

Nonalcoholic Fatty Liver Disease Without overlapping Metabolic

Associated Fatty Liver Disease and the risk of incident type 2 diabetes

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Supplementary Table 1. Estimated* mean values (95% CI) and adjusted* proportions (95% CI) of the baseline characteristics of study participants with respect to fatty liver disease category among women (n = 120,137)

Characteristics	Neither NAFLD nor MAFLD	NAFLD-only	MAFLD
Number of participants	108,511	1,543	10,083
Age (years)	36.6 (36.6-36.7)	38.3 (38.1-38.5)	39.1 (39.1-39.2)
Alcohol intake (%) [†]	11.0 (10.8-11.1)	10.5 (8.9-12.1)	12.2 (11.5-12.9)
Current smoker (%)	1.8 (1.7-1.8)	2.4 (1.6-3.2)	2.3 (2.0-2.6)
Education level (%) [‡]	80.9 (80.7-81.2)	82.4 (80.5-84.3)	70.2 (69.3-71.1)
HEPA (%) [§]	13.4 (13.2-13.6)	11.4 (9.9-12.9)	12.4 (11.8-13.0)
History of hypertension (%)	2.1 (2.0-2.2)	1.2 (0.8-1.6)	5.4 (5.1-5.7)
History of CVD (%)	0.5 (0.5-0.5)	0.3 (0.1-0.5)	0.6 (0.4-0.7)
Lipid-lowering medication use (%)	0.8 (0.8-0.9)	1.6 (1.2-2.1)	1.7 (1.5-1.8)
Family history of diabetes (%)	15.4 (15.2-15.6)	18.7 (16.8-20.6)	20.8 (20.0-21.6)
Obesity (%)	6.8 (6.6-6.9)	0	59.2 (58.2-60.2)
Body mass index (kg/m ²)	21.1 (21.0-21.1)	21.1 (21.0-21.2)	26.2 (26.2-26.3)
Waist circumference (cm)	74.0 (74.0-74.1)	74.7 (74.3-75.0)	86.5 (86.3-86.6)
SBP (mmHg)	101.1 (101-101.2)	100.1 (99.6-100.6)	109.2 (109.0-109.4)
DBP (mmHg)	64.5 (64.5-64.6)	64.1 (63.7-64.5)	69.2 (69.0-69.4)
Fasting glucose (mg/dL)	90.1 (90.1-90.2)	90.8 (90.4-91.2)	95.1 (94.9-95.2)
HbA1c (%)	5.5 (5.5-5.5)	5.5 (5.5-5.5)	5.5 (5.5-5.5)
Total cholesterol (mg/dL)	183.9 (183.7-184.0)	190.7 (189.1-192.2)	197.8 (197.2-198.4)
LDL-C (mg/dL)	107.8 (107.7-108.0)	115.9 (114.5-117.2)	127.6 (127.0-128.1)
HDL-C (mg/dL)	67.6 (67.5-67.6)	65.0 (64.3-65.7)	53.9 (53.7-54.2)
Triglycerides (mg/dL)	75.1 (74.8-75.3)	81.4 (79.4-83.4)	127.8 (127.0-128.6)
GTP (U/L)	14.9 (14.9-15.0)	17.3 (16.6-18.0)	25.1 (24.8-25.4)
ALT (U/L)	14.2 (14.1-14.3)	16.7 (16.1-17.3)	24.4 (24.2-24.7)
AST (U/L)	18.1 (18.0-18.2)	18.7 (18.2-19.1)	21.6 (21.4-21.8)
hs-CRP (mg/L)	0.74 (0.72-0.75)	0.63 (0.51-0.75)	1.80 (1.75-18.47)
HOMA-IR	1.17 (1.16-1.18)	1.31 (1.26-1.36)	2.45 (2.43-2.47)

*Adjusted for age; [†]≥10 g/day; [‡]≥college graduate; [§] health-enhancing physical activity; ^{||} BMI ≥25 kg/m²
Abbreviations: ALT, alanine aminotransferase; AST, aspartate transaminase; GTP, glutamyl transpeptidase;
BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure;
HbA1c, glycated hemoglobin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein
cholesterol; hs-CRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin
resistance; NAFLD, non-alcoholic fatty liver disease; SBP, systolic blood pressure

Supplementary Table 2. Estimated* mean values (95% CI) and adjusted* proportions (95% CI) of the baseline characteristics of study participants with respect to fatty liver disease category among men (n = 126,287)

Characteristics	Neither NAFLD nor MAFLD	NAFLD-only	MAFLD
Number of participants	75,635	3,896	46,756
Age (years)	36.6 (36.6-36.7)	38.3 (38.1-38.5)	39.1 (39.1-39.2)
Alcohol intake (%) [†]	46.4 (46.1-46.8)	38.2 (36.7-39.7)	47.6 (47.1-48.0)
Current smoker (%)	29.9 (29.5-30.2)	29.3 (27.8-30.7)	33.2 (32.8-33.6)
Education level (%) [‡]	90.1 (89.9-90.3)	93.4 (92.6-94.2)	90.8 (90.5-91.0)
HEPA (%) [§]	19.0 (18.7-19.3)	12.1 (11.1-13.1)	14.5 (14.1-14.8)
History of hypertension (%)	6.4 (6.2-6.5)	3.1 (2.6-3.7)	12.2 (11.9-12.5)
History of CVD (%)	0.9 (0.9-1.0)	1.1 (0.8-1.4)	0.9 (0.8-1.0)
Lipid-lowering medication use (%)	1.3 (1.2-1.3)	1.2 (0.9-1.6)	2.6 (2.5-2.8)
Family history of diabetes (%)	11.6 (11.4-11.8)	14.3 (13.2-15.4)	15.7 (15.4-16.0)
Obesity (%)	21.1 (20.8-21.4)	0	67.7 (67.3-68.1)
Body mass index (kg/m ²)	23.2 (23.2-23.2)	21.9 (21.9-22.0)	26.5 (26.5-26.5)
Waist circumference (cm)	82.3 (82.3-82.4)	80.8 (80.5-81.0)	91.0 (90.9-91.0)
SBP (mmHg)	112.3 (112.2-112.3)	110.1 (109.8-110.5)	117.1 (117.0-117.2)
DBP (mmHg)	71.4 (71.4-71.5)	70.6 (70.4-70.9)	75.2 (75.2-75.3)
Fasting glucose (mg/dL)	93.7 (93.7-93.8)	93.1 (92.8-93.3)	96.7 (96.6-96.8)
HbA1c (%)	5.5 (5.5-5.5)	5.5 (5.5-5.5)	5.6 (5.6-5.6)
Total cholesterol (mg/dL)	192.2 (192.0-192.4)	197.9 (196.9-199.0)	206.5 (206.2-206.8)
LDL-C (mg/dL)	123.2 (123.0-123.5)	130.4 (129.4-131.3)	138.1 (137.8-138.4)
HDL-C (mg/dL)	56.6 (56.5-56.7)	54.3 (53.9-54.7)	47.4 (47.3-47.5)
Triglycerides (mg/dL)	104.7 (104.2-105.3)	108.8 (106.5-111.2)	164.6 (163.9-165.3)
GTP (U/L)	29.5 (29.3-29.8)	32.5 (31.4-33.5)	47.5 (47.2-47.8)
ALT (U/L)	22.2 (22.1-22.4)	27.6 (26.9-28.2)	40.6 (40.5-40.8)
AST (U/L)	21.8 (21.7-21.9)	22.8 (22.4-23.2)	27.7 (27.5-27.8)
hs-CRP (mg/L)	1.00 (0.98-1.03)	0.78 (0.68-0.89)	1.45 (1.42-1.48)
HOMA-IR	1.17 (1.17-1.18)	1.20 (1.17-1.23)	2.07 (2.06-2.08)

*Adjusted for age; [†]≥10 g/day; [‡]≥college graduate; [§] health-enhancing physical activity; ^{||} BMI ≥25 kg/m²
Abbreviations: ALT, alanine aminotransferase; AST, aspartate transaminase; GTP, glutamyl transpeptidase;
BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure;
HbA1c, glycated hemoglobin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein
cholesterol; hs-CRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin
resistance; NAFLD, non-alcoholic fatty liver disease; SBP, systolic blood pressure

Supplementary Table 3. Absolute and relative estimates of diabetes incidence with respect to fatty liver disease category

Fatty liver disease category	PY	Incident cases	Incidence rate (/10 ³ PY)	Multivariable-adjusted HR* (95% CI)
Total				
Neither NAFLD nor MAFLD	993,873	2,885	2.9	1.00 (reference)
NAFLD-only	29888	152	5.1	1.77 (1.48-2.13)
NAFLD-only plus high FIB-4	45	1	22.1	8.57 (1.21-60.91)
MAFLD	294453	5,350	17.7	3.16 (2.99-3.34)
MAFLD plus high FIB-4	469	15	19.3	2.75 (1.47-5.12)
Women				
Neither NAFLD nor MAFLD	576,185	1,001	1.7	1.00 (reference)
NAFLD-only	7,911	33	4.2	2.31 (1.56-3.41)
NAFLD-only plus high FIB-4	10	1	103.2	57.17 (8.02-407.5)
MAFLD	47,513	1,046	22.0	5.76 (5.18-6.40)
MAFLD plus high FIB-4	79	4	50.3	3.63 (0.90-14.59)
Men				
Neither NAFLD nor MAFLD	417,688	1,884	4.5	1.00 (reference)
NAFLD-only	21,976	118	5.4	1.53 (1.25-1.88)
NAFLD-only plus high FIB-4	36	0	0	-
MAFLD	246,940	4,304	17.4	2.60 (2.44-2.76)
MAFLD plus high FIB-4	389	11	28.3	2.50 (1.24-5.01)

The *p*-value for the interaction of sex and fatty liver disease category with the risk of diabetes was <0.001 (multivariable model).

* Estimated from Cox proportional hazards models; the multivariable model was adjusted for age, center, year of screening examination, alcohol consumption, smoking status, physical activity, education level, use of lipid-lowering medication, family history of diabetes, prediabetes and history of hypertension.