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Gender Disparities in Alcohol Use Disorder Treatment among Privately Insured Patients with Alcohol-associated Cirrhosis

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Abstract

Background: The burden of alcohol-associated cirrhosis (AC) is high, and though alcohol cessation improves mortality, many patients fail to engage in alcohol use (AUD) treatment and continue drinking. Our aim was to determine rates, predictors, and outcomes of AUD treatment utilization in AC patients with private insurance. **Methods**: We collected data from persons with AC (diagnosed by ICD-9/ICD-10 codes), ages 18-64, enrolled in the Truven MarketScan Commerical Claims and Encounters database (2009-2016). We determined rates and predictors of substance abuse treatment visits as well as rates of alcohol relapse prevention medication prescriptions, weighted to the national employer-sponsored insured population. Effects of AUD treatment utilization on decompensation rates were calculated using proportional hazards regression with propensity score adjustment. **Results:** 66,053 AC patients were identified, 32% female, mean age at diagnosis was 54.5 years. 72% had insurance coverage for substance abuse treatment. Overall, AUD treatment utilization rates were low, with only 10% receiving a face-to-face mental health or substance abuse visit and only 0.8% receiving an

FDA-approved relapse prevention medication within 1 year of index diagnosis. Women were less likely to receive a face-to-face visit (HR 0.84, p<0.001) or a FDA-approved relapse prevention medication (0.89, p=0.05) than men. AC patients who had a clinic visit for AUD treatment or used FDA-approved relapse medication showed decreased risk of decompensation at 1 year (HR 0.85, p<0.001 for either). **Conclusions:** AUD treatment utilization is associated with lower decompensation rates among privately insured patients with AC. Women were less likely to utilize AUD treatment visits. Efforts to reduce gender-specific barriers to treatment are urgently needed to improve outcomes.

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Introduction

Alcohol-associated liver disease (ALD) is a spectrum of liver damage caused by heavy alcohol use over time, ranging from bland hepatic steatosis, to more severe forms of liver damage, such as acute alcoholic hepatitis (AAH) and alcohol-associated cirrhosis (AC) (O'Shea *et al.*, 2010; Schwartz and Reinus, 2012). The health care and economic burden of ALD is high, both in the United States (US) and worldwide, where AC is estimated to be reponsible for nearly half the liver-related deaths (Rehm, Samokhvalov and Shield, 2013; Mellinger, Shedden, *et al.*, 2018). In the US, AC comprises over half the total costs of cirrhosis amongst the privately insured and is a major reason for liver transplantation (O'Shea *et al.*, 2010; Goldberg *et al.*, 2017; Mellinger, Shedden, *et al.*, 2018). Ongoing alcohol use is the strongest predictor of mortality in ALD patients, particularly those with alcoholic hepatitis (AH) (Louvet *et al.*, 2016). Between 2002 and 2013, the prevalence of past 12-month alcohol use disorder (AUD) in the US increased 49.4% (Grant *et al.*, 2017). Alcohol use is also increasing worldwide, and in the US, alcohol-related mortality is increasing (World Health Organization, 2014; Dwyer-Lindgren *et al.*, 2018). Given that AC develops only after years of heavy alcohol use, these increases may result in rising AC morbidity and mortality(Guirguis *et al.*, 2015). Alcohol cessation is the primary intervention which arrests and, in some cases, reverses ALD (Thiele *et al.*, 2018). Yet utilization and effectiveness of AUD treatment in this population are poorly described.

Behavioral and medication-related therapies for AUD are well-studied in the general population, with moderate effect sizes demonstrated in multiple trials, though little evidence to suggest one treatment modality is superior to another across all population categories(Jonas *et al.*, 2014; Klimas *et al.*, 2014; Donoghue *et al.*, 2015). For example, in the general population, the number-needed-to-treat (NNT) to prevent a return to any drinking for acamprosate was 12 and for oral naltrexone was 20 (Jonas *et al.*, 2014). Despite documented benefits, access to AUD treatment in the general population is low, with recent large-scale epidemiologic surveys showing a treatment utilization rate of 7.7% for past year AUD, and 19.8% for lifetime AUD (Hasin and Grant, 2015). Individuals with AUD that do seek treatment tend to be older (≥ 30 years-old), are more likely to be men, report more severe and longer histories of substance use problems, and have co-occurring mood disorders(S. Khan *et al.*, 2013). There are various reasons individuals with AUD forgo treatment(Greenfield *et al.*, 2007; S. Khan *et al.*, 2013). Structural barriers such as lack of insurance coverage are experienced by both men and women (Verissimo and Grella, 2017). Women, however, report more attitudinal barriers, more perceived stigma and financial problems, as well as conflicting family and child care responsibilities (Green, Rockhill and Furrer, 2009; S. Khan *et al.*, 2013; Verissimo and Grella, 2017).

Utilization of AUD treatment in patients with ALD has been less well evaluated. A recent systematic review of psychosocial, abstinence-focused treatments for AUDs among patients with chronic liver disease found only five randomized controlled trials in the literature, three of which included AC patients exclusively (Kuchipudi *et al.*, 1990; Willenbring and Olson, 1999; Weinrieb *et al.*, 2011; A. Khan *et al.*, 2016). Only one randomized controlled trial of combined motivational enhancement therapy and cognitive-behavioral therapy embedded in the medical clinic showed significantly higher rates of abstinence in the treatment group compared to controls (Willenbring and Olson, 1999). In terms of medication-based treatments, research in AC patients is even more scarce, with only a single randomized trial of baclofen, an off-label relapse prevention medication, demonstrating a two-fold increase in abstinence among 42 AC patients receiving baclofen for 12 weeks versus placebo (Addolorato *et al.*, 2007).

Given the clearly established benefits of alcohol cessation in AC patients and the dearth of research on treatment utilization, the aims of our study were to: 1) assess the rates and predictors of AUD treatment utilization among adults with AC in a large, nationally-representative dataset of privately insured Americans; and 2) determine if utilization of AUD treatment is associated with improved clinical outcomes.

Materials and Methods

Population

The cohort of AC patients was drawn from the Truven Analytics Marketscan Commercial Claims and Encounters (CCAE) database from 2009-2016. In the US, private insurance accounts for approximately 50% of the total insurance market, with the overwhelming majority of privately insured individuals receiving coverage via their employer. Marketscan compiles claims from >100 million employed persons and their dependents across all regions of the US, representing well over 50% of the employer sponsored insurance market. Marketscan data includes claims for enrollees across inpatient, outpatient, facility, and pharmaceutical claims and has been used in multiple large-scale medical and surgical studies of healthcare delivery and costs (Mellinger, Shedden, *et al.*, 2018).

Inclusion Criteria and Alcoholic Cirrhosis Case Ascertainment

The initial dataset included all patients from 2009-2016, ages 18-64, who had at least a single ICD-9 or ICD-10 code for cirrhosis and at least 1 year of continuous enrollment, including the

index cirrhosis diagnosis date (see Appendix A). Age was capped at 64 given that most patients age 65 and older transition onto Medicare and are thus lost from the dataset. All data were restricted to the continuous enrollment period containing the cirrhosis diagnosis. AC was defined using previously published criteria as a single ICD-9 or ICD-10 code for alcohol-associated cirrhosis *or* a code for cirrhosis without mention of alcohol *plus* a code for alcohol use or an alcohol-related comorbidity (see Appendix A)(Beste *et al.*, 2015; Mellinger, Shedden, *et al.*, 2018). Patients with both AC and hepatitis C (HCV) codes were counted as having AC. Cirrhosis-related complications, such as ascites and hepatic encephalopathy, were defined by ICD-9 or ICD-10 codes (see Appendix A). Decompensated AC was defined as an AC diagnosis code *and* a diagnosis code for a portal hypertensive complication (ascites, hepatic encephalopathy, or variceal bleeding). Single diagnosis codes for cirrhosis and for portal hypertensive complications have been validated in administrative data and found to have positive predictive values of 80% or greater (Kramer *et al.*, 2008; Nehra *et al.*, 2013). Medical comorbidities were estimated using the Elixhauser comorbidity scale with the liver disease and alcohol abuse categories excluded as these were accounted for separately in our models (Elixhauser *et al.*, 1998). An indicator variable for whether or not the enrollee had insurance coverage for mental health and substance abuse (MHSA) care was included. Census regions were used as geographic variables for predictors of AUD treatment access with census region 3 (South) as the reference region.

Mental Health and Substance Abuse (MHSA) Treatment Ascertainment

We defined comorbid depression or anxiety by ICD-9 or ICD-10 codes. Because substance use is frequently assessed and treated alongside other mental health issues and is often comorbid with alcohol use and misuse, alcohol use treatment was defined as *either* a substance use or mental health outpatient visit *or* a prescription for a US Food and Drug Administration (FDA) approved alcohol relapse prevention medication. We performed additional analyses of non-FDA approved alcohol relapse prevention medications. A mental health/substance abuse (MHSA) treatment visit was defined as a Current Procedural Terminology (CPT) code for a face-to-face outpatient visit combined with a claims-based service category code indicating a substance abuse related claim was submitted on the same day or a CPT code for a face-to-face outpatient visit with a provider code indicating that the visit was conducted by a psychiatrist or psychologist. FDA-approved (disulfiram, naltrexone, and acamprosate) and non-FDA approved medications (baclofen, gabapentin, and topiramate) for alcohol relapse prevention were identified in the pharmaceutical claims dataset. Enrollees were required to have a 90-day or

greater continuous prescription in order to eliminate short courses of treatment which would be expected to have less influence on alcohol use. Analyses of medication prescriptions were restricted to enrollees with prescription drug coverage.

Statistical Methods

We calculated baseline proportions of covariates present at index diagnosis. AC, HCV, and diabetes were treated as time invariant, meaning that if a diagnosis appeared at any time in the enrollment period, enrollees were counted as having these diagnoses. We calculated pre- and post-index cirrhosis diagnosis rates of MHSA treatment utilization. Rates for medication use (antidepressants, alcohol relapse prevention medications) were calculated in the population of patients with prescription drug coverage, while rates of MHSA clinic visits were calculated in the total population with or without prescription drug coverage. We modelled the cumulative event rates for major events of interest (prescriptions for FDA or non-FDA approved relapse prevention medication and MHSA outpatient visits) at 1 month, 1 year, and 2 years post-index diagnosis and weighted these to reflect the national population with private, employer-sponsored insurance as previously reported (Mellinger, Shedden, *et al.*, 2018). To identify predictors of treatment utilization, we used proportional hazards regression with propensity score adjustment based on multiple covariates and 100 strata to model the hazard from the index AC diagnosis to the first occurrence of a given form of alcohol use treatment (visit or medication). Models were fit using standard methods for proportional hazard estimation in the setting of time-varying covariates. Patients who received liver transplant were censored at time of transplant. For additional analyses of non-FDA approved relapse prevention medications, diabetes was considered an independent predictor given the high occurrence of gabapentin use for diabetic neuropathy.

Clinical Outcomes

Our primary clinical outcome was hepatic decompensation defined as ascites, hepatic encephalopathy, or variceal bleeding. We assessed the association between MHSA treatment and decompensation using proportional hazards regression with time-varying covariates as in the above methods for predictors of treatment access. Patients with decompensation diagnoses at index diagnosis were excluded from the model. Propensity score adjustment based on multiple covariates and 100 strata were used as in the access model above. The effects of MHSA treatment on decompensation were assessed in three separate models: 1)

FDA approved medications alone, 2) MHSA treatment visits alone, and 3) FDA approved medications and MHSA treatment visits as a composite variable.

Results

Patient Characteristics

66,053 patients with AC were identified, approximately one-third were female (see *Table 1*). Mean age at diagnosis was 53.5 years. Of these, 72% had MHSA coverage under their insurance plans and 87% had prescription drug coverage. Roughly one quarter (28%) also had HCV and 53% were decompensated. Depression and anxiety were present in 16% and 12%, respectively at index cirrhosis diagnosis. Baseline FDA-approved alcohol relapse prevention medication prescriptions were rare (0.4%) while non-FDA approved relapse medications were more common (3.2%). Gabapentin made up the greatest proportion of non-FDA approved relapse prevention medication prescriptions at index cirrhosis diagnosis (2.6%) (see *Figure 1*).

Rates of AUD Treatment and Alcohol Relapse Prevention Utilization After Index AC Diagnosis in the National Employer-Sponsored Insurance Population

FDA-approved alcohol relapse prevention medication use and MHSA visits increased over time, from 0.2% for medications and 3.0% for MHSA visits at 1 month after AC diagnosis to 0.8% and 10.1%, respectively, at 1 year; and to 1.2% and 14.5%, respectively, at 2 years (see *Figure 2*). MHSA visits alone accounted for most of the AUD treatment utilization. Rates of FDA-approved alcohol relapse prevention medications alone were low, increasing from 0.2% at 1 month to 1.2% at 2 years, with similar rates of acamprosate and naltrexone usage and a lower rate of usage of disulfiram. Use of non-FDA-approved medications that have been suggested to prevent alcohol relapse was more common, and dominated by gabapentin use (8.3% at 2 years post-diagnosis).

Predictors of AUD Treatment Utilization in the MarketScan Population

Women were less likely to utilize face-to-face MHSA clinic visits (HR 0.84, $p<0.001$) and FDA-approved alcohol relapse prevention medications (HR 0.89, $p=0.05$) (see *Figure 3*). In analyses of separate outcomes (MHSA visits or FDA-approved relapse prevention medications), patients with MHSA insurance coverage were more likely to utilize MHSA clinic visits (HR 1.32, $p<0.001$) and FDA-approved alcohol relapse prevention medications (HR 1.88, $p<0.001$) than those who did not. Older patients and those with decompensation were less likely to have attended a face-

to-face MHSA clinic visit (HR 0.97 and HR 0.89, p<0.001 for both) while patients with depression and anxiety diagnoses were much more likely to have such visits (HR 2.17 and HR 1.47, p<0.001 for both). See *Table 2* for findings from the composite outcome of either MHSA visit or FDA approved relapse prevention medicine.

Within the cohort of AC patients with prescription drug coverage, women were less likely to receive FDA-approved alcohol relapse prevention medication prescriptions (HR 0.89, p=0.05) than men and those with MHSA insurance coverage were more likely to receive these prescriptions (HR 1.88, p<0.001) than those without MHSA insurance coverage. Having a depression diagnosis was the strongest predictor of FDA-approved alcohol relapse prevention medication utilization (HR 3.62, p<0.001) as was having an anxiety diagnoses though the effect was attenuated compared to depression (HR 1.32, p<0.001). In additional analyses examining utilization of non-FDA approved relapse prevention medications, women were more likely to receive these prescriptions as well even after discounting gabapentin use (any non-FDA medication: HR 1.33, p<0.001; topiramate and baclofen only (no gabapentin): HR 1.84, p<0.001).

Clinical Outcome: Hepatic Decompensation in the MarketScan Population

Approximately one-fifth (19%) of patients had new diagnosis codes for hepatic decompensation within 1 year after index diagnosis of AC. In multivariate models, utilization of an MHSA clinic visit alone had a protective effect on risk of decompensation (HR 0.89, p<0.001). Although the number was small, use of FDA-approved alcohol relapse prevention medication alone had a greater effect on decreasing the risk of decompensation (HR 0.65, p<0.001). In a composite model analyzing effects of having either an MHSA visit or an FDA-approved relapse medication, reduction in risk of decompensation was similar to that of MHSA visit alone likely due to infrequent use of FDA-approved relapse medication (HR 0.85, p<0.001) (see *Table 3)*. Older age was associated with a minimally lower risk of decompensation (HR 0.998, p<0.001). There was a gender and Elixhauser interaction resulting in slightly lower risk of decompensation (HR 0.96, p<0.001). Diagnoses of depression and use of antidepressant medications were both associated with lower rates of hepatic decompensation (HR 0.77 and HR 0.99, p<0.001 for both). In both models of MHSA visits and FDA medications, primary care visits were associated with decreased risk for decompensation (HR 0.82 and 0.83, p<0.001 for both).

Discussion

In this large study of privately insured patients with AC, overall utilization of AUD treatment was low, despite a high rate of MHSA insurance coverage. Gender influenced utilization, with women being less likely to obtain both a face-to-face MHSA clinic visit and FDA-approved relapse prevention medications. Those who utilized alcohol use treatment, whether men or women, were significantly less likely to decompensate at one year after index diagnosis compared to those who did not utilize such treatment, even when adjusting for comorbidities, such as hepatitis C and diabetes. In a best-case scenario, men and women who access AUD treatment early, whether relapse prevention medications or MHSA clinic visits may avoid progression to AC and decompensation with its subsequent high mortality and possible need for transplant. Those who fail to access AUD treatment and continue drinking, may go on to further decompensate, bringing with it higher mortality, more inpatient hospital admissions, higher costs, and potential need for transplant. For those that don't access formal AUD treatment, transplant may be denied given the requirement for alcohol cessation and formal AUD treatment at most US liver transplant centers.

Similar to reported low rates of MHSA utilization in the general population, only 10% of privately insured AC patients utilized a MHSA clinic visit within 1 year after their index diagnosis. While lack of insurance coverage is frequently cited as a major reason for lack of utilization of AUD treatment, our study population had private insurance with a high rate of MHSA coverage, and MHSA coverage was weakly correlated with utilization. This fits with existing data showing that barriers to AUD treatment are related more to patient attitudes than to structural insurance issues (S. Khan *et al.*, 2013; Verissimo and Grella, 2017). The gender imbalance in alcohol treatment utilization in the privately insured AC population is consistent with research in the broader AUD population indicating women are less likely to receive inpatient, outpatient, emergency room, or other face-to-face treatment for AUD relative to men and are less likely to attend specialty addiction treatment services (S. Khan *et al.*, 2013). In a mixed-methods study of AC patients, men and women identified attitudinal barriers as major causes for lack of AUD treatment uptake (Mellinger, Scott Winder, *et al.*, 2018).

Barriers to AUD treatment differ between men and women with women experiencing more barriers relative to men, including higher perceived stigma and other 'attitudinal' barriers as well as higher economic and time barriers (Green, Rockhill and Furrer, 2009; S. Khan *et al.*, 2013; Verissimo and Grella, 2017). Diagnosis of AUDs in women is challenging as alcohol screening

tools have lower specificity among women and opportunites for diagnosis are frequently missed (Volk *et al.*, 1997; Bradley *et al.*, 1998). For example, amongst AC patients in the UK, women were less likely to have alcohol use recorded and were overall less likely to interact with the healthcare system in the period prior to their AC diagnosis (Otete *et al.*, 2015). Despite evidence that women are less likely to seek face-to-face treatment, when women do access psychosocial treatment, they may have better treatment outcomes than men (Green, Rockhill and Furrer, 2009; Sugarman *et al.*, 2017). Low treatment utilization among women is particularly concerning given a higher proportion of American women now meet criteria for AUD than ever before, with rates rising more rapidly in women than in men (Grant *et al.*, 2017). In the liver disease population, women frequently develop AC and alcoholic hepatitis at lower amounts of alcohol consumed and shorter time-frames compared to men, suggesting that rates of ALD, as demonstrated in our earlier study, will rise more rapidly in women, increasing the urgency for connection to professional AUD treatment (Nielsen *et al.*, 2017; Mellinger, Shedden, *et al.*, 2018; Szabo, 2018).

We found that only a very small fraction (0.8%) of AC patients received an FDA-approved relapse prevention medication despite having insurance coverage for healthcare and prescriptions. It is possible that this under-utilization of is related to concerns about liver toxicity for naltrexone and disulfiram. Acamprosate, which is not metabolized by the liver, has no reported instances of clinically significant hepatotoxicity and may be safe, but it has not been explicitly tested in those with advanced liver disease. Only baclofen, a non-FDA approved relapse prevention medication, has been tested in a small randomized trial in patients with AC, showing a benefit at 12 weeks of treatment with baclofen 10 mg three times daily with an acceptable side effect profile (Addolorato *et al.*, 2007). In our study, baclofen use, like other relapse prevention medications, was low.

We found that a 90 day prescription for an FDA-approved alcohol relapse prevention medication was associated with an even greater reduction in decompensation compared to an MHSA clinic visit. While our findings do not demonstrate causation, given alcohol's deleterious effects on cirrhosis and portal hypertensive complications, one possible mechanism for their positive influence may be via improved rates of alcohol abstinence, similar to the mechanism for MHSA visit effect (Lucey *et al.*, 2008). Our additional analyses indicated that non-FDA approved relapse prevention medications also had a large effect on decompensation rates. Gabapentin, a neuromodulator typically prescribed for seizures or peripheral neuropathy, has an increasing

literature base supporting its effects on relapse prevention, primarily through modulation of alcohol craving, and was the most common relapse prevention medication prescribed, though it is likely much more frequently prescribed for other indications such as neuropathy (Mason *et al.*, 2014). Similarly, topiramate has some evidence, though with smaller studies, for reducing alcohol use (Johnson *et al.*, 2003; 2007). While the indication for use of gabapentin, topiramate and baclofen in our patient population cannot be determined, the associated beneficial effect on decompensation rates is worthy of further study.

Diagnoses of depression and anti-depressant medication use were associated with increased utilization of MHSA care (both visits and FDA-approved relapse medications) and lower rates of decompensation. This effect may be related to the fact that patients diagnosed with depression or anxiety and prescribed anti-depressant medications to treat these conditions are connected to the medical system and likely utilize care overall to a greater degree. Comorbid mental illness is common in AUD patients and associated with increased, though inconsistent, utilization of primary medical care (Ford *et al.*, 2005). The complex psychosocial milieu and medical comorbidities AC patients confront combined with complex medication prescribing in advanced liver disease, warrant the establishment of integrated clinics with co-located substance use professionals working alongside hepatologists to appropriately care for these complex patients.

There were several limitations to our study. First, this database only assesses those with private insurance and a claim for healthcare services and may thus lack generalizability to non-privately insured populations. Second, alternate supports for sobriety in the community, such as mutual aid societies like Alcoholics Anonymous, would not be reflected in our data and are difficult to measure. Third, behavioral interventions for alcohol treatment, such as psychoeducation or other brief interventions, are frequently delivered by non-addiction specialists and may have occurred outside MHSA visits. We attempted to mitigate this limitation by broadening our ascertainment to include both visits conducted by a psychiatrist or psychologist as well as visits where a service category code related to substance abuse treatment was entered, regardless of the specialty of the medical provider entering the code. Fourth, we are unable to determine the content of the substance abuse intervention and cannot ascertain the effectiveness of different modalities of alcohol use treatment. Fifth, AUD treatment efficacy may be influenced by endogenous factors influencing a patient's motivation to take up alcohol treatment such that patients who engage in treatment are more likely to stop drinking for

reasons other than the treatment effectiveness. Sixth, the requirement for 1 year of continuous enrollment may have biased the population towards a healthier population by excluding those who died within 1 year of diagnosis or lost insurance due to disability.

In conclusion, patients with AC utilize AUD treatment at low rates within 1 year after AC diagnosis, with women less likely to receive AUD treatment compared to men. Alcohol cessation is the only intervention known to improve mortality in patients with ALD , and receipt of AUD treatment in our study was significantly associated with improved outcomes. As such, efforts to improve utilization rates of MHSA care, including treatment of comorbid mental health conditions, are necessary. Integrated care combining professional mental health and hepatology care as well as the development of novel behavioral treatments for this population are urgently needed.

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Figure Legends

Figure 1. Proportion of alcohol relapse prevention medication prescriptions at index diagnosis, by type of prescription.

Figure 2. Rates of MHSA treatment utilization at 1 month, 1 and 2 years post index diagnosis.

Figure 3. Gender differences in MHSA treatment utilization.

Table 1. Population characteristics at index alcoholic cirrhosis diagnosis.

Characteristics	**Total AC patients n=66053 N (%)**
Female	21442 (32%)
Mean age (years)	53.5
Mental Health/ Substance Abuse Treatment Coverage	47505 (72%)
Prescription Drug Coverage	57,632 (87%)
Mean Elixhauser	3.53
Hepatitis C	18817 (28%)
Decompensation*	35069 (53%)
Anxiety	7642 (12%)
Depression	10652 (16%)
Any FDA Approved Alcohol Relapse Prevention Medication	275 (0.4%)
Acamprosate	122 (0.2%)
Disulfiram	133 (0.2%)
Naltrexone	99 (0.1%)

*Decompensation defined as presence of ascites, variceal bleeding, or hepatic encephalopathy

Table 2. Predictors of access to MHSA visits or FDA alcohol relapse prevention medications

Variable	**Hazard Ratio (95% Confidence Interval)**	**P Value**
MHSA Insurance Coverage	1.34 (1.28-1.40)	<0.001
Female	0.85 (0.82-0.88)	<0.001
Decompensated Cirrhosis	0.89 (0.86-0.92)	<0.001
Diabetes	0.79 (0.76-0.82)	<0.001
Age at diagnosis	0.97 (0.97-0.98)	<0.001
Hepatitis C	1.00 (0.97-1.04)	0.70
Anxiety	1.47 (1.41-1.53)	<0.001
Depression	2.21 (2.13-2.30)	<0.001
Elixhauser	1.41 (1.37-1.44)	<0.001
PCP Visit	1.60 (1.54-1.67)	<0.001
GI Clinic Visit	1.07 (1.03-1.11)	<0.001
South*	1.00	*
Northeast	1.33 (1.27-1.39)	<0.001
Midwest	1.20 (1.15-1.26)	<0.001
West	1.53 (1.46-1.60)	<0.001

*indicates reference category census region

Table 3. Substance abuse treatment utilization effects on occurrence of hepatic decompensation within 1 year following index cirrhosis diagnosis.

Variable	**HR (95% Confidence Interval)**	**P value**
Composite MHSA Visit and/or FDA medication	0.85 (0.82-0-.87)	<0.001
Female: Elixhauser[#]	0.96 (0.94-0.97)	<0.001
Diabetes	0.98 (0.96-0.99)	<0.001
Age at diagnosis	0.998 (0.998-0.999)	0.02
HCV	1.22 (1.20-1.24)	<0.001
Hepatorenal Syndrome	2.63 (2.51-2.76)	<0.001
Acute Kidney Injury	1.37 (1.34-1.40)	<0.001
Infection	1.16 (1.14-1.18)	<0.001
Depression	0.77(0.76-0.79)	<0.001
Anti-depressant medication prescription	0.99 (0.97-1.01)	<0.001
PCP Visit	0.83 (0.82-0.84)	<0.001
GI Visit	1.36 (1.35-1.38)	<0.001
South*	1.00	*
Northeast	0.95 (0.93-0.97)	<0.001
Midwest	1.03 (1.01-1.05)	0.002
West	1.06 (1.04-1.08)	<0.001

[#]Interaction between gender and Elixhauser score

*Indicates reference category for geographic comparisons

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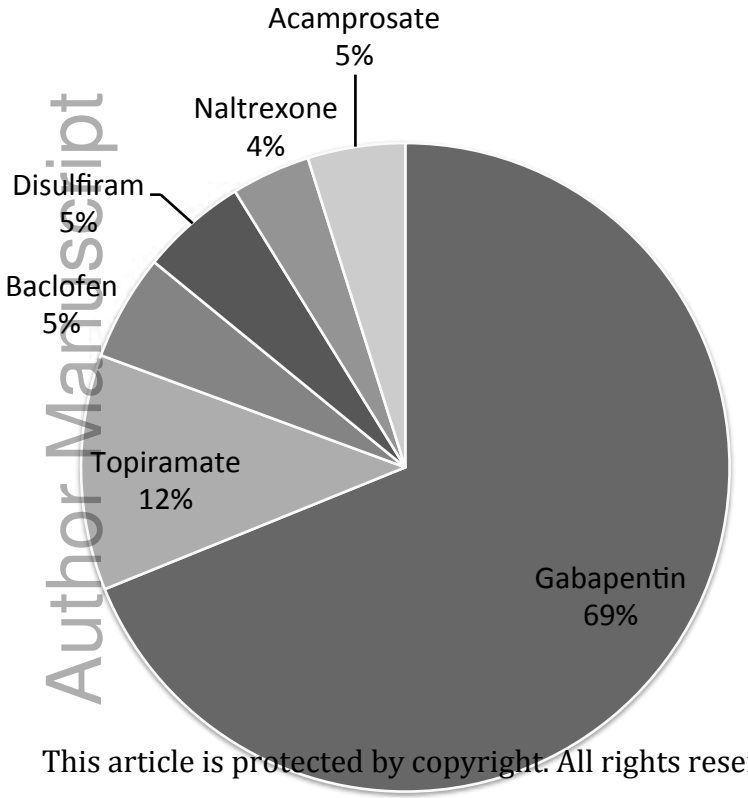

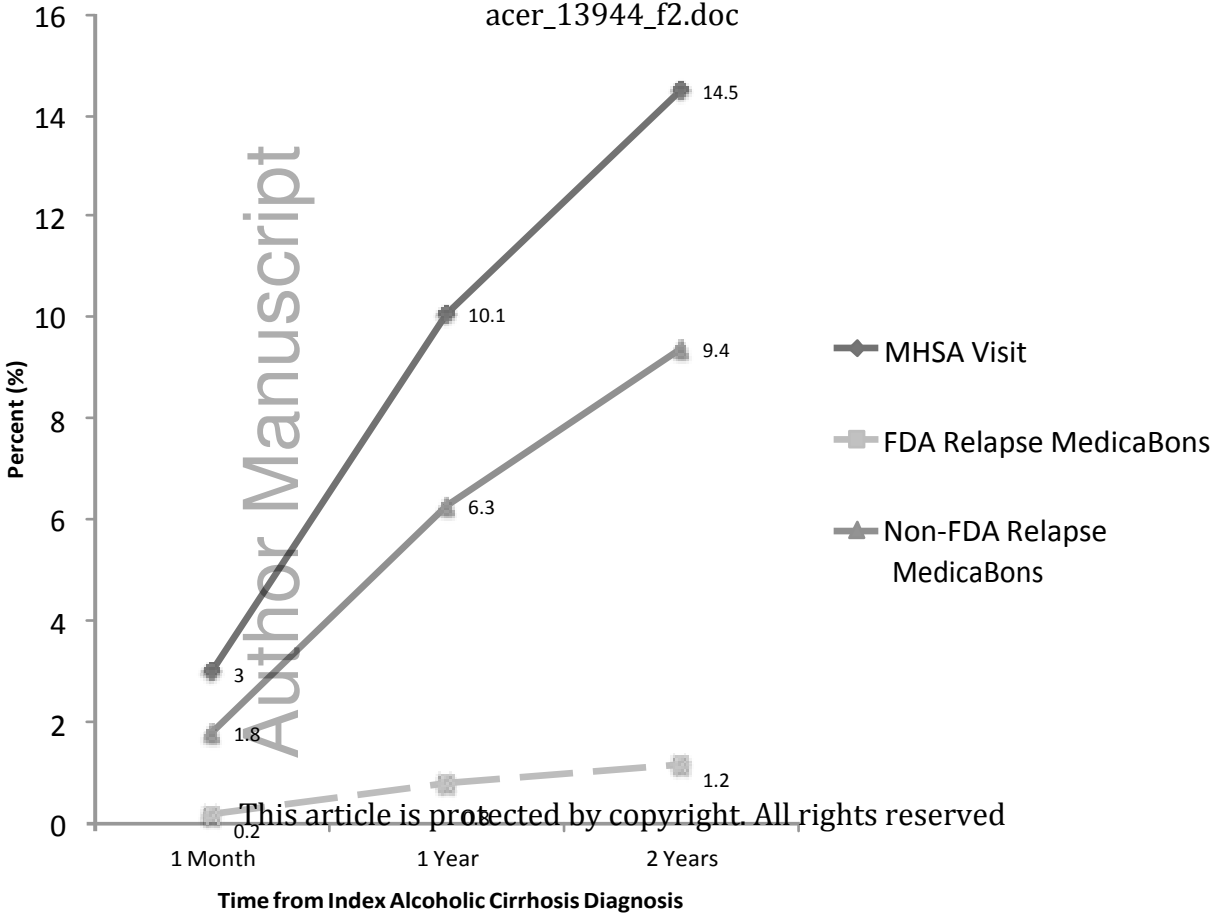

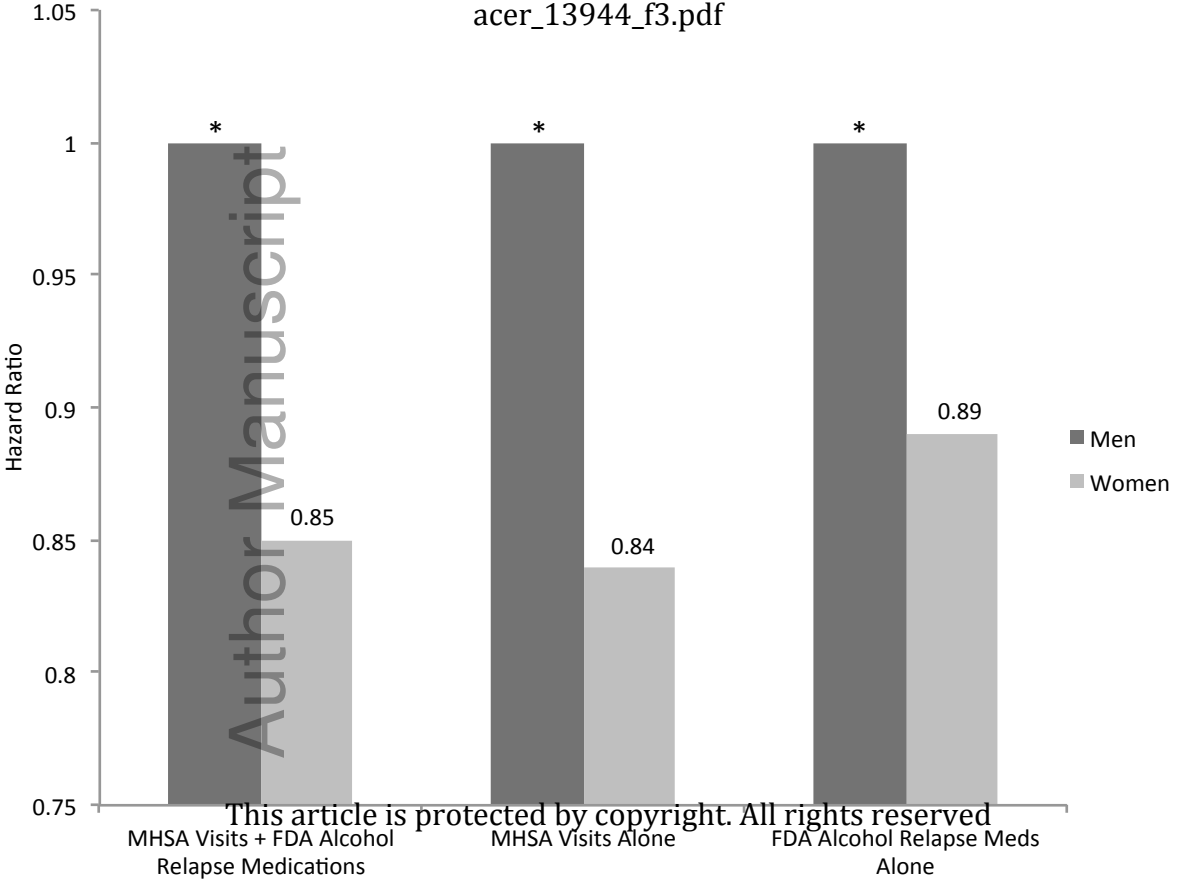

*indicates reference category (HR = 1.0). P values <0.001 for MHSA Visit + FDA Meds and MHSA visits alone; p=0.05 for FDA Relapse Meds Alone