

Supplementary Table 1. Baseline characteristics according to follow-up

Characteristics	Overall	No follow-up	Follow-up	P value
Number	42,168	3,869	38,299	
Age (years) [*]	36.7 (4.5)	36.4 (4.7)	36.7 (4.4)	<0.001
BMI(kg/m ²)	23.3 (3.1)	23.2 (3.1)	23.3 (3.1)	0.023
Male (%)	62.4	57.3	62.9	<0.001
Current smoke (%)	30.4	29.4	30.5	0.157
Alcohol intake (%) [§]	29.2	27.5	29.3	0.015
Regular exercise (%) [§]	41.7	39.9	41.9	0.013
Obesity (%)	28.2	27.5	28.3	0.263
Hypertension (%)	8.4	8.1	8.4	0.543
Metabolic syndrome (%)	12.4	12.2	12.4	0.739
Systolic BP (mmHg) [*]	112.1 (12.8)	111.9 (12.8)	112.1 (12.9)	0.243
Diastolic BP (mmHg) [*]	72.3 (9.2)	72.0 (9.3)	72.3 (9.2)	0.089
Glucose (mg/dl) [*]	92.4 (8.0)	92.2 (8.0)	92.4 (8.0)	0.137
HbA1c (%)	5.3 (0.3)	5.3 (0.3)	5.3 (0.3)	0.803
Total cholesterol (mg/dl) [*]	187.0 (32.1)	186.3 (32.2)	187.1 (32.1)	0.142
LDL-C (mg/dl) [*]	107.3 (27.2)	106.4 (27.1)	107.4 (27.2)	0.035
HDL-C (mg/dl) [*]	53.4 (12.0)	54.3 (12.5)	53.4 (11.9)	<0.001
Uric acid (mg/dl) [*]	5.44 (1.47)	5.32 (1.45)	5.45 (1.47)	<0.001
Triglycerides (mg/dl) [†]	102 (72–151)	99 (70–145)	103 (72–151)	<0.001
AST (U/l) [†]	22 (19–27)	22 (19–26)	22 (19–27)	0.076
ALT (U/l) [†]	21 (16–30)	20 (15–30)	21 (16–30)	0.284
GGT (U/l) [†]	19 (12–33)	18 (11–31)	19 (12–33)	<0.001
hsCRP (mg/l) [†]	0.40 (0.20–0.90)	0.40 (0.20–0.90)	0.40 (0.20–0.90)	0.190
HOMA-IR [†]	1.90 (1.52–2.44)	1.89 (1.53–2.46)	1.90 (1.52–2.44)	0.348

Data are ^{*} means (standard deviation), [†] medians (interquartile range), or percentages.

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein-cholesterol; hsCRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance.

§ ≥ 1 time per week.

Supplementary Table 2. Adjusted hazard ratios (aHR) of incidence of diabetes in relation to nonalcoholic fatty liver disease (NAFLD) and its severity based on NAFLD fibrosis score (NFS)

	Multivariate HR [*] (95% CI)			
	Model 1	Model 2	Model 2	Model 2
No NAFLD	1.00 (reference)	1.00 (reference)		
NAFLD, Low NFS	2.00 (1.79–2.24)	1.81 (1.61–2.04)	1.00 (reference)	1.00 (reference)
NAFLD, Intermediate or high NFS	4.74 (3.67–6.13)	3.84 (2.93–5.02)	2.38 (1.84–3.04)	2.12 (1.64–2.74)
<i>P</i> for trend	<0.001	<0.001		

^{*} Estimated from Cox proportional hazard models.

^{*} Model 1: adjustment for, sex, smoking status, alcohol intake, regular exercise, family history of diabetes, total cholesterol, triglyceride, HDL-cholesterol, HOMA-IR and hsCRP; model 2: model 1 plus adjustment for age and BMI

Abbreviations: CI, confidence intervals; HR, hazard ratios; NAFLD, nonalcoholic fatty liver disease; NFS, NAFLD fibrosis score

Supplementary Table 3. Adjusted hazard ratios (aHR) of incidence of diabetes in relation to nonalcoholic fatty liver disease (NAFLD) and its severity based on FIB-4 or aspartate transaminase to platelet ratio index (APRI)

	Person- years	Incident case	Incidence Density (1000 person- year)	Crude HR (95% CI)	Multivariate HR* (95% CI)		HR (95% CI) [‡] in the model using time-dependent variables
					Model 1	Model 2	
Based on FIB-4							
No NAFLD	129836.1	1,127	8.7	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD, Low FIB-4	45541.3	884	19.4	2.24 (2.05–2.44)	2.14 (1.92–2.40)	1.87 (1.66–2.10)	1.55 (1.38–1.74)
NAFLD, Intermediate or high FIB-4	639.8	14	21.9	2.50 (1.48–4.23)	2.15 (1.26–3.68)	2.17 (1.27–3.70)	1.33 (0.85–2.08)
<i>P</i> for trend				<0.001	<0.001	<0.001	<0.001
Based on APRI							
No NAFLD	129836.1	1,127	8.7	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD, Low APRI	43945.0	818	18.6	2.15 (1.96–2.35)	2.08 (1.86–2.34)	1.82 (1.62–2.05)	1.50 (1.34–1.69)
NAFLD, Intermediate or high APRI	2236.2	80	35.8	4.11 (1.38–5.15)	3.62 (2.84–4.63)	2.97 (2.31–3.80)	3.06 (2.40–3.89)
<i>P</i> for trend				<0.001	<0.001	<0.001	<0.001

* Estimated from Cox proportional hazard models

* Model 1: adjustment for age, sex, BMI, smoking status, alcohol intake and regular exercise; model 2: model 1 plus adjustment for total cholesterol, triglyceride, HDL-cholesterol, HOMA-IR and family history of diabetes except that the results for “based on FIB-4” were not adjusted for age.

[‡]Estimated from extended Cox proportional hazard models with NAFLD category as a time-dependent categorical variable adjusted for other covariates (BMI, smoking status, alcohol intake, BMI, regular exercise, triglyceride, HDL-cholesterol and HOMA-IR over time as time-dependent variables).

FIB-4 was calculated by the following formula: $\text{FIB-4} = (\text{age [years]} \times \text{AST [U/L]}) / (\text{platelet count [109/L]} \times (\text{ALT [U/L]}^{1/2})$ [26]. Published cutoff values were used to define low (FIB-4 <1.30), intermediate, and high (FIB-4 >2.67) probability of advanced fibrosis [26]. Aspartate transaminase (AST) to platelet index (APRI) was calculated by the following formula[27]: $\text{APRI} = ([\text{AST/upper limit of normal}]/\text{platelet count [109/L]}) \times 100$. Published cutoff values were used to define low (APRI <0.5), intermediate, and high (APRI >1.5) probability of advanced fibrosis.

Abbreviations: CI, confidence intervals; HR, hazard ratios; NAFLD, nonalcoholic fatty liver disease; AAR, aspartate transaminase to alanine aminotransferase ratio; APRI, aspartate transaminase to platelet ratio index

Supplementary Table 4. Adjusted hazard ratios (aHR) of incidence of diabetes in relation to nonalcoholic fatty liver disease (NAFLD) and its severity based on NAFLD fibrosis score (NFS) in clinically relevant subgroups.

	NAFLD category, aHR ^a (95% CI)			<i>P</i> for trend	<i>P</i> for interaction
	No NAFLD	NAFLD Low NFS	NAFLD Intermediate, high NFS		
Sex					0.038
Men (N=24,071)	1.00 (reference)	2.04 (1.79–2.33)	4.88 (3.69–6.46)	<0.001	
Women (N=14,220)	1.00 (reference)	1.92 (1.53–2.41)	4.48 (2.27–8.87)	<0.001	
Glucose					<0.001
<100 mg/dl (<i>n</i> = 31,791)	1.00 (reference)	1.59 (1.35–1.87)	-	<0.001	
≥100 mg/dl (<i>n</i> = 6,500)	1.00 (reference)	2.05 (1.73–2.42)	2.30 (1.74–3.04)	<0.001	
HbA1c					<0.001
<5.8% (<i>n</i> =35,267)	1.00 (reference)	1.55 (1.35–1.79)	3.74 (2.57–5.45)	<0.001	
≥5.8% (<i>n</i> =2,827)	1.00 (reference)	1.79 (1.46–2.19)	2.21 (1.52–3.21)	<0.001	
BMI					0.083
< 25 kg/m ² (<i>n</i> =27,439)	1.00 (reference)	1.77 (1.49–2.10)	5.09 (2.71–9.57)	<0.001	
≥ 25 kg/m ² (<i>n</i> =10,844)	1.00 (reference)	1.88 (1.58–2.23)	4.15 (3.07–5.60)	<0.001	
Metabolic syndrome					0.069
No (<i>n</i> =33,535)	1.00 (reference)	1.55 (1.34–1.80)	4.13 (2.32–7.36)	<0.001	
Yes (<i>n</i> =4,753)	1.00 (reference)	2.02 (1.63–2.50)	3.10 (2.24–4.30)	<0.001	
HOMA-IR					<0.001
<2.5 (<i>n</i> =29,435)	1.00 (reference)	1.81 (1.55–2.10)	4.16 (2.55–6.78)	<0.001	
≥2.5 (<i>n</i> =8,856)	1.00 (reference)	2.04 (1.70–2.44)	4.88 (3.55–6.70)	<0.001	

^aAdjustment for sex, smoking status, alcohol intake and regular exercise, total cholesterol, triglyceride, HDL-cholesterol, HOMA-IR and family history of diabetes except obesity, HOMA-IR and metabolic syndrome in the table. The results for metabolic syndrome were adjusted for age, sex, smoking status, alcohol intake and regular exercise, total cholesterol, HOMA-IR, and family history of diabetes.