozenge from one side of your mouth to the other on time. It usually takes 20 to 30 minutes for a single lozenge to dissolve.

3. Avoid Eating or Drinking: For fifteen minutes prior to applying the lozenges and while it is in your mouth, refrain from eating or drinking. Coffee, juice, and soda are examples of acidic beverages that can hinder the absorption of nicotine.

4. Reduce Use Gradually: To remove yourself off of nicotine, gradually cut back on the quantity of lozenges you take each day, just like with other types of NRT.

Marketed preparation:

Brand name	Manufacturer	Doses strength
Nicorette	Pfizer	2mg, 4mg
Commit	GlaxoSmithKline	2mg, 4mg
Thrive	Johnson & Johnson	2mg, 4mg, 6mg
Nicogel	Novartis	2mg, 4mg
Quitmax	Teva	2mg, 4mg

4. Nicotine Oral Inhaler:

Inhalers can only be available with a prescription. A narrow plastic tube with a mouthpiece and a nicotine-containing plastic cartridge makes up the nicotine inhaler. The nicotine inhaler distributes the largest amount of the nicotine vapor to the mouth and throat, where it is absorbed into the circulation, in contrast to other

inhalers that deliver the most of the medication to the lungs. Some people find that using a nicotine inhaler, which is FDA-approved and most similar to smoking a cigarette, helps them stop. Inhalers are currently the most expensive type of NRT on the market.

How to use nicotine oral inhaler:

1. Place the Inhaler Together: The inhaler is made up of a nicotine cartridge and a plastic mouthpiece. After inserting a nicotine cartridge into the inhaler, securely hold the mouthpiece.

2. How to Inhale: Because nicotine is mainly absorbed through the lining of your tongue rather than your lungs, take shallow breaths rather than deep ones. A tiny quantity of nicotine is delivered with each inhalation, and it passes through the oral mucosa into the circulation.

3. Continue to a Dosing Schedule: Depending on your nicotine cravings, you will usually take the inhaler 6–16 times a day.

4. Use for Short, Regular Sessions: Each cartridge lasts for approximately 20 minutes for constant use, but you may divide that time up into smaller bursts throughout the day.

5. Avoid Eating or Drinking Before Using: For 15 minutes before or during inhaler use, avoid eating or drinking anything, especially acidic liquids (such as coffee, juice, or soda), as this can block the absorption of nicotine.

Marketed preparation:

Brand name	Manufacturer	Doses strength
Nicorette	Johnson & Johnson	10 mg/cartridge
Nicotrol	Pfizer	4 mg/inhalation
Commit	GlaxoSmithKline	15 mg/cartridge
Nicogel	Novartis	10 mg/cartridge
Thrive	Johnson & Johnson	10 mg/cartridge

5. Nicotine Nasal Spray:

Nicotine nasal spray is available with a prescription. Because nicotine is absorbed through the nose, it is made to quickly deliver doses to the bloodstream. Customers can purchase a multidose container that contains a pump mechanism attached to a nozzle that dispenses 0.5 mg of nicotine per 50-uL squirt. By reducing cravings and withdrawal symptoms, it is intended for helping smokers in cessation.

How to use nicotine nasal spray:

1. Read directions: Make sure you always carefully read and abide by the product's directions.

2. Prime the Spray: You should prime the spray if this is your first time using it or if you haven't used it in a day. A light mist will form after a few sprays of the spray into the air.

3. Blow Your Nose: To guarantee that the spray is adequately absorbed, clear your nasal passages before using.

4. Apply the spray: softly tilt your head back. Aim the spray bottle's tip toward the back of your nose rather than the septum as you insert it into one nostril. Breathe slowly through your lips and spray one dose (typically one spritz) into one nostril. The spray may irritate your throat if you sniff it or take a deep breath.

5. Wait Between Sprays: Spray into the other nostril if you require a second dosage. The average person uses one or two sprays every hour.

6. Reduce Usage Gradually: To wean off of nicotine, reduce gradually the number of sprays.

Marketed preparation:

Brand name	manufacturer	Doses strength
Nicorette	Pfizer	0.5mg/spray
Nicotrol	Johnson & Johnson	0.5mg/spray
Commit	GlaxoSmithKline	0.5mg/spray
Nicogel	Novartis	0.5mg/spray
Niccare	Teva	0.5mg/spray

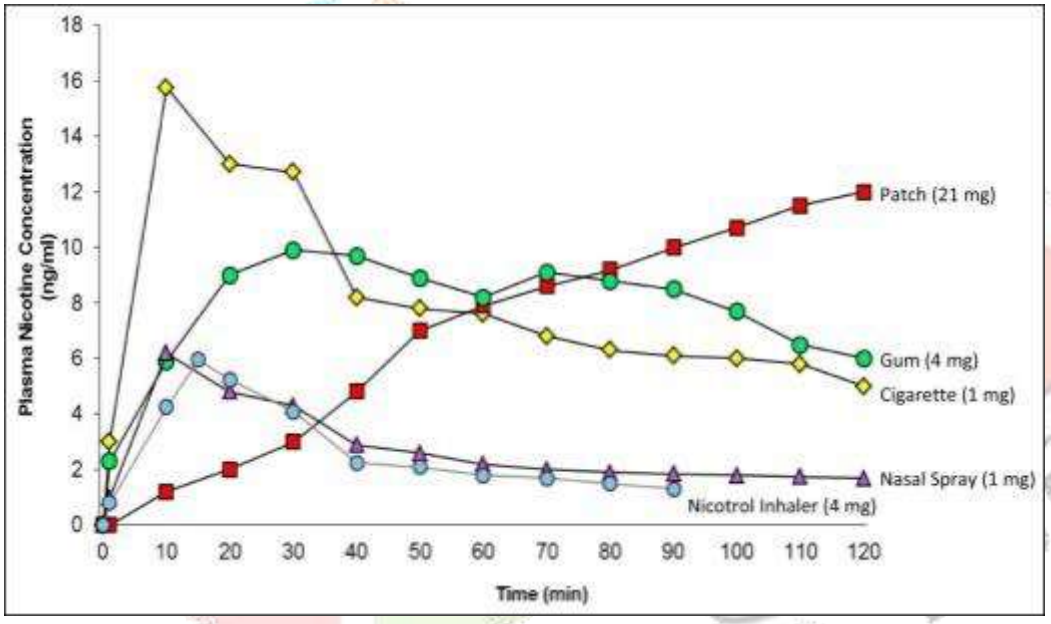

Fig. 4 NRT Formulations

Nicotine replacement therapy formulations:

Nicotine products	Available doses	Cautions/warning	Uses	Adverse events
Transdermal patches	5 mg, 10 mg, 15 mg doses worn over 16 hours 7 mg, 14 mg, 21 mg doses worn over 24 hours	For smokers with insomnia, they should be removed before bedtime.	One daily on clean, unbroken skin; remove before bed (16 h patch) or next morning (24 h); new patch, fresh site.	Local skin reactions, disrupt sleep (insomnia), nausea, vomiting
Chewing gum	2 mg and 4 mg doses	Avoid consumption of acidic drinks.	Chew gum until taste is strong, then rest gum between gum and cheek; chew again when taste has faded. Try	Mouth pain, mouth sores, jaw aches, jaw fatigue

			not to swallow excessively.	
Lozenge	1 mg, 2 mg, and 4 mg doses	Do not eat or drink 15 minutes before or during use.	Allow to dissolve in mouth (about 20–30 minutes), moving from side-to-side from time-to-time. Try not to swallow excessively. Do not chew or swallow whole.	Heartburn, nausea, and mouth soreness
Nasal spray	0.5 mg dose/spray	Not for patients with asthma	Take shallow puffs approximately every 2 seconds, or alternatively, take four puffs every minute. Continue for up to 30 minutes.	Nasal irritation, sneezing, teary eyes, coughing
Oral inhaler	Cartridge containing 10 mg	May irritate mouth/throat at first	Spray into the mouth, avoiding the lips. Do not breathe while spraying. Use when cigarettes would usually be smoked or if cravings emerge. Do not swallow for a few seconds after spraying.	Local irritation of mouth and throat

Conclusion:

The primary barrier to quitting smoking and maintaining long-term abstinence is nicotine addiction. We advise all tobacco users who do not have any medical contraindications to use one of the many nicotine treatments currently available in a variety of forms, dosages, and flavors. All of the currently available forms of NRT such as gum, transdermal patches, nasal sprays, inhalers, and lozenges increase their chances that they will effectively quit smoking, according to current research. The rate of quitting increases by 50–70% with NRT. As an entire approach for supporting quitting smoking, nicotine replacement therapy is successful. In the end, people who are willing to quit find that these NRT products such as nicotine transdermal patches, nicotine chewing gum, nicotine lozenges, nicotine oral inhalers, and nicotine nasal sprays are more effective. NRT is appropriate for therapeutic smoking cessation applications because it is effective in reducing the rate of withdrawal, reducing tobacco dependency, relieving withdrawal symptoms, and reducing daily smoking.

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