

Table 1. Estimated^a mean values (95% CI) and adjusted^a proportions (95% CI) of baseline characteristics for population strata defined by sex and menopausal and NAFLD status (N=245,054)

Characteristics	Premenopausal women		Postmenopausal women		Men	
	No NAFLD	NAFLD	No NAFLD	NAFLD	No NAFLD	NAFLD
Number of participants	100,354	9,456	3,505	1,453	78,114	52,172
Age (years)	35.3 (35.2-35.3)	38.5 (38.4-38.6)	58.3 (58.1-58.5)	59.0 (58.7-59.3)	37.3 (37.2-37.4)	38.8 (38.7-38.8)
Alcohol intake (%) ^b	11.1 (10.9-11.3)	12.1 (11.4-12.8)	5.7 (4.9-6.4)	6.4 (5.2-7.7)	46.6 (46.3-47.0)	47.0 (46.6-47.4)
Current smoker (%)	1.7 (1.6-1.8)	2.4 (2.1-2.7)	1.9 (1.4-2.4)	1.8 (1.1-2.6)	29.9 (29.6-30.2)	33.1 (32.7-33.5)
Education level (%) ^d	83.6 (83.4-83.9)	73.7 (72.8-74.7)	39.4 (37.8-41.0)	36.6 (34.0-39.1)	90.1 (89.9-90.4)	91.2 (91.0-91.5)
HEPA (%)	12.4 (12.2-12.7)	11.9 (11.2-12.5)	22.3 (20.8-23.7)	20.9 (18.7-23.1)	18.9 (18.7-19.2)	14.2 (13.9-14.5)
History of hypertension (%)	1.3 (1.2-1.3)	4.0 (3.6-4.3)	20.8 (19.5-22.1)	31.6 (29.3-33.9)	6.5 (6.3-6.6)	11.6 (11.4-11.9)
History of CVD (%)	0.3 (0.3-0.4)	0.4 (0.2-0.5)	3.5 (2.9-4.1)	3.9 (3.0-4.9)	0.9 (0.9-1.0)	1.0 (0.9-1.0)
Anti-lipid medication use (%)	0.3 (0.3-0.4)	0.9 (0.8-1.0)	12.4 (11.3-13.5)	17.7 (15.7-19.6)	1.3 (1.2-1.4)	2.6 (2.5-2.7)
Family history of diabetes (%)	15.1 (14.9-15.3)	20.6 (19.8-21.4)	16.3 (15.1-17.5)	19.2 (17.2-21.3)	11.6 (11.3-11.8)	15.6 (15.3-15.9)
Obesity (%) ^e	6.3 (6.2-6.5)	51.9 (50.9-53.0)	15.6 (14.4-16.8)	49.2 (46.7-51.8)	21.1 (20.9-21.4)	62.6 (62.1-63.0)
Body mass index (kg/m ²) ^e	21.0 (21.0-21.0)	25.7 (25.6-25.7)	22.5 (22.4-22.6)	25.2 (25.1-25.4)	23.2 (23.2-23.2)	26.1 (26.1-26.2)
Waist circumference (cm)	73.8 (73.7-73.8)	85.1 (84.9-85.2)	78.3 (78.0-78.5)	85.5 (85.1-85.9)	82.3 (82.2-82.3)	90.2 (90.1-90.2)

SBP (mmHg)	100.5 (100.5-100.6)	107.8 (107.6-108)	111.7 (111.3-112.1)	114.8 (114.1-115.5)	112.3 (112.2-112.4)	116.6 (116.5-116.7)
DBP (mmHg)	64.2 (64.1-64.2)	68.4 (68.3-68.6)	70.1 (69.8-70.4)	71.9 (71.4-72.3)	71.5 (71.4-71.5)	74.9 (74.9-75.0)
Glucose (mg/dl)	89.8 (89.8-89.9)	94.3 (94.2-94.5)	94.4 (94.1-94.7)	97.8 (97.4-98.2)	93.7 (93.6-93.7)	96.4 (96.3-96.5)
HbA1c (%)	5.5 (5.5-5.5)	5.6 (5.6-5.6)	5.7 (5.7-5.7)	5.8 (5.8-5.8)	5.5 (5.5-5.5)	5.6 (5.6-5.6)
Total cholesterol (mg/dl)	182.9 (182.7-183.1)	196.2 (195.6-196.9)	209.7 (208.5-210.9)	214.3 (212.4-216.1)	192.2 (192.0-192.4)	205.8 (205.5-206.1)
LDL-C(mg/dl)	106.8 (106.6-106.9)	125.7 (125.1-126.2)	133.9 (132.7-135)	142.3 (140.6-144.1)	123.2 (123.0-123.5)	137.5 (137.2-137.8)
HDL-C (mg/dl)	67.8 (67.7-67.9)	55.3 (55.0-55.6)	66.4 (65.9-66.9)	56.6 (55.9-57.4)	56.7 (56.6-56.8)	47.9 (47.8-48.0)
Triglycerides (mg/dl)	74.2 (73.9-74.4)	120.9 (120.1-121.7)	94.6 (92.7-96.4)	130.4 (127.6-133.2)	104.7 (104.1-105.2)	160.3 (159.6-160.9)
GTP (U/L)	14.5 (14.5-14.6)	23.8 (23.5-24.0)	21.0 (20.3-21.7)	27.6 (26.5-28.7)	29.5 (29.3-29.7)	46.2 (45.9-46.5)
ALT (U/L)	13.9 (13.8-14.0)	23.4 (23.2-23.7)	19.2 (18.8-19.6)	25.9 (25.2-26.5)	22.2 (22.1-22.4)	39.6 (39.4-39.7)
AST (U/L)	17.8 (17.8-17.9)	21.0 (20.8-21.2)	23.6 (23.3-24.0)	25.4 (24.9-25.9)	21.8 (21.7-21.9)	27.3 (27.2-27.4)
hs-CRP (mg/L)	0.73 (0.71-0.74)	1.69 (1.64-1.74)	0.83 (0.75-0.91)	1.29 (1.17-1.41)	1.01 (0.99-1.03)	1.40 (1.37-1.43)
HOMA-IR	1.17 (1.17-1.18)	2.36 (2.34-2.38)	1.16 (1.12-1.20)	1.89 (1.82-1.95)	1.18 (1.17-1.18)	2.01 (2.01-2.02)

^aAdjusted for age; ^b≥10 g/day; ^c health-enhancing physical activity; ^d≥college graduate; ^e BMI ≥25 kg/m²

Abbreviations: ALT, alanine aminotransferase; AST, aspartate transaminase; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; NAFLD, nonalcoholic fatty liver disease; SBP, systolic blood pressure

Table 2. Absolute and relative estimates of diabetes incidence for population strata defined by sex and menopausal and NAFLD status

	Person- years	Incident cases	Incidence density (/ 10 ³ PY)	Age adjusted HR (95% CI)	Multivariable-adjusted HR ^a (95% CI)		HR (95% CI) ^b in a model with time-dependent variables
					Model 1	Model 2	
					Premenopausal women (N= 109,810)		
No NAFLD	527,498	803	1.5	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD	45,142	842	18.7	11.09 (10.07-12.22)	4.63 (4.17-5.14)	3.11 (2.79-3.46)	3.02 (2.73-3.35)
Postmenopausal women (N= 4,958)							
No NAFLD	13,208	82	6.2	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD	5,204	143	27.5	4.30 (3.28-5.64)	2.65 (2.02-3.48)	2.14 (1.63-2.81)	1.67 (1.31-2.14)
Men (N= 130,286)							
No NAFLD	427,315	1,941	4.5	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
NAFLD	275,667	4,570	16.6	3.51 (3.32-3.70)	2.16 (2.04-2.29)	1.56 (1.47-1.66)	1.59 (1.50-1.69)

The *P*-value for the interaction of sex, menopausal status, and NAFLD status with the risk of diabetes was <0.001 (Model 2).

^a Estimated from Cox proportional hazards models; multivariable Model 1 was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, hyperlipidemia medication, family history of diabetes, history of hypertension, and BMI. Model 2: Model 1 plus adjustments for SBP; total cholesterol, HDL-C, and triglyceride levels; HOMA-IR; and hs-CRP level

^b Estimated from Cox proportional hazard models with NAFLD status, smoking status, alcohol consumption, physical activity, BMI, hyperlipidemia medication, history of hypertension, SBP, total cholesterol, HDL-C, triglyceride, HOMA-IR, and hs-CRP as time-dependent categorical variables, and baseline age, center, year of screening examination, family history of diabetes, and education level as time-fixed variables

Abbreviations: BMI, body mass index; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; hs-CRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; NAFLD, nonalcoholic fatty liver disease; PY, person-years; SBP, systolic blood pressure

Table 3. Comparison of the discriminatory power of NAFLD for diabetes incidence by sex and menopausal status, with the base model adjusted for age, family history of diabetes, hypertension, BMI, and waist circumference

	AUROC (95% CI)		NRI ^a		IDI	
	Harrell's C (95% CI)	<i>P</i> value	Index	<i>P</i> value	Index	<i>P</i> value
Premenopausal women						
Base model	0·823 (0·812–0·835)	reference		reference		reference
+ NAFLD	0·838 (0·826–0·849)	<0·001	0·170	<0·001	0·012	<0·001
Postmenopausal women						
Base model	0·708 (0·671–0·744)	reference		reference		reference
+ NAFLD	0·743 (0·708–0·779)	0·001	0·264	<0·001	0·015	<0·001
Men						
Base model	0·744 (0·738–0·750)	reference		reference		reference
+ NAFLD	0·758 (0·752–0·764)	<0·001	0·079	<0·001	0·005	<0·001

^a Risk cutoffs of 5% and 10% were used.

Abbreviations: AUROC, area under the receiver operating characteristic curve; BMI, body mass index; CI, confidence interval; IDI, integrated discrimination improvement; NAFLD, nonalcoholic fatty liver disease; NRI, net reclassification improvement