Eight-Year Trends of Cardiometabolic Morbidity and Mortality in Patients with Schizophrenia

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Abstract

Objective—We examined cardiometabolic disease and mortality over eight years among individuals with and without schizophrenia.

Method—We compared 65,362 patients in the Veteran Affairs (VA) health system with schizophrenia to 65,362 VA patients without serious mental illness (non-SMI) matched on age, service access year, and location. The annual prevalence of diagnosed cardiovascular disease, diabetes, dyslipidemia, hypertension, obesity, and all-cause and cause-specific mortality were compared for fiscal years 2000–2007. Mean years of potential life lost (YPLL) was calculated annually.

Results—The cohort was mostly male (88%) with a mean age of 54 years. Cardiometabolic disease prevalence increased in both groups with non-SMI patients having higher disease prevalence in most years. Annual between-group differences ranged from < 1% to 6%. Annual mortality was stable over time for schizophrenia (3.1%) and non-SMI patients (2.6%). Annual mean YPLL increased from 12.8 to 15.4 in schizophrenia and from 11.8 to 14.0 for non-SMI groups.

Conclusions—VA patients with and without schizophrenia show increasing but similar prevalence rates of cardiometabolic diseases. YPLLs were high in both groups and only slightly higher among patients with schizophrenia. Findings highlight the complex population served by the VA while suggesting a smaller mortality impact from schizophrenia than previously reported.

Keywords

schizophrenia; cardiovascular disease; morbidity; mortality; cardiometabolic

Introduction

Researchers estimate that individuals with schizophrenia have a life expectancy 15–30 years shorter than the general population [1, 2]. This disparity has been observed consistently in clinical and population-based studies in the U.S. and elsewhere [3–7]. Although some excess mortality is due to trauma and suicide, the majority has been associated with natural causes, such as cancer, respiratory diseases, and most notably, cardiovascular disease (CVD) [2, 8]. Cardiovascular disease is the leading cause of premature mortality in persons with schizophrenia with cancer-related deaths reported nearly as frequently in some studies [2, 9], a trend consistent with the leading causes of death among the general U.S. population [11].

Premature mortality from natural causes of death among people with schizophrenia is commonly attributed to socioeconomic factors (e.g., poverty, poor education), behavioral factors (e.g., cigarette smoking, physical inactivity) and treatment factors (e.g., fragmentation of physical and mental health care, disparities in quality of medical care) and possibly to the cardiometabolic side effects of atypical antipsychotic medications [12–15]. However, the increased risk for CVD mortality existed prior to the advent of atypical antipsychotics, with some evidence indicating that first-generation antipsychotic medications might confer a greater risk for premature mortality [13]. Epidemiological evidence from time-trend studies and meta-analyses suggests that rates of premature death among individuals with schizophrenia have increased over the past three decades [3, 16, 17] although recent studies indicate that these rates may be in decline in settings with better mental health care [2, 18].

Approximately 3.5 million adults in the US have schizophrenia (1.5% of U.S adult population) [19, 20]. The Substance Abuse and Mental Health Services Administration (SAMHSA) recognizes the need to reduce health and health care disparities for individuals with mental illness and in 2010 set a goal of reducing premature mortality by 10 years within 10 years [21]. Some have suggested health insurance reforms may diminish disparities through expansion of publicly-funded insurance programs at the state level [22]. To more fully understand the health needs of people with schizophrenia and care delivery models that may be effective for them, it is essential to understand the current and recent health states of this population.

Published studies addressing excess mortality among individuals with serious mental illness, and cardiometabolic morbidity and mortality specifically in people with schizophrenia, have been relatively small, with cohorts ranging from 72 to 7217 subjects, and either cross-sectional or with a limited follow-up [3, 7, 23]. Until recently, the literature lacked prospective cohort studies conducted at a population level that apply national patient registries to monitor changes in cardiovascular risk factors and mortality over time. Moreover, even in studies from countries with national data registries, results are difficult to interpret due to the absence of comparison groups that are matched by appropriate demographic characteristics [2].

The goals of this study were to examine the unadjusted crude prevalence rates and trends of five cardiometabolic morbidities as well as trends in overall and cause-specific, unadjusted crude mortality rates associated with schizophrenia for a national cohort spanning 8 years. Our large cohort consisted of individuals receiving care from the U.S. Department of

Veterans Affairs (VA) health system. The VA health system is one of the largest providers of care to people with mental illness in the U.S. With a national electronic medical record system, integrated care design, and emphasis on care of the mentally ill, the VA represents a unique context to examine trends in morbidity and mortality of people with schizophrenia [24, 25].

Method

Setting and Design

Subjects with schizophrenia were identified from the VA National Psychosis Registry (NPR). Details of this registry have been described elsewhere [26]. Briefly, the registry includes administrative records for all VA patients who have received a diagnosis of psychosis in inpatient settings at some point since fiscal year (FY) 1988 or in outpatient settings since FY1997. The registry includes records of patient demographics, inpatient and outpatient services use, diagnoses, and prescription medication dispensing, vital signs and laboratory results.

From the NPR, our study cohort included patients with one or more diagnoses of schizophrenia in inpatient or outpatient settings from fiscal year (FY) 2000 through FY 2007 (10/1/99-9/30/07) (See Appendix for ICD-9 codes). We excluded patients with dementia diagnoses prior to the first diagnosis of schizophrenia as we believe these patients represent a distinct population with distinct care patterns and needs. A comparison population of VA patients was identified from annual random-sample cohorts of patients maintained in conjunction with NPR. This was achieved by matching each patient with one randomly selected comparison patient of the same age (within 2 years), sex, a VA clinic or inpatient visit within the same VA medical center system within 6 months of the schizophrenia patient's index diagnosis date, and with no diagnosis of serious mental illness (schizophrenia, bipolar disorder, or other psychosis diagnosis) in the study period.

Outcome measures

The main outcomes were 1) annual prevalence of cardiometabolic diseases: diabetes mellitus type 2 (T2DM), hypertension (HTN), dyslipidemia, and cardiovascular disease (CVD); 2) obesity, determined by Body Mass Index (BMI); and 3) rates of all-cause and cause-specific mortality. Year and cause of death were obtained from National Death Index data. These data are requested annually for all patients who did not have VA health care utilization in FY 2008 or 2009 [27, 28]. To determine annual prevalence of each of four cardiometabolic disease states, we identified diseases using ICD-9 diagnosis codes and prescription medication fills. Patients having either a diagnosis or a prescription fill specific to the disease of interest (e.g. oral hypoglycemic agents were deemed indicative of T2DM) were classified as having the corresponding condition. The diagnosis or medication fill date that occurred earliest in the study period was considered the index date of onset of the disease. Once a patient was classified as having a disease (except for obesity) we assumed the condition continued in all study follow-up years.

Obesity was defined as having a body mass index (BMI) 30. BMI was calculated from height and weight measures obtained from the VA vital signs files included among NPR data holdings. Patients categorized as obese in a given year were not assumed to be obese in subsequent years; for each year, they were categorized as obese only if a height and weight were recorded and BMI was 30 or greater.

Patient and Care System Characteristics

Covariates included in descriptive analyses were patient age, race (categorized as black, white, Hispanic and other), sex, Category C cost-share status (a VA measure of income sufficient to pay cost-share), military service connected disability status (a VA indicator of illness related to military service), marital status (dichotomized as married, not-married), and non-SMI psychiatric comorbidities (post traumatic stress disorder [PTSD], anxiety, depression, substance abuse or dependence). Tobacco exposure was based on diagnoses of chronic obstructive lung disease and/or tobacco use. Veterans Affairs Medical Center (VAMC) was assigned based on the site of the index diagnosis of schizophrenia or of index visit for the comparison population. Further methods details are provided in the Appendix.

Follow-up and censoring

Patients were followed from their index date through the end of the study period, 9/30/2007, or until they met one of the following censoring criteria: (1) no VA visits for 13 months (censored 12 months from last recorded visit or prescription fill), (2) death date identified from the NDI, (3) admission to a VA community living center (formerly known as nursing homes) lasting more than 30 days (patients were censored 30 days after admission)

Statistical analysis

Descriptive statistics were used to compare the schizophrenia and comparison population with regard to demographic characteristics, non-SMI psychiatric diagnoses, tobacco exposure, and inpatient and outpatient services use. Comparisons were conducted using methods for paired designs such as paired t-tests. For each year and group, we calculated the prevalence of each cardiometabolic morbidity, proportion of the group with BMI 30, and annual all-cause and cause-specific mortality.

The number of years of potential life lost (YPLL) was calculated for each decedent using current life expectancy tables for the U.S. population, published by the Centers for Disease Control and Prevention [29]. This measure of premature death uses the difference between a patient's age at death and the current life expectancy for cohorts of the same age and sex as the decedent in the year of death. Individual-level YPLL were used to calculate annual mean YPLL for each group (schizophrenia and non-SMI) by summing all YPLL in each group and dividing the sum by the number of group members decedents each year [10]. We also calculated the mean age at death for each group. YPLL was performed to put our observation comparing two VA populations into the context of the general U.S. population.

Results

We identified 65,362 patients with schizophrenia meeting inclusion criteria and an equal number of matched non-SMI comparison patients. Mean (SD) age was 53.6 years (14.8), 87.9% were male, and 32.1% were ethnic/racial minorities (Table 1). Race and income distribution differed somewhat between the schizophrenia and comparison groups. Among patients with schizophrenia, 27.9% were black, 13.2% met Category C income criteria, and 27.0% were married; this compares to the non-SMI group in which 19.9% of patients were black, 26.3% met Category C income criteria, and 45.9% were married. Substance abuse, tobacco use/tobacco related disease, and cumulative prevalence of non-SMI mental illness (anxiety, depression) were all more common in the schizophrenia group than the comparison group. Patients with schizophrenia used inpatient and outpatient services more intensely than the comparison group as well.

Figure 1 (and Appendix Table 2) presents morbidity measures by year. In the earlier years, diabetes and obesity were more prevalent among the schizophrenia group relative to the

comparison group. T2DM affected 17.9% to 21.1% of the schizophrenia group in the first three study years and 15.8% to 18.5% of the comparison group. In the early years, the prevalence of obesity was also greater among the schizophrenia patients (25.6% to 29.2%) relative to the comparison group (24.1% to 27.7%). These differences diminished in later years. In all years, prevalence of diagnosed HTN, CAD, and hyperlipidemia were consistently lower in the schizophrenia group than the comparison group. In 2007, the prevalence of diagnosed CAD was 22.4% in the schizophrenia population and 27.1% in the comparison group. Both groups experienced a substantial increase in cardiometabolic diagnoses over the study period. Notably diagnosed dyslipidemia nearly doubled from 25.2% of the schizophrenia group and 26.9% of the comparison group in 2000 to 55.9% and 61.7%, respectively in 2007.

Compared to cardiometabolic morbidity, mortality rates varied more substantially across the two groups. The schizophrenia group experienced significantly higher rates of mortality due to all-causes as well as from trauma/accidents in nearly all years and from suicide in most years. (Figure 2, Table 2). For all-cause mortality, the difference in annual rates never exceeded 0.9% between the cohorts. The most substantial difference across groups in annual all cause-mortality occurred in 2003 when schizophrenia patients experienced a death rate 1.6% higher than the comparison population. Annual mean YPLL increased from 12.8 to 15.4 for schizophrenia patients and from 11.8 to 14.0 for non-SMI patients, in each year the difference between the two populations was statistically significant ($p < 0.01$) (See Figure 3).

Discussion

Our large, retrospective study of the prevalence of cardiometabolic disease as well as all-cause and cause-specific mortality rates among patients diagnosed with schizophrenia relative to a matched comparison cohort revealed unexpectedly small overall differences across the cohorts in morbidity and mortality. While there were significantly higher annual mortality rates in the schizophrenia group the overall mortality-gap with comparison group was not as large as reported in the literature. The difference in the all-cause mortality rates of the two cohorts over the 8-year observation period appears predominantly attributable to mortality from atherosclerosis/HTN, suicide, and other causes that are consistently more common among the schizophrenia patients compared to the comparison population.

We find an overall increase in cardiometabolic disease for both the schizophrenia and the comparison populations. This is likely due to many factors including intensified screening and lower diagnostic thresholds (for T2DM for example). The observed increasing prevalence of obesity mirrors that of the general U.S. population and likely explains at least some of the rise in prevalence of other morbidities for which obesity is an important risk factor [30, 31]. For some cardiometabolic conditions, prevalence was lower in the schizophrenia group than the comparison group despite substantially higher rates of tobacco exposure, comparable rates of obesity, and the added cardiometabolic risk associated with some second generation antipsychotics. This may result from lower levels of diagnostic testing in this population, due in part to the clinical demands of managing mental illness. Although schizophrenia patients had higher rates of health care encounters (psychiatric and non-psychiatric) compared to the non-SMI group, these encounters may focus on acute conditions or consequences of mental illness rather than screening and prevention which may explain some differences in documented disease prevalence [32, 33]. While lower rates of testing may explain relative low prevalence of some diseases in the schizophrenia population, the modest differences in cardiometabolic mortality suggest that disease prevalence in the two populations is not dramatically different [34].

Rates of much morbidity in the schizophrenia group are comparable with non-SMI Veteran population, yet for both groups, rates were significantly greater than the general U.S. population. For example, the prevalence of diabetes and obesity (BMI 30) in 2005 for men between the ages of 40–59 years old averaged 7.9% and 39.7% respectively in objectively measured samples of American adults [35, 36], whereas the concurrent rates in the cohort of non-SMI Veterans averaged 24.1% and 40.7% and 24.9% and 40.6% in the schizophrenia group. VHA FY 2010 operational data indicate that the combined prevalence of overweight/obesity is 77% among VA patients (39% for obesity only), 10% greater than the general U.S. population [37]. These figures underscore the morbidity burden in the VA patient population that distinguishes it from general U.S. population and validate our choice of Veterans without SMI as the best comparison population.

Mortality is a critical measure of effectiveness of specific clinical treatment strategies [2, 16]. Our findings support conclusions of a 2009 publication reporting a 1.5-year difference in life expectancy among the general population of VA patients with and without SMI [38]. Likewise, a 2010 survey-based publication [39] comparing the mortality for VA patients with and without schizophrenia found that the hazards ratio for death for Veterans with schizophrenia compared to those with no mental illness was 1.2, significantly lower than the average 2.5 mortality ratio reported in community samples [3]. The similar rates in mortality among Veterans with and without SMI treated through VA healthcare facilities contrasts reports of a life expectancy gap of over 20–30 years among persons with schizophrenia compared to the general population even in settings with socialized medicine including the Nordic countries and Taiwan [6, 7, 18]. Gaps in mortality of this magnitude among people with serious mental illnesses have also been observed in the U.S. and in other countries [1, 3, 13].

While not the primary focus of the current study, mortality rates for cancer and suicide were notably lower than reported in other studies [2, 9, 40]. A number of methodological issues can obscure clear comparisons between the causes of mortality from suicide or specific cancers including the age of the cohort, the length and decade of follow-up, the cohort size, patient access to quality integrated and preventive health care services, and the reliability of data to measure causes of death. However, crude and unadjusted mortality findings from the current study are consistent with results from a recent retrospective study [41] examining causes of death and years of potential life lost (YPLL) among decedents with a serious mental illness persons from the general population in a Midwestern U.S. state. Researchers found that heart disease was the leading cause of death in both groups while cancer was the second leading cause of death in the general population but only the fifth cause of death for SMI patients (suicide was not in the top 10 causes of death for SMI patients overall). However, suicide, accidents, and cancer were leading causes of premature mortality (YPLL), causing the authors to conclude that community mental health clinics should place more emphasis on integrated care and preventive screening for these risks. In addition, mortality and morbidity results from the current study not only parallel similar findings reported by Bouza and colleagues in Spain [42], but also the leading cause of death (CVD) and mortality gap (i.e., 8 years) in a community-based study of American patients with mental disorders published by Druss et al. [43]

Indeed the relatively small disparities observed for patients *within* VA may be due to the unique, nationally and regionally integrated nature of this system. The VA's nationally integrated health care system is unique compared to other national health systems because of the high-risk population that the VA serves. Unlike many health systems, patients not only have access to mental and physical health care, but also receive targeted services to screen for and prevent both suicide and many forms of common cancers that might be attributed to exposures incurred during military service. The VA has made integrated care a priority for

patients with psychotic disorders since landmark studies were published in 2001 suggesting this approach improves outcomes [33, 44]. Patients with schizophrenia have greater access to substance abuse treatment services [45], inpatient and intensive case management to facilitate recovery, and immediate access to primary care in the same facility. As one of the largest single providers of mental health care in the U.S., the VA has also been at the forefront in implementing mental health parity, notably through the Mental Health Strategic Plan and the Uniform Mental Health Services Handbook. We speculate that lower unadjusted prevalence rates for cancer and suicide most likely reflect significant efforts to enact quality improvement efforts to target these risks for VA patients in general. Not only are older Veterans more likely to receive preventive screening for conditions like cancer than similar individuals outside the VA [46, 47], but patients who often do not receive preventive screenings in community settings due to conditions like obesity are actually more likely to be screening in the VA [48]. Finally, while quality improvement initiatives such as the implementation of a national electronic medical records system has radically improved care for all Veterans [24], efforts to improve coordination of care between specialty mental health and medical health providers is an ongoing process.

Present findings do not adjust for the prevalence of common psychiatric comorbidities that may raise CVD risk such as anxiety or depressive disorders. However, in a 9-year retrospective cohort study of 559,985 VA patients that examined the effects of mental health diagnoses on all-cause mortality, Chwastiak and colleagues [39] reported that only VA patients with schizophrenia and substance abuse disorders had an increased risk for all-cause mortality, even after adjustment for *psychiatric* and medical comorbidity, obesity, current smoking, and exercise frequency. While Chwastiak et al. did not address CVD mortality specifically, Kilbourne and colleagues [49] conducted a similar 8-year retrospective study of 147,193 VA patients with and without mental disorders, and found that VA patients with schizophrenia or other psychotic disorders, were more likely to die from heart disease-related mortality than Veterans diagnosed with depression or bipolar disorder, even after adjusting for sociodemographic factors, co-occurring diagnoses, and behavioral variables, including smoking and physical inactivity. These two studies offer support to the validity of the current study's findings despite limitations raised by analyses unadjusted for covariates. Subsequent studies will report the influence of important confounding variables including, exposure to specific psychiatric medications suggested to affect the onset and progression of CVD (e.g., antipsychotic medications).

Our finding of a mortality gap much smaller than that reported by other studies may also result from our choice of matched Veterans as our comparison population. We believe the relative homogeneity of U.S. Veterans making up both our schizophrenia and non-SMI groups, permits us to isolate more than other researchers to date, the impact of schizophrenia on mortality, at least for schizophrenia patients similar to our cohort. Other explanations for the small mortality gap we observed include possible selection effects. VA SMI patients are often diagnosed after enlistment and during military service, and may have had higher premorbid functioning compared to the general U.S. population with schizophrenia prior to their first psychotic episode. Additionally, early diagnosis and access to appropriate and continuous mental health care may help to mitigate the pathophysiological effects of psychosis on disease risk factors and help to identify common and avoidable medical conditions that can contribute to premature mortality if untreated (e.g., infectious disease, lung disease).

Perhaps most importantly, we note morbidity and mortality among Veterans with and without schizophrenia did not improved appreciably in the 8 years studied. This suggests, like the general U.S. population additional efforts are needed to improve the health of Veterans.

Limitations

Observational studies based on computerized administrative data have well-understood limitations that include unmeasured confounding factors. However, by matching schizophrenia Veterans with non-SMI Veterans, we believe we address major unmeasured confounders. We did not have a sufficient sample size or accurate measure to permit matching on race/ethnicity, but given the lower life expectancy of racial minorities in the U.S, we expect matching on race would result in even smaller difference across our study group. We also lack data on important cardiometabolic risk factors including: education, physical activity, diet, and environment. By intention, we did not adjust our analyses for comorbidities because our aim was to describe the relative health experiences of the two populations matched on age, gender, geography and visit timing. We expect such adjustment would move our observations closer to the null.

We relied on ICD-9 diagnosis codes from VA administrative data to identify patients' psychiatric and medical diagnoses, our measures depend on the accuracy and completeness of the codes recorded. Such data frequently underestimate the prevalence of psychiatric morbidity which affected both groups in this study [33]. Similarly, the prevalence of smoking is likely underestimated because VA providers often do not report this ubiquitous behavior with a formal diagnostic code. We additionally rely on the NDI Plus data for mortality statistics and cause of death; these data may lack sufficient sensitivity to accurately identify the primary cause of death [50, 51]. Finally, we were limited to an eight-year observation because VA pharmacy data used to confirm inclusion in both cohorts only became linked to the National Psychosis Registry starting in FY 2000. Future reports will explore differential effects of treatment with specific classes of psychotrophic drugs on morbidity and mortality outcomes, adjusting for key confounding variables such as demographic and comorbid health conditions.

Conclusions

This study described and compared the prevalence of cardiometabolic morbidity and mortality in a matched cohort of VA patients with and without schizophrenia diagnoses and found that while the burden of cardiometabolic disease continues to increase in all Veterans, schizophrenia does not appear associated with substantially higher differences in these diseases. Observed differences in mortality of patients with and without schizophrenia are significantly lower than reported in the literature and do not appear to have widened over this time period. We note that atherosclerotic disease stands out as the single greatest cause of the mortality gap we observed. Future research should further assess the modifiable causes of this excess atherosclerotic mortality and interventions and care models specific to these patients should be developed to address this. Exploration of such causes should include, in addition to behavioral factors, the potential contribution of cardiometabolically offensive psychotropic medications, especially second generation antipsychotics.

Acknowledgments

Appendices

Appendix Table 1

Annual Prevalence of Cardiometabolic Diseases among Veterans Diagnosed with Schizophrenia and Matched Veterans without Serious Mental Illness Diagnosis, 2000 through 2007. N = 130,724 (62,362 from each group)

		2000	2001	2002	2003	2004	2005	2006	2007
		%	%	%	%	%	%	%	%
Diabetes	**Schizophrenia**	17.9[*]	19.6[*]	21.1[*]	22.5[*]	23.5	24.9[*]	25.9	26.8
	Non-SMI	15.9	16.7	18.5	21.1	23.1	24.1	25.7	26.5
Coronary Artery Disease	**Schizophrenia**	17.2[*]	19.0[*]	20.1[*]	20.9[*]	21.6[*]	22.1[*]	22.3[*]	22.5[*]
	Non-SMI	19.6	20.7	22.2	24.6	26.2	26.2	27.3	27.1
Hypertension	**Schizophrenia**	42.8[*]	46.7[*]	49.7	52.8[*]	55.4[*]	58.0[*]	59.9[*]	61.6[*]
	Non-SMI	40.6	45.0	49.6	55.4	59.61	60.8	63.6	64.3
Dyslipidemia	**Schizophrenia**	25.2[*]	29.9[*]	35.1[*]	40.0[*]	45.0[*]	49.9[*]	53.2[*]	55.9[*]
	Non-SMI	26.9	33.1	39.0	46.2	52.1	55.6	59.7	61.7
Obesity	**Schizophrenia**	34.9	35.6	37.4	38.6	39.3	40.6	41.1	41.9
	Non-SMI	35.6	36.1	37.4	38.9	39.7	40.7	41.7	42.4
No medical Cardio-metabolic morbidities	**Schizophrenia**	37.0[*]	33.4[*]	30.4[*]	27.3[*]	24.7[*]	22.1[*]	20.5[*]	19.6[*]
	Non-SMI	38.3	35.3	31.3	26.0	22.0	20.7	18.9	18.4

Chi-squared tests assessed significance of difference across the groups.

Non-SMI group is matched on age, gender, parent Veterans Administration medical center and visit date. Non-SMI comparison group has no diagnosis of psychotic disorder. Annual prevalence based on ICD-9 diagnoses and disease-specific pharmacotherapy, once diagnosed patients with chronic conditions are assumed to continue with that condition until death or censorship. Obesity is defined as Body Mass Index ≥ 30 kg/m^2. Annual prevalence of obesity is based on annual body mass index measures. Patients obese in one year are not assumed obese in subsequent years.

[*]
p<0.05.

Appendix Table 2

Annual Mortality Rate (per 10,000) by Fiscal Year Among Veterans Diagnosed with Schizophrenia and Matched Veterans without Serious Mental Illness Diagnosis

		2000		2001		2002		2003		2004		2005		2006		2007	
		Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N
All Cause	Schizophrenia	257*	477	331*	893	315*	986	313*	1129	330*	1299	328*	1328	309*	1317	311*	1369
	Non-SMI	196	213	243	592	264	880	276	967	285	1041	274	1131	279	1169	247	1127
Atherosclerosis/HTN	Schizophrenia	81	150	105*	282	110*	344	99	358	106	415	101*	409	109*	463	103*	451
	Non-SMI	64	69	78	189	90	300	94	329	96	352	86	356	89	372	84	384
Suicide	Schizophrenia	8	14	10	27	8	24	12	42	11*	45	13*	54	6	27	7*	30
	Non-SMI	5	5	7	18	7	25	8	29	5	17	5	21	5	23	4	16
Trauma/accident	Schizophrenia	15	27	19*	50	19	60	23*	83	19	73	22	91	23*	96	26*	114
	Non-SMI	13	14	12	28	15	49	16	57	15	53	19	79	16	65	13	59
Malignancy	Schizophrenia	56	104	77	207	56	176	65	235	67	265	71	287	60	257	62	271
	Non-SMI	58	63	74	180	58	193	62	218	70	255	66	271	65	271	59	269
Pulmonary Disease	Schizophrenia	19*	36	23*	63	31*	98	22	79	23	90	23	95	18	75	23	101
	Non-SMI	8	9	12	28	20	67	20	70	18	64	18	73	19	81	20	90
Other causes	Schizophrenia	80*	146	100*	264	93*	284	94*	332	107*	411	99*	392	96	399	93*	402
	Non-SMI	50	53	62	149	75	246	77	264	84	300	82	331	87	357	69	309

Chi-squared tests assessed significance of difference across the groups. Death rate is calculated as number of deaths per 10,000 person years. SMI= serious mental illness. Patients in the non-SMI group are matched with the schizophrenia patients on age, gender, parent medical center and visit date; they have no diagnosis of psychotic illness. Cause of death as categorized by the National Death Index Plus data. Deaths attributed to "atherosclerotic/HTN" are those categorized in this data set as death due to: atherosclerosis hypertension, coronary heart disease, cerebrovascular disease, and aortic aneurysm.

*
 p<0.05

Appendix Table 3

Years of Potential Life Lost Patients with Schizophrenia and Matched Comparison Population with No Serious Mental Illness, by Year Mean(SD)

	2000	2001	2002	2003	2004	2005	2006	2007
Schizophrenia	12.8 (10)	13.2 (10)	13.8 (10.1)	14.4 (10.1)	15.0 (10.0)	14.8 (10.0)	15.3 (10.0)	15.4 (9.8)
Non-SMI	11.8 (9.6)	12.5 (9.3)	13.3 (9.3)	13.5 (9.3)	13.8 (9.5)	13.6 (9.5)	13.9 (9.6)	14.0 (9.5)
P Value	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

Statistical test of difference of YPLL between the two cohorts: t-test was used

Appendix Table 4

Psychiatric and Neurocognitive ICD-9 Codes

Schizophrenia **Exclusion Criteria**	295.0 – 295.9 schizophrenia disorders
Dementia	290.0 Senile dementia uncomplicated
	290.1 Presenile dementia uncomplicated
	290.11 Presenile dementia with delirium
	290.12 Presenile dementia with delusional features
	290.13 Presenile dementia with depressive features
	290.20 Senile dementia with delusional features
	290.21 Senile dementia with depressive features
	290.30 Senile dementia with delirium
	290.40 Vascular dementia uncomplicated
	290.41 Vascular dementia with delirium
	290.42 Vascular dementia with delusions
	290.43 Vascular dementia with depressed mood
	290.8 Other specified senile psychotic conditions
	290.9 Unspecified senile psychotic condition
	291.2 Alcohol-induced persisting dementia
	294.0 Amnestic disorder CCE[a]
	294.1 Dementia in CCE[a]
	294.10 Dementia CCE without behavioral disturbance[a]
	294.11 Dementia CCE w/ behavioral disturbances[a]
	294.8 Other persistent mental disorder due CCE[a]
	294.9 Unspecified persistent mental disorder due to CCE[a]
	331.0 Alzheimers disease
	331.2 Senile degeneration of brain
	333.4 Huntington's chorea
	331.19 Other frontotemporal dementia
	331.82 Dementia with Lewy bodies
	331.11 Pick's disease
	797.0 Senility without mention of psychosis

[a]CCE = Conditions classified elsewhere

Appendix Table 5

Cardiometabolic Disease ICD-9 Diagnosis Codes

Included Diagnoses	**ICD-9 codes**
Diabetes mellitus type 2	250.xx Diabetes mellitus (except 250.1 – with ketoacidosis)
Coronary artery disease	411 Other acute and subacute forms of ischemic heart disease
	413 Angina pectoris
	414 Other forms of chronic ischemic heart disease

Included Diagnoses	ICD-9 codes
Hyperlipidemia	272.0 Pure hypercholesterolemia
	272.1 Pure hyperglyceridemia
	272.2 Mixed hyperlipidemia
	272.3 Hyperchylomicronemia, other and unspecified
	272.4 Hyperlipidemia
Acute myocardial infarction	410 AMI inpatient diagnosis only
Obesity	278.00 Obesity
	278.01 Morbid obesity
	783.1 Abnormal weight gain
Hypertension	401 Essential hypertension
Cerebrovascular accident (Inpatient diagnosis only)	431 Intracerebral hemorrhage
	434.01 Cerebral thrombosis with cerebral infarction
	434.11 Cerebral embolism with cerebral infarction
	434.91 Cerebral artery occlusion unspecified with cerebral infarction

Appendix Table 6

Prescription Drug Classes Used to Identify Disease Prevalence and Morbidity

Disease	VA Medication Code	Prescription Classification
Diabetes	HS500	Blood glucose regulation agents
	HS501	Insulin
	HS502	Oral hypoglycemic agents
	HS503	Anti-hypoglycemics
Coronary Artery Disease/Arrythmia (Heart disease)	CV050	Digitalis glycosides
	CV250	Antianginals
	CV300	Antiarrhthmics
	CV900	Other cardiovascular agents
Hyperlipidmia	CV350	
Hypertension	CV701	Thiazides - related diuretics
	CV150	Alpha blockers
Coronary Artery Disease and/or Hypertension	CV100	Beta blocker
	CV200	Calcium channel blockers
	CV400	Antihypertensive combinations
	CV490	Other antihypertensives

Disease	VA Medication Code	Prescription Classification
	CV500	Peripheral vasodilators[a]
	CV703	Carbonic anhydrase inhibitor diuretics
	CV800	Ace inhibitors (no diabetes mellitus)
	CV805	Angiotensin II inhibitor (no diabetes mellitus)
	Cv806	Direct rennin inhibitor[a]

[a]No prescriptions for this class found in VA formulary

Appendix Table 7

Psychiatric Comorbidity Codes

Included Diagnoses	ICD-9 codes
Anxiety disorders	300.00 Anxiety disorder unspecified
	300.01 Panic disorder without agoraphobia
	300.02 Generalized anxiety disorder
	300.09 Other anxiety disorders
	300.10 Dissociative, conversion and factitious disorders
	300.20 Phobia unspecified
	300.21 Agoraphobia with panic attacks
	300.22 Agoraphobia without panic attacks
	300.23 Social phobia
	300.29 Other isolated or specific phobias
Post traumatic stress disorder	309.81 Posttraumatic stress disorder
Bipolar Disorders	296.0 Bipolar I, single manic episode
	296.1 Manic disorder recurrent episode
	296.4 Bipolar I disorder, most recent episode manic
	296.5 Bipolar I disorder, most recent episode depressed
	269.6 Bipolar I disorder, most recent episode mixed
	269.7 Bipolar I disorder most recent episode unspecified
	296.8 Other and unspecified bipolar disorders
Depression	293.83 Mood disorder in conditions classified elsewhere
	296.2 Major depressive disorder single episode
	296.3 Major depressive disorder recurrent episode
	296.9 Unspecified episodic mood disorder
	296.99 Other specified episodic mood disorder
	298.0 Depressive type psychosis
	300.4 Dysthymic disorder
	301.12 Chronic depressive personality disorder
	309.0 Adjustment disorder with depressed mood
	309.1 Adjustment reaction with prolonged depressive reaction
	311.0 Depressive disorder not elsewhere classified

| Included Diagnoses	ICD-9 codes
Substance abuse disorder	303.0 Acute alcoholic intoxication
	291 Alcohol withdrawal delirium
	292 Drug-induced mental disorders
	303.9 Other and unspecified alcohol dependence
	304.1 Sedative, hypnotic or anxiolytic dependence
	304.4 Amphetamine and other psychostimulant dependence
	304.5 Hallucinogen dependence
	304.6 Other specified drug dependence
	304.8 Combinations of drug dependence excluding opioid type drug
	304.9 Unspecified drug dependence
	305.0 Nondependent alcohol abuse
	305.2 Nondependent cannibus abuse
	305.3 Nondependent hallucinogen abuse
	305.4 Nondependent sedative, hypnotic, or anxiolytic abuse
	305.5 Nondependent opioid abuse
	305.6 Nondependent cocaine abuse
	305.7 Nondependent amphetamine/acting sympathommetic abuse
	305.8 Nondependent antidepressant type abuse
	305.9 Nondependent other mixed or unspecified drug abuse
Tobacco Exposure Measure (tobacco related disease or diagnosis of tobacco use)	Chronic Non-Asthmatic Lung Disease: ICD-9 Dx code: 415.0, 416.8, 416.9, 491.0, 492.0, 494.0, 496.0
	Tobacco use: ICD-9 305.1, V15.82, 989.84 tobacco
	649.0 Tobacco use disorder complicating pregnancy, childbirth, puerperium

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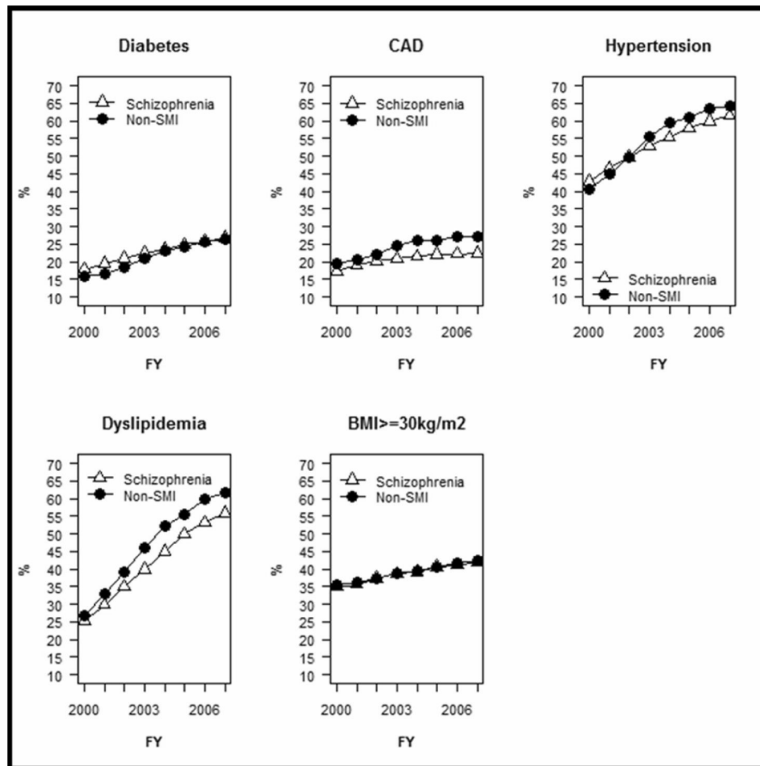
Figure 1. Annual Prevalence of Diagnosed Cardiometabolic Diseases Among Veterans with Schizophrenia and a Matched Comparison Group of Veterans Without Serious Mental Illness 2000–2007

Non-SMI group is matched on age, gender, parent Veterans Administration medical center and visit date, and has no diagnosis of psychotic disorder. Annual prevalence based on ICD-9 diagnoses and disease-specific pharmacotherapy. Once diagnosed patients with chronic conditions are assumed to continue with that condition until death or censorship. Annual prevalence of obesity is based on annual body mass index ≥ 30 kg/m^2. Patients obese in one year are not assumed obese in subsequent years. FY = fiscal year, CAD= Coronary Artery Disease, BMI = Body Mass Index (weight in kilograms/height in meters squared). See appendix table 1 for annual rates.
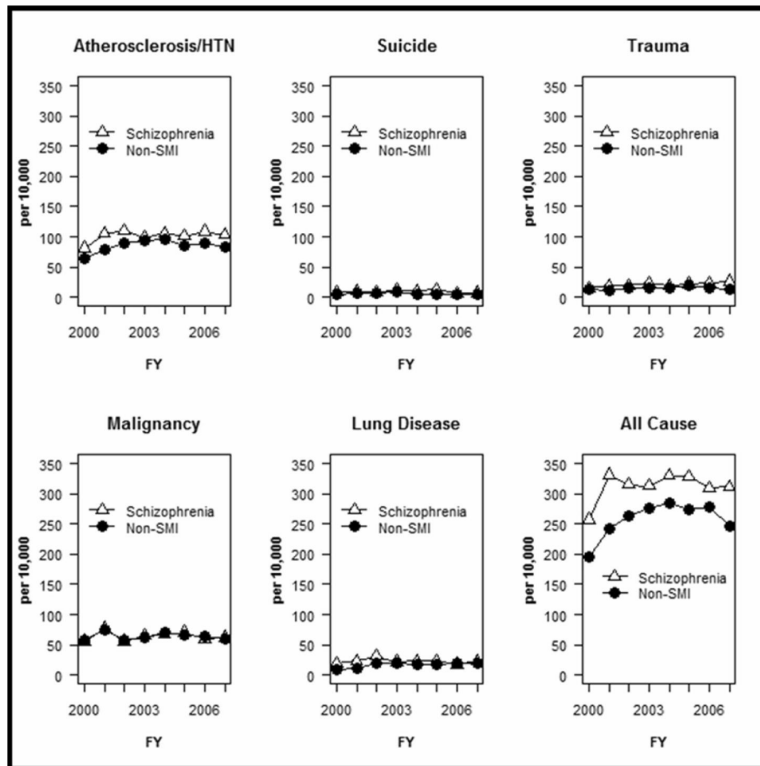
Figure 2. Annual Death Rate per 10,000 Person Years Overall and by Specific Causes, for Veterans with Schizophrenia and a Matched Comparison Group of Veterans without Serious Mental Illness, 2000–2007

Non-SMI group is matched on age, gender, parent Veterans Administration medical center and visit date. Non-SMI comparison group has no diagnosis of psychotic disorder (schizophrenia, bipolar disorder or other psychosis). Cause of death as categorized by the National Death Index Plus data. Deaths attributed to "atherosclerotic/HTN" are those categorized in this data set as death due to: atherosclerosis hypertension, coronary heart disease, cerebrovascular disease, and aortic aneurysm. Annual mortality rates are presented in Appendix Table 2.
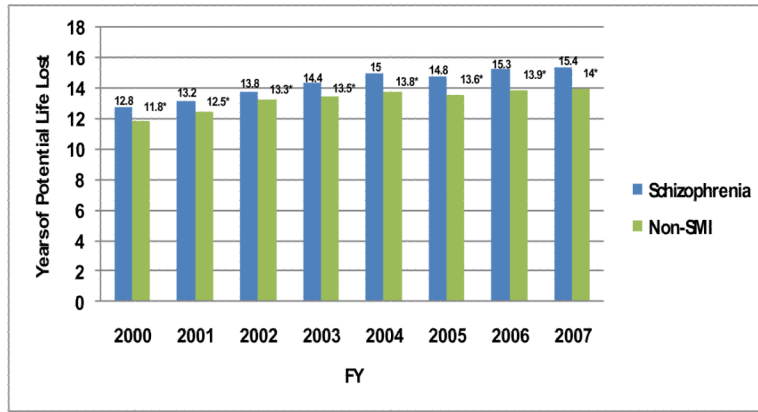
Age at Death	Mean (SD)							
	2000	2001	2002	2003	2004	2005	2006	2007
Schizophrenia	69.3(13.3)	68.8(13.5)	68.5(13.7)	68.0(13.9)	67.7(14.0)	67.8(14.0)	67.7(14.1)	67.9(13.8)
Non-SMI	71.0(13.2)	69.8(13.1)	69.4(13.2)	69.6(13.1)	69.8(13.1)	69.5(13.2)	69.6(13.3)	70.0(13.3)

Figure 3. Years of Potential Life Lost and Age at Death, 2000–2007, for Veterans with Schizophrenia and a Matched Comparison Population with no Serious Mental Illness
The number of years of potential life lost (YPLL) was calculated for each decedent using current life expectancy tables for the U.S. population, published by the Centers for Disease Control and Prevention. This measure of premature death uses the difference between a patient's age at death and the current life expectancy for cohorts of the same age and sex as the decedent in the year of death. Individual-level YPLL were used to calculate annual mean YPLL for each group (schizophrenia and non-SMI) by summing all YPLL in each group and dividing the sum by the number of group members decedents each year.[1] We also calculated the mean age at death for each group. T-test was used to assess statistical significance between groups. * denotes p< 0.01

Table 1

Demographics, Psychiatric Comorbidities and Service Use of Patients with Schizophrenia and the Comparison Population with No Serious Mental Illness 2000–2007

Characteristics	Overall (N=130,724)	Schizophrenia Group (N=65,362)	Non-SMI Comparison Group (N=65,362)
Mean age SD	53.6 (14.8)[*]	53.4 (14.9)	53.8(14.6)
White: N (%)	78220 (67.9)[*]	37960 (64.2)	40260(72.0)
Black: N (%)	27608 (23.9)	16470 (27.9)	11138(19.9)
Hispanic: N (%)	6184 (5.4)	3099 (5.2)	3085(5.5)
Other Race: N (%)	3054 (2.7)	1619 (2.7)	1435(2.6)
Male: N (%)	115006 (87.9)	57503 (87.9)	57503(87.9)
Meets Category C Cost Share Means Test: N (%)	24850 (19.7)[*]	8408 (13.2)	16442(26.3)
Service Connected: N (%)	62317 (47.7)[*]	31928 (48.9)	30389(46.5)
Married: N (%)	47507 (36.5)[*]	17493 (27.0)	30014(45.9)
Substance Abuse Disorder Diagnosis: N (%)	39618 (30.3)[*]	26442 (40.5)	13176(20.2)
Post Traumatic Stress Disorder: N (%)	29074 (22.2)[*]	16026 (24.5)	13048(19.9)
Anxiety not PTSD: N (%)	30936 (23.7)[*]	17979 (27.5)	12957(19.8)
Depression: N (%)	71243 (54.5)[*]	37413 (57.2)	33830(51.8)
Tobaccos Exposure Diagnoses: N (%)	45675 (34.9)[*]	27005 (41.3)	18670(28.6)
No-Mental Illness Diagnosis: N (%)			47579(72.8)
Inpatient and Outpatient Service Use			
Psychiatric inpatient days/person year	1.84	3.52	0.19
Non-Psychiatric inpatient days/person years	2.95	4.27	1.65
Psychiatric outpatient clinic visits/person year	9.89	15.83	4.04
Non-Psychiatric outpatient clinic visits/person year	18.05	20.39	15.74

Tobacco exposure measure is defined as a diagnosis of tobacco-associated lung disease or diagnosis of tobacco use. Category C is a Veterans Administration means tested benefit categorization, Category C patients have sufficient income to be held responsible for cost-share payments on select services. Prevalence of psychiatric and tobacco associated comorbidities presented are **cumulative** over the 8-year study period. Inpatient and outpatient service use rates presented are calculated for all patients during all years. Chi squared and T tests used to determine statistical difference across groups.

[*] Indicates p< 0.05.