Unemployment, Homelessness, and Other Societal Outcomes Among US Veterans With Schizophrenia Relapse:
A Retrospective Cohort Study

Dee Lin, PharmD, MS[a],[*]; Hyunchung Kim, MPP[b]; Keiko Wada, MA[b]; Maya Aboumrad, MPH[c]; Ethan Powell, BA[c]; Gabrielle Zwain, BA[c]; Carmela Benson, MS, MSHP[a]; and Aimee M. Near, MPH[b]

ABSTRACT

Objective: To evaluate societal outcomes including unemployment and homelessness among US veterans with schizophrenia with a history of relapse.

Methods: A retrospective cohort study was conducted using US Veterans Health Administration (VHA) data from January 1, 2013, to September 30, 2019. Veterans with ≥ 2 diagnoses of schizophrenia, schizotypal disorder, and/or schizoaffective disorders (*ICD-9-CM* 295.xx, *ICD-10-CM* F20.x, F21, or F25.x) during the study period on different days were identified. The index date was the earliest observed diagnosis. Two cohorts were created and propensity score matched: (1) the relapse cohort of veterans with ≥ 1 prior relapse, defined as hospitalization or emergency department visit associated with a schizophrenia diagnosis during the 12-month preindex period, and (2) the nonrelapse cohort of veterans with no evidence of relapse during the preindex period. The frequencies of unemployment, divorce, homelessness, incarceration, and premature death were compared between matched cohorts using standardized mean difference (SMD ≥ 0.1 indicating imbalance).

Results: Each cohort included 16,862 veterans (92.0% male, 57.0% White, median age of 58–59 years). In the relapse cohort, 67.4% and 42.0% of veterans had a history of substance use disorder and non-schizophrenia mental health disorder, respectively, compared to 43.5% and 23.8% in the matched nonrelapse cohort (both SMD > 0.1). The relapse cohort had a higher frequency of unemployment (75.4% vs 71.4%), divorce (35.6% vs 33.7%), homelessness (38.9% vs 23.7%), incarceration (0.6% vs 0.4%), and premature death (23.3% vs 16.9%) compared to the nonrelapse cohort (all SMD > 0.1).

Conclusions: Schizophrenia relapse is associated with increased adverse societal outcomes in the VHA population.

Prim Care Companion CNS Disord 2022;24(5):21m03173

Schizophrenia is a debilitating and severe mental health disorder, that according to the Global Burden of Disease Study, affects approximately 21 million people worldwide, including more than 1 million people in the United States.[1,2] The prevalence of schizophrenia, as well as other mental health disorders, is particularly high among US veterans. Of the 4 million US veterans evaluated in 2010 and 2011, approximately 164,000 were reported to have serious mental illness such as schizophrenia and bipolar disorder.[3]

Relapse in schizophrenia is common and characterized by acute psychotic exacerbation; relapse has been associated with disease progression, poorer response to treatment, and worsening of clinical symptoms.[4–7] Relapse has a detrimental impact on patients, caregivers, society, and health care systems.[6] Reported relapse rates in schizophrenia ranged from 41% to 79% over a period of 12 months after treatment discontinuation[5,8–12]; the wide range reflects inconsistent definitions of relapse across the studies.[6] A US-based claims database study using data from 1997 to 2010 suggests that patients with schizophrenia had an average of 9 relapse episodes over 5.5 years.[13] Key drivers of relapse include poor treatment adherence, chronic nature of schizophrenia, inappropriate treatment leading to nonadherence (eg, an increased dose of medication prescribed to prevent relapse may increase the side effects, which can result in nonadherence), psychological stress (such as traumatic experience and social isolation), and substance abuse.[5,14–17] It has been estimated that 1 in 5 patients will have poorer long-term outcomes following relapse[18] and that only 1 in 7 will achieve long-term recovery.[19] Furthermore, 1 episode of relapse has been identified as an important predictor of subsequent relapse.[20]

Relapse leads to increased socioeconomic burden to the patients, their families, and society.[4–7] For example, a physician and patient survey study[21] reported that having a relapse in the past 12 months was associated with homelessness, unemployment, history of incarceration, challenges in maintaining employment, impairment in work ability, inability to live independently, and poor quality of life. A systematic literature review[22] of 16 studies estimated that the excess health care cost of relapse in the United States ranges from $6,033 to $32,753. Relapse episodes most often lead to emergency department (ED) visits and hospitalizations,[23] which are generally the largest contributors to the economic burden.[22] Furthermore, costs associated with treatments received after relapse may account for the largest proportion of treatment costs associated with schizophrenia.[14] Despite these previous studies on economic burden of schizophrenia and its

Clinical Points

- The impact of schizophrenia relapse on societal burden, outside of clinical and economic burden, is substantial.
- Schizophrenia-related relapse was associated with significantly increased frequency of unemployment, divorce, homelessness, and incarceration, as well as increased risk of premature death and subsequent relapse.
- Clinically preventing relapse and managing comorbid mental health and substance abuse conditions, while addressing social determinants of health, may improve societal and clinical outcomes for patients.

relapse, the literature describing the non–health care societal burden of schizophrenia remains sparse.

The aim of this study was to evaluate societal outcomes such as unemployment, divorce, homelessness, incarceration, and premature death among veterans with schizophrenia with a history of relapse who receive care within the US Veterans Health Administration (VHA) system, wherein the prevalence of schizophrenia is high. This study will fill the existing gap in the literature on the impact of schizophrenia relapse outside of clinical and economic burden and provides a unique opportunity to identify areas for improvement with respect to social determinants of health, particularly in the US VHA population.
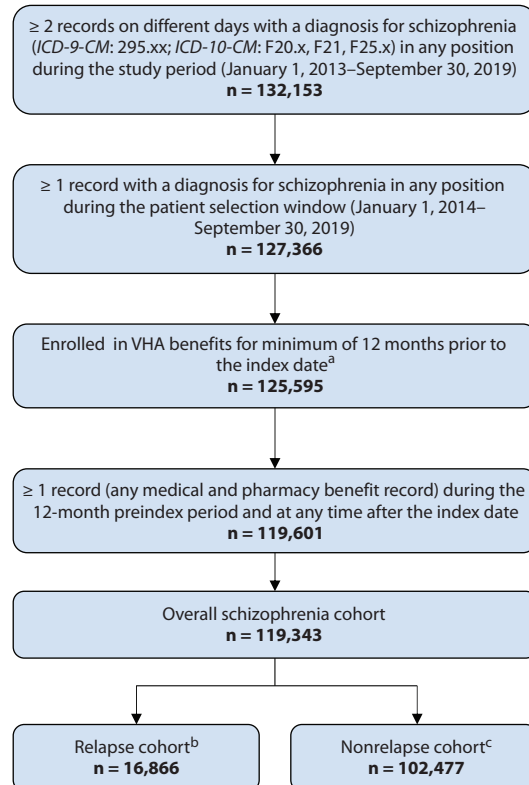
METHODS

Data Source

The VHA is the largest integrated health care system in the United States, providing comprehensive health care services to over 9 million veterans.[24] For this study, data were extracted from the integrated database of the VHA Corporate Data Warehouse (CDW). The VHA CDW contains medical records of inpatient, outpatient, and ED visits of veterans as well as demographic and mortality information collected from multiple VHA and non-VHA sources including Medicare Vital Status and the National Death Index. CDW data are updated daily. Data for employment, marital, housing, and incarceration statuses were obtained through linkage to the Veterans Benefits Administration Corporate Database, which is updated biannually. All study procedures were carried out in compliance with federal and institutional ethical guidelines. The Veterans Affairs Central Institutional Review Board (IRB; Study ID:1478231–1) provided approval for this study on December 17, 2019. The requirement to obtain informed consent from study participants was waived. The IRB deemed this study to involve no more than a minimal risk to the privacy of individuals. Data used in the study were deidentified, all analyses were conducted within the Veterans Affairs (VA) system, and only aggregated results were provided to non-VA individuals involved with this study.

Study Design

This was a retrospective cohort study using VHA data from January 1, 2013, to September 30, 2019 (study period).

Figure 1. Patient Selection Criteria Flowchart

≥ 2 records on different days with a diagnosis for schizophrenia (*ICD-9-CM*: 295.xx; *ICD-10-CM*: F20.x, F21, F25.x) in any position during the study period (January 1, 2013–September 30, 2019)
n = 132,153

↓

≥ 1 record with a diagnosis for schizophrenia in any position during the patient selection window (January 1, 2014–September 30, 2019)
n = 127,366

↓

Enrolled in VHA benefits for minimum of 12 months prior to the index date[a]
n = 125,595

↓

≥ 1 record (any medical and pharmacy benefit record) during the 12-month preindex period and at any time after the index date
n = 119,601

↓

Overall schizophrenia cohort
n = 119,343

↓

Relapse cohort[b]	Nonrelapse cohort[c]
n = 16,866	**n = 102,477**

[a]The index date was defined as the first observable diagnosis of schizophrenia with at least 12 months of enrollment in Veterans Affairs benefits preindex (baseline period) and postindex (observation period).
[b]Patients with ≥ 1 schizophrenia-related relapse anytime during the 12-month baseline period, defined as an inpatient stay or emergency department visit with a diagnosis code for schizophrenia (*ICD-9-CM*: 295. xx, *ICD-10-CM*: F20.x, F21, F25.x) in any position.
[c]Patients with no schizophrenia-related relapse anytime during the 12-month baseline period, defined as no inpatient stay or emergency department visit with a diagnosis code for schizophrenia in any position.
Abbreviation: VHA = US Veterans Health Administration.

The study included veterans receiving care within the VHA who had ≥ 2 diagnoses of schizophrenia, schizotypal disorder, or schizoaffective disorders (*ICD-9-CM* 295.xx, *ICD-10-CM* F20.x, F21, or F25.x) on different days during the study period. At least 1 of these diagnoses was required to be in the patient selection window of January 1, 2014, through September 30, 2019, to allow for a 12-month preindex period and variable follow-up period. The index date was the date of the earliest diagnosis observed during the selection window. Two schizophrenia cohorts, the relapse and nonrelapse cohorts, were created based on a history of schizophrenia-related relapse, defined as an inpatient stay or ED visit with 1 of the schizophrenia diagnoses in any position in the preindex period. The complete inclusion and exclusion criteria are provided in Figure 1.

Baseline Measures

Patient sociodemographic and baseline clinical characteristics from the 12-month preindex period were reported. Clinical characteristics included the Charlson Comorbidity Index (CCI),[25] mental health and substance

Table 1. Demographic and Baseline Clinical Characteristics of the Study Population

Variable	Relapse Cohort (n = 16,862)	Nonrelapse Cohort (n = 16,862)	Absolute SMD[a]	Variable	Relapse Cohort (n = 16,862)	Nonrelapse Cohort (n = 16,862)	Absolute SMD
Age at index, y				**Comorbidities of interest, n (%)**			
Mean (SD)	56.4 (13.3)	56.6 (13.0)	0.01	Hypertension	9,511 (56.4)	6,064 (36.0)	0.42
Median (Q1, Q3)	58 (51, 64)	59 (51, 65)		Hyperlipidemia	7,525 (44.6)	4,807 (28.5)	0.34
Minimum	20	20		Diabetes	5,170 (30.7)	5,103 (30.3)	0.01
Maximum	99	98		Obesity	2,907 (17.2)	1,900 (11.3)	0.17
Age categories, n (%)			**0.00**	Hepatitis	2,205 (13.1)	1,054 (6.3)	0.23
18–34	1,655 (9.8)	1,621 (9.6)		Coronary artery disease	1,911 (11.3)	1,063 (6.3)	0.18
35–44	1,182 (7.0)	1,206 (7.2)		Liver disease	1,684 (10.0)	704 (4.2)	0.23
45–54	3,021 (17.9)	3,021 (17.9		Congestive heart failure	1,082 (6.4)	469 (2.8)	0.17
55–64	6,793 (40.3)	6,797 (40.3)		Chronic obstructive pulmonary disease	869 (5.2)	197 (1.2)	0.23
≥65	4,211 (25.0)	4,217 (25.0)		Cancer	842 (5.0)	587,581 (3.4)	0.08
Sex, n (%)			**0.01**	Mental health conditions of interest (any)	7,082 (42.0)	4,010 (23.8)	0.40
Male	15,499 (91.9)	15,529 (92.1)		Trauma- and stressor-related disorders[b]	3,601 (21.4)	2,816 (16.7)	0.12
Race, n (%)			**0.08**	PTSD	3,094 (18.3)	2,579 (15.3)	0.08
White	9,669 (57.3)	9,697 (57.5)		Other stressor-related disorders[c]	757 (4.5)	334 (2.0)	0.14
Black	5,944 (35.3)	5,950 (35.3)		Anxiety disorders	2,606 (15.5)	1,522 (9.0)	0.20
Hawaiian Pacific islander	158 (0.9)	151 (0.9)		Suicide ideation	3,321 (19.7)	368 (2.2)	0.58
Asian	138 (0.8)	127 (0.8)		Suspected suicide attempt[d]	372 (2.2)	62 (0.4)	0.16
Native American	102 (0.6)	85 (0.5)		History of substance abuse[e]	11,368 (67.4)	7,332 (43.5)	0.50
Unknown/decline	851 (5.1)	852 (5.0)		**PHQ-2 score, n (%)[f]**	9,472 (56.1)	10,848 (64.4)	
Geographic region, n (%)			**0.00**	Mean (SD)	1.1 (1.7)	1.0 (1.6)	0.09
South	5,281 (31.3)	5,288 (31.4)		Median (Q1, Q3)	0 (0, 2)	0 (0, 2)	
Northeast	5,054 (30.0)	5,038 (29.9)		Minimum	0	0	
Midwest	3,492 (20.7)	3,507 (20.8)		Maximum	6	6	
West	3,035 (18.0)	3,029 (18.0)					
Residence, n (%)			**0.00**				
Urban	13,276 (78.7)	13,296 (78.9)					
CCI							
Mean (SD)	2.5 (2.7)	2.4 (2.4)	**0.05**				
Median (Q1, Q3)	2 (0, 4)	2 (0, 4)					
Minimum	0	0					
Maximum	20	18					
CCI categories, n (%)			**0.00**				
0	4,542 (26.9)	4,545 (27.0)					
1	3,435 (20.4)	3,418 (20.3)					
2	2,313 (13.7)	2,306 (13.7)					
3	1,952 (11.6)	1,965 (11.7)					
≥4	4,620 (27.4)	4,628 (27.4)					

[a]The bolded values indicate the variables used in the propensity score model.
[b]Includes both PTSD and other stressor-related disorders.
[c]Includes adjustment disorders, reaction to stress, and state of emotional shock and stress.
[d]Suspected suicide attempt was identified with *ICD* codes for suicide attempt and *ICD* codes related to intentional self-harm and self-inflicted poisoning and injury, which may result in death.
[e]Substance abuse disorders identified through diagnosis codes of nicotine, opioid, alcohol, cocaine, cannabis, amphetamine, antidepressant, sedative, hypnotic or anxiolytic, or hallucinogen and other psychoactive substance or inhalant dependence, misuse, or abuse.
[f]Score ranges from 0 to 6; a score ≥3 is considered the optimal cut point when using the PHQ-2 to screen for depression.
Abbreviations: CCI = Charlson Comorbidity Index, PHQ-2 = Patient Health Questionnaire-2, PTSD = posttraumatic stress disorder, Q1 = quartile 1, Q3 = quartile 3, SMD = standardized mean difference.

use comorbidities, and the self-reported Patient Health Questionnaire-2 (PHQ-2)[26] score.

Study Outcomes

The frequency of unemployment, divorce, homelessness, incarceration, and premature death (defined as death before aged 80 years[27]), based on the most recent nonmissing data during the study period, was reported for each cohort. The number and proportion of veterans with missing data for each of these variables were reported as a separate category. The frequency of death and relapse, as well as time from index to relapse, was reported based on the variable follow-up period.

Statistical Analysis

Veterans in the relapse cohort were matched 1:1 with veterans in the nonrelapse cohort using propensity scores (PS); greedy nearest neighbor matching without replacement (caliper of 0.01) was used. The PS model included age category, sex, race, geographic region of residence, urban or rural residence, index year, and CCI. The matched cohorts were considered well-balanced for a given variable if the absolute standardized mean difference (SMD) was < 0.1 between the cohorts.

For descriptive analyses, categorical measures were reported as frequency and percentage, and continuous variables were described as mean, standard deviation (SD),

Table 2. Relapse and Death During Follow-Up for the Study Population

Variable	Relapse Cohort (n = 16,862)	Nonrelapse Cohort (n = 16,862)	Absolute SMD
Length of follow-up, mo			
Mean (SD)	56.8 (20.7)	58.8 (17.6)	0.10
Median (Q1, Q3)	68.7 (49.4, 69.7)	67.2 (59.4, 69.3)	
Minimum	0.0	0.1	
Maximum	70.0	70.0	
Relapse			
Patients with relapse during follow-up, n (%)	12,942 (76.8)	7881 (46.7)	0.65
Mean (SD), mo	12.3 (15.6)	19.9 (19.4)	0.43
Median (Q1, Q3), mo	5.7 (0.9, 17.6)	14.0 (2.3, 33.0)	
Death status, n (%)			
Died during the follow-up	4,511 (26.8)	3,296 (19.5)	0.17
Patient age at death, y			
Mean (SD)	67.0 (10.6)	67.4 (10.7)	0.03
Median (Q1, Q3)	67.0 (61.0, 72.0)	67.0 (61.0, 73.0)	
Minimum	23	25	
Maximum	100	98	
Patients with premature death (aged < 80 y), n (%)	3,932 (23.3)	2,847 (16.9)	0.16

Abbreviations: Q1 = quartile 1, Q3 = quartile 3, SMD = standardized mean difference.

first quartile (Q1), median, third quartile (Q3), minimum, and maximum. The matched cohorts were compared using SMD, with any value ≥ 0.1 considered statistically meaningful. Data were analyzed using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Baseline Demographic and Clinical Characteristics

A total of 119,343 veterans with schizophrenia met the selection criteria, resulting in 16,866 patients in the relapse cohort and 102,477 in the nonrelapse cohort prior to matching (Figure 1). After PS matching, 16,862 veterans remained in each cohort.

The matched cohorts were well-balanced in terms of demographic characteristics (Table 1). Nearly all veterans were male (91.9% of the relapse cohort, 92.1% of the nonrelapse cohort); the median age was 58–59 years in both cohorts. The majority of veterans were White (57.3% of the relapse cohort and 57.5% of the nonrelapse cohort), and most of the remaining veterans were Black (35.3% for both cohorts, all SMD < 0.1). CCI scores were also similar between the matched cohorts, with a median score of 2 (SMD = 0.05). The key differences between the cohorts were observed in baseline comorbidities, with the relapse cohort having a higher frequency of both non–mental health and mental health comorbidities compared to the nonrelapse cohort, including hypertension (56.4% vs 36.0%, SMD = 0.42), hyperlipidemia (44.6% vs 28.5%, SMD = 0.34), and liver disease (10.0% vs 4.2%, SMD = 0.23) (Table 1). Furthermore, compared to the nonrelapse cohort, the relapse cohort had a higher frequency of substance use disorder (67.4% vs 43.5%, SMD = 0.50), posttraumatic

Table 3. Non–Health Care Societal Burden Among the Matched Cohorts

Variable	Relapse Cohort (n = 16,862)	Nonrelapse Cohort (n = 16,862)	Absolute SMD
Employment status, n (%)			0.20
Full-time employment	577 (5.4)	908 (5.4)	
Part-time employment	284 (1.7)	428 (2.5)	
Unemployed	12,721 (75.4)	12,043 (71.4)	
Retired	2,661 (15.8)	2,889 (17.1)	
Self-employed	68 (0.4)	93 (0.6)	
Missing data	551 (3.3)	501 (3.0)	
Marital status, n (%)			0.21
Divorced	6,006 (35.6)	5,689 (33.7)	
Married	2,751 (16.3)	4,099 24.3)	
Single	7,270 (43.1)	6,257 (37.1)	
Widowed	104 (0.6)	112 (0.7)	
Data missing	731 (4.3)	705 (4.2)	
Housing status, n (%)			0.33
Evidence of homelessness	6,558 (38.9)	3,997 (23.7)	
No evidence of homelessness	10,304 (61.1)	12,865 (76.3)	
Incarcerated patients, n (%)			0.15
Yes	101 (0.6)	62 (0.4)	
No	5,733 (34.0)	6,085 (36.1)	
Missing data	11,028 (65.4)	10,715 (63.5)	

Abbreviation: SMD = standard mean difference.

stress disorder (18.3% vs 15.3%, SMD = 0.08), and anxiety disorders (15.5% vs 9.0%, SMD = 0.20). Suicidal ideation was also observed in 19.7% of the relapse cohort compared to 2.2% in the nonrelapse cohort (SMD = 0.58). The frequency of suicide attempt was low in both cohorts but numerically higher for the relapse cohort (2.2% vs 0.4%, SMD = 0.16). PHQ-2 scores were similar with a mean of 1.1 in the relapse cohort compared to 1.0 in the nonrelapse cohort (SMD = 0.09).

Relapse During Follow-Up

The mean follow-up was 4.7 years for the relapse cohort and 4.9 years for the nonrelapse cohort (SMD = 0.10). The frequency of relapse during the follow-up period were significantly higher for the relapse cohort compared to the nonrelapse cohort (76.8%

Figure 2. Non–Health Care Societal Burden Among Matched Relapse Schizophrenia and Nonrelapse Schizophrenia Cohorts
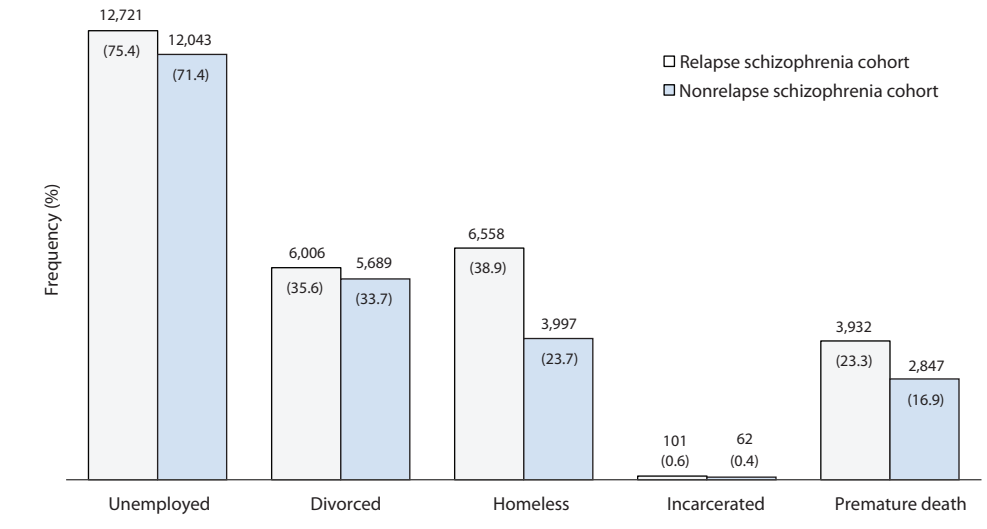
vs 46.7%, respectively, SMD = 0.65). The mean time from index to the first relapse during follow-up was also shorter in the relapse cohort (12.3 months vs 19.9 months for the nonrelapse cohort, SMD = 0.43) (Table 2).

Non–Health Care Societal Burden

A higher proportion of the relapse cohort experienced unemployment (75.4% vs 71.4%), divorce (35.6% vs 33.7%), homelessness (38.9% vs 23.7%), and incarceration (0.6% vs 0.4%) (all SMD > 0.1, Table 3, Figure 2). Similarly, a higher proportion of the relapse cohort died during the follow-up period compared to the nonrelapse cohort (26.8% vs 19.5%, SMD = 0.17) (Table 2). The proportion of veterans considered to have died prematurely was also higher for the relapse cohort (23.3%) compared to the nonrelapse cohort (16.9%; SMD = 0.16).

DISCUSSION

Our study included 16,862 veterans in each cohort (veterans with schizophrenia with and without a prior schizophrenia-related relapse). Nearly all veterans were male (92.0%), more than half of veterans were White (57.0%), and the median age was 58–59 years. In the relapse cohort, 67.4% and 42.0% of veterans had a history of substance use disorder and non-schizophrenia mental health disorder, respectively, compared to 43.5% and 23.8% in the matched nonrelapse cohort (both SMD > 0.1). The relapse cohort had a higher frequency of unemployment (75.4% vs 71.4%), divorce (35.6% vs 33.7%), homelessness (38.9% vs 23.7%), incarceration (0.6% vs 0.4%), and premature death (23.3% vs 16.9%) compared to the nonrelapse cohort (all SMD > 0.1).

The results of this study fill an important knowledge gap on the frequency of non–health care, societal outcomes among US veterans with schizophrenia with a history of relapse who receive care within the VHA. An early phase of this study shed light on the increased societal burden of

schizophrenia[28]; therefore, in the present study, we chose to evaluate the additional burden of relapse, which is common among patients with schizophrenia.[5]

Our findings suggest that veterans who had a prior schizophrenia-related relapse have a higher frequency of unemployment, divorce, homelessness, and incarceration. These findings are consistent with those reported in a prior cross-sectional survey of psychiatrists and their patients with schizophrenia in the United States,[21] which reported an increased likelihood of negative societal outcomes among patients with relapse(s) in the past 12 months compared to those with no relapse. For example, patients with relapse had a 67% lower likelihood of being employed compared to those without relapse (risk ratio = 0.3, P = .001), and patients with 3 prior relapses or more were 24 times more likely to lose their homes compared to those without relapse (odds ratio = 23.6, P < .001).[21] Furthermore, our study found that 77% of the relapse cohort experienced a subsequent relapse during follow-up compared to 47% of veterans without prior relapse. It is important to note that our study did not investigate treatment utilization or compliance. Our findings are consistent with the literature reporting a high frequency of relapse among those who had relapse at least once.[20]

Veterans with prior relapse in our study also had more comorbidities, including mental health conditions, compared to their nonrelapse counterparts. Although balanced on overall CCI score from PS matching, veterans with relapse had a higher frequency of not only mental health comorbidities including trauma and stressor-related disorders and anxiety disorders, but also hypertension, hyperlipidemia, obesity, and chronic obstructive pulmonary disease. Moreover, a higher frequency of liver disease and hepatitis was observed among patients with a history of relapse. Additionally, a large proportion of veterans (67% of the relapse cohort and 44% of the nonrelapse cohort) included in our study had experienced substance use disorder. Similar findings were observed in a large prospective observational study of the

US Schizophrenia Care and Assessment Program[20] in which patients who had not experienced relapse prior to or during the study period were less likely to have comorbid substance use disorder. This high rate of substance use disorder has been frequently reported among the US veteran population, and a comparison of schizophrenia patients to nonschizophrenia controls showed nearly 20% higher frequency of substance use disorder in those with schizophrenia.[28]

Suicidal ideation in the relapse cohort was high (1 in 5 veterans)—10 times more than that in the nonrelapse cohort (2%). Although rare in the study population and likely underdocumented in the database, suspected suicide attempts were 5 times more common in the relapse cohort (more than 2% of the relapse cohort). These findings are consistent with several global studies[4,17,20,29–31] that have identified a strong correlation between relapse and suicide ideation and/or attempt. Another UK-based study revealed that patients with relapse had 4 times the odds of suicide attempt compared to those without relapse.[4] Similarly, a US cross-sectional study[21] conducted in 2019 suggested an increasing trend in the mean number of suicide attempts with increasing number of relapses. To that end, some studies[20,23] have also considered self-harm, suicide attempts, and suicide ideation as indicators of relapse, substantiating their correlation.

Strengths of this study include use of the most recent VHA data, which provided large sample size and long-term follow-up; this enabled the comprehensive evaluation of non–health care societal burden of schizophrenia relapse in recent years. Further, this study provides valuable insights on societal outcomes in a patient population with more severe schizophrenia who have a higher risk of medical comorbidities and mental health disorders,[32,33] a population often understudied in the literature. Several limitations of this study should be noted. First, the VHA population differs considerably from the general US population; for example, the population in this study was 92% male. While the characteristics of the veterans in our study are consistent with other studies on schizophrenia leveraging the VHA data,[34,35] the generalizability of our findings to a broader population is limited. Second, our study did not investigate treatment utilization or compliance. This information in particular would help interpret our finding on the high frequency of relapse during the follow-up period for both cohorts. Third, because a cross-sectional approach was used in examining societal outcomes across the full study period, no temporality was applied between the exposure (relapse) and the outcomes of interest. Therefore, it is important to note that the nonrelapse cohort may have had a relapse during follow-up, which occurred prior to their most recent societal burden measure captured in this study. Finally, although consistent with prior real-world studies,[6] our study defined an episode of relapse as an inpatient stay or ED visit with a diagnosis code for schizophrenia in any position, as opposed to a confirmed relapse based on clinical measures and noted in patient medical records.

CONCLUSION

Among a US veteran population, schizophrenia-related relapse was associated with significantly increased frequency of unemployment, divorce, homelessness, and incarceration, as well as increased risk of premature death and subsequent relapse. Preventing relapse, managing comorbid mental health and substance use conditions, and providing services to help with employment and housing for this vulnerable population may improve societal and clinical outcomes for patients.

REFERENCES

1. GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390(10100):1211–1259.

2. Charlson FJ, Ferrari AJ, Santomauro DF, et al. Global epidemiology and burden of schizophrenia: findings from the Global Burden of Disease Study 2016. *Schizophr Bull*. 2018;44(6):1195–1203.

3. Trivedi RB, Post EP, Sun H, et al. Prevalence, comorbidity, and prognosis of mental health among US veterans. *Am J Public Health*. 2015;105(12):2564–2569.

4. Almond S, Knapp M, Francois C, et al. Relapse in schizophrenia: costs, clinical outcomes and quality of life. *Br J Psychiatry*. 2004;184(4):346–351.

5. Emsley R, Chiliza B, Asmal L, et al. The nature of relapse in schizophrenia. *BMC Psychiatry*. 2013;13(1):50.

6. Olivares JM, Sermon J, Hemels M, et al. Definitions and drivers of relapse in patients with schizophrenia: a systematic literature review. *Ann Gen Psychiatry*. 2013;12(1):32.

7. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. *Schizophr Bull*. 1995;21(3):419–429.

8. Chen EY, Hui CL, Lam MM, et al. Maintenance treatment with quetiapine versus discontinuation after one year of treatment in patients with remitted first episode psychosis: randomized controlled trial. *BMJ*. 2010;341:c4024.

9. Emsley R, Oosthuizen PP, Koen L, et al. Symptom recurrence following intermittent treatment in first-episode schizophrenia successfully treated for 2 years: a 3-year open-label clinical study. *J Clin Psychiatry*. 2012;73(4):e541–e547.

10. Gaebel W, Riesbeck M, Wölwer W, et al; German Study Group on First-Episode Schizophrenia. Relapse prevention in first-episode schizophrenia–maintenance vs intermittent drug treatment with prodrome-based early intervention: results of a randomized controlled trial within the German Research Network on Schizophrenia. *J Clin Psychiatry*. 2011;72(2):205–218.

11. Gitlin M, Nuechterlein K, Subotnik KL, et al. Clinical outcome following neuroleptic discontinuation in patients with remitted recent-onset schizophrenia. *Am J Psychiatry*. 2001;158(11):1835–1842.

12. Kane JM, Rifkin A, Quitkin F, et al. Fluphenazine

vs placebo in patients with remitted, acute first-episode schizophrenia. *Arch Gen Psychiatry*. 1982;39(1):70–73.

13. Lafeuille MH, Gravel J, Lefebvre P, et al. Patterns of relapse and associated cost burden in schizophrenia patients receiving atypical antipsychotics. *J Med Econ*. 2013;16(11):1290–1299.

14. Alphs L, Nasrallah HA, Bossie CA, et al. Factors associated with relapse in schizophrenia despite adherence to long-acting injectable antipsychotic therapy. *Int Clin Psychopharmacol*. 2016;31(4):202–209.

15. Doering S, Müller E, Köpcke W, et al. Predictors of relapse and rehospitalization in schizophrenia and schizoaffective disorder. *Schizophr Bull*. 1998;24(1):87–98.

16. San L, Bernardo M, Gómez A, et al. Factors associated with relapse in patients with schizophrenia. *Int J Psychiatry Clin Pract*. 2013;17(1):2–9.

17. Chabungbam G, Avasthi A, Sharan P. Sociodemographic and clinical factors associated with relapse in schizophrenia. *Psychiatry Clin Neurosci*. 2007;61(6):587–593.

18. Zipursky RB, Reilly TJ, Murray RM. The myth of schizophrenia as a progressive brain disease. *Schizophr Bull*. 2013;39(6):1363–1372.

19. Zipursky RB, Agid O, Remington G. Improving outcomes in schizophrenia by preventing early relapses. *Lancet Psychiatry*. 2018;5(5):384–386.

20. Ascher-Svanum H, Zhu B, Faries DE, et al. The cost of relapse and the predictors of relapse in the treatment of schizophrenia. *BMC Psychiatry*. 2010;10(1):2.

21. Lin D, Joshi K, Keenan A, et al. Associations between relapses and psychosocial outcomes in patients with schizophrenia in real-world settings in the United States. *Front Psychiatry*. 2021;12:695672.

22. Pennington M, McCrone P. The cost of relapse in schizophrenia. *Pharmacoeconomics*. 2017;35(9):921–936.

23. Lader M. What is relapse in schizophrenia? *Int Clin Psychopharmacol*. 1995;9(suppl 5):5–10.

24. Veterans Health Administration. US Department of Veteran Affairs website. Updated August 15, 2022. Accessed August 19, 2022. https://www.va.gov/health/aboutVHA. asp#:~:text=The%20Veterans%20Health%20 Administration%20(VHA,Veterans%20 enrolled%20in%20the%20VA

25. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383.

26. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003;41(11):1284–1292.

27. *Centers for Disease Control and Prevention, National Health Report Highlights*. 2014. Accessed August 19, 2022. https://www.cdc. gov/healthreport/previous/2014/publications/ Compendium.pdf

28. Lin DKH, Aboumrad M, Wada K, et al. Non-healthcare societal burden of schizophrenia among veterans. Poster no. 177. Presented at Psych Congress; September 10–13, 2020; Nashville, Tennessee.

29. Geddes J, Mercer G, Frith CD, et al. Prediction of outcome following a first episode of schizophrenia: follow-up study of Northwick Park first episode study subjects. *Br J Psychiatry*. 1994;165(5):664–668.

30. Johnson DA. The significance of depression in the prediction of relapse in chronic schizophrenia. *Br J Psychiatry*. 1988;152(3):320–323.

31. Shepherd M, Watt D, Falloon I, et al. The natural history of schizophrenia: a five-year follow-up study of outcome and prediction in a representative sample of schizophrenics. *Psychol Med Monogr suppl*. 1989;15:1–46.

32. Nichter B, Norman S, Haller M, et al. Psychological burden of PTSD, depression, and their comorbidity in the US veteran population: suicidality, functioning, and service utilization. *J Affect Disord*. 2019;256:633–640.

33. Rafferty LA, Cawkill PE, Stevelink SAM, et al. Dementia, post-traumatic stress disorder and major depressive disorder: a review of the mental health risk factors for dementia in the military veteran population. *Psychol Med*. 2018;48(9):1400–1409.

34. Davis CL, Kilbourne AM, Blow FC, et al. Reduced mortality among Department of Veterans Affairs patients with schizophrenia or bipolar disorder lost to follow-up and engaged in active outreach to return for care. *Am J Public Health*. 2012;102(suppl 1):S74–S79.

35. Thorp SR, Sones HM, Glorioso D, et al. Older patients with schizophrenia: does military veteran status matter? *Am J Geriatr Psychiatry*. 2012;20(3):248–256.