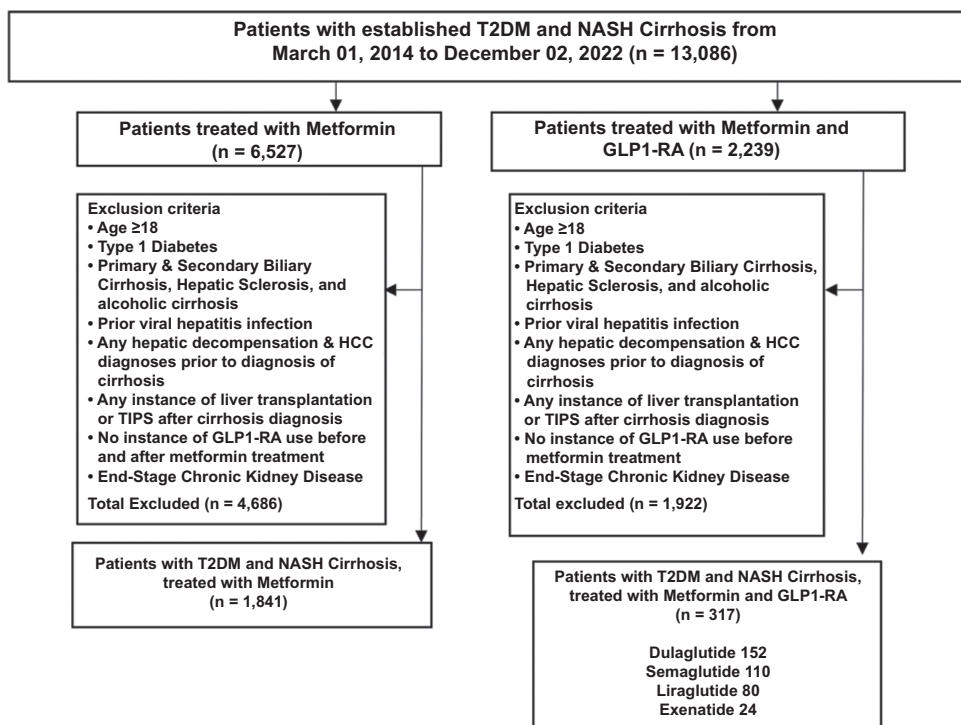
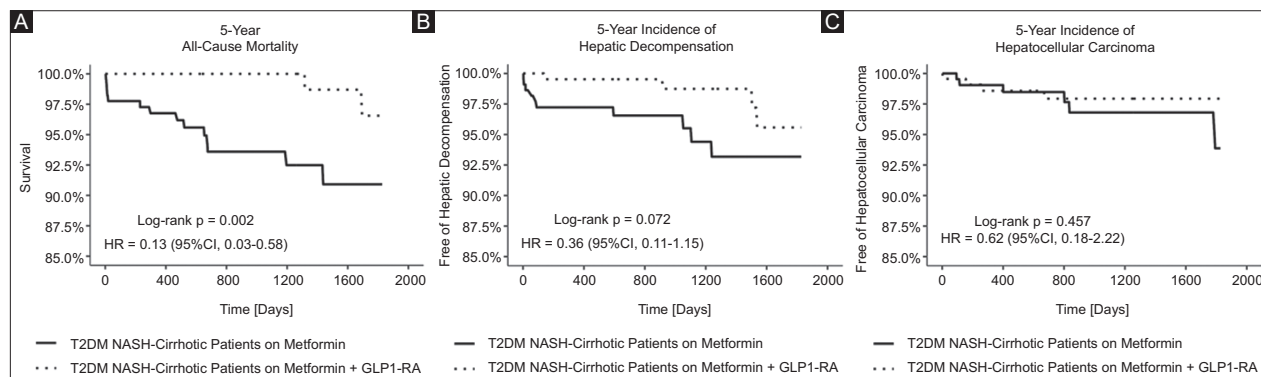


Supplementary material



Supplementary Figure 1 Cohort construction for T2DM patients with NASH cirrhosis Cohort Construction. Inclusion and exclusion criteria for patient cohort selection was based on ICD-10 coding, Current Procedural Terminology, and RxNorm terminology. For details review materials and methods

T2DM, type 2 diabetes mellitus; GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis



Supplementary Figure 2 Five-year all-cause mortality, composite hepatic decompensation, and hepatocellular carcinoma for T2DM patients with NASH cirrhosis Five-year outcomes for T2DM patients with NASH cirrhosis on metformin vs. metformin and GLP1-RA therapy. Kaplan-Meier probability values are percent free of death (A), composite hepatic decompensation (B) and hepatocellular carcinoma (C). P values indicate P log-rank test

T2DM, type 2 diabetes mellitus; NASH, nonalcoholic steatohepatitis; GLP1-RA, glucagon-like peptide-1 receptor; HR, hazard ratio; CI, confidence interval

Supplementary Table 1 Complete baseline characteristics before and after propensity score matching for T2DM cirrhosis patients

Characteristic ID	Characteristic name	Before propensity score matching			After propensity score matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
Age	Current Age	62.44±14.34	58.41±12.76	<0.001	58.69±14.99	58.53±12.84	0.770
AI	Age at Index	58.04±14.23	56.23±12.76	<0.001	56.39±14.92	56.24±12.85	0.778
F	Female	10093 (50.33)	889 (62.52)	0.001	804 (61.09)	805 (61.17)	0.968
M	Male	9959 (49.66)	533 (37.48)	<0.001	512 (38.91)	511 (38.83)	0.968
UN	Unknown Gender	10 (0.05)	0 (0)	0.400	0 (0)	0 (0)	NA
2106-3	White	13315 (66.4)	1007 (70.82)	<0.001	943 (71.66)	934 (70.97)	0.698
1002-5	American Indian or Alaska Native	202 (1.01)	11 (0.77)	0.390	11 (0.84)	11 (0.84)	>0.99
2028-9	Asian	571 (2.85)	30 (2.11)	0.103	30 (2.28)	29 (2.2)	0.895
2054-5	Black or African American	2960 (14.76)	205 (14.42)	0.723	163 (12.39)	181 (13.75)	0.298
2076-8	Native Hawaiian or Other Pacific Islander	25 (0.12)	10 (0.7)	<0.001	10 (0.76)	10 (0.76)	>0.99
2131-1	Unknown Race	2980 (14.86)	168 (11.81)	<0.001	168 (12.77)	160 (12.16)	0.637
2135-2	Hispanic or Latino	2096 (10.45)	157 (11.04)	0.484	132 (10.03)	149 (11.32)	0.283
2186-5	Not Hispanic or Latino	13202 (65.84)	1009 (70.96)	<0.001	944 (71.73)	929 (70.59)	0.519
UN	Unknown Ethnicity	4755 (23.71)	256 (18)	<0.001	240 (18.24)	238 (18.09)	0.919
N17-N19	Acute kidney failure and chronic kidney disease	2242 (11.18)	313 (22.01)	<0.001	280 (21.28)	272 (20.67)	0.702
F50-F59	Behavioral syndromes associated with physiological disturbances and physical factors	654 (3.26)	143 (10.06)	<0.001	101 (7.68)	113 (8.59)	0.392
K00-K95	Diseases of the digestive system	12223 (60.95)	1224 (86.08)	<0.001	1088 (82.67)	1120 (85.11)	0.090
E00-E89	Endocrine, nutritional and metabolic diseases	15091 (75.26)	1320 (92.83)	<0.001	1176 (89.36)	1214 (92.25)	0.010
I50	Heart failure	1824 (9.1)	174 (12.24)	<0.001	149 (11.32)	165 (12.54)	0.336
I10-I16	Hypertensive diseases	10834 (54.03)	1054 (74.12)	<0.001	927 (70.44)	956 (72.64)	0.210
I20-I25	Ischemic heart diseases	3231 (16.11)	361 (25.39)	<0.001	327 (24.85)	336 (25.53)	0.686
F10-F19	Mental and behavioral disorders due to psychoactive substance use	5044 (25.15)	471 (33.12)	<0.001	423 (32.14)	434 (32.98)	0.647
E70-E88	Metabolic disorders	9761 (48.68)	1083 (76.16)	<0.001	948 (72.04)	980 (74.47)	0.159
E13	Other specified diabetes mellitus	385 (1.92)	83 (5.84)	<0.001	72 (5.47)	65 (4.94)	0.539
E65-E68	Overweight, obesity and other hyperalimentation	5755 (28.7)	883 (62.1)	<0.001	763 (57.98)	781 (59.35)	0.476
K76.0	Fatty (change of) liver, not elsewhere classified	4937 (24.62)	782 (54.97)	<0.001	697 (52.95)	663 (50.36)	0.172
K75.8	Other specified inflammatory liver diseases	1717 (8.56)	437 (30.75)	<0.001	338 (25.72)	330 (25.07)	0.695
K70.3	Alcoholic cirrhosis of liver	1099 (5.48)	73 (5.16)	0.583	60 (4.54)	69 (5.26)	0.379
B18.2	Chronic viral hepatitis C	2805 (13.99)	163 (11.43)	<0.01	154 (11.67)	152 (11.53)	0.906

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Supplementary Table 1 (Continued)

Characteristic ID	Characteristic name	Before propensity score matching			After propensity score matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
B18.1	Chronic viral hepatitis B without delta-agent	461 (2.3)	28 (1.99)	0.420	25 (1.87)	27 (2.02)	0.783
B18.0	Chronic viral hepatitis B with delta-agent	22 (0.11)	9 (0.62)	<0.001	9 (0.72)	0 (0)	<0.01
K74.6	Other and unspecified cirrhosis of liver	5103 (25.45)	718 (50.5)	<0.001	574 (43.59)	590 (44.81)	0.516
K75.4	Autoimmune hepatitis	176 (0.88)	21 (1.49)	0.014	27 (2.02)	19 (1.44)	0.244
E83.11	Hemochromatosis	199 (0.99)	21 (1.49)	0.054	17 (1.3)	19 (1.44)	0.744
E88.01	Alpha-1-antitrypsin deficiency	32 (0.16)	10 (0.62)	<0.001	9 (0.72)	9 (0.72)	>0.99
1003143	Surgery	10719 (53.45)	1083 (76.16)	<0.001	954 (72.49)	984 (74.77)	0.184
1006964	Surgical Procedures on the Digestive System	3656 (18.23)	502 (35.3)	<0.001	430 (32.67)	437 (33.21)	0.772
CV800	Ace inhibitors	5339 (26.62)	655 (46.06)	<0.001	576 (43.77)	583 (44.3)	0.783
CV805	Angiotensin ii inhibitor	2554 (12.74)	383 (26.93)	<0.001	325 (24.7)	324 (24.62)	0.964
CV300	Antiarrhythmics	5619 (28.02)	749 (52.67)	<0.001	668 (50.76)	667 (50.68)	0.969
BL110	Anticoagulants	5000 (24.93)	560 (39.38)	<0.001	516 (39.21)	513 (38.98)	0.905
CV490	Antihypertensives, other	2550 (12.72)	328 (23.07)	<0.001	297 (22.57)	304 (23.1)	0.745
HS503	Antihypoglycemics	3857 (19.23)	510 (35.87)	<0.001	459 (34.88)	450 (34.2)	0.712
CV350	Antilipemic agents	6533 (32.58)	853 (59.99)	<0.001	779 (59.2)	761 (57.83)	0.476
CV100	Beta blockers/related	5998 (29.91)	668 (46.98)	<0.001	603 (45.82)	604 (45.9)	0.969
CV200	Calcium channel blockers	3886 (19.38)	453 (31.86)	<0.001	392 (29.79)	403 (30.62)	0.641
CV700	Diuretics	6416 (32)	741 (52.11)	<0.001	641 (48.71)	664 (50.46)	0.370
BL117	Platelet aggregation inhibitors	5268 (26.27)	637 (44.8)	<0.001	559 (42.48)	573 (43.54)	0.582
HS509	Hypoglycemic agents, other	10 (0.05)	10 (0.7)	<0.001	10 (0.76)	10 (0.76)	>0.99
HS501	Insulin	5372 (26.79)	777 (54.64)	<0.001	712 (54.1)	681 (51.75)	0.226
16681	a-carbose	49 (0.23)	10 (0.66)	<0.01	10 (0.84)	10 (0.84)	>0.99
30009	Miglitol	10 (0.05)	0 (0)	0.395	0 (0)	0 (0)	-
593411	Sitagliptin	1749 (8.31)	285 (18.71)	<0.001	217 (18.3)	204 (17.2)	0.485
1100699	Linagliptin	441 (2.1)	71 (4.66)	<0.001	59 (4.98)	50 (4.22)	0.377
1368001	Alogliptin	81 (0.38)	21 (1.38)	<0.001	16 (1.35)	13 (1.1)	0.575
857974	Saxagliptin	150 (0.71)	20 (1.31)	<0.01	21 (1.77)	16 (1.35)	0.407
73044	Repaglinide	100 (0.48)	15 (0.98)	<0.01	15 (1.26)	10 (0.84)	0.315
274332	Nateglinide	29 (0.14)	10 (0.66)	<0.001	10 (0.84)	10 (0.84)	>0.99
1545653	Empagliflozin	559 (2.66)	177 (11.62)	<0.001	132 (11.13)	114 (9.61)	0.225
1373458	Canagliflozin	279 (1.33)	77 (5.06)	<0.001	60 (5.06)	48 (4.05)	0.237
1488564	Dapagliflozin	265 (1.26)	70 (4.6)	<0.001	48 (4.05)	45 (3.79)	0.751
1992672	Ertugliflozin	24 (0.11)	10 (0.66)	<0.001	12 (1.01)	10 (0.84)	0.668
4821	Glipizide	2471 (11.74)	328 (21.54)	<0.001	270 (22.77)	249 (21)	0.297
25789	Glimepiride	1360 (6.46)	165 (10.83)	<0.001	127 (10.71)	120 (10.12)	0.638
4815	Glyburide	684 (3.25)	71 (4.66)	<0.01	44 (3.71)	54 (4.55)	0.302

(Contd...)

Supplementary Table 1 (Continued)

Characteristic ID	Characteristic name	Before propensity score matching			After propensity score matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
10633	Tolazamide	10 (0.05)	0 (0)	0.395	0 (0)	0 (0)	-
2404	Chlorpropamide	10 (0.05)	0 (0)	0.395	0 (0)	0 (0)	-
10635	Tolbutamide	10 (0.05)	0 (0)	0.395	0 (0)	0 (0)	-
33738	Pioglitazone	625 (2.97)	114 (7.48)	<0.001	78 (6.58)	80 (6.74)	0.869
84108	Rosiglitazone	39 (0.18)	10 (0.66)	<0.001	10 (0.84)	10 (0.84)	>0.99
9044	Alanine aminotransferase [Enzymatic activity/volume] in Serum, Plasma or Blood	47.68 ± 71.81	44.84 ± 56.96	0.207	46.96 ± 97.39	45.39 ± 58.9	0.664
9045	Albumin [Mass/volume] in Serum, Plasma or Blood	3.86 ± 0.62	3.98 ± 0.52	<0.001	3.9 ± 0.62	3.98 ± 0.53	<0.01
9046	Alkaline phosphatase [Enzymatic activity/volume] in Serum, Plasma or Blood	101.36 ± 71.93	99.29 ± 60.36	0.362	103.06 ± 76.28	99.63 ± 62.15	0.277
16362-6	Ammonia [Moles/volume] in Plasma	131.34 ± 2036.12	37.76 ± 25.49	0.727	42.66 ± 28.43	37.71 ± 25.89	0.344
9047	Aspartate aminotransferase [Enzymatic activity/volume] in Serum or Plasma	45.04 ± 68.15	40.49 ± 54.79	0.034	40.71 ± 42.34	40.86 ± 56.83	0.948
9048	Bilirubin. direct [Mass/volume] in Serum or Plasma	0.39 ± 1.19	0.3 ± 1.11	0.070	0.37 ± 1.19	0.31 ± 1.17	0.387
9049	Bilirubin. indirect [Mass/volume] in Serum or Plasma	0.65 ± 0.83	0.61 ± 0.92	0.612	0.62 ± 0.79	0.55 ± 0.55	0.409
9050	Bilirubin. total [Mass/volume] in Serum, Plasma or Blood	0.77 ± 1.18	0.65 ± 1.01	<0.001	0.71 ± 1	0.66 ± 1.06	0.330
9083	BMI	33.12 ± 7.28	36.38 ± 7.04	<0.001	34.86 ± 7.59	36.36 ± 7.09	<0.001
9081	Body weight	207.26 ± 57.75	227.02 ± 62.27	<0.001	215.77 ± 59.45	226.93 ± 62.73	<0.001
9022	Calcium [Mass/volume] in Serum, Plasma or Blood	9.17 ± 0.77	9.35 ± 0.63	<0.001	9.17 ± 0.79	9.35 ± 0.64	<0.001
9024	Creatinine [Mass/volume] in Serum, Plasma or Blood	0.88 ± 2.05	0.88 ± 0.41	0.983	0.83 ± 0.41	0.88 ± 0.42	<0.01
9051	Gamma glutamyl transferase [Enzymatic activity/volume] in Serum or Plasma	151.17 ± 266.53	155.2 ± 285.52	0.823	143.36 ± 233.63	158.06 ± 299.43	0.576
9025	Glucose [Mass/volume] in Serum, Plasma or Blood	153.86 ± 78.54	177.88 ± 81.11	<0.001	154.12 ± 78.41	178.24 ± 82.08	<0.001
9037	Hemoglobin A1c/ Hemoglobin.total in Blood	7.24 ± 1.93	8.16 ± 2.12	<0.001	7.21 ± 1.98	8.16 ± 2.15	<0.001
9032	INR in Plasma or Blood	1.22 ± 0.98	1.15 ± 0.64	0.052	1.19 ± 0.91	1.15 ± 0.66	0.331
9020	Platelets [# /volume] in Blood	210.97 ± 92.08	221.22 ± 86.43	<0.001	215.12 ± 89.75	219.34 ± 86.01	0.282
9030	Urea nitrogen [Mass/volume] in Serum, Plasma or Blood	14.94 ± 7.97	15.59 ± 7.48	0.010	15.4 ± 7.89	15.5 ± 7.5	0.768

Characteristics ID defines baseline characteristics based on ICD-10 for diagnoses, RxNorm for medications, and CPT for procedures

BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; FIB-4, fibrosis-4; GLP1-RA, glucagon-like peptide-1 receptor agonist; INR, international normalized ratio; HbA1c, hemoglobin A1c; MELD-Na, model for end-stage liver disease; NASH, nonalcoholic steatohepatitis; T2DM, type 2 diabetes mellitus

Supplementary Table 2 Patient cohort count

Patient Count	Before Propensity Score Matching		After Propensity Score Matching	
	Metformin	Metformin + GLP1-RA	Metformin	Metformin + GLP1-RA
All	20053	1422	1316	1316
Demographic Subgroup				
Men	9959	533	397	397
Women	10093	889	774	774
White	13315	1007	737	737
Non-White	3585	233	192	192
Hispanic	2096	157	132	132
Non-Hispanic	13202	1009	857	857
Age 35-59	5742	564	491	491
Age 60-85	12429	715	644	644
NASH	1841	317	229	229

Patient cohort count was reported before and after propensity score matching

GLP1-RA, *glucagon-like peptide-1 receptor agonist*; NASH, *nonalcoholic steatohepatitis*

Supplementary Table 3 Full before and after propensity score-matched baseline characteristics for T2DM patients with NASH cirrhosis

Characteristic ID	Characteristic Name	Before Propensity Score Matching			After Propensity Score Matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
Age	Current Age	61.63±13.03	57.74±11.32	<0.001	57.95±15.12	57.83±11.53	0.923
AI	Age at Index	58.49±12.92	54.61±11.17	<0.001	54.35±14.99	54.27±11.36	0.950
F	Female	1182 (64.2)	214 (67.51)	0.256	148 (64.63)	154 (67.25)	0.554
M	Male	659 (35.8)	103 (32.49)	0.256	81 (35.37)	75 (32.75)	0.554
UN	Unknown Gender	0 (0)	0 (0)	-	0 (0)	0 (0)	-
2106-3	White	1449 (78.71)	253 (79.81)	0.657	183 (79.91)	185 (80.79)	0.814
1002-5	American Indian or Alaska Native	10 (0.54)	10 (3.16)	<0.001	10 (4.37)	10 (4.37)	>0.99
2028-9	Asian	43 (2.34)	10 (3.16)	0.384	10 (4.37)	10 (4.37)	>0.99
2054-5	Black or African American	99 (5.38)	18 (5.68)	0.827	12 (5.24)	13 (5.68)	0.837
2076-8	Native Hawaiian or Other Pacific Islander	10 (0.54)	0 (0)	0.188	0 (0)	0 (0)	-
2131-1	Unknown Race	236 (12.82)	37 (11.67)	0.570	28 (12.23)	24 (10.48)	0.556
2135-2	Hispanic or Latino	207 (11.24)	29 (9.15)	0.269	26 (11.35)	20 (8.73)	0.351
2186-5	Not Hispanic or Latino	1318 (71.59)	229 (72.24)	0.813	172 (75.11)	166 (72.49)	0.524
UN	Unknown Ethnicity	316 (17.17)	59 (18.61)	0.530	31 (13.54)	43 (18.78)	0.128
N17-N19	Acute kidney failure and chronic kidney disease	232 (12.6)	37 (11.67)	0.643	29 (12.66)	26 (11.35)	0.666
F50-F59	Behavioral syndromes associated with physiological disturbances and physical factors	150 (8.15)	27 (8.52)	0.825	18 (7.86)	18 (7.86)	>0.99
K00-K95	Diseases of the digestive system	1698 (92.23)	304 (95.9)	0.020	215 (93.89)	216 (94.32)	0.843
E00-E89	Endocrine, nutritional and metabolic diseases	1731 (94.03)	308 (97.16)	0.024	220 (96.07)	220 (96.07)	>0.99
I50	Heart failure	177 (9.61)	26 (8.2)	0.426	21 (9.17)	17 (7.42)	0.498
I10-I16	Hypertensive diseases	1363 (74.04)	230 (72.56)	0.580	157 (68.56)	164 (71.62)	0.475
I20-I25	Ischemic heart diseases	398 (21.62)	65 (20.51)	0.655	50 (21.83)	45 (19.65)	0.564

(Contd...)

Supplementary Table 3 (Continued)

Characteristic ID	Characteristic Name	Before Propensity Score Matching			After Propensity Score Matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
F10-F19	Mental and behavioral disorders due to psychoactive substance use	345 (18.74)	60 (18.93)	0.937	37 (16.16)	45 (19.65)	0.330
E70-E88	Metabolic disorders	1422 (77.24)	250 (78.86)	0.523	166 (72.49)	171 (74.67)	0.596
E13	Other specified diabetes mellitus	62 (3.37)	14 (4.42)	0.349	10 (4.37)	10 (4.37)	>0.99
E65-E68	Overweight, obesity and other hyperalimentionation	1114 (60.51)	216 (68.14)	<0.01	139 (60.7)	150 (65.5)	0.287
1003143	Surgery	1397 (75.88)	251 (79.18)	0.202	179 (78.17)	173 (75.55)	0.506
1006964	Surgical Procedures on the Digestive System	810 (44)	130 (41.01)	0.322	95 (41.49)	94 (41.05)	0.924
CV800	Ace inhibitors	726 (39.44)	138 (43.53)	0.169	79 (34.5)	91 (39.74)	0.246
CV805	Angiotensin ii inhibitor	500 (27.16)	91 (28.71)	0.568	60 (26.2)	63 (27.51)	0.752
CV300	Antiarrhythmics	873 (47.42)	157 (49.53)	0.488	106 (46.29)	106 (46.29)	>0.99
BL110	Anticoagulants	629 (34.17)	109 (34.39)	0.940	82 (35.81)	75 (32.75)	0.491
CV490	Antihypertensives, other	300 (16.3)	59 (18.61)	0.306	39 (17.03)	38 (16.59)	0.901
HS503	Antihypoglycemics	472 (25.64)	90 (28.39)	0.302	59 (25.76)	59 (25.76)	>0.99
CV350	Antilipemic agents	1108 (60.19)	216 (68.14)	<0.01	151 (65.94)	150 (65.5)	0.922
CV100	Beta blockers/related	811 (44.05)	135 (42.59)	0.627	94 (41.05)	90 (39.3)	0.703
CV200	Calcium channel blockers	491 (26.67)	87 (27.45)	0.774	55 (24.02)	61 (26.64)	0.519
CV700	Diuretics	856 (46.5)	157 (49.53)	0.318	98 (42.8)	104 (45.42)	0.572
BL117	Platelet aggregation inhibitors	765 (41.55)	141 (44.48)	0.330	101 (44.11)	101 (44.11)	>0.99
HS509	Hypoglycemic agents, other	0 (0)	88 (27.76)	<0.001	0 (0)	0 (0)	-
HS501	Insulin	627 (34.06)	147 (46.37)	<0.001	106 (46.29)	97 (42.36)	0.397
16681	a-carbose	10 (0.52)	10 (2.91)	<0.001	0 (0)	0 (0)	-
30009	Miglitol	0 (0)	0 (0)	-	0 (0)	0 (0)	-
593411	Sitagliptin	252 (13.04)	57 (16.57)	0.079	42 (18.42)	39 (17.1)	0.713
1100699	Linagliptin	39 (2.02)	16 (4.65)	<0.01	11 (4.82)	10 (4.39)	0.823
1368001	Alogliptin	10 (0.52)	10 (2.91)	<0.001	10 (4.39)	10 (4.39)	>0.99
857974	Saxagliptin	19 (0.98)	10 (2.91)	<0.01	10 (4.39)	10 (4.39)	>0.99
73044	Repaglinide	10 (0.52)	10 (2.91)	<0.001	0 (0)	0 (0)	-
274332	Nateglinide	10 (0.52)	10 (2.91)	<0.001	10 (4.39)	10 (4.39)	>0.99
1545653	Empagliflozin	98 (5.07)	43 (12.5)	<0.001	34 (14.91)	25 (10.96)	0.209
1373458	Canagliflozin	47 (2.43)	22 (6.4)	<0.001	10 (4.39)	10 (4.39)	>0.99
1488564	Dapagliflozin	39 (2.02)	14 (4.07)	0.020	10 (4.39)	10 (4.39)	>0.99
1992672	Ertugliflozin	10 (0.52)	10 (2.91)	<0.001	10 (4.39)	0 (0)	<0.01
4821	Glipizide	224 (11.59)	78 (22.67)	<0.001	37 (16.23)	44 (19.3)	0.391
25789	Glimepiride	172 (8.9)	45 (13.08)	0.015	28 (12.28)	25 (10.96)	0.661
4815	Glyburide	48 (2.48)	16 (4.65)	0.025	13 (5.7)	10 (4.39)	0.521
10633	Tolazamide	0 (0)	0 (0)	-	0 (0)	0 (0)	-
2404	Chlorpropamide	0 (0)	0 (0)	-	0 (0)	0 (0)	-

(Contd...)

Supplementary Table 3 (Continued)

Characteristic ID	Characteristic Name	Before Propensity Score Matching			After Propensity Score Matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
10635	Tolbutamide	0 (0)	0 (0)	-	0 (0)	0 (0)	-
33738	Pioglitazone	75 (3.88)	34 (9.88)	<0.001	17 (7.46)	15 (6.58)	0.714
84108	Rosiglitazone	10 (0.52)	10 (2.91)	<0.001	10 (4.39)	10 (4.39)	>0.99
9044	Alanine aminotransferase [Enzymatic activity/volume] in Serum, Plasma or Blood	60.47±56.3	63.71±46.53	0.384	54.07±43.04	65.97±48.87	0.013
9045	Albumin [Mass/volume] in Serum, Plasma or Blood	4.07±0.51	4.08±0.5	0.834	4.03±0.52	4.09±0.48	0.286
9046	Alkaline phosphatase [Enzymatic activity/volume] in Serum, Plasma or Blood	99.48±62.6	97.2±39.23	0.576	97.84±46.64	95.35±38.87	0.579
16362-6	Ammonia [Moles/volume] in Plasma	38.45±28.71	42.4±20.33	0.689	38.94±14.73	41.71±20.83	0.735
9047	Aspartate aminotransferase [Enzymatic activity/volume] in Serum or Plasma	50.6±44.95	56.05±42.22	0.074	45.94±27.94	56.57±43.82	<0.01
9048	Bilirubin. direct [Mass/volume] in Serum or Plasma	0.22±0.36	0.21±0.2	0.764	0.26±0.66	0.22±0.23	0.618
9049	Bilirubin. indirect [Mass/volume] in Serum or Plasma	0.54±0.39	0.73±1.43	0.088	0.52±0.33	0.79±1.59	0.310
9050	Bilirubin. total [Mass/volume] in Serum, Plasma or Blood	0.66±0.64	0.6±0.48	0.144	0.59±0.43	0.63±0.54	0.495
9083	BMI	35.02±6.55	37.37±5.99	<0.001	34.11±7.36	36.85±6.06	<0.01
9081	Body weight	218.64±58.45	231.93±64.74	<0.01	223.68±60.35	226.02±62.96	0.736
9022	Calcium [Mass/volume] in Serum, Plasma or Blood	9.4±0.68	9.48±0.54	0.058	9.43±0.92	9.48±0.55	0.480
9024	Creatinine [Mass/volume] in Serum, Plasma or Blood	0.83±0.31	0.82±0.33	0.860	0.8±0.29	0.82±0.34	0.454
9051	Gamma glutamyl transferase [Enzymatic activity/volume] in Serum or Plasma	109.43±154.43	136.32±267.56	0.266	104.95±105.36	109.18±100.82	0.854
9025	Glucose [Mass/volume] in Serum, Plasma or Blood	149±64.98	165.53±77.65	<0.001	147.01±69.08	162.79±72.17	0.032
9037	Hemoglobin A1c/Hemoglobin.total in Blood	7.1±1.55	7.74±1.84	<0.001	7.11±1.72	7.69±1.79	<0.01
9032	INR in Plasma or Blood	1.21±2.37	1.07±0.17	0.381	1.12±0.4	1.06±0.19	0.119
9020	Platelets [# /volume] in Blood	213.85±80.74	221.76±77.01	0.148	220.56±88.04	219.91±74.34	0.940
9030	Urea nitrogen [Mass/volume] in Serum, Plasma or Blood	13.8±6.57	14.3±5.68	0.271	14.04±5.72	14.03±5.31	0.974

Characteristics ID defines baseline characteristics based on ICD-10 for diagnoses, RxNorm for medications, and CPT for procedures

BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GLP1-RA, glucagon-like peptide-1 receptor agonist; INR, international normalized ratio; HbA1c, hemoglobin A1c; T2DM, type 2 diabetes mellitus

Supplementary Table 4 Cohort baseline FIB-4 scores

	Before PS-matching characteristics		After PS-matching characteristics	
	Metformin	Metformin + GLP1-RA	Metformin	Metformin + GLP1-RA
	FIB-4	FIB-4	FIB-4	FIB-4
All	1.79	1.54	1.56	1.64
Demographic Subgroup				
Men	2.32	1.99	2.15	1.86
Women	1.64	1.42	1.46	1.44
White	1.90	1.66	1.61	1.58
Non-White	1.79	1.25	1.49	1.30
Hispanic	1.61	1.43	1.53	1.45
Non-Hispanic	1.73	1.54	1.56	1.57
Age 35-59	1.32	1.17	1.39	1.18
Age 60-85	2.16	2.09	2.20	2.11
NASH	1.78	1.73	1.54	1.72

FIB-4 scores were calculated for each cohort based on average lab values reported by TriNetX. T2DM Cirrhosis patients treated with Metformin and GLP1-RA were further divided into demographic subgroups. T2DM NASH cirrhosis patients treated with metformin and GLP1-RA were propensity score-matched to the NASH cirrhosis metformin (n=1,841) group.

FIB-4, Fibrosis-4; GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis; T2DM, type 2 diabetes mellitus

Supplementary Table 5 Cohort baseline MELD-Na scores

	Before PS-matching characteristics		After PS-matching characteristics	
	Metformin	Metformin + GLP1-RA	Metformin	Metformin + GLP1-RA
	MELD-Na	MELD-Na	MELD-Na	MELD-Na
All	6.43	5.08	5.28	5.17
Demographic subgroup				
Men	9.15	8.18	8.92	7.55
Women	4.39	3.42	4.35	3.49
White	7.10	5.39	6.84	5.01
Non-White	6.73	4.63	4.95	4.87
Hispanic	5.22	5.20	2.92	2.90
Non-Hispanic	6.18	5.18	6.67	5.40
Age 35-59	6.22	3.58	5.11	3.26
Age 60-85	6.55	6.68	6.29	6.69
NASH	5.19	3.36	3.56	3.48

MELD-Na scores were calculated for each cohort based on average lab values reported by TriNetX. T2DM Cirrhosis patients treated with Metformin and GLP1-RA were further divided into demographic subgroups. T2DM NASH cirrhosis patients treated with metformin and GLP1-RA were propensity score-matched to the NASH cirrhosis metformin (n=1,841) group

GLP1-RA, glucagon-like peptide-1 receptor agonist; model for end-stage liver disease; NASH, nonalcoholic steatohepatitis; T2DM, type 2 diabetes mellitus

Supplementary Table 6 Study definitions

Diagnosis	ICD-10 Code For Inclusion
Type 2 diabetes	E11
Cirrhosis	K70.3, K74, K74.6, K74.2
Nonalcoholic steatohepatitis NASH	K76.0, K75.8
Ascites	R18, R18.8
Varices	I85, I85.0, I85.1, I86.4, I85.11
Hepatic Encephalopathy	G93.40, G93.41, G93.49, K72.91
Diagnosis	ICD-10 Code For Exclusion
Type 1 Diabetes	E10
Primary and Secondary Biliary Cirrhosis and Hepatic Sclerosis	K74.3, K74.1, K74.4
Viral Hepatitis	B17.1, B18.2, B19.2, B16.0, B17.0, B18.0, B19.1, B17.9, B18.1, B19.9
End Stage Chronic Kidney Disease (Stage 4 & 5)	N18.4, N18.5
Hepatocellular Carcinoma	C22.0
Procedures	Current Procedural Terminology
Transvenous intrahepatic portosystemic shunt (TIPS)	06180ZY, 37183
Liver Transplantation	47135
Medications	RxNorm
Metformin	6809
GLP1-RA	475968 liraglutide, 1534763 albiglutide, 60548 exenatide, 1991302 semaglutide, 1551291 dulaglutide
Demographics	
Non-White	Non-White is defined as Black or African American, Asian, Native Hawaiian or Pacific Islander, Alaskan Native or American Indian.
Age	Defined as Age of Patients at the index of receiving mono or dual treatment

Inclusion and exclusion criteria for patient cohort selection were based on ICD-10 coding, current procedural terminology and RxNorm terminology. For details review Materials and methods

Supplementary Table 7 Cirrhosis cohort etiology

Code	Cirrhosis etiology	Before propensity score matching			After propensity score matching		
		Metformin	Metformin + GLP1-RA	P-value	Metformin	Metformin + GLP1-RA	P-value
K76.0	Fatty (change of) liver, not elsewhere classified	4937 (24.62)	782 (54.97)	<0.001	697 (52.95)	663 (50.36)	0.172
K75.8	Other specified inflammatory liver diseases	1717 (8.56)	437 (30.75)	<0.001	338 (25.72)	330 (25.07)	0.695
K70.3	Alcoholic cirrhosis of liver	1099 (5.48)	73 (5.16)	0.583	60 (4.54)	69 (5.26)	0.379
B18.2	Chronic viral hepatitis C	2805 (13.99)	163 (11.43)	<0.01	154 (11.67)	152 (11.53)	0.906
B18.1	Chronic viral hepatitis B without delta-agent	461 (2.3)	28 (1.99)	0.420	25 (1.87)	27 (2.02)	0.783
B18.0	Chronic viral hepatitis B with delta-agent	22 (0.11)	9 (0.62)	<0.001	9 (0.72)	0 (0)	<0.01
K74.6	Other and unspecified cirrhosis of liver	5103 (25.45)	718 ((50.5)	<0.001	574 (43.59)	590 (44.81)	0.516
K75.4	Autoimmune hepatitis	176 (0.88)	21 (1.49)	0.014	27 (2.02)	19 (1.44)	0.244
E83.11	Hemochromatosis	199 (0.99)	21 (1.49)	0.054	17 (1.3)	19 (1.44)	0.744
E88.01	Alpha-1-antitrypsin deficiency	32 (0.16)	9 (0.62)	<0.001	9 (0.72)	9 (0.72)	>0.99

Baseline diagnoses of T2DM (E11) patients with cirrhosis (K70.3, K74, K74.6, K74.2) on metformin (n=20,053) or metformin and GLP1-RA (n=1,316) before and after propensity score matching. NASH cirrhosis is defined by patients with both ICD-10 codes K76.0 and K75.8 concurrently. Values are n (%)

GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis; T2DM, type 2 diabetes mellitus

Supplementary Table 8 Before and after propensity score matching, mortality outcomes for T2DM cirrhosis and T2DM patients with NASH cirrhosis

5-year survival rate	Kaplan-Meier estimates							
	Before propensity score matching				After propensity score matching			
	Metformin	Metformin + GLP1-RA	P-value	HR (95%CI)	Metformin	Metformin + GLP1-RA	P-value	HR (95%CI)
All	86.19	88.59	0.001	0.61 (0.45-0.82)	85.29	88.53	0.011	0.61 (0.42-0.89)
Demographic Subgroup								
Men	79.52	88.13	0.004	0.55 (0.36-0.83)	77.76	86.34	0.046	0.55 (0.3-0.97)
Women	89.11	91.42	0.014	0.56 (0.36-0.9)	85.97	91.28	0.012	0.5 (0.29-0.87)
White	81.96	91.36	<0.0001	0.39 (0.27-0.57)	86.96	88.99	0.014	0.55 (0.33-0.89)
Non-White	91.10	68.88	0.557	1.2 (0.64-2.27)	88.82	69.26	0.839	0.91 (0.35-2.33)
Hispanic	91.42	97.50	0.325	0.5 (0.12-2.04)	96.34	96.26	0.939	1.08 (0.15-7.69)
Non-Hispanic	87.42	86.82	0.034	0.67 (0.46-0.97)	88.09	86.57	0.278	0.77 (0.48-1.23)
Age 35-59	92.26	91.61	0.174	0.66 (0.36-1.2)	95.96	91.56	0.639	0.82 (0.36-1.89)
Age 60-85	85.82	84.74	0.176	0.78 (0.53-1.12)	83.35	84.64	0.114	0.68 (0.42-1.1)
NASH	92.50	96.75	0.002	0.15 (0.04-0.62)	90.92	96.56	0.002	0.13 (0.03-0.58)

K-M probability values are percent free of death. P values indicate P log-rank test. T2DM patients with cirrhosis treated with metformin and GLP1-RA were further divided into demographic subgroups. They were propensity score-matched to the metformin group by sex, race, ethnicity, and age groups. T2DM NASH cirrhosis patients treated with metformin and GLP1-RA were propensity score matched to the NASH cirrhosis metformin (n=1841) group

T2DM, type 2 diabetes mellitus; GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis; HR, hazard ratio; CI, confidence interval; K-M, Kaplan-Meier

Supplementary Table 9 Before and after propensity score matching, composite hepatic decompensation outcomes for T2DM cirrhosis and T2DM patients with NASH cirrhosis

Kaplan-Meier estimates								
5-year absence of hepatic decompensation	Before propensity score matching				After propensity score matching			
	Metformin	Metformin + GLP1-RA	P-value	HR (95%CI)	Metformin	Metformin + GLP1-RA	P-value	HR (95%CI)
All	86.68	87.77	0.044	0.75 (0.56-0.99)	82.01	87.87	0.020	0.65 (0.46-0.93)
Demographic Subgroup								
Men	87.55	89.35	0.463	0.85 (0.54-1.32)	87.56	92.42	0.438	0.75 (0.36-1.56)
Women	89.21	90.08	0.055	0.65 (0.42-1.01)	88.60	90.23	0.021	0.54 (0.31-0.92)
White	88.72	91.54	0.033	0.66 (0.44-0.97)	88.65	92.54	0.021	0.51 (0.29-0.92)
Non-White	88.65	89.62	0.715	0.88 (0.45-1.72)	85.60	90.10	0.067	0.44 (0.18-1.09)
Hispanic	90.58	97.61	0.451	0.65 (0.2-2.04)	88.22	97.83	0.428	0.51 (0.09-2.78)
Non-Hispanic	87.62	89.37	0.130	0.76 (0.53-1.09)	87.07	90.00	0.006	0.52 (0.32-0.83)
Age 35-59	90.12	90.64	0.859	0.96 (0.6-1.52)	92.87	90.69	0.455	1.3 (0.65-2.63)
Age 60-85	85.12	84.19	0.157	0.76 (0.52-1.11)	81.89	84.77	0.005	0.51 (0.32-0.83)
NASH	92.09	94.83	0.054	0.48 (0.22-1.03)	93.18	95.58	0.072	0.36 (0.11-1.15)

K-M probabilities values are percent free of decompensation. P values indicate P Log-rank Test. T2DM cirrhosis patients treated with metformin and GLP1-RA were further divided into demographic subgroups and were propensity score matched to the metformin group by sex, race, ethnicity, and age groups. T2DM NASH cirrhosis patients treated with metformin and GLP1-RA were propensity score matched to the NASH cirrhosis metformin (n=1,841) group. Composite hepatic decompensation is defined as any instance of ascites, variceal bleeding, or hepatic encephalopathy

T2DM, type 2 diabetes mellitus; GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis; HR, hazard ratio; CI, confidence interval; K-M, Kaplan-Meier

Supplementary Table 10 Before and after propensity score matching, hepatocellular carcinoma outcomes for T2DM cirrhosis and T2DM patients with NASH cirrhosis

Kaplan-Meier estimates								
5-year absence of hepatocellular carcinoma	Before propensity score matching				After propensity score matching			
	Metformin	Metformin + GLP1-RA	P-value	HR (95%CI)	Metformin	Metformin + GLP1-RA	P-value	HR (95%CI)
All	93.43	95.01	0.239	0.76 (0.49-1.19)	91.15	94.94	0.001	0.44 (0.26-0.74)
Demographic Subgroup								
Men	94.66	98.60	0.167	0.5 (0.19-1.35)	96.67	99.04	0.262	0.47 (0.12-1.82)
Women	92.06	92.63	0.628	0.88 (0.53-1.45)	87.05	92.53	0.073	0.58 (0.32-1.06)
White	92.00	95.20	0.411	0.8 (0.47-1.37)	90.63	96.04	0.200	0.61 (0.28-1.32)
Non-White	94.34	93.75	0.125	0.24 (0.03-1.72)	97.52	95.91	0.790	1.3 (0.18-9.09)
Hispanic	94.00	96.11	0.770	0.81 (0.2-3.33)	96.60	96.67	0.665	0.59 (0.05-6.67)
Non-Hispanic	92.54	93.37	0.552	0.86 (0.53-1.41)	87.93	93.49	0.001	0.37 (0.21-0.67)
Age 35-59	90.71	91.33	0.288	0.71 (0.38-1.33)	89.31	91.15	0.021	0.43 (0.21-0.88)
Age 60-85	95.36	97.64	0.366	0.71 (0.33-1.49)	91.65	97.74	0.029	0.37 (0.15-0.93)
NASH	96.01	97.48	0.823	0.91 (0.38-2.17)	93.87	97.93	0.457	0.62 (0.18-2.22)

K-M probability values are percent free of hepatocellular carcinoma. P values indicate P log-rank test. T2DM cirrhosis patients treated with metformin and GLP1-RA were further divided into demographic subgroups and were propensity score matched to the metformin group by sex, race, ethnicity and age groups. T2DM NASH cirrhosis patients treated with metformin and GLP1-RA were propensity score matched to the NASH cirrhosis metformin (n=1,841) group

T2DM, type 2 diabetes mellitus; GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis; HR, hazard ratio; CI, confidence interval; K-M, Kaplan-Meier

Supplementary Table 11 Six-month, 1-year, 2-year, 3-year and 5-year Kaplan-Meier estimates for mortality, hepatic decompensation and hepatocellular carcinoma in T2DM cirrhosis patients

Cumulative outcome probabilities for T2DM patients with cirrhosis								
Outcome	Before propensity score matching				After propensity score matching			
	Metformin (n=20,053)	Metformin + GLP1 RA (n=1422)	P-value	HR (95%CI)	Metformin (n=1316)	Metformin + GLP1-RA (n=1316)	P-value	HR (95%CI)
All-cause mortality								
6 months	97.17	98.82	<0.001	0.41 (0.24-0.69)	98.01	98.74	0.154	0.62 (0.32-1.20)
1 year	95.80	97.12	0.011	0.61 (0.42-0.89)	96.35	97.09	0.264	0.75 (0.46-1.23)
2 years	93.37	95.48	<0.01	0.62 (0.44-0.86)	93.67	95.43	0.113	0.71 (0.46-1.09)
3 years	91.20	94.76	<0.001	0.58 (0.42-0.81)	90.13	94.70	<0.01	0.59 (0.4-0.88)
5 years	86.19	88.59	<0.01	0.61 (0.45-0.82)	85.29	88.53	0.011	0.61 (0.42-0.89)
Hepatic decompensation								
6 Months	97.32	98.51	0.014	0.55 (0.34-0.89)	97.14	98.41	0.048	0.56 (0.31-1.01)
1 year	95.93	97.34	0.015	0.62 (0.58-0.92)	95.93	97.20	0.081	0.65 (0.4-1.06)
2 years	93.60	95.78	0.012	0.65 (0.46-0.91)	92.57	95.61	0.029	0.63 (0.41-0.95)
3 years	91.36	94.45	<0.01	0.64 (0.47-0.88)	89.68	94.56	<0.01	0.59 (0.4-0.75)
5 years	86.68	87.77	0.044	0.75 (0.56-0.99)	82.01	87.87	0.020	0.65 (0.46-0.93)
Hepatocellular carcinoma								
6 Months	99.22	99.40	0.602	0.82 (0.38-1.75)	98.51	99.36	0.076	0.46 (0.19-1.11)
1 year	98.65	99.28	0.167	0.61 (0.33-1.23)	97.13	99.23	<0.01	0.38 (0.21-0.69)
2 years	97.54	97.89	0.398	0.8 (0.48-1.33)	92.92	97.82	<0.001	0.39 (0.24-0.67)
3 years	95.96	97.12	0.199	0.73 (0.45-1.18)	91.15	97.05	<0.001	0.44 (0.26-0.74)
5 years	93.43	95.01	0.239	0.76 (0.49-1.19)	97.13	94.94	<0.01	0.46 (0.19-1.11)

K-M probabilities values are percent free of death, decompensation, and hepatocellular carcinoma. P values indicate P log-rank test

T2DM, type 2 diabetes mellitus; GLP1-RA, glucagon-like peptide-1 receptor agonist; HR, hazard ratio; CI, confidence interval; K-M, Kaplan-Meier

Supplementary Table 12 Six-month, 1-year, 2-year, 3-year and 5-year Kaplan-Meier estimates for mortality, hepatic decompensation and hepatocellular carcinoma in T2DM patients with NASH cirrhosis

Outcome	Before propensity score matching				After propensity score matching			
	Metformin (n=1841)	Metformin + GLP1-RA (n=317)	P-value	HR (95%CI)	Metformin (n=229)	Metformin + GLP1-RA (n=229)	P-value	HR (95%CI)
All-cause mortality								
6 Months	98.79	100	0.055	-	99.11	100	0.156	-
1 year	98.18	100	0.022	-	97.05	100	0.012	-
2 years	96.24	100	<0.01	-	96.27	100	<0.01	-
3 years	95.48	100	<0.01	-	96.27	100	<0.01	-
5 years	92.50	96.75	<0.01	0.15 (0.04-0.62)	90.92	96.56	<0.01	0.13 (0.03-0.58)
Hepatic decompensation								
6 Months	98.03	99.31	0.121	0.34 (0.08-1.43)	98.62	99.52	0.312	0.33 (0.03-3.12)
1 year	97.33	98.94	0.102	0.39 (0.12-1.27)	98.62	99.52	0.312	0.33 (0.03-3.12)
2 years	95.74	98.45	0.042	0.36 (0.13-1.01)	98.02	99.52	0.166	0.24 (0.03-2.13)
3 years	94.79	97.77	0.042	0.4 (0.16-1)	98.02	98.74	0.358	0.46 (0.08-2.56)
5 years	92.09	94.83	0.054	0.48 (0.22-1.03)	93.18	95.58	0.072	0.36 (0.11-1.15)
Hepatocellular carcinoma								
6 Months	99.47	99.32	0.776	1.25 (0.27-5.88)	99.53	99.08	0.578	1.96 (0.18-20)
1 year	99.04	98.53	0.481	1.47 (0.49-4.55)	99.53	97.93	0.337	2.86 (0.3-25)
2 years	98.56	97.48	0.283	1.64 (0.66-4)	99.53	97.93	0.207	3.7 (0.42-33.33)
3 years	96.97	97.48	0.997	1 (0.42-2.38)	98.60	97.93	0.486	1.82 (0.33-10)
5 years	96.01	97.48	0.823	0.91 (0.38-2.17)	93.87	97.93	0.457	0.62 (0.18-2.22)

K-M probabilities values are percent free of death, decompensation, and hepatocellular carcinoma. P values indicate P log-rank test

T2DM, type 2 diabetes mellitus; GLP1-RA, glucagon-like peptide-1 receptor agonist; NASH, nonalcoholic steatohepatitis; HR, hazard ratio; CI, confidence interval; K-M, Kaplan-Meier