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History of marijuana use does not affect outcomes on the liver transplant waitlist

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Abstract

Background—Data are limited on marijuana use and its impact on liver transplant (LT) waitlist outcomes. We aimed to assess the risk of waitlist mortality/delisting and likelihood of LT among prior marijuana users, and to determine the prevalence and factors associated with marijuana use.

Methods—Retrospective cohort of adults evaluated for LT over 2 years at a large LT center. Marijuana use defined by self-report in psychosocial assessment and/or positive urine toxicology. Ongoing marijuana use was not permitted for LT listing during study period.

Results—884 adults were evaluated and 585 (66%) were listed for LT (median follow up 1.4 years, IQR 0.5–2.0). Prevalence of marijuana use was 48%, with 7% being recent users and 41% prior users. Marijuana use had statistically significant association with alcoholic cirrhosis (IRR=1.9) and hepatitis C (IRR=2.1) vs. hepatitis B, tobacco use (prior IRR=1.4; recent IRR=1.3 vs. never), alcohol use (never IRR 0.1; heavy use/abuse IRR 1.2 vs. social), and illicit drug use (prior IRR=2.3; recent =1.9 vs. never). In adjusted competing risk regression, marijuana use was not associated with the probability of LT (prior HR 0.9; recent HR=0.9 vs. never) or waitlist mortality/delisting (prior HR 1.0; recent HR 1.0 vs. never). However, recent illicit drug use was associated with higher risk of death or delisting (HR 1.8, p=0.004 vs. never).

Conclusions—Unlike illicit drug use, marijuana use was not associated with worse outcomes on the LT waitlist. Prospective studies are needed to assess ongoing marijuana use on the LT waitlist and post-LT outcomes.

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Conflict of Interest

The authors declare no conflicts of interest

Introduction

Medical marijuana has moderate-to-high-quality evidence to treat conditions including chronic pain, neuropathic pain, spasticity due to multiple sclerosis, and chemotherapy associated nausea and vomiting¹⁻³. There has been growing interest in standardized trials to determine efficacy and side effects using standardized dosing⁴. Marijuana is also increasingly recognized as a promising therapeutic target in various digestive disorders including inflammatory bowel disease, irritable bowel syndrome, secretion and motility-related disorders⁵.

Data on marijuana use and progression of liver disease are limited and have yielded conflicting results. Cross-sectional studies⁶⁻⁸ have reported a correlation between daily marijuana use and increase in liver fibrosis and steatosis among hepatitis C (HCV) patients. However, several subsequent cohort studies⁹⁻¹¹ did not confirm the association between marijuana use and accelerated progression to fibrosis or cirrhosis in HCV or HIV/HCV co-infected patients.

Whether marijuana use should be a contraindication for liver transplant (LT) is unclear. In a recent survey of transplant physicians, 47% identified marijuana use as a “controversial characteristic”¹². In fact, there is little consensus within the LT community whether marijuana users should be eligible for transplant listing at all¹³⁻¹⁵. Despite this debate, there are few reports on overall survival (pre and posttransplant) among chronic liver disease patients who use marijuana. Consequently, marijuana use among LT candidates remains a controversial topic^{12,13}.

Yet, in July 2015, California adopted Assembly Bill 258, the Medical Cannabis Organ Transplant Act, which prohibits transplant institutions from denying transplantation to medical marijuana users based on their use of marijuana alone¹⁶. In fact, 6 other states have adopted similar measures protecting medical cannabis users: Arizona, Delaware, Illinois, Minnesota, New Hampshire and Washington¹⁵. In addition, 6 states passed legislation or ballot measures to legalize medical marijuana in 2016 alone, bringing the total number of states with legalization of marijuana to twenty-eight in addition to the District of Columbia. Given the increasing trend towards legalization and protection of medical marijuana, understanding the impact of marijuana use on LT outcomes is not only practical but also essential.

In the only prior study assessing LT-related outcomes among marijuana users, Ranney et al¹⁷ found no survival difference among LT candidates whether they consumed marijuana or not. However, in this study, more than a third of eligible patients (n = 803) on the LT waitlist were excluded due to missing tobacco, toxicology or psychiatric history. This large proportion of patients with missing toxicology data is likely to include many substance users who might be reluctant to undergo drug screening for fear of delisting or had poor follow up. Despite exclusion of these potentially high-risk patients, marijuana users were significantly less likely to receive LT (21.8% vs. 14.8%). Given the proportion of missing data, it is plausible that this study may not have adequately captured adverse outcomes like death or delisting among marijuana users on the LT waitlist.

In light of the limited data on LT waitlist outcomes, in the present study, we aimed to assess several outcomes among historical marijuana users who were evaluated for LT at our institution, including death or delisting on the LT waiting list and probability of receiving LT. In addition, we also sought to evaluate the prevalence of and factors associated with marijuana use among all patients undergoing LT evaluation at our center to guide future studies among this population.

Methods

Study Population & Design

All adults (age ≥ 18 years) presenting for a LT evaluation at University of California, San Francisco (UCSF) over a 2-year period, from January 1, 2012 through December 31, 2013, were included in this retrospective cohort study. The study was reviewed and approved by the UCSF institutional review board.

During the study period, the UCSF LT program had a policy of not listing patients with active marijuana use. Prior to listing, patients were required to abstain from marijuana use and, therefore, all marijuana use among listed patients is likely to be historical. Marijuana use was defined as ‘recent’ if subjects self-reported ongoing marijuana use at the time of first LT evaluation and/or had positive drug toxicology on screening laboratory evaluation. These patients were generally asked to abstain from marijuana use before being listed for LT. ‘Prior’ use refers to self-reported historical use of marijuana. Similarly, tobacco, alcohol and illicit substance (heroin, cocaine, amphetamines, hallucinogens, stimulants, nonprescription opiate/BDZ etc.) use was defined by combination of self-report and urine toxicology and further categorized as ‘prior’ and ‘recent’.

Outcomes

For the primary outcome, we assessed (1) the risk of waitlist death or delisting and (2) the risk of transplant among historical marijuana users and nonusers who were listed for LT. We also report factors associated with death and/or delisting on the waitlist and receiving LT. Secondary outcomes include prevalence of marijuana use and factors associated with marijuana use.

Sample size

In this retrospective cohort study, the primary end point is risk of waitlist death or delisting among historical marijuana users and nonusers who were listed for transplant at UCSF. A sample size of 570 is obtained by setting the alpha (two-tailed) at 0.05, beta at 0.2, assuming a baseline event rate (delisting/death/transplant) of 50% among nonmarijuana users (based on historic data), over a median follow up of 2 years, estimating censoring at 15%, and assuming a relative hazard of 1.35. Since about 300 patients are listed for LT at UCSF each year, a study period of 2 years would provide sufficient data to reach the desired sample size.

Data Collection & Analysis

Patient demographic and clinical data were collected by individual health record review and/or programmed capture from electronic medical record databases (data was abstracted in

December 2015). Substance use, including marijuana, information was obtained from review of detailed psychosocial assessment conducted by trained social workers at the time of first LT evaluation. Statistical analyses were performed using STATA versions 12 and 14 software (Stata Corporation, College Station, Texas).

Marijuana use was defined as combination of self-report on psychosocial assessment or positive urine toxicology during initial LT evaluation and work up. Urine drug screening was performed at the discretion of the LT team based on perceived risk of drug use on the LT waitlist. Our study includes the initial urine drug screen with further data captured at the end of the study period via final LT status (i.e. those with ongoing drug use were delisted and this was captured at the end of the study). Marijuana use was further categorized as ‘prior’ or ‘recent’ at the time of first LT evaluation, as described previously. Factors associated with marijuana use were analyzed using a multivariable log-link Poisson regression with robust standard errors to estimate adjusted incidence rate ratios (IRR). Using this method, the calculated IRR approximates the prevalence ratio¹⁸. All risk factors with p-values of less than 0.05 were retained in the multivariable model.

Among those listed for LT, we calculated the cumulative incidence of death or delisting within strata of marijuana use. Similarly, we also calculated the cumulative incidence of receiving LT within strata of marijuana use. Observation time was measured from date of first LT evaluation to the first of dropout, waitlist death, or transplant. Cumulative incidence estimates accounted for competing events and patients remaining on the waiting list were censored at the last known date on the list. Using Fine and Gray competing risk regression¹⁹ we estimated the hazard ratios (HR) and 95% CI for risk of the 2 outcomes of interest, (1) waitlist death or delisting and (2) receiving transplant on the waitlist. Factors with a univariate $p < 0.2$ and the primary explanatory variable, marijuana use, were included in the multivariable modeling process. The final multivariable models were selected by backward elimination with $p > 0.05$ for removal while retaining marijuana use.

Results

Demographics of study participants

884 adults (age 18 years) had an initial LT evaluation at UCSF over the 2-year study period and all patients were included in this analysis. The median age of the cohort was 58 years (IQR 51–63) with 37% women, 56% white, 25% Hispanic/Latino, and 64% with a college degree. The most common etiology of liver disease was HCV cirrhosis (49%), majority of patients had MELD < 20 (71%) and 33% had hepatocellular carcinoma (HCC). 66% of evaluated patients ($n = 585$) were listed for liver transplant and had median follow up of 1.4 (IQR 0.5–2.0) years during the study. Demographic and clinical characteristics of study subjects are listed in Table 1.

Marijuana and other substance use

The vast majority (89%) of the cohort ($N = 788/884$) underwent urine drug screening during initial LT evaluation while the remaining 96 subjects (11%) underwent psychosocial assessment alone or had missing toxicology data. Prevalence of marijuana use was 48% with

7% being recent users at the time of evaluation (Table 2). Among marijuana users, 13% had a self-reported history of weekly use while 16% had been daily users. History of tobacco use was comparable at 55% with 8% reporting recent use at the time of LT evaluation. History of alcohol use was higher at 89% among all candidates with 54% having a history of heavy use/abuse, while 5% had recent alcohol use. Notably, 46% had a history of illicit drug use with 14% being recent users. Further, 22% of candidates had recent opiate or benzodiazepine prescriptions. Figure 1 presents drug use within strata marijuana use – recent and prior marijuana users were prevalent across all categories and types of substance use, except never users of alcohol had limited use of marijuana (3%).

Factors associated with marijuana use

After multivariable adjustment, history of marijuana use was associated with age 18–29 vs. 30–44 years (IRR 2.6, 95% CI 1.6–4.0), white vs. other race (IRR 1.2, 95% CI 1.1–1.4), alcoholic cirrhosis (IRR 1.9, 95% CI 1.0–3.7) and HCV (IRR 2.1, 95% CI 1.1–4.0) vs. HBV, MELD <20 (IRR 1.2, 95% CI 1.1–1.5), tobacco use ('prior' IRR 1.4, 95% CI 1.2–1.7 and 'recent' IRR 1.3, 95% CI 1.1–1.6 compared to 'never'), alcohol use frequency ('never' IRR 0.1, 95% CI 0.04–0.3 and 'heavy use/abuse' IRR 1.2, 95% CI 1.0–1.3 compared to 'social') and illicit drug use ('prior' IRR 2.3, 95% CI 1.9–2.7 and 'recent' IRR 1.9, 95% CI 1.5–2.4 compared to 'never') (Table 3). Notably, male gender, BMI, HCC and prescription opiate/BDZ use were associated with marijuana use in univariate analysis but not after multivariable adjustment.

Listing and waitlist outcomes

Of all 884 LT candidates, 585 (66%) were listed for LT. Among them, 205 (35%) died or were delisted while 287 (49%) received LT. Among never users of marijuana, 69% (319/460) were listed for LT. While, 65% (234/359) and 51% (33/65) of prior and recent users of marijuana were listed for LT, respectively. Listing and waitlist outcomes for all participants are outlined in Figure 2.

Among those listed for LT, there was no statistically significant difference in the cumulative incidence of death or delisting on the LT waiting list within strata of marijuana use (Figure 3). Similarly, there was no statistically significant difference in the cumulative incidence of receiving LT within strata of marijuana use (Figure 4).

Reasons for delisting from the LT waitlist are presented in Table 4. The most common reasons for delisting included 'too sick for transplant' (45%) and 'death' (31%). There were isolated cases of 'substance abuse relapse' (n = 8) with no significant differences between recent, prior and never users of marijuana (Pearson exact chi-square – recent vs. never, p=0.42 & prior vs. never, p=1.00).

Competing risk regression

Using competing risk regression, no statistically significant difference in risk of death or delisting was identified among patients with recent (HR 1.0, 95% CI 0.5–1.8, p=0.9) or prior (HR 1.0, 95% CI 0.7–1.4, p=0.9) marijuana use compared to never use in univariate or multivariable adjusted analysis (Table 5). In univariate analysis, alcohol use severity and

illicit substance use had statistically significant associations with risk of death or delisting (Table 5). However, after multivariable adjustment, only recent use of illicit drugs (HR 1.8, 95% CI 1.2–2.8, $p=0.004$ vs. never) was statistically significantly associated with higher risk of death or delisting on the LT waiting list (Table 5).

Similarly, compared to never users, probability of receiving a LT was not statistically significantly decreased among patients with recent (HR 0.9, 95% CI 0.6–1.6, $p=0.8$) or prior (HR 0.9, 95% CI 0.7–1.2, $p=0.4$) marijuana use in univariate or multivariable adjusted analysis (Table 6). In univariate analysis, alcohol use severity and MELD ≥ 20 were statistically significantly associated with risk of receiving LT. However, after multivariable adjustment, only MELD ≥ 20 (HR 1.6, 95% CI 1.2–2.2, $p=0.001$) and HCC (HR 1.3, 95% CI 1.0–1.7, $p=0.02$) were statistically significantly associated with higher probability of receiving LT (Table 6).

Discussion

Our study presents a comprehensive assessment of marijuana use among LT candidates. We found no statistically significant association between the risk of waitlist removal or death and historical marijuana use. On the other hand, notably, a history of recent illicit drug use was associated with higher risk of death or delisting. This finding could be related to a number of possibilities including recidivism to drug abuse which would prompt delisting from LT waitlist, or perhaps higher rate of medical illness from complications of drug use resulting in death or delisting. Illicit drug use may also reflect worse social circumstances and lack of support leading to delisting. On the other hand, a similar association with marijuana use was not found. This observation supports major differences in the impact of a history of marijuana use vs. illicit drug use among LT candidates. Similarly, in unadjusted and adjusted competing risk regression, we were unable to detect a statistically significant association between receiving LT and history of marijuana use. Factors associated with higher chance of receiving LT included MELD score ≥ 20 and HCC – both of which are consistent with and reflect current LT allocation practices (i.e. MELD exception points for HCC).

Marijuana use was highly prevalent among LT candidates at our institution. Almost half of all evaluated patients (48%) had a history of marijuana use and a considerable proportion (7%) were recent users at the time of evaluation. Among users, 13% had a self-reported history of weekly use while 16% had been daily users. Substance use, beyond marijuana, was a common feature among LT candidates – we found high prevalence of historical tobacco use (55%), alcohol use (89%), illicit drug use (47%) and prescription opiate/BDZ use (31%). More than half of all alcohol users (54%) had a history of heavy use/abuse, and a significant proportion (14%) of candidates were recent users of illicit substances. We also found that almost a quarter (22%) of evaluated patients had recent opiate/BDZ prescriptions. Though detailed and systematic data about substance abuse among all LT candidates are limited²⁰, our findings are similar to prior reports²⁰, including those assessing patients with alcoholic liver disease^{21,22}.

We also identify several factors associated with marijuana use, including younger age (18–29 years) and white race. Marijuana use was closely associated with other substance use – persons with alcoholic and HCV cirrhosis were more likely to have been marijuana users compared to those with HBV cirrhosis. Tobacco use, both prior and recent, was also associated with higher prevalence of marijuana use. Similarly, prior and recent illicit drug users had higher prevalence of marijuana use. Notably, never users of alcohol had much lower prevalence of marijuana use – this likely reflects a small proportion of LT candidates who have been abstinent or had very limited exposure to any substance use. There have been prior conflicting reports regarding an association between marijuana use and lower BMI^{23–26}. In univariate analysis, marijuana users were less likely to be obese (BMI 30–34.9, IRR 0.8) compared to overweight (BMI 25–29.9), though this association was not significant after multivariable adjustment (Table 3). This is the first study to present detailed data on prevalence and multivariable adjusted factors associated with marijuana use among LT candidates. Our findings are consistent with limited prior reports of marijuana use patterns among LT candidates¹⁷. Recent national drug use surveys²⁷ have found that 6.5% of adults older than 25 had active marijuana use. These nationally representative estimates are in close agreement with our finding of 7% recent marijuana use among LT candidates. It is also important to note that marijuana use was not just limited to those with a history of substance abuse but was rather distributed across the spectrum of substance use, as demonstrated in Figure 1. Yet, in our study, despite noting a high prevalence of marijuana use and its associations with other substance use, we were unable to detect worse outcomes with historical marijuana use itself; whereas, illicit substance use did confer higher risk of death or delisting on the waitlist. In a recent study, Greenan et al²⁸ also found that isolated recreational marijuana was not associated with poorer outcomes among kidney transplant patients.

Though most patients (89%) underwent urine drug screening in addition to psychosocial evaluation to identify marijuana use in our cohort, we assessed for differences in sensitivity of marijuana use assessment between urine drug screening and psychosocial screening. Most marijuana users had positive urine toxicology – among ‘recent’ marijuana users 80% (N=52) had positive urine toxicology (of whom 52% also self-reported marijuana use) while an additional 20% (N=13) were identified based on self-report alone. Therefore, sensitivity of drug screening alone was 80% (N=52 of 65) while that of self-report alone was 62% (N=40 of 65).

We also assessed for differences in outcomes between those who tested negative for marijuana and those who were not tested with urine drug screening. A similar proportion of subjects with and without urine drug screen were positive for marijuana use – 48% (N=380 of 788) and 46% (N=44 of 96), respectively, with no statistical difference detected (chi-square $p=0.66$). When comparing subjects *without marijuana use* by presence or absence of the urine test, risk of death/delisting (univariate HR 0.69 urine test yes vs. no, 95% CI 0.36–1.32, $p=0.26$) and LT (univariate HR 0.92 urine test yes vs. no, 95% CI 0.52–1.62, $p=0.77$) failed to differ statistically. Regardless of screening method, a similar proportion of patients were positive for marijuana use and waitlist outcomes were similar.

Despite broad implications, there is limited data on clinical outcomes for patients who use marijuana before and after LT and no consensus within the transplant community surrounding marijuana use^{12–14,29}. Approximately 15,000 patients are currently listed for LT in the US according to the Organ Procurement and Transplantation Network (OPTN)³⁰. Therefore, given the rising prevalence of marijuana use, LT listing policies around marijuana use may affect several thousand patients in the US alone. Using psychosocial assessment and urine toxicology, our study is the first report on the prevalence and frequency of marijuana use and its effect on LT waitlist outcomes among a cohort of LT candidates in the United States. In the only prior study evaluating LT-related outcomes among marijuana users, Ranney et al¹⁷ found that marijuana users were less likely to receive LT but had similar overall survival rates as nonusers. Their study, however, was limited by the exclusion of a large portion of LT waitlist candidates. They also did not assess waitlist outcomes like rate of delisting in this study and their use of urine toxicology alone to define marijuana led to a low prevalence estimate (~10%) and may have led to misclassification of marijuana users. In contrast, we used a more robust definition of marijuana use based on psychosocial interviews combined with urine toxicology to describe the frequency and patterns of marijuana and other substance use among LT candidates. We also used a competing risk model to assess for rates of death or delisting in addition to receiving LT among marijuana users and nonusers.

Our study, and that of Ranney et al., did not find clear evidence of harm associated with historical marijuana use, and raises the question whether ongoing marijuana use could be considered safe on the LT waitlist. This question is especially relevant given recent passage of laws that protect medical marijuana users from transplant restrictions across several states in the United States. Further, could medical marijuana have a potential therapeutic role for LT candidates? A recent report documents successful use of prescription marijuana to decrease opiate use following liver transplantation³¹. Perhaps marijuana could be effectively used for appetite stimulation, treating nausea, reducing opiate addiction, or postoperative pain relief. This is especially relevant considering that almost a quarter of LT candidates at our institution had recent opiate/BDZ prescriptions.

It is important to note that our understanding of the metabolism and effects of marijuana is still developing – marijuana use affects the endocannabinoid system, including the hepatic cannabinoid (CB) receptors, which are also modulated by chronic liver disease. Upregulation of the CB1 receptor in chronic liver disease has been implicated in progression of liver fibrosis^{32,33}. However, CB2 is also upregulated in liver disease and prevents fibrosis progression. It has been postulated that the balance between CB1 and CB2 receptor activation may modulate liver fibrosis – if both receptors are targeted equally then they may not be any net effect on liver fibrosis. However, there have been isolated cases of invasive aspergillosis related to marijuana use among posttransplant patients^{34,35}. A recent report also suggests potential for calcineurin inhibitor toxicity with heavy marijuana use³⁶.

Our study has several important limitations and should be interpreted with caution. We could not assess impact of ongoing marijuana use on waitlist outcomes because our institutional policy did not allow LT listing for active marijuana users. Those with active marijuana use, including heavy users, had to demonstrate abstinence prior to listing for LT. Therefore, based

on our data we cannot comment on active marijuana use and our results should only be applied to *historical marijuana use prior to LT listing*. Those subjects who were able to satisfy the selection committee concerns and demonstrate abstinence from marijuana use were classified as ‘recent’ users in our study. All outcomes are presented in strata of ‘recent’ and ‘prior’ marijuana use to capture any differences between these 2 groups. Accordingly, we also cannot provide relevant data on the effects of ongoing marijuana use on post-LT outcomes. Though we attempt to adjust for confounding variables, given the limited prior work in this field there is potential for unmeasured confounding in our analysis. Further, our definition of marijuana use does not incorporate duration or method of marijuana use, as these data were not collected systematically at our institution. Finally, we defined marijuana use via combination of self-report in a psychosocial assessment and urine toxicology, which likely yields an underestimate of the true prevalence since patients had a conflict of interest in self-reporting marijuana use and urine toxicology to detect marijuana is an imperfect test.

In conclusion, we found a high prevalence of historical marijuana use that did not have clear adverse effects on LT waitlist outcomes. Recent use of illicit substances was, however, associated with higher risk of death or delisting from the LT waitlist. This suggests historical marijuana use alone may not be equivalent to use of other illicit drugs. Yet, this data should be interpreted with restraint as further research is needed to assess the impact of ongoing marijuana use among candidates on the LT waitlist. Further, posttransplant outcomes must also be followed in these patients to determine safety of continued marijuana use after LT. Recent passage of laws protecting medical marijuana users has created an urgent need to further study LT-related outcomes among this population.

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Abbreviations

BDZ	benzodiazepine
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HR	hazard ratio
IRR	incidence rate ratio
LT	liver transplant
MELD	model for end-stage liver disease
NAFLD	nonalcoholic fatty liver disease

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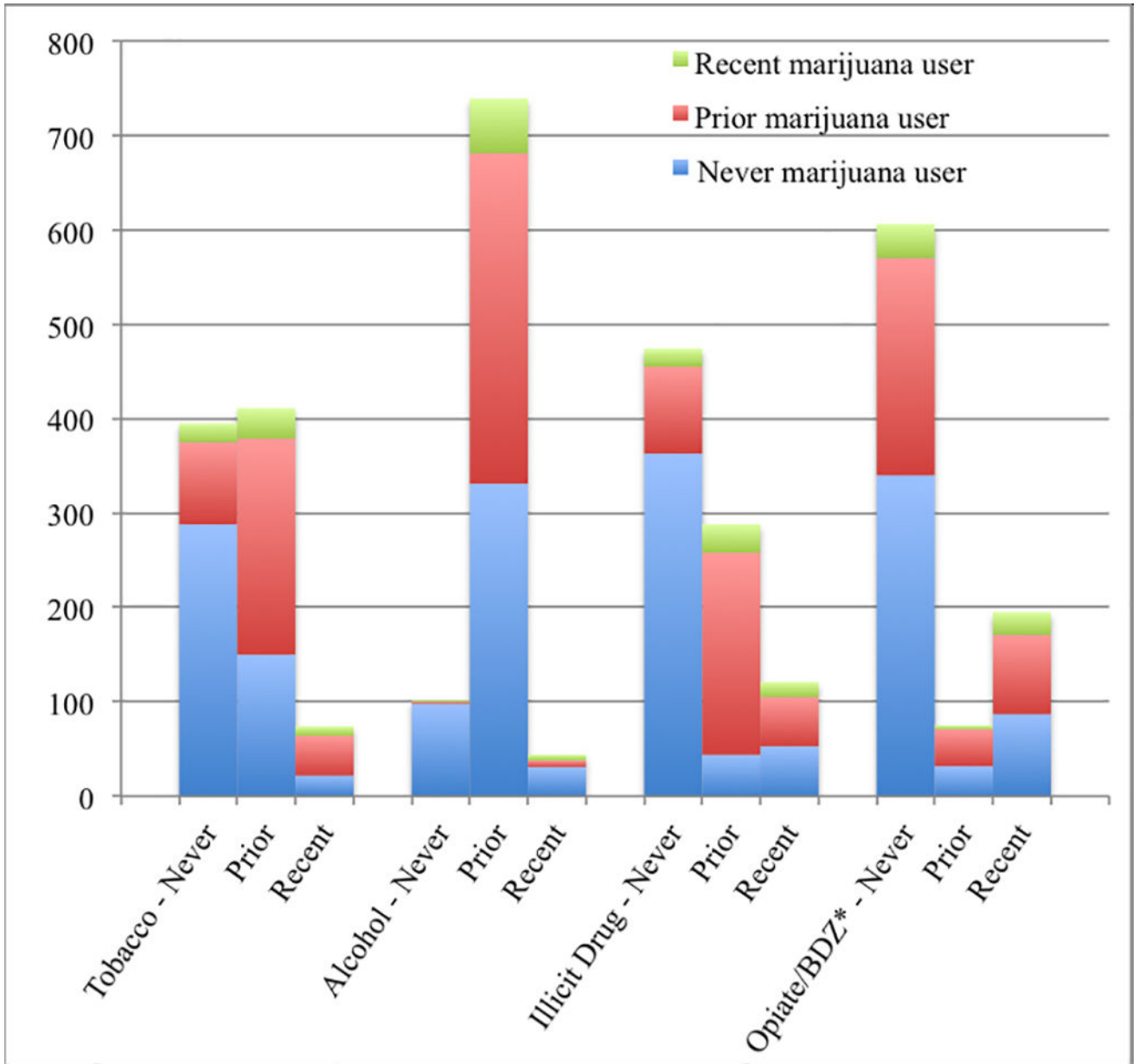


Figure 1.
Drug use among all subjects in strata of marijuana use
*Prescription opiate and benzodiazepine use

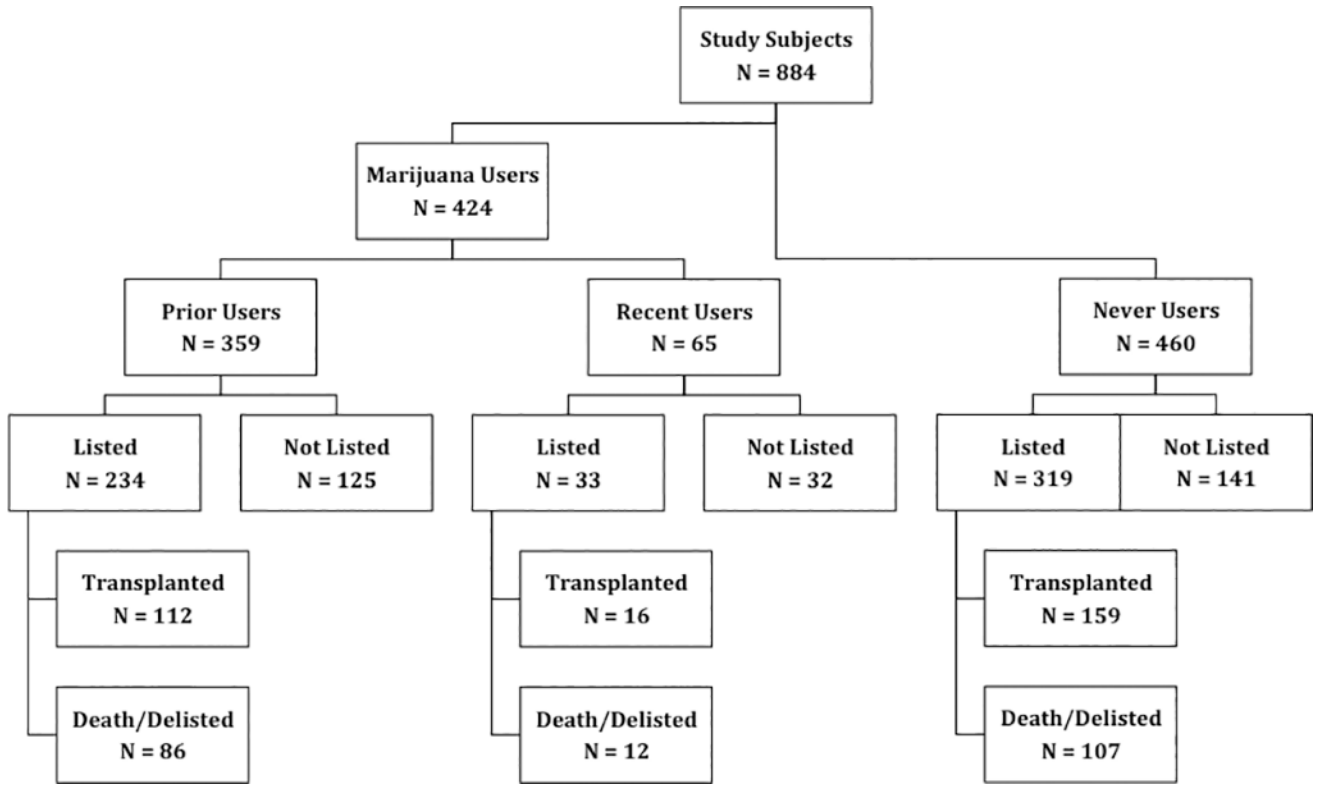


Figure 2.
Listing and waitlist outcomes

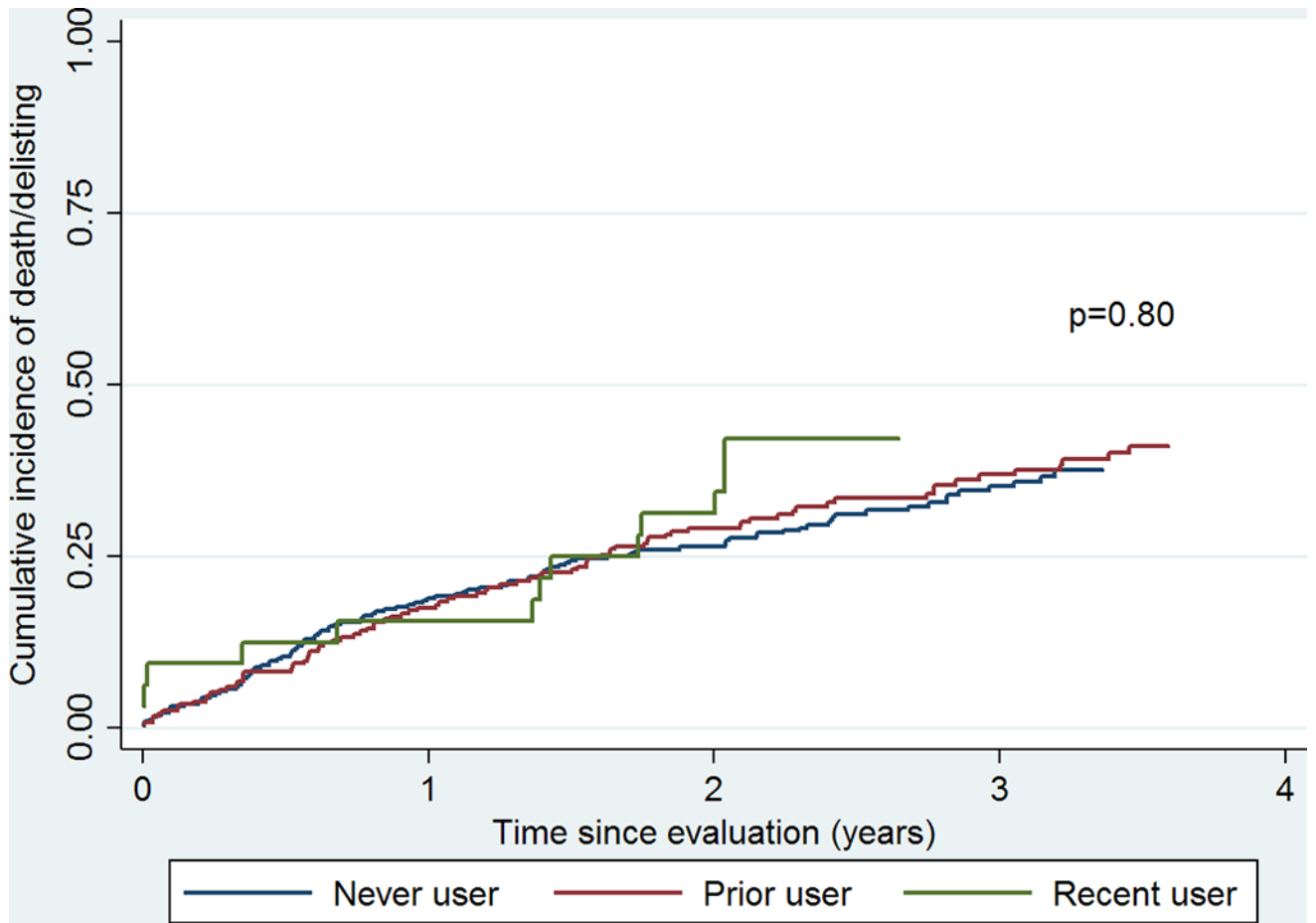


Figure 3. Cumulative incidence of death or delisting on the transplant waitlist by marijuana use

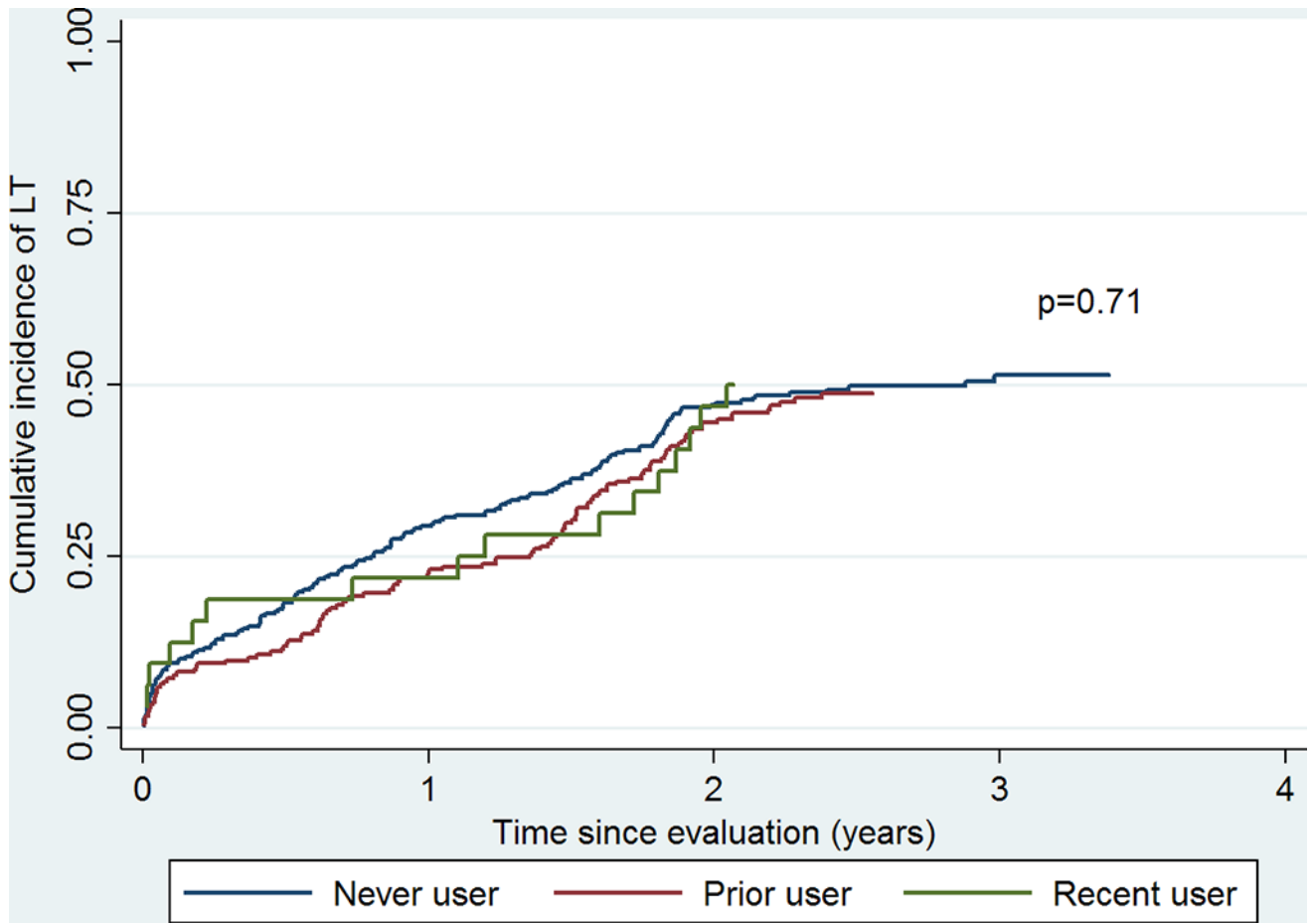


Figure 4. Cumulative incidence of receiving liver transplant (LT) on the transplant waitlist by marijuana use

Table 1

Demographics and clinical characteristics of study participants

	N (%)		
	Not listed N=299	Listed N=585	Total N=884
Age (years)			
18–29	10 (3)	14 (2)	24 (3)
30–44	39 (13)	47 (8)	86 (10)
45–59	142 (47)	280 (48)	422 (48)
60	108 (36)	244 (42)	352 (40)
Gender			
Women	122 (41)	202 (35)	324 (37)
Men	177 (59)	383 (65)	560 (63)
BMI			
<25	72 (27)	171 (29)	243 (28)
25–29.9	102 (38)	200 (34)	302 (35)
30–34.9	52 (19)	109 (19)	161 (10)
35	42 (16)	105 (18)	147 (17)
Race/Ethnicity			
White	159 (59)	317 (54)	476 (56)
African American	13 (5)	27 (5)	40 (5)
Asian	27 (10)	72 (12)	99 (12)
Native Hawaiian/Pacific Islander	3 (1)	9 (2)	12 (1)
American Indian/Other	7 (3)	9 (2)	16 (2)
Hispanic/Latino	61 (23)	151 (26)	212 (25)
Education			
Less than high school	18 (10)	33 (8)	51 (9)
Finished high school	62 (34)	100 (25)	162 (28)
College or beyond	101 (56)	270 (67)	371 (64)
Etiology of liver disease			
Alcoholic cirrhosis	50 (18)	86 (15)	136 (16)
HCV cirrhosis	137 (49)	284 (49)	421 (49)
HBV cirrhosis	15 (5)	43 (7)	58 (7)
NAFLD	32 (11)	48 (8)	80 (9)
Other	48 (17)	124 (21)	172 (20)
MELD			
<20	203 (68)	429 (73)	632 (71)
20	96 (32)	156 (27)	252 (29)
HCC			
No	220 (78)	358 (61)	578 (67)

	N (%)		
	Not listed N=299	Listed N=585	Total N=884
Yes	62 (22)	227 (39)	289 (33)

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Table 2

Substance use among study subjects

	N (%)		
	Not listed N=299	Listed N=585	Total N=884
Marijuana use*			
Never	141 (47)	319 (55)	460 (52)
Prior	125 (42)	234 (40)	359 (41)
Recent	33 (11)	32 (5)	65 (7)
Marijuana use frequency[§]			
Less than weekly	55 (36)	113 (43)	168 (40)
Weekly	21 (14)	31 (12)	52 (13)
Daily	27 (18)	40 (15)	67 (16)
Unknown	50 (33)	80 (30)	130 (31)
Tobacco use			
Never	131 (44)	264 (45)	395 (45)
Prior	122 (41)	289 (49)	411 (47)
Recent	42 (14)	32 (5)	74 (8)
Alcohol use			
Never	35 (12)	66 (11)	101 (11)
Prior	245 (82)	494 (84)	739 (84)
Recent	19 (6)	25 (4)	44 (5)
Alcohol use frequency[¶]			
Social use	105 (40)	259 (50)	364 (46)
Heavy use/abuse	159 (60)	260 (50)	419 (54)
Illicit drug use*			
Never	146 (49)	328 (56)	474 (54)
Prior	103 (35)	185 (32)	288 (33)
Recent	49 (16)	72 (12)	121 (14)
Prescription opiate/BDZ use[§]			
Never	187 (63)	419 (72)	606 (69)
Prior	22 (7)	53 (9)	75 (9)
Recent	86 (29)	109 (19)	195 (22)

* Self-report and/or urine toxicology

[§]Self-report[¶]Social use: 7 drinks/week for women or 14 drinks/week for men.

Table 3

Poisson regression to determine factors associated with marijuana use (recent or prior)

	Univariable		Multivariable	
	IRR (95% CI)	p-value	IRR (95% CI)	p-value
Age (years)				
18–29	1.7 (1.1 – 2.6)	0.02	2.6 (1.6 – 4.0)	<0.001
30–44	1		1	
45–59	1.6 (1.1 – 2.1)	0.005	1.0 (0.7 – 1.3)	0.8
>60	1.2 (0.9 – 1.7)	0.2	0.9 (0.6 – 1.2)	0.3
Gender*				
Female	1			
Male	1.4 (1.2 – 1.6)	0.0001		
BMI				
<25	1.0 (0.8 – 1.2)	0.8		
25–29.9	1			
30–34.9	0.8 (0.6 – 1.0)	0.02		
35	0.9 (0.8 – 1.1)	0.4		
Race/Ethnicity				
White	1		1.2 (1.1 – 1.4)	0.001
Non-white	0.6 (0.5 – 0.7)	<0.0001	1	
Education				
Did not finish high school	1			
Finished high school	1.4 (0.9 – 2.1)	0.09		
College or beyond	1.3 (0.9 – 1.9)	0.2		
Etiology of liver disease				
Alcoholic cirrhosis	3.6 (1.8 – 7.0)	<0.0001	1.9 (1.0 – 3.7)	0.05
HCV	4.8 (2.5 – 9.2)	<0.0001	2.1 (1.1 – 4.0)	0.02
HBV	1		1	
NAFLD	1.4 (0.7 – 3.2)	0.3	1.6 (0.8 – 3.2)	0.2
Other	1.9 (1.0 – 3.9)	0.06	1.6 (0.8 – 3.0)	0.2
MELD				
<20	1.2 (1.1 – 1.5)	0.01	1.2 (1.1 – 1.5)	0.005
20	1		1	
HCC*				
No	1			
Yes	1.2 (1.0 – 1.4)	0.02		
Tobacco use				
Never	1		1	
Prior	2.3 (2.0 – 2.8)	<0.0001	1.4 (1.2 – 1.7)	<0.001

	Univariable		Multivariable	
	IRR (95% CI)	p-value	IRR (95% CI)	p-value
Recent	2.6 (2.1 – 3.2)	<0.0001	1.3 (1.1 – 1.6)	0.006
Alcohol use frequency				
Never	0.1 (0.02 – 0.2)	<0.0001	0.1 (0.04 – 0.3)	<0.001
Social use	1		1	
Heavy use/abuse	1.7 (1.4 – 1.9)	<0.0001	1.2 (1.0–1.3)	0.03
Illicit drug use				
Never	1		1	
Prior	3.6 (3.1 – 4.3)	<0.0001	2.3 (1.9 – 2.7)	<0.001
Recent	2.4 (1.9 – 3.0)	<0.0001	1.9 (1.5 – 2.4)	<0.001
Prescription opiate/BDZ use*				
Never user	1			
Prior user	1.3 (1.1 – 1.6)	0.02		
Recent user	1.3 (1.1 – 1.5)	0.003		

* Composite p-value <0.05 but not statistically significant in multivariable model.

Table 4

Reasons for removal from the liver transplant waitlist by marijuana use (N = 205)

	Marijuana use N (%)		
	Never user (N = 107)	Prior user (N = 86)	Recent user (N = 12)
Died	51 (48)	39 (45)	3 (25)
Patient condition deteriorated, too sick for transplant	35 (33)	27 (31)	2 (17)
Patient improved, transplant not needed	4 (4)	6 (7)	2 (17)
Transferred to another center	2 (2)	3 (3)	0
Lack of social support	0	2 (2)	0
Substance abuse relapse	4 (4)	3 (3)	1 (8)
Refused transplant	5 (5)	1 (1)	1 (8)
Other	3 (3)	3 (3)	3 (25)

Table 5

Competing risk regression to determine factors associated with death/delisting on the liver transplant waitlist

	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Marijuana use				
Never	1.0		1.0	
Prior	1.1 (0.8–1.4)	0.54	1.0 (0.7–1.4)	0.9
Recent	1.1 (0.6–2.0)	0.70	1.0 (0.5–1.8)	0.9
Age				
18–29	1.0			
30–44	0.5 (0.2–1.5)	0.22		
45–59	0.7 (0.3–1.8)	0.46		
>=60	0.7 (0.3–1.7)	0.42		
Gender				
Female	1.0			
Male	1.1 (0.8–1.5)	0.41		
Race				
White	1.0			
Non-White	1.0 (0.8–1.3)	0.96		
MELD				
<20	1.0			
20	1.3 (1.0–1.8)	0.06		
HCC				
No	1.0			
Yes	1.2 (0.9–1.6)	0.24		
Etiology of liver disease				
Alcoholic cirrhosis	1.0			
HCV cirrhosis	1.4 (0.9–2.0)	0.14		
HBV cirrhosis	1.1 (0.6–2.0)	0.86		
NAFLD	0.8 (0.4–1.6)	0.60		
Other	1.0 (0.6–1.7)	0.90		
Education				
Did not finish high school	1.0			
Finished high school	1.8 (0.9–3.6)	0.08		
College or beyond	1.4 (0.7–2.6)	0.33		
Unknown	1.4 (0.8–2.8)	0.26		
Tobacco use				
Never	1.0			
Prior	0.9 (0.7–1.2)	0.72		
Recent	1.3 (0.7–2.2)	0.41		

	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Alcohol use severity				
Never	1.1 (0.7–1.7)	0.71		
Social	1.0			
Heavy user/Abuse	1.4 (1.0–1.8)	0.03		
Illicit use				
Never	1.0		1.0	
Prior	1.2 (0.9–1.6)	0.19	1.2 (0.9–1.8)	0.2
Recent	1.8 (1.2–2.8)	0.004	1.8 (1.2–2.8)	0.004
Prescription opiate/BDZ use				
Never	1.0			
Prior	0.9 (0.6–1.5)	0.78		
Recent	1.1 (0.8–1.5)	0.65		

Table 6

Competing risk regression to determine factors associated with receiving liver transplant

	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Marijuana use				
Never	1.0		1.0	
Prior	0.9 (0.7–1.1)	0.41	0.9 (0.7–1.2)	0.4
Recent	0.9 (0.6–1.5)	0.77	0.9 (0.6–1.6)	0.8
Age				
18–29	1.0			
30–44	1.1 (0.5–2.4)	0.86		
45–59	0.8 (0.4–1.6)	0.48		
>=60	0.8 (0.4–1.6)	0.45		
Gender				
Female	1.0			
Male	1.0 (0.8–1.3)	0.98		
Race				
White	1.0			
Non-White	1.1 (0.9–1.4)	0.41		
MELD				
<20	1.0		1.0	
20	1.5 (1.1–2.0)	0.005	1.6 (1.2–2.2)	0.001
HCC				
No	1.0		1.0	
Yes	1.1 (0.9–1.4)	0.24	1.3 (1.0–1.7)	0.02
Etiology of liver disease				
Alcoholic cirrhosis	1.0			
HCV cirrhosis	1.0 (0.7–1.4)	0.86		
HBV cirrhosis	1.5 (0.9–2.4)	0.12		
NAFLD	1.2 (0.7–1.9)	0.58		
Other	1.2 (0.8–1.8)	0.30		
Education				
Did not finish high school	1.0			
Finished high school	0.6 (0.4–1.0)	0.05		
College or beyond	0.7 (0.5–1.2)	0.20		
Unknown	0.8 (0.5–1.3)	0.40		
Tobacco use				
Never	1.0			
Prior	1.1 (0.9–1.4)	0.41		
Recent	0.8 (0.4–1.3)	0.33		

	Univariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Alcohol severity				
Never	1.5 (1.0–2.1)	0.04		
Social	1.0			
Heavy use/Abuse	0.9 (0.7–1.2)	0.39		
Illicit use				
Never	1.0			
Prior	0.9 (0.7–1.1)	0.30		
Recent	0.8 (0.5–1.2)	0.25		
Prescription opiate/BDZ use				
Never	1.0			
Prior	0.8 (0.5–1.2)	0.30		
Recent	0.8 (0.5–1.0)	0.08		