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# Patients with Persistently Low MELD-Na Scores Continue to be at Risk of Liver Related Death

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## Abstract

**Background:** The vast majority of patients with cirrhosis have low Model for End Stage Liver Disease-Sodium (MELD-Na) scores, however the ability for the MELD-Na score to predict patient outcomes at low scores is unclear.

**Methods:** Adult patients in a multicenter, Chicago-wide database of medical records with ICD-9 codes of cirrhosis and without a history of hepatocellular carcinoma were included. Records were linked with the state death registry and death certificates were manually reviewed. Deaths were classified as “liver related”, “nonliver related”, and “nondescript” as adjudicated by a panel comprised of a transplant surgeon, a hepatologist, and an internist. A sensitivity analysis was performed where patients with hepatocellular carcinoma were included.

**Results:** Among 7922 identified patients, 3999 patients had MELD-Na scores that were never higher than 15. In total, 2137 (27%) patients died during the study period with higher mortality rates for the patients in the high MELD-Na group (19.4 (41.6%) vs 4.1 (12.6%) per 100 person years, p<0.001). The high MELD-Na group died of a liver related cause in 1142/1632 (70%) as compared to 240/505 (47.5%) deaths in the low MELD-Na group. There was no difference in the

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3. Contributed new analytic tools
4. Participated in data analysis
5. Participated in the writing of the paper

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distribution of subcategory of liver related death between low and high MELD-Na groups. Among subclassification of liver related deaths, the most common cause of death was ‘Infectious’ in both groups.

**Conclusions:** Despite persistently low MELD-Na scores, patients with cirrhosis still experience high rates of liver related mortality.

## 1. Introduction:

According to estimates by the Center for Disease Control and Prevention (CDC) liver disease is a major cause of death with over 40 000 patients dying each year.[1] While it is well known that liver disease is a major driver of mortality in patients with high Model for End Stage Liver Disease-Sodium (MELD-Na) scores, very little is known about the leading causes of death in patients with cirrhosis and low MELD-Na.[2,3] This population is notable as patients with low MELD-Na scores comprise the vast majority of patients with cirrhosis in large national samples of waitlisted patients.[4,5] One single-center study of listed patients with MELD score less than 22 suggests that these patients succumb to liver related complications and have a mortality rate upwards of 30% over 2 years.[6] Unfortunately the above studies are limited by the inherent selection bias related to the transplant listing process. The generalizability of the results are also unclear as listed patients comprise a tiny minority of patients with cirrhosis, with only 10 636 patients listed nationwide in 2015 as compared to an estimated 600 000 patients with prevalent liver cirrhosis-- slightly less than 2%.[7,8] This leaves the majority of patients with cirrhosis uncaptured by the widely studied United Network for Organ Sharing (UNOS) database. Therefore, the objective of this study was to explore the burden of liver related death by describing the causes of death in patients with low MELD-Na and high MELD-Na scores in a unique, multicenter, population based cohort within a large metropolitan area.

## Materials and Methods:

### 2.1 Patient Population

All patients age 18 or older greater seen from January 1, 2006 through December 31, 2012 at 1 of 6 large healthcare institutions in Chicago were included if they were associated with 1 of 3 diagnosis codes for cirrhosis as defined by the International Classification of Disease Ninth edition (ICD-9 codes 571.2, 571.5, or 571.6), a validated method used in administrative studies of cirrhosis.[9–11] MELD-Na scores were calculated with serum creatinine, bilirubin, INR, and sodium using the standard method from the Organ Procurement and Transplantation Network (OPTN). For patients missing any values, future values were used for MELD-Na calculation. The maximum time span allowed between the values used for 1 calculation was 30 days. If multiple scores were available, the peak score was used for analysis to truly identify a population that consistently had low MELD-Na scores. If no scores were available from the EHR and patients were listed for transplant, biological MELD-Na was manually calculated from United Network for Organ Sharing (UNOS) data. Patients were excluded if they had insufficient data for even a single MELD-Na calculation or if they were ever taking warfarin. Patients were allowed to contribute time at risk up until transplantation, but were censored at date of surgery. Given concern that

patients who developed hepatocellular carcinoma have an altered disease course which may not manifest in an elevation of MELD-Na score, these patients were included in a sensitivity analysis.

### 2.2 Data sources

Patient records from 6 large healthcare institutions in Chicago were linked into a deidentified, community based cohort, the HealthLNK database.[12] These institutions include 5 major academic healthcare centers: Northwestern Medicine, University of Chicago Hospitals and Clinic, Rush University Medical Center, University of Illinois at Chicago Medical Center, and Loyola University Medical Center; and 1 large county health system, Cook County Health and Hospitals System. HealthLNK contains more than 2.4 million unique patient records and encompasses ~42% of all inpatient beds in Chicago, IL spanning from January 1, 2006 to December 31, 2012. These records were merged with the OPTN database, the Illinois Department of Public Health (IDPH) Death registry, and deidentified prior to analysis. The OPTN database comprises national registry data of all patients waitlisted and transplanted in the US. The IDPH is a governmental agency with death certificates for all patients who have died in Illinois. All databases were linked in 2015. For patients meeting inclusion, demographics, procedure codes, medications, laboratory measurements, and diagnostic codes from all inpatient, outpatient, and emergency department encounters at the participating institutions were abstracted. Northwestern IRB approval of study protocols was obtained prior to data acquisition and analysis.

### 2.3 Cause of death ascertainment and adjudication

We manually reviewed death certificate data obtained from the Department of Public Health on all included patients who died during the follow up period above. Death certificates listed the “Immediate cause of death” as completed by the physician caring for the patient at the time of death. Each patient could also have up to 14 associated conditions or contributing causes which were reported on the death certificate after the immediate cause. Classification of causes of death was performed in 2 stages (See Supplementary Digital Content, SDC, http://links.lww.com/TP/B823).

In the first stage, the “immediate cause of death” as listed on the death certificate was reviewed by a panel consisting of a transplant surgeon, transplant hepatologist, and internist who were blinded to all other patient data. Patients’ deaths were classified as “liver related”, “nonliver related”, “nondescript”, or ‘missing’ by an in person consensus according to specified rules similar to past studies (See Supplementary Digital Content, SDC, http://links.lww.com/TP/B823)[6,13] If the decision was not unanimous, the death certificate was flagged for further review. These debated cases as well as those labeled ‘Nondescript, ‘missing’, or liver related were included in a secondary review.

Upon secondary review, indeterminate death certificates were categorized based on the up to 14 contributing causes and associated conditions listed on the death certificate. Causes of death and subcategory assignment were allocated based on ordinal interpretation of death certificates and according to specified rules (See Supplementary Digital Content, SDC, http://links.lww.com/TP/B823). Specifically, contributing causes of death listed earlier in the

death certificate were considered to be more immediately contributory to the patient's cause of death compared to later causes. For example, patients with intracerebral hemorrhage required listing of coagulopathy or a cirrhosis related diagnosis to be classified as 'liver-related' and 'bleeding'. Any patient with a 'liver related' cause of death was further categorized into 6 subcategories: Infectious, Oncologic, Portal hypertensive, Variceal Bleeding, Bleeding, and Other similar to previous studies.[6,13] Patients with an Oncologic causes of death were retroactively removed from the primary analysis and included in the sensitivity analysis. Patients whose death certificates noted death post liver transplant and who were not noted to have been listed or transplanted in the UNOS database during the study period were assumed to be posttransplant and therefore excluded.

### 2.4 Statistical analysis

T tests and chi-squared tests were performed for statistical inference for continuous and categorical variables respectively. R statistical software version 3.4.3, Rstudio version 1.1.419 were used for data processing, analysis, and graphics generation. The 'icd' package was used to translate ICD-9 and ICD-10 codes.[14] The 'tableone' package was used to compute the above statistical tests and generate tables.[15] A p value of 0.05 was considered significant.

## 2. Results

### 3.1 Population Characteristics

Over the study period, 18 690 patients had an ICD-9 code for cirrhosis and were not on warfarin. Among the remaining patients, 9719 patients were pretransplant at the start of their follow up and had sufficient data to calculate a MELD-Na score. Of these patients 1797 were excluded due to a diagnosis of HCC. The remaining 7922 were included in the analysis below (Table 1). Patients had a mean age of 55 years and were generally white (n=3219, 41.9%), male (n=4610; 58%), and insured by public insurance (n=3381; 42.7%). During the follow up period, 440 patients underwent liver transplantation. After stratification by maximal MELD-Na score attained, 3999 (50.4%) patients never had a MELD-Na score greater than 15. The average mean peak MELD-Na in the 2 groups were 25.3 vs 10.1 ($p<0.001$). Patients in the low MELD-Na group were less likely to have alcohol related cirrhosis (32% vs 59%, $p<0.001$) or complications of liver disease such as ascites, hepatic encephalopathy, esophageal varices/banding, spontaneous bacterial peritonitis, or hepatorenal syndrome ($p<0.001$ for each, Table 1). In contrast patients with lower MELD-Na scores were more likely to have HCV (41% vs 35%, $p<0.001$), identify as female (46.5% vs 37.2%, $p<0.001$), or have a cholestatic etiology of cirrhosis (11% vs 9%, $p<0.001$).

### 3.1 Patient Outcomes

In total, 2137 (27%) patients died during the study period with higher mortality rates for the patients in the high MELD-Na group (19.4 (41.6%) vs 4.1 (12.6%) per 100 person years, $p<0.001$). Death certificates were available for all but 81 patients (3.7% missing). Results of the death certificate review after stratification by MELD-Na score are displayed in Table 2. Patients in the high MELD-Na group died of a liver related cause in 1142/1632 (70%) as compared to 240/505 (47.5%) deaths in the low MELD-Na group. Among subclassification

of liver related deaths, the most common cause of death was ‘Infectious’ in both groups. There was no difference in the distribution of subcategory of death between low and high MELD-Na groups. A high percentage of liver-related deaths did not have enough information to further classify into a subcategory (663/1632; 56.4% vs 127/505; 51.0%).

When patients were stratified based on the presence of common portal hypertensive complications (hepatic encephalopathy, varices, or ascites) in the medical chart, patients with more complications were more likely to die from a liver related cause based on their death certificate (169/374 45.2% vs 1213/1763 68.8% p<0.001, Table S1, SDC, http://links.lww.com/TP/B823). Similarly, when patients were stratified based on variceal status (none, present, or history of bleeding; Table S2, SDC, http://links.lww.com/TP/B823) in the medical chart, patients with worse variceal status had higher rates of liver related death (721/1268 56.9% vs 452/603 75.0% vs 209/266 78.6% p<0.001 respectively) and liver related death in the variceal bleeding subcategory (31/721 4.2% vs 16/452 3.4% vs 27/209 12.6% respectively, p<0.001).

The sensitivity analysis that included the 1797 patients with HCC demonstrated that patients in both groups were even more likely to die of a liver-related cause (Table 3). Patients in the high MELD-Na group died of a liver related cause in 1698/2253 (75.4%) cases as compared to 448/736 (60.9%) deaths in the low MELD-Na group. Inclusion of these patients also significantly altered the previously similar distribution of cause of liver-related death. The subclassification of ‘Oncologic’ now accounted for the most common cause of death in the low MELD-Na group (158/736; 34.4% vs 352/2253; 20.2%, p<0.001).

## 3. Discussion

Organ allocation is an essential aspect of the field of transplantation in lieu of an adequate donor supply. Intrinsic to the success of organ allocation is prediction of which patients would succumb to their liver disease soonest and thus who may attain the most benefit from such a scarce resource. This study was not designed to examine the benefit of transplantation in patients with high MELD-Na scores--this is well known and forms the basis for current transplant policy. Instead, we sought to examine the cause of death for patients with low MELD-Na scores, considered to be ‘low risk’ of liver related death. Given that incorporation of hyponatremia into the MELD benefits patients with lower scores to a higher degree, examination of patients with persistently low MELD-Na scores creates a new group of the ‘lowest’ risk patients.[3,16] Surprisingly, patients in the low MELD-Na group did not have a different distribution of causes of death as compared to the higher scoring group. Additionally, nearly half of them died of a liver related cause with a relatively high (12%) mortality over the 6 year study period, an adjusted rate of 4.1 deaths per 100 patient years. This implies that 1 in 25 of all patients with persistently low MELD scores will die of their liver disease each year. Although on first glance this may seem like a relatively low rate, this finding becomes significant as the vast majority of patients with cirrhosis fall into this category, with a 2004 study finding 92% of waitlisted patients had a MELD score of 18 or less and a more recent 2014 analysis noting 73.4% of patients were initially listed with a MELD less than 16.[4,5] Although many studies have used databases such as UNOS or SRTR which are comprised of patients who have passed stringent screening and are listed for

transplant, our study is one of the largest to our knowledge that examines outcomes for all patients with low MELD-Na scores, not just those who are listed. This is highlighted by the fact that only about 5% of patients in this study (1.8 per 100 patient-years) underwent transplantation over the 6 year study period as compared to the national rate of around 40 per 100 years during the same period.[7] Our findings suggest that the vast majority of patients with cirrhosis do not receive transplant and, despite low MELD-Na scores, succumb to complications related to their liver disease.

Our study is also unique in that we examined each patient's death certificate to attribute mortality to a liver-related or liver-unrelated cause as compared to using all-cause mortality. This was intended to characterize the burden of liver related mortality in the low MELD-Na group as a surrogate for potential benefit from transplantation.

Prior retrospective analyses of waitlisted patients using the UNOS dataset suggest that a small group of patients with low MELD scores may benefit from transplant but, on average, have an increased 1 year all-cause mortality if transplanted.[17,18] Additionally, retrospective studies of living donor liver transplant suggested a benefit for all patients regardless of MELD score.[19,20] Taken together, these findings are consistent with our results in supporting that liver transplantation could benefit a subset of low MELD-Na patients who suffer liver-related death. Additional studies would be needed to identify which of these low MELD-Na patients should be selected.

On sensitivity analysis, when patients with HCC were included the mortality rate increased to 1 in 20. However given that we censored patients at time of transplant, the inclusion of HCC patients could enrich the low MELD group with transplant-ineligible patients. Alternatively, the high rates of oncologic death in the low MELD-Na patient group found on sensitivity analysis may have several explanations. Perhaps, a patient with chronically compensated disease may fall out of screening guidelines and specialist care only to present at a more advanced stage. Our study was not designed to control for specialist care or screening adherence. Another possibility is that patients with high MELD scores die much more quickly of more acute issues and so do not have time to develop oncologic complications. Alternatively the oncogenicity of various etiologies of cirrhosis may correlate with their likelihood to produce a high MELD score.

Our study has several limitations. First, we could not adjust for other covariates when calculating mortality rates. However, we would expect adjusting for nonliver factors in the slightly older, more female, and longer lived low-MELD-Na group to further enlarge the proportion of patients with liver related death. Second we excluded patients without a MELD-Na score in the database. We considered the lack of a single MELD-Na lab over the 6 year study period even allowing for a relatively broad, 30 day lab grace period to signify that the patient was not receiving liver-minded care and therefore may not be generalizable to the patients of the intended audience of this article. Third, manual review of death certificate data may introduce subjectivity to outcomes, although this was avoided as much as possible by implementing a diverse review panel, with defined rules, and by blinding reviewers to other patient data. Furthermore, when this blinded review of death certificate data was compared with an EHR-based history of decompensation and varices, patients

appeared to correspondingly have increased rates of liver related death and variceal bleeding suggesting validity of our death certificate classifications. Finally, the accuracy of the clinically determined cause of death listed on death certificates has been questioned compared to the gold standard of autopsy.[21–23] However this inaccuracy appears to be mainly in cases of cardiovascular death, with a meta-analysis suggesting that a clinical diagnosis of cirrhosis or hepatobiliary carcinoma had sensitivities and specificities of 57–70% and 99% respectively.[21] Thus our use of cirrhosis related diagnoses in death certificate data are likely underestimates of the true rate of death due to a liver related cause.

In conclusion, this study suggests that the vast majority of patients with cirrhosis, those with a low MELD-Na score, are not free from liver-related death. Future studies should center on distinguishing which of these patients are not as 'low risk' as previously thought. Determining which patients with a low MELD-Na score are at highest risk may allow transplant providers to explore mechanisms to avert liver related death such as living donor liver transplant or donation after circulatory death.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations:

| | |
|---|---|
| **HCC** | Hepatocellular Carcinoma |
| **ICD-9** | International Classification of Disease Ninth edition |
| **IDPH** | Illinois Department of Public Health |
| **MELD** | Model for End-Stage Liver Disease |
| **Na** | Sodium |
| **OPTN** | Organ Procurement and Transplantation Network |

## References

1. Murphy SL, Xu J, Kochanek KD, et al. Deaths: Final Data for 2015. National Vital Statistics Reports. 2015;66(6):1–75. Available at https://www.cdc.gov/. Published November 27, 2017. Accessed October 23, 2018.
2. Malinchoc M, Kamath PS, Gordon FD, et al. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31(4):864–871. doi:10.1053/he.2000.5852 [PubMed: 10733541]
3. Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and Mortality among Patients on the Liver-Transplant Waiting List. N Engl J Med. 2008;359:1018–1026. Available at http://www.nejm.org/doi/pdf/10.1056/NEJMoa0801209. Accessed April 3, 2018. [PubMed: 18768945]

4. Trotter JF, Osgood MJ. MELD scores of liver transplant recipients according to size of waiting list: impact of organ allocation and patient outcomes. JAMA. 2004;291(15):1871–1874. doi:10.1001/jama.291.15.1871 [PubMed: 15100206]
5. Yi Z, Mayorga ME, Orman ES, et al. Trends in Characteristics of Patients Listed for Liver Transplantation Will Lead to Higher Rates of Waitlist Removal Due to Clinical Deterioration. Transplantation. 2017;101(10):2368–2374. doi:10.1097/TP.0000000000001851 [PubMed: 28858174]
6. Kwong AJ, Lai JC, Dodge JL, et al. Outcomes for liver transplant candidates listed with low model for end-stage liver disease score. Liver Transpl. 2015;21(11):1403–1409. doi:10.1002/lt.24307 [PubMed: 26289624]
7. Kim WR, Lake JR, Smith JM, et al. OPTN/SRTR 2017 Annual Data Report: Liver. Am J Transplant. 2019;19:184–283. doi:10.1111/ajt.15276 [PubMed: 30811890]
8. Scaglione S, Kliethermes S, Cao G, et al. The Epidemiology of Cirrhosis in the United States: A Population-based Study. J Clin Gastroenterol. 2015;49(8):690–696. doi:10.1097/MCG.0000000000000208 [PubMed: 25291348]
9. Nehra MS, Ma Y, Clark C, et al. Use of administrative claims data for identifying patients with cirrhosis. J Clin Gastroenterol. 2013;47(5):e50–54. doi:10.1097/MCG.0b013e3182688d2f [PubMed: 23090041]
10. Lo Re V III, Haynes K, Goldberg D, et al. Validity of diagnostic codes to identify cases of severe acute liver injury in the US Food and Drug Administration's Mini-Sentinel Distributed Database. Pharmacoepidemiol Drug Saf. 2013;22(8):861–872. doi:10.1002/pds.3470 [PubMed: 23801638]
11. Goldberg D, Lewis J, Halpern S, et al. Validation of three coding algorithms to identify patients with end-stage liver disease in an administrative database. Pharmacoepidemiol Drug Saf. 2012;21(7):765–769. doi:10.1002/pds.3290 [PubMed: 22674685]
12. Kho AN, Cashy JP, Jackson KL, et al. Design and implementation of a privacy preserving electronic health record linkage tool in Chicago. J Am Med Inform Assoc. 2015;22(5):1072–1080. doi:10.1093/jamia/ocv038 [PubMed: 26104741]
13. Tapper EB, Parikh ND. Mortality due to cirrhosis and liver cancer in the United States, 1999–2016: observational study. BMJ. 2018;362:k2817. doi:10.1136/bmj.k2817 [PubMed: 30021785]
14. Wasey Jack O.. icd: Comorbidity Calculations and Tools for ICD-9 and ICD-10 Codes. R package version 3.3. Available at https://cran.r-project.org/package=icd. Published 2018.
15. Yoshida K, Chipman J, Bohn J. tableone: Create 'Table 1' to Describe Baseline Characteristics. R package version 0.9.3. https://cran.r-project.org/package=tableone. Published 2018.
16. Biggins SW, Kim WR, Terrault NA, et al. evidence-based incorporation of serum sodium concentration into MELD. Gastroenterology. 2006;130:1652–1660. doi:10.1053/j.gastro.2006.02.010 [PubMed: 16697729]
17. Schaubel DE, Guidinger MK, Biggins SW, et al. Survival benefit-based deceased-donor liver allocation. Am J Transplant. 2009;9(4p2):970–981. doi:10.1111/j.1600-6143.2009.02571.x [PubMed: 19341419]
18. Merion RM, Schaubel DE, Dykstra DM, et al. The survival benefit of liver transplantation. Am J Transplant. 2005;5(2):307–313. doi:10.1111/j.1600-6143.2004.00703.x [PubMed: 15643990]
19. Perumpail RB, Yoo ER, Cholankeril G, et al. Underutilization of Living Donor Liver Transplantation in the United States: Bias against MELD 20 and Higher. J Clin Transl Hepatol. 2016;4(3):169–174. doi:10.14218/JCTH.2016.00029 [PubMed: 27777886]
20. Berg CL, Merion RM, Shearon TH, et al. Liver transplant recipient survival benefit with living donation in the model for endstage liver disease allocation era. Hepatology. 2011;54(4):1313–1321. doi:10.1002/hep.24494 [PubMed: 21688284]
21. Roulson J, Benbow EW, Hasleton PS. Discrepancies between clinical and autopsy diagnosis and the value of post mortem histology; a meta-analysis and review. Histopathology. 2005;47(6):551–559. doi:10.1111/j.1365-2559.2005.02243.x [PubMed: 16324191]
22. Boers M, Nieuwenhuyzen Kruseman AC, Eulderink F, et al. Value of autopsy in internal medicine: a 1-year prospective study of hospital deaths. Eur J Clin Invest. 1988;18(3):314–320. doi:10.1111/j.1365-2362.1988.tb01265.x [PubMed: 3138134]

23. Blake JE, Compton KV, Schmidt W, et al. Accuracy of death certificates in the diagnosis of alcoholic liver cirrhosis. Alcohol Clin Exp Res. 1988;12(1):168–172. doi:10.1111/j.1530-0277.1988.tb00154.x [PubMed: 3279851]

**Table 1.**

Baseline Patient Demographics

| | | Full Cohort | MELD-Na >15 | MELD-Na 15 or less | p |
|---|---|---|---|---|---|
| N | | 7922 | 3923 | 3999 | |
| Age (Mean (SD)) | | 55.06 (11.27) | 54.87 (11.09) | 55.24 (11.45) | 0.141 |
| Gender (%) | Female | 3312 (41.9) | 1458 (37.2) | 1854 (46.5) | <0.001 |
| | | | | | 0.052 |
| | White | 3219 (40.6) | 1640 (41.8) | 1579 (39.5) | |
| | Black | 1707 (21.5) | 848 (21.6) | 859 (21.5) | |
| Race (%) | Hispanic | 1690 (21.3) | 827 (21.1) | 863 (21.6) | |
| | Asian | 182 (2.3) | 76 (1.9) | 106 (2.7) | |
| | Other | 1124 (14.2) | 532 (13.6) | 592 (14.8] | |
| | | | | | <0.001 |
| | Medicare/Medicaid | 3381 (42.7) | 1730 (44.1) | 1651 (41.3) | |
| Insurance (%) | Private | 2521 (31.8) | 1114 (29.7) | 1357 (33.9) | |
| | Other | 2020 (25.5) | 1029 (26.2) | 991 (24.8) | |
| Median days of follow up (IQR) | | 823 (306–1461) | 580 (153–1218) | 976 (548–1706) | <0.001 |
| | | | | | |
| | | | | | |
| Mean Elixhauser Comorbidity Index (SD) | | 5.41 (3.24) | 6.53 (3.26) | 4.31 (2.82) | <0.001 |
| MELD-Na | Median number of Measurements (IQR) | 4 (2–8) | 4 (2–10) | 4 (2–7) | <0.001 |
| during follow up | Average Minimum (S | 12.87 (6.95) | 17.05 (7.59) | 8.79 (2.32) | <0.001 |
| | Average Maximum (SD) | 17.62 (9.15) | 25.30 (6.68) | 10.08 (2.71) | <0.001 |
| MELD during follow up | Average Maximum (SD) | 16.36 (8.43) | 22.96 (7.17) | 9.92 (2.50) | <0.001 |
| Listed Patients | | 998 (12.6) | 787 (20.1) | 211 (5.3) | <0.001 |
| Median days on Waitlist (IQR) | | 187 (26–1,208) | 113 (17–607) | 1916 (674–2557) | <0.001 |
| Transplants | | 440 (5.4) | 418 (10.7) | 22 (0.6) | <0.001 |
| | HCV | 38% | 35% | 41% | <0.001 |
| | HBV | 8% | 8% | 8% | 0.588 |
| Etiology (%) | Alcohol | 45% | 59% | 32% | <0.001 |
| | NASH | 19% | 18% | 19% | 0.177 |
| | Cholestatic | 10% | 9% | 11% | <0.001 |
| | | | | | |
| | Ascites | 41% | 64% | 18% | <0.001 |
| | HE | 37% | 58% | 16% | <0.001 |
| Complications (%) | Varices | 34% | 43% | 26% | <0.001 |
| | SBP | 8% | 14% | 1% | <0.001 |
| | HRS | 8% | 15% | 1% | <0.001 |

**Table 2.**

Results of Death Certificate review

| | | Peak MELD-Na >15 | Peak MELD-Na 15 or less | p |
|---|---|---|---|---|
| Cohort n | | 3923 | 3999 | |
| Total # deaths (%) | | 1632 (41.6) | 505 (12.6) | <0.001 |
| Person-Years at risk | | 8,412 | 12,261 | |
| Rate of death per 100 person-years | | 19.4 | 4.1 | |
| Cause of death n (%) | | | | <0.00 |
| | Liver | 1142 (70.0) | 240 (47.5) | |
| | Nonliver | 428 (26.2) | 246 (48.7) | |
| | Nondescript | 62 (3.8) | 19 (3.8) | |
| Subcategory if Liver Related n (%) | | | | 0.546 |
| | Bleeding | 42 (3.6) | 12 (4.8) | |
| | Infectious | 325 (27.6) | 75 (30.1) | |
| | Other | 663 (56.4) | 127 (51.0) | |
| | Portal HTN | 85 (7.2) | 22 (8.8) | |
| | Varices | 61 (5.2) | 13 (5.2) | |

**Table 3.**

Sensitivity analysis including patients with HCC or Cholangiocarcinoma

| | | Peak MELD-Na >15 | Peak MELD-Na 15 or less | p |
|---|---|---|---|---|
| N | | 4993 | 4726 | |
| Total # deaths (%) | | 2253 (45.1) | 736 (15.3) | <0.001 |
| Person-Years at risk | | 10,412 | 14,060 | |
| Rate of death per 100 person-years | | 21.6 | 5.2 | |
| Cause of death n (%) | | | | <0.001 |
| | Liver | 1698 (75.4) | 448 (60.9) | |
| | Nonliver | 477 (21.2) | 264 (35.9) | |
| | Nondescript | 78 (3.5) | 24 (3.3) | |
| Subcategory if Liver Related n (%) | | | | <0.001 |
| | Bleeding | 47 (2.7) | 14 (3.1) | |
| | Infectious | 378 (21.7) | 89 (19.4) | |
| | Oncologic | 352 (20.2) | 158 (34.4) | |
| | Other Portal hypertensive | 104 (6.0) | 27 (5.9) | |
| | Varices | 74 (4.2) | 17 (3.7) | |
| | Other | 787 (45.2) | 154 (33.6) | |