

Premature mortality across most psychiatric disorders

The evidence is robust and disheartening: As if the personal suffering and societal stigma of mental illness are not bad enough, psychiatric patients also have a shorter life-span.¹ In the past, most studies have focused on early mortality and loss of potential life-years in schizophrenia,² but many subsequent reports indicate that premature death occurs in all major psychiatric disorders.

Here is a summary of the sobering facts:

- **Schizophrenia.** In a study of 30,210 patients with schizophrenia, compared with >5 million individuals in the general population in Denmark (where they have an excellent registry), mortality was 16-fold higher among patients with schizophrenia if they had a single somatic illness.³ The illnesses were mostly respiratory, gastrointestinal, or cardiovascular.³ The loss of potential years of life was staggeringly high: 18.7 years for men, 16.3 years for women.⁴ A study conducted in 8 US states reported a loss of 2 to 3 decades of life across each of these states.⁵ The causes of death in patients with schizophrenia were mainly heart disease, cancer, stroke, and pulmonary diseases. A national database in Sweden found that unmedicated patients with schizophrenia had a significantly higher death rate than those receiving antipsychotics.^{6,7} Similar findings were reported by

researchers in Finland.⁸ The Swedish study by Tiihonen et al⁶ also found that mortality was highest in patients receiving benzodiazepines along with antipsychotics, but there was no increased mortality among patients with schizophrenia receiving antidepressants.

- **Bipolar disorder.** A shorter life expectancy has also been reported in bipolar disorder,⁹ with a loss of 13.6 years for men and 12.1 years for women. Early death was caused by physical illness (even when suicide deaths were excluded), especially cardiovascular disease.¹⁰

- **Major depressive disorder (MDD).** A reduction of life expectancy in persons with MDD (unipolar depression) has been reported, with a loss of 14 years in men and 10 years in women.¹¹ Although suicide contributed to the shorter lifespan, death due to accidents was 500% higher among persons with unipolar depression; the largest causes of death were physical illnesses. Further, Zubenko et al¹² reported alarming findings about excess mortality among first- and second-degree relatives of persons with early-onset depression (some of whom were bipolar). The relatives died an average of 8 years earlier than the local population, and 40% died before reaching age 65. Also, there was a 5-fold increase in infant mortality (in the first year of life) among the relatives. The most common causes of death in adult relatives were heart disease, cancer, and stroke.



Henry A. Nasrallah, MD
Editor-in-Chief

Psychiatric brain disorders are associated with multiple medical diseases that lead to a shorter lifespan

To comment on this editorial or other topics of interest:
henry.nasrallah
@currentpsychiatry.com



continued

Editorial Staff

EDITOR **Jeff Bauer**
SENIOR EDITOR **Sathya Achia Abraham**
ASSISTANT EDITOR **Jason Orsz**
WEB ASSISTANTS
Tyler Mundhenk, Kathryn Wighton

Art & Production Staff

CREATIVE DIRECTOR **Mary Ellen Niatas**
ART DIRECTOR **Pat Fopma**
DIRECTOR, JOURNAL MANUFACTURING
Michael Wendt
PRODUCTION MANAGER **Donna Pituras**

Publishing Staff

PUBLISHER **Sharon Finch**
DIRECTOR eBUSINESS DEVELOPMENT
Alison Paton
SENIOR DIRECTOR OF SALES
Tim LaPella
CONFERENCE MARKETING MANAGER
Kathleen Wenzler

Editor-in-Chief Emeritus

James Randolph Hillard, MD

Frontline Medical Communications

SVP, FINANCE **Steven Resnick**
VP, OPERATIONS **Jim Chicca**
VP, SALES **Mike Guire**
VP, SOCIETY PARTNERS **Mark Branca**
VP, EDITOR IN CHIEF **Mary Jo Dales**
VP, EDITORIAL DIRECTOR, CLINICAL CONTENT
Karen Clemments
VP, DIGITAL CONTENT & STRATEGY
Amy Pfeiffer
PRESIDENT, CUSTOM SOLUTIONS **JoAnn Wah**
VP, CUSTOM SOLUTIONS **Wendy Raupers**
VP, MARKETING & CUSTOMER ADVOCACY
Jim McDonough
VP, HUMAN RESOURCES & FACILITY
OPERATIONS **Carolyn Caccavelli**
DATA MANAGEMENT DIRECTOR **Mike Fritz**
CIRCULATION DIRECTOR **Jared Sonners**
CORPORATE DIRECTOR, RESEARCH
& COMMUNICATIONS **Lori Raskin**
DIRECTOR, CUSTOM PROGRAMS
Patrick Finnegan

**In affiliation with Global Academy for
Medical Education, LLC**

PRESIDENT **David J. Small, MBA**



7 Century Drive, Suite 302
Parsippany, NJ 07054
Tel: (973) 206-3434
Fax: (973) 206-9378
www.frontlinemedcom.com

Subscription Inquiries:
subscriptions@mdedge.com

Published through an
educational partnership with



It is obvious that MDD has a significant negative impact on health and longevity in both patients and their relatives.

- **Attention-deficit/hyperactivity disorder (ADHD).** A 220% increase in mortality was reported in persons with ADHD at all ages.¹³ Accidents were the most common cause of death. The mortality rate ratio (MRR) was 1.86 for ADHD before age 6, 1.58 for ADHD between age 6 to 17, and 4.25 for those age ≥18. The rate of early mortality was higher in girls and women (MRR = 2.85) than boys and men (MRR = 1.27).

- **Obsessive-compulsive disorder (OCD).** A study from Denmark of 10,155 persons with OCD followed for 10 years reported a significantly higher risk of death from both natural (MRR = 1.68) and unnatural causes (MRR = 2.61), compared with the general population.¹⁴ Patients with OCD and comorbid depression, anxiety, or substance use had a further increase in mortality risk, but the mortality risk of individuals with OCD without psychiatric comorbidity was still 200% higher than that of the general population.

- **Anxiety disorders.** One study found no increase in mortality among patients who have generalized anxiety, unless it was associated with depression.¹⁵ Another study reported that the presence of anxiety reduced the risk of cardiovascular mortality in persons with depression.¹⁶ The absence of increased mortality in anxiety disorders was also confirmed in a meta-analysis of 36 studies.¹⁷ However, a study of postmenopausal women with panic attacks found a 3-fold increase in coronary artery disease and stroke in that cohort,¹⁸ which confirmed the findings of an older study¹⁹ that demonstrated a 2-fold increase of mortality among 155 men with panic disorder after a 12-year follow-up. Also, a 25-year follow-up study found that suicide accounted for 20% of deaths in the anxiety group

compared with 16.2% in the depression group,²⁰ showing a significant risk of suicide in panic disorder, even exceeding that of depression.

- **Oppositional defiant disorder (ODD) and conduct disorder (CD).** In a 12-year follow-up study of 9,495 individuals with “disruptive behavioral disorders,” which included ODD and CD, the mortality rate was >400% higher in these patients compared with 1.92 million individuals in the general population (9.66 vs 2.22 per 10,000 person-years).²¹ Comorbid substance use disorder and ADHD further increased the mortality rate in this cohort.

- **Posttraumatic stress disorder (PTSD).** Studies show that there is a significantly increased risk of early cardiovascular mortality in PTSD,²² and that the death rate may be associated with accelerated “DNA methylation age” that leads to a 13% increased risk for all-cause mortality.²³

- **Borderline personality disorder (BPD).** A recent longitudinal study (24 years of follow-up with evaluation every 2 years) reported a significantly higher mortality in patients with BPD compared with those with other personality disorders. The age range when the study started was 18 to 35. The rate of suicide death was >400% higher in BPD (5.9% vs 1.4%). Also, non-suicidal death was 250% higher in BPD (14% vs 5.5%). The causes of non-suicidal death included cardiovascular disease, substance-related complications, cancer, and accidents.²⁴

- **Other personality disorders.** Certain personality traits have been associated with shorter leukocyte telomeres, which signal early death. These traits include neuroticism, conscientiousness, harm avoidance, and reward dependence.²⁵ Another study found shorter telomeres in persons with high neuroticism and low agreeableness²⁶ regardless of age or sex. Short

continued on page 12

Our psychiatric patients are at high risk for potentially fatal medical conditions that require ongoing collaborative care with primary care clinicians

continued from page 10

telomeres, which reflect accelerated cellular senescence and aging, have also been reported in several major psychiatric disorders (schizophrenia, bipolar disorder, MDD, and anxiety).²⁷⁻²⁹ The cumulative evidence is unassailable; psychiatric brain disorders are not only associated with premature death due to high suicide rates, but also with multiple medical diseases that lead to early mortality and a shorter lifespan. The shortened telomeres reflect high oxidative stress and inflammation, and both those toxic processes are known to be associated with major psychiatric disorders. Compounding the dismal facts about early mortality due to mental illness are the additional grave medical consequences of alcohol and substance use, which are highly comorbid with most psychiatric disorders, further exacerbating the premature death rates among psychiatric patients.

There is an important take-home message in all of this: Our patients are at high risk for potentially fatal medical conditions that require early detection, and intensive ongoing treatment by a primary care clinician (not “provider”; I abhor the widespread use of that term for physicians or nurse practitioners) is an indispensable component of psychiatric care. Thus, collaborative care is vital to protect our psychiatric patients from early mortality and a shortened lifespan. Psychiatrists and psychiatric nurse practitioners must not only win the battle against mental illness, but also diligently avoid losing the war of life and death.



Henry A. Nasrallah, MD
Editor-in-Chief

References

1. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry*. 2015;72(4):334-341.

2. Laursen TM, Wahlbeck K, Hällgren J, et al. Life expectancy and death by diseases of the circulatory system in patients with bipolar disorder or schizophrenia in the Nordic countries. *PLoS One*. 2013;8(6):e67133. doi: 10.1371/journal.pone.0067133.
3. Kugathasan P, Stubbs B, Aagaard J, et al. Increased mortality from somatic multimorbidity in patients with schizophrenia: a Danish nationwide cohort study. *Acta Psychiatr Scand*. 2019. doi: 10.1111/acps.13076.
4. Laursen TM. Life expectancy among persons with schizophrenia or bipolar affective disorder. *Schizophr Res*. 2011;131(1-3):101-104.
5. Colton CW, Manderscheid RW. Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. *Prev Chronic Dis*. 2006;3(2):A42.
6. Tiihonen J, Mittendorfer-Rutz E, Torniainen M, et al. Mortality and cumulative exposure to antipsychotics, antidepressants, and benzodiazepines in patients with schizophrenia: an observational follow-up study. *Am J Psychiatry*. 2016;173(6):600-606.
7. Torniainen M, Mittendorfer-Rutz E, Tanskanen A, et al. Antipsychotic treatment and mortality in schizophrenia. *Schizophr Bull*. 2015;41(3):656-663.
8. Tiihonen J, Lönnqvist J, Wahlbeck K, et al. 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). *Lancet*. 2009;374(9690):620-627.
9. Wilson R, Gaughran F, Whitburn T, et al. Place of death and other factors associated with unnatural mortality in patients with serious mental disorders: population-based retrospective cohort study. *BJPsych Open*. 2019;5(2):e23. doi: 10.1192/bjo.2019.5.
10. Ösby U, Westman J, Hällgren J, et al. Mortality trends in cardiovascular causes in schizophrenia, bipolar and unipolar mood disorder in Sweden 1987-2010. *Eur J Public Health*. 2016;26(5):867-871.
11. Laursen TM, Musliner KL, Benros ME, et al. Mortality and life expectancy in persons with severe unipolar depression. *J Affect Disord*. 2016;193:203-207.
12. Zubenko GS, Zubenko WN, Spiker DG, et al. Malignancy of recurrent, early-onset major depression: a family study. *Am J Med Genet*. 2001;105(8):690-699.
13. Dalsgaard S, Østergaard SD, Leckman JF, et al. Mortality in children, adolescents, and adults with attention deficit hyperactivity disorder: a nationwide cohort study. *Lancet*. 2015;385(9983):2190-2196.
14. Meier SM, Mattheisen M, Mors O, et al. Mortality among persons with obsessive-compulsive disorder in Denmark. *JAMA Psychiatry*. 2016;73(3):268-274.
15. Holwerda TJ, Schoevers RA, Dekker J, et al. The relationship between generalized anxiety disorder, depression and mortality in old age. *Int J Geriatr Psychiatry*. 2007;22(3):241-249.
16. Ivanovs R, Kivite A, Ziedonis D, et al. Association of depression and anxiety with the 10-year risk of cardiovascular mortality in a primary care population of Latvia using the SCORE system. *Front Psychiatry*. 2018;9:276.
17. Miloyan B, Bulley A, Bandeen-Roche K, et al. Anxiety disorders and all-cause mortality: systematic review and meta-analysis. *Soc Psychiatry Psychiatr Epidemiol*. 2016;51(11):1467-1475.
18. Smoller JW, Pollack MH, Wassertheil-Smoller S, et al. Panic attacks and risk of incident cardiovascular events among postmenopausal women in the Women’s Health Initiative Observational Study. *Arch Gen Psychiatry*. 2007;64(10):1153-1160.

continued on page 34

From the Editor

continued from page 12

19. Coryell W, Noyes R Jr, House JD. Mortality among outpatients with anxiety disorders. *Am J Psychiatry*. 1986;143(4):508-510.
20. Coryell W, Noyes R, Clancy J. Excess mortality in panic disorder. A comparison with primary unipolar depression. *Arch Gen Psychiatry*. 1982;39(6):701-703.
21. Scott JG, Giørtz Pedersen M, Erskine HE, et al. Mortality in individuals with disruptive behavior disorders diagnosed by specialist services - a nationwide cohort study. *Psychiatry Res*. 2017;251:255-260.
22. Burg MM, Soufer R. Post-traumatic stress disorder and cardiovascular disease. *Curr Cardiol Rep*. 2016; 18(10):94.
23. Wolf EJ, Logue MW, Stoop TB, et al. Accelerated DNA methylation age: associations with PTSD and mortality. *Psychosom Med*. 2017. doi: 10.1097/PSY.0000000000000506.
24. Temes CM, Frankenburg FR, Fitzmaurice MC, et al. Deaths by suicide and other causes among patients with borderline personality disorder and personality-disordered comparison subjects over 24 years of prospective follow-up. *J Clin Psychiatry*. 2019;80(1). doi: 10.4088/JCP.18m12436.
25. Sadahiro R, Suzuki A, Enokido M, et al. Relationship between leukocyte telomere length and personality traits in healthy subjects. *Eur Psychiatry*. 2015;30(2):291-295.
26. Schoormans D, Verhoeven JE, Denollet J, et al. Leukocyte telomere length and personality: associations with the Big Five and Type D personality traits. *Psychol Med*. 2018;48(6):1008-1019.
27. Muneer A, Minhas FA. Telomere biology in mood disorders: an updated, comprehensive review of the literature. *Clin Psychopharmacol Neurosci*. 2019; 17(3):343-363.
28. Vakonaki E, Tsiminikaki K, Plaitis S, et al. Common mental disorders and association with telomere length. *Biomed Rep*. 2018;8(2):111-116.
29. Malouff JM, Schutte NS. A meta-analysis of the relationship between anxiety and telomere length. *Anxiety Stress Coping*. 2017;30(3):264-272.