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The Dual Epidemic of Tobacco Dependence and Obesity Among Those With Severe Mental Illness

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Smoking and obesity are both more common in persons with severe mental illness (SMI) than in the general population, occurring in 50%–80% and 45%–55%, respectively, of those with SMI.^{1,2} Importantly, both smoking and obesity contribute to the increased mortality of persons with SMI, which is 2 to 3 times higher than that of the overall United States population and primarily due to cardiovascular disease (CVD).^{1,2} Thus, both smoking cessation and weight management are crucial to enhancing the health of people with SMI.

Weight gain after smoking, an important complication of tobacco abstinence, does not alter the reduced risk of CVD from stopping smoking.³ Until now, however, this relationship has not been explored in persons with SMI. In this month's issue, Thorndike and colleagues⁴ provide important findings that postcessation weight gain does not decrease the cardiovascular benefits of tobacco abstinence among people with SMI. The authors evaluated a subgroup of 65 outpatient smokers with schizophrenia, schizoaffective disorder, or bipolar disorder who completed a 1-year randomized controlled trial of varenicline for maintenance of abstinence from smoking. Participants in the abstinent group had a greater weight gain and a greater decrease in 10-year Framingham general CVD risk scores than those in the nonabstinent group, despite high prevalences of obesity (mean body mass index [BMI] = 31 mg/kg), diabetes (31%), dyslipidemia (55%), and hypertension (34%). In other words, despite being associated with significant weight gain, smoking cessation still decreased 10-year CVD risk. These very encouraging findings suggest that people with SMI who stop smoking will reduce their risk for cardiovascular events despite gaining weight and having high baseline levels of metabolic dysregulation. However, a number of unresolved issues remain.

First, these findings cannot be generalized to periods of tobacco abstinence beyond 1 year. Thorndike and colleagues⁴ note that postcessation weight gain in people with SMI may have a more severe trajectory over time as compared to that in people without SMI. Indeed, postcessation weight gain in their study sample continued throughout the 12 months of

abstinence. An important unresolved question, therefore, is whether there is a point at which continued postcessation weight gain in those with SMI might attenuate the beneficial effects of quitting smoking and actually increase CVD risk. For example, in a 3-year outcome study of 914 people who tried to stop smoking, quitting smoking was associated with an increased risk of diabetes and impaired fasting glucose.⁵

Another issue is that the Framingham model predicts only cardiovascular events, and people with SMI have elevated mortality from other general medical disorders and suicide.^{1,2} Smoking cessation might reduce cardiovascular risk, but weight gain could increase the mortality risk from other disorders related to obesity (eg, diabetes, dyslipidemia, and metabolic syndrome). Thus, metabolic syndrome (of which abdominal obesity, diabetes, and dyslipidemia are components) is associated with a 2- to 3-fold increase in cardiovascular mortality and a 2-fold increase in all-cause mortality.⁶ Moreover, the presence of obesity in persons with SMI is associated with a more severe course of the mental disorder, including higher rates of suicide attempts.⁷ This has been hypothesized to be due in part to the adverse effects that obesity has on the central nervous system.

Additionally, it is unknown how well the 10-year Framingham risk score predicts cardiovascular events among those with SMI, as people with SMI were excluded from studies that led to development of the Framingham risk score equations. In a recent study of cardiovascular risk models for people with SMI in which 38,824 people with SMI were followed a median of 5.6 years, the PRIMROSE lipid model and the PRIMROSE BMI model (the latter to be used when laboratory values are not available) were each superior to the Framingham model for predicting cardiovascular events.⁸ Unlike the Framingham model, the PRIMROSE models include variables for psychiatric diagnosis, psychotropic medications at baseline, harmful use of alcohol, and a social deprivation score. Thus, psychiatric diagnosis, psychiatric medications, alcohol use, and social deprivation are important to consider in the prediction of CVD events among those with SMI.

This leads to the question of how to best treat the person with SMI who has postcessation weight gain, especially if he or she is obese. In a meta-analysis of treatments for postcessation weight gain,⁹ dexfenfluramine, phenylpropanolamine, and naltrexone were found to limit weight gain shortly after stopping smoking, but not at 6 or 12 months. Also, dexfenfluramine and phenylpropanolamine have been removed from the market because of safety concerns. Exercise did not mitigate weight gain at end of treatment but did so at 12 months. Importantly, weight

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management education was not effective for reducing postcessation weight gain and possibly reduced abstinence.

There may be gender effects in the treatment of postcessation weight gain: naltrexone may mitigate postcessation weight gain in women but not men,¹⁰ while topiramate promotes smoking cessation and weight loss in men but not women.¹¹ Finally, in a review of 12 studies of combination pharmacotherapy for smoking cessation,¹² 7 found that combination therapy was associated with less postcessation weight gain than monotherapy or placebo, raising the question of whether combination pharmacotherapy would be more efficacious than monotherapy for treatment of postcessation weight gain, as has been found for the treatment of obesity. Could the postcessation weight gain associated with successful varenicline treatment be mitigated by coadministration of an opioid antagonist or topiramate? Would the combination of bupropion and naltrexone be efficacious for smoking cessation while mitigating weight gain? In an open-label trial¹³ of the combination therapy weight loss agent bupropion sustained release (SR) and naltrexone SR in 30 overweight or obese smokers, 48% of participants achieved sustained abstinence at week 12 with no change in body weight. Would any of the other newly US Food and Drug Administration–approved treatments for weight loss in persons with obesity (eg, lorcaserin, the combination of topiramate extended release [ER] and phentermine ER, or liraglutide 3 mg/d) be efficacious for postcessation weight gain in people with SMI?

Another possibility is that there are different subgroups of patients with SMI and tobacco dependence, and these subgroups may require differential treatment for optimal outcomes. Obesity is a reason given for nonadherence with antipsychotic medications,¹⁴ and women with psychosis are more likely than men with psychosis to report that they smoke to prevent weight gain.¹⁵ Indeed, there is a subgroup of women who smoke primarily to control their weight, termed “female weight-control smokers.”¹⁶ Perhaps in obese women with SMI who smoke as a means to control their weight, initial management of obesity might enhance the chances of successful treatment of tobacco dependence.

Finally, it is important to remember how difficult it is for persons with SMI to adopt a healthy lifestyle. Of 203 participants enrolled in Thorndike and colleagues’ study, 87 (43%) were abstinent at week 12, and 33 (16%) were abstinent at week 52. Thus, the majority of participants were unable to achieve or maintain abstinence. More effective treatments for tobacco dependence that also prevent postcessation weight gain are greatly needed.

In short, Thorndike and colleagues⁴ present compelling findings that smoking cessation improves CVD risk in people with SMI despite significant weight gain and substantial baseline levels of obesity and related diseases. Thus,

clinicians may encourage their patients with SMI to stop smoking while educating them that they are reducing their CVD risk even if they gain weight. However, postcessation weight gain and its complications must be monitored and addressed, especially among patients with obesity, diabetes, or metabolic syndrome.

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