Severe Mental Illness and Risk of Cardiovascular Disease

John W. Newcomer, MD
Charles H. Hennekens, MD

Cardiovascular Disease (CVD), including coronary heart disease (CHD), stroke, and peripheral vascular disease, is the leading cause of death in the United States and most developed Western countries, and will remain so during the 21st century. In 2004, CVD was listed as the underlying cause of death in 871,517 of all 2,398,000 deaths (36.3%), or 1 of every 2.8 deaths in the United States, with CHD accounting for 52% and stroke for 17%. During the past several decades, CVD mortality has markedly declined in the United States, from more than 50% to approximately 36% as the underlying cause of death. Recent data suggest that the decline is largely due to improved diagnosis and treatment rather than to major successes in primary prevention. In contrast, patients with severe mental illnesses, such as schizophrenia, bipolar disorder, and depression that together affect 5% to 10% of the US population, lose 25 or more years of life expectancy, with the majority of the excess premature deaths due to CVD, not suicide. In this Commentary, we summarize disparities in CVD mortality and prevention efforts comparing the general population and individuals with severe mental illnesses and suggest the urgent need for new paradigms.

In the general US population, cigarette consumption has been the leading avoidable cause of all premature deaths, with the amount currently smoked representing a key measure of risk. Smoking rates in the general population have declined from more than 50% in the 1950s to approximately 25% at present. However, among patients with diagnosable mental illness, 50% to 80% are smokers and consume 34% to 44% of all cigarettes in the United States. Although patients with severe mental illness are overrepresented in state programs like Medicaid, some states do not cover any form of tobacco-dependence treatment. In addition, only a few states cover all treatments recommended in the US Preventive Services Task Force guidelines on smoking cessation. Moreover, some states that cover tobacco-dependence treatment require cost sharing, a serious disincentive for disabled patients with fixed income.

Beginning in 1972, the National High Blood Pressure Education Program and, beginning in 1988, the National Cholesterol Education Program (NCEP) have contributed to substantial increases in the proportions of individuals in the general population diagnosed and treated for hypertension and dyslipidemia. With respect to NCEP guidelines, secondary prevention targets are defined as those patients with prior occlusive events involving the heart, brain, or peripheral vessels, as well as other very high-risk patients with 10-year risks of a first CHD event of 20% or greater, and patients with diabetes who have equivalent risk. Although the initial goal for low-density lipoprotein cholesterol was less than 100 mg/dL, recent modifications have defined an optional goal of less than 70 mg/dL. Furthermore, in patients with moderate risk, defined as 10-year risks of a first CHD event of 10% to 19%, the prior goal was 130 mg/dL but the recent modified optional goal is less than 100 mg/dL. These recent modifications are based on randomized trials comparing more intensive vs usual doses of statins. These trials demonstrate that patients who achieve the new optional goals with intensive statin therapy have lower risks of CHD, stroke, and vascular deaths than those who achieve the previous goals with usual statin therapy.

In the general US population during the last decade, most of the observed reductions in CVD mortality were due to improvements in the treatment of acute events and in long-term secondary prevention. For example, decreases in the case fatality rate for hospitalized myocardial infarction (MI) have been attributed to increases in the acute utilization of aspirin, thrombolitics, β-blockers, and angiotensin-converting enzyme (ACE) inhibitors. Subsequent long-term post-MI use of aspirin, β-blockers, ACE inhibitors, and statins, as well as therapeutic lifestyle change, have all contributed to reductions in mortality.

In contrast, patients with severe mental illness who experience an acute MI are significantly less likely than the general population to receive these therapies. Although the reasons for this disparity are complex, they include diagnostic underrecognition of CVD in psychiatric illness, delayed hospital presentation, and undertreatment due to symptom overlap with psychiatric illness. In addition, patients with severe illness who present with CVD are generally older, have a higher rate of prior adverse cardiovascular events, and are more likely to have co-morbidities (e.g., hypertension, diabetes, obesity, and hyperlipidemia) than the general population. All of these factors likely explain why patients with severe mental illness remain at increased risk for CVD even after acute care hospitalization compared with age- and sex-matched general population controls. The current paucity of data regarding the prevention of CVD exacerbations and assessment of cardiovascular risk in patients with severe mental illness is striking. Further studies are needed to determine whether the risk of CHD events in the general population can be applied to individuals with severe mental illness.
general population to receive drug therapies of proven benefit, including thrombolytics, aspirin, β-blockers, and ACE inhibitors. Patients with severe mental illness are also significantly less likely to undergo cardiac catheterizations and receive emergency angioplasties or coronary artery bypass graft surgery. In a study of more than 88,000 Medicare patients hospitalized for MI, mortality in the follow-up period was increased by 19% in the presence of any mental disorder and by 34% in persons with schizophrenia, with increases in mortality related to reductions in the quality of care.11

Regarding CVD prevention, individuals with severe mental illness have approximately 1.5 to 2 times the general population prevalence of diabetes, dyslipidemia, hypertension, and obesity.12-14 The high prevalence of modifiable CVD risk factors can be explained in part by underdiagnosis and undertreatment and in part by contributions related to the mental illness, including effects of the medications used for treatment, some of which have unfavorable effects on various metabolic risk factors for CVD.14-16

Among the approximately 1500 patients with chronically treated schizophrenia entering the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, which was conducted at 57 US sites spanning a range of academic and public sector treatment settings, 88% of patients with dyslipidemia were receiving no lipid-lowering pharmacotherapy, 30% with diabetes were receiving no antidiabetic medications, and 62% with hypertension were receiving no antihypertensive medications.17

In general, screening for hyperglycemia and dyslipidemia occurs at very low rates in individuals with serious mental disorders, even in the context of treatment with medications such as antipsychotics. Evidence from controlled studies including large-scale randomized trials indicates that some but not all antipsychotic drugs can adversely affect adiposity as well as glucose and lipid metabolism.14,16 A recent cohort study involving Medicaid claims data for 55,436 enrollees with mental illness from 4 states observed that in the 4 months before and after a new antipsychotic prescription, less than one-third of patients overall received any plasma glucose measurement and less than 10% received any plasma lipid measurement.18 Low levels of screening are likely to contribute to observed low levels of diagnosis and treatment for modifiable CVD risk factors in this population.

The NCEP guidelines recommend that patients with diabetes be treated as aggressively as patients with prior MI or stroke who do not have diabetes.8 However, patients with diabetes and severe mental illness are less likely than patients with diabetes and no mental illness to receive standard-of-care treatments. In a study of more than 300,000 patients with diabetes in the Veterans Administration system, the presence of mental illnesses like schizophrenia and bipolar disorder significantly increased the risk of not receiving appropriate elements of care, such as eye examinations, plasma lipid testing, and glycated hemoglobin monitoring.19

With respect to high-risk prevention targets, the NCEP guidelines define the metabolic syndrome as a constellation of at least 3 of 5 risk factors including abdominal obesity, low high-density lipoprotein, high triglycerides, increased blood pressure, and elevated fasting blood glucose, targeting insulin resistance-related changes in risk for CVD and diabetes.20 The metabolic syndrome is a common condition in the US general population, especially in the presence of obesity, affecting more than 25% of all adults21 and 50% to 60% of those with a body mass index of more than 30.22 Such individuals have a 10-year risk of a first CHD event of approximately 16% to 18%. In the baseline evaluation of patients with chronic schizophrenia entering the CATIE study,13 prevalence of the metabolic syndrome was approximately twice that of age-matched general population controls, accounted for by increased prevalence of all individual metabolic syndrome criteria.13

These considerations all contribute to the markedly reduced life expectancy of patients with severe mental illnesses, in whom the majority of excess premature deaths are due to CVD. These data indicate a crucial need for new approaches for prevention and treatment of CVD in patients with serious mental illnesses, including closer attention to choice of psychotropic drug treatment regimens and more aggressive use of monitoring and interventions to identify and reduce risk. Almost a decade ago, US Surgeon General Satcher suggested that mental health is “inextricably intertwined” with general medical health, and high-quality mental health systems must integrate medical care with psychiatric treatment.23 Similarly, a recent Institute of Medicine report concerning the need to improve overall health care for patients with mental illness underscored the importance of integrating and co-localizing psychiatric and medical services.24 However, the need for new approaches and better coordination of services faces short-term and long-term challenges, ranging from fiscal concerns to lack of awareness, knowledge, or comfort among clinicians, administrators, and support staff who might play key roles.

The majority of cardiovascular clinicians who provide care for patients with severe mental illness are primary care physicians or cardiologists who are likely to be less familiar than psychiatrists and other mental health care professionals with the existing situation or the potential solutions. Improvements in secondary prevention will therefore necessarily involve better education and involvement of primary care clinicians, endocrinologists, and cardiologists to reduce disparities in the level and quality of treatment services received by individuals with mental illness requiring treatment for CVD, CVD risk-equivalent conditions like diabetes, and other CVD risk factors. In the short term, substantial effort must come from the existing...
mental care system, reallocating existing resources to coordinate screening, interventions including needed referrals, and required follow-up monitoring. Mental health professionals and systems need to improve working relationships with primary care and specialty collaborators, including proactive efforts to facilitate evaluation and follow-up for patients where extra communication and staffing may be needed in relation to either the mental disorder or treatment choices.

Improvements in primary prevention offer the largest potential for reducing CVD mortality in individuals with severe mental illness. Careful attention and future research should be directed at key issues, such as the appropriate role of antipsychotic and other psychotropic drug therapies less likely to adversely affect cardiometabolic risk compared with the role of adjunctive pharmacotherapies that might target excess weight, dyslipidemia, hypertension, and hyperglycemia in this population. New approaches and models that include nonpsychiatric clinicians evaluating more patients with severe mental illness will require access to supportive services and psychiatric consultations necessary to implement recommendations. Without the future collaborative efforts of primary care clinicians, endocrinologists, and cardiologists with psychiatrist, the large burden of avoidable premature mortality from CVD in patients with severe mental illness is likely to continue and increase in severity.

Financial Disclosures: Dr Newcomer reports receiving research grant support from the National Institute of Mental Health, the National Alliance for Research on Schizophrenia and Depression, the Sidney R. Baer Jr Foundation, Janssen, Pfizer, Bristol-Myers Squibb, and Wyeth; serving as a consultant for Janssen, Pfizer, Bristol-Myers Squibb, AstraZeneca, GlaxoSmithKline, Solvay, and Wyeth; being a member of a data and safety monitoring board for Organon; serving as a legal consultant regarding medication effects; and receiving royalties for a metabolic screening form from Clinical Clinics. Dr Hennekens reports being funded by the Department of Biomedical Science and Center of Excellence at Florida Atlantic University (FAU) as principal investigator on 2 investigator-initiated research grants funded to FAU by Bayer, testing the effects of aspirin dose on platelet biomarkers, inflammatory markers, nitric oxide formation, and endothelial function; serving as a consultant, including as chair or member on data and safety monitoring boards, for Actelion, Amgen, AstraZeneca, Bayer, Biovail, Bristol-Myers Squibb, Chatteron, Delacor, Dechert, US Food and Drug Administration, GlaxoSmithKline, Keryx, McKinnell, Merck, National Association for Continuing Education, National Institutes of Health, Novartis, Pfizer, Practice, Reliant, Solvay, TAP, United BioSource Corporation, UpToDate, and Wyeth; serving on speakers bureaus for the International Atherosclerosis Society, AstraZeneca concerning lipids and heart failure, as well as Bristol-Myers Squibb, Reliant, and Pfizer concerning lipids; receiving royalties for authorship or editorship of 3 textbooks; receiving royalties as coinventor on patents concerning inflammatory markers and cardiovascular disease, which are held by Brigham and Women’s Hospital, and having an investment management relationship with SunTrust Bank, who has sole discretionary investment authority.

Funding/Support: This work was supported in part by grants MH-63985 and MH-72512 from the National Institute of Mental Health.

Role of the Sponsor: No funding organization played a role in the preparation, review, or approval of the manuscript.

Disclaimer: Dr Newcomer chairs an American Psychiatric Association Workgroup on Antipsychotics and Metabolic Risk, and the Missouri Medicaid Drug Utilization Review Board, but the opinions expressed herein are his own and do not necessarily express the opinions of any of these groups.

Additional Contributions: Glennon M. Floyd, MA, Managing Editor, Department of Psychiatry, Washington University School of Medicine, provided editorial assistance on the manuscript. He received no specific additional compensation in relation to this particular project.

REFERENCES