TABLE 1. Baseline characteristics of the general population with no known liver disease

Characteristic	Total	Sex			Mortality		
		Female	Male	*P* Value	Alive	Death	*P* Value
Number	200,479	103,826 (51.8)	96,653 (48.21)		199,450 (99.49)	1,029 (0.051)	
Men, n (%)					95,975 (48.12)	678 (65.89)	<.001
Age, years	36.4±7.7	36.2±7.6	36.7±7.9	<.001	36.4±7.7	46.6±13.2	<.001
Smoking status				<.001			<.001
Non/former smoker	148,388 (74.02)	93,902 (90.44)	54,486 (56.37)		147,711 (74.06)	677 (65.79)	
Current smoker	41,952 (20.93)	2,589 (2.49)	39,363 (40.73)		41,630 (20.87)	322 (31.29)	
Unknown	10,139 (5.06)	7,335 (7.06)	2,804 (2.9)		10,109 (5.07)	30 (2.92)	
Alcohol intake, g/day	4 (0-12)	0 (0-4)	10 (4-20)	<.001	4 (0-12)	6 (0-15)	.004
Obesity							
Body mass index, kg/m^2	22.3±2.7	21.3±2.5	23.3±2.5	<.001	22.3±2.7	23.1±2.8	<.001
<25	168,817 (84.21)	95,148 (91.64)	73,669 (76.22)	<.001	168,039 (84.25)	778 (75.61)	<.001
≥25	31,662 (15.79)	8,678 (8.36)	22,984 (23.78)		31,411 (15.75)	251 (24.39)	

				p			p
Exercise measure, times/week				<.001			<.001
<3	168,808 (84.2)	88,684 (85.42)	80,124 (82.9)		168,008 (84.24)	800 (77.75)	
≥3	28935 (14.43)	13,522 (13.02)	15,413 (15.95)		28,723 (14.4)	212 (20.6)	
Unknown	2,736 (1.36)	1,620 (1.56)	1,116 (1.15)		2,719 (1.36)	17 (1.65)	
Education (%)				<.001			<.001
≤High school	31,929 (15.93)	20,659 (19.9)	11,270 (11.66)		31,591 (15.84)	338 (32.85)	
≥College graduate	113,040 (56.38)	53,723 (51.74)	59,317 (61.37)		112,563 (56.44)	477 (46.36)	
Unknown	55,510 (27.69)	29,444 (28.36)	26,066 (26.97)		55,296 (27.72)	214 (20.8)	
T2DM, %	2,446 (1.22)	754 (0.73)	1,692 (1.75)	<.001	2,374 (1.19)	72 (7)	<.001
Glucose, mg/dL	91.8±11	90±9.2	93.6±12.3	<.001	91.7±10.9	96±20.3	<.001
HbA1c, %	5.5±0.4	5.5±0.3	5.4±0.4	<.001	5.5±0.4	5.6±0.7	.004
Hypertension, %	17,569 (8.76)	4,695 (4.52)	12,874 (13.32)	<.001	17,302 (8.67)	267 (25.95)	<.001
Systolic BP, mmHg	110±13.2	105.3±12.4	115.1±12.1	<.001	110±13.2	117.8±15.9	<.001
Diastolic BP, mmHg	70.7±9.6	67.2±8.8	74.5±9.1	<.001	70.7±9.6	75.8±10.8	<.001
Triglycerides, mg/dl	85 (62-120)	72 (55-96)	103 (76-144)	<.001	85 (62-119)	105 (76-142)	<.001
Total cholesterol, mg/dl	188.3±32.6	184±31.9	193±32.6	<.001	188.3±32.5	196.9±36.2	<.001

HDL-C, mg/dl	59±13.5	63.1±13.7	54.6±11.7	<.001	59±13.5	56.7±13.2	<.001
LDL-C, mg/dl	109.2±28.3	103.4±27.1	115.5±28.4	<.001	109.2 ± 28.3	114.5±30.1	<.001
FIB-4				<.001			<.001
Low, %	189,134 (94.34)	98,792 (95.15)	90,342 (93.47)		188,391 (94.46)	743 (72.21)	
Intermediate, %	10,835 (5.4)	4,886 (4.71)	5,949 (6.16)		10,589 (5.31)	246 (23.91)	
High, %	510 (0.25)	148 (0.14)	362 (0.37)		470 (0.24)	40 (3.89)	
APRI				<.001			<.001
Low, %	199,859 (99.69)	103,689 (99.87)	96,170 (99.5)		198,865 (99.71)	994 (96.6)	
Intermediate, %	436 (0.22)	103 (0.1)	333 (0.34)		411 (0.21)	25 (2.43)	
High, %	184 (0.09)	34 (0.03)	150 (0.16)		174 (0.09)	10 (0.97)	

Abbreviations: APRI, Aspartate aminotransferase to platelet ratio index; BP, blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

TABLE 2. All-cause mortality and cancer-related mortality according to FIB-4 score in the general population with no known liver disease

	Person-years	Number of events	Mortality rate (per 10^5 PY)	Age as time scale Sex-adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI) Model 1	Model 2	HR (95% CI) in the model using time-dependent variables
All-cause mortality							
FIB-4							
Low	1,803,630	653	36.2 (33.53-39.09)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Intermediate	160,681	293	182.35 (162.62-204.47)	1.35 (1.14-1.61)	1.41 (1.19-1.68)	1.46 (1.22-1.79)	1.35 (1.15-1.59)
High	7,221	83	1,149.46 (926.96-1,425.36)	5.16 (3.93-6.78)	5.52 (4.20-7.26)	5.94 (4.42-7.98)	5.98 (4.61-7.77)
Cancer-related mortality							
FIB-4							
Low	1,803,630	301	16.69 (14.91-18.68)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Intermediate	160,681	160	99.58 (85.28-116.26)	1.65 (1.31-2.08)	1.75 (1.38-2.2)	1.73 (1.35-2.21)	1.65 (1.31-2.07)

High	7,221	50	692.44 (524.81-913.61)	8.55 (6.04-12.10)	9.41 (6.65-13.32)	10.35 (7.19-14.89)	8.55 (6.06-12.05)

Model 1 was adjusted for sex, year of screening examination, center, BMI, smoking status, regular exercise, educational level, history of diabetes, and history of hypertension.

Model 2 was model 1 and adjustment for LDL-C, HDL-C, triglycerides, systolic blood pressure, glucose, alcohol intake.

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HDL-C, high density lipoprotein cholesterol; HR, hazard ratio; LDL-C, low density lipoprotein cholesterol; PY, patient years.

TABLE 3. All-cause mortality and cancer-related mortality according to APRI score in the general population with no known liver disease

	Person-years	Number of events	Mortality rate (per 10^5 PY)		Age as time scale			HR (95% CI) in the model using time-dependent variables
					Sex-adjusted HR (95% CI)	Multivariable-adjusted HR (95% CI)		
						Model 1	Model 2	
All-cause mortality								
APRI								
<1	1,965,250	983	50.02	(46.99-53.25)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
1 to 2	4,632	30	647.61	(452.8-926.23)	8.38 (5.82-12.06)	8.16 (5.65-11.78)	7.88 (5.37-11.57)	7.97 (5.53-11.49)
≥2	1,649	16	970.2	(594.38-1583.67)	14.22 (8.66-23.34)	13.85 (8.43-22.76)	13.34 (8.07-22.04)	12.84 (7.74-21.31)
Cancer related mortality								
APRI								
<1	1,965,250	482	24.53	(22.43-26.82)	1 (reference)	1 (reference)	1 (reference)	1 (reference)

1 to 2	4,632	19	410.15 (261.62-643.02)	10.72 (6.77-16.99)	10.21 (6.43-16.23)	10.56 (6.60-16.88)	9.83 (6.18-15.63)
≥2	1,649	10	606.38 (326.26-1126.98)	18.06 (9.63-33.84)	17.04 (9.08-31.97)	16.63 (8.79-31.43)	14.26 (7.29-27.91)

Model 1 was adjusted for sex, year of screening examination, center, BMI, smoking status, regular exercise, educational level, history of diabetes, and history of hypertension.

Model 2 was model 1 and adjustment for LDL-C, HDL-C, triglycerides, systolic blood pressure, glucose, alcohol intake.

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HDL-C, high density lipoprotein cholesterol; HR, hazard ratio; LDL-C, low density lipoprotein cholesterol; PY, patient years.

TABLE 4. Causes of death in the general population with no known liver disease

	N	%
Entire population	200,479	100
All deaths		
All cause deaths	1,029	0.51
Cancer-related deaths	511	0.25
CVD-related deaths	109	0.05
Other deaths	409	0.20
Cancer-related deaths		
All cancer-related deaths	511	0.25
Liver cancer deaths		
Malignant neoplasm of liver and intrahepatic bile ducts	80	0.04
Common Non-liver cancer deaths		
Malignant neoplasm of bronchus and lung	95	0.05
Malignant neoplasm of stomach	50	0.02
Malignant neoplasm of pancreas	43	0.02
Malignant neoplasm of breast	30	0.01
Myeloid leukaemia	26	0.01
Malignant neoplasm of colon	23	0.01
Malignant neoplasm of brain	21	0.01
Malignant neoplasm of rectum	15	0.01
Other cancer-related deaths[†]		
CVD-related deaths		
All CVD-related deaths	109	0.05
Angina pectoris	29	0.01

Acute myocardial infarction	15	0.01
Chronic ischaemic heart disease	15	0.01
Pulmonary embolism	13	0.01
Cardiomyopathy	12	0.01
Other CVD-related deaths[‡]		

[†]All other cancer-related deaths individually <0.01% of entire population

[‡]All other CVD-related deaths individually <0.01% of entire population

Abbreviations: CVD, cardiovascular disease.

TABLE 5. Liver cancer and lung cancer mortality according to FIB-4 and APRI score in the general population with no known liver disease

	Deaths	Model 1	Model 2
Person-years		1,741,899	1,741,899
Liver cancer mortality			
FIB-4			
Low	5	1 (reference)	1 (reference)
Intermediate	41	39.69 (14.91-105.67)	39.12 (14.62-104.73)
High	34	629.10 (228.74-1730.2)	588.95 (212.03-1635.94)
P for linear trend		<.001	<.001
APRI			
1	57	1 (reference)	1 (reference)
1-2	15	49.38 (26.22-92.98)	49.06 (25.58-94.06)
2	8	80.42 (34.37-188.18)	88.00 (37.41-206.99)
P for linear trend		<.001	<.001
Lung cancer mortality			
FIB-4			
Low	61	1 (reference)	1 (reference)
Intermediate	34	0.93 (0.51-1.66)	0.72 (0.38-1.37)
High	0	†	†
P for linear trend		N/A	N/A
APRI			
1	95	1 (reference)	1 (reference)
1-2	0	†	†
2	0	†	†

P for linear trend	N/A	N/A

[†]No lung cancer deaths in high FIB-4, intermediate APRI or high APRI categories.

Model 1 was adjusted for sex, year of screening examination, centre, BMI, smoking status, regular exercise, educational level, history of diabetes, and history of hypertension for LDL-C, HDL-C, triglycerides, systolic blood pressure, glucose.

Model 2 was model 1 + adjustment for alcohol amount grams.

Abbreviations: APRI, Aspartate aminotransferase to platelet ratio index; BMI, body mass index; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.