Received: 11 August 2023 | Accepted: 4 October 2023

DOI: 10.1097/HC9.0000000000000352

ORIGINAL ARTICLE

OPEN

The changing epidemiology of adult liver transplantation in the United States in 2013-2022: The dominance of metabolic dysfunction–associated steatotic liver disease and alcohol-associated liver disease

Zobair M. Younossi[1,2] | **Maria Stepanova**[1,2] | **Reem Al Shabeeb**[1] | **Katherine E. Eberly**[1] | **Dipam Shah**[1] | **Veronica Nguyen**[1] | **Janus Ong**[2,3] | **Linda Henry**[1,2,4] | **Saleh A. Alqahtani**[1,4,5]

[1]Beatty Liver and Obesity Research Program, Inova Health System, Falls Church, Virginia, USA

[2]The Global NASH Council, Washington, District of Columbia, USA

[3]Department of Internal Medicine, College of Medicine, University of the Philippines, Manila, Philippines

[4]Center for Outcomes Research in Liver Diseases, Washington, District of Columbia, USA

[5]Epidemiology & Scientific Computing Department, Liver Transplant Center and Biostatistics, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

Correspondence
Zobair M. Younossi, The Global NASH Council, Washington DC 20037, USA.
Email: Zobair.younossi@cldq.org

Abstract

Background: The high prevalence of obesity in the United States drives the burden of NASH, recently renamed as metabolic dysfunction–associated steatohepatitis (MASH). We assessed the most recent trends in liver transplantation in the United States.

Methods: The Scientific Registry of Transplant Recipients (SRTR 2013-2022) was used to select adult (18 years or above) candidates who underwent liver transplant.

Results: There were 116,292 candidates who underwent liver transplant with known etiology of chronic liver disease. In candidates without HCC, the most common etiology was alcohol-associated liver disease (ALD), increasing from 23% (2013) to 48% (2022), followed by NASH/MASH, which increased from 19% to 27%; the rates of viral hepatitis decreased (chronic hepatitis C: 28%–4%; chronic hepatitis B: 1.8%–1.1%) (all trend $p < 0.01$). The proportion of HCC decreased from 25% (2013–2016) to 17% (2021-2022). Among HCC cohort, the proportion of chronic hepatitis C decreased from 60% (2013) to 27% (2022), NASH/MASH increased from 10% to 31%, alcohol-associated liver disease increased from 9% to 24% (trend $p < 0.0001$), and chronic hepatitis B remained stable between 5% and 7% (trend $p = 0.62$). The rapid increase in the proportion of NASH/MASH in HCC

Abbreviations: ALD, alcohol-associated liver disease; CVD, cardiovascular disease; HRSA, Health Resources and Services Administration; MASH, metabolic dysfunction–associated steatohepatitis; MASLD, metabolic dysfunction–associated steatotic liver disease; OPTN, Organ Procurement and Transplantation Network; SRTR, Scientific Registry of Transplant Recipients; T2D, type 2 diabetes.

The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the US Government.

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.hepcommjournal.com.

continued during the most recent study years [20% (2018), 28% (2020), 31% (2022)]; the trend remained significant after adjustment for age, sex, ethnicity, obesity, and type 2 diabetes.

Conclusions: Liver transplant etiologies in the United States have changed over the last decade. Alcohol-associated liver disease and NASH/MASH remain the 2 most common indications for transplantation among those without HCC, and NASH/MASH is the most common in patients with HCC.

INTRODUCTION

Liver transplantation remains the curative treatment for end-stage liver disease. According to the data from the Global Burden of Disease study, the absolute incidence, cumulative prevalence, and the number of deaths and disability-adjusted life years attributable to liver cirrhosis increased significantly between 1990 and 2019. At the same time, there was also a noted decrease in the age-standardized incidence of cirrhosis from 25.7 per 100,000 in 1990 to 25.3 per 100,000 in 2019, accompanied by even more substantial decreases in age-adjusted cirrhosis-associated deaths and disability-adjusted life years.[1] These decreases appear to be driven by fewer cases of viral hepatitis-related cirrhosis which, in turn, is most likely attributable to increasing availability of curative drugs for HCV, prevention vaccination for HBV infection, and effective viral suppression treatments for those with chronic HBV.[1–3] On the other hand, these investigators and others have found that cirrhosis due to NAFLD (now called metabolic dysfunction–associated steatotic liver disease, or MASLD) and alcohol use are increasing around the world, especially in Asia, Europe, and North America.[4–9] As such, the need for liver transplantation may change in parallel with the changes seen among those with cirrhosis. To build upon ours and others' prior work on the liver transplant landscape,[10–14] we aimed to describe the trends of liver transplantation in the United States using the national solid organ transplant registry from the most recent decade.

METHODS

Data source

In this study, we used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, waitlisted candidates, and recipients of transplant in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration (HRSA) and US Department of Health and Human Services provide oversight to the activities of the OPTN and SRTR contractors. All research was conducted in accordance with both the Declarations of Helsinki and Istanbul; all research was approved by the appropriate ethics and/or institutional review committee at Inova Health Systems and provided a waiver of consent.

For the study, we included all the candidates who underwent liver transplant and recipients of at least 18 years of age who were waitlisted and/or transplanted during the most recent decade (2013-2022). The most common primary listing diagnoses were collected from subjects' medical history; HCC could have been recorded as a primary or secondary diagnosis. Subjects with a listing diagnosis indicative of acute liver disease or with missing listing diagnosis data were excluded.

For candidates who underwent transplant, the outcome was removal from the transplant list as of the study cutoff (March 2, 2023); the main causes of removal from the list could be receiving a transplant, death, removal due to deterioration (too sick to transplant) or due to improvement (no longer qualify), refusal, and transfer to another center. For recipients of transplant, the primary outcomes were time to post-transplant mortality (determined by matching with the Social Security Death Master File provided by SRTR) and graft loss (defined by either a documented retransplant or by a cause of death being graft failure). Patients undergoing retransplants included in the mortality analysis only with their most recent transplants. Patients with no documented date of death were presumed alive as of the study cutoff date (March 2, 2023).

Statistical analysis

All collected clinical and demographic parameters of included recipients of transplant were summarized as mean $\pm$ SD or N (%) in subjects with and without HCC separately. Trends over time were evaluated using univariate generalized or logistic regression with calendar year being an independent variable; a multivariable logistic regression was used when a trend was evaluated with adjustment for confounders (age, sex, ethnicity, obesity, and type 2 diabetes).

To evaluate changes in outcomes over time, the association of the year of listing/transplantation with the study outcomes (time to transplantation for candidates, with being removed from the list due to death or deterioration as competing risks in cause-specific hazards models, follow-up time censored at death or removal for deterioration or the study cutoff date; time to post-transplant mortality for recipients of transplant) was assessed by Cox proportional hazard models adjusted for potential confounders. Given the limited availability of demographic and clinical parameters in the SRTR data collection, the list of potential confounders included age, sex, ethnicity, the type of insurance coverage, functional status score (0-100), body mass index, history of pretransplant type 2 diabetes and nonhepatic cancer, chronic liver disease etiology, indicators of liver disease severity such as MELD score, the presence of ascites (moderate or severe), HE (grade 1–4), bacterial peritonitis, PVT, history of TIPS, and receiving a liver retransplant.

All analyses were run in SAS 9.4 (SAS Institute, Cary, NC). The study was granted an exemption from IRB review as a non-human subject research by the Inova Institutional Review Board.

RESULTS

There were 121,544 adult candidates who underwent liver transplant in 2013-2022. Of those, 116,292 had chronic liver disease (CLD) with a known etiology and were included in this study, including 24,657 (21%) with HCC and 91,635 without HCC. During the study period, the prevalence of HCC among candidates who underwent liver transplant decreased from 24% to 25% in 2013–2016 to 22% in 2017-2018 to 19% in 2019-2020 to 17% in 2021-2022 (trend $p < 0.0001$).

Liver transplant candidates with HCC

A total of 24,657 candidates with HCC who underwent transplant were included in this study. The absolute number of HCC listings was the highest in 2016 (n = 2745); it decreased to its lowest observed value in 2022 (n = 2057). During the study period, the average age of a candidate with HCC who underwent transplant increased from 60 to 63 years, along with a decrease in the proportion of non-Hispanic Whites (65%–61%) and Blacks (10%–6%) contrasted by an increase in the proportion of Hispanics (16%–24%) (all $p < 0.01$) (Table 1). There was also a substantial increase in the proportion of patients covered by Medicare: 28%–39% ($p < 0.0001$) (Table 1). The proportions of obesity and type 2 diabetes increased from 35% to 43% and 30% to 40%, respectively (both $p < 0.0001$) (Table 1).

Considering etiologies of CLD among candidates with HCC, the proportion of chronic hepatitis C (CHC) decreased from 60% (2013) to 27% (2022), while NASH/MASH increased from 10% to 31% and alcohol-associated liver disease (ALD) from 9% to 24%, respectively (all trend $p < 0.0001$) (Table 1, Figure 1). On the other hand, the proportion of chronic hepatitis B remained stable at 5%–7% (trend $p = 0.62$) (Table 1, Figure 1). Among candidates with HCC, the rapid increase in the proportion of NASH was observed throughout the study duration and, importantly, also continued during the most recent study years: 20% (2018) to 28% (2020) to 31% (2022) (Figure 1). As a result, in 2022, NASH/MASH became the most common etiology of CLD among candidates who underwent liver transplant surpassing CHC (year 2021: 29% NASH vs. 30% CHC vs. 21% ALD; year 2022: 31% NASH vs. 27% CHC vs. 24% ALD). Furthermore, the increasing trend remained significant after adjustment for candidates' age, sex, ethnicity, obesity, and type 2 diabetes, and the average magnitude of increase in the proportion of NASH/MASH in candidates with HCC in 2018–2022 was +2.8 percentage points per year ($p < 0.0001$).

Of the included candidates with HCC who underwent transplant, 62% eventually received a transplant, 6% died on the list, 14% were removed due to deterioration, 2% refused a transplant, 2% improved, 8% were removed from the list for other causes, and 6% were still waiting as of the time of the study. Since the proportion of candidates whose waitlist outcome was unknown (still waiting) was 31% for the years 2021-2022, we excluded these 2 most recent study years from the analysis of trends in waitlist outcomes. As a result, we observed a trend toward decreasing rates of transplantation and longer wait times among candidates with HCC: of those listed in 2013-2014, 30% received a transplant within 6 months versus 19% in 2019-2020 ($p < 0.0001$) (Table 2). At the same time, the proportions of those who died on the list or were removed due to deterioration (too sick to transplant) remained unchanged: 21% in 2013-2014 versus 20% in 2019-2020 (Table 2). In time-to-event regression analysis, there was a significant association of a more recent calendar year with a lower chance of receiving a transplant among candidates with HCC [adjusted HR (95% CI) = 0.972 (0.965–0.980) per calendar year, $p < 0.0001$] (Supplemental Table S1, http://links.lww.com/HC9/A714).

Candidates without HCC who underwent liver transplant

A total of 91,635 adult candidates without HCC underwent liver transplant. The absolute number of listings without HCC increased from n = 8279 in 2013 to 10,352 in 2022. During the study period, the average age of a candidate without HCC who underwent transplant decreased from 55 to 54 years, the proportion of male subjects decreased from 62% to 59%, the proportion of non-Hispanic Blacks decreased

TABLE 1 Changes in clinicodemographic parameters of liver transplant candidates with HCC over the last decade (2013-2022)

	2013-2014, n (%)	2015-2016, n (%)	2017-2018, n (%)	2019-2020, n (%)	2021-2022, n (%)	p[a]	All, n (%)
N	5142	5463	5259	4617	4176	—	24,657
Age, y	60.3 ± 6.8	61.1 ± 6.9	61.9 ± 7.0	62.3 ± 7.7	62.8 ± 8.0	< 0.0001	61.6 ± 7.3
Male	3949 (76.8)	4168 (76.3)	4096 (77.9)	3483 (75.4)	3132 (75.0)	0.03	18,828 (76.4)
Non-Hispanic White	3317 (64.5)	3491 (63.9)	3238 (61.6)	2924 (63.3)	2525 (60.5)	< 0.0001	15,495 (62.8)
Non-Hispanic Black	527 (10.2)	570 (10.4)	461 (8.8)	346 (7.5)	264 (6.3)	< 0.0001	2168 (8.8)
Asian	408 (7.9)	361 (6.6)	409 (7.8)	315 (6.8)	324 (7.8)	0.82	1817 (7.4)
Hispanic	831 (16.2)	951 (17.4)	1061 (20.2)	952 (20.6)	998 (23.9)	< 0.0001	4793 (19.4)
Other race/ethnicity	59 (1.1)	90 (1.6)	90 (1.7)	80 (1.7)	65 (1.6)	0.06	384 (1.6)
US citizen	4834 (94.0)	5115 (93.6)	4887 (92.9)	4313 (93.4)	3845 (92.1)	0.0006	22,994 (93.3)
College-educated	1144 (23.3)	1258 (23.5)	1192 (23.0)	1132 (25.2)	1085 (26.8)	< 0.0001	5811 (24.2)
Insurance: private	2678 (52.5)	2641 (48.6)	2361 (44.9)	2046 (44.4)	1798 (43.3)	< 0.0001	11,524 (46.9)
Insurance: Medicare	1449 (28.4)	1760 (32.4)	1842 (35.1)	1731 (37.6)	1613 (38.9)	< 0.0001	8395 (34.2)
Insurance: Medicaid	776 (15.2)	809 (14.9)	800 (15.2)	601 (13.0)	535 (12.9)	0.0006	3521 (14.3)
Insurance: other	51 (1.0)	55 (1.0)	71 (1.4)	82 (1.8)	72 (1.7)	< 0.0001	331 (1.3)
Insurance: none	17 (0.3)	10 (0.2)	5 (0.1)	8 (0.2)	2 (0.0)	0.001	42 (0.2)
On life support	37 (0.7)	46 (0.8)	41 (0.8)	33 (0.7)	39 (0.9)	0.63	196 (0.8)
Ascites	2547 (49.5)	2652 (48.5)	2450 (46.6)	2217 (48.0)	2042 (48.9)	0.45	11,908 (48.3)
Bacterial peritonitis	173 (3.4)	170 (3.1)	175 (3.3)	158 (3.4)	162 (3.9)	0.09	838 (3.4)
HE	1993 (38.8)	2043 (37.4)	1946 (37.0)	1789 (38.7)	1640 (39.3)	0.22	9411 (38.2)
PVT	286 (5.6)	356 (6.5)	453 (8.6)	403 (8.7)	387 (9.3)	< 0.0001	1885 (7.7)
TIPS	181 (3.5)	257 (4.9)	271 (5.2)	246 (5.5)	234 (5.8)	< 0.0001	1189 (4.9)
BMI, kg/m^2	28.7 ± 5.2	29.1 ± 5.4	29.4 ± 5.4	29.7 ± 5.8	29.7 ± 5.7	< 0.0001	29.3 ± 5.5
Obese (BMI > = 30)	1817 (35.4)	2107 (38.7)	2178 (41.5)	2007 (43.6)	1773 (42.7)	< 0.0001	9882 (40.2)
Type 2 diabetes	1506 (29.8)	1813 (33.5)	1834 (35.2)	1629 (35.6)	1655 (39.9)	< 0.0001	8437 (34.6)
Functional status (0–100)	72.6 ± 16.9	70.7 ± 17.5	70.2 ± 17.5	71.0 ± 17.7	71.0 ± 18.4	0.0001	71.1 ± 17.6
MELD score	14.6 ± 8.7	14.1 ± 8.3	13.8 ± 7.9	14.0 ± 7.9	13.9 ± 7.9	0.0001	14.1 ± 8.2
Re-transplant	78 (1.5)	76 (1.4)	72 (1.4)	76 (1.6)	65 (1.6)	0.54	367 (1.5)
Primary listing diagnosis							
Chronic hepatitis B (CHB)	271 (6.2)	234 (4.7)	266 (5.8)	218 (5.6)	204 (5.9)	0.62	1193 (5.6)
Chronic hepatitis C (CHC)	2662 (60.6)	2657 (53.9)	2107 (46.1)	1417 (36.6)	984 (28.6)	< 0.0001	9827 (46.4)
NASH/MASH	456 (10.4)	743 (15.1)	855 (18.7)	990 (25.6)	1033 (30.1)	< 0.0001	4077 (19.2)
Autoimmune hepatitis	44 (1.0)	60 (1.2)	49 (1.1)	46 (1.2)	55 (1.6)	0.06	254 (1.2)
Alcoholic liver disease (ALD)	409 (9.3)	631 (12.8)	705 (15.4)	689 (17.8)	782 (22.8)	< 0.0001	3216 (15.2)
ALD+CHC	350 (8.0)	366 (7.4)	389 (8.5)	265 (6.9)	173 (5.0)	< 0.0001	1543 (7.3)
Primary biliary cholangitis	31 (0.7)	44 (0.9)	49 (1.1)	44 (1.1)	47 (1.4)	0.004	215 (1.0)
Primary sclerosing cholangitis	21 (0.5)	16 (0.3)	19 (0.4)	23 (0.6)	16 (0.5)	0.31	95 (0.4)
Other known CLD etiology	147 (3.3)	178 (3.6)	136 (3.0)	176 (4.6)	143 (4.2)	0.02	780 (3.7)

[a]*p*-value indicates significance of a trend over time returned by a regression model.

Abbreviations: ALD, alcohol-associated liver disease; BMI, body mass index; CHB, chronic hepatitis B; CHC, chronic hepatitis C; CLD, chronic liver disease; MASH, metabolic dysfunction–associated steatohepatitis; MELD, model for end-stage liver disease.

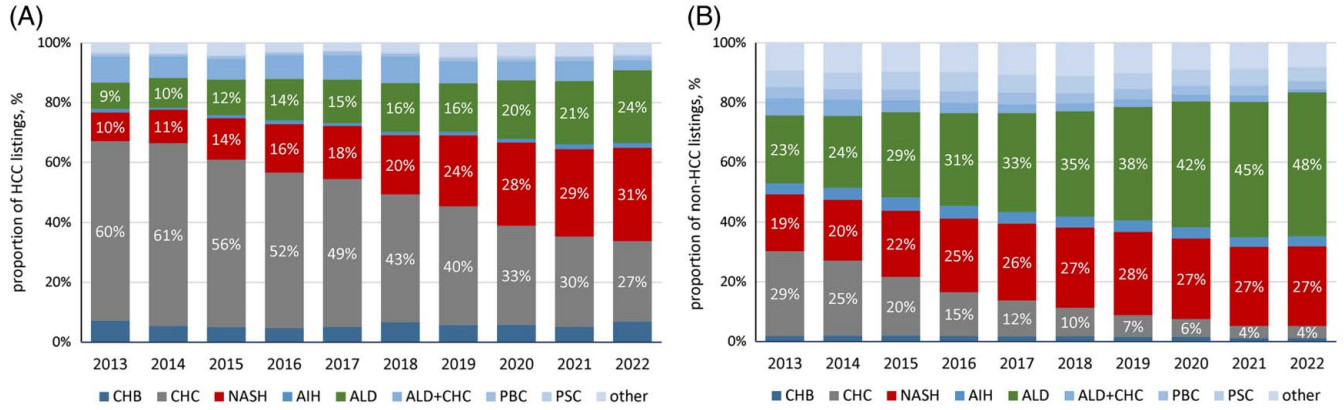

FIGURE 1 Distributions of CLD etiologies among adult candidates with and without HCC who underwent liver transplant. Abbreviations: AIH, ALD, alcohol-associated liver disease; CHB, chronic hepatitis B; CHC, chronic hepatitis C; CLD, chronic liver disease; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis.

from 9% to 6% while the proportion of Hispanics increased from 14% to 17% (all trend $p < 0.01$) (Table 3). The proportion of patients covered by Medicaid increased from 17% to 19%, while the proportion of those on Medicare decreased from 25% to 22% ($p < 0.0001$) (Table 3). In addition, there was evidence of increasing severity of liver disease manifested via increased rates of ascites, bacterial peritonitis, HE, and PVT (all $p < 0.0001$), although there was no concurrent increase in the average MELD score: 23.1 in 2013-2014 versus 22.5 in 2021-2022 (Table 3).

TABLE 2 Waitlist outcomes of candidates with and without HCC who underwent liver transplant in 2013-2020

	2013-2014	2015-2016	2017-2018	2019-2020		2013-2020
Candidates with HCC						
Transplanted in 3 mo	816 (16.4)	765 (14.4)	618 (12.1)	588 (13.1)	< 0.0001	2787 (14.0)
Transplanted in 6 mo	1506 (30.2)	1236 (23.3)	864 (16.9)	856 (19.0)	< 0.0001	4462 (22.4)
Transplanted in 12 mo	2356 (47.3)	2592 (48.9)	2535 (49.7)	2124 (47.2)	0.87	9607 (48.3)
Transplanted in 18 mo	2888 (57.9)	3169 (59.8)	3005 (58.9)	2462 (54.7)	0.0009	11,524 (58.0)
Transplanted in 24 mo	3171 (63.6)	3371 (63.7)	3147 (61.7)	2610 (58.0)	< 0.0001	12,299 (61.9)
Died on the list	346 (6.7)	302 (5.5)	292 (5.6)	236 (5.1)	Nc	1176 (5.7)
Removed due to deterioration	727 (14.1)	814 (14.9)	775 (14.7)	675 (14.6)	Nc	2991 (14.6)
Refused transplant	89 (1.7)	95 (1.7)	100 (1.9)	87 (1.9)	Nc	371 (1.8)
Transferred to another center	75 (1.5)	69 (1.3)	51 (1.0)	49 (1.1)	Nc	244 (1.2)
Removed due to improvement	87 (1.7)	101 (1.8)	127 (2.4)	98 (2.1)	Nc	413 (2.0)
Removed for other reasons	363 (7.1)	417 (7.6)	459 (8.7)	419 (9.1)	Nc	1658 (8.1)
Still on the list	11 (0.2)	20 (0.4)	56 (1.1)	184 (4.0)	Nc	271 (1.3)
Candidates without HCC						
Transplanted in 3 mo	4296 (27.0)	5412 (33.2)	6110 (34.7)	7807 (41.5)	< 0.0001	23,625 (34.4)
Transplanted in 6 mo	5490 (34.5)	6695 (41.0)	7655 (43.4)	9340 (49.6)	< 0.0001	29,180 (42.5)
Transplanted in 12 mo	6698 (42.1)	8037 (49.3)	9239 (52.4)	10,813 (57.5)	< 0.0001	34,787 (50.7)
Transplanted in 18 mo	7281 (45.8)	8725 (53.5)	9990 (56.7)	11,409 (60.6)	< 0.0001	37,405 (54.5)
Transplanted in 24 mo	7690 (48.3)	9084 (55.7)	10,334 (58.6)	11,750 (62.4)	< 0.0001	38,858 (56.6)
Died on the list	2259 (13.7)	1907 (11.3)	1826 (10.0)	1637 (8.5)	Nc	7629 (10.8)
Removed due to deterioration	1971 (11.9)	1667 (9.9)	1544 (8.5)	1312 (6.8)	Nc	6494 (9.2)
Refused transplant	103 (0.6)	136 (0.8)	124 (0.7)	108 (0.6)	Nc	471 (0.7)
Transferred to another center	369 (2.2)	268 (1.6)	216 (1.2)	148 (0.8)	Nc	1001 (1.4)
Removed due to improvement	1173 (7.1)	1048 (6.2)	1147 (6.3)	1054 (5.5)	Nc	4422 (6.2)
Removed for other reasons	1436 (8.7)	1307 (7.8)	1276 (7.0)	1092 (5.6)	Nc	5111 (7.2)
Still on the list	157 (1.0)	273 (1.6)	591 (3.2)	1397 (7.2)	Nc	2418 (3.4)

Note: Nc—cumulative outcomes with unequal follow-up duration were not compared cross-sectionally.

TABLE 3 Changes in clinicodemographic parameters of candidates without HCC liver transplant over the last decade (2013-2022)

	2013-2014, n (%)	2015-2016, n (%)	2017-2018, n (%)	2019-2020, n (%)	2021-2022, n (%)	*p*	All, n (%)
N	16,513	16,847	18,245	19,337	20,693		91,635
Age, y	54.9 ± 10.5	54.6 ± 10.9	54.8 ± 11.3	54.7 ± 11.5	53.9 ± 11.7	< 0.0001	54.6 ± 11.2
Male	10,206 (61.8)	10,239 (60.8)	10,860 (59.5)	11,512 (59.5)	12,290 (59.4)	< 0.0001	55,107 (60.1)
Non-Hispanic White	12,038 (72.9)	12,124 (72.0)	13,296 (72.9)	13,906 (71.9)	14,932 (72.2)	0.12	66,296 (72.3)
Non-Hispanic black	1418 (8.6)	1338 (7.9)	1325 (7.3)	1254 (6.5)	1265 (6.1)	< 0.0001	6600 (7.2)
Asian	518 (3.1)	572 (3.4)	554 (3.0)	592 (3.1)	638 (3.1)	0.33	2874 (3.1)
Hispanic	2310 (14.0)	2552 (15.1)	2753 (15.1)	3236 (16.7)	3473 (16.8)	< 0.0001	14,324 (15.6)
Other race/ ethnicity	229 (1.4)	261 (1.5)	317 (1.7)	349 (1.8)	385 (1.9)	< 0.0001	1541 (1.7)
US citizen	15,743 (95.4)	15,970 (94.8)	17,353 (95.1)	18,319 (94.8)	19,454 (94.9)	0.04	86,839 (95.0)
College-educated	4037 (26.0)	4463 (27.6)	5161 (29.0)	5692 (30.4)	6528 (33.0)	< 0.0001	25,881 (29.4)
Insurance: private	8965 (54.8)	9107 (54.4)	9535 (52.5)	10,149 (52.6)	10,981 (53.8)	0.002	48,737 (53.6)
Insurance: Medicare	4014 (24.5)	4081 (24.4)	4698 (25.8)	4785 (24.8)	4510 (22.1)	< 0.0001	22,088 (24.3)
Insurance: Medicaid	2717 (16.6)	2913 (17.4)	3223 (17.7)	3587 (18.6)	3963 (19.4)	< 0.0001	16,403 (18.0)
Insurance: other	174 (1.1)	224 (1.3)	272 (1.5)	333 (1.7)	445 (2.2)	< 0.0001	1448 (1.6)
Insurance: none	92 (0.6)	65 (0.4)	50 (0.3)	51 (0.3)	47 (0.2)	< 0.0001	305 (0.3)
On life support	648 (3.9)	733 (4.4)	760 (4.2)	803 (4.2)	787 (3.8)	0.72	3731 (4.1)
Ascites	12,688 (76.8)	13,129 (77.9)	14,356 (78.7)	15,497 (80.2)	17,084 (82.6)	< 0.0001	72,754 (79.4)
Bacterial peritonitis	1466 (9.0)	1536 (9.2)	1918 (10.6)	2123 (11.0)	2451 (12.0)	< 0.0001	9494 (10.4)
HE	10,975 (66.5)	11,272 (66.9)	12,257 (67.2)	13,102 (67.8)	14,253 (68.9)	< 0.0001	61,859 (67.5)
PVT	1084 (6.7)	1295 (7.7)	1586 (8.7)	1678 (8.7)	1782 (8.7)	< 0.0001	7425 (8.2)
TIPS	1605 (9.8)	1603 (9.8)	1684 (9.3)	1755 (9.4)	1717 (8.6)	0.0001	8364 (9.4)
BMI, kg/m^2	28.8 ± 6.0	28.9 ± 6.1	29.1 ± 6.2	29.1 ± 6.3	28.9 ± 6.2	0.03	29.0 ± 6.2
Obese (BMI ≥ 30)	6206 (37.8)	6398 (38.1)	7042 (38.8)	7593 (39.6)	7803 (38.1)	0.05	35,042 (38.5)
Type 2 diabetes	3937 (24.3)	4436 (26.6)	4840 (26.7)	5133 (26.7)	5134 (25.2)	0.28	23480 (25.9)
Cancer (other than HCC)	1483 (9.2)	1618 (9.6)	1906 (10.4)	1988 (10.3)	2175 (10.6)	< 0.0001	9170 (10.1)
Functional status (0–100)	59.7 ± 22.7	56.6 ± 22.0	56.1 ± 21.2	56.3 ± 21.7	55.4 ± 22.3	< 0.0001	56.7 ± 22.0
MELD score	23.1 ± 10.4	23.0 ± 10.4	22.2 ± 10.0	22.4 ± 9.9	22.5 ± 9.8	< 0.0001	22.6 ± 10.1
Retransplant	905 (5.5)	837 (5.0)	826 (4.5)	846 (4.4)	795 (3.8)	< 0.0001	4209 (4.6)
Primary listing diagnosis							
Chronic hepatitis B (CHB)	292 (1.8)	307 (1.9)	296 (1.7)	276 (1.5)	223 (1.1)	< 0.0001	1394 (1.6)
Chronic hepatitis C (CHC)	4259 (26.9)	2781 (17.1)	1913 (10.9)	1236 (6.6)	809 (4.1)	< 0.0001	10,998 (12.5)
NASH/MASH	3093 (19.5)	3818 (23.5)	4641 (26.3)	5109 (27.5)	5266 (26.6)	< 0.0001	21,927 (24.9)
Autoimmune hepatitis	617 (3.9)	700 (4.3)	662 (3.8)	714 (3.8)	649 (3.3)	0.0002	3342 (3.8)
Alcohol-associated liver disease (ALD)	3713 (23.4)	4850 (29.8)	6017 (34.1)	7426 (39.9)	9229 (46.7)	< 0.0001	31,235 (35.4)
ALD+CHC	877 (5.5)	619 (3.8)	498 (2.8)	447 (2.4)	307 (1.6)	< 0.0001	2748 (3.1)
Primary biliary cholangitis	584 (3.7)	603 (3.7)	638 (3.6)	606 (3.3)	589 (3.0)	< 0.0001	3020 (3.4)

TABLE 3. (*continued*)

	2013-2014, n (%)	2015-2016, n (%)	2017-2018, n (%)	2019-2020, n (%)	2021-2022, n (%)	*p*	All, n (%)
Primary sclerosing cholangitis	880 (5.6)	1011 (6.2)	1033 (5.9)	990 (5.3)	1015 (5.1)	0.0006	4929 (5.6)
Other known CLD etiology	1532 (9.7)	1591 (9.8)	1930 (10.9)	1789 (9.6)	1694 (8.6)	0.0001	8536 (9.7)

[a]*p*-value indicates significance of a trend over time returned by a regression model.
Abbreviations: ALD, alcohol-associated liver disease; BMI, body mass index; CHB, chronic hepatitis B; CHC, chronic hepatitis C; CLD, chronic liver disease; MASH, metabolic dysfunction–associated steatohepatitis; MELD, model for end-stage liver disease.

Among candidates without HCC, the most common CLD etiology was ALD, which increased from 23% (2013) to 48% (2022) (Table 2, Figure 1). The second most common indication for non-HCC liver transplantation was NASH/MASH, the proportion of which increased from 19% (2013) to 27% (2022) (Table 2, Figure 1). In contrast, rates of CHC decreased from 28% (2013) to 4% (2022), and chronic hepatitis B declined from 1.8% (2013) to 1.1% (2022) (all trend $p < 0.01$) (Table 2, Figure 1).

Of the included candidates without HCC who underwent transplant, 61% eventually received a transplant, 10% died on the list, 8% were removed due to deterioration, <1% refused a transplant, 5% improved, 6% were removed from the list for other causes, and 8% were still waiting as of the time of the study. There was a consistent trend toward increasing rates of transplantation and shorter wait times among candidates without HCC: 35% received a transplant within 6 months in 2013-2014 versus 50% in 2019-2020 (all $p < 0.0001$) (Table 2). At the same time, the rates of death or deterioration on the list decreased: 26% in 2013-2014 versus 15% in 2019-2020 (Table 2). In time-to-event analysis, there was a significant association of a more recent year of listing with the higher chance of receiving a transplant among candidates without HCC [adjusted HR (95% CI) = 1.067 (1.063–1.071) per calendar year, $p < 0.0001$] (Supplemental Table S2, http://links.lww.com/HC9/A714).

Post-transplant outcomes with and without HCC

Of those who received a transplant, post-transplant mortality was assessed over time (Table 4). Among candidates with HCC who underwent liver transplant, there was a decrease in 1-year mortality from 8.4% in 2013-2014 to 6.1% in 2017-2018, followed by an increase of 6.9% in 2019-2020 (Table 4). However, there were no significant differences in mortality outcomes when assessed later in follow-up (all $p > 0.01$) (Table 4). The cumulative rate of graft failure was 4.5% among those transplanted in 2013-2014 vs. 2.9% in 2019-2020 (Table 4). The most common cause of death among recipients of liver transplant with HCC was malignancy, followed by infections and cardiovascular causes (Table 4). In multivariable survival analysis, the association of the risk of post-transplant mortality with calendar year among recipients of transplant with HCC was not significant: $p = 0.05$ (Supplemental Table S3, http://links.lww.com/HC9/A714).

Among candidates without HCC who underwent liver transplant, there was a decreasing trend in post-transplant mortality over time: 1-year mortality 9.6% in 2013-2014 versus 6.8% in 2019-2020 ($p < 0.0001$) (Table 4); the trend was also observed later in follow-up (trend $p < 0.01$ until post-transplant year 6). After adjustment for changes in the distributions of CLD etiologies and other confounders in a Cox proportional hazards model, the association of a more recent year of transplantation with the lower risk of post-transplant mortality in recipients of transplant without HCC was significant (adjusted HR = 0.968 (0.959–0.978) per calendar year, $p < 0.0001$) (Supplemental Table S4, http://links.lww.com/HC9/A714). The cumulative rate of graft loss decreased over time, similar to the HCC sample (Table 4). The most common causes of death among recipients of liver transplant without HCC were infections followed by cardiovascular disease (Table 4).

DISCUSSION

Along with changes in demographics observed in the United States,[15] the portrait of a candidate who underwent liver transplant in the United States has evolved over time. At present, candidates with HCC who underwent liver transplant in the United States have an average age of 62 years and are most commonly white, male, without a college degree, covered by private insurance or Medicare, presenting with ascites or HE as indicators of hepatic decompensation. These patients are also commonly overweight or obese, with NASH/MASH, CHC, or ALD being the most likely etiologies of their underlying liver disease. During the study period, there was a significant increase in Hispanic patients with HCC noted. In fact, in 2021-2022 almost 1 out of every 4 patients with HCC were Hispanic, a change from 1 out of every 6 in 2013-2014. Additionally, more patients with HCC were on Medicare, most likely due to the increasing age of the recipients of

TABLE 4 Changes in the outcomes of liver transplant recipients during the study period (2013-2022).

	2013-2014	2015-2016	2017-2018	2019-2020	2021-2022	*p*	All
Transplantations with HCC							
N	3088	3343	3435	2926	2704		15,496
Discharged alive	2963 (96.9)	3227 (97.3)	3341 (97.9)	2824 (97.2)	2569 (97.5)	0.13	14,924 (97.4)
6-mo mortality	157 (5.2)	148 (4.5)	125 (3.7)	133 (4.6)	91 (4.2)	0.05	654 (4.5)
1-y mortality	252 (8.4)	229 (7.0)	205 (6.1)	198 (6.9)	108 (7.3)	0.009	992 (7.1)
3-y mortality	488 (16.3)	461 (14.1)	480 (14.2)	238 (13.4)	—	0.02	1667 (14.6)
5-y mortality	644 (21.5)	652 (20.0)	454 (22.7)	—	—	0.05	1750 (21.2)
8-y mortality	884 (29.5)	98 (34.5)	—	—	—	0.08	982 (29.9)
Graft failure	139 (4.5)	117 (3.5)	95 (2.8)	84 (2.9)	62 (2.3)	Nc	497 (3.2)
Causes of death							
Graft failure	48 (6.5)	45 (7.1)	37 (6.4)	30 (8.3)	12 (7.7)	Nc	172 (7.0)
Infection	99 (13.4)	98 (15.4)	93 (16.1)	72 (20.0)	31 (19.9)	Nc	393 (15.9)
Cardiovascular	105 (14.2)	102 (16.1)	67 (11.6)	50 (13.9)	29 (18.6)	Nc	353 (14.3)
Pulmonary	46 (6.2)	39 (6.1)	47 (8.2)	23 (6.4)	17 (10.9)	Nc	172 (7.0)
Cerebrovascular	19 (2.6)	13 (2.0)	11 (1.9)	11 (3.1)	2 (1.3)	Nc	56 (2.3)
Hemorrhage	18 (2.4)	11 (1.7)	9 (1.6)	11 (3.1)	8 (5.1)	Nc	57 (2.3)
Malignancy	320 (33.1)	262 (30.4)	254 (33.8)	128 (29.4)	35 (19.2)	Nc	999 (31.2)
Other	82 (11.1)	65 (10.2)	58 (10.1)	35 (9.7)	22 (14.1)	Nc	262 (10.6)
Transplantations without HCC							
N	8504	9951	11,019	12,938	14,155		56,567
Discharged alive	8042 (95.4)	9452 (95.8)	10,516 (96.1)	12,413 (96.7)	13,378 (96.8)	< 0.0001	53,801 (96.2)
6-mo mortality	602 (7.4)	604 (6.3)	614 (5.7)	628 (5.0)	574 (5.0)	< 0.0001	3022 (5.7)
1-y mortality	782 (9.6)	808 (8.4)	821 (7.6)	861 (6.8)	511 (6.5)	< 0.0001	3783 (7.7)
3-y mortality	1261 (15.4)	1284 (13.3)	1369 (12.8)	913 (12.5)	—	< 0.0001	4827 (13.4)
5-y mortality	1644 (20.1)	1727 (17.9)	1140 (18.4)	—	—	0.0007	4511 (18.8)
8-y mortality	2323 (28.4)	197 (26.2)	—	—	—	0.20	2520 (28.2)
Graft failure	503 (5.9)	437 (4.4)	396 (3.6)	429 (3.3)	276 (1.9)	Nc	2041 (3.6)
Causes of death							
Graft failure	183 (9.9)	153 (9.0)	136 (9.2)	129 (10.4)	67 (9.2)	Nc	668 (9.5)
Infection	410 (22.2)	388 (22.8)	343 (23.1)	326 (26.2)	180 (24.6)	Nc	1647 (23.5)
Cardiovascular	291 (15.7)	346 (20.4)	319 (21.5)	233 (18.7)	174 (23.8)	Nc	1363 (19.4)
Pulmonary	174 (9.4)	142 (8.4)	124 (8.4)	124 (10.0)	60 (8.2)	Nc	624 (8.9)
Cerebrovascular	66 (3.6)	57 (3.4)	55 (3.7)	36 (2.9)	40 (5.5)	Nc	254 (3.6)
Hemorrhage	86 (4.6)	62 (3.6)	79 (5.3)	71 (5.7)	52 (7.1)	Nc	350 (5.0)
Malignancy	330 (13.1)	268 (11.8)	215 (10.8)	135 (8.3)	49 (5.3)	Nc	997 (10.7)
Other	310 (16.7)	284 (16.7)	212 (14.3)	188 (15.1)	108 (14.8)	Nc	1102 (15.7)

Note: Nc—cumulative outcomes with unequal follow-up duration were not compared cross-sectionally.

transplant. Candidates were also more likely to be obese and have type 2 diabetes (T2D), which is not unexpected, given the increasing prevalence of these metabolic conditions and their association with NASH/MASH and NASH-related cirrhosis, the liver disease that saw the largest increase among candidates with HCC who underwent transplant (an increase from 1 in 10 for NASH/MASH in 2013-2014 to 1 in 3 in 2022). This is in line with the sociodemographic characteristics of NAFLD/MASLD, the most common chronic liver disease in the world.[5–9]

Our analysis also provided some encouraging data suggesting a significant decrease in CHC-related HCC being listed for liver transplantation. Although in 2013-2014, over 60% of candidates who underwent transplant had CHC-related HCC, in 2021-2022, less than 30% of cases were related to CHC. We believe this is most likely due to the wide availability of curative therapy for chronic HCV infection, which reduces the rates of HCC.[2,16–19] Notably, the proportion of those with HBV-HCC requiring a transplant remained low and decreased further over time, suggesting the positive impact of antiviral therapy and preventive HBV vaccination.[3,4]

In contrast to candidates with HCC who underwent liver transplant, liver transplant candidates without HCC

were younger, more commonly White, females with private insurance. Similarly, they were typically overweight and presented with ascites and HE as frequent complication of cirrhosis. Also, their most common primary diagnosis was ALD followed by NASH/MASH. During the study period, we noted a decrease in the average age of candidates without HCC who underwent transplant, an increase in the percentage of females requiring a transplant, and an increase in the rate of Medicaid coverage. There were also increases in cirrhosis complications (ascites, HE, and bacterial peritonitis) among those listed without HCC. Similar to the HCC group, the proportion of candidates with CHC who received liver transplant among those without HCC has dropped substantially from over 26% in 2013-2014 to 4% by 2020-2022. Although both NASH/MASH and ALD increased significantly, ALD incurred the largest increase over time and now comprises almost half of all candidates without HCC who underwent transplant. These trends may be reflective of the new changes in the transplant policy where not only are the sickest patients allocated to the top of the waiting list but organs are allowed to be dispersed to a wider geographical area than in prior years.[20,21] Additionally, there has also been an increase in the use of deceased donor livers, livers that have been infected with HCV, and the removal of the requirement for alcohol abstinence for 6 months or longer before being waitlisted for a liver transplant.[22–29] As a result, candidates with ALD meeting the newer eligibility criteria for liver transplantation may not experience long waiting times for an organ.[28,29] The increase in ALD as a cause for liver transplantation also helps to explain the decrease in age and the increase in females among the candidates who underwent transplant as the latest reports have highlighted the increasing rates of alcohol use disorder among the 18–34 years and females in particular.[30–39]

Considering waitlist outcomes over time, fewer candidates with HCC who received liver transplant were transplanted within 2 years of being placed on the list. On the other hand, those listed for transplant without HCC saw positive changes over time, where more candidates were transplanted in the first 3 months through 2 years. These outcomes are also most likely reflective of the policy changes in which the sickest patients are trying to be addressed, but in doing so, changes in other areas had to be made due to the finite number of organs available for transplant.[20–23]

In addition to waitlist outcomes, we assessed post-transplant outcomes. In this context, post-transplant outcomes for those with HCC showed that 86.6% of patients were still alive at 3 years post-transplant (2019-2020), a significant improvement since 2013-2014. A similar finding was noted for those transplanted without HCC. In both cohorts, the cumulative percent of graft failures decreased over time, suggesting improvements in post-transplant management. The leading cause of short-term death among both HCC and non-HCC cohorts was infection, which, as of the study date, accounted for approximately 20% of the deaths in patients transplanted in 2021-2022. However, among those with HCC, malignancy was the second leading cause of death, which also accounted for almost 20% of deaths in 2021-2022, but unlike infection that had increased during the study period, deaths from malignancy decreased from 33% in 2013-2014 to 19% in patients transplanted in 2021-2022. It is important to note that the observed changes in the causes of death are likely biased by the available duration of follow-up for the respective groups in which recurrence of HCC and malignancy-related deaths would occur later and/or are postponed by surveillance while infection-related deaths are more commonly observed shortly after the transplantation when the immunosuppressive regimen is typically the most aggressive.

Among the non-HCC cohort, cardiovascular disease (CVD) was the second most common cause of death, also accounting for almost 20% of short-term deaths. Notably, the proportion of CVD as a cause of death has increased from 16% in the earlier study years to 24% in the most recent years. This finding may not be surprising given that more patients are now on the transplant list with CVD risk factors to include obesity, T2D, and NASH/MASH.[40] On the other hand, these results suggest that careful evaluation of patients with CVD risk factors needs to be undertaken prior to transplantation, especially among those with NASH, as the presence of T2D in this population has been shown to independently increase the risk of mortality by as much as 40%.[41–43] Patients with NASH/MASH also tend to be older and, as noted in our study as others, older age can be associated with increased mortality, although many older patients do well post-transplant.[10,44] Additionally, the presence of sarcopenia (surrogate of which could be the functional score) has been associated with poorer outcomes following liver transplantation; this is a concern for those with NASH/MASH as sarcopenia is known to be associated with an increase in mortality in that population.[45–48] Therefore, careful assessment and management of the comorbidities present in those with NASH/MASH is needed prior to liver transplant to maximize the chance for positive outcomes. As NASH-HCC is now the number one indication for liver transplantation among those with HCC, hepatology and transplantology experts will need to develop such management guidelines.

The limitations of the study are related to its observational design, the quality of data, which is not centrally controlled and may vary across centers and over time, and the lack of potentially important confounding factors such as relevant comorbidities, laboratory parameters, and unaccounted socio-economic factors. Nevertheless, the large sample size and availability of pretransplant and post-transplant outcomes provide a great opportunity to assess factors associated with outcomes in liver transplantation.

In conclusion, these results from a recent registry-based study suggest that although criteria for being transplanted have expanded and some outcomes have shown improvement, overall older, sicker patients with T2D have a lower chance to fare well with a liver transplant. On the other hand, the alarming increase in the need for liver transplant among younger adults due to ALD as well as the increase of liver transplant among those with NASH-HCC are both areas that may benefit from public health interventions. Through increased awareness campaigns, mental health advocacy, and the provision of healthy foods at affordable prices, these trends may be able to be reversed. However, simultaneous to these campaigns, experts will need to continue to assess candidates who undergo liver transplant and work to optimize the liver candidate's chances of survival post-transplant through a thorough pretransplant assessment and aggressive management of pretransplant and *de novo* comorbidities.

AUTHOR CONTRIBUTIONS

Zobair M. Younossi: substantial contributions to conception and design, acquisition of data, or analysis, and interpretation of data; drafting the article or revising it critically for important intellectual content; final approval of the version to be published. Maria Stepanova: substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; final approval of the version to be published. Reem Al Shabeeb: revising the manuscript critically for important intellectual content; final approval of the version to be published. Katherine E. Eberly: revising the manuscript critically for important intellectual content; final approval of the version to be published. Dipam Shah: revising the manuscript critically for important intellectual content; final approval of the version to be published. Veronica Nguyen: revising the manuscript critically for important intellectual content; final approval of the version to be published. Janus Ong: revising the manuscript critically for important intellectual content; final approval of the version to be published. Linda Henry: substantial contributions to the interpretation of data; drafting the article or revising it critically for important intellectual content; final approval of the version to be published. Saleh A. Alqahtani: revising the manuscript critically for important intellectual content; final approval of the version to be published.

ACKNOWLEDGMENTS

The authors thank the Hennepin Healthcare Research Institute (HHRI) for the data supplied as the contractor for the Scientific Registry of Transplant Recipients (SRTR).

CONFLICTS OF INTEREST

The authors have no conflicts to report.

ORCID

Zobair M. Younossi https://orcid.org/0000–0001–9313–577x

REFERENCES

1. Wu Z, Wang W, Zhang K, Fan M, Lin R. Trends in the incidence of cirrhosis in global from 1990 to 2019: A joinpoint and age-period-cohort analysis. J Med Virol. 2023;95:e28858.
2. Ogawa E, Chien N, Kam L, Yeo YH, Ji F, Huang DQ, et al. Association of direct-acting antiviral therapy with liver and nonliver complications and long-term mortality in patients with chronic hepatitis C. JAMA Intern Med. 2023;183:97–105.
3. Hsu YC, Huang DQ, Nguyen MH. Global burden of hepatitis B virus: Current status, missed opportunities and a call for action. Nat Rev Gastroenterol Hepatol. 2023;20:524–37.
4. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. (senior); NAFLD Nomenclature consensus group. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. Ann Hepatol. 2023;29:101133.
5. Paik JM, Kabbara K, Eberly KE, Younossi Y, Henry L, Younossi ZM. Global burden of NAFLD and chronic liver disease among adolescents and young adults. Hepatology. 2022;75:1204–7.
6. Paik JM, Golabi P, Younossi Y, Mishra A, Younossi ZM. Changes in the Global Burden of Chronic Liver Diseases from 2012 to 2017: The growing impact of NAFLD. Hepatology. 2020;72:1605–16.
7. Golabi P, Paik JM, AlQahtani S, Younossi Y, Tuncer G, Younossi ZM. Burden of non-alcoholic fatty liver disease in Asia, the Middle East and North Africa: Data from Global Burden of Disease 2009-2019. J Hepatol. 2021;75:795–809.
8. Paik JM, Golabi P, Younossi Y, Srishord M, Mishra A, Younossi ZM. The growing burden of disability related to nonalcoholic fatty liver disease: Data from the Global Burden of Disease 2007-2017. Hepatol Commun. 2020;4:1769–80.
9. Paik JM, Golabi P, Younossi Y, Saleh N, Nhyira A, Younossi ZM. The growing burden of disability related to chronic liver disease in the United States: Data from the Global Burden of Disease Study 2007-2017. Hepatol Commun. 2021;5:749–59.
10. Stepanova M, Kabbara K, Mohess D, Verma M, Roche-Green A, AlQahtani S, et al. Nonalcoholic steatohepatitis is the most common indication for liver transplantation among the elderly: Data from the United States Scientific Registry of Transplant Recipients. Hepatol Commun. 2022;6:1506–15.
11. Younossi Z, Stepanova M, Ong JP, Jacobson IM, Bugianesi E, Duseja A, et al. Global Nonalcoholic Steatohepatitis Council. Nonalcoholic steatohepatitis is the fastest growing cause of hepatocellular carcinoma in liver transplant candidates. Clin Gastroenterol Hepatol. 2019;17:748–55.e3.
12. Younossi ZM, Stepanova M, Ong J, Trimble G, AlQahtani S, Younossi I, et al. Nonalcoholic steatohepatitis is the most rapidly increasing indication for liver transplantation in the United States. Clin Gastroenterol Hepatol. 2021;19:580–9.e5.
13. Younossi ZM, Harring M, Younossi Y, Ong JP, Alqahtani SA, Stepanova M. The impact of NASH to liver transplantations with hepatocellular carcinoma in the United States. Clin Gastroenterol Hepatol. 2022;20:2915–7.e1.
14. Golabi P, Bush H, Stepanova M, Locklear CT, Jacobson IM, Mishra A, et al. Liver transplantation (LT) for cryptogenic cirrhosis (CC) and nonalcoholic steatohepatitis (NASH) cirrhosis: Data from the Scientific Registry of Transplant Recipients (SRTR): 1994 to 2016. Medicine (Baltimore). 2018;97:e11518.
15. United States Census. Accessed July 17, 2023. https://www2.census.gov/programs-surveys/popest/

16. Xie C, Kuo YF, Singal AK. Changing population of liver transplant recipients in the era of direct-acting antiviral therapy. J Clin Transl Hepatol. 2020;8:262–6.
17. Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: A modelling study. Lancet Gastroenterol Hepatol. 2022;7:396–415.
18. Tabrizian P, Saberi B, Holzner ML, Rocha C, Kyung Jung Y, et al. Outcomes of transplantation for HBV- vs. HCV-related HCC: Impact of DAA HCV therapy in a national analysis of > 20,000 patients. HPB (Oxford). 2022;24:1082–90.
19. Arora SS, Axley P, Ahmed Z, Satapathy SK, Wong R, Kuo YF, et al. Decreasing frequency and improved outcomes of hepatitis C-related liver transplantation in the era of direct-acting antivirals —a retrospective cohort study. Transpl Int. 2019;32:854–64.
20. Organ Procurement and Transplantation Network (OPTN). 2022 organ transplants again set annual records; organ donation from deceased donors continues 12-year record-setting trend. https://optn.transplant.hrsa.gov/news/2022-organ-transplants-again-set-annual-records-organ-donation-from-deceased-donors-continues-12-year-record-setting-trend/ 7/17/2023
21. Liver and Intestinal Transplantation Committee. OPTN Policy Notice Liver and Intestine Distribution Using Distance from Donor Hospital. Accessed July 17, 2023. https://optn.transplant.hrsa.gov/media/2788/liver_policynotice_201901.pdf
22. OPTN. Briefing to the OPTN Board of Directors on Enhance Transplant Program Performance Monitoring System. Accessed July 17, 2023. https://optn.transplant.hrsa.gov/media/yctffgt2/20211206-bp-mpsc-enhnc-tx-prgrm-prfrmnc-mntrng-syst.pdf
23. Ferrarese A, Battistella S, Germani G, Russo FP, Senzolo M, Gambato M, et al. Nash up, virus down: How the waiting list is changing for liver transplantation: Single center experience from Italy. Medicina (Kaunas). 2022;58:290.
24. Delman AM, Ammann AM, Shah SA. The current status of virus-positive liver transplantation. Curr Opin Organ Transplant. 2021;26:160–7.
25. Shaikh OS, Rogal S, Malik A, Sharma V, Cacciarelli T. Liver transplant from increased-risk donors in the era of direct-acting antivirals for hepatitis C. Exp Clin Transplant. 2020;18:605–11.
26. Wanis KN, Madenci AL, Dokus MK, Tomiyama K, Al-Judaibi BM, Hernán MA, et al. The effect of the opioid epidemic on donation after circulatory death transplantation outcomes. Transplantation. 2019;103:973–9.
27. Durand CM, Bowring MG, Thomas AG, et al. The drug overdose epidemic and deceased-donor transplantation in the United States: A national registry study. Ann Intern Med. 2018;168:702–11.
28. Lee BP, Vittinghoff E, Dodge JL, Cullaro G, Terrault NA. National trends and long-term outcomes of liver transplant for alcohol-associated liver disease in the United States. JAMA Intern Med. 2019;179:340–8.
29. Asrani SK, Trotter J, Lake J, Ahmad A, Bonagura A, Cameron A, et al. Meeting report: The Dallas consensus conference on liver transplantation for alcohol associated hepatitis. Liver Transplant. 2020;26:127–40.
30. Haldar D, Kern B, Hodson J, Armstrong MJ, Adam R, Berlakovich G, et al. Outcomes of liver transplantation for non-alcoholic steatohepatitis: A European Liver Transplant Registry study. J Hepatol. 2019;71:313–22.
31. Kardashian A, Serper M, Terrault N, Nephew LD. Health disparities in chronic liver disease. Hepatology. 2023;77:1382–403.
32. Maddur H, Shah VH. Alcohol and liver function in women. Alcohol Res Curr Rev. 2020;40:10.
33. Harding KD, Whittingham L, McGannon KR. #sendwine: An analysis of motherhood, alcohol use and #winemom culture on Instagram. Subst Abuse Res Treat. 2021;15:11782218211015196.
34. Sohal A, Khalid S, Green V, Gulati A, Roytman M. The pandemic within the pandemic: Unprecedented rise in alcohol-related hepatitis during the COVID-19 pandemic. J Clin Gastroenterol. 2022;56:e171–5.
35. Wong T, Dang K, Ladhani S, Singal AK, Wong RJ. Prevalence of alcoholic fatty liver disease among adults in the United States, 2001–2016. JAMA. 2019;321:1723–5; 37.
36. Mellinger JL, Shedden K, Winder GS, Tapper E, Adams M, Fontana RJ, et al. The high burden of alcoholic cirrhosis in privately insured persons in the United States. Hepatology. 2018;68:872–82.
37. Pinedo M. A current re-examination of racial/ethnic disparities in the use of substance abuse treatment: Do disparities persist? Drug Alcohol Depend. 2019;202:162–7.
38. Rogal S, Youk A, Zhang H, Gellad WF, Fine MJ, Good CB, et al. Impact of alcohol use disorder treatment on clinical outcomes among patients with cirrhosis. Hepatology. 2020;71:2080–92.
39. Moon AM, Yang JY, Barritt AS, Bataller R, Peery AF. Rising mortality from alcohol-associated liver disease in the United States in the 21st century. Am J Gastroenterol. 2020;115:79–87.
40. Henson JB, Wilder JM, Kappus MR, Barbas AS, Moylan CA, Niedzwiecki D, et al. Transplant outcomes in older patients with nonalcoholic steatohepatitis compared to alcohol-related liver disease and hepatitis C. Transplantation. 2020;104:e164–73.
41. Tsochatzis EA, Watt KD, VanWagner LB, Verna EC, Berzigotti A. Evaluation of recipients with significant comorbidity—patients with cardiovascular disease. J Hepatol. 2023;78:1089–4.
42. VanWagner LB, Lapin B, Levitsky J, Wilkins JT, Abecassis MM, Skaro AI, et al. High early cardiovascular mortality after liver transplantation. Liver transplant. 2014;20:1306–6.
43. De Luca L, Kalafateli M, Bianchi S, Alasaker N, Buzzetti E, Rodríguez-Perálvarez M, et al. Cardiovascular morbidity and mortality is increased post-liver transplantation even in recipients with no pre-existing risk factors. Liver Int. 2019;39:1557–65.
44. Minich A, Arisar FAQ, Shaikh NS, Herman L, Azhie A, Orchanian-Cheff A, et al. Predictors of patient survival following liver transplant in non-alcoholic steatohepatitis: A systematic review and meta-analysis. EClinicalMedicine. 2022;50:101534.
45. Van Dongen C, Paik JM, Harring M, Younossi Y, Price JK, Kabbara K, et al. Sarcopenia, healthy living, and mortality in patients with chronic liver diseases. Hepatol Commun. 2022;6:3140–53.
46. Harring M, Golabi P, Paik JM, Shah D, Racila A, Cable R, et al. Sarcopenia among patients with nonalcoholic fatty liver disease (NAFLD) is associated with advanced fibrosis. Clin Gastroenterol Hepatol. 2023;21:2876–88.e5.
47. Golabi P, Gerber L, Paik JM, Deshpande R, de Avila L, Younossi ZM. Contribution of sarcopenia and physical inactivity to mortality in people with non-alcoholic fatty liver disease. JHEP Rep. 2020;2:100171.
48. Tandon P, Zanetto A, Piano S, Heimbach JK, Dasarathy S. Liver transplantation in the patient with physical frailty. J Hepatol. 2023;78:1105–7.

How to cite this article: Younossi ZM, Stepanova M, Al Shabeeb R, Eberly KE, Shah D, Nguyen V, et al. The changing epidemiology of adult liver transplantation in the United States in 2013-2022: The dominance of metabolic dysfunction–associated steatotic liver disease and alcohol-associated liver disease. Hepatol Commun. 2024;8:e0352. https://doi.org/10.1097/HC9.0000000000000352