

## Supplementary Information

Supplemental Table 1. ICD-10 codes for definition of comorbidity complexes

Comorbidity	ICD-10 codes
Hypertension	I10 - I15
Dyslipidemia	E780 - E785
Type 2 diabetes	E11
Osteoporosis	M80 - M82
Insomnia	G470
Depression	F30 - F39
Hepatic cirrhosis	K743 - K746
Liver cancer	C22
Colon cancer	C18
Cancer	C00 - C96, D00 - D48, D370 - D386, D390 - D392, D397, D399, D410 - D414, D417, D419, D440 - D449
Colorectal adenomas	D126
Chronic kidney disease	N18
Gastroesophageal reflux disease	K21
Cardiovascular disease	I20 - I25, I60 - I69
Sleep apnea syndrome	G473

Supplemental Table 2. Baseline patient demographics and characteristics for NASH and non-NASH group

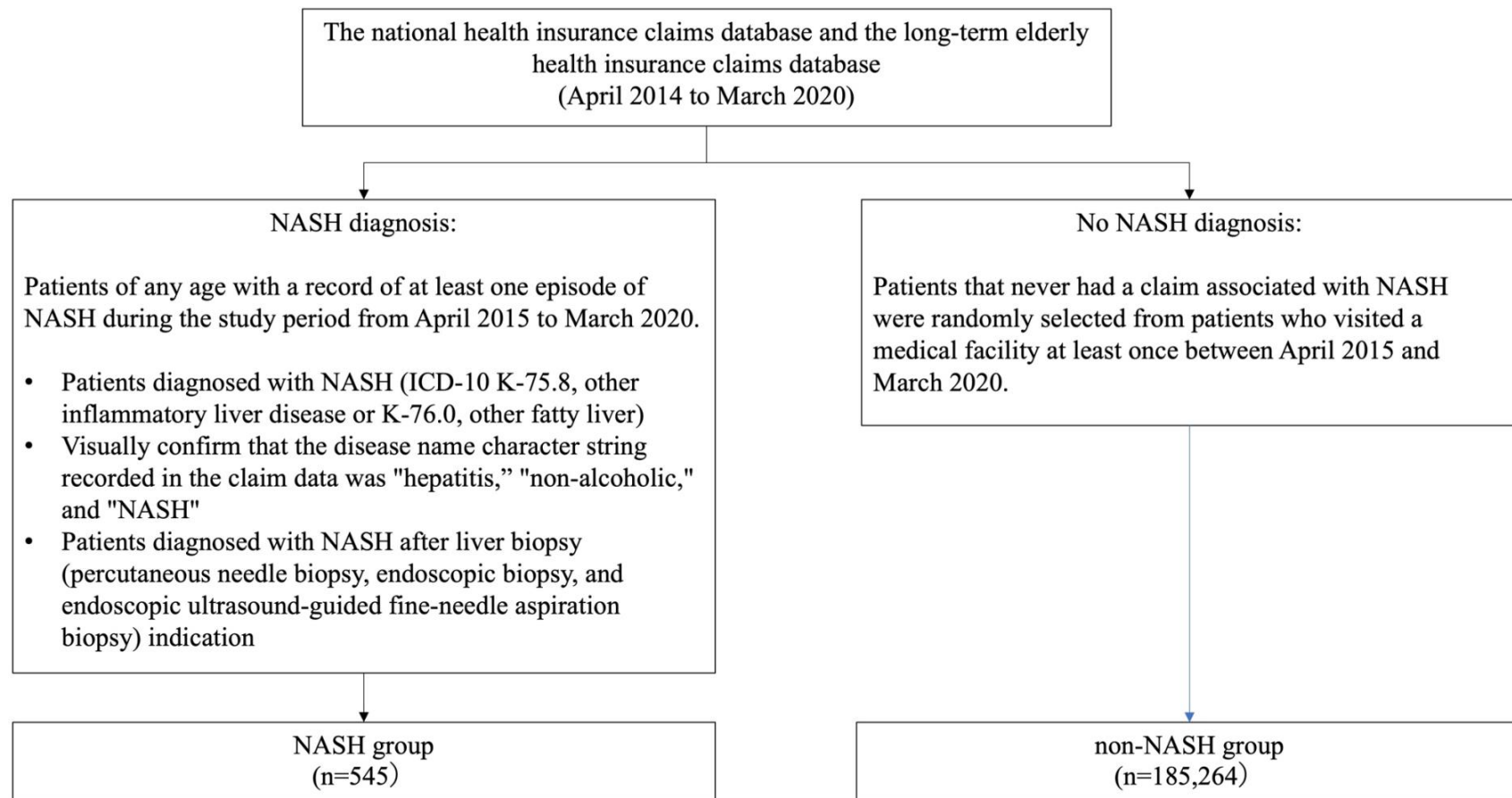
	NASH group N=545		non-NASH group N=185,264		<i>p</i> -value	
Age years; Median (IQR)	68	(63.00-75.00)	65	(44.00-74.00)	<0.001	
Gender n (%)						
Male	209	(38.3%)	80,051	(43.2%)	0.022	
Female	336	(61.7%)	105,213	(56.8%)		
Death n (%)	24	(4.4%)	6,696	(3.6%)	0.300	
Prescribed drugs for treatment of NASH during analysis period						
	Pioglitazone	16	(2.9%)	1,600	(0.9%)	<0.001
Type 2 diabetes	GLP1 agonist	18	(3.3%)	794	(0.4%)	<0.001
	SGLT2	61	(11.2%)	2,851	(1.5%)	<0.001
Dyslipidemia	Statins	290	(53.2%)	39,692	(21.4%)	<0.001
Hypertension	ARB	250	(45.9%)	41,202	(22.2%)	<0.001
	ACEi	34	(6.2%)	5,220	(2.8%)	<0.001
None	Vitamin E	66	(12.1%)	5,057	(2.7%)	<0.001

NASH, nonalcoholic steatohepatitis; IQR, Interquartile range; GLP1, Glucagon-like peptide-1; SGLT2, Sodium-glucose cotransporter 2; ARB, Angiotensin II receptor blocker; ACEi, Angiotensin converting enzyme inhibitor.

Supplemental Table 3. Risk adjusted odds ratio with NASH onset and NASH-related comorbidities relationship.

	Hepatic cirrhosis		Liver cancer		Gastroesophageal reflux diseases		Colorectal adenomas		Colon cancer		Cancer	
	OR (95%CI)		OR (95%CI)		OR (95%CI)		OR (95%CI)		OR (95%CI)		OR (95%CI)	
NASH vs. non-NASH	28.81	(21.79-38.08)	18.38	(12.56-26.89)	3.08	(2.53-3.73)	2.54	(1.25-5.16)	2.36	(1.70-3.28)	2.16	(1.79-2.62)
Gender (female)	0.70	(0.60-0.81)	0.45	(0.37-0.55)	0.92	(0.90-0.94)	0.41	(0.35-0.49)	0.62	(0.59-0.66)	0.57	(0.55-0.59)
Age	1.04	(1.03-1.04)	1.06	(1.05-1.07)	1.04	(1.04-1.04)	1.02	(1.02-1.03)	1.05	(1.05-1.05)	1.05	(1.05-1.05)
Hypertension	1.78	(1.45-2.19)	1.31	(1.03-1.67)	1.90	(1.85-1.95)	1.54	(1.25-1.90)	1.36	(1.25-1.47)	1.22	(1.17-1.26)
Dyslipidemia	0.73	(0.62-0.86)	0.86	(0.70-1.04)	1.72	(1.68-1.76)	1.72	(1.45-2.05)	1.1	(1.03-1.18)	1.08	(1.04-1.11)
Type 2 diabetes	2.15	(1.82-2.54)	2.56	(2.10-3.13)	1.58	(1.54-1.63)	1.46	(1.23-1.74)	1.62	(1.51-1.74)	1.69	(1.63-1.75)
	Sleep apnea syndrome		Cardiovascular diseases		Osteoporosis		Depression		Insomnia		Chronic kidney diseases	
	OR (95%CI)		OR (95%CI)		OR (95%CI)		OR (95%CI)		OR (95%CI)		OR (95%CI)	
NASH vs. non-NASH	1.82	(1.20-2.76)	1.40	(1.16-1.69)	1.25	(1.02-1.53)	1.11	(0.87-1.41)	1.12	(0.94-1.34)	0.81	(0.58-1.12)
Gender (female)	0.34	(0.31-0.37)	0.74	(0.72-0.76)	6.68	(6.47-6.91)	1.43	(1.38-1.48)	1.35	(1.31-1.38)	0.58	(0.56-0.61)
Age	1.00	(1.00-1.00)	1.07	(1.07-1.07)	1.08	(1.07-1.08)	1.02	(1.02-1.02)	1.04	(1.03-1.04)	1.06	(1.05-1.06)
Hypertension	3.19	(2.80-3.62)	2.99	(2.90-3.07)	1.50	(1.45-1.55)	1.32	(1.27-1.38)	1.78	(1.73-1.83)	4.33	(4.00-4.68)
Dyslipidemia	2.02	(1.84-2.22)	2.08	(2.03-2.13)	1.68	(1.64-1.73)	1.24	(1.19-1.28)	1.38	(1.34-1.41)	1.35	(1.29-1.41)
Type 2 diabetes	1.57	(1.43-1.72)	1.78	(1.72-1.83)	1.23	(1.18-1.27)	1.22	(1.17-1.27)	1.32	(1.29-1.36)	2.08	(1.99-2.18)

NASH, nonalcoholic steatohepatitis; OR, odds ratio; CI, confidence interval



Supplemental Figure 1. Flowchart of case-control selection of patients with NASH from the national health insurance and the long-term elderly health insurance claims database in Japan.