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## Tobacco Cessation Counseling Interventions: An update on Current Approaches

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### ABSTRACT

Tobacco smoking is globally far more widespread than use of any other form of substance abuse. Its use remains the leading preventable cause of morbidity and mortality, each year causing more than 6 million deaths globally. The World Health Organization estimates there are 1.3 billion smokers worldwide and each year 5 million smokers die because of tobacco-related diseases. Data suggest that up to 70% of current smokers want to quit and 40% attempt to do so each year. Timely intervention in smoking cessation not only reduces the risk of major disease, but also modifies the clinical course and outcome of certain diseases. There are various pharmacological and non pharmacological measures available which need to be implemented properly and timely. Strategies for assisting smoking cessation include non-pharmacological therapies to enhance motivation and to support attempts to quit and pharmacological intervention to reduce nicotine reinforcement and withdrawal from nicotine. The pharmacological interventions include nicotine replacement therapy (NRT) and antidepressants. Non-pharmacologic interventions includes behavioral interventions, cognitive behavioral therapy (CBT), individual or group counseling, telephone counseling and self-help counseling. The present review aims at analyzing the current knowledge of various smoking cessation strategies

**Keywords:** tobacco addiction, pharmacological, no pharmacological, vaccines.

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## INTRODUCTION

The World Health Organization (WHO) considers smoking as “the single biggest preventable cause of death” in the contemporary society.<sup>1</sup> Tobacco addiction is currently considered a chronic disorder that accounts for nearly 6 million premature deaths worldwide and causes hundreds of billions of dollars of economic damage.<sup>2,3</sup> India is the 2nd largest producer and 3rd largest consumer of tobacco worldwide. With 274.9 million tobacco users in the country, India’s tobacco problem is more complex and the usage prevailing among the people as a part of tradition and custom.<sup>4</sup> There are 3 billion cigarette smokers worldwide of which 112 million are in India.<sup>1</sup> Cigarette smoking is estimated to cause 800,000 deaths annually in India. The WHO predicts that tobacco deaths in India may exceed 1.5 million annually by 2020.<sup>5</sup> Addiction is the result of heavy drug use that changes the structure and function of the brain, the International Classification of Diseases-10 has categorized tobacco addiction as a mental and behavioral disorder.<sup>4,6,7</sup>

Nicotine is the main active ingredient in tobacco products that reinforces individual to tobacco addiction behavior. Nicotine is mostly absorbed via the buccal mucosa metabolized by liver, lungs and kidneys and excreted via the urine.<sup>8</sup> Addiction begins when nicotine acts on nicotinic acetylcholine receptor (nACh receptors) leading to down-regulation of CNS ACh receptor, needing nicotine reinforcement to maintain elevated mood and thus causing dependence. Nicotine activates the brain reward centre (in nucleus accumbens) by increasing the release of adrenaline and dopamine.<sup>9</sup> This improves mood and reinforces the behavior induces pleasure and reduces stress and anxiety.<sup>8</sup> When smokers try to quit, lack of nicotine leads to withdrawal symptoms – both physical as well as mental. Physically, the body reacts to absence of nicotine. Mentally, smokers are, faced with giving up a habit, which calls for a major change in behavior.<sup>5</sup>

The Indian government in accordance with the WHO has been taking measures to curtail the usage through various tobacco control initiatives such as raising taxes, alternative crop for farmers, cultivating the cash crop in South-East Asia, and enforcing bans on tobacco advertising, promotion, and sponsorship.<sup>10, 11</sup> Dentist and other health care professionals play a significant role in the intervention of the tobacco related epidemic.<sup>4</sup>

Current and available smoking cessation (SC) interventions are divided into two main categories i.e non pharmacological and pharmacological therapies [Table 1]. The most effective approach to SC appears to result from the combination of these modalities. The pharmacological interventions include nicotine replacement therapy (NRT) and antidepressants. Non-pharmacologic interventions includes behavioral interventions, cognitive behavioral therapy (CBT), individual or group counseling, telephone counseling and

self –help counseling. Non-pharmacologic interventions support SC through broader public health and clinical approaches.<sup>4,12</sup>

## **NON PHARMACOLOGICAL APPROACHS**

### **Behavioral Interventions**

Behavioural support, with multiple sessions of individual or group counselling, assists SC in the form of advice, discussion, encouragement, and other activities designed to help quit attempts succeed. Both individual and group therapy have been shown to improve quit rates beyond those seen with self-help materials alone.<sup>13</sup> Three types of counselling and behavioural therapies have been shown to produce higher abstinence rates: 1) providing smokers with problem-solving/skills training (e.g. avoiding situations where other people are smoking, identifying triggers to smoking); 2) providing social support as part of treatment; and 3) helping smokers to obtain social support outside of treatment.<sup>4</sup>

Hall and colleagues were able to achieve abstinence rates exceeding 40% by extending therapist-guided behavioral treatment over a 52-week period.<sup>14</sup> Lancaster and Stead recently reviewed the literature on the efficacy of individual behavioral treatment for smoking cessation. As might be expected, behavioral treatment was found to be superior to no treatment control. However, the review failed to detect a greater effect of intensive counseling compared to brief counseling.<sup>15</sup>

Behavioral change is inherently an unstable and unsteady process with frequent lapses and relapses. Hence, it is imperative that support should be provided at all stages of change from precontemplation to maintenance to prevent relapse.<sup>16</sup>

Behavioral change techniques for SC are complex and work in multiple ways but in last 20 years there has been no improvement in this technique.<sup>15, 17</sup> In an attempt to rectify this deficit, the UK Medical Research Council has recently funded the Behavior Change Techniques Taxonomy (BCTT) project. The aim of BCTT is to develop a reliable method for specifying behavior change techniques, linking them to relevant theory, and detailing the behaviors necessary to implement them.<sup>18</sup>

### **Cognitive Behavioral Therapy (CBT)**

CBT therapy is usually ‘problem-focused’ and ‘action-based’, actively engaging the person in changing their own smoking habits and behaviours.<sup>19</sup> CBT is promising psychological intervention for people who want to quit smoking because changing and restructuring thought processes, combined with new learning behaviour, is essential for people who want to effectively quit smoking and maintain cessation. CBT targets a thinking pattern or belief that is inconsistent with a desired change. This is a therapeutic treatment for providing smokers

with skills for changing unproductive thoughts and behaviours that sabotage their quit process.<sup>20</sup>

CBT tends to be more effective when conducted one-on- one with healthcare professionals as this allows them to personalize the therapy to individual thoughts and behaviours. Studies have shown that pharmacotherapy combined with CBT achieve high and stable abstinence rates.<sup>21</sup>

The intervention in CBT constituted (1) provision of cognition (by self-identification of the cause of initiation of the habit, identification of the conditioned daily routines, and learning to reduce and cope with negative mood or urge to smoke associated with nicotine withdrawal) (2) provision of counseling to achieve behavioral change (by breaking the routine, managing the temptation to use tobacco, and the various day-to-day stresses which enhance the usage) (3) motivational interviewing to understand and accept the reality (through usage of questions, insight was provided regarding importance to quit tobacco usage), and (4) relapse prevention strategies were taught and asked to be followed.<sup>4, 22, 23</sup>

Webb *et al.*<sup>24</sup> from his study concluded that CBT was effective in tobacco cessation of African-American smokers. Raja M *et al.*<sup>25</sup> conducted study on 40 subjects to evaluate the effectiveness of CBT in comparison with basic health education for tobacco cessation. Author concluded that tobacco users intervened by CBT had higher decrease in the Fagerstrom's addiction scores, yet there was no statistical difference considering basic health education as equally effective.

Social cognitive theory acknowledges that, as people change their behaviour, this will cause/require changes in both their environment (including interpersonal relationships) and in themselves. Social cognitive theory evolved from social learning theory, which suggests that people learn not only from their own experiences but by observing the actions of others (modelling). Social cognitive theory is a complex model and includes personal, behavioural and environmental factors that can be leveraged by the quit line counsellor to help smokers increase their self-efficacy in their ability to quit and gain insight into their use of tobacco.<sup>20, 22, 23</sup>

Various environmental and social factors such as peer influence, job-related stresses, family issues, and smoking environment cause lapse and relapse to tobacco usage and CBT helps overcoming these social stigmas associated with tobacco use initiation and relapse prevention.<sup>26,27</sup> The other most common and readily available interventions are brief advice/interventions, individual behavioral counseling, group behavior therapy programs, motivational interviewing, behavioural contracting, telephone counseling, and self-help materials.<sup>13</sup>

### Brief Advice/Interventions

Brief advice on smoking cessation from a health care professional is effective in promoting cessation. It is also called as Short therapy, referred to as “5 A therapy”, [Table 2] takes only a few minutes and can be given during every routine medical visit. This treatment can be provided (and should be provided) by all health operators involved in first- and second-level assistance, especially general physicians.<sup>1,5</sup>

**Table 1: Different types of interventions for smoking cessation.**<sup>4,20-23, 30-36</sup>

Interventions	
None pharmacological therapy	<ul style="list-style-type: none"> <li>• Brief counselling (in person: individual or group)</li> <li>• Cognitive Behavioral Therapy (CBT)</li> <li>• Psychotherapy</li> <li>• Motivational interviewing</li> <li>• Biofeedback mechanism therapy</li> <li>• Health education</li> <li>• Practical problem-solving (skill-building)</li> <li>• Modelling</li> <li>• Reinforcement</li> <li>• Behavioural contracting</li> </ul>
Pharmacological approach	<ul style="list-style-type: none"> <li>• Nicotine replacement therapy (transdermal patches, chewing gums, lozenge, sublingual tablets, oral inhaler and nasal spray)</li> <li>• Non nicotine Medications (Bupropion, Varenicline Clonidine, nortriptyline, and cytosine)</li> </ul>
Mind – body interventions	<ul style="list-style-type: none"> <li>• E-cigarettes</li> <li>• Mind –body therapies</li> <li>• Yoga</li> <li>• Hypnosis</li> <li>• Biofeedback</li> </ul>
Others	<ul style="list-style-type: none"> <li>• Acupuncture</li> <li>• Phone or distance counseling</li> <li>• Mobile phone interventions (text message reminders from a health care provider)</li> <li>• Self-help, noninteractive audio-visual materials</li> <li>• Internet and social media-based interactive interventions</li> <li>• School-based cessation programs</li> </ul>

**Table 2: The 5 A’s Method for counseling smoking cessation.**<sup>13,15, 28</sup>

5 A’S	Description	Suggested Questions
Ask	Ask about tobacco use: For all teens, at every visit and without parents present	Have you ever smoked cigarettes or e-cigarettes? How often do you smoke? How many cigarettes did you smoke yesterday/last week/ last month? Why do you think it would be a good/bad idea to quit? • Do you use other forms of tobacco?

Advise	Strongly urge all tobacco users to quit	<ul style="list-style-type: none"> <li>• Did you know that quitting is (one of) the single most important thing(s) you can do to protect your health and the health of those around you?</li> </ul>
Assess	Determine readiness to quit by assessing willingness to attempt to quit: within the next 30 days(preparation) within the next six months or • beyond six months	<ul style="list-style-type: none"> <li>• Would you be ready to quit smoking in the next 30 days?</li> <li>• In the next six months?</li> <li>• Have you ever tried to quit?</li> <li>• What do you think made you start smoking again?</li> </ul>
Assist	Provide help for teens attempting to quit (including pharmacotherapy, when indicated) by setting a date and directing the teen toward supportive materials or groups Counsel on the risks associated with taking up replacement substances, such as marijuana or alternate forms of tobacco	<ul style="list-style-type: none"> <li>• When do you think would be a good time/day for you to quit?</li> <li>• Do you have friends or family who can support you when things get difficult?</li> </ul>
Arrange	Arrange follow-up to review progress and re-evaluate pharmacotherapy use and problems, as appropriate	<ul style="list-style-type: none"> <li>• When can we meet again to talk about your progress?</li> </ul>

The 5As approach assists initially in identifying smokers by encouraging health professionals to ‘ask’ patients/clients if they smoke/use tobacco. It then suggests that they ‘assess’ willingness to stop smoking, ‘advise’ on the importance of quitting, offer ‘assistance’ in the form of pharmacotherapy and/or referral for behavioral support, and ‘arrange’ a follow-up appointment, if possible, with those patients who wish to stop smoking. Brief interventions are said only to take 5 to 10 minutes.<sup>13</sup>

A systematic review by Lancaster and Stead estimated that a brief advice intervention by a physician can increase quitting by a further 1%–3% when unassisted quit rate was assumed to be 2%–3%. At the end of 6 months after health education as intervention, the abstinence from smoking was 15% which was higher than previous studies.<sup>28</sup>

“Very brief advice” (VBA) on smoking, is considered to have a greater level of utility when compared with the traditional 5As approach. VBA on smoking is a simple, person/patient centered approach that professionals can deliver effectively in less than 60 seconds if time pressures are such that this is required. When using VBA, professionals are encouraged to ask patients about their smoking, acknowledging that they may have tried to stop many times in the past, and to discuss the options that exist to support a quit attempt, that is, behavioral support and pharmacotherapy.<sup>29,30</sup>

### **Behavioural Contracting**

This is a formal agreement outlining a promise to adhere to a behavior change plan. Well written plans are SMART (specific, measurable, attainable, relevant and timely). Behavioural

contracts can include rewards for performing the behaviour or consequences for not following through with the plan. Creating a sense of accountability to increase the chances that a patient will follow up on specific behavioural strategies.<sup>20</sup>

Enhancing motivation is an important part of the overall treatment for tobacco addiction as it increases smokers' enthusiasm, sense of purpose, and will to quit. Interventions may also seek to maximize self-regulatory capacity and skills (eg, strategies for reducing exposure to smoking cues) and include adjuvant activities such as giving advice on pharmacotherapy and encouraging social support (eg, among group members or from family).<sup>31</sup>

### **Motivational Interviewing (MI)**

This is a directive counselling approach that is used to facilitate the change process. The goal is to enhance motivation for change by enabling the smoker to identify and resolve ambivalence. This strategy is useful for smokers who are not ready to quit. Using open-ended questions and reflections with the objective of resolving a person's diminished motivation to quit. MI involves building intrinsic motivation for change, uses the OARS (Open-ended questions, Affirmations, Reflective listening, Summarizing) strategies to resolve ambivalence and build motivation for change and strengthening commitment to change and developing a plan to accomplish it. MI is a directive, patient-centre counselling approach that enhances motivation for change by helping patients to clarify and resolve ambivalence about behaviour change. The goal of MI is to increase the person's intrinsic motivation based on his or her own personal goals and values. Intrinsic motivation is a state of readiness to change. It relates to the importance of change and confidence in one's ability to change. MI is based on three key elements: collaboration, evocation and autonomy. The core principles of MI include: expressing empathy, supporting self-efficacy, developing discrepancies, rolling with resistance.<sup>20, 32</sup>

### **Reinforcement**

This is used to express confidence in the success the smoker has achieved and the steps he or she has taken to engage successfully in the quitting process. When a smoker has been actively engaged and is successful in quitting, reinforcement can be used to help the person sustain these effective actions. An example of this is when the counsellor supports smoker in the way they have been using their quit medications and the strategies they have used to manage urges to smoke after quitting. In this situation reinforcement is used to encourage smokers to continue doing what they have been doing as it has yielded success. This strategy is effective in enhancing the smoker's self-efficacy and it enhances both motivation and confidence in them to stay quit.<sup>20,33</sup>

### **Modeling**

This is used to help smokers learn from the success of others in their life who have had success in quitting tobacco or in making other significant changes in behaviour that can be applied to quitting tobacco. The process of learning new behaviours or skills by watching the actions of other people and the outcomes of their actions.<sup>20</sup>

### **Individual behavioral counseling**

This type of counseling involves scheduled face-to-face appointments with a trained smoking cessation counselor. It includes both behavior change techniques and motivational interviewing to enhance a person's impetus to change their behavior. This patient-centered approach enhances an individual's motivation for change through self-examination and identification of ambivalence to change and the subsequent resolution leading to sustained positive behavior change. Usually sessions are weekly over a period of at least 4 weeks after a quit date, and this is normally combined with prescribed pharmacotherapy.<sup>13,15</sup> Involves guided smoking, where the patient smokes intensively, often to the point of discomfort, nausea and/or vomiting. Aversion therapy pairs the pleasurable stimulus of smoking a cigarette with some unpleasant stimulus.<sup>4</sup>

### **Group behavior therapy**

This form of therapy is offered to small groups. Group support allows individuals to learn behavioral techniques, and group participants provide peer support. The chances of quitting are doubled for those who attend group behavioral programs compared with those who receive self-help material.<sup>13,17</sup>

### **Telephone counseling**

Telephone counseling and quit lines provide support and encouragement to individuals who smoke and want to quit or individuals who have recently quit. Telephone counseling is more effective than self-help materials, brief advice, or pharmacotherapy. Those who have 1 or more additional phone calls after an initial contact increase their chance of quitting by 25% to 50%. Counseling using quitlines can be provided as part of a national, regional, or local health program or as part of a SC service and potentially can reach large numbers of people without medical referral.<sup>34,35</sup> Telephone quit lines, which provide smokers with convenient access to cessation information and support, have been proved to be both effective and cost effective in helping smokers to quit.<sup>36</sup>

### **Self-help materials**

Self-help materials include manuals or structured programs that are used by individuals without the help of health professionals, trained counselors, or support groups. These are usually written materials provided by health charities and government health departments with formats including leaflets, audio recordings, videos/DVDs, or computer programs, and

Web/Internet-based materials. Current evidence suggests there is likely to be a small effect from the use of standard self-help materials on quit rates compared with no intervention.<sup>13</sup>

Generic self-help materials are no better than brief advice from a health professional, but are more effective than no intervention, and they have the advantage of being able to reach large numbers of people at relatively low per-person cost; thus they can be cost-effective, even though not as efficacious as medication. Printed materials are most common and may range from a brief guide and tips sheet to a structured manual with exercises to guide quit attempts. The increasing accessibility of the Internet should increase opportunities for individually tailored self-help therapies.<sup>13, 37</sup>

### **New technologies**

With the advent of new technology, such as smart phones and easier Internet access, other types of intervention are available. The use of text messaging (eg, txt2stop and txt2Quit) has been developed using motivational messages with some success in the United Kingdom and the United States.<sup>35,38</sup>

Other alternative method includes Cold Turkey method: means abrupt cessation of all nicotine use. National Institute of Health (NIH) recommends chewing cinnamon sticks to help curb the urge to smoke. Biochemical feedback methods includes: estimation of carbon monoxide, cotinin level during follow-up. Acupuncture (Needles are placed in certain parts of the body, including outside of the ear, Aims to relieve discomfort from nicotine withdrawal.), Laser (low-intensity ) therapy, aromatherapy and hypnosis.<sup>5,9,19,39-41</sup>

### **PHARMACOLOGICAL APPROACH**

The development of pharmacotherapies to treat nicotine dependence has focused on the alleviation of tobacco-withdrawal symptoms. There are currently two categories of medication that are available for smoking cessation: Nicotine Replacement Therapy (NRT) and non-nicotine medications (antidepressants).

NRTs reduce withdrawal symptoms by partially replacing the nicotine normally achieved by smoking. Antidepressants such as bupropion, varenicline and nortriptyline may be efficacious for smoking cessation because of their reduction of the cessation-induced depression that is related to nicotine withdrawal.<sup>1,2,8,42</sup>

### **Forms of Nicotine Replacement Therapy**

NRT products are available in number of forms [Table 3]. Transdermal patches are a common form of NRT that is applied to the skin. Acute dosing of nicotine products include gum, lozenge, sublingual tablet, oral inhaler, and nasal spray and Electronic nicotine delivery systems (ENDS). Acute dosing products are self-dosing system which reduces craving in

contrast to transdermal patches which delivers a constant, low level of nicotine, and thus help reduce unpleasant effect of nicotine withdrawal symptoms.<sup>8,42,43</sup>



**Table 3: Types of Pharmacotherapy treatment.**<sup>1,3,4,44-53</sup>

<b>Nicotine Replacement Therapy</b>						
<b>Types of NRT</b>	<b>Dosage</b>	<b>How To Use Them</b>	<b>warning/ Caution</b>	<b>Adverse effects</b>	<b>Availability</b>	<b>Brand names</b>
Transdermal patches	5 mg, 10 mg, 15 mg doses worn over 16 hours 7 mg, 14 mg, 21 mg doses worn over 24hours	One daily on clean, unbroken skin; remove before bed (16 h patch) or next morning (24 h); new patch, fresh site. Gives a small and steady amount of nicotine	Place on the skin Gives a small and steady amount of nicotine	Local skin reaction Insomnia	US FDA (OTC) MHRA (OTC)	Habitrol, Nicoderm CQ, Nicotrol
Chewing gum	2 mg and 4 mg doses	Chew to release nicotine Chew until you get a tingling feeling, then place between cheek and gums	TMJ disease Caution with dentures Do not eat or drink 15 min before or during use	Mouth soreness, Hiccups, Dyspepsia and Jaw ache	US FDA (OTC) MHRA (OTC)	Nicorette, Nulife, Nicotex chew gum
Sublingual tablet	2 mg dose	Rest under tongue until dissolved	Nicotine dependence, insomnia	Mouth soreness	MHRA (Rx) Regulatory	-
Lozenge	1mg, 2 mg and 4 mg doses	Place in the mouth like hard candy Releases nicotine as it slowly dissolves in the mouth. 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	Do not eat or drink 15 minutes before or during use One lozenge at a time Limit 20 in 24 hours	Nausea/ Heartburn	US FDA (OTC) MHRA (OTC)	Commit
Nicotine inhaler	Cartridge containing 10mg	Cartridge attached to a mouthpiece Inhaling through the mouthpiece gives a specific amount of nicotine Spray into the mouth, avoiding the lips. Do not inhale while spraying. Use when cigarettes would usually be	May irritate mouth/throat at first	Local irritation of mouth and throat	US FDA (Rx) MHRA (Rx)	Nicotrol inhaler

		smoked or if cravings emerge. Do not swallow for a few seconds after spraying				
Nasal Spray	0.5mg dose/spray	Pump bottle containing nicotine Put into nose and spray Take shallow puffs approximately every 2 seconds or alternatively take four puffs every minute. Continue for up to 30 minutes.	Not for patients with asthma May cause dependence	Nasal irritation	US FDA (Rx) MHRA	Nicotrol ® inhaler
Electronic cigarette	-	E-Cigarette vapor is drawn very slowly in to mouth, then held there for a second or two. Then, it can be inhaled if desired. The vapor is then expelled through the mouth or nose	May cause dependence	Mouth and airway irritation, chest pain, and palpitation (26, 27)	Untill now, it is not approved by any agency	Vaporfi, V <sub>2</sub> CIGS, JUUL, South Beach Smoke, HALO CIGS
<b>NON NICOTINE MEDICATIONS</b>						
Varenicline	1mg once or twice daily for period 12 weeks	Varenicline tablet started 2 week before your Quit Day. Take it after meals, the daily dose increases over the first 8 days for a period of 12 weeks.	Allergy, reduced doses) are recommended for patients with renal impairment	Nausea Vomiting, Headache Mood or behavior changes Constipation ,Changes in taste, Skin rashes	Rx OTC	Chantix
Bupropion	150 mg tablets once or twice per day.	Bupropion tablet started 2 week before your Quit Day.	Seizures (it can cause or worsen seizures) Heavy alcohol use Cirrhosis, A serious head injury, Dose reduction is necessary in patients with hepatic or renal disease	Difficulty in concentrating, insomnia, nightmares, headache, dry mouth, nausea and anxiety.	Rx OTC	Zyban, Wellbutrin, or Aplenzin

\*US FDA: U S Food and Drug Administration; MHRA: Medicines and Health care products Regulatory; Rx: Prescription; OTC: Over the counter.

These NRTs, in a Cochrane review, increased the chances of quitting smoking by 50 - 70% compared to placebo or to no treatment.<sup>5</sup> Recent evidence suggests that all NRT products have different levels of efficacy and variable rates of nicotine absorption. Combined NRT formulations have been shown to result in higher abstinence rates than single NRT, and they are most effective when the consumer also receives parallel cessation-counseling.<sup>4, 3, 44,45</sup>

Schnoll RA *et al.*,<sup>46</sup> recruited 525 treatment-seeking smokers for a randomized clinical trial to compare 8 (standard), 24 (extended), and 52 (maintenance) weeks of nicotine patch treatment for promoting tobacco abstinence and the results findings support the safety of long-term use of nicotine patch treatment, although they do not support efficacy beyond 24 weeks of treatment in a broad group of smokers.

Joseph AM *et al.*,<sup>47</sup> and colleagues found that extended treatment with nicotine gum, patches, or lozenges for 52 weeks significantly increased smoking cessation rates compared with 4 weeks of treatment. Strasser AA *et al.*,<sup>48</sup> did study to know the better understanding, use, and exposure of using e-cigarettes on 28 cigarette smokers. Author concluded that E-cigarettes are not liked as much as cigarettes, provide significantly lower nicotine replacement, reduce carbon monoxide exposure, and mitigate withdrawal and craving. The current evidence suggests that ENDS are an effective smoking cessation tool, but more research is needed to confirm its long-term effectiveness and safety.<sup>49</sup>

### **NON NICOTINE MEDICATIONS**

Varenicline is a nicotine receptor partial agonist, act by maintaining levels of dopamine to mitigate withdrawal symptoms and also reduces the craving for nicotine.<sup>50</sup> It is hypothesized that varenicline has a dual mechanism of action: (i) it acts as a partial agonist at the a4b2 receptor that reduces the smoking cessation-induced drop in mesolimbic dopamine concentrations, potentially relieving withdrawal symptoms and (ii), it antagonizes the activity of nicotine at the a4b2 receptor and blocks nicotine-induced dopaminergic activation, potentially reducing the reward from smoking relapse.<sup>51</sup> Varenicline is recommended to start a week or two before the patient stops smoking. The dose is gradually increased and treatment continues for 12 weeks. Varenicline can be combined safely with NRT and this may further improve abstinence rates at six months. The plasma half-life of varenicline is approximately 24 h it does not undergo significant hepatic metabolism and is excreted in the urine so reduced doses (or alternative treatments) are recommended for patients with renal impairment.<sup>1,3 52</sup>

Bupropione is an oral antidepressive agent that belongs to the chemical class of aminoketones. It mainly acts as a catecholamine (noradrenaline and dopamine) neuronal reuptake inhibitor and partly as a serotonin inhibitor.<sup>1</sup> It has equivalent efficacy to NRT but

less efficacy than varenicline and is therefore considered a second-line option. Bupropion is metabolized into three active metabolites by cytochrome 2B6. The recommended dosage of bupropion is 150 mg twice daily. It is contraindicated in patients with a history of seizures. Common adverse effects include difficulty concentrating, insomnia, nightmares, headache, dry mouth, nausea and anxiety. Dose reduction is necessary in patients with hepatic or renal disease.<sup>3,52</sup>

Ebbert JO *et al.*,<sup>53</sup> conducted randomized clinical trial to determine efficacy and safety of varenicline and bupropion sustained-release compared with varenicline monotherapy on 506 adult cigarette smokers. The study concludes that among cigarette smokers, combined use of varenicline and bupropion, compared with varenicline alone, increased prolonged abstinence but not 7-daypoint prevalence at 12 and 26 weeks. Neither outcome was significantly different at 52 weeks. Further research is required to determine the role of combination therapy in smoking cessation.

Nortriptyline and clonidine have been proposed as second line pharmacotherapies by the US clinical practice guidelines for treating tobacco use and dependence. Nortriptyline, a tricyclic antidepressant, is believed to block the re-uptake of norepinephrine and serotonin and, by this mechanism, reduce tobacco withdrawal symptoms.<sup>3,54</sup>

### **NICOTINE VACCINES**

Nicotine vaccines represent a newer novel therapeutic concept to treat the nicotine dependence. Because nicotine is a small molecule and an incomplete antigen, it is linked to a carrier protein order to stimulate the necessary immune response.<sup>8</sup> Nicotine vaccines can be used both for relapse prevention and as preparation for a quit attempt.<sup>55</sup> The mechanism of immunization against nicotine can be achieved by active or passive immunization. Active immunization refers to the administration of an immunogenic substrate that causes T and B cell activation, leading to the formation of specific antibodies within the studied individual. Passive immunization is defined as the administration of preformed monoclonal or polyclonal high-affinity antibodies and it offers immediate protection.<sup>56</sup>

A number of organizations have developed vaccines [Table 4] for smoking cessation, with NicVAX developed by Nabi Biopharmaceuticals being perhaps the best known. A potential drawback of vaccines to treat tobacco dependence is the fact that smokers will often compensate for decreases in the actions of nicotine, as would be expected when a vaccine decreases concentrations of nicotine penetrating into brain tissues, by increasing their tobacco consumption to overcome this effect.<sup>57</sup> Other potential issues related to the successful use of vaccines include difficulties achieving sufficiently high antibody titers, the fact that vaccines

are generally short lived, and significant inter-individual variation in response to the vaccine typically observed.<sup>55-57</sup>

**Table 4: Vaccines for tobacco cessation.**<sup>8, 55-57</sup>

Vaccine	Construction of vaccine	Company	Clinical trial phases	Results
<b>NicVax</b> (Bacterial exoprotein Conjugate vaccine)	3-AmNic-rEPA (3'-aminomethylnicotine Pseudomonas aeruginosa r-exoprotein A)	Nabi Biopharmaceutics	III	The preliminary results of the trials showed that the primary endpoint of 16 weeks abstinence measured at 12 months was not met; there was no statistically difference between the NicVAXW and placebo group Interim analysis showed that the primary endpoint (continuous abstinence from smoking from weeks 8–12 after start of treatment) was not achieved, possibly because NIC002 failed to induce sufficiently high antibody titers.
<b>NIC002</b> (Nicotine Qbeta or CYT002-NicQb)	Recombinantly produced virus-like protein	Novartis	II	Not declared
<b>TA-NIC</b> (a recombinant cholera toxin conjugate vaccine)	Nicotine butyric acid covalently linked to recombinant cholera toxin B	Celtic Pharma	II	Not declared
<b>SEL-068</b> (Synthetically engineered nanoparticle)	Synthetically engineered nanoparticle	Selecta Biosciences	I	Not declared

WHO- World Health Organization

nACh receptors- nicotinic acetylcholine receptors

CNS- Central nervous system

SC – Smoking cessation

NRT- Nicotine replacement therapy

CBT- cognitive behavioral therapy

BCTT- Behavior change techniques taxonomy

VBA- Very brief advice

SMART - specific, measurable, attainable, relevant and timely

MI- Motivational Interviewing

OARS -Open-ended questions, Affirmations, Reflective listening, Summarizing

NIH- National Institute of Health

ENDS - Electronic nicotine delivery systems

US-FDA- U S Food & Drug Administration

CO- carbon monoxide

MHRA- Medicines and Health care products Regulatory;

Rx- Prescription;

OTC- Over the counter

## CONCLUSION

There is a wide range of treatment options that have been proved effective, including behavioural and pharmacological therapies. There is no single approach that should be emphasized to the exclusion of others because the therapies vary widely in their efficacy, their acceptability, their cost-effectiveness, and their cost on an individual.

Furthermore, public health approaches such as mass media campaigns, Quit and Win competitions and telephone help lines serve to play an important role in changing societal norms and promoting smoking cessation. Working with individual smokers to change their smoking behaviour is an important goal but has limited impact if the environmental factors that promote and support smoking are not also addressed. Hence, population based interventions should be thought of as complementary approaches to individual based behavioural or pharmacological interventions.

To achieve a smoke free society, a comprehensive health programme is required which includes effective information and education activities, legislative restriction, fiscal measures, and smoking cessation programme. Health care professionals can play a key role in helping and making informed decisions related to tobacco consumption and cessation. Finally, as noted above, while the 5As approach is commonly used, recent evidence suggests the VBA may be more appropriate in facilitating effective conversations about smoking in time-limited situations. In combination, these different levels of support, combined with pharmacotherapy, significantly increase an individual's chance of managing to stop smoking successfully. International and national associations for oral health professionals and all oral health professionals can act as advocates to promote population, community, and individual initiatives in the support of tobacco use prevention and cessation counseling, including integration in undergraduate and graduate dental curricula.

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