



## **CURRENT ISSUE: SMOKING CESSATION, THE PATIENT, THE PHYSICIAN AND THE POLICY MAKERS**

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### **ABSTRACT**

*Tobacco smoking continues to be a bane in the US. Nearly 540, 000 people die annually because of cigarette smoking. These deaths are preventable. Smoking is implicated in lung cancer and many other medical conditions. Billions of dollars have been spent on health issues related to smoking. Lung cancer affects men and women. Nicotine addiction is the culprit in continued smoking and understanding its role is important in promoting smoking cessation. Smoking cessation is important and scientific evidence and approaches exist in the literature. We have explored traditional, non-traditional and novel modalities for smoking cessation and the need for physicians to be actively involved in recommending smoking cessation. We have also discussed special populations that have special requirements for smoking cessation.*

**Keywords:** Cigarettes, Smoking cessation, Nicotine, Lung cancer, Healthy care policy.

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### **Contribution/ Originality**

This paper's primary contribution is making stakeholders aware of the implications of smoking and the role of the physicians and policy makers in reducing the incidence of cigarette related deaths. It also emphasizes how available smoking cessation methods may be beneficial to smokers.

### **1. INTRODUCTION**

More than half a million people die each year in America because of cigarettes and this includes current user or a past user of cigarette [1, 2]. Smoking is the main causative factor in lung cancer [1]. People have continued to die from lung cancer in spite of treatment modalities available in healthcare [3]. Tobacco usage is a significant cause of morbidity and mortality in the US [4, 5]. Smoking is implicated in other diseases such as coronary disease, respiratory and oral diseases [1, 6]. The total number of cigarettes smoked by an individual is highly significant and it is related to lung cancer risk and death [1, 6]. Research has shown that smoking cessation will reduce morbidity and mortality [4, 5, 7, 8]. Tobacco advertisements and businesses flourish and may be partly responsible for the global acceptance of tobacco smoking in spite of the negative implications of smoking [9, 10]. Considering the health and financial implications of cigarette smoking in the US, it is imperative that smoking cessation programs and policy should be advocated for in our communities [10-12].

### 1.1. Epidemiology of Smoking and Lung Cancer

There are approximately 40 million cigarette smokers in America. The financial implications of smoking show that about 150 billion dollars have been lost as a result of cigarette smoking [4]. Lung cancer is the number one cancer in the United States and the world [13].

The US had the third highest rate of lung cancer in women in 2012 as compared to the rest of the world. In the US, lung cancer places second in men and women for newly diagnosed cases with over 100, 000 in both genders when compared to the rest of the world [13-16].

When prostate, breast and colon cancers are added together, they do not account for as many deaths as lung cancer [13, 17]. There were over 400, 000 people living with lung cancer in the US alone in 2011 [17]. Cigarette smoking is responsible for 540, 000 deaths annually in the US [18]. The five-year survival rate in the US for lung cancer is about 17% [19, 20]. Median age of diagnosis of lung cancer and death is 70 and 72 respectively [17, 20]. The number of new cases per 100, 000 persons is highest in black males with 93 new cases per 100, 000 persons [19, 20]. More than 15% of lung cancer is diagnosed at the local stage and if this happens, the 5-year survival for this stage is over 50%; however, nearly 60% would have metastasized at presentation with a less than 5% survival in a 5-year survival period [20]. Black and white males have the highest numbers of deaths per 100, 000 persons which is about 76 per 100, 000 black males and 40 per 100, 000 for white males [20].

Kentucky has the highest incidence of lung cancer and Utah has the lowest incidence of lung cancer and these correspond to the highest and lowest smoking prevalence across the United States [18, 20]. The following have been implicated in lung cancer based on different studies: cigarette smoking, passive smoking, food and diet supplements, alcohol, exercise and physical inactivity, air pollution, occupational exposure and susceptibility genes for lung cancer such as Epidermal Growth Factor Receptor (EGFR), Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS), anaplastic lymphoma receptor tyrosine kinase (ALK) and Ret Proto-Oncogene (RET) [2, 9, 15, 21, 22].

### 1.2. Nicotine Addiction: Pathophysiology

The addictive substance in tobacco is nicotine. It is chiefly responsible for the continued use of tobacco. Its effects are as a result of the large surface absorptive area in the lungs and its eventual pathway to the cerebral circulation, nicotine receptor interaction and final distribution to the system. These are all contributory to the almost instantaneous rise in nicotine levels in the systemic circulation [8, 23]. The main effects derived from tobacco use include reduced anxiety and creating a state of euphoria. The connection between excitement and pleasure effects with precipitating factors such as environmental conditions such as stressful situations, constant desire for tobacco and displeasurable effects experienced in the bid to quit smoking are all because of nicotine [8, 23]. The symptoms of withdrawal include but are not limited to anger, irritation fits, dysphoria, depression, anxiousness, restlessness, lack of concentration, insomnia, weight gain and excessive appetite [8, 23]. Once inhalation of cigarette smoke has occurred, nicotine levels rise considerably based on the absorptive surface area in the pulmonary system. Blood moves quickly from the heart and lungs into the cerebral circulation containing nicotine. Known to be a weak base with a pKa value is 8.0; at a pH of 8.0, nicotine is almost 50% ionized [24].

The binding of nicotine to pentameric alpha and beta nicotinic acetylcholine receptors in the mesolimbic dopaminergic system (reward center of the brain) as well as its stimulation in the reward center which causes changes in structure and conformation is critical to understanding nicotine dependence. The result is an increase in the release of dopamine, which further establishes nicotine effects [8, 23, 25]. Abstinence is difficult when nicotine interacts with receptors in the brain; dependence develops over time [8, 23, 25].

### 1.3. Smoking Cessation Methods Available

So many challenges in the promulgation of procedures and strategies for counseling and providing advice on smoking cessation exist. The department of Health and Human Services initiated an action plan to put a final stop to smoking [26]. This has suffered setback because of a lack of implementation and the myriad of debates about the habit. Smokers who have attempted quitting smoking sometimes fail because of lack of motivation [27]. For smokers who are knowledgeable about the adverse effects of smoking, 75% are interested in quitting the habit [28]. Smokers are likely to lose about 10 years of life expectancy compared to their counterparts who have never smoked. If smoking cessation occurs prior to the fourth decade of life, the risk of death associated with smoking significantly reduces [12]. Special consideration should be given to specific patient groups such as pregnant women, adolescents and patients with heart disease [23, 29-31]. For example, pregnant women require one on one intervention because of the side effects of nicotine therapy such as possible adverse fetal effects [23, 29-31]. Considering the cardiac side effects of bupropion, delicate care should be exercised in administering this medication to smokers with coronary artery disease since QRS complexes prolongation are typically a side effect of this medication [23, 29-31]. Unfortunately, little evidence is known about smoking cessation programs in adolescents because they are a very mobile population and may not adhere to smoking cessation recommendations [29] however motivation may prove useful in adolescents. Furthermore, the use of nortriptyline and clonidine for smoking cessation has been discouraged as first line because of its side effect profile. Side effects such as sedation, dizziness and constipation are common [23].

Smoking cessation methods can be grouped into three parts: traditional pharmacological, non-pharmacological and novel methods.

### 1.4. Traditional Pharmacological Methods

Pharmacotherapy with the use of nicotine replacement therapy, which, includes nicotine patch, inhaler, spray and gum and sustained release bupropion and varenicline, are most popular forms of smoking cessation therapy [23, 28, 30, 32, 33]. Pharmacotherapy is the most superior form of treatment in addition to brief counseling at the outset of treatment [31]. It is therefore imperative to deal with this issue through the education and engagement of the public and the healthcare community [34]. When smokers receive sustained release bupropion with or Without the nicotine patch, these methods are associated with higher rates of smoking cessation compared to nicotine therapy alone, studies have shown higher abstinence rates at 12 months [33]. Varenicline is a partial agonist at the alpha 4 and beta 2 nicotinic acetylcholine receptor [8]. It is known to be a blocker; however, it does have partial receptor activator properties; it penetrates the brain and stimulates dopamine release in the reward center. A study on the effect of varenicline for 6 months and one year on smoking cessation via smoking reduction, when compared to placebo was shown to drastically reduce smoking in participants [8, 22, 23, 30, 35].

Table-1. Pharmacologic methods available for smoking cessation; prices are for generic brands [references 10,26, 37-38, 40 and CVS pharmacy website [8]; [36]; [33]; [30].

Cessation modality	Mode of action	Efficacy	Side effects	Advantages	Doctor's visit	Cost of medication	Insurance coverage
Nicotine patch	Absorbed through the skin	Effective at 2 months at the minimum	Insomnia, headache, skin irritation at the site	Placed on the skin easily	Receivable over the counter	\$37.99 for 24-hour 14 patches	Not covered by Medicare because OTC medications are excluded from Medicare Part D coverage by law
Nicotine gum	Absorbed by the mucous membrane of the buccal cavity	When combined with the patch, it proves to be effective	GI irritation, difficult to use with dentures	Effective in weight gain	Receivable over the counter	\$39.99 for 100 2mg pieces	Not covered by Medicare because OTC medications are excluded from Medicare Part D coverage by law
Nicotine inhaler	Replaces nicotine through inhalation but does not get to the small airways	Has been shown to be superior to placebo inhalers for smoking cessation in 6 month-trials	Cough	Close to actual cigarette smoking but particles do not get to the airway where it can have carcinogenic effects.	Prescription is required	\$288.17 for 168 10mg cartridges	Covered by Medicare
Nicotine lozenges	Nicotine is bound to ion exchange resin known as polacrilex.	Has been proven to have long and short-term smoking cessation rates	Irritation on the mouth and throat	Lozenges can be matched for the level of nicotine dependence	Available over the counter	\$41 for 2mg mini- 81 lozenges	Not covered by Medicare because OTC medications are excluded from Medicare Part D coverage by law
Nicotine nasal spray	Produces droplets causing a replacement of nicotine in plasma	If maintained, it leads to twice the rates while being actively used.	Nasal and throat irritation, cough, sneezing and watering eyes	Delivers more nicotine than gum	Prescription is required	\$300 for 40 ml	Covered by Medicare
Bupropion	norepinephrine-dopamine reuptake inhibitor -nicotine anatonagonist	Very effective if combined with a nicotine replacement therapy. Therapy begins long before and continues 6 months after quit date.	Insomnia, dry mouth, seizures	Useful in smokers with depression	Prescription is required	\$26.20 for 30 150mg tablets	Covered by Medicare
Varenicline	Selective alpha and beta nicotinic receptor partial agonist	Varenicline group had significantly higher continuous abstinence rates after 6 months (32%) compared to	Headache, insomnia, nausea and flatulence, suicide risk	Combination with a nicotine replacement therapy is not required	Prescription is required	\$292 for 53 tablets	Covered by Medicare

		placebo group [35]. Therapy begins before and continues months after quit date.					
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### 1.5. Non-Pharmacological Methods

While Yoga, exercises and acupuncture are not recommended by the USPHS guidelines for tobacco treatment, they have been reported to reduce stress levels by way of postures and breathing techniques as well as exercises, which improve mood and cause stimulation effects on the stretch pulmonary receptors which is analogous to the deep inhalations in cigarette smoking [37]. Mood has been shown to impact stress, which is significantly responsible for quitting smoking or relapses for people who have quit smoking already [37]. Financial gain increased smoking quitting rates [7]. In addition, studies have shown that following physician advice to quit smoking, patients feel motivated to quit; however, physicians do not take advantage of this opportunity [4-6, 32, 34, 38].

### 1.6. Individual Behavioral Therapy

Smoking cessation intervention and strategies, individual therapy, a form of behavioral intervention has been assessed and compared to group therapy in more than 20 trials with more than 7000 participants [38]. It showed that when compared to contact at a minimum level, smoking cessation was achieved [38]. It also showed that when individual counseling is rigorous (consisting of between 10-15 cognitive behaviorally known relapse prevention sessions), it is more beneficial than brief counseling and will lead to improved rates of smoking cessation [38].

### 1.7. Group Behavioral Therapy

There are advantages of group therapy; they include skills and knowledge acquisition for smokers, provision of opportunities to discuss personal experiences in quitting smoking as well as exploring reasons for quitting smokers amongst intending quitters [38]. In studies where group interventions were compared to self-interventions, group interventions were shown to increase cessation rates (n=4395, OR 2.04, 95% CI: 1.60-2.60) [25]. Group therapies are scientifically proven to be better than no intervention (n= 815, OR 2.17, 95% CI: 1.37-3.45) [38]. Many studies have also discussed the effectiveness of combining group therapies with nicotine replacement therapies [27, 38].

### 1.8. Novel Methods

Novel areas being explored include cigarette-smoking vaccine, cytisine and e- cigarettes. The induction by the immune system to make antibodies expected to have affinity to nicotine is a first step in the nicotine vaccine method. Blood brain barrier crossing is prevented and there is no action on brain receptors [25]. Dopamine release is suppressed as a result of nicotine vaccination. While nicotine vaccination promises to prevent relapses in abstainers in the first few months of quitting smoking, a period very significant and sensitive in smokers who may suffer a relapse, there isn't significant evidence that it is a smoking cessation intervention [25]. Cytisine is not yet available in the US, however studies by Walker et.al have shown that after a month, abstinence from smoking cigarettes could occur [39] in 40% of known smokers who used cytisine (partial agonist of nicotinic acetyl choline receptors) when compared to 30% who used nicotine replacement therapy [40]. Furthermore, when combined with behavioral therapy for an interim period, it was superior to nicotine replacement therapy. However, significant

differences exist in smoking cessation between placebo and cytisine than previous studies when compared to varenicline and nicotine replacement therapy (RR 3.4, 2.3 and 1.6 respectively) [40]. The food and Drug administration (FDA) spent almost a decade by 2014 to announce its intent to regulate E-cigarettes [36, 41, 42]. Even though Americans have spent over 2 billion dollars on E-cigarettes, the safety of E-cigarettes cannot be guaranteed. Trials and evidence are still not sufficiently strong on the justification for use, legislation and inferences in regards to smoking cessation [36, 41, 42].

### 1.9. Smoking Cessation Recommendations for Health Professionals

Several recommendations and policies for smoking cessation exist. It is imperative however, to be sure of their efficacy, score rating and evidence to support the guidelines [31, 32]. The following recommendations have been tested as having evidence rating of letter grade A. Grade A is defined by the United States Preventive Services Task Force (USPSTF) as 'certainty that the net benefit is substantial and practices should offer the service' [31]. Certainty is also defined by the USPSTF as 'the likelihood that the USPSTF assessment of the net benefit of a preventive service is correct' [31]. These concepts are based on scientific evidence.

**Table-2.** Summary of revised recommendations for smoking cessation [31]

<b>Recommendations</b>	<b>Grade based on evidence</b>
Most recent and up to date information about nicotine replacement therapy should be offered	A
Assessment of the smoking situation of patients at each encounter in the clinic	A
Recommendation for smokers to cease smoking	A
All smokers should be screened for cigarette smoking	A
Intending quitters should be offered assistance	A
Specialist cessation may be helpful if and when required	A
Nicotine replacement therapy should be recommended for intending quitters	A

### 1.10. Smoking Cessation Policy Changes

Smoking cessation can be dealt with in three sections: the patient and the environment, the healthcare provider and agencies already involved in smoking cessation and the available treatment modalities. Patients have been stratified into three main groups: current tobacco user now willing to make a quit attempt, current tobacco user unwilling to make quit attempt and a former tobacco user who has recently quit based on the clinical practice guidelines for treating tobacco use and dependence (CPGTD). The willingness of smokers is the most important factor for success in a smoking cessation program.

Considering the healthcare providers perform the first two As of the 5As recommended by the CPGTD which are training Ask, Advice, Assess, Assist and Arrange for smoking cessation [4, 5, 22, 23, 34, 43]. The most consistent barrier across different studies on smoking cessation practices as it relates to medical practitioners is competing time for other counseling topics in a visit [4, 5, 22, 23, 27, 34, 43]. Other barriers include lack of incentives, deficient and lack of awareness [4, 5, 22, 23, 27, 34, 43]. In addition, most providers think that it is majorly the responsibility of the primary care physician to provide smoking cessation counseling. The impact of healthcare providers cannot be overemphasized in smoking cessation practices. Studies have shown that patients advised by their physician on smoking and recommended for them to quit smoking are twice likely to quit than those not receiving any form of counseling [4, 5, 22, 23, 27, 34, 43]. Interventions in this regard may be necessary for health workers and would improve their counseling skills on smoking for their patients. Healthcare workers will significantly gain from effective training on smoking cessation. Some studies also suggest that physicians use less than 5As recommended by the CPGTD [4, 5]. For several years, the environment has played a great role in smoking cessation programs. These include smoke free workplaces, price as well as significant tax payments to

reduce tobacco demands [32]. The importance of media campaigns cannot be overemphasized positively as they impact behavioral change in all age groups of smokers. The ban of public smoking in many countries as well as increased awareness about smoking health implications related to smoking have been impactful. The printing of health warnings on cigarettes smoking labels by manufacturers of cigarettes have also proved useful [32]. Smoking cessation has its advantages. Scientific and other evidence based recommendations and approaches for reducing the effect of smoking on public health does exist in the medical literature. They include increases in taxes paid on cigarettes, campaigns in the mass media, behavioral approaches and medication assistance [32]. A study conducted by Jha et al. showed that smokers who quit at a young age before 35 with a median age of 29 years showed a survival curve similar to counterparts who had never smoked cigarettes and they were able to add an additional decade to their lives [12].

In each year that a smoker does not quit cigarette smoking after reaching 35 years of age, the smoker in question arguably loses life expectancy to the tune of a quarter of a year [12]. Considering the addictive nature of the habit, it is a difficult course to follow through for patients making the decision to quit smoking. So many smokers who might have made prior solo attempts to quit smoking find themselves in the same vicious cycle of failure especially in the first year [12]. Medications that enable smokers quit smoking exist, however from a medical standpoint, while they may be effective, it is imperative to note that some clients or patients will not use these prescribed medications for different reasons which include but are not limited to cost of medications, lack of health insurance, medications side effect profile, contraindications and interactions as well as lack of insight into the effects of nicotine on their health [12, 32]. While studies have suggested that physician smoking cessation counseling at hospital or clinic visits may prove beneficial, it has been argued that physicians may not strictly follow laid down guidelines or protocol in this practice [43]. This is based on a study in the United Arab Emirates and these findings may not be representative or applicable to the US or the rest of the world. Unfortunately, physicians do not obtain smoking status or histories from patients, neither might they have the skill set to offer counseling for smoking cessation or know the resources for referral [43]. As a follow up, a study conducted in Ohio in a pulmonary clinic showed that new smokers did receive smoking cessation interventions and type of intervention was physician dependent and varied across physician [44].

### 1.11. Smoking Cessation versus Low Dose CT Scan Screening

Smoking cessation albeit alone is more beneficial than screening with a CT scan alone or CT scan combined with smoking cessation. There is an ongoing debate by healthcare policy makers on how best to spend our healthcare dollars on smoking cessation [3]. There is a school of thought that feels we should invest on primary smoking cessation method as this focuses on prevention; preventing teenagers from smoking and advocating for new smokers to quit. However, the other school of thought feels that since we are not winning the war on cessation, it might be prudent to focus on secondary prevention of lung cancer by screening via low dose CT imaging. The advocates for this method feel that we might prevent deaths from this approach. According to the national screening trial research team, there was a 20% reduction in lung cancer mortality with low-dose computed tomographic screening [45].

The critics of this approach opine that there is a focus on treatment rather than prevention; also that there are significant adverse effects from imaging such as radiation, over testing, unwarranted follow up testing such as biopsy of benign nodules and anxiety from patients. In addition, the costs to the society versus benefits have to be considered [3]. Others believe that both approaches should be adopted but in reality because of unlimited resources, making a choice becomes imminent as we continue to wage war on reducing healthcare expenditure in the US.

## 2. CONCLUSION

Cigarette smoking all over the world continue to remain a challenge because of the significant medical and psychological issues associated with the habit. Lung cancer continues to cause significant morbidity and mortality. Smoking cessation has been proven to reduce heart disease, lung cancer and stroke. Many recommendations exist for smoking cessation but most importantly in summary are that the physician should always ask about tobacco use, provide cessation interventions to those who use tobacco products. It is important to consider special populations when considering smoking cessation programs and recommendations. Very importantly, tobacco usage history should be sought from pregnant women as well as provision of tailored counseling to pregnant women who smoke. These recommendations have been graded A by USPSTF.

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