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ORIGINAL RESEARCH

Multiple Admissions for Alcohol Withdrawal

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Objective The objective was to identify risk factors for multiple admissions for alcohol withdrawal syndrome (AWS) in patients admitted to a general medicine service.

Methods: A retrospective study was performed examining records of patients admitted for AWS between January 1, 2006 and December 31, 2008 to an academic tertiary referral hospital. Patients with a single admission were compared to patients with multiple admissions with respect to demographic and clinical variables.

Results: Three hundred and twenty-two patients accounted for 788 admissions. Of the 322 patients, 142 (44%) had multiple admissions. Compared to patients with a single admission, patients with multiple admissions were more likely to have a high school education or less ($p=0.0071$), a higher Charlson comorbidity index score ($p=0.0010$), a positive urine drug screen for non-alcohol drug ($p=0.0002$), psychiatric comorbidity ($p=0.0303$) and a higher CIWA-Ar maximum total score ($p<0.0001$).

Conclusion: In patients with AWS, we identified demographic and clinical variables associated with multiple admissions to a general medicine service. Our results indicate areas for a targeted multidisciplinary and multispecialty approach at initial intervention, which is especially important given the high rates of recidivism in this patient population. *Journal of Hospital Medicine* 2012;7:617–621. © 2012 Society of Hospital Medicine.

Many patients are admitted and readmitted to acute care hospitals with alcohol-related diagnoses, including alcohol withdrawal syndrome (AWS), and experience significant morbidity and mortality. In patients with septic shock or at risk for acute respiratory distress syndrome (ARDS), chronic alcohol abuse is associated with increased ARDS and severity of multiple organ dysfunction.[1] Among intensive care unit (ICU) patients, those with alcohol dependence have higher morbidity, including septic shock, and higher hospital mortality.[2] Patients who experience AWS as a result of alcohol dependence may experience life-threatening complications, such as seizures and delirium tremens.[3,4] In-hospital mortality from AWS is historically high,[5] but with benzodiazepines used in a symptom-driven manner to treat the complications of alcohol use, hospital mortality rates are more recently reported at 2.4%.[6]

As inpatient outcomes[1,2,7] and hospital mortality[8–10] are negatively affected by alcohol abuse, the post-hospital course of these patients is also of interest. Specifically, patients are often admitted and readmitted with alcohol-related diagnoses or AWS to acute care hospitals, but relatively little quantitative data exist on readmission factors in this population.[11] Patients readmitted to detoxification units or alcohol and substance abuse units have been studied, and factors associated with readmission include psychiatric disorder,[12–17] female gender,[14,15] and delay in rehabilitation aftercare.[18]

These results cannot be generalized to patients with AWS who are admitted and readmitted to acute-care hospitals. First, patients hospitalized for alcohol withdrawal symptoms are often medically ill with more severe symptoms, and more frequent coexisting medical and psychiatric illnesses, that complicate the withdrawal syndrome. Detoxification units and substance abuse units require patients to be ''medically stable'' before admission, because they do not have the ability to provide a high level of supervision and treatment. Second, much of what we know regarding risk factors for readmission to detoxification centers and substance abuse units comes from studies of administrative data of the Veterans Health Administration,[12,13] Medicare Provider Analysis and Review file,[16] privately owned outpatient substance abuse centers,[14] and publicly funded detoxification centers.[18] These results may be difficult to generalize to other patient populations. Accordingly, the objective of this study was to identify demographic and clinical factors associated with multiple admissions to a general medicine service for treatment of AWS over a 3-year period. Characterization of these high-risk patients and their hospital course may help focus intervention and reduce these revolving door admissions.

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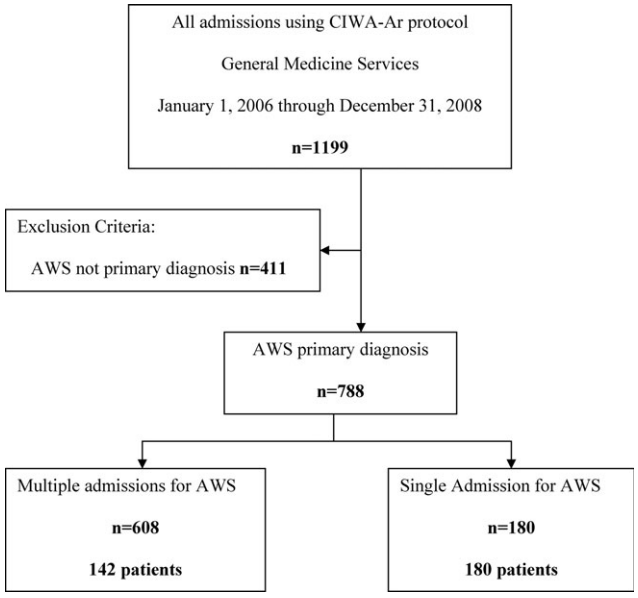

FIG. 1. Study design. Abbreviations: AWS, alcohol withdrawal syndrome; CIWA-Ar, Clinical Institute Withdrawal Assessment—Alcohol Revised.

METHODS

The Mayo Clinic Institutional Review Board deemed the study exempt.

Patient Selection

The study was conducted at an 1157-bed academic tertiary referral hospital, located in the Midwest, that has approximately 15,000 inpatient admissions to general medicine services annually and serves as the main referral center for the region. Patients included in this study were adults admitted to general medicine services and treated with symptom-triggered Clinical Institute Withdrawal Assessment—Alcohol Revised (CIWA-Ar) protocol[19] between January 1, 2006 and December 31, 2008. Patients were identified using the Mayo Clinic Quality Improvement Resource Center database, as done in a previous CIWA-Ar study.[20] Patients were excluded if the primary diagnosis was a non–alcohol-related diagnosis (Figure 1).

Patients were placed in 1 of 2 groups based on number of admissions during the study period, either a single-admission group or a multiple-admissions group. While most readmission studies use a 30-day mark from discharge, we used 3 years to better capture relapse and recidivism in this patient population. The 2 groups were then compared retrospectively. To insure that a single admission was not arbitrarily created by the December 2008 cutoff, we reviewed the single-admission group for additional admissions through June of 2009. If a patient did have a subsequent admission, then the patient was moved to the multiple-admissions group.

Clinical Variables

Demographic and clinical data was obtained using the Mayo Data Retrieval System (DRS), the Mayo Clinic Life Sciences System (MCLSS) database, and electronic medical records. Clinical data for the multiple-admissions group was derived from the first admission of the study period, and subsequently referred to as "index" admission. Specific demographic information collected included age, race, gender, marital status, employment status, and education. Clinical data collected included admitting diagnosis, comorbid medical disorders, psychiatric disorders, and CIWA-Ar evaluations including highest total score (CIWA-Ar score [max] and component scores). The CIWA-Ar protocol is a scale to assess the severity of alcohol withdrawal, based on 10 symptoms of alcohol withdrawal ranging from 0 (not present) to 7 (extremely severe). The protocol requires the scale to be administered hourly, and total scores guide the medication dosing and administration of benzodiazepines to control withdrawal symptoms. Laboratory data collected included serum ammonia, alanine aminotransferase (ALT), and admission urine drug screen. For the purposes of this study, a urine drug screen was considered positive if a substance other than alcohol was present. Length of stay (LOS) and adverse events during hospitalization (delirium tremens, intubations, rapid response team [RRT] calls, ICU transfers, and in-hospital mortality) were also collected.

Medical comorbidity was measured using the Charlson Comorbidity Index (CCI).[21] The CCI was scored electronically using diagnoses in the institution's medical index database dating back 5 years from patient's first, or index, admission. Originally validated as a prognostic tool for mortality 1 year after admission in medical patients, the CCI was chosen as it accounts for most medical comorbidities.[21] Data was validated, by another investigator not involved in the initial abstracting process, by randomly verifying 5% of the abstracted data.

Statistical Analysis

Standard descriptive statistics were used for patient characteristics and demographics. Comparing the multiple-admissions group and single-admission group, categorical variables were evaluated using the Fisher exact test or Pearson chi-square test. Continuous variables were evaluated using 2-sample t test. Multivariate logistic model analyses with stepwise elimination method were used to identify risk factors that were associated with multiple admissions. Age, gender, and variables that were statistically significant in the univariate analysis were used in stepwise regression to get to the final model. A P value of ≤ 0.05 was considered statistically significant. All statistical analyses were performed using SAS version 9.3 software (SAS Institute, Cary, NC).

RESULTS

The CIWA-Ar protocol was ordered on 1199 admissions during the study period. Of these, 411 (34.3%)

TABLE 1. Univariate Analysis of Demographic Variables and Multiple Admissions

Variable	Single Admission N = 180	Multiple Admissions N = 142	*P* Value
Age, years (SD)	47.85 (12.84)	45.94 (12)	0.170
Male, No. (%)	122 (68)	109 (77)	0.080
Race/Ethnicity, No. (%)			0.270
White	168 (93)	132 (93)	
African American	6 (3)	3 (2)	
Asian	0 (0)	1 (1)	
Middle Eastern	3 (2)	0 (0)	
Other	3 (2)	6 (4)	
Relationship status, No. (%)			0.160
Divorced	49 (27)	55 (39)	0.028*
Married	54 (30)	34 (24)	0.230
Separated	9 (5)	4 (3)	0.323
Single	59 (33)	38 (27)	0.243
Widowed	5 (3)	3 (2)	0.703
Committed	4 (2)	7 (5)	0.188
Unknown	0 (0)	1 (1)	0.259
Education, No. (%)			0.002*
High school graduate, GED, or less	49 (28)	67 (47)	
Some college or above	89 (49)	60 (42)	
Unknown	41 (23)	15 (11)	
Employment, No. (%)			0.290
Retired	26 (14)	12 (8)	
Employed	72 (40)	51 (36)	
Unemployed	51 (28)	51 (36)	
Homemaker	9 (5)	4 (3)	
Work disabled	20 (11)	23 (16)	
Student	1 (1)	0 (0)	
Unknown	1 (1)	1 (1)	

Abbreviations: GED, General Educational Development; SD, standard deviation. *$P \leq 0.05$ and significant.

admissions were excluded because AWS was not the primary diagnosis, leaving 788 (65.7%) admissions for 322 patients, which formed the study population. Of the 322 patients, 180 (56%) had a single admission and 142 (44%) had multiple admissions.

Univariate analyses of demographic and clinical variables are shown in Tables 1 and 2, respectively. Patients with multiple admissions were more likely divorced ($P = 0.028$), have a high school education or less ($P = 0.002$), have a higher CCI score ($P < 0.0001$), a higher CIWA-Ar score (max) ($P < 0.0001$), a higher ALT level ($P = 0.050$), more psychiatric comorbidity ($P < 0.026$), and a positive urine drug screen ($P < 0.001$). Adverse events were not significantly different between the 2 groups (Table 2).

Multivariate logistic model analysis was performed using the variables age, male gender, divorced marital status, high school education or less, CIWA-Ar score (max), CCI score, psychiatric comorbidity, and positive urine drug screen. With a stepwise elimination process, the final model showed that multiple admissions were associated with high school education or less ($P = 0.0071$), higher CCI score ($P = 0.0010$), higher CIWA-Ar score (max) ($P < 0.0001$), a positive urine drug screen ($P = 0.0002$), and psychiatric comorbidity ($P = 0.0303$) (Table 3).

TABLE 2. Univariate Analysis of Clinical Variables and Multiple Admissions

Variable	Single Admission N = 180	Multiple Admissions N = 142	*P* Value
LOS, mean (SD)	3.71 (7.10)	2.72 (3.40)	0.130
Charlson Comorbidity Index, mean (SD)	1.7 (2.23)	2.51 (2.90)	0.005*
Medical comorbidity, No. (%)			
Diabetes mellitus	6 (3)	16 (11)	0.005*
Cardiovascular disease	6 (3)	15 (11)	0.050*
Cerebrovascular disease	0 (0)	3 (2)	0.009*
Hypertension	53 (30)	36 (25)	0.400
Cancer	17 (7)	10 (9)	0.440
Psychiatric comorbidity, No. (%)	97 (54)	94 (66)	0.026*
Adjustment disorder	0 (0)	6 (4)	0.005*
Depressive disorder	85 (47)	76 (54)	0.260
Bipolar disorder	6 (3)	10 (7)	0.130
Psychotic disorder	4 (2)	6 (4)	0.030*
Anxiety disorder	30 (17)	25 (18)	0.820
Drug abuse	4 (2)	4 (3)	0.730
Eating disorder	0 (0)	3 (2)	0.050*
CIWA-Ar scores			
CIWA-Ar score (max), mean (SD)	15 (8)	20 (9)	<0.000*
Component, mean (SD)			
Agitation†	20 (11)	36 (25)	0.001*
Anxiety†	23 (13)	38 (27)	0.001*
Auditory disturbance†	4 (2)	9 (6)	0.110
Headache†	11 (6)	26 (18)	0.001*
Nausea/vomiting†	5 (3)	17 (12)	0.003*
Orientation‡	52 (29)	72 (51)	0.001*
Paroxysm/sweats†	9 (5)	17 (12)	0.023*
Tactile disturbance‡	25 (14)	54 (38)	0.001*
Tremor†	35 (19)	47 (33)	0.004*
Visual disturbance‡	54 (30)	77 (54)	0.001*
ALT (U/L), mean (SD)	76 (85)	101 (71)	0.050*
Ammonia (mcg N/dl), mean (SD)	25 (14)	29 (29)	0.530
Positive urine drug screen, No. (%)	25 (14)	49 (35)	<0.001*
Tetrahydrocannabinol	14 (56)	19 (39)	
Cocaine	8 (32)	8 (16)	
Benzodiazepine	6 (24)	11 (22)	
Opiate	4 (16)	13 (26)	
Amphetamine	2 (8)	2 (4)	
Barbiturate	1 (4)	0 (0)	
Adverse event, No. (%)			
RRT	1 (1)	1 (1)	0.866
ICU transfer	32 (18)	20 (14)	0.550
Intubation	12 (7)	4 (3)	0.890
Delirium tremens	7 (4)	4 (3)	0.600
In-hospital mortality	0 (0)	0 (0)	

Abbreviations: ALT, alanine aminotransferase; CIWA-Ar, Clinical Institute Withdrawal Assessment–Alcohol Revised; ICU, intensive care unit; LOS, length of stay (days); RRT, rapid response team; SD, standard deviation. *$P \leq 0.05$ and significant. †Score >5. ‡Score >3.

TABLE 3. Multivariate Analysis of Variables Associated With Multiple Admissions

Variable	Adjusted Odds Ratio (95% CI)	*P* Value
High school education or less	2.074 (1.219, 3.529)	0.0071*
CIWA-Ar score (max)	1.074 (1.042, 1.107)	<0.0001*
Charlson Comorbidity Index	1.232 (1.088, 1.396)	0.0010*
Psychiatric comorbidity	1.757 (1.055, 2.928)	0.0303*
Positive urine drug screen	3.180 (1.740, 5.812)	0.0002*

Abbreviations: CI, confidence interval; CIWA-Ar, Clinical Institute Withdrawal Assessment–Alcohol Revised. *$P \leq 0.05$ and significant.

DISCUSSION

We provide important information regarding identification of individuals at high risk for multiple admissions to general medicine services for treatment of AWS. This study found that patients with multiple admissions for AWS had more medical comorbidity. They had more cases of diabetes mellitus, cardiovascular disease, and cerebrovascular disease, and their CCI scores were higher. They also had higher CIWA-Ar (max) scores, as well as higher CIWA-Ar component scores, indicating a more severe withdrawal.

Further, psychiatric comorbidity was also associated with multiple admissions. Consistent with the high prevalence in alcoholic patients, psychiatric comorbidity was common in both patients with a single admission and multiple admissions. We also found that a positive urine drug screen was associated with multiple admissions. Interestingly, few patients in each group had a diagnosis recorded in the medical record of an additional substance abuse disorder, yet 14% of patients with a single admission and 29% of patients with multiple admissions had a positive urine drug screen for a non-alcohol substance. Psychiatric comorbidity, including additional substance abuse, is a well-established risk factor for readmission to detoxification centers.[12–15,17,22,23] Also, people with either an alcohol or non-alcohol drug addiction, are known to be 7 times more likely to have another addiction than the rest of the population.[24] This study suggests clinicians may underrecognize additional substance abuse disorders which are common in this patient population.

In contrast to studies of patients readmitted to detoxification units and substance abuse units,[14,15,18,22] we found level of education, specifically a high school education or less, to be associated with multiple admissions. In a study of alcoholics, Greenfield and colleagues found that lower education in alcoholics predicts shorter time to relapse.[25] A lack of education may result in inadequate healthcare literacy. Poor health behavior choices that follow may lead to relapse and subsequent admissions for AWS. With respect to other demographic variables, patients in our study population were predominantly men, which is not surprising. Gender differences in alcoholism are well established, with alcohol abuse and dependence more prevalent in men.[26] We did not find gender associated with multiple admissions.

Our findings have management and treatment implications. First, providers who care for patients with AWS should not simply focus on treating withdrawal signs and symptoms, but also screen for and address other medical issues, which may not be apparent or seem stable at first glance. While a comorbid medical condition may not be the primary reason for hospital admission, comorbid medical conditions are known to be a source of psychological distress[27] and have a negative effect on abstinence. Second, all patients should be screened for additional substance abuse. Initial laboratory testing should include a urine drug screen. Third, before discharging the patient, providers should establish primary care follow-up for continued surveillance of medical issues. There is evidence that primary care services are predictive of better substance abuse treatment outcomes for those with medical problems.[28,29]

Finally, inpatient psychiatric consultation, upon admission, is essential for several reasons. First, the psychiatric team can help with initial management and treatment of the alcohol withdrawal regardless of stage and severity, obtain a more comprehensive psychiatric history, and assess for the presence of psychiatric comorbidities that may contribute to, aggravate, or complicate the clinical picture. The team can also address other substance abuse issues when detected by drug screen or clinical history. The psychiatric team, along with chemical-dependency counselors and social workers, can provide valuable input regarding chemical-dependency resources available on discharge and help instruct the patient in healthy behaviors. Because healthcare illiteracy may be an issue in this patient population, these instructions should be tailored to the patient's educational level. Prior to discharge, the psychiatry team, social workers, or chemical-dependency counselors can also assist with, or arrange, rehabilitation aftercare for patients. Recent work shows that patients were less likely to be readmitted to crisis detoxification if they entered rehabilitation care within 3 days of discharge.[18]

Our study has significant limitations. This study was performed with data at a single academic medical center with an ethnically homogeneous patient population, limiting the external validity of its results. Because this is a retrospective study, data analyses are limited by the quality and accuracy of data in the electronic medical record. Also, our follow-up period may not have been long enough to detect additional admissions, and we did not screen for patient admissions prior to the study period. By limiting data collection to admissions for AWS to general medical services, we may have missed cases of AWS when admitted for other reasons or to subspecialty services, and we may have missed severe cases requiring admission to an intensive care unit. While we believe we were able to capture most admissions, we may underreport this number since we cannot account for those events that may have occurred at other facilities and locations. Lastly, without a control group, this study is limited in its ability to show an association between any variable and readmission.

In our study, 142 patients accounted for 608 admissions during the 3-year study period, which speaks to the high recidivism rates for patients with AWS. This disease is associated with high morbidity, high medical costs, and high utilization of healthcare. Our study provides insight regarding identification of patients at high risk of multiple admissions with respect to

demographic (lower level of education) and clinical characteristics (worse withdrawal severity, more medical and psychiatric comorbidity, and polysubstance abuse). We believe collaboration between social services, chemical-dependency counselors, psychiatry, and medicine is necessary to effectively treat this population of patients and assist with the crucial transition to the outpatient setting. Future studies should include key social factors, such as health literacy in the readmission risk assessment, as well as primary care follow-up and rehabilitation aftercare.

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References

1. Moss M, Burnham EL. Chronic alcohol abuse, acute respiratory distress syndrome, and multiple organ dysfunction. *Crit Care Med*. 2003;31(4 suppl):S207–S212.
2. O'Brien JM Jr, Lu B, Ali NA, et al. Alcohol dependence is independently associated with sepsis, septic shock, and hospital mortality among adult intensive care unit patients. *Crit Care Med*. 2007;35(2): 345–350.
3. Foy A, March S, Drinkwater V. Use of an objective clinical scale in the assessment and management of alcohol withdrawal in a large general hospital. *Alcohol Clin Exp Res*. 1988;12(3):360–364.
4. Sarff M, Gold JA. Alcohol withdrawal syndromes in the intensive care unit. *Crit Care Med*. 2010;38(9 suppl):S494–S501.
5. Moore M, Gray M. Alcoholism at the Boston City Hospital—V. The causes of death among alcoholic patients at the Haymarket Square Relief Station, 1923–1938. *N Engl J Med*. 1939;221(July 13):58–59.
6. Puerta Louro R, Otero Anton E, Lorenzo Zuniga V. Epidemiology of alcohol withdrawal syndrome: mortality and factors of poor prognosis [in Spanish]. *An Med Interna (Madrid)*. 2006;23(7):307–309.
7. Saitz R, Ghali WA, Moskowitz MA. The impact of alcohol-related diagnoses on pneumonia outcomes. *Arch Intern Med*. 1997;157(13): 1446–1452.
8. Monte R, Rabunal R, Casariego E, Lopez-Agreda H, Mateos A, Pertega S. Analysis of the factors determining survival of alcoholic withdrawal syndrome patients in a general hospital. *Alcohol Alcohol*. 2010;45(2):151–158.
9. Khan A, Levy P, DeHorn S, Miller W, Compton S. Predictors of mortality in patients with delirium tremens. *Acad Emerg Med*. 2008; 15(8):788–790.
10. Campos J, Roca L, Gude F, Gonzalez-Quintela A. Long-term mortality of patients admitted to the hospital with alcohol withdrawal syndrome. *Alcohol Clin Exp Res*. 2011;35(6):1180–1186.
11. Raven MC, Carrier ER, Lee J, Billings JC, Marr M, Gourevitch MN. Substance use treatment barriers for patients with frequent hospital admissions. *J Subst Abuse Treat*. 2010;38(1):22–30.
12. Moos RH, Brennan PL, Mertens JR. Diagnostic subgroups and predictors of one-year re-admission among late-middle-aged and older substance abuse patients. *J Stud Alcohol*. 1994;55(2):173–183.
13. Moos RH, Mertens JR, Brennan PL. Rates and predictors of four-year readmission among late-middle-aged and older substance abuse patients. *J Stud Alcohol*. 1994;55(5):561–570.
14. Mertens JR, Weisner CM, Ray GT. Readmission among chemical dependency patients in private, outpatient treatment: patterns, correlates and role in long-term outcome. *J Stud Alcohol*. 2005;66(6): 842–847.
15. Luchansky B, He L, Krupski A, Stark KD. Predicting readmission to substance abuse treatment using state information systems. The impact of client and treatment characteristics. *J Subst Abuse*. 2000; 12(3):255–270.
16. Brennan PL, Kagay CR, Geppert JJ, Moos RH. Elderly Medicare inpatients with substance use disorders: characteristics and predictors of hospital readmissions over a four-year interval. *J Stud Alcohol*. 2000;61(6):891–895.
17. Tomasson K, Vaglum P. The role of psychiatric comorbidity in the prediction of readmission for detoxification. *Compr Psychiatry*. 1998;39(3):129–136.
18. Carrier E, McNeely J, Lobach I, Tay S, Gourevitch MN, Raven MC. Factors associated with frequent utilization of crisis substance use detoxification services. *J Addict Dis*. 2011;30(2):116–122.
19. Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *Br J Addict*. 1989; 84(11):1353–1357.
20. Hecksel KA, Bostwick JM, Jaeger TM, Cha SS. Inappropriate use of symptom-triggered therapy for alcohol withdrawal in the general hospital. *Mayo Clin Proc*. 2008;83(3):274–279.
21. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383.
22. Ponzer S, Johansson S-E, Bergman B. A four-year follow-up study of male alcoholics: factors affecting the risk of readmission. *Alcohol*. 2002;27(2):83–88.
23. Walker RD, Howard MO, Anderson B, et al. Diagnosis and hospital readmission rates of female veterans with substance-related disorders. *Psychiatr Serv*. 1995;46(9):932–937.
24. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990;264(19): 2511–2518.
25. Greenfield SF, Sugarman DE, Muenz LR, Patterson MD, He DY, Weiss RD. The relationship between educational attainment and relapse among alcohol-dependent men and women: a prospective study. *Alcohol Clin Exp Res*. 2003;27(8):1278–1285.
26. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2007; 64(7):830–842.
27. Shih M, Simon PA. Health-related quality of life among adults with serious psychological distress and chronic medical conditions. *Qual Life Res*. 2008;17(4):521–528.
28. Saitz R, Horton NJ, Larson MJ, Winter M, Samet JH. Primary medical care and reductions in addiction severity: a prospective cohort study. *Addiction*. 2005;100(1):70–78.
29. Mertens JR, Flisher AJ, Satre DD, Weisner CM. The role of medical conditions and primary care services in 5-year substance use outcomes among chemical dependency treatment patients. *Drug Alcohol Depend*. 2008;98(1–2):45–53.