

**Supplemental Table 1. Definition of patient characteristics based on diagnostic ICD9 codes recorded at least twice in inpatient or outpatient records.**

<b>Characteristic</b>	<b>Definition</b>
Cirrhosis	571.2 Alcoholic Cirrhosis Of Liver 571.5 Cirrhosis Of Liver Without Mention Of Alcohol 456.0 Esophageal Varices With Bleeding 456.1 Esophageal Varices Without Mention Of Bleeding 456.20 Esophageal Varices In Diseases Classified Elsewhere, With Bleeding 456.21 Esophageal Varices In Diseases Classified Elsewhere, Without Mention Of Bleeding 789.5 Ascites 567.23 Spontaneous Bacterial Peritonitis 572.2 Hepatic Coma or hepatic encephalopathy 070.44 Chronic hepatitis C with coma 572.4 Hepatorenal syndrome
Decompensated cirrhosis	456.0 Esophageal Varices With Bleeding 456.1 Esophageal Varices Without Mention Of Bleeding 456.20 Esophageal Varices In Diseases Classified Elsewhere, With Bleeding 456.21 Esophageal Varices In Diseases Classified Elsewhere, Without Mention Of Bleeding 789.5 Ascites 567.23 Spontaneous Bacterial Peritonitis 572.2 Hepatic Coma or hepatic encephalopathy 070.44 Chronic hepatitis C with coma 572.4 Hepatorenal syndrome
Compensated cirrhosis	571.2 Alcoholic Cirrhosis Of Liver 571.5 Cirrhosis Of Liver Without Mention Of Alcohol
Hepatocellular carcinoma	ICD9 155.0 Hepatocellular carcinoma
Diabetes Mellitus Type 2	250.00-250.92 Diabetes
Alcohol Use Disorders	305.0-305.03 alcohol abuse disorders 303.9-303.93 alcohol dependence 291.81 alcohol withdrawal 291.0 alcohol withdrawal delirium 291.8 other specified alcohol-induced mental disorders 291.9 unspecified alcohol-induced mental disorders 303.00 Acute alcohol intoxication 577 pancreatitis 2/2 etoh 357 alcoholic polyneuropathy 425.5 cardiomyopathy 2/2 alcohol 980.9 toxic effect of alcohol 305.00 Non-dependent alcohol abuse 571.0x alcoholic fatty liver 571.1x acute alcoholic hepatitis 571.3x alcoholic liver damage, unspec 571.2 alcoholic cirrhosis of liver
Hemochromatosis	275.0 hemochromatosis (MUST exclude 275.1, 275.2 etc)
Primary Biliary Cirrhosis	571.6 primary biliary cirrhosis
Autoimmune hepatitis	571.32 autoimmune hepatitis
Primary sclerosing cholangitis	576.1 cholangitis

**Supplemental Table 2. Definitions of categories for etiology of cirrhosis<sup>35</sup>**

Etiology of Cirrhosis*	Definition
Hepatitis C virus (HCV)	Patients with a positive serum HCV RNA were categorized as HCV regardless of any additional etiologies
Alcoholic liver disease (ALD)	Patients with ICD-9 codes for alcohol use disorders in the absence of serological markers of chronic HCV or HBV infection and in the absence if ICD9 codes for hemochromatosis, primary biliary cirrhosis, primary sclerosing cholangitis, and autoimmune hepatitis
Non-alcoholic fatty liver disease (NAFLD)	Patients with diabetes (ICD-9 code 250- 250.92, recorded at least twice) or body mass index (BMI) $\geq 30$ kg/m <sup>2</sup> prior to the diagnosis of cirrhosis, who <i>did not have</i> HCV, HBV, ALD (defined as above) or ICD9 codes for hemochromatosis, primary biliary cirrhosis, primary sclerosing cholangitis, and autoimmune hepatitis. NAFLD-related cirrhosis does not have pathognomonic serological, radiological, or histological features - even hepatic steatosis is frequently absent after cirrhosis develops. Hence, we adapted a clinical definition of NAFLD based on previous work that reflects the diagnostic process used in clinical practice, in which NAFLD is suspected in the presence of risk factors such as obesity and diabetes after exclusion of other etiologies.
Other	All other patients not meeting criteria above for HCV, ALD or NAFLD

\* These definitions were necessarily designed to be mutually exclusive.

**Supplemental Table 3. Determination of whether an abdominal ultrasound scan was done for screening or non-screening indications.**

Assignment of Indication	Indication reported in ultrasound report or in the ordering provider progress notes before and after the USS was ordered and performed
a. Definitely screening*	HCC (or hepatoma, or liver cancer) screening or surveillance in patients with no new symptoms, signs or tests suggestive of HCC. <u>Indications completely unrelated to liver disease such as:</u> Abdominal aortic aneurysm screening; Follow-up renal cysts etc
b. Definitely non-screening	<u>As workup of any symptoms or signs that might be suggestive of HCC including:</u> Elevated (or worsening) liver function tests; New ascites; Weight loss; Abdominal pain; Abdominal tenderness; Abdominal mass; Abdominal distension; Abdominal bloating; Enlarged liver; Palpable liver; Failure to thrive; Jaundice; Increased bilirubin; Variceal Bleeding; Fever.  <u>As a follow-up of another positive test suggestive of HCC:</u> Abnormal AFP; Liver abnormality on abdominal ultrasound; Liver abnormality on abdominal CT or MRI scan.  Any test done in the Emergency Room or as an Inpatient.
c. Probably screening	Screen for HCC and patient also has ascites or encephalopathy (when the ascites or encephalopathy are long-standing or unchanged)†.
d. Probably non-screening	Unclear if patient has symptoms or signs suspicious of HCC

\* Only record as “definitely screening” if there is no simultaneous “non-screening” indication.

† This refers to tests where the provider seems to be ordering the USS with the intention of screening for HCC but also wants a comment on the degree of ascites that is long-standing and being treated, without any obvious concern that development of HCC might have contributed to the ascites or encephalopathy.

**Supplemental Table 4. Determination of whether a serum AFP test was done for screening or non-screening indications.**

Assignment of Indication	Indication reported in the ordering provider progress notes before and after the serum AFP test was ordered and performed
a. Definitely screening*	HCC (or hepatoma, or liver cancer) screening or surveillance in patients with no new symptoms, signs or tests suggestive of HCC.
b. Definitely non-screening	<p><i>As workup of any symptoms or signs that might be suggestive of HCC including:</i> Elevated (or worsening) liver function tests; New ascites; Weight loss; Abdominal pain; Abdominal tenderness; Abdominal mass; Abdominal distension; Abdominal bloating; Enlarged liver; Palpable liver; Failure to thrive; Jaundice; Increased bilirubin; Variceal Bleeding; Fever.</p> <p><i>As a follow-up of another positive test suggestive of HCC:</i> Abnormal AFP; Liver abnormality on abdominal ultrasound; Liver abnormality on abdominal CT or MRI scan.</p> <p>Any test done in the Emergency Room or as an Inpatient.</p>
c. Probably screening	Screen for HCC and patient also has ascites or encephalopathy (when the ascites or encephalopathy are long-standing or unchanged)†.
d. Probably non-screening	R/O HCC – but unclear based on documentation if patient has symptoms or signs suspicious of HCC

\* Only record as “definitely screening” if there is no simultaneous “non-screening” indication.

† This refers to serum AFP tests ordered in patients who have ascites or encephalopathy that are long-standing and being treated, without any obvious concern that development of HCC might have contributed to the ascites or encephalopathy.

**Supplemental Table 5. Comparison of cases and controls with respect to occurrence of screening for HCC with BOTH serum AFP AND USS versus only one of the two tests or none.**

	Controls N=238 n (%)	Cases N=238 n (%)	Odd Ratio (95% CI) <u>BOTH vs USS only</u>	Adjusted* OR (95% CI) <u>BOTH vs USS only</u>	Odds Ratio (95% CI) BOTH vs AFP only	Adjusted* OR (95% CI) BOTH vs AFP only	Odds Ratio (95% CI) BOTH vs NONE	Adjusted* OR (95% CI) BOTH vs NONE
<i>0-4 years prior to index date</i>								
<b>NONE</b>	49 (20.6%)	45 (18.9%)					1	1
<b>USS only</b>	14 (5.9%)	15 (6.3%)			1	1		
<b>AFP only</b>	60 (25.2%)	67 (28.2%)	1	1				
<b>BOTH</b>	115 (48.3%)	111 (46.6%)	0.86 (0.29- 2.55)	1.35 (0.38- 4.82)	0.97 (0.58- 1.61)	1.09 (0.63- 1.88)	0.90 (0.49- 1.68)	0.87 (0.44- 1.72)
<i>0-3 years prior to index date</i>								
<b>NONE</b>	61 (25.6%)	56 (23.5%)					1	1
<b>USS only</b>	13 (5.5%)	14 (5.9%)			1	1		
<b>AFP only</b>	60 (25.2%)	70 (29.4%)	1	1				
<b>BOTH</b>	104 (43.7%)	98 (41.2%)	0.86 (0.29- 2.55)	1.23 (0.35- 4.33)	0.75 (0.44- 1.27)	0.84 (0.48- 1.48)	1.15 (0.63- 2.09)	1.21 (0.63- 2.33)
<i>0-2 years prior to index date</i>								
<b>NONE</b>	78 (32.8%)	73 (30.7%)					1	1
<b>USS only</b>	15 (6.3%)	14 (5.9%)			1	1		
<b>AFP only</b>	65 (27.3%)	74 (31.1%)	1	1				
<b>BOTH</b>	80 (33.6%)	77 (32.4%)	1.67 (0.40- 6.97)	2.07 (0.44- 9.66)	0.63 (0.34- 1.16)	0.79 (0.41- 1.53)	1.28 (0.69- 2.37)	1.33 (0.69- 2.57)
<i>0-1 years prior to index date</i>								
<b>NONE</b>	111 (46.6%)	95 (39.9%)					1	1
<b>USS only</b>	18 (7.6%)	22 (9.2%)			1	1		
<b>AFP only</b>	65 (27.3%)	73 (30.7%)	1	1				
<b>BOTH</b>	44 (18.5%)	48 (20.2%)	0.60 (0.14- 2.51)	0.65 (0.12- 3.62)	0.87 (0.41- 1.82)	0.97 (0.44- 2.16)	1.67 (0.81- 3.41)	1.57 (0.73- 3.34)

**\* Adjusted for age, etiology of cirrhosis, MELD score at cirrhosis diagnosis, race/ethnicity, year of cirrhosis diagnosis, diabetes, alcohol use disorders, body mass index, receipt of abdominal CT or MRI during the period of interest and eradication of HCV by antiviral treatment.**

**Supplemental Table 6. Comparison of cases and controls with respect to occurrence of DEFINITE OR PROBABLE screening ultrasound, screening AFP or either USS or AFP at given time intervals prior to the index date.**

	<b>Controls N=238 n (%)</b>	<b>Cases N=238 n (%)</b>	<b>OR (95% CI)</b>	<b>Adjusted* OR (95% CI)</b>
<i>0-4 years prior to index date</i>				
<b>USS</b>	131 (55.0%)	128 (53.8%)	0.95 (0.66-1.37)	0.94 (0.63-1.41)
<b>AFP</b>	175 (73.5%)	178 (74.8%)	1.07 (0.70-1.65)	1.09 (0.67-1.76)
<b>USS or AFP</b>	190 (79.8%)	193 (81.1%)	1.09 (0.68-1.75)	1.07 (0.66-1.75)
<i>0-3 years prior to index date</i>				
<b>USS</b>	119 (50.0%)	113 (47.5%)	0.90 (0.63-1.30)	0.89 (0.59-1.34)
<b>AFP</b>	165 (69.3%)	168 (70.6%)	1.07 (0.71-1.59)	1.13 (0.72-1.77)
<b>USS or AFP</b>	178 (74.8%)	182 (76.5%)	1.10 (0.72-1.69)	1.10 (0.70-1.73)
<i>0-2 years prior to index date</i>				
<b>USS</b>	97 (40.8%)	91 (38.2%)	0.89 (0.61-1.31)	0.88 (0.57-1.35)
<b>AFP</b>	146 (61.3%)	152 (63.9%)	1.13 (0.76-1.69)	1.22 (0.78-1.91)
<b>USS or AFP</b>	161 (67.6%)	166 (69.7%)	1.12 (0.74-1.68)	1.13 (0.73-1.74)
<i>0-1 years prior to index date</i>				
<b>USS</b>	65 (27.3%)	70 (29.4%)	1.11 (0.74-1.67)	1.08 (0.70-1.68)
<b>AFP</b>	110 (46.2%)	122 (51.3%)	1.24 (0.85-1.79)	1.25 (0.84-1.86)
<b>USS or AFP</b>	128 (53.8%)	144 (60.5%)	1.33 (0.92-1.92)	1.40 (0.95-2.07)

\* Adjusted for age, etiology of cirrhosis, MELD score at cirrhosis diagnosis, race/ethnicity, year of cirrhosis diagnosis, diabetes, alcohol use disorders, body mass index, receipt of abdominal CT or MRI during the period of interest and eradication of HCV by antiviral treatment. Also, the USS analysis was adjusted for serum AFP and the serum AFP analysis was adjusted for USS.

**Supplemental Table 7. Comparison of cases and controls with respect to occurrence of DEFINITE OR PROBABLE screening for HCC with BOTH serum AFP AND USS versus only one of the two tests or none.**

	Controls N=238 n (%)	Cases N=238 n (%)	Odd Ratio (95% CI) <u>BOTH vs USS only</u>	Adjusted* OR (95% CI) <u>BOTH vs USS only</u>	Odds Ratio (95% CI) <u>BOTH vs AFP only</u>	Adjusted* OR (95% CI) <u>BOTH vs AFP only</u>	Odds Ratio (95% CI) <u>BOTH vs NONE</u>	Adjusted* OR (95% CI) <u>BOTH vs NONE</u>
<i>0-4 years prior to index date</i>								
<b>NONE</b>	48 (20.2%)	45 (18.9%)					1	1
<b>USS only</b>	15 (6.3%)	15 (6.3%)			1	1		
<b>AFP only</b>	59 (24.8%)	65 (27.3%)	1	1				
<b>BOTH</b>	116 (48.7%)	113 (47.5%)	0.86 (0.29- 2.55)	1.37 (0.38- 4.93)	0.97 (0.58- 1.61)	1.06 (0.61- 1.83)	0.95 (0.52- 1.76)	0.93 (0.48- 1.82)
<i>0-3 years prior to index date</i>								
<b>NONE</b>	60 (25.2%)	56 (23.5%)					1	1
<b>USS only</b>	13 (5.5%)	14 (5.9%)			1	1		
<b>AFP only</b>	59 (24.8%)	69 (29.0%)	1	1				
<b>BOTH</b>	106 (44.5%)	99 (41.6%)	0.86 (0.29- 2.55)	1.23 (0.35- 4.33)	0.75 (0.44- 1.27)	0.84 (0.48- 1.48)	1.09 (0.61- 1.95)	1.12 (0.60- 2.08)
<i>0-2 years prior to index date</i>								
<b>NONE</b>	77 (32.4%)	72 (30.3%)					1	1
<b>USS only</b>	15 (6.3%)	14 (5.9%)			1	1		
<b>AFP only</b>	64 (26.9%)	75 (31.5%)	1	1				
<b>BOTH</b>	82 (34.5%)	77 (32.4%)	1.67 (0.40- 6.97)	2.07 (0.44- 9.66)	0.63 (0.34- 1.16)	0.77 (0.40- 1.47)	1.15 (0.63- 2.09)	1.18 (0.63- 2.23)
<i>0-1 years prior to index date</i>								
<b>NONE</b>	110 (46.2%)	94 (39.5%)					1	1
<b>USS only</b>	18 (7.6%)	22 (9.2%)			1	1		
<b>AFP only</b>	63 (26.5%)	74 (31.1%)	1	1				
<b>BOTH</b>	47 (19.7%)	48 (20.2%)	0.60 (0.14- 2.51)	0.65 (0.12- 3.62)	0.81 (0.39- 1.69)	0.88 (0.40- 1.93)	1.43 (0.72- 2.83)	1.31 (0.64- 2.67)

\* Adjusted for age, etiology of cirrhosis, MELD score at cirrhosis diagnosis, race/ethnicity, year of cirrhosis diagnosis, diabetes, alcohol use disorders, body mass index, receipt of abdominal CT or MRI during the period of interest and eradication of HCV by antiviral treatment.