Review Article

Tobacco-Related Disparities Among Individuals Affected by Mental Illness

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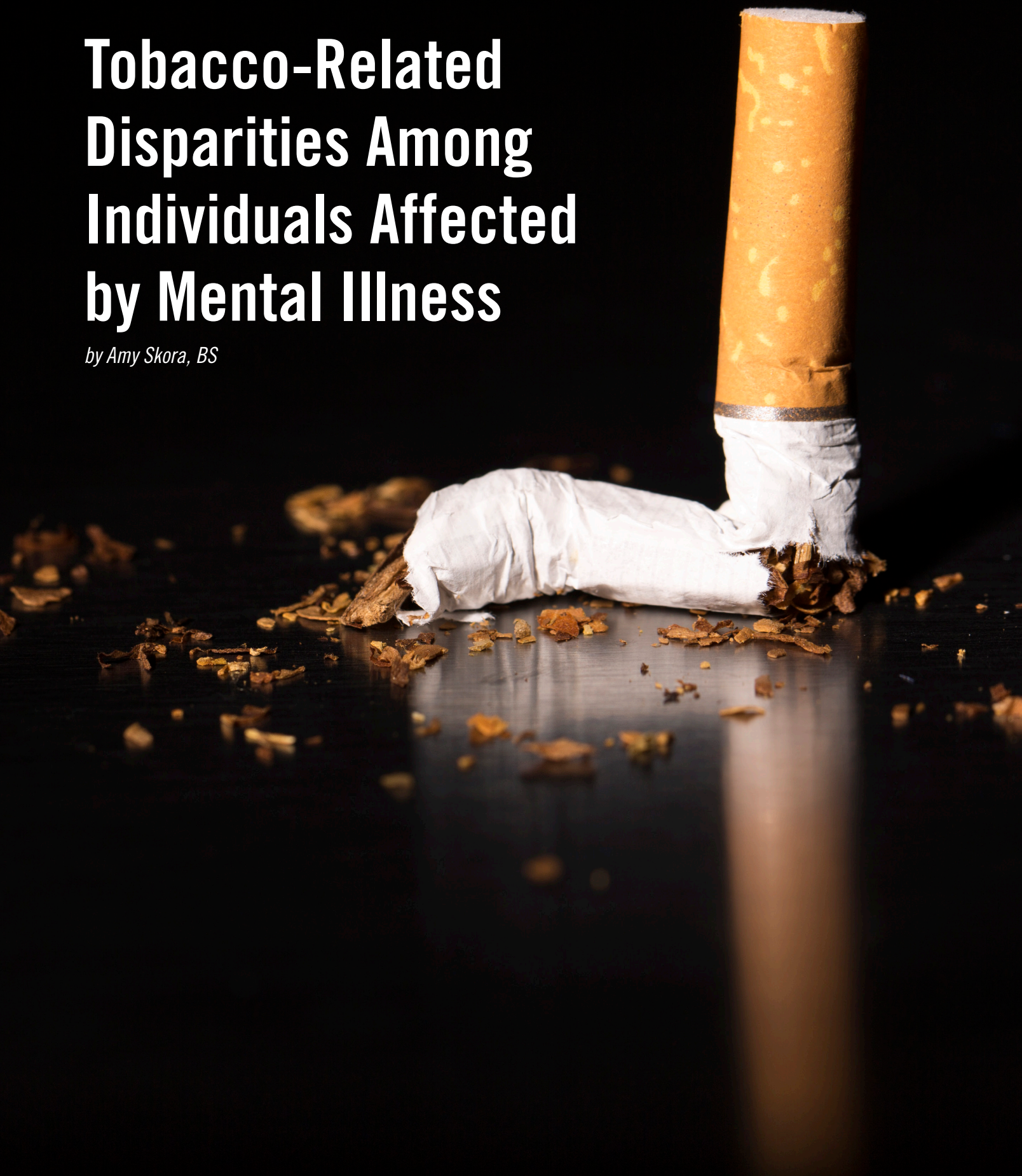


Tobacco use is still the leading cause of preventable death in the United States.[1] Although fewer Americans are smoking today than in years past—about 15% of adults currently smoke[1]—and while this rate continues to decrease for the general population, certain groups have experienced far less smoking reduction. Individuals affected by mental illness are disproportionately impacted by the burden of tobacco, and a large disparity remains between this group and the general population of smokers.[2] Smoking rates are significantly higher among individuals affected by mental illness as compared to the general population. One in four adults in the U.S. have some form of mental illness; this subset uses 40% of all cigarettes smoked by adults in the U.S. People affected by mental illness are approximately twice as likely to smoke as those without mental illness.[3] Nearly 50% of those with more severe mental illness smoke, or about 194% more than the smoking rate in the general population.[3]

Smoking leads to serious consequences for the psychological and physical health of this vulnerable, underserved population. To help reduce the tobacco-related disparities associated with individuals affected by mental illness, concerted efforts need to be taken to assist this population in quitting smoking and to deliver effective, evidence-based treatments for tobacco dependence.[4]

This article will help clinicians understand the challenges facing smokers affected by mental illness, review the importance of providing evidence-based tobacco-dependence treatments, including behavioral counseling and recommended pharmacotherapies, and highlight the mental health benefits of quitting.

Comorbidity of Mental Illness and Smoking

The disproportionately high rates of smoking among those affected by mental illness are likely due to a combination of biological, psychological, and social factors that work together to create a unique vulnerability for tobacco dependence.[5] People affected by mental illness are more likely to have stressful living conditions, have low annual household income, and lack access to health insurance, health care, and cessation support.[6,7] These factors do not only affect the likelihood of smoking among this population, but also can make it more challenging to quit smoking.

In addition to higher smoking rates, those affected by mental illness also smoke in greater amounts and more frequently than the general population, resulting in greater nicotine dependence which contributes to an increased difficulty in quitting.[8] Nicotine has mood-altering effects that can mask the negative symptoms of mental illness, putting people affected by mental illness at a higher risk for cigarette use and nicotine addiction.[6] Based on the National Epidemiological Survey on Alcohol and Related Conditions, the quit rate of smokers without mental illness is 22.3%; for those with any mental illness, 18.4%; and for those with psychosis, 12.5%.[9]

Consequently, the high rates of smoking and nicotine addiction among people affected by mental illness put them at a higher risk for devastating health consequences. People with mental illness are more likely to die from tobacco use than from their mental illness.[10] In fact, individuals affected by mental illness die up to 25 years earlier than the general population. A primary cause of this premature death is smoking. The most common causes of death among people affected by mental illness are heart disease, cancer, and lung disease, all of which are smoking-related diseases.[11] People diagnosed with schizophrenia, for example, face double the risk of death due to cardiovascular problems and triple the risk of respiratory disease and lung cancer.[5,12-14] This increased morbidity and mortality associated with mental illness is due in large part to treatable medical conditions that are attributed to smoking.

One common misconception is that quitting smoking impairs mental health recovery. However, research shows that those affected by a mental illness who smoke actually have increased psychiatric complications.[15-17] Among patients affected by mental illness who smoke, there are higher rates of psychiatric symptoms, more psychiatric hospitalizations, and poorer treatment outcomes. Fortunately, smoking cessation provides benefits to the individual's mental health, overall quality of life, and longevity.

Due to the unique challenges faced by those affected by mental illness, another misconception is that these patients cannot quit smoking. However, those affected by mental illness who smoke are able to quit. Their quit rates may not be as high as the general population, but patients affected by mental illness can successfully quit smoking when provided support and assistance.[9] This underscores the importance of utilizing every opportunity to provide tobacco dependence treatments to every individual affected by mental illness.

Evidence-Based Tobacco Dependence Treatment

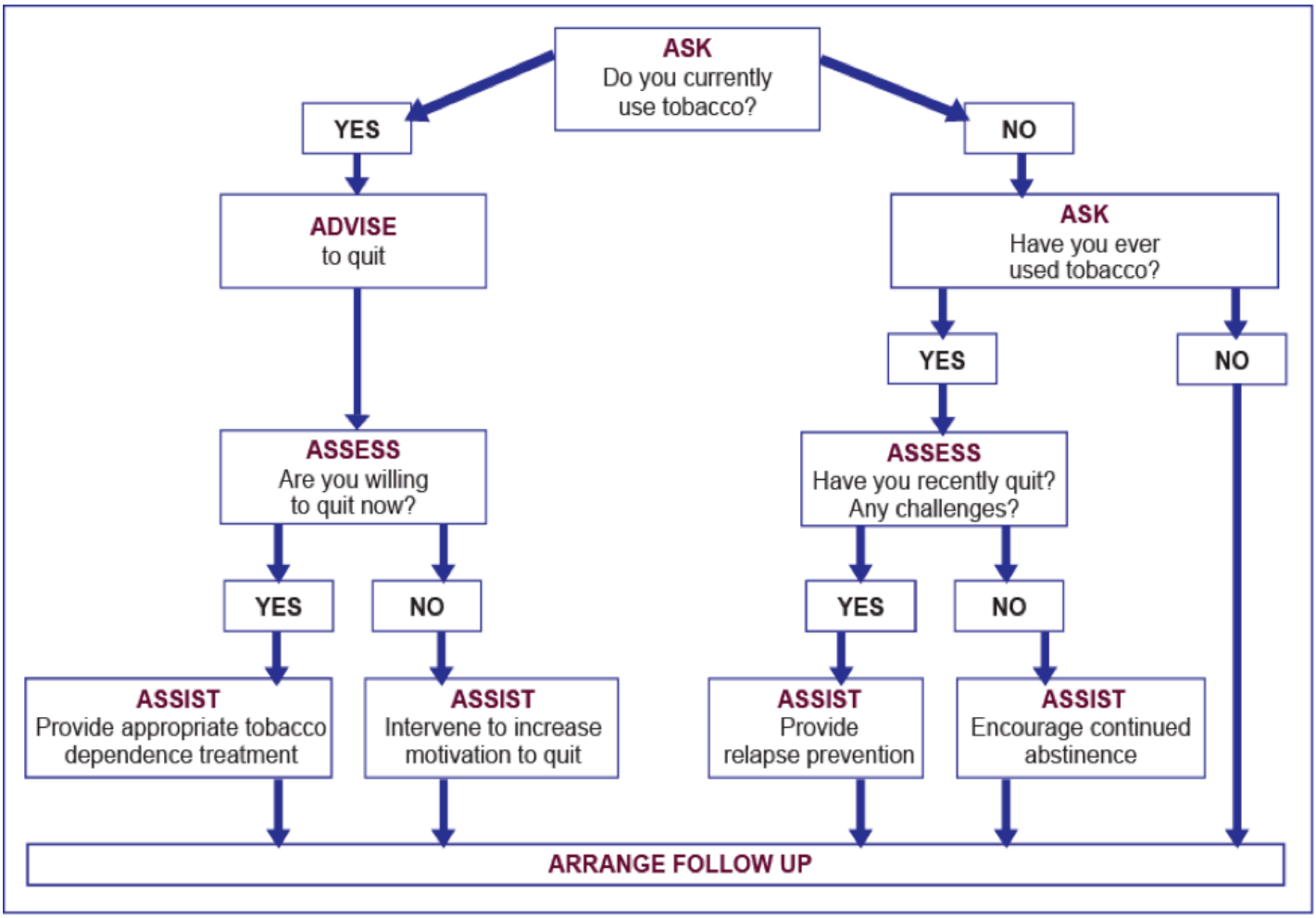
The 2008 United States Public Health Service Clinical Practice Guideline Treating Tobacco Use and Dependence provides recommendations to deliver effective tobacco-dependence interventions.[4] The Clinical Practice Guideline identifies tobacco-dependence treatments, including medications and behavioral counseling, that are effective across a broad range of populations. These evidence-based treatments can work well to assist individuals affected by mental illness in quitting smoking.

Despite increased rates of smoking and high levels of tobacco dependence in this population, people affected by mental illness are just as likely to want to quit smoking as those without such conditions.[18] However, the chronic nature of tobacco dependence often requires multiple attempts to successfully quit and the need for repeated intervention.[4] Fortunately, research has shown that adult smokers affected by mental illness can successfully quit, and benefit from receiving proven smoking-cessation treatments.[18]

Clinicians can make a difference with even a minimal (three minute or less) intervention.[4] The guideline recommends the 5A model for a brief intervention to systematically identify tobacco users and consistently give the message that they can help them quit smoking (Figure 1). The 5A mnemonic follows:

- Ask about tobacco use at every visit
- Advise smokers to quit in a clear, strong, personalized manner

FIGURE 1. Tobacco Dependence Treatment 5A Brief Intervention[4]



- Assess smoker's willingness to make a quit attempt within 30 days
- Assist in the quit attempt by providing counseling and pharmacotherapy
- Arrange to follow-up with the smoker to prevent relapse

Smokers who receive all of the 5As during a medical encounter are more likely to use counseling and medication to quit, compared to smokers who receive one or none of the 5As.[19] All smokers trying to quit, including those affected by mental illness, should be encouraged to use both counseling and pharmacotherapy as they are more effective when combined.[20-24]

Counseling

Providing cessation counseling is an essential component of an effective treatment intervention. Clinicians should assist tobacco users with developing a quit plan, including setting a quit date within thirty days, and provide counseling that focuses on problem solving to recognize smoking triggers and develop coping skills.

The Wisconsin Tobacco Quit Line (800-QUIT-NOW) can serve as an extension of a clinical tobacco intervention by providing ongoing, intensive telephone cessation support to Wisconsin tobacco users. Counseling from the Wisconsin Tobacco Quit Line can quadruple the chances of a tobacco user quitting permanently.[25] The free services of the Quit Line are available 24 hours per day/7 days per week and include individualized telephone counseling on strategies for quitting, self-help materials, and access to a two-week supply of nicotine replacement therapy medication.

Pharmacotherapy

Seven first-line pharmacotherapy treatments are approved by the United States Food and Drug Administration (FDA) and have an established record of effectiveness and safety for treating tobacco dependence. Clinicians should not be reluctant to provide pharmacotherapy to individuals affected by mental illness. This section will highlight the two pharmacotherapy treatments that have been shown to be particularly effective for all populations of smokers, including individuals affected by mental illness. Varenicline and the combination of nicotine patch plus short-acting nicotine replacement therapy (NRT) are roughly equivalent first-line choices.[26] A Cochrane meta-analysis showed that both varenicline and combination NRT were superior to NRT monotherapy in increasing the odds of quitting. Other meta-analyses and large individual clinical trials also support the superiority of varenicline and combination NRT relative to monotherapies.[4,22,27,28]

Nicotine replacement therapy

There are five forms of nicotine replacement therapy: patch, gum, lozenge, inhaler, and nasal spray.[4] The nicotine patch is available with a prescription or can be purchased over the counter. Patches are a long-acting product designed to provide a steady dose of nicotine through the skin over 16-24 hours, depending on the product. Combining the patch with a short-acting NRT, such as the gum or lozenge, yields the best results to help with physical withdrawal symptoms and to resist the urge to smoke. This combination can be particularly helpful for smokers with high dependence or repeated failures with using only one NRT. Nicotine replacement therapy also does not interfere with antidepressants or antipsychotics so is an optional choice for individuals affected by mental illness.

The FDA made changes to NRT labeling in 2013 that many tobacco users, and some clinicians, are not aware of.[29] The changes removed unnecessary warnings that were no longer necessary to ensure safe use of these products. The FDA removed the warning that consumers should not use an NRT product if they are using tobacco or a nicotine-containing product, including another NRT. There are no significant safety concerns associated with using more than one NRT at the same time, or using NRT at the same time as another nicotine-containing product—including a cigarette. If an individual is using NRT to help them quit smoking but slips and smokes a cigarette, they should not stop using the NRT. Rather, it is safe and advantageous for them to keep using the NRT and keep trying to quit despite the cigarette use.

The FDA also supports research that has shown NRT products do not appear to have significant potential for abuse or dependence.[29] Some tobacco users need to continue using NRT for an extended time in order to successfully quit, and it is safe to do so in most cases. Many individuals affected by mental illness who smoke have high nicotine dependence and need more intense treatments.[6] Combination NRT and extended use of NRT is safe and may be beneficial for quitting success and relapse prevention for patients affected by mental illness.[30]

Varenicline

Varenicline is a partial agonist activating the α4β2 nicotinic receptor to prevent cravings and relieve withdrawal symptoms.[31] It also acts as a partial antagonist by occupying receptor sites and blocking nicotine-binding leading to a reduction in the satisfaction gained by smoking.[31,32] Studies have shown that varenicline increases the odds of quitting about three fold.[4]

On December 16, 2016, the FDA removed the black box warning regarding serious neuropsychiatric events from the tobacco cessation medications, varenicline and bupropion SR. Based on a review of a large clinical trial, the FDA determined the risk of serious side effects on mood, behavior, or thinking is lower than previously suspected.[33] The risk of these mental health side effects is still present, especially in those currently being treated for mental illnesses or who have been treated for mental illnesses in the past. However, most people who had these side effects did not have serious consequences, such as hospitalization. The results of the clinical trial confirm that the benefits of stopping smoking typically outweigh the risks of these medications.

For information on all of the seven FDA-approved tobacco-cessation medications, a comprehensive medication chart, including dosing and use instructions, is available on the University of Wisconsin Center for Tobacco Research and Intervention Website: www.ctri.wisc.edu.[34] As of February 2016, Medicaid/BadgerCare covers all seven of the FDA-approved smoking-cessation medications, allowing repeated courses of treatment, combination therapy, and no copays or costs to the patient.[35]

Special Considerations for Treatment for Individuals Affected by Mental Illness

Traditional cessation treatments, such as monotherapies and standard medication dosing/duration, may be inadequate for people affected by mental illness.[36] This population often faces unique challenges in quitting smoking and may benefit from additional services, such as more intensive counseling, longer use of (or combination of) cessation medications, and follow-up care.[36-38]

Clinicians should keep an open mind around flexibility in setting quit dates and gradual reduction in smoking to eventually reach abstinence. Often times, "practice quit attempts" are beneficial to this population. Practice quit attempts are unofficial quitting attempts to gain confidence and skills in quitting; they are a practice experience to get ready for an official quit.[39] These practice attempts present less pressure to succeed and help individuals build self-efficacy over time.

Another strategy to assist patients affected by mental illness in successful quitting and to motivate reluctant smokers to make a quit attempt is partially replacing cigarettes with NRT.[40] Patients who smoke can begin to reduce the amount of cigarettes smoked while supplementing with NRT. This is an opportunity for individuals to become comfortable with using the medications, lessen withdrawal symptoms while working on behavior change, and increase confidence in their ability to quit. Researchers have found the use of the NRT patch prior to the quit date, or for smoking reduction as part of a quit attempt, is safe and may increase smoking abstinence.

Extra assistance and tailored strategies to succeed in quitting should be offered to individuals affected by mental illness who smoke. With support, people affected by mental illness can, and do, quit smoking successfully.[36,37]

Benefits of Tobacco Cessation in Individuals Affected by Mental Illness

Improvements in Mental Health

The acute effects of nicotine withdrawal include mood swings, irritability, sleep disturbance, and depressed affect, which need to be managed.[41] However, in the long term quitting smoking is associated with mental health benefits. A recent systematic review and meta-analysis examined 26 studies that assessed mental health and smoking status of participants to examine changes in mental health between people who quit smoking and those who continued to smoke.[42] The meta-analysis found that smoking cessation was

TABLE 1. Effect of Smoking Cessation on Mental Health

Outcome	# of studies	Standardized mean difference (95% CI)
		Original effect estimate
Anxiety	4	–0.37 (-0.70 to -0.03)
Depression	9	–0.25 (-0.37 to -0.12)
Mixed anxiety and depression	4	–0.31 (-0.47 to -0.14)
Psychological quality of life	4	0.22 (0.09 to 0.36)
Positive affect	1	0.40 (0.09 to 0.71)
Stress	2	–0.27 (-0.40 to -0.13)

[a] A comparison of the differences in mental health outcomes in people who quit smoking or continued to smoke.
[b] Adapted from Taylor G, McNeil A, Farley A, Girling A, Linson-Hawley N, Avegard P. Change in mental health after smoking cessation: systematic review and meta-analysis. *BMJ*. 2014;348:g1151

associated with marked improvements in mental health over time, whereas continued smoking was associated with little change over the same period. Over time, cessation actually improves depression, anxiety, stress levels, and lowers the risk of suicide.[43-46] The meta-analysis also found that, compared to those that did not quit, those that quit smoking experienced significant improvements in depression and anxiety and significant reductions in stress (Table 1).[42] The amount of reduction in anxiety and depression was equal to or greater than what would have been expected from medications used to treat anxiety and depression.

The evidence shows that quitting smoking does not jeopardize the stability of a primary mental health disorder or recovery.[42] Assistance to quit tobacco is and should be a part of recovery from a mental illness. Quitting smoking will not hinder progress and can be beneficial in improving both physical and mental health.

Decreased Medication Burden

Quitting smoking may reduce psychiatric medication burden. Since tobacco smoke increases the metabolism of certain psychiatric medications, quitting may produce rapid, significant increase in blood levels of psychotropic medications.[47] Side effects of using the pre-quit dosages of psychiatric medication can appear once someone quits smoking. This underscores the importance of psychiatric monitoring during the quit attempt. Following cessation, it is often possible to lower medication dosages, which can benefit the patient. Mental health patients often need to lower doses of psychotropic medications and see a decrease in side effects of these medications after quitting.[47]

For a comprehensive list of psychotropic drug interactions with tobacco use, please see the resource, Drug Interactions with Tobacco Smoke, from Rx for Change.[48]

Conclusion

In summary, clinicians can do their part in helping reduce tobacco disparities among people affected by mental illness by making tobacco dependence treatment an integral part of their standard of care. The majority of individuals affected by mental illness who smoke want to quit and can successfully quit with assistance.[36,37] When this vulnerable population is provided evidence-based tobacco treatments and interventions, with appropriate modifications such as increased dosage and extended use of the cessation medications, they increase their chance of quitting successfully and reduce the tobacco-related disparities associated with mental illness.

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Additional Resources

Visit www.ctri.wisc.edu/providers/behavioral-health/ to learn more about how to help people with mental health conditions quit smoking.[49] University of Wisconsin Center for Tobacco Research and Intervention Regional Outreach staff can provide assistance to your organization to help implement evidence-based practices to help patients quit.[50] Find your Regional Outreach Specialist here: www.ctri.wisc.edu/providers/contact-specialist/

The Wisconsin Nicotine Treatment Integration Project (WiNTiP) works with mental health and substance use disorder treatment providers to integrate tobacco dependence into their services.[49] Learn more about how WiNTiP is changing the culture and helping this vulnerable population break their addiction tobacco here: www.HelpUsQuit.org

References

1. Fermin J. 11 Scary Statistics About StressCenters for Disease Control and Prevention. Current cigarette smoking among adults—united states, 2005-2015. *Morbidity and Mortality Weekly Report*. 2016;65(44):1205–1211.
2. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Adults with mental illness or substance use disorder account for 40 percent of all cigarettes smoked. https://www.samhsa.gov/data/sites/default/files/spot104-cigarettes-mental-illness-substance-use-disorder/spot104-cigarettes-mental-illness-substance-use-disorder.pdf. Published March 20, 2013. Accessed October 19, 2017.
3. Szatkowski L, McNeill A. The delivery of smoking cessation interventions to primary care patients with mental health problems. *Addiction*. 2013;108(8):1487-1894.
4. Fiore MC, Jaén CR, Baker TB, et al. Treating tobacco use and dependence: 2008 update. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service; 2008.
5. Ziedonis D, Hitsman B, Beckham J, et al. Tobacco use and cessation in psychiatric disorders: national institute of mental health report. *Nicotine and Tob Resh*. 2008;10(12):1691-1715.
6. Centers for Disease Control and Prevention. Vital signs fact sheet: adult smoking focusing on people with mental illness 2013. https://www.cdc.gov/vitalsigns/smokingandmentalillness/index.html. Published February 2013. Updated February 5, 2013. Accessed January 2, 2018.
7. Centers for Disease Control and Prevention. Vital signs: current cigarette smoking among adults aged ≥18 years with mental illness—united states, 2009–2011. *Morbidity and Mortality Weekly Report.* 2013;62(5):81-87.
8. Lipari RN, Van Horn SL. The CBHSQ Report. Smoking and mental illness among adults in the united states. The CBHSQ Report. https://www.samhsa.gov/data/sites/default/files/report_2738/ShortReport-2738.html. Published March 30, 2017. Accessed October 17, 2017.
9. Smith, PH, Mazure CM, McKee, SA. Smoking and mental illness in the U.S. population. *Tobacco Control.* 2014;23:e147-153.
10. Prochaska JJ, Hall SE, Delucchi K, Hall S. Efficacy of initiating tobacco dependence treatment in inpatient psychiatry: a randomized controlled trial. *Am J Public Health*. 2014;104(8):1557-1565.
11. Druss BG, Zhao L, Von Esenwein S, Morrato EH, Marcus SC. Understanding excess mortality in persons with mental illness: 17-year follow up of a nationally representative us survey. *Med Care.* 2011;49(6):599–604.
12. Curkendall SM, Mo J, Glasser DB, Rose Stang M, Jones JK. Cardiovascular disease in patients with schizophrenia in Saskatchewan, Canada. *J Clin Psychiatry.* 2004;65(5),715-720.
13. Joukamaa M, Heliövaara M, Knekt P, Aromaa A, Raitasalo R, Lehtinen V. Mental disorders and cause-specific mortality. Br J Psychiatry. 2001;179:498-502.
14. Lichtermann D, Ekelund J, Pukkala E, Tanskanen A, Lönnqvist J. Incidence of cancer among persons with schizophrenia and their relatives. *Arch Gen Psychiatry.* 2001;58(6):573-578.
15. Dalack GW, Glassman AH, Rivelli S, Covey L, Stetner F. Mood, major depression, and fluoxetine response in cigarette smokers. *Am J Psychiatry.* 1995;152(3):398-403.
16. Prochaska JJ, Gill P, Hall SM. Treatment of tobacco use in an inpatient psychiatric setting. *Psychiatr Serv.* 2004;55(11):1265-1270.
17. Ziedonis DM, Kosten TR, Glazer WM, Frances RJ. Nicotine dependence and schizophrenia. *Hosp Community Psychiatry.* 1994;45(3):204-206.
18. Siru R, Hulse GK, Tait RJ. Assessing motivation to quit smoking in people with mental illness: a review. *Addiction*. 2009;104(5):719-733.
19. Kruger J, O'Halloran A, Rosenthal AC, Babb SD, Fiore MC. Receipt of evidence-based brief cessation interventions by health professionals and use of cessation assisted treatments among current adult cigarette-only smokers: National Adult Tobacco Survey, 2009-2010. *BMC Public Health*. 2016;16:141.
20. Rigotti NA. Strategies to help a smoker who is struggling to quit. JAMA. 2012;308(15):1573-1580.
21. Gonzales D, Rennard SI, Nides M, et al; Varenicline phase 3 study group. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. *JAMA.* 2006;296(1):47-55.
22. Jorenby DE, Hays JT, Rigotti NA, et al; Varenicline Phase 3 study group. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. *JAMA*. 2006;296(1):56-63.
23. Tonstad S, Tonnesen P, Hajek P, Williams KE, Billing CB, Reeves KR. Varenicline phase 3 study group. effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. *JAMA.* 2006;296(1):64-71.
24. Benowitz NL. Nicotine addiction. *N Engl J Med.* 2010;362(24):2295-2303.
25. Smith SS, Keller PA, Kobinsky KH, et al. Enhancing tobacco quitline effectiveness: identifying a superior pharmacotherapy adjuvant. *Nicotine Tob Res.* 2013;15(3):718–728.
26. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological intervetnions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev.* 2013;5:CD009329.
27. Eisenberg MJ, Filion KB, Yavin D, et al. Pharmocotherapies for smoking cessation: a meta-analysis of randomized controlled trials. *CMAJ.* 2008;179(2):135-144.
28. Hsueh KC, Hsueh SC, Chou MY, et al. Varenicline versus transdermal nicotine patch: a 3-year follow-up in a smoking cessation clinic in Taiwan. *Psychopharmacology* (Berl). 2014;231(14):2819-2823.
29. Food and Drug Administration. Modifications to labeling of nicotine replacement therapy products for over-the-counter human use. *Federal Register.* 2013;78(63):19718-19721.
30. Agboola S, McNeill A, Coleman T, Leonardi Bee J. A systematic review of the effectiveness of smoking relapse prevention interventions for abstinent smokers. *Addiction*. 2010;105(8):1362-1380.
31. Prochaska JJ, Hilton JF. Risk of cardiovascular serious adverse events associated with varenicline use for tobacco cessation: systematic review and meta-analysis. *BMJ.* 2012;344:e2856.
32. Hajek P, Smith KM, Dhanji AR, McRobbie H. Is a combination of varenicline and nicotine patch more effective in helping smokers quit than varenicline alone? A randomised controlled trial. B*MC Med.* 2013;11:140.
33. University of Wisconsin Center for Tobacco Research and Intervention. FDA removes boxed warning from 2 quit-smoking medications. https://ctri.wisc.edu/2017/01/11/fda-removes-boxed-warnings-from-2-quit-smoking-medications-2/. Published January 11, 2017. Accessed February 27, 2018.
34. University of Wisconsin Center for Tobacco Research and Intervention. Tobacco dependence treatment medications. https://ctri.wiscweb.wisc.edu/wp-content/uploads/sites/240/2017/09/2.CMEpharmacotherapytable.pdf. Updated December 2017. Accessed February 27, 2018.

35. University of Wisconsin Center for Tobacco Research and Intervention. Fact sheet #3: medicaid/badgercare. https://ctri.wisc.edu/fact-sheets/quit-tobacco-series-fact-sheet-3-medicaid-badgercare/. Updated May 2016. Accessed February 27, 2018.
36. Evins AE, Cather C, Laffer A. Treatment of tobacco use disorders in smokers with serious mental illness: Toward clinical best practices. *Harv Rev Psychiatry.* 2015;23(2):90-98.
37. Tidey JW, Miller ME. Smoking cessation and reduction in people with chronic mental illness. *BMJ.* 2015;351:h4065.
38. Centers for Disease Control and Prevention. Best practices user guide: health equity in tobacco prevention and control. https://www.cdc.gov/tobacco/stateandcommunity/best-practices-health-equity/pdfs/bp-health-equity.pdf. Published 2015. Accessed October 30, 2017.
39. Carpenter MJ, Hughes JR, Gray KM, Wahlquist AE, Saladin ME, Alberg AJ. Nicotine therapy sampling to induce quit attempts among smokers unmotivated to quit: a randomized clinical trial. *Arch Intern Med.* 2011;171(21):1901-1907.
40. Shiffman S, Ferguson SG. Nicotine patch therapy prior to quitting smoking: a meta-analysis. *Addiction.* 2008;103(4):557-563.
41. Hughes, JR. Effects of abstinence from tobacco: valid symptoms and time course. *Nicotine Tob Res.* 2007;9(3):315-327.
42. Taylor G, McNeil A, Girling A, Farley A, Lindson-Hawley N, Aveyard P. Change in mental health after smoking cessation: systematic review and meta-analysis. *BMJ.* 2014;348: g1151.
43. Khaled SM, Bulloch AG, Williams JV, Hill JC, Lavorato DH, Patten SB. Persistent heavy smoking as risk factor for major depression (md) incidence: evidence from a longitudinal Canadian cohort of the national population health survey. *J Psychiatr Res.* 2012;46(4):436-443.
44. Berlin I, Hakes JK, Hu MC, Covey, LS. Tobacco use and suicide attempt: longitudinal analysis with retrospective reports. *PLoS One.* 2015;10(4):e0122607.
45. Kahler CW, Spillane NS, Busch AM, Leventhal AM. Time-varying smoking abstinence predicts lower depressive symptoms following smoking cessation treatment. *Nicotine Tob Res.* 2011;13(2):146-150.
46. Cavazos-Rehg PA, Breslau N, Hatsukami D, et al. Smoking cessation is associated with lower rates of mood/anxiety and alcohol use disorders. *Psychol Med.* 2014;44(12)P:2523-2535.
47. Zevin S, Benowitz NL. Drug interactions with tobacco smoking. an update. *Clin Pharmacokinet.* 1999;36(6):425-438.
48. Rx for Change. Drug interactions with tobacco smoke. https://ctri.wiscweb.wisc.edu/wp-content/uploads/sites/240/2017/09/meds_aoda_mh.pdf. Published 2009. Accessed February 27, 2018.
49. University of Wisconsin Center for Tobacco Research and Intervention. Behavioral health and quitting smoking. https://ctri.wisc.edu/providers/behavioral-health/. Accessed October 30, 2017.
50. University of Wisconsin Center for Tobacco Research and Intervention. Provider/system training. https://ctri.wisc.edu/providers/contact-specialist/. Accessed October 30, 2017.