

Supplementary Table 1. Sensitivity analysis of logistic regression for combining amylase at entry [E] and annual**change rate of amylase [R] regarding the odds ratio (OR) for type 2 diabetes mellitus according to baseline age,****HbA1c, and BMI**

A : Age (year)	≤48			≥49		
	n	event	OR(95%CI)	n	event	OR(95%CI)
E ≤57 and R ≤-2.0	138	54	4.18(2.68-6.5)	81	34	3.84(2.28-6.46)
E ≤57 and R ≥-1.9	717	104	1.41(1.06-1.9)	550	78	0.97(0.72-1.32)
E ≥58 and R ≤-2.0	603	164	3.48(2.66-4.55)	637	176	3.34(2.61-4.27)
E ≥58 and R ≥-1.9	1859	168	1.00(ref.)	2332	243	1.00(ref.)
B : HbA1c (%)	≤5.5			≥5.6		
	n	event	OR(95%CI)	n	event	OR(95%CI)
E ≤57 and R ≤-2.0	140	46	4.19(2.7-6.5)	79	42	3.57(2.09-6.1)
E ≤57 and R ≥-1.9	892	95	1.35(1.02-1.79)	375	87	1.02(0.74-1.4)
E ≥58 and R ≤-2.0	913	202	3.89(3.08-4.9)	327	138	2.66(1.97-3.57)
E ≥58 and R ≥-1.9	3060	200	1.00(ref.)	1131	211	1.00(ref.)
C : BMI (kg/m ²)	≤24.9			≥25.0		
	n	event	OR(95%CI)	n	event	OR(95%CI)
E ≤57 and R ≤-2.0	120	37	3.57(2.26-5.64)	99	51	4.85(2.91-8.08)
E ≤57 and R ≥-1.9	871	114	1.19(0.93-1.54)	396	68	1.19(0.81-1.75)
E ≥58 and R ≤-2.0	997	252	3.16(2.58-3.89)	243	88	4.3(2.91-6.35)
E ≥58 and R ≥-1.9	3504	327	1.00(ref.)	687	84	1.00(ref.)

ORs were adjusted for age, sex, BMI, SBP, eGFR, fatty liver, current smoking, current physical activity, current**drinking habits, diabetes family history, and HbA1c**

Supplementary Table 2. Characteristics of participants according to serum amylase at entry and annual change

rate of serum amylase

A: Baseline serum amylase (IU/L)	Q1: ≤57	Q2:58-67	Q3:68-78	Q4:79-94	Q5: ≥95	P for
n	1486	1285	1389	1439	1318	trend
T2DM (%)	270(18.2)	190(14.8)	203(14.6)	213(14.8)	145(11)	<0.001
Male sex (%)	1182(79.5)	977(76)	1008(72.6)	1013(70.4)	875(66.4)	<0.001
Age (year)	48±8	48±8	49±9	50±9	53±9	<0.001
Diabetes family history (%)	225(15.1)	204(15.9)	202(14.5)	231(16.1)	212(16.1)	0.494
BMI (kg/m²)	24±3.1	23.2±2.9	22.7±2.7	22.4±2.8	21.7±2.6	<0.001
<18.5	29(2)	54(4.2)	68(4.9)	95(6.6)	118(9)	<0.001
≥25.0	495(33.3)	310(24.1)	251(18.1)	240(16.7)	129(9.8)	<0.001
Systolic blood pressure (mmHg)	125±16	125±16	123±15	124±15	122±15	<0.001
HbA1c (%)	5.4±0.3	5.3±0.3	5.4±0.3	5.4±0.3	5.3±0.3	0.023
(mmol/mol)	35±4	35±4	35±4	35±4	35±4	0.023
Fasting plasma glucose (mg/dL)	97±8	96±9	95±8	95±8	93±8	<0.001
Fatty liver (%)	589(39.6)	383(29.8)	330(23.8)	317(22)	203(15.4)	<0.001
ALT (IU/L)	28±21	26±16	24±15	24±26	23±16	<0.001
γ-GTP (IU/L)	57±60	51±57	47±56	44±57	38±44	<0.001
non-HDL cholesterol (mg/dL)	151±33	149±33	147±33	146±32	148±33	0.002
eGFR (mL/min/1.73m²)	77±15	74±15	73±15	72±15	68±14	<0.001
Serum amylase at censor (IU/L)	52±13	65±11	75±14	86±16	111±29	<0.001
Annual change rate of amylase (%)	1.4±5.9	0.6±3.8	0.5±4	0.0±4.9	-0.5±4.6	<0.001
Current smoking (%)	424(28.5)	293(22.8)	248(17.9)	198(13.8)	146(11.1)	<0.001
Current physical activity (%)	686(46.2)	623(48.5)	697(50.2)	712(49.5)	680(51.6)	0.005
Current drinking habits (%)	1293(87)	1064(82.8)	1099(79.1)	1110(77.1)	942(71.5)	<0.001

B: Annual change rate of amylase (%)	Q1: ≤-2.0	Q2:-1.9 ~ -0.6	Q3:-0.5 ~ 0.8	Q4:0.9 ~ 2.6	Q5: ≥2.7	P for
n	1459	1357	1434	1347	1320	trend
T2DM (%)	428(29.3)	136(10)	103(7.2)	108(8)	246(18.6)	<0.001
Male sex (%)	1035(70.9)	986(72.7)	1038(72.4)	1014(75.3)	982(74.4)	0.011
Age (year)	49±9	50±9	49±9	50±9	50±9	0.003
Diabetes family history (%)	325(22.3)	211(15.5)	214(14.9)	165(12.2)	159(12)	<0.001
BMI (kg/m²)	23±3.1	22.8±2.9	22.8±2.8	22.8±2.8	22.8±3	0.166
<18.5	68(4.7)	80(5.9)	72(5)	73(5.4)	71(5.4)	0.590
≥25.0	342(23.4)	260(19.2)	300(20.9)	269(20)	254(19.2)	0.023

Systolic blood pressure (mmHg)	124±15	124±16	124±16	123±15	124±16	0.854
HbA1c (%)	5.4±0.4	5.3±0.3	5.3±0.3	5.3±0.3	5.4±0.3	<0.001
(mmol/mol)	35±4	35±4	35±4	35±4	36±4	<0.001
Fasting plasma glucose (mg/dL)	95±9	95±8	95±8	95±8	97±9	<0.001
Fatty liver (%)	439(30.1)	348(25.6)	337(23.5)	350(26)	348(26.4)	0.044
ALT (IU/L)	26±26	25±15	25±16	24±16	25±21	0.019
γ -GTP (IU/L)	49±63	46±46	46±46	47±52	52±67	0.923
non-HDL cholesterol (mg/dL)	149±33	150±32	148±32	148±33	146±33	0.001
eGFR (mL/min/1.73m ²)	75±15	72±15	72±15	72±15	74±15	0.408
Serum amylase at entry (IU/L)	83±26	79±24	75±23	73±22	71±22	<0.001
Serum amylase at censor (IU/L)	69±21	73±22	76±23	81±24	90±35	<0.001
Current smoking (%)	295(20.2)	232(17.1)	257(17.9)	257(19.1)	268(20.3)	0.580
Current physical activity (%)	654(44.8)	657(48.4)	741(51.7)	664(49.3)	682(51.7)	<0.001
Current drinking habits (%)	1126(77.2)	1078(79.4)	1149(80.1)	1093(81.1)	1062(80.5)	0.014

Supplementary Table 3. Comparison of characteristics between participants included and excluded in the analysis because of missing data

Characteristics	Participants included in the analysis		Excluded from the analysis because of missing data		p value
	6917	n			
Incident T2DM (%)	1021(14.8)	237	34(14.3)	0.859	
Age (year)	50±9	237	54±10	<0.001	
Male sex (%)	5055(73.1)	237	130(54.9)	<0.001	
Diabetes family history (%)	1074(15.5)	237	9(3.8)	<0.001	
BMI (kg/m ²)	22.8±2.9	237	22.5±2.8	0.082	
<18.5	364(5.3)	237	15(6.3)	0.471	
≥25.0	1425(20.6)	237	48(20.3)	0.896	
Systolic blood pressure (mmHg)	124±16	237	123±15	0.264	
HbA1c (%)	5.4±0.3	237	5.5±0.3	<0.001	
(mmol/mol)	35±4	237	36±4	<0.001	
Fasting plasma glucose (mg/dL)	95±8	237	95±8	0.837	
Fatty liver (%)	1822(26.3)	233	51(21.9)	0.128	
ALT (IU/L)	25±19	237	22±11	<0.001	
γ-GTP (IU/L)	48±55	237	37±35	<0.001	
Non-HDL cholesterol (mg/dL)	148±33	237	153±33	0.026	
eGFR (mL/min/1.73m²)	73±15	237	75±15	0.048	
Serum amylase level at entry (IU/L)	76±24	237	74±24	0.136	
Serum amylase level at censor (IU/L)*	77±27	237	77±24	0.727	
Annual change rate of amylase (%)	0.4±4.8	236	1.3±4.2	0.004	
Current smoking (%)	1309(18.9)	30	1(3.3)	0.029	
Current physical activity (%)	3398(49.1)	41	31(75.6)	0.001	
Current drinking habits (%)	5508(79.6)	58	41(70.7)	0.093	

*"at censor" means serum amylase level at the end of the study period in non-T2DM controls or when T2DM was ascertained in T2DM cases.

Supplemental figure 1. The receiver operating characteristic curve to determine the cut-off value for the annual change in amylase, a predictor of T2DM.

