Original Investigation

Premature Mortality Among Adults With Schizophrenia in the United States

Mark Olfson, MD, MPH; Tobias Gerhard, PhD; Cecilia Huang, PhD; Stephen Crystal, PhD; T. Scott Stroup, MD, MPH

IMPORTANCE Although adults with schizophrenia have a significantly increased risk of premature mortality, sample size limitations of previous research have hindered the identification of the underlying causes.

OBJECTIVE To describe overall and cause-specific mortality rates and standardized mortality ratios (SMRs) for adults with schizophrenia compared with the US general population.

DESIGN, SETTING, AND PARTICIPANTS We identified a national retrospective longitudinal cohort of patients with schizophrenia 20 to 64 years old in the Medicaid program (January 1, 2001, to December 31, 2007). The cohort included 1 138 853 individuals, 4 807 121 years of follow-up, and 74 003 deaths, of which 65 553 had a known cause.

MAIN OUTCOMES AND MEASURES Mortality ratios for the schizophrenia cohort standardized to the general population with respect to age, sex, race/ethnicity, and geographic region were estimated for all-cause and cause-specific mortality. Mortality rates per 100 000 person-years and the mean years of potential life lost per death were also determined. Death record information was obtained from the National Death Index.

RESULTS Adults with schizophrenia were more than 3.5 times (all-cause SMR, 3.7; 95% CI, 3.7-3.7) as likely to die in the follow-up period as were adults in the general population. Cardiovascular disease had the highest mortality rate (403.2 per 100 000 person-years) and an SMR of 3.6 (95% CI, 3.5-3.6). Among 6 selected cancers, lung cancer had the highest mortality rate (74.8 per 100 000 person-years) and an SMR of 2.4 (95% CI, 2.4-2.5). Particularly elevated SMRs were observed for chronic obstructive pulmonary disease (9.9; 95% CI, 9.6-10.2) and influenza and pneumonia (7.0; 95% CI, 6.7-7.4). Accidental deaths (119.7 per 100 000 person-years) accounted for more than twice as many deaths as suicide (52.0 per 100 000 person-years). Nonsuicidal substance-induced death, mostly from alcohol or other drugs, was also a leading cause of death (95.2 per 100 000 person-years).

CONCLUSIONS AND RELEVANCE In a US national cohort of adults with schizophrenia, excess deaths from cardiovascular and respiratory diseases implicate modifiable cardiovascular risk factors, including especially tobacco use. Excess deaths directly attributable to alcohol or other drugs highlight threats posed by substance abuse. More aggressive identification and management of cardiovascular risk factors, as well as reducing tobacco use and substance abuse, should be leading priorities in the medical care of adults with schizophrenia.

Editorial page 1166

Supplemental content at jamapsychiatry.com

Author Affiliations: Department of Psychiatry and New York State Psychiatric Institute, College of Physicians and Surgeons, Columbia University, New York (Olfson, Stroup); Center for Health Services Research on Pharmacotherapy, Chronic Disease Management, and Outcomes, Institute for Health, Health Care Policy and Aging Research, Rutgers, The State University of New Jersey, New Brunswick (Gerhard, Huang, Crystal); Department of Pharmacy Practice and Administration, Ernest Mario School of Pharmacy, Rutgers School of Health Related Professions, Piscataway, New Jersey (Gerhard).

Corresponding Author: Mark Olfson, MD, MPH, Department of Psychiatry and New York State Psychiatric Institute, College of Physicians and Surgeons, Columbia University, 1051 Riverside Dr, New York, NY 10032 (mo49@cumc.columbia.edu).

JAMA Psychiatry. 2015;72(12):1172-1181. doi:10.1001/jamapsychiatry.2015.1737
Published online October 28, 2015.

Adults with schizophrenia are at markedly increased risk of premature death.[1,2] Despite elevated rates of suicide and other unnatural causes of death, most of the excess mortality has been attributed to cardiovascular disease, respiratory disease, and other natural causes.[3] One analysis from the United Kingdom found that suicide, homicide, and accidental deaths collectively accounted for 21 of 164 schizophrenia deaths.[4] Accurate characterizations of premature mortality patterns are important to inform clinical and policy initiatives to improve services and reduce preventable deaths in this patient population.

Many factors, including economic disadvantage, negative health behaviors, and difficulties accessing and adhering to medical treatments, are thought to contribute to premature mortality in schizophrenia.[5] Smoking,[6] limited physical activity,[7] obesity,[8] elevated serum glucose level,[9] hypertension,[10] and dyslipidemia[11] are all significantly more common in schizophrenia than in the general population. Adults with schizophrenia are also less likely than age-matched peers to receive adequate treatment for major medical conditions,[12] which may compound risk of premature mortality.[13]

Research on early mortality in schizophrenia primarily derives from Western Europe.[2] Because the United States differs from most Western European countries in its health and social welfare systems[14] and in several relevant health indexes (including life expectancy,[15] obesity,[16] blood pressure,[17] and tobacco use[18]), Western European mortality estimates for schizophrenia may not directly generalize to the United States.

In the United States, premature mortality has been well documented in diagnostically mixed samples of patients with severe mental illness.[19,20] Investigations in the United States limited to schizophrenia have primarily involved small samples (<1000 patients) published more than a quarter century ago.[21,22] A recent US study[23] comparing mortality for schizophrenia research participants with a demographically matched general population reference group reported a standardized mortality ratio (SMR) of 2.80, with all 25 deaths in the schizophrenia group occurring from natural causes. In a large cohort of US military veterans, it was further found that veterans with schizophrenia were significantly more likely than those without mental disorders to die of heart disease.[24]

We conducted a national examination of premature mortality among adults with schizophrenia in the Medicaid program, the largest payer of health services for persons with schizophrenia in the United States.[25] Mortality rates and mortality ratios standardized to the general population by age, sex, race/ethnicity, and geographic region were used to characterize the burden and excess mortality from several common medical diseases overall and stratified by demographic characteristics. By characterizing key sources of excess mortality in a large cohort with schizophrenia, the results provide a more comprehensive picture than was previously available of the gap in mortality, highlighting the need for more effective strategies to improve the medical care of this patient population.

Methods

Sources of Data

The total resident population and death information were obtained from the January 1, 2001, to December 31, 2007, US Compressed Mortality File.[26] Age, sex, race/ethnicity, and year-specific life expectancy data were obtained from the 2006 United States Life Tables.[27] The schizophrenia cohort was extracted from the national Medicaid Analytic eXtract (MAX) data from the Centers for Medicare & Medicaid Services.[63] It included data from 45 states, not including Arizona, Delaware, Nevada, Oregon, and Rhode Island. Dates and cause of death information for the schizophrenia cohort were derived from linkage to the National Death Index (NDI), which provides a complete accounting of state-recorded deaths in the United States and is the most complete resource for tracing mortality in national samples.[28] The data, which are deidentified, were determined to be exempt from human participants review by the Rutgers University Institutional Review Board.

Schizophrenia Cohort Assembly and Follow-up

We identified a national retrospective longitudinal cohort of patients with schizophrenia 20 to 64 years old who received at least 2 outpatient claims or at least 1 inpatient claim for schizophrenia (*ICD-10-CM* code 295).[29] The first observed day on which the inclusion criteria were met defined the start of follow-up. The cohort was followed forward until the loss of Medicaid eligibility, the date of death, or December 31, 2007 (end of NDI-linked MAX data), whichever came first.

Causes of Death

All causes of death were first divided into natural and unnatural causes. Natural causes were partitioned into cardiovascular disease, cancer, diabetes mellitus, renal failure, influenza and pneumonia, sepsis, chronic obstructive pulmonary disease (COPD), liver disease, and other natural causes. Cardiovascular disease was subpartitioned into ischemic heart disease, nonischemic heart disease, stroke, and other circulatory diseases. Cancer was subpartitioned into lung, colon, breast, liver, pancreas, hematologic, and other cancer. Unnatural causes were partitioned into suicide, accidents, assault (homicide), and injuries with undetermined intent and other injuries (eTable 1 in the Supplement). In addition, an alternative overlapping Centers for Disease Control and Prevention classification was used to define substance-induced deaths, including drug-induced and alcohol-induced deaths, and firearm-related deaths.[30] Drug-induced nonsuicidal deaths were also partitioned into those induced by drugs of abuse (opioids, cannabinoids, sedatives or hypnotics, cocaine, stimulants, and volatile solvents) and others. Deaths related to legal interventions (eg, encounters with law enforcement officials) were also examined (eTable 2 in the Supplement).

Sociodemographic Characteristics

Based on Medicaid eligibility data, cohort members were classified by sex, age group (20-34, 35-44, 45-54, and 55-64 years), and race/ethnicity (Hispanic, white non-Hispanic

[white], black non-Hispanic [black], and other non-Hispanic [other], including American Indian/Alaskan native, Asian, native Hawaiian/other Pacific Islander, and more than 1 race/ethnicity. Cohort members were also classified by geographic region (West, Midwest, South, and Northeast).

Statistical Analysis

In the schizophrenia cohort, person-years of follow-up, number of deaths, and mortality rates per 100 000 person-years of follow-up were determined overall and stratified by demographic characteristics. To facilitate comparisons of the mean years of lost life per death across causes of death, the mean years of potential lost life per death were calculated overall and for each cause of death as the mean of the remaining life expectancy in years for each deceased schizophrenia cohort member at the age at death, as determined from the 2006 United States Life Tables based on the age at death, sex, and race/ethnicity.

Cause-specific mortality rates and SMRs with 95% CIs were calculated for the entire schizophrenia cohort and stratified by age, sex, and race/ethnicity. Standardized mortality ratios are the ratio of the observed number of deaths in the schizophrenia cohort to the number of deaths expected in the same cohort based on data from the general US population (January 1, 2001, to December 31, 2007, US Compressed Mortality File). A software program (SAS PROC STDRATE; SAS Institute Inc) was used to derive SMRs indirectly standardized by age, sex, race/ethnicity, and geographic region.

Results

All-Cause Mortality

The schizophrenia cohort included 1 138 853 individuals, 4 807 121 years of follow-up, and 74 003 deaths, of which 65 553 had a known cause. The cohort sample sizes are stratified by state and payer type in eTable 3 in the Supplement, and the death counts are stratified by demographic group and specific mortality in eTable 4 in the Supplement.

The crude all-cause mortality rate for adults with schizophrenia was higher for men than for women and increased with age. The rate was higher for persons of white race/ethnicity than for other racial/ethnic groups. These results are detailed in eTable 5 in the Supplement.

Compared with the general population, the all-cause SMR for the schizophrenia cohort was significantly increased in the total sample and in each demographic group. The all-cause SMRs were higher for women than for men, for older adults than for younger or middle-aged adults, and for persons of white race/ethnicity than for the "other" racial/ethnic group, Hispanics, and blacks (**Tables 1**, **2**, and **3**). Standardized mortality ratios varied across the leading causes of death and age groups (**Figure**).

Natural Causes of Death

All Natural-Cause Mortality

In the schizophrenia cohort, natural causes accounted for most of the known-cause deaths. Standardized mortality ratios from all natural causes of death were significantly elevated in the total schizophrenia cohort and in each demographic subgroup (Tables 1, 2, and 3).

Cardiovascular Mortality

Cardiovascular disease had the highest mortality rate of all disease groups examined, accounting for approximately one-third of all natural deaths. Approximately one-half of cardiovascular deaths were due to ischemic heart disease. The cardiovascular disease mortality rate was higher for men than for women, increased with age, and was highest for persons of white race/ethnicity and lowest for the "other" ethnic/racial group. Standardized mortality ratios for cardiovascular disease were significantly elevated in each demographic group, particularly among women (4.6; 95% CI, 4.5-4.7), young adults (4.5; 95% CI, 4.1-4.8), and individuals of white race/ethnicity (4.9; 95% CI, 4.8-5.0) (Tables 1, 2, and 3).

Cancer Mortality

Cancer accounted for approximately 1 in 6 natural deaths. Lung cancer had the highest mortality rate of the 6 selected specific cancers. The lung cancer mortality rate was higher for men than for women, for persons of white race/ethnicity than for other racial/ethnic groups, and for older adults than for middle-aged or younger adults.

The SMR for cancer was significantly elevated in the total cohort but was only approximately half as large as the SMR for cardiovascular disease. The cancer SMR was significantly elevated among all demographic groups except young adults (Tables 1, 2, and 3). The SMR for lung cancer was considerably larger than SMRs for the other specific cancers (Table 1).

Other Natural Causes of Death

Among the other specific natural causes of death, COPD, diabetes mellitus, and influenza and pneumonia had the highest mortality rates (Table 1). For each of these diseases, SMRs were significantly increased overall and in each demographic subgroup. Particularly high SMRs were evident for COPD and influenza and pneumonia except among black adults with schizophrenia. The diabetes mellitus SMR was significantly higher among young adults than among middle-aged or older adults (Table 2).

Unnatural Causes of Death

Unnatural causes of death accounted for approximately 1 in 7 known-cause deaths. Mortality due to unnatural causes was higher for men than for women and for middle-aged adults than for younger or older adults. Accidents followed a similar pattern. Among accidental deaths, poisoning and nonpoisoning accounted for similar numbers of deaths, although SMRs for poisoning were significantly larger than those for nonpoisoning accidental deaths except among older adults.

Suicide accounted for approximately one-quarter of unnatural deaths. Among all causes of death, suicide was associated with the highest mean years of potential life lost per death. Suicide mortality was higher in men than in women, decreased with age, and was highest for persons of white race/ethnicity. Suicide SMRs were significantly elevated in all demographic groups. The homicide SMR was not significantly in-

Table 1. Observed Deaths, Years of Potential Life Lost per Death, Mortality Rates, and Standardized Mortality Ratios of Adult Medicaid Beneficiaries Diagnosed as Having Schizophrenia by Disease Category and Sex (January 1, 2001, to December 31, 2007)[a]

	Total				Male		Female	
Cause of Death	Observed Deaths	Potential Life Lost per Death, Mean, y	Mortality Rate	SMR (95% CI)	Mortality Rate	SMR (95% CI)	Mortality Rate	SMR (95% CI)
All causes	74 003	28.5	1539.5	3.7 (3.7-3.7)	1576.3	3.3 (3.3-3.3)	1497.0	4.3 (4.3-4.4)
Natural deaths	55 741	27.0	1159.6	3.3 (3.3-3.3)	1152.1	3.0 (3.0-3.0)	1168.2	3.7 (3.7-3.8)
Cardiovascular disease	19 381	26.8	403.2	3.6 (3.5-3.6)	416.6	3.1 (3.0-3.1)	387.7	4.6 (4.5-4.7)
Ischemic heart disease	10 096	25.6	210.0	3.7 (3.6-3.8)	228.9	3.1 (3.0-3.2)	188.4	5.2 (5.0-5.4)
Nonischemic heart disease	5988	28.9	124.6	3.9 (3.8-4.0)	123.3	3.4 (3.3-3.5)	126.0	4.8 (4.6-5.0)
Cerebrovascular disease	1561	24.9	32.5	2.2 (2.1-2.3)	29.5	2.0 (1.8-2.1)	35.9	2.5 (2.3-2.6)
Other circulatory disease	1736	25.8	36.1	3.8 (3.7-4.0)	35.0	3.3 (3.1-3.5)	37.4	4.6 (4.3-4.9)
Cancer	9638	25.6	200.5	1.8 (1.7-1.8)	185.3	1.7 (1.7-1.8)	217.9	1.8 (1.8-1.8)
Lung	3595	24.6	74.8	2.4 (2.4-2.5)	78.6	2.4 (2.3-2.5)	70.4	2.5 (2.4-2.6)
Colon	679	24.9	14.1	1.7 (1.6-1.8)	13.1	1.6 (1.4-1.8)	15.3	1.9 (1.7-2.1)
Breast	995	27.5	20.7	1.6 (1.5-1.7)	0.6	3.6 (1.8-5.4)	43.8	1.6 (1.5-1.7)
Liver	315	24.7	6.6	1.4 (1.2-1.5)	8.9	1.3 (1.1-1.5)	3.8	1.5 (1.2-1.9)
Pancreas	401	24.5	8.3	1.4 (1.2-1.5)	8.8	1.3 (1.2-1.5)	7.8	1.4 (1.2-1.6)
Hematologic	648	27.9	13.5	1.4 (1.3-1.6)	14.4	1.4 (1.3-1.6)	12.4	1.5 (1.3-1.7)
Other cancer	3005	26.1	62.5	1.5 (1.4-1.5)	60.8	1.4 (1.3-1.7)	64.5	1.6 (1.5-1.7)
Diabetes mellitus	2969	27.3	61.8	4.2 (4.0-4.3)	52.8	3.4 (3.2-3.6)	72.1	5.2 (4.9-5.4)
Renal failure	327	26.0	6.8	3.6 (3.2-4.0)	6.8	3.5 (3.0-4.0)	6.8	3.8 (3.2-4.4)
Influenza and pneumonia	1602	26.0	33.3	7.0 (6.7-7.4)	34.2	6.5 (6.1-7.0)	32.4	7.8 (7.2-8.4)
Sepsis	1254	25.7	26.1	4.6 (4.3-4.8)	22.9	4.1 (3.8-4.5)	29.7	5.0 (4.6-5.4)
COPD	4304	24.4	89.5	9.9 (9.6-10.2)	83.8	9.9 (9.5-10.3)	96.2	10.0 (9.6-10.4)
Liver disease	1391	29.0	28.9	2.0 (1.9-2.1)	35.8	1.9 (1.8-2.0)	21.0	2.1 (1.9-2.3)
Other natural deaths	14 875	29.4	309.4	4.2 (4.1-4.3)	313.8	3.8 (3.7-3.9)	304.4	4.8 (4.7-5.0)
Unnatural deaths	9812	35.7	204.1	3.1 (3.0-3.2)	241.7	5.0 (4.8-5.2)	160.9	2.5 (2.5-2.6)
Suicide	2498	38.3	52.0	3.9 (3.8-4.1)	63.7	3.2 (3.0-3.3)	38.5	6.9 (6.5-7.4)
Homicide assault	582	35.6	12.1	1.1 (1.0-1.2)	16.4	0.9 (0.8-1.0)	7.2	1.9 (1.6-2.2)
Accidents	5753	34.5	119.7	3.2 (3.1-3.2)	140.0	2.6 (2.5-2.7)	96.3	4.7 (4.5-4.9)
Poisoning	2846	36.8	59.2	4.8 (4.6-4.9)	67.6	4.1 (3.9-4.3)	49.5	6.5 (6.1-6.9)
Nonpoisoning	2907	32.3	60.5	2.4 (2.3-2.4)	72.4	2.0 (1.9-2.1)	46.8	3.6 (3.4-3.9)
Undetermined intent and other	979	36.1	20.4	5.9 (5.5-6.3)	21.7	5.0 (4.6-5.4)	18.8	7.8 (7.1-8.6)

Abbreviations: COPD, chronic obstructive pulmonary disease; SMR, standardized mortality ratio (standardized for age, sex, race/ethnicity, and geographic region).

[a] Schizophrenia mortality data are from the National Death Index of Medicaid beneficiaries. General population mortality data are from the Centers for Disease Control and Prevention WONDER data.[64] Mortality rates are expressed per 100 000 person-years. The deaths of 8450 individuals were classified as unknown, undetermined, or unspecified. Male and female SMRs are standardized for age, race/ethnicity, and geographic region.

creased in the total schizophrenia cohort, although it was significantly increased among women, middle-aged and older adults, and persons of white race/ethnicity (Tables 1, 2, and 3).

Deaths From Substances, Firearms, and Legal Intervention

Under the alternative Centers for Disease Control and Prevention classification, substance-induced deaths accounted for 8.2% of known-cause deaths and were most commonly nonsuicide deaths. Alcohol-induced and drug-induced deaths from drugs of abuse collectively accounted for most substance-induced deaths that were not classified as suicides. Standardized mortality ratios were significantly elevated for substance-induced suicide and nonsuicide deaths, firearm deaths, and deaths due to legal interventions (**Table 4**).

Discussion

Nonelderly adults with schizophrenia in the Medicaid program die at approximately 3.5 times the rate of the general

Table 2. Mortality Rates and Standardized Mortality Ratios of Adult Medicaid Beneficiaries Diagnosed as Having Schizophrenia by Disease Category and Age Group (January 1, 2001, to December 31, 2007)[a]

	20-34 y		35-54 y		55-64 y	
Cause of Death	Mortality Rate	SMR (95% CI)	Mortality Rate	SMR (95% CI)	Mortality Rate	SMR (95% CI)
All causes	459.6	3.6 (3.5-3.7)	1233.5	3.4 (3.4-3.5)	3707.2	4.0 (4.0-4.1)
Natural deaths	190.1	3.8 (3.6-4.0)	868.7	3.0 (3.0-3.0)	3157.6	3.6 (3.6-3.7)
Cardiovascular disease	54.9	4.5 (4.1-4.8)	296.4	3.2 (3.1-3.3)	1128.4	4.0 (3.9-4.0)
Ischemic heart disease	14.8	5.2 (4.4-6.0)	142.5	3.3 (3.2-3.4)	640.9	4.1 (4.0-4.2)
Nonischemic heart disease	32.0	4.7 (4.2-5.2)	111.2	3.9 (3.7-4.0)	269.2	4.0 (3.8-4.1)
Cerebrovascular disease	3.0	2.2 (1.4-2.9)	18.5	1.5 (1.4-1.6)	109.7	3.0 (2.8-3.2)
Other circulatory disease	5.0	3.9 (2.8-5.0)	24.1	3.2 (2.9-3.4)	108.7	4.5 (4.3-4.8)
Cancer	10.7	1.2 (1.0-1.4)	131.9	1.6 (1.5-1.6)	628.8	1.9 (1.9-2.0)
Lung	0.5	1.4 (0.2-2.7)	45.5	2.4 (2.2-2.5)	250.3	2.5 (2.4-2.6)
Colon	0.8	1.5 (0.5-2.6)	8.6	1.4 (1.2-1.6)	46.6	2.0 (1.8-2.2)
Breast	0.8	1.0 (0.3-1.8)	14.4	1.3 (1.2-1.4)	62.9	1.9 (1.7-2.1)
Liver	0.2	0.7 (0.0-1.6)	4.7	1.1 (1.0-1.3)	19.5	1.6 (1.4-1.8)
Pancreas	0.2	1.6 (0.0-3.7)	5.3	1.2 (1.0-1.4)	27.1	1.4 (1.2-1.6)
Hematologic	3.3	1.4 (1.0-1.9)	10.1	1.5 (1.3-1.6)	35.4	1.4 (1.3-1.6)
Other cancer	4.9	1.1 (0.8-1.4)	43.4	1.4 (1.3-1.4)	187.0	1.6 (1.5-1.7)
Diabetes mellitus	13.2	7.3 (6.0-8.5)	45.7	4.1 (3.9-4.3)	166.6	4.1 (3.9-4.3)
Renal failure	1.4	6.2 (3.0-9.5)	4.2	3.0 (2.4-3.5)	21.2	4.1 (3.5-4.7)
Influenza and pneumonia	5.2	5.6 (4.1-7.1)	21.2	5.2 (4.8-5.6)	103.0	9.4 (8.8-10.0)
Sepsis	2.8	3.2 (2.0-4.4)	16.1	3.5 (3.2-3.8)	83.7	5.8 (5.4-6.2)
COPD	1.4	9.7 (4.6-14.8)	47.2	11.0 (10.4-11.6)	322.1	9.5 (9.2-9.9)
Liver disease	3.2	2.8 (1.8-3.8)	30.6	2.0 (1.8-2.1)	51.9	1.9 (1.8-2.1)
Other natural deaths	97.3	4.1 (3.9-4.4)	275.4	3.7 (3.6-3.8)	651.9	5.1 (5.0-5.2)
Unnatural deaths	203.6	2.6 (2.5-2.8)	214.8	3.2 (3.1-3.3)	170.6	3.5 (3.3-3.7)
Suicide	73.9	5.3 (4.9-5.7)	51.0	3.7 (3.5-3.8)	30.8	2.9 (2.6-3.3)
Homicide assault	15.1	0.7 (0.6-0.8)	12.4	1.3 (1.2-1.5)	7.7	2.1 (1.6-2.6)
Accidents	97.2	2.6 (2.4-2.8)	127.9	3.2 (3.1-3.3)	118.2	3.8 (3.5-4.0)
Poisoning	55.0	5.7 (5.2-6.2)	71.3	4.6 (4.4-4.8)	25.3	4.1 (3.5-4.6)
Nonpoisoning	42.2	1.5 (1.4-1.7)	56.6	2.3 (2.2-2.4)	92.9	3.7 (3.4-3.9)
Undetermined intent and other	17.4	6.4 (5.5-7.4)	23.4	6.0 (5.5-6.4)	13.9	5.0 (4.2-5.9)

Abbreviations: COPD, chronic obstructive pulmonary disease; SMR, standardized mortality ratio (standardized for age, sex, race/ethnicity, and geographic region).

[a] Schizophrenia mortality data are from the National Death Index of Medicaid beneficiaries. General population mortality data are from the Centers for Disease Control and Prevention WONDER data.[64] Mortality rates are expressed per 100 000 person-years. The deaths of 8450 individuals were classified as unknown, undetermined, or unspecified.

population. Their increased risk of mortality was distributed across several diseases but was particularly elevated for COPD, influenza and pneumonia, diabetes mellitus, cardiovascular disease, and suicide. In absolute terms, the leading identified causes of death were cardiovascular disease, cancer, and accidents. These patterns have implications for the medical care of patients with schizophrenia.

The 3.7 SMR for all-cause mortality was higher than the corresponding 2.98 SMR from a meta-analysis of 38 studies that collectively included 22 296 deaths.[3] Our higher figure is consistent with a trend in the meta-analysis toward an increasing all-cause SMR in recent decades (the statistical test in the meta-analysis was significant at $P = .03$).[3] A French study[31] of 3470 patients with schizophrenia aged 18 to 64 years old, conducted between 1993 and 2005, reported all-cause SMRs of 3.6 for men and 4.3 for women, resembling the present findings.

Increased relative risk of cardiovascular mortality was observed for 3 age groups (20-34, 35-54, and 55-64), both sexes, and all 4 racial/ethnic groups. The number of age groups was reduced in the cause of death analysis to simplify the data presentation. Previous schizophrenia studies have reported significant, although smaller, increases in the relative risk for cardiovascular mortality for men,[32] women,[33] and younger adults.[34] Incomplete follow-up, sampling from hospital discharges, and short follow-up periods may have depressed prior estimates. The relative risk of cardiovascular mortality was lower among black adults than among white or Hispanic adults in part because of the higher background cardiovascular mor-

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.