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REVIEW

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Smoking Use and Cessation Among People with Serious Mental Illness

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Smoking rates in people with serious mental illness (SMI†) are disproportionately high compared to the general population. It is a leading contributor to the early mortality in this population. Smoking cessation rates are low in this group, though patients are motivated to quit. Unfortunately, health care providers do not always prioritize smoking cessation for this population. This review provides an overview of prevalence rates, biological effects that maintain smoking, and evidence-based treatments for smoking cessation in SMI. In addition, objective and qualitative data from a chart review of 78 patients with SMI prescribed smoking cessation treatment at one community mental health center are described. Of these, 30 (38.5 percent) were found to either quit (16/78) or reduce (14/78) smoking. Varenicline appeared to be particularly effective. Review of the literature and results of this study suggest that smoking cessation pharmacotherapies are effective for SMI patients and should be offered to those who smoke.

INTRODUCTION

Since the 1964 landmark U.S. Surgeon General report outlining evidence of harmful health effects of smoking, comprehensive programs and public campaigns have greatly reduced smoking prevalence. Nonetheless, smoking continues to be the leading cause of preventable disease and death in the United States [1]. Currently, the prevalence rate of cigarette smoking for women and men is 20.5 percent and 15.3 percent, respectively [2]. The prevalence of smoking in people with mental illness is much higher [3,4], and people with mental illness comprise a large majority of cigarette smokers [5]. Smoking rates in this group have declined much less than in those without mental illness [6].

Serious mental illness (SMI) is defined as a diagnosable mental disorder of sufficient duration to meet diagnostic criteria specified within the *Diagnostic and Statistical Manual* (DSM), resulting in substantial functional impairment [7]. A meta-analysis of mortality in mental disorders showed a significantly higher rate of mortality than in the comparison population, and a total of 67.3 percent of deaths were from medical causes [8]. People with SMI have a reduced lifespan of at least 10 years [8,9]. Smoking, along with obesity, contributes to the health risks in this population [10,11].

There is a perception that patients with mental illness are not interested in quitting [12], and few mental health providers offer smoking cessation treatment. However, there are effective evidence-based interventions for this population.

This review summarizes the literature on smoking and smoking cessation in patients with SMI. The paper also describes the experience of patients with SMI who received pharmacotherapy for smoking cessation at one community mental health center.

PREVALENCE

The U.S. 2009-2011 national survey of substance use and health estimated a prevalence of cigarette smoking at 36.1 percent in those with any behavioral disorder [13]. The Substance Abuse and Mental Health Services Administration (SAMHSA) reports a 50 percent prevalence [3]. Data from the National Comorbidity Survey found a smoking rate of 55.3 percent in those with lifetime mental illness [4].

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†Abbreviations: SMI, serious mental illness; DSM, Diagnostic and Statistical Manual; SAMHSA, Substance Abuse and Mental Health Services Administration; NRT, nicotine replacement therapy; CMHC, Connecticut Mental Health Center; FDA, Food and Drug Administration.

Keywords: smoking prevalence; smoking predisposition; tobacco cessation treatment; seriously mentally ill

Conflict of interest: Stephanie O'Malley, PhD, has received donated medications from Pfizer.

The association of smoking and psychiatric diagnoses remains even after controlling for other substance use, which is highly prevalent in people with mental illness [14]. Smoking prevalence increases with severity of mental illness, and rates are high in the SMI population [15]. In one sample of 991 SMI patients, the prevalence was 64 percent in schizophrenia and 44 percent in bipolar disorder patients [16].

Smoking-related mortality is also high in this population, with half of all deaths attributable to smoking [3]. In a large cohort of more than 600,000 patients, tobacco-related conditions comprised 53 percent of total deaths in schizophrenia, 48 percent in bipolar disorder, and 50 percent in major depressive disorder patients [17].

Chronic lung disease and obstructive sleep apnea are highly prevalent in the SMI population [18,19] and contribute to the increased smoking-related mortality risk.

Although people with mental illness are as motivated to quit as the general population [20], smoking quit rates are lower [6]. Data from the 2007 National Health Interview Survey on 23,393 adults showed lower success rates of quitting in mentally ill people [15].

Possible reasons for high prevalence of smoking and low quit rates in the SMI population are explored in the next section.

FACTORS LEADING TO MAINTENANCE OF SMOKING IN MENTALLY ILL PATIENTS

Smoking incidence in patients at the onset of illness is comparable to the general population but increases significantly as early as 1 year after treatment initiation [11]. Both biologic and social factors likely play a role in this escalation.

Several studies suggest a strong predisposition to smoking and less likelihood of cessation in people with depression [21]. The worsening of symptoms seen in depressive disorders [22,23] leads to the hypothesis that tobacco is a form of self-medication. Nicotine in cigarette smoke binds to nicotinic acetylcholine receptors in the brain, and while it causes an immediate increase in receptor activity, there is a long-term decrease due to receptor desensitization. It is postulated that increased cholinergic activity causes a state of depression and smoking alleviates symptoms due to nicotinic acetylcholine receptor desensitization [24]. However, there is evidence that clinically depressed smokers can receive treatment for smoking without worsening in depressive symptoms [25].

Among patients with schizophrenia, nicotine may normalize neuronal deficits; this effect may contribute to the high rate of smoking in this population [26]. Nicotinic acetylcholine receptors have been found to be important for maintaining optimal cognitive performance [27], and so smoking may improve cognitive deficits seen in schizophrenia. Cigarette smoking is also thought to normalize several sensory deficits seen in schizophrenia such as abnormal auditory sensory gating (P50) and smooth pursuit eye movements [28,29]. The P50 system measures the response with 50ms latency to paired auditory stimuli; in people with schizophrenia, the normal decrease in response to the second stimuli does not occur. Smooth pursuit eye movements refer to the movement of the eyes when tracking an object. It is abnormal in those with schizophrenia due to deficits in attention and failure of inhibitory cortical control.

In addition, the role of nicotine in the dopaminergic mesolimbic pathway is well characterized [30]. The net effect of nicotine is to increase dopamine, and this may result in use of smoking to ameliorate negative symptoms or, alternatively, represent an attempt to overcome dopamine blockade by antipsychotic medications. Also, nicotine alters pharmacokinetics of many psychotropic medications, resulting in lower drug levels [31] and leading to a hypothesis that people with SMI use smoking as a means to alleviate adverse effects from antipsychotics. Haloperidol, a potent dopamine blocking agent, is associated with an increase in smoking [32], and clozapine, a highly effective atypical agent, is associated with a decrease in smoking [33]. Clozapine impacts the P50 system [34], and this may also contribute to its role in smoking reduction.

Co-existing substance use is highly prevalent in people with mental illness, and there is some suggestion that treatment for substance dependence is associated with lower odds of quitting smoking [35]. However, this may be due to providers not addressing smoking during treatment for active substance dependence. A meta-analysis of 19 studies evaluating outcomes for smoking cessation treatment for people in addictions treatment or recovery showed positive results for short-term smoking cessation and long-term abstinence from alcohol and illicit drugs [36].

Finally, social reasons contribute to smoking in the SMI population. Historically, mental health providers have been permissive toward tobacco smoking among patients [37]. A survey of mental health providers at community mental health settings showed that only a minority advised or assisted in smoking cessation [12]. Barriers cited were a lack of training of providers and a perception that patients were not interested in quitting. In recent years, however, mental health centers are moving toward becoming tobacco-free [38], and this will help foster the recognition of tobacco dependence as a serious health problem for mentally ill patients.

Given the social and biologic predisposition to smoking and its maintenance, it is not surprising that people with serious mental illnesses have a very high prevalence. However, there are effective evidence-based treatments for this population.

TREATMENT OF TOBACCO DEPENDENCE

Treatment of Tobacco Dependence in the General Population

Effective tobacco cessation treatments exist in the general population and in those with SMI [39]. Tobacco cessation treatment requires involvement of health care professionals at multiple levels. Combination of medications and counseling is more effective than either alone.

Counseling includes practical problem solving skills and supportive engagement and can be delivered in telephone, group, and individual counseling formats.

Bupropion, nicotine replacement therapy (NRT), and varenicline are all considered first line medications. Bupropion is an antidepressant, but effect on smoking cessation seems independent of antidepressant effect [40]. Varenicline is a nicotinic receptor partial agonist and simultaneously stimulates dopamine and blocks nicotine receptors. A 2013 large Cochrane review of a total of 101,804 adults showed that all three agents are superior to placebo; all forms of NRT are effective; and varenicline is superior to bupropion and to single type of NRT but not combination NRT. Adverse effects from the active treatments were not significantly different from each other or significantly higher than placebo [41]. Combination of long-acting NRT such as a patch and a short-acting NRT such as a gum, lozenge, or inhaler is more effective than a single type of NRT [42]. There is some evidence that combination of varenicline with the nicotine patch, a form of NRT, is more effective than varenicline alone [43].

In 2009 and 2011, the U.S. Food and Drug Administration (FDA) issued a boxed warning for varenicline alerting health care professionals to unusual mood or behavior changes and suicidality; recently, it also added a risk of seizures and reduced tolerance to alcohol [44]. However, many studies have demonstrated superior efficacy of varenicline without increased neuropsychiatric adverse effects [45-48]. The FDA is continuing to evaluate the risk of neuropsychiatric effects of varenicline, and further updates to the label are pending. In weighing risks, the prescribing label notes the significant efficacy of varenicline and that the benefits of quitting smoking are "immediate and substantial."

Given the high relapse rate after smoking cessation treatment, multiple approaches have been studied for relapse prevention. A 2013 Cochrane review did not find evidence for any specific behavioral intervention; extended treatment with varenicline had some efficacy in preventing relapse [49].

Treatment of Tobacco Dependence in Seriously Mentally Ill People

Evidence shows that smoking cessation treatments are effective in the SMI population. In large meta-analyses, response to treatment is seen to be less robust in people with SMI compared to those without mental illness [41,50]; however, individual studies have shown similar success rates in people with and without mental illness [51]. For patients with schizophrenia, a Cochrane review showed significantly high cessation rates with varenicline and bupropion compared to placebo (risk ratio RR 4.74, 95% confidence interval CI 1.34 to 16.71 and RR 3.03, 95% CI 1.69 to 5.42 respectively). Evidence was insufficient for the efficacy of NRT in this group [50], though there may be some utility of NRT for long-term maintenance [52]. Varenicline appears to be well tolerated in those with SMI [53,54]. Varenicline may even improve sensory deficits and some cognitive deficits in schizophrenia [55].

There is insufficient evidence to recommend specialized psychosocial interventions tailored to people with schizophrenia [56]. There is some evidence for utility of cognitive behavioral treatment and motivational interviewing techniques along with pharmacological treatment [57-59]. Financial contingency reinforcement has shown short-term improvement in smoking reduction and cessation [50]. Maintenance treatment with continued pharmacological therapies and cognitive behavioral treatment was effective in reducing high relapse rates [60,61]. A longer duration of treatment may be effective in maintenance of cessation. Smoking reduction is also a potential goal. Varenicline recently has been shown to increase abstinence rates in smokers who initially were only willing to reduce smoking [62]. This strategy of initial reduction may predict future abstinence in the schizophrenia population as well [63].

For patients with current or past depression, NRT and buproprion have shown efficacy in smoking cessation [64]. Varenicline also was found to increase smoking cessation rates in stably treated depressed smokers without symptom recurrence [65]. Behavioral mood management and staged care interventions with motivational feedback and psychological counseling may also be effective [64,66]. Patients with bipolar disorder also have high rates of smoking and increased vulnerability to treatment failure [67]. Some treatment trials of people with SMI included those with bipolar disorder, but there are very few trials specifically studying smoking cessation treatments in this group. One small trial showed varenicline was safe and showed efficacy for smoking cessation at 3 months compared to placebo [68].

The majority of data show no worsening of psychiatric symptoms with smoking cessation treatment [50]. Abstinence from smoking is not associated with an increase in depressive episodes in those with a history of depression [23], and, in fact, symptoms have been shown to improve with cessation [25,69]. However, more research is needed on long-term effects of smoking cessation on mental health, especially after the initial years of smoking cessation.

Electronic cigarettes have been considered as a mechanism for harm reduction in smokers. There is limited evidence of efficacy of electronic cigarettes as a means to smoking cessation [70]. But there is concern that they may serve as a gateway to continued smoking or even serve to initiate smoking behavior. Currently, these products are unregulated, although the FDA recently announced its intention to regulate the devices [71]. At this time, given that the risks and benefits of electronic cigarettes are unknown, they are not recommended for use in treatment.

SMOKING CESSATION DATA FROM ONE COMMUNITY MENTAL HEALTH CENTER

Purpose

The Connecticut Mental Health Center (CMHC) adopted a smoke-free policy in 2008 [72]. As part of a multifaceted approach, patients who wished to quit smoking were

Table 1. Initial response to pharmacotherapy for smoking cessation.

	Category	Quit smoking	Reduced smoking	Total quit or reduced
	All patients (n=78)	16 (20.5%)	14 (17.9%)	30[a] (38.5%)
By type of pharmacotherapy	Varenicline (n=44)	12[b](27.3%)	10(22.7%)	22 (50%)
	Nicotine replacement therapy (n=34)	4 (11.8%)	4 (11.8%)	8 (23.5%)
	• Nicotine patch (n=20)	3 (15%)	0	3 (15%)
	• Nicotine gum (n=8)	1 (12.5%)	2 (25%)	3 (37.5%)
	• Nicotine patch + gum (n=6)	0	2 (33.3%)	2 (33.3%)
By diagnosis	Schizophrenia and other psychotic disorders (n=33)	6 (18.2%)	6 (18.2%)	12 (36.4%)
	• Varenicline (n=24)	5 (20.8%)	5 (20.8%)	10 (41.7%)
	• NRT (n=9)	1 (11.1%)	1 (11.1%)	2 (22.2%)
	Major depressive disorder (n=22)	4 (18.2%)	4 (18.2%)	8 (36.4%)
	• Varenicline (n=12)	4 (33.3%)	2 (16.7%)	6 (50%)
	• NRT (n=10)	0	2 (20%)	2 (20%)
	Bipolar disorder (n=12)	4 (33.3%)	3 (25%)	7 (58.3%)
	• Varenicline (n=7)	3 (42.9%)	2 (28.6%)	5 (71.4%)
	• NRT (n=5)	1 (20%)	1 (20%)	2 (40%)
	Others (n=11)[c]	2 (18.2%)	1 (9.1%)	3 (27.3%)
	• Varenicline (n=1)	0	1 (100%)	1 (100%)
	• NRT (n=10)	2 (20%)	0	2 (20%)

[a]Three patients who initially tried NRT with no response subsequently tried varenicline, and two of them reduced smoking; including these patients, the overall quit/reduction rate for the sample is 32/78 (41%), reduction rate for varenicline is 12/44 (27.3%), and total quit/reduction rate for varenicline is 24/44 (54.5%).
[b]Three of the 12 people relapsed within 30 days following early discontinuation of varenicline.
[c]Includes people with anxiety disorders, unspecified mood disorders and primary substance use disorders.

provided either a type of NRT or varenicline by the center pharmacy free of cost. A chart review was conducted to describe the experience of patients who were prescribed these medications for smoking cessation.

Method

Seventy-eight patients who received smoking cessation pharmacotherapy in 2009 were identified from pharmacy records. Each chart was reviewed retrospectively by one of two reviewers. Data was obtained from the pharmacy database and the physical chart. Information was collected on type of pharmacotherapy, side effects, number of cigarettes smoked, number of days quit, motivation to quit, self-reported cravings, and self-reported emotional state during smoking cessation. The study was approved by the Yale Human Investigation Committee.

Results

Among the 78 people who received smoking cessation treatment, there were 32 males and 46 females. Mean age was 45. The major psychiatric diagnoses were schizophrenia and other psychotic disorders (42.3 percent), major depressive disorder (28.2 percent), and bipolar disorder (15.4 percent). Forty-four patients were prescribed varenicline and 34 NRT as the initial pharmacotherapy.

Sixteen of 78 people (20.5 percent) quit smoking, and an additional 14 (17.9 percent) reduced smoking, making a total of 30 people (38.5 percent) who either quit or reduced. The number was higher with varenicline (22/44) than with NRT (8/34) (Table 1). Also, three in the NRT group who failed treatment subsequently initiated varenicline and two reduced smoking, bringing the total quit/reduction number for varenicline to 24 (54.5 percent). Higher quit rates were seen with varenicline irrespective of diagnostic group (Table 1). The average duration of varenicline treatment was 63.5 days for all patients. Among the 12 people who quit on varenicline, three relapsed within a month soon after varenicline was stopped due to adverse effects.

Among 12 patients who reported side effects, nine were on varenicline but only four reported neuropsychiatric complaints (irritability, nightmares, anxiety, paranoia). Two people reported nausea. At least two people did not start the prescribed varenicline, citing fear of psychiatric side effects.

Among motivators to quit, personal or family history of physical illness such as lung disease, cardiac illness, and cancer was common. Less common reasons were planning pregnancy, preparation for surgery, and housing restrictions. Many people were motivated to initiate treatment in spite of previous failed attempts. People who quit reported feeling good, though some complained about weight gain. Even people who did not reduce smoking reported decrease in cravings on varenicline and wanted to continue treatment.

A few patients received specific education and counseling to address anxiety or other symptoms experienced from nicotine withdrawal. People who were using other addictive substances did not report increased cravings for those substances. Many patients were on more than one psychotropic medication and did not report any medication changes during the immediate smoking cessation treatment period.

Discussion

In this naturalistic follow-up of patients on smoking cessation pharmacotherapy at CMHC, a clinically significant percentage of people with SMI achieved abstinence with pharmacotherapy and no other targeted interventions. An equal number of people reduced smoking, which has health benefits and may lead to future abstinence. Quit rates were lower than reported in studies of people without mental illness, consistent with lower rates seen in some studies of individuals with SMI. This SMI group showed motivation to quit for reasons similar to people without mental illness. However, the limited qualitative data on self-reported motivators to quit and cravings during treatment did not allow for assessment of these factors in predicting smoking cessation. Overall, patients had a positive experience with treatment, regardless of actual outcome on abstinence.

CONCLUSION

Patients with SMI have a much higher prevalence of cigarette smoking than the general population, and this contributes to the already high medical morbidity and mortality in this group. Smoking is hypothesized as a form of self-medication in people with SMI. But SMI people are motivated to quit, and treatments are effective for smoking cessation and maintenance. SMI people report an overall positive experience with treatment. Mental health providers, as well as primary care providers, should routinely offer evidence-based treatments for smoking cessation for people with SMI.

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