Final Report

OPTN Liver and Intestine Transplantation Committee | Descriptive Data Request

Update Liver Diagnosis Code Nomenclature and Treatment Options for Hepatocellular Carcinoma (HCC) Exceptions Six-Month Monitoring Report

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Executive Summary

This report provides a review of the six months after implementation of updates to treatment options for hepatocellular carcinoma (HCC) exceptions and liver diagnosis code nomenclature.

After the implementation of updates to treatment options for HCC exceptions:

- 4 HCC exception forms utilized "Histotripsy" as a locoregional treatment option post-implementation.
- 44 HCC exception forms utilized "Other" as a locoregional treatment option post-implementation.

As for the updates of liver diagnosis nomenclature codes on Transplant Candidate Registration (TCR) forms:

- 18.5% of the included TCR forms listed "Cirrhosis: Fatty Liver (NASH)" (diagnosis code 4214) as the primary diagnosis pre-implementation.
- 15.9% of the included TCR forms listed "Cirrhosis: metabolic dysfunction-associated steatohepatitis (MASH)" (diagnosis code 4221) as the primary diagnosis post-implementation.
- 3.2% of the included TCR forms listed "Cirrhosis: Metabolic Dysfunction And Alcohol-Related - Associated Liver Disease (MetALD)" (diagnosis code 4222) as the primary diagnosis post-implementation.

As for the updates of liver diagnosis nomenclature codes on Transplant Recipient Registration (TRR) forms:

- 18.5% of the included TRR forms listed "Cirrhosis: Fatty Liver (NASH)" (diagnosis code 4214) as the primary diagnosis pre-implementation.
- 15.9% of the included TRR forms listed "Cirrhosis: metabolic dysfunction-associated steatohepatitis (MASH)" (diagnosis code 4221) as the primary diagnosis post-implementation.
- 2.3% of the included TRR forms listed "Cirrhosis: Metabolic Dysfunction And Alcohol-Related - Associated Liver Disease (MetALD)" (diagnosis code 4222) as the primary diagnosis post-implementation.

Background/Purpose

In March 2024, the OPTN Executive Committee approved updates to treatment options for hepatocellular carcinoma (HCC) exceptions and liver diagnosis code nomenclature.[1]

The first implementation phase, implemented 08/01/2024, updated the OPTN Waiting List to include 'Histotripsy' and 'Other' as locoregional treatment options for initial and extension exception requests for liver candidates with HCC. The addition of 'Histotripsy' and 'Other' as locoregional treatment options affected only the HCC exception form. Histotripsy is a recently approved therapy for the treatment of liver cancer. It is considered to be an innovative, non-invasive treatment for liver cancer that uses a robotic machine to target and destroy cancer tissue with ultra-precise sound waves and has been approved by the U.S. Food and Drug Administration (FDA).[2]

The second phase, implemented 10/10/2024, deactivated the diagnosis code of "Cirrhosis: fatty liver (NASH)" (diagnosis code 4214) and added two new diagnosis codes: "Cirrhosis: metabolic dysfunction-associated steatohepatitis (MASH)" (diagnosis code 4221) and "Cirrhosis: metabolic dysfunction and alcohol-related/associated liver disease (MetALD)" (diagnosis code 4222). These nomenclature changes affected Transplant Candidate Registration (TCR) forms, Transplant Recipient Registration (TRR) forms, and Transplant Recipient Followup (TRF) forms. These proposed changes result from a recent multisociety Delphi consensus statement that terminology related to nonalcoholic fatty liver disease (NAFLD) was outdated. It has been noted that while the nomenclature is widely used, it has been appreciated that the term "nonalcoholic" did not accurately capture what the etiology of the disease was, and notably, the term "fatty" has been considered to be stigmatizing by some.[3]

Monitoring Plan

Monitoring of these changes will be performed at approximately 6 months and 1 year post-implementation.

Relevant analyses for locoregional treatment options, stratified by various features as sample size permits:

- Table and figure: Number and proportion of treatment options used in the pre-implementation era compared to the post-implementation era

This report also includes the following metrics to evaluate the impact of the diagnosis nomenclature changes, stratified by various features as sample size permits:

- Table to compare the counts and proportions of TCR diagnoses selected in the pre-implementation era compared to the post-implementation era

Data, Methods, and Cohorts

Data Sources:

These analyses use data from the OPTN Waiting List, TCR forms, TRR forms, and HCC exception forms. Analyses are based on OPTN data as of June 13, 2025 and are subject to change based on future data submission or correction.

Methods and Cohorts:

The locoregional therapy cohort included initial and extension HCC forms submitted between 01/31/2024 - 07/31/2024 (pre-implementation) and 08/01/2024 - 01/30/2025 (post-implementation).

The diagnosis nomenclature cohort included any validated TCR form between 04/10/2024 - 10/09/2024 (pre-implementation) and 10/10/2024 - 04/10/2025 (post-implementation). The TCR form's validation date determined the pre- or post-implementation era. If a TCR form's diagnosis was updated, the most recent form in each era was used in these analyses. This same approach was applied for the TRR forms.

Counts and percentages were used to summarize categorical variables or characteristics.

Analyses are based on OPTN data as of June 13, 2025 and are subject to change based on future data submission or correction.

Results

Locoregional Treatment Therapies

This section of the report examines the utilization of the various locoregional treatment options in the pre- and post-implementation eras.

There were 7590 HCC exception forms included in these analyses. The proportion of initial and extension forms were similar in the pre- and post-implementation era.

Table 1. Initial and Extension HCC Request Forms Submitted by Implementation Era

	Pre-Implementation Era	Post-Implementation Era
Application Type	N (%)	N (%)
Initial	1,593 (40.9%)	1,532 (41.5%)
Extension	2,306 (59.1%)	2,159 (58.5%)
Total	3,899 (100.0%)	3,691 (100.0%)

Based on OPTN data as of 2025-06-13.

Data subject to change based on future data submission or correction.

Across the pre- and post-implementation eras, 44.5% of HCC exception forms (n = 7590) listed any locoregional therapy treatments (43.7% pre-implementation and 45.3% post-implementation). 7.9% of forms had more than one locoregional therapy treatment listed.

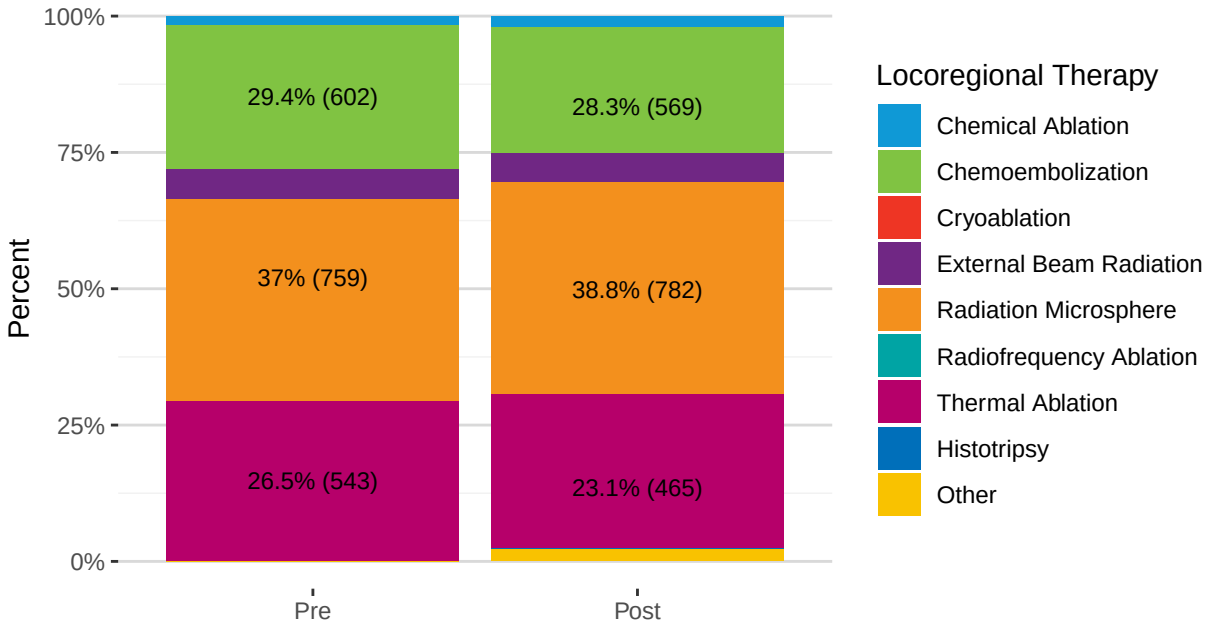
There were 4 forms that utilized histotripsy in the post-implementation era. Of these, 1 was an initial submission and 3 were extensions. Further, 3 of these were auto-approved (all extension forms) and the remaining form (initial) was reviewed by the National Liver Review Board (NLRB).

Table 2. Locoregional Treatment Therapies by Implementation Era

	Pre-Implementation Era	Post-Implementation Era
Treatment	N (%)	N (%)
Chemical Ablation	34 (1.7%)	41 (2.0%)
Chemoembolization	543 (26.5%)	465 (23.1%)
Cryoablation	0 (0.0%)	0 (0.0%)
External Beam Radiation	111 (5.4%)	108 (5.4%)
Radiation Microsphere	759 (37.0%)	782 (38.8%)
Radiofrequency Ablation	0 (0.0%)	0 (0.0%)
Thermal Ablation	602 (29.4%)	569 (28.3%)
Histotripsy	0 (0.0%)	4 (0.2%)
Other	0 (0.0%)	44 (2.2%)
Total	2,049 (100.0%)	2,013 (100.0%)

4062 locoregional therapy treatments from 3375 unique candidates; 4215 candidates with no reported locoregional therapy treatments reported excluded.
Based on OPTN data as of 2025-06-13.
Data subject to change based on future data submission or correction.

Figure 1. Locoregional Treatment Therapies by Implementation Era



Label is omitted for categories containing <10% of forms.
4062 locoregional therapy treatments from 3375 unique candidates.
4215 candidates with no reported locoregional therapy treatments reported excluded.
Based on OPTN data as of 2025−06−13.
Data subject to change based on future data submission or correction.

Liver Diagnosis Code Nomenclature

This section of the report examines the utilization of liver diagnoses in the pre- and post-implementation eras.

Throughout this section, diagnoses are grouped into the following larger categories:

- The "Cirrhosis: Fatty Liver (NASH)" diagnosis group contains the following diagnosis codes: 4214.
- The "Cirrhosis: Metabolic Dysfunction - Associated Steatohepatitis (MASH)" diagnosis group contains the following diagnosis codes: 4221.
- The "Cirrhosis: Metabolic Dysfunction And Alcohol-Related - Associated Liver Disease (MetALD)" diagnosis group contains the following diagnosis codes: 4222.
- The "Acute Hepatic Necrosis" diagnosis group contains the following diagnosis codes: 4100, 4101, 4102, 4103, 4104, 4105, 4106, 4107, 4108, 4110.
- The "Cirrhosis" diagnosis group contains the following diagnosis codes: 4200, 4201, 4202, 4203, 4204, 4205, 4206, 4207, 4208, 4209, 4210, 4212, 4213, 4218, 4219.
- The "Alcohol-Related Liver Disease" diagnosis group contains the following diagnosis codes: 4215, 4216, 4217.
- The "Cholestatic Liver Disease/Cirrhosis" diagnosis group contains the following diagnosis codes: 4220, 4260.
- The "PSC/SSC" diagnosis group contains the following diagnosis codes: 4230, 4231, 4235, 4240, 4241, 4242, 4245.
- The "Biliary Atresia" diagnosis group contains the following diagnosis codes: 4270, 4275.
- The "Metabolic Disease" diagnosis group contains the following diagnosis codes: 4300, 4301, 4302, 4303, 4304, 4305, 4306, 4307, 4308, 4315.
- The "Malignant Neoplasms" diagnosis group contains the following diagnosis codes: 4400, 4401, 4402, 4403, 4404, 4405, 4410.
- The "Benign Neoplasms" diagnosis group contains the following diagnosis codes: 4450, 4451, 4455.
- The "Graft Failure" diagnosis group contains the following diagnosis codes: 4598.

There were 15229 TCR forms validated across both eras (7629 in the pre-implementation era and 7600 in the post-implementation era).

18.5% of the included forms in the pre-implementation era had a primary diagnosis of Cirrhosis: Fatty Liver (NASH). As intended, there were 0 NASH cases in the post-implementation era.

15.9% of the included forms in the post-implementation era had a primary diagnosis of Cirrhosis: Metabolic Dysfunction - Associated Steatohepatitis (MASH). As intended, there were 0 MASH cases in the pre-implementation era.

3.2% of the included forms in the post-implementation era had a primary diagnosis of Cirrhosis: Metabolic Dysfunction And Alcohol-Related/Associated Liver Disease (MetALD). As intended, there were 0 MetALD cases in the pre-implementation era.

Roughly 50% of all TCR forms listed Cirrhosis as the primary diagnosis in both eras.

Table 3. TCR Primary Diagnoses by Era

	Pre-Implementation Era	Post-Implementation Era
Primary Diagnosis	N (%)	N (%)
NASH	1,413 (18.5%)	0 (0.0%)
MASH	0 (0.0%)	1,211 (15.9%)
MetALD	0 (0.0%)	245 (3.2%)
Acute Hepatic Necrosis	152 (2.0%)	160 (2.1%)
Benign Neoplasms	67 (0.9%)	77 (1.0%)
Biliary Atresia	121 (1.6%)	145 (1.9%)
Cholestatic Liver Disease/Cirrhosis	186 (2.4%)	174 (2.3%)
Graft Failure	140 (1.8%)	156 (2.1%)
Metabolic Disease	155 (2.0%)	147 (1.9%)
Malignant Neoplasms	823 (10.8%)	814 (10.7%)
PSC/SSC	251 (3.3%)	284 (3.7%)
Cirrhosis	3,876 (50.8%)	3,661 (48.2%)
Other Specify	343 (4.5%)	415 (5.5%)
Other	102 (1.3%)	111 (1.5%)
Total	7,629 (100.0%)	7,600 (100.0%)

Based on OPTN data as of 2025-06-13.

Data subject to change based on future data submission or correction.

3.6% of the included forms in the pre-implementation era had a secondary diagnosis of Cirrhosis: Fatty Liver (NASH). As intended, there were 0 NASH cases in the post-implementation era.

2.8% of the included forms in the post-implementation era had a secondary diagnosis of Cirrhosis: Metabolic Dysfunction - Associated Steatohepatitis (MASH). As intended, there were 0 MASH cases in the pre-implementation era.

0.5% of the included forms in the post-implementation era had a secondary diagnosis of Cirrhosis: Metabolic Dysfunction And Alcohol-Related/Associated Liver Disease (MetALD). As intended, there were 0 MetALD cases in the pre-implementation era.

In both the pre- and post-implementation eras, most of the TCR forms did not list a secondary diagnosis, but, of those that did, cirrhosis was the most common.

Table 4. TCR Secondary Diagnoses by Era

	Pre-Implementation Era	Post-Implementation Era
Primary Diagnosis	N (%)	N (%)
NASH	274 (3.6%)	0 (0.0%)
MASH	0 (0.0%)	214 (2.8%)
MetALD	0 (0.0%)	40 (0.5%)
Acute Hepatic Necrosis	24 (0.3%)	23 (0.3%)
Benign Neoplasms	1 (0.0%)	2 (0.0%)
Biliary Atresia	4 (0.1%)	2 (0.0%)
Cholestatic Liver Disease/Cirrhosis	34 (0.4%)	42 (0.6%)
Graft Failure	10 (0.1%)	3 (0.0%)
Metabolic Disease	67 (0.9%)	44 (0.6%)
Malignant Neoplasms	376 (4.9%)	355 (4.7%)
PSC/SSC	48 (0.6%)	48 (0.6%)
Cirrhosis	564 (7.4%)	498 (6.6%)
Other Specify	90 (1.2%)	101 (1.3%)
Other	4 (0.1%)	11 (0.1%)
None listed	6,133 (80.4%)	6,217 (81.8%)
Total	7,629 (100.0%)	7,600 (100.0%)

Based on OPTN data as of 2025-06-13.

Data subject to change based on future data submission or correction.

There were 11676 TRR forms validated across both eras (5918 in the pre-implementation era and 5758 in the post-implementation).

18.5% of the included forms in the pre-implementation era had a primary diagnosis of Cirrhosis: Fatty Liver (NASH). The 2 cases of NASH in the post-implementation era were validated on the day of implementation.

15.9% of the included forms in the post-implementation era had a primary diagnosis of Cirrhosis: Metabolic Dysfunction - Associated Steatohepatitis (MASH). As intended, there were 0 MASH cases in the pre-implementation era.

2.3% of the included forms in the post-implementation era had a primary diagnosis of Cirrhosis: Metabolic Dysfunction And Alcohol-Related/Associated Liver Disease (MetALD). As intended, there were 0 MetALD cases in the pre-implementation era.

Roughly 50% of all TRR forms listed Cirrhosis as the diagnosis in both eras.

Table 5. TRR Primary Diagnoses by Era

	Pre-Implementation Era	Post-Implementation Era
Primary Diagnosis	N (%)	N (%)
NASH	1,095 (18.5%)	2 (0.0%)
MASH	0 (0.0%)	915 (15.9%)
MetALD	0 (0.0%)	133 (2.3%)
Acute Hepatic Necrosis	95 (1.6%)	79 (1.4%)
Benign Neoplasms	40 (0.7%)	63 (1.1%)
Biliary Atresia	114 (1.9%)	94 (1.6%)
Cholestatic Liver Disease/Cirrhosis	163 (2.8%)	151 (2.6%)
Graft Failure	111 (1.9%)	116 (2.0%)
Metabolic Disease	142 (2.4%)	131 (2.3%)
Malignant Neoplasms	670 (11.3%)	665 (11.5%)
PSC/SSC	220 (3.7%)	214 (3.7%)
Cirrhosis	2,941 (49.7%)	2,752 (47.8%)
Other Specify	241 (4.1%)	373 (6.5%)
Other	86 (1.5%)	70 (1.2%)
Total	5,918 (100.0%)	5,758 (100.0%)

Based on OPTN data as of 2025-06-13.

Data subject to change based on future data submission or correction.

Conclusion

In the six months following the implementation of histotripsy as a locoregional therapy option, relatively few hepatocellular carcinoma candidates who submitted medical urgency exception forms utilized histotripsy.

In the six months following the implementation of the new diagnosis codes, the proportions of candidates with a listed diagnosis of Cirrhosis: Fatty Liver (NASH) prior to implementation were comparable to the sum of the proportions of Cirrhosis: metabolic dysfunction-associated steatohepatitis (MASH) and Cirrhosis: Metabolic Dysfunction And Alcohol-Related - Associated Liver Disease (MetALD) diagnoses post-implementation, across both primary and secondary diagnoses in the TCR and TRR forms.

References

1. Organ Procurement and Transplantation Network. (2024, March 19). Liver and Intestinal Organ Committee: Mini briefing paper [PDF]. U.S. Department of Health & Human Services. https://optn.transplant.hrsa.gov/media/1xepyey0/20240319_optn_liver-and-intestinal-organ-committee_minibrief.pdf
2. University of Chicago Medicine. (n.d.). Histotripsy – Cancer types & treatments. Retrieved July 17, 2025, from https://www.uchicagomedicine.org/cancer/types-treatments/histotripsy
3. Rinella, Lazarus, et al. (2023). A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology, 78(6), 1966–1986. https://doi.org/10.1097/HEP.0000000000000520