

Classifying Patients into Disease Severity Cohorts

The first diagnosis of NAFLD marked the NAFLD index quarter.

Patients with NAFLD index quarter, having continuous enrollment for 1 year before and after the index quarter and no evidence of NAFLD or advanced liver disease within 1 year preceding the index quarter constituted the ‘NAFLD’ cohort.

Out of them, patients who were not diagnosed with any advanced liver disease at any time during the study period were categorized as ‘NAFLD non-progressors’.

Following the NAFLD index quarter, the subsequent first diagnosis of a more severe stage marked the index quarter for that stage (stage-specific index quarter). The diagnosis of disease severity stages was based on the presence of ≥ 1 ICD-10-GM or OPS (Operationen-und Prozedurenschlüssel [German procedure classification] or DRG (Diagnosis Related Group) codes.

Patients were included in ≥ 1 disease severity stage, if they had (i) continuous enrollment for 1 year before and after the stage-specific index quarter, and (ii) no evidence of more severe stage in the 1 year preceding the stage-specific index quarter.

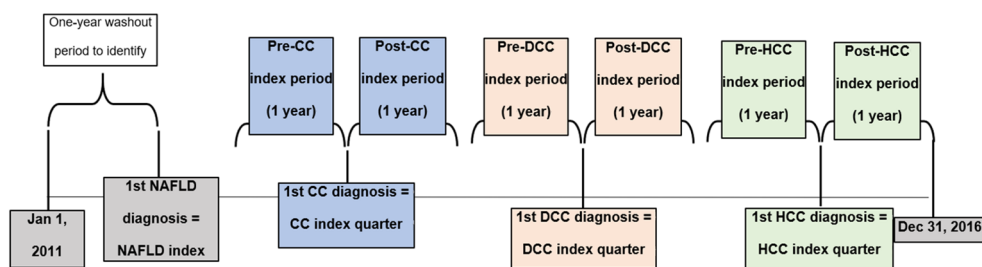


Figure S1 Study schema. LT index quarter was captured in a similar manner. CC: compensated cirrhosis; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LT: liver transplant; NAFLD: nonalcoholic fatty liver disease.

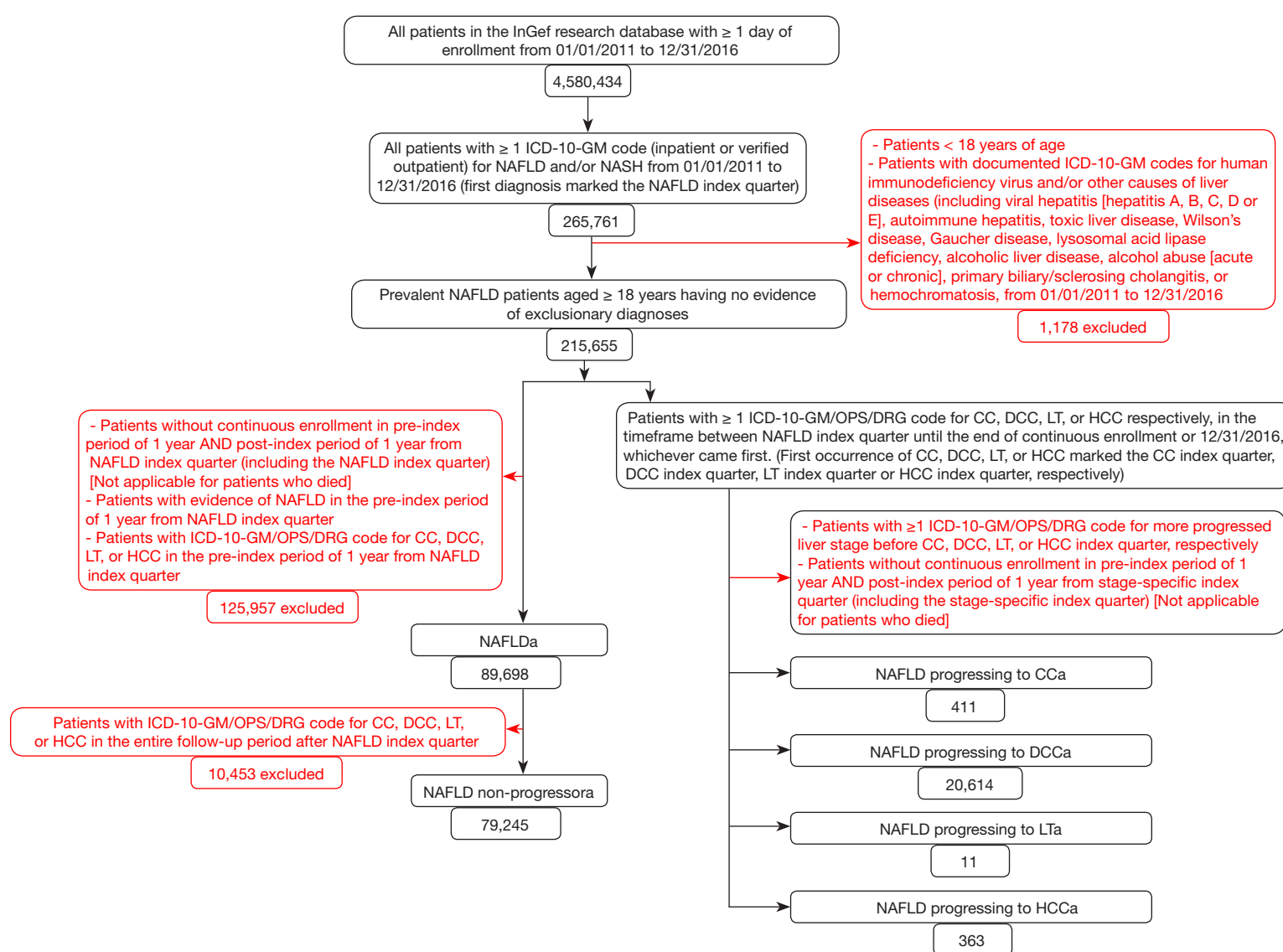


Figure S2 Detailed patient attrition. aLiver disease severity cohorts are not mutually exclusive because patients are included in >1 severity cohort. CC: compensated cirrhosis; DCC: decompensated cirrhosis; DRG: Diagnosis Related Group; HCC: hepatocellular carcinoma; ICD-10-GM: International Classification of Diseases, Tenth Edition, German Modification; InGef: Institut für angewandte Gesundheitsforschung; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; NASH: nonalcoholic steatohepatitis; OPS: Operationen-und Prozedurenschlüssel (German procedure classification).

Table S1 Annual all-cause healthcare resource utilization, stratified by T2DM^a

		Severity of liver disease									
		NAFLD (n=89,698)		NAFLD non-progressor (n=79,245)		CC (n=411)		DCC (n=20,614)		HCC (n=363)	
		With T2DM n=24,127	Without T2DM n=65,571	With T2DM n=20,587	Without T2DM n=58,658	With T2DM n=223	Without T2DM n=188	With T2DM n=8,498	Without T2DM n=12,116	With T2DM n=191	Without T2DM n=172
All-cause hospitalizations											
Number of patients with hospitalizations											
n (%)	Pre-index	5,999 (24.86)	10,411 (15.88)*	4,779 (23.21)	8,857 (15.10)*	87 (39.01)	46 (24.47)*	4,044 (47.59)	3,881 (32.03)*	88 (46.07)	83 (48.26)
	Post-index	9,993 (41.42)	17,852 (27.23)†	7,733 (37.56)	14,824 (25.27)†	146 (65.47)	95 (50.53)†	6,629 (78.01)	6,846 (56.50)†	171 (89.53)	137 (79.65)†
Number of admissions for patients with ≥1 admission											
Mean (SD)	Pre-index	1.65 (1.36)	1.48 (1.08)*	1.62 (1.38)	1.44 (0.98)*	2.07 (1.35)	1.7 (1.07)	2.19 (1.83)	2.03 (1.90)*	2.43 (2.03)	2.33 (3.13)
	Post-index	2.48 (2.56)	2.09 (2.08)†	1.92 (1.70)	1.65 (1.38)†	2.52 (2.01)	2.48 (2.27)	3.83 (3.14)	3.16 (2.97)†	5 (3.29)	4.89 (3.77)
Median	Pre-index	1	1	1	1	2	1	2	1	2	1
	Post-index	2	1	1	1	2	2	3	2	4	4
Length of stay for patients with ≥1 admission, days											
Mean (SD)	Pre-index	12.91 (18.93)	10.57 (17.85)*	12.31 (17.96)	10.23 (17.70)*	21.06 (26.20)	12.93 (14.64)*	21.06 (28.14)	16.72 (24.14)*	24.72 (45.21)	21.57 (33.49)
	Post-index	24.42 (40.92)	17.51 (32.85)†	16.33 (25.46)	12.36 (21.71)†	26.11 (29.80)	20.70 (26.50)	50.84 (62.93)	38.38 (56.68)†	54.40 (49.54)	52.11 (77.97)
Median	Pre-index	7	5	7	5	13	9.50	12	9	11.50	8
	Post-index	10	7	8	6	16	10	29	17.17	42	36
All-cause outpatient visits											
Number of patients with outpatient visits											
n (%)	Pre-index	23,696 (98.21)	62,234 (94.91)*	20,189 (98.07)	55,598 (94.78)*	223 (100)	187 (99.47)	8,463 (99.59)	11,948 (98.61)*	191 (100)	171 (99.42)
	Post-index	24,087 (99.83)	65,523 (99.93)†	20,566 (99.90)	58,624 (99.94)	221 (99.10)	187 (99.47)	8,313 (97.82)	11,976 (98.84)†	188 (98.43)	169 (98.26)
Number of outpatient visits for patients with ≥1 visit											
Mean (SD)	Pre-index	24.91 (16.69)	16.33 (13.69)*	24.12 (15.88)	15.84 (13.17)*	30.71 (16.02)	22.39 (18.45)*	33.42 (22.88)	23.91 (18.31)*	33.88 (21.82)	24.26 (15.32)*
	Post-index	29.84 (17.77)	20.51 (15.12)†	28.55 (16.48)	19.40 (13.95)†	34.72 (15.52)	26.84 (19.51)†	37.45 (24.81)	28.23 (19.65)†	42.35 (29.71)	37.94 (24.58)†
Median	Pre-index	22	13	21	13	28	19	29	20	30	22
	Post-index	26	17	25	16	32	23	32	24	36.67	32

^aResults for patients with LT are not reported owing to small sample size. *p <0.05 for pre-index with T2DM vs. without T2DM. †p <0.05 for post-index with T2DM vs. without T2DM. CC: compensated cirrhosis; DCC: decompensated cirrhosis; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; SD: standard deviation; T2DM: type 2 diabetes mellitus.

Table S2 Annual all-cause healthcare resource utilization, stratified by CVD^a

		Severity of liver disease									
		NAFLD (n=89,698)		NAFLD non-progressor (n=79,245)		CC (n=411)		DCC (n=20,614)		HCC (n=363)	
		With CVD n=36,412	Without CVD n=53,286	With CVD n=30,525	Without CVD n=48,720	With CVD n=257	Without CVD n=154	With CVD n=13,943	Without CVD n=6,671	With CVD n=246	Without CVD n=117
All-cause hospitalizations											
Number of patients with hospitalizations											
n (%)	Pre-index	9,875 (27.12)	6,535 (12.26)*	7,832 (25.66)	5,804 (11.91)*	102 (39.69)	31 (20.13)*	6,493 (46.57)	1,432 (21.47)*	129 (52.44)	42 (35.90)*
	Post-index	16,120 (44.27)	11,725 (22)†	12,411 (40.66)	10,146 (20.83)†	168 (65.37)	73 (47.40)†	10,657 (76.43)	2,818 (42.24)†	221 (89.84)	87 (74.36)†
Number of admissions for patients with ≥1 admission											
Mean (SD)	Pre-index	1.64 (1.23)	1.39 (1.11)*	1.60 (1.18)	1.37 (1.08)*	2.05 (1.32)	1.58 (0.99)*	2.16 (1.81)	1.92 (2.09)*	2.44 (2.82)	2.19 (1.85)
	Post-index	2.52 (2.50)	1.83 (1.85)†	1.94 (1.63)	1.50 (1.28)†	2.78 (2.12)	1.88 (1.97)†	3.74 (3.09)	2.54 (2.83)†	5.17 (3.66)	4.40 (3.01)
Median	Pre-index	1	1	1	1	2	1	2	1	1	1
	Post-index	2	1	1	1	2	1	3	1	4	4
Length of stay for patients with ≥1 admission, days											
Mean (SD)	Pre-index	12.32 (17.82)	10.08 (18.90)*	11.82 (17.55)	9.79 (18.11)*	19.79 (23.47)	13.16 (21.58)	19.83 (26.54)	14.87 (25.04)*	22.95 (41.90)	23.9 (33.30)
	Post-index	24.12 (39.86)	14.31 (29.26)†	15.93 (24.79)	11.01 (20.63)†	27.62 (30.81)	15.58 (20.59)†	49.20 (62.32)	26.78 (47.15)†	54.08 (45.83)	51.61 (95.35)
Median	Pre-index	7	5	6	5	12.50	7	11	7	10	8
	Post-index	10	6	8	5	17	7	28	10	44	26
All-cause outpatient visits											
Number of patients with outpatient visits											
n (%)	Pre-index	35,718 (98.09)	50,212 (94.23)*	29,922 (98.02)	45,865 (94.14)*	256 (99.61)	154 (100)	13,863 (99.43)	6,548 (98.16)*	246 (100)	116 (99.15)
	Post-index	36,352 (99.84)	53,258 (99.95)†	30,494 (99.90)	48,696 (99.95)†	255 (99.22)	153 (99.35)	13,650 (97.90)	6,639 (99.52)†	242 (98.37)	115 (98.29)
Number of outpatient visits for patients with ≥1 visit											
Mean (SD)	Pre-index	23.82 (16.90)	15.06 (12.41)*	23.01 (16.05)	14.81 (12.19)*	30.30 (19.02)	21.29 (13.35)*	31.36 (21.98)	20.42 (15.89)*	31.85 (20.34)	24.01 (16.80)*
	Post-index	28.81 (18.25)	19.07 (13.68)†	27.36 (16.84)	18.28 (12.88)†	34.42 (19.43)	25.59 (13.27)†	35.62 (23.77)	24.59 (16.92)†	42.76 (29.42)	35.01 (21.98)†
Median	Pre-index	21	12	20	12	27	19	27	17	29	22
	Post-index	25	16	24	15	32	24	31	21	38.33	29

^aResults for patients with LT are not reported owing to small sample size. *p <0.05 for pre-index with CVD vs. without CVD. †p <0.05 for post-index with CVD vs. without CVD. CC: compensated cirrhosis; CVD: cardiovascular diseases; DCC: decompensated cirrhosis; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; SD: standard deviation.

Table S3 Annual all-cause healthcare resource utilization, stratified by renal disease^a

		Severity of liver disease									
		NAFLD (n=89,698)		NAFLD non-progressor (n=79,245)		CC (n=411)		DCC (n=20,614)		HCC (n=363)	
		With renal disease n=22,108	Without renal disease n=67,590	With renal disease n=18,289	Without renal disease n=60,956	With renal disease n=182	Without renal disease n=229	With renal disease n=9,977	Without renal disease n=10,637	With renal disease n=197	Without renal disease n=166
All-cause hospitalizations											
Number of patients with hospitalizations											
n (%)	Pre-index	6,251 (28.27)	10,159 (15.03)*	4,828 (26.40)	8,808 (14.45)*	74 (40.66)	59 (25.76)*	4,977 (49.88)	2,948 (27.71)*	103 (52.28)	68 (40.96)*
	Post-index	10,242 (46.33)	17,603 (26.04)†	7,712 (42.17)	14,845 (24.35)†	126 (69.23)	115 (50.22)†	8,004 (80.22)	5,471 (51.43)†	183 (92.89)	125 (75.30)†
Number of admissions for patients with ≥1 admission											
Mean (SD)	Pre-index	1.74 (1.36)	1.42 (1.06)*	1.70 (1.31)	1.40 (1.02)*	2.31 (1.38)	1.47 (0.92)*	2.26 (1.89)	1.86 (1.81)*	2.64 (2.95)	1.99 (1.94)
	Post-index	2.74 (2.67)	1.93 (1.95)†	2.08 (1.79)	1.57 (1.29)†	3.11 (2.59)	1.85 (1.11)†	4.06 (3.15)	2.65 (2.76)†	5.14 (3.53)	4.67 (3.47)
Median	Pre-index	1	1	1	1	2	1	2	1	2	1
	Post-index	2	1	1	1	2	2	3	2	4	4
Length of stay for patients with ≥1 admission, days											
Mean (SD)	Pre-index	13.57 (18.90)	10.11 (17.77)*	13.03 (18.75)	9.83 (17.18)*	23.89 (23.94)	11.17 (20.12)*	21.59 (27.62)	14.44 (23.37)*	26.61 (46.41)	18 (26.63)
	Post-index	27.76 (44.77)	15.47 (29)†	18.02 (28.31)	11.48 (19.56)†	31.39 (33.21)	15.84 (19.65)†	55.63 (66.73)	28.25 (44.22)†	57.95 (71.17)	46.70 (50.26)
Median	Pre-index	8	5	7	5	16	6	13	7	12	7
	Post-index	11	7	9	6	21	8	34	12	45	30
All-cause outpatient visits											
Number of patients with outpatient visits											
n (%)	Pre-index	21,623 (97.81)	64,307 (95.14)*	17,858 (97.64)	57,929 (95.03)*	182 (100)	228 (99.56)	9,924 (99.47)	10,487 (98.59)*	197 (100)	165 (99.40)
	Post-index	22,065 (99.81)	67,545 (99.93)†	18,267 (99.88)	60,923 (99.95)†	180 (98.90)	228 (99.56)	9,718 (97.40)	10,571 (99.38)†	192 (97.46)	165 (99.40)
Number of outpatient visits for patients with ≥1 visit											
Mean (SD)	Pre-index	24.19 (18.30)	16.85 (13.32)*	23.21 (17.25)	16.46 (13.01)*	31.47 (20.50)	23.28 (14)*	32.67 (23.79)	23.29 (16.39)*	32.13 (20.70)	26 (17.70)*
	Post-index	29.28 (19.84)	20.97 (14.54)†	27.68 (18.35)	20 (13.62)†	36.04 (20.36)	27.22 (14.55)†	36.94 (25.88)	27.48 (17.38)†	45.85 (31.34)	33.76 (20.33)†
Median	Pre-index	21	14	20	13	29	21	28	20	29	22
	Post-index	25	18	24	17	33.50	24	32	24	40.50	30

^aResults for patients with LT are not reported owing to small sample size. *p <0.05 for pre-index with renal disease vs. without renal disease. †p <0.05 for post-index with renal disease vs. without renal disease. CC: compensated cirrhosis; DCC: decompensated cirrhosis; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; SD: standard deviation.

Table S4 Annual all-cause healthcare costs, stratified by T2DM*

	Healthcare service component									
	Total costs, €		Inpatient costs, €		Outpatient costs, €		Pharmacy costs, €		Devices and aids costs, €	
	With T2DM n=24,127	Without T2DM n=65,571	With T2DM n=24,127	Without T2DM n=65,571	With T2DM n=24,127	Without T2DM n=65,571	With T2DM n=24,127	Without T2DM n=65,571	With T2DM n=24,127	Without T2DM n=65,571
NAFLD (n=89,698)										
Pre-index										
Mean (SD)	3,857.44 (6,350.20)	2,064.95 (6,787.56)*	1,438.3 (4,289.13)	781.04 (3,183.87)*	969.76 (1,505.12)	628.93 (1,040.03)*	1,102.81 (2,773.85)	484.72 (5,230.63)*	346.57 (1,068.90)	170.27 (1,287.48)*
Median	1,877.32	704.80	0	0	712.55	409.48	501.63	93.84	46.62	0
Post-index										
Mean (SD)	8,192.37 (23,541.54)	4,165.02 (15,899.55)†	5,001.61 (22,313.82)	2,356.21 (13,964.63)†	1,279.29 (1,727.06)	903.96 (1,271.10)†	1,436.27 (3,669.19)	682.45 (5,634.99)†	475.20 (2,135.17)	222.39 (1,413.46)†
Median	3,030.56	1,174.36	0	0	942.51	621.79	652.87	129.59	78.54	0
Percentage increase, % ^a	112.38	101.70	247.75	201.68	31.92	43.73	30.24	40.79	37.11	30.61
NAFLD non-progressor (n=79,245)										
Pre-index										
Mean (SD)	3,561.55 (5,801.01)	1,929.87 (6,732.87)*	1,305.41 (4,103.71)	716.51 (2,865.28)*	928.29 (1,345.89)	607.24 (980.47)*	1,008.88 (2,276.37)	444.44 (5,415.65)*	318.98 (997.04)	161.69 (1,329.13)*
Median	1,740.67	674.16	0	0	692.54	396.53	460.54	87.73	29.45	0
Post-index										
Mean (SD)	5,780.11 (11,151.48)	3,129.80 (9,151.21)†	2,847.02 (9,205.07)	1,478.80 (5,954.89)†	1,203.06 (1,545.24)	845.13 (1,157.04)†	1,304.59 (3,334.31)	600.19 (5,685.38)†	425.44 (2,103.37)	205.67 (1,386.68)†
Median	2,706.90	1,076.67	0	0	911.40	592.51	595.50	120.70	74.97	0
Percentage increase, % ^a	62.29	62.18	118.09	106.39	29.60	39.18	29.31	35.05	33.38	27.20
CC (n=411)										
Pre-index										
Mean (SD)	6,257.45 (7,665.12)	4,146.48 (6,811.04)*	2,990.36 (6,072.44)	1,561.83 (4,370.71)*	1,221.07 (940.24)	1,028.37 (2,411.04)	1,504.84 (2,293.64)	1,093.34 (3,983.27)	541.17 (1,210.83)	462.94 (1,227.84)
Median	3,389.60	1,482.88	0	0	950.14	673.16	713.28	270.30	82.20	63.11
Post-index										
Mean (SD)	12,285.57 (15,572.17)	7,924.85 (12,132.89)†	7,910.06 (13,164.06)	4,549.01 (8,777.77)†	1,433.33 (1,004.89)	1,277.35 (2,396.12)	2,264.76 (5,420.01)	1,623.28 (6,123.38)	677.42 (1,590.52)	475.21 (1,141.07)
Median	6,996.02	3,085.10	3,562.11	493.72	1,223.91	856.73	1,000.20	334.19	160.18	66.94
Percentage increase, % ^b	96.34	91.12	164.52	191.26	17.38	24.21	50.50	48.47	25.18	2.65
DCC (n=20,614)										
Pre-index										
Mean (SD)	8,817.13 (14,360.92)	5,120.57 (10,343.94)*	4,404.46 (9,955.16)	2,480.54 (7,182.55)*	1,505.55 (2,889.71)	1,029.21 (1,720.93)*	2,229.97 (7,346.96)	1,268.37 (4,849.2)*	677.15 (1,814.14)	342.45 (1,291.18)*
Median	4,190.40	1,601.88	82.32	0	987.69	680.88	975.38	251.41	151.45	0
Post-index										
Mean (SD)	30,451.01 (62,138.51)	17,027.50 (47,042.50)†	24,817.45 (61,137.72)	13,192.80 (45,263.57)†	1,891.69 (3,467.28)	1,373.7 (2,250.90)†	2,677.08 (6,900.78)	1,864.45 (6,703.18)†	1,064.78 (2,549.26)	596.56 (2,126.47)†
Median	13,304.95	3,885.25	8,329.80	1,782.03	1,155.79	895.37	1,163.15	328.15	255.95	75.40
Percentage increase, % ^b	245.36	232.53	463.46	431.85	25.65	33.47	20.05	46.99	57.24	74.21
HCC (n=363)										
Pre-index										
Mean (SD)	10,865.18 (22,082.32)	8,708.17 (14,673.20)	4,983.53 (12,498.09)	4,473.52 (10,489.91)	1,675.83 (2,674.13)	1,167.34 (1,163.37)*	3,653.71 (12,303.03)	2,724.58 (8,377.69)	552.11 (1,398.71)	342.73 (753.06)
Median	3,930.84	2,955.24	0	220.88	1,038.34	772.94	975.85	324.13	132.64	0
Post-index										
Mean (SD)	32,733.09 (29,480.10)	39,437.87 (119,196.52)	21,810.31 (24,378.6)	29,702.25 (119,441)	2,787.10 (4,397.09)	2,508.16 (2,582.83)	7,002.21 (13,688.04)	6,447.01 (11,763.18)	1,133.47 (3,114.28)	780.45 (1,446.59)
Median	26,696.58	23,152.17	18,175.48	12,765.05	1,622.72	1,760.36	1,649.68	1,112.86	335.36	207.06
Percentage increase, % ^b	201.27	352.88	337.65	563.96	66.31	114.86	91.65	136.62	105.30	127.71

*Results for patients with LT are not reported owing to small sample size. ^bPercentage increase from the pre-index to the post-index period. *p <0.05 for pre-index with T2DM vs. without T2DM. †p <0.05 for post-index with T2DM vs. without T2DM. CC: compensated cirrhosis; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; SD: standard deviation; T2DM: type 2 diabetes mellitus.

Table S5 Annual all-cause healthcare costs, stratified by CVD^a

	Healthcare service component									
	Total costs, €		Inpatient costs, €		Outpatient costs, €		Pharmacy costs, €		Devices and aids costs, €	
	With CVD n=36,412	Without CVD n=53,286	With CVD n=36,412	Without CVD n=53,286	With CVD n=36,412	Without CVD n=53,286	With CVD n=36,412	Without CVD n=53,286	With CVD n=36,412	Without CVD n=53,286
NAFLD (n=89,698)										
Pre-index										
Mean (SD)	3,768.80 (6,732.56)	1,712.27 (6,582.10)*	1,549.38 (4,471.38)	553.60 (2,623.39)*	960.02 (1,646.46)	557.01 (690.56)*	937.57 (3,274.26)	455.14 (5,464.18)*	321.83 (1,069.13)	146.53 (1,331.85)*
Median	1,681.60	610.40	0	0	690.10	368.60	338.90	77.40	26	0
Post-index										
Mean (SD)	8,358.01 (25,376.81)	3,123.33 (10,779.71)†	5,404.19 (24,129.25)	1,471.22 (7,975)†	1,279.43 (1,858.43)	817.33 (968.81)†	1,240.21 (4,078.70)	642.63 (5,817.65)†	434.17 (1,881.83)	192.15 (1,449.20)†
Median	2,897.40	1,019.10	0	0	923.50	573	430.10	110.90	68.70	0
Percentage increase, % ^b	121.77	82.41	248.80	165.76	33.27	46.74	32.28	41.19	34.91	31.13
NAFLD non-progressor (n=79,245)										
Pre-index										
Mean (SD)	3,494.71 (6,281.64)	1,638.92 (6,601.65)*	1,425.64 (4,215.04)	521.05 (2,379.57)*	921.87 (1,522.72)	545.77 (669.22)*	845.52 (3,035.81)	431.65 (5,635.69)*	301.67 (1,054.81)	140.45 (1,359.27)*
Median	1,568.10	594.30	0	0	669	361.70	310.20	74.50	0	0
Post-index										
Mean (SD)	5,780.34 (11,498.61)	2,589.04 (8,295.10)†	3,099.99 (9,517.03)	1,041.22 (4,550.11)†	1,199.12 (1,696.24)	774.59 (888.11)†	1,091.41 (3,756.37)	590.07 (5,901.92)†	389.82 (1,829.46)	183.16 (1,444.38)†
Median	2,528.10	962.80	0	0	886.50	553.60	384.70	106.10	66.10	0
Percentage increase, % ^b	65.40	57.97	117.44	99.83	30.07	41.93	29.08	36.70	29.22	30.41
CC (n=411)										
Pre-index										
Mean (SD)	6,307.25 (7,816.98)	3,597.31 (6,169.09)*	2,976.16 (5,966.89)	1,270.13 (4,099.83)*	1,265.98 (2,157.16)	910.89 (739.68)*	1,421.15 (2,343.43)	1,142.16 (4,230.93)	643.96 (1,409.97)	274.13 (749.37)*
Median	2,946.40	1,546.70	0	0	911.50	712.20	633.10	255.60	112.20	0
Post-index										
Mean (SD)	12,344.84 (15,459.98)	6,863.18 (11,208.19)†	8,064.47 (12,969.10)	3,549.27 (7,673.78)†	1,504.02 (2,121.80)	1,124.93 (935.65)†	2,034.66 (5,004.25)	1,865.66 (6,841.63)	741.69 (1,586.68)	323.32 (983.21)†
Median	6,996	3,085.10	3,374.20	164.60	1,185.70	870.10	904	387.10	218.10	43.60
Percentage increase, % ^b	95.72	90.79	170.97	179.44	18.80	23.50	43.17	63.35	15.18	17.94
DCC (n=20,614)										
Pre-index										
Mean (SD)	8,019.22 (13,380.73)	3,771.08 (8,991.50)*	4,140.89 (9,539.90)	1,461.09 (5,256.91)*	1,394.84 (2,628.94)	871.81 (1,247.15)*	1,900.04 (6,335.20)	1,173.08 (5,283.65)*	583.44 (1,676.61)	265.11 (1,166.30)*
Median	3,665.20	1,054.80	0	0	920.40	560.40	694.80	157.30	107.70	0
Post-index										
Mean (SD)	28,789.41 (61,955.20)	9,543.87 (28,274.06)†	23,612.65 (60,871.07)	6,222.68 (25,190.95)†	1,787.84 (3,245.22)	1,167.97 (1,563.68)†	2,425.29 (6,784.48)	1,727.42 (6,799.28)†	963.63 (2,566.73)	425.81 (1,640.06)†
Median	12,031.50	2,097.90	7,503	0	1,113	790.30	888.70	198.30	198.40	0
Percentage increase, % ^b	259.01	153.08	470.23	325.89	28.18	33.97	27.64	47.26	65.16	60.61
HCC (n=363)										
Pre-index										
Mean (SD)	10,084.45 (19,887.75)	9,335.73 (16,851.24)	4,889.53 (11,914.82)	4,431.41 (10,875.85)	1,510.69 (2,340.87)	1,275.51 (1,516.05)	3,139.84 (10,766.76)	3,368.25 (10,353.17)	544.38 (1,311.09)	260.56 (623.7)*
Median	4,328.10	2,493.50	1,030.80	0	987.90	781.30	860.70	292	93.50	0
Post-index										
Mean (SD)	33,775.26 (33,103.88)	40,398.46 (141,627.34)	23,484.99 (30,085.32)	29,891.02 (141,818.81)	2,861.96 (4,075.74)	2,219.64 (2,489.18)	6,338.71 (12,513.79)	7,581.06 (13,390.78)	1,089.60 (2,828.6)	706.74 (1,438.42)
Median	27,061.70	21,887.60	17,561.50	10,410.10	1,691.20	1,633.70	1,648.80	841.40	358.50	125.20
Percentage increase, % ^b	234.92	332.73	380.31	574.53	89.45	74.02	101.88	125.07	100.15	171.24

^aResults for patients with LT are not reported owing to small sample size. ^bPercentage increase from the pre-index to the post-index period. *p <0.05 for pre-index with CVD vs. without CVD. †p <0.05 for post-index with CVD vs. without CVD. CC: compensated cirrhosis; CVD: cardiovascular diseases; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; SD: standard deviation.

Table S6 Annual all-cause healthcare costs, stratified by renal disease^a

	Healthcare service component									
	Total costs, €		Inpatient costs, €		Outpatient costs, €		Pharmacy costs, €		Devices and aids costs, €	
	With renal disease n=22,108	Without renal disease n=67,590	With renal disease n=22,108	Without renal disease n=67,590	With renal disease n=22,108	Without renal disease n=67,590	With renal disease n=22,108	Without renal disease n=67,590	With renal disease n=22,108	Without renal disease n=67,590
NAFLD (n=89,698)										
Pre-index										
Mean (SD)	4,115.74 (7,598.04)	2,034.01 (6,322.71)*	1,733.39 (5,005.76)	704.15 (2,838.43)*	996.31 (1,919.81)	630.42 (806.09)*	1,045.51 (3,742.27)	521.93 (4,973.95)*	340.53 (1,072.53)	177.51 (1,281.11)*
Median	1,726.10	768	0	0	691.70	431.70	348.90	111.30	26.60	0
Post-index										
Mean (SD)	9,777.11 (31,240.07)	3,766.97 (10,917.26)†	6,584.98 (29,902.99)	1,917.33 (8,420.17)†	1,335.15 (2,165.54)	896.9 (1,042.92)†	1,400.11 (4,770.53)	716.79 (5,310.35)†	456.87 (1,353.94)	235.94 (1,723.53)†
Median	3,119.60	1,258.20	0	0	926.90	641.60	438.90	152	69.80	0
Percentage increase, % ^b	137.55	85.20	279.89	172.29	34.01	42.27	33.92	37.34	34.17	32.92
NAFLD non-progressor (n=79,245)										
	With renal disease n=18,289	Without renal disease n=60,956	With renal disease n=18,289	Without renal disease n=60,956	With renal disease n=18,289	Without renal disease n=60,956	With renal disease n=18,289	Without renal disease n=60,956	With renal disease n=18,289	Without renal disease n=60,956
Pre-index										
Mean (SD)	3,760.11 (7,036.27)	1,931.81 (6,326.75)*	1,564.75 (4,559.38)	660.90 (2,692.40)*	944.45 (1,739.17)	614.49 (793.73)*	939.48 (3,588.87)	486.54 (5,112.88)*	311.43 (1,024.06)	169.88 (1,312.49)*
Median	1,567.90	738.70	0	0	667.40	421	311.60	105.20	0	0
Post-index										
Mean (SD)	6,460.16 (13,734.39)	3,025.68 (8,063.77)†	3,596.53 (11,580.6)	1,305.50 (4,664.83)†	1,238.51 (1,947.30)	847.99 (976.64)†	1,225.46 (4,529.33)	650.49 (5,362.13)†	399.65 (1,067.4)	221.7 (1,734.21)†
Median	2,659.30	1,165.60	0	0	888.10	617	384.40	143.40	65	0
Percentage increase, % ^b	71.81	56.62	129.85	97.53	31.14	38	30.44	33.70	28.33	30.50
CC (n=411)										
	With renal disease n=182	Without renal disease n=229	With renal disease n=182	Without renal disease n=229	With renal disease n=182	Without renal disease n=229	With renal disease n=182	Without renal disease n=229	With renal disease n=182	Without renal disease n=229
Pre-index										
Mean (SD)	7,228.60 (8,607.51)	3,752.59 (5,749.72)*	3,570.08 (6,593.45)	1,356.86 (3,974.22)*	1,353.58 (2,467.17)	957.56 (862.14)*	1,563.61 (2,656.36)	1,120.30 (3,538.68)	741.33 (1,560.35)	317.87 (808.82)*
Median	3,560.10	1,651.70	0	0	977.30	722.20	690.70	342.40	215.50	0
Post-index										
Mean (SD)	14,145.75 (17,697.43)	7,227.19 (9,768.77)†	9,505.64 (14,981.93)	3,882.66 (6,688)†	1,621.31 (2,438.26)	1,155.87 (941.89)†	2,208.73 (5,964.12)	1,782.67 (5,587.63)	810.06 (1,769.66)	406, (995.31)†
Median	7,924.10	3,710.10	4,007.20	400.70	1,258.20	912.80	862.80	552.60	232.30	65.90
Percentage increase, % ^b	95.69	92.59	166.26	186.15	19.78	20.71	41.26	59.12	9.27	27.72
DCC (n=20,614)										
	With renal disease n=9,977	Without renal disease n=10,637	With renal disease n=9,977	Without renal disease n=10,637	With renal disease n=9,977	Without renal disease n=10,637	With renal disease n=9,977	Without renal disease n=10,637	With renal disease n=9,977	Without renal disease n=10,637
Pre-index										
Mean (SD)	9,142.51 (15,043.26)	4,301.40 (8,333.76)*	4,824.66 (10,768.88)	1,818.91 (5,150.71)*	1,511.36 (3,057.48)	957.52 (1,111.09)*	2,159.22 (7,160.27)	1,201.03 (4,669.98)*	647.27 (1,848.21)	323.94 (1,151.66)*
Median	4,256.30	1,512.20	400	0	951.70	674.20	795.60	257.80	125.80	0
Post-index										
Mean (SD)	34,209.56 (70,285.98)	11,635.72 (28,456.91)†	28,496.53 (69,175.87)	8,125.67 (26,344.62)†	1,933.96 (3,705.38)	1,262.02 (1,550.79)†	2,715.91 (7,673.48)	1,715.04 (5,815.62)†	1,063.15 (2,753.85)	532.98 (1,787.80)†
Median	15,542.30	3,230.50	10,471.60	771.10	1,130.20	900.20	998.70	333.30	237.70	70.90
Percentage increase, % ^b	274.18	170.51	490.64	346.73	27.96	31.80	25.78	42.80	64.25	64.53
HCC (n=363)										
	With renal disease n=197	Without renal disease n=166	With renal disease n=197	Without renal disease n=166	With renal disease n=197	Without renal disease n=166	With renal disease n=197	Without renal disease n=166	With renal disease n=197	Without renal disease n=166
Pre-index										
Mean (SD)	11,677.31 (22,027.04)	7,666.40 (14,214.96)*	5,972.73 (13,937.79)	3,281.16 (7,703.01)*	1,597.22 (2,611.2)	1,242.25 (1,269.16)	3,507 (10,463.75)	2,865.11 (10,827.01)	600.37 (1,449.12)	277.89 (559.73)*
Median	4,631.60	2,938.40	1,060.20	0	992.80	845.30	871.20	420	97.10	0.30
Post-index										
Mean (SD)	45,736.74 (112,231.75)	24,248.17 (23,136.01)†	34,408.32 (112,032.48)	15,036.85 (19,727.30)†	3,060.83 (4,490.14)	2,173.22 (2,200.14)†	7,114.07 (13,030.41)	6,294.19 (12,540.54)	1,153.52 (3,088.41)	743.90 (1,408.30)
Median	28,895.20	19,051.20	19,438.80	9,017	1,794.90	1,440.30	1,866	960.60	360.10	142
Percentage increase, % ^b	291.67	216.29	476.09	358.28	91.64	74.94	102.85	119.68	92.13	167.69

^aResults for patients with LT are not reported owing to small sample size. ^bPercentage increase from the pre-index to the post-index period. *p <0.05 for pre-index with renal disease vs. without renal disease. †p <0.05 for post-index with renal disease vs. without renal disease. CC: compensated cirrhosis; DCC: decompensated cirrhosis; HCC: hepatocellular carcinoma; LT: liver transplantation; NAFLD: nonalcoholic fatty liver disease; SD: standard deviation.