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2    **Healthy Overweight Individuals**

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## Supplementary Methods

### *Study population: The Kangbuk Samsung Health Study cohort*

The Kangbuk Samsung Health Study is a cohort study of Korean men and women who underwent comprehensive annual or biennial health examinations at one of the Kangbuk Samsung Hospital Total Healthcare Centers in Seoul and Suwon, South Korea.<sup>1, 2</sup> The Industrial Safety and Health Law in South Korea requires annual or biennial health screening for employees; over 80% of participants were employees of companies, local governmental organizations, or their spouses, and the remaining voluntarily purchased the health screening programs. This study uses data routinely collected during health screening examinations, including questionnaires, blood tests, imaging examinations, and procedures (e.g., endoscopy).<sup>1</sup>

### *Measurements*

Data regarding medical history, medication use, diet, lifestyle factors, and education level were collected using a standardized, self-administered questionnaire. Smoking status was categorized as never, former, or current smoking. Average alcohol consumption was estimated by calculating the frequency of drinking per week and the amount consumed per drinking day. Physical activity levels were evaluated using the validated Korean version of the International Physical Activity Questionnaire Short Form.<sup>3, 4</sup> Health-enhancing physical activity (HEPA) was physical activity that complied with the following criteria: 1) vigorous activity  $\geq 3$  d/week with  $\geq 1,500$  accumulated metabolic equivalent(MET)-min/week, or 2) 7 days of a combination of walking or moderate to vigorous intensity activities accumulating  $\geq 3,000$  MET min/week.<sup>4</sup>

Anthropometric measures, blood pressure (BP), and blood samples after at least 10 hours of fasting were obtained by trained personnel.<sup>5</sup> Height was measured to the nearest mm using a

stadiometer with the subject standing barefoot. Weight was measured to the nearest 0.1 kilogram (kg) by using a bioimpedance analyser (InBody 720, Biospace Co., Seoul, Korea), which had been validated for reproducibility and accuracy.<sup>6</sup> Body mass index (BMI) was calculated as weight in kg divided by height in meters squared, and was classified according to Asian-specific criteria<sup>7</sup>: overweight, BMI of 23–25 kg/m<sup>2</sup>, and obese, BMI  $\geq$ 25 kg/m<sup>2</sup>. Asians have increased all-cause mortality risk compared to Caucasians at lower BMI units, and the risk increases beginning at BMI  $\geq$ 25 kg/m<sup>2</sup>.<sup>8</sup>

Fasting blood tests included glucose (FBG), insulin, total cholesterol, low density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, triglycerides, aspartate aminotransferase, alanine aminotransferase (ALT), high sensitivity C-reactive protein (hsCRP), platelet count, and albumin, as previously described.<sup>1</sup> Insulin resistance was assessed by the homeostatic model assessment–insulin resistance (HOMA-IR) calculation: fasting blood insulin (uU/mL)  $\times$  FBG (mmol/L) / 22.5.

### ***Assessment of NAFLD and liver fibrosis***

Hepatic steatosis (HS) diagnosis was based on abdominal ultrasound examined by experienced radiologists who were blinded to the aim of the present study. Standard criteria, including diffuse increase of fine echoes in the liver parenchyma in comparison to the kidney or spleen, attenuation of deep beam, and brightness in vessel walls were used for the determination of disease presence or absence.<sup>9</sup> Inter-observer reliability values were substantial (kappa statistic: 0.74), and intra-observer reliability values were excellent (kappa statistic: 0.94) for HS diagnosis.<sup>10</sup>

Two non-invasive indices of liver fibrosis were used to assess the risk of fibrosis progression during follow-up: the fibrosis 4 score (FIB-4) and NAFLD fibrosis score (NFS).<sup>11, 12</sup> Subjects with NAFLD were classified into three groups based on the probability of advanced fibrosis: low (FIB-4: <1.30), intermediate (FIB-4: 1.30–2.66), and high (FIB-4:  $\geq$ 2.67).<sup>11</sup> Participants were also categorized into three groups reflecting the probability of advanced fibrosis based on NFS: high (NFS >0.676), intermediate (NFS: 0.676 to -1.455), and low (NFS < -1.455).<sup>12</sup>

### ***Statistical analysis: mediation criteria***

The following criteria for mediation analysis were used: 1) the predictor of interest (weight change) was significantly related to the mediator (HOMA-IR, hsCRP, and metabolic components), 2) the mediator (HOMA-IR, hsCRP, and metabolic components) was significantly related to the outcome (HS and HS plus fibrosis), and 3) the addition of the mediator (HOMA-IR, hsCRP, and metabolic components) to the model attenuated the predictor's coefficient while having a statistically significant mediation effect.

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**Supplementary Table 1.** Development of hepatic steatosis according to weight change category by sex among metabolically healthy overweight or obese individuals

Weight change category <sup>c</sup>	Person- years (PY)	Incident cases	Incidence rate (/1,000 PY)	Age adjusted HR (95% CI)	Multivariable- adjusted HR <sup>a</sup> (95% CI)	HR (95% CI) <sup>b</sup> in model using time- dependent variables
<b>Women</b>						
>-5.0%	5821.1	121	20.8	0.59 (0.48–0.74)	0.55 (0.44–0.69)	0.16 (0.11–0.24)
-1.0 to -5.0%	8249.0	288	34.9	0.93 (0.78–1.11)	0.94 (0.79–1.12)	0.49 (0.37–0.64)
-0.9 to 0.9%	5836.7	219	37.5	1.00 (reference)	1.00 (reference)	1.00 (reference)
1.0 to 5.0%	9618.7	437	45.4	1.25 (1.06–1.47)	1.25 (1.07–1.48)	1.33 (1.08–1.64)
> 5.0%	6059.5	312	51.5	1.58 (1.33–1.88)	1.56 (1.31–1.86)	2.90 (2.39–3.51)
<i>P</i> for trend				< 0.001	< 0.001	< 0.001
<b>Men</b>						
>-5.0%	2631.8	77	29.3	0.56 (0.44–0.71)	0.49 (0.38–0.62)	0.20 (0.13–0.30)
-1.0 to -5.0%	9865.7	418	42.4	0.78 (0.69–0.90)	0.77 (0.67–0.88)	0.49 (0.39–0.61)
-0.9 to 0.9%	8712.6	456	52.3	1.00 (reference)	1.00 (reference)	1.00 (reference)

1.0 to 5.0%	14989.8	879	58.6	1.19 (1.06–1.33)	1.19 (1.06–1.33)	1.68 (1.45–1.95)
> 5.0%	5009.7	332	66.3	1.50 (1.30–1.73)	1.51 (1.30–1.74)	3.30 (2.85–3.81)
<i>P</i> for trend				< 0.001	< 0.001	< 0.001

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*P* = 0.413 for the overall interaction between sex and weight change category for hepatic steatosis incidence (multivariable-adjusted model)

HR, hazard ratio; CI, confidence interval.

<sup>a</sup> Estimated from parametric proportional hazard models. The multivariable model was adjusted for age, sex, center, year of screening exam, educational level, smoking status, alcohol intake, physical activity, body mass index, and total energy intake.

<sup>b</sup> Estimated from parametric proportional hazard models with weight change category, alcohol intake, smoking status, physical activity, total energy intake as a time-dependent categorical variables and baseline age, sex, center, year of screening exam, BMI, and education level as time-fixed variables.

<sup>c</sup> The negative numbers in each weight change category, expressed with a “-“ sign before each number, refer to weight loss during follow-up.



**Supplementary Table 2.** Development of hepatic steatosis and hepatic steatosis plus intermediate or high probability of advanced fibrosis by intention of weight loss among metabolically healthy overweight or obese individuals

Weight change category <sup>c</sup>	Multivariable-adjusted HR <sup>a</sup> (95% CI)		
	Hepatic steatosis	Hepatic steatosis plus	
		intermediate / high probability of advanced	
		fibrosis	
		Based on FIB-4	Based on NFS
<b>Unintentional weight loss</b>			
>-5.0%	0.52 (0.41–0.66)	0.28 (0.07–1.22)	0.30 (0.10–0.84)
- 1.0 to -5.0%	0.85 (0.73–1.00)	0.96 (0.53–1.73)	0.67 (0.41–1.11)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
<i>P</i> for trend	< 0.001	0.731	0.001
<b>Intentional weight loss</b>			
>-5.0%	0.46 (0.37–0.57)	0.22 (0.05–0.96)	0.31 (0.12–0.80)
-1.0 to -5.0%	0.79 (0.69–0.91)	0.94 (0.52–1.68)	0.91 (0.57–1.47)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
<i>P</i> for trend	< 0.001	0.042	< 0.001
<i>P</i> for interaction	0.646	0.722	0.881

HR, hazard ratio; CI, confidence interval; FIB-4, Fibrosis-4; NFS, non-alcoholic fatty liver disease fibrosis Score.

<sup>a</sup> Estimated from parametric proportional hazard models. The multivariable model was adjusted for age, sex, center, year of screening exam, educational level, smoking status, alcohol intake,

physical activity, body mass index (not for NFS), and total energy intake.

<sup>c</sup> The negative numbers in each weight change category, expressed with a “-“ sign before each number, refer to weight loss during follow-up.

**Supplementary Table 3.** Mediation analysis of the association between weight change category and development of hepatic steatosis and hepatic steatosis plus intermediate or high probability of advanced fibrosis among metabolically healthy overweight or obese individuals

Weight change category <sup>b</sup>	HR (95% CI) <sup>a</sup> in model using time-dependent variables		
	Hepatic steatosis	Hepatic steatosis plus	
		intermediate / high probability of advanced	
		fibrosis	
		Based on FIB-4	Based on NFS
Model 1 <sup>c</sup>			
>-5%	0.52 (0.44–0.60)	0.29 (0.10–0.80)	0.38 (0.19–0.77)
-1 to -5%	0.83 (0.75–0.92)	0.96 (0.63–1.46)	0.83 (0.59–1.18)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.21 (1.10–1.33)	1.02 (0.68–1.51)	1.17 (0.86–1.59)
> 5%	1.51 (1.36–1.69)	1.02 (0.57–1.85)	1.51 (1.02–2.24)
<i>P</i> for trend	< 0.001	0.095	<0.001
Model 1 <sup>c</sup> + adjusting for HOMA-IR			
>-5%	0.52 (0.44–0.60)	0.30 (0.11–0.83)	0.38 (0.19–0.77)
-1 to -5%	0.82 (0.74–0.91)	0.96 (0.63–1.45)	0.82 (0.58–1.16)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.22 (1.11–1.33)	1.03 (0.69–1.53)	1.18 (0.87–1.60)
> 5%	1.56 (1.39–1.74)	1.04 (0.57–1.88)	1.56 (1.05–2.32)
<i>P</i> for trend	< 0.001	0.091	< 0.001
Model 1 <sup>c</sup> + adjusting for hsCRP			

>-5%	0.51 (0.43–0.60)	0.28 (0.10–0.80)	0.37 (0.18–0.75)
-1 to -5%	0.82 (0.74–0.92)	0.96 (0.63–1.46)	0.83 (0.59–1.17)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.20 (1.10–1.32)	1.01 (0.68–1.51)	1.17 (0.86–1.58)
> 5%	1.52 (1.36–1.70)	1.02 (0.56–1.85)	1.51 (1.02–2.24)
<i>P</i> for trend	< 0.001	0.097	< 0.001
<hr/> Model 1 <sup>c</sup> + adjusting for HOMA-IR and hsCRP			
>-5%	0.51 (0.43–0.60)	0.29 (0.10–0.83)	0.37 (0.18–0.75)
-1 to -5%	0.81 (0.73–0.90)	0.95 (0.63–1.45)	0.82 (0.58–1.15)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.21 (1.10–1.33)	1.02 (0.68–1.52)	1.18 (0.87–1.60)
> 5%	1.56 (1.40–1.74)	1.03 (0.57–1.87)	1.56 (1.05–2.32)
<i>P</i> for trend	< 0.001	0.092	< 0.001
<hr/> Model 1 <sup>c</sup> + adjusting for total cholesterol			
>-5%	0.51 (0.44–0.60)	0.28 (0.10–0.80)	0.38 (0.19–0.77)
-1 to -5%	0.83 (0.75–0.92)	0.96 (0.64–1.46)	0.83 (0.59–1.18)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.21 (1.10–1.33)	1.02 (0.68–1.51)	1.17 (0.86–1.59)
> 5%	1.52 (1.36–1.70)	1.03 (0.57–1.85)	1.51 (1.02–2.25)
<i>P</i> for trend	< 0.001	0.093	< 0.001
<hr/> Model 1 <sup>c</sup> + adjusting for HDL			
>-5%	0.51 (0.44–0.60)	0.29 (0.10–0.80)	0.38 (0.19–0.76)
-1 to -5%	0.83 (0.75–0.92)	0.96 (0.63–1.46)	0.83 (0.59–1.18)

-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.21 (1.10–1.33)	1.02 (0.68–1.52)	1.17 (0.86–1.59)
> 5%	1.54 (1.37–1.72)	1.03 (0.57–1.86)	1.52 (1.03–2.26)
<i>P</i> for trend	< 0.001	0.092	< 0.001
<hr/> Model 1 <sup>c</sup> + adjusting for triglyceride			
>-5%	0.51 (0.43–0.59)	0.28 (0.10–0.80)	0.37 (0.19–0.75)
- 1 to -5%	0.82 (0.73–0.91)	0.96 (0.63–1.46)	0.83 (0.59–1.17)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.22 (1.11–1.34)	1.02 (0.69–1.52)	1.18 (0.87–1.61)
> 5%	1.58 (1.41–1.77)	1.04 (0.57–1.88)	1.57 (1.06–2.33)
<i>P</i> for trend	< 0.001	0.084	< 0.001
<hr/> Model 1 <sup>c</sup> + adjusting for glucose			
>-5%	0.52 (0.44–0.61)	0.28 (0.10–0.80)	0.39 (0.19–0.78)
- 1 to -5%	0.83 (0.74–0.92)	0.96 (0.64–1.46)	0.83 (0.59–1.17)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.21 (1.10–1.33)	1.01 (0.68–1.51)	1.19 (0.88–1.62)
> 5%	1.52 (1.36–1.70)	1.01 (0.56–1.83)	1.60 (1.08–2.37)
<i>P</i> for trend	< 0.001	0.104	< 0.001
<hr/> Model 1 <sup>c</sup> + adjusting for SBP			
>-5%	0.52 (0.44–0.61)	0.29 (0.10–0.81)	0.39 (0.19–0.79)
- 1 to -5%	0.83 (0.75–0.92)	0.96 (0.63–1.46)	0.85 (0.60–1.19)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.21 (1.10–1.33)	1.00 (0.67–1.49)	1.19 (0.87–1.62)

> 5%	1.51 (1.35–1.69)	1.02 (0.57–1.85)	1.53 (1.03–2.28)
<i>P</i> for trend	< 0.001	0.108	< 0.001
Model 1 <sup>c</sup> + adjusting for all metabolic profiles <sup>d</sup>			
>-5%	0.50 (0.42–0.59)	0.29 (0.10–0.82)	0.35 (0.17–0.70)
- 1 to -5%	0.81 (0.73–0.90)	0.95 (0.62–1.44)	0.80 (0.57–1.14)
-0.9 to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1 to 5%	1.22 (1.11–1.34)	1.00 (0.67–1.49)	1.24 (0.91–1.69)
> 5%	1.61 (1.44–1.80)	1.03 (0.57–1.87)	1.65 (1.11–2.46)
<i>P</i> for trend	< 0.001	0.099	< 0.001

HR, hazard ratio; CI, confidence interval; FIB-4, Fibrosis-4; NFS, non-alcoholic fatty liver disease fibrosis score.

<sup>a</sup> Estimated from parametric proportional hazard models

<sup>b</sup> The negative numbers in each weight change category, expressed with a “-“ sign before each number, refer to weight loss during follow-up.

<sup>c</sup> Model 1 was adjusted for age, sex, center, year of screening exam, educational level, smoking status, alcohol intake, physical activity, body mass index (not for NFS), and total energy intake.

<sup>d</sup> All metabolic profiles refer to all metabolic components in this table: HOMA-IR, hsCRP, total cholesterol, HDL, triglyceride, glucose, and SBP.

**Supplementary Table 4.** Estimated<sup>a</sup> mean values (95% CI) and adjusted<sup>a</sup> proportion (95% CI) of characteristics at follow-up according to weight change category among metabolically healthy overweight or obese individuals (n = 14,779)

Characteristics	weight change category <sup>b</sup>					P for trend
	>-5.0%	-1.0 to -5.0%	-0.9 to 0.9%	1.0 to 5.0%	>5.0%	
Number	1,550	3,411	2,835	4,811	2,172	
Body mass index (kg/m <sup>2</sup> )	22.8 (22.7–22.9)	23.9 (23.9–24.0)	24.5 (24.5–24.6)	25.2 (25.1–25.2)	26.5 (26.5–26.6)	<0.001
Systolic BP (mmHg)	104.8 (104.4–105.3)	105.9 (105.6–106.2)	106.4 (106.0–106.7)	107.2 (106.9–107.4)	109.0 (108.7–109.4)	<0.001
Diastolic BP (mmHg)	67.0 (66.6–67.3)	67.3 (67.1–67.5)	67.5 (67.3–67.8)	67.8 (67.5–68.0)	68.9 (68.6–69.2)	<0.001
Glucose (mg/dl)	89.6 (89.3–90.0)	90.9 (90.7–91.2)	91.3 (91.0–91.5)	92.1 (91.9–92.3)	93.0 (92.8–93.3)	<0.001
Total cholesterol (mg/dL)	185.2 (183.6–186.7)	190.0 (189.0–191.0)	192.3 (191.2–193.4)	193.7 (192.8–194.5)	198.2 (196.9–199.5)	<0.001
LDL-C (mg/dL)	111.1 (109.7–112.5)	117.0 (116.1–117.9)	120.1 (119.1–121.1)	121.9 (121.1–122.7)	126.7 (125.5–127.9)	<0.001
HDL-C (mg/dL)	70.1 (69.2–71.0)	66.8 (66.1–67.4)	65.8 (65.1–66.5)	64.2 (63.7–64.8)	63.8 (63.1–64.6)	<0.001
Triglycerides (mg/dL)	71.5 (69.6–73.4)	79.6 (78.4–80.9)	85.1 (83.8–86.5)	91.2 (90.2–92.3)	101.8 (100.2–103.4)	<0.001
ALT (U/L)	17.2 (16.7–17.8)	17.1 (16.7–17.5)	18.0 (17.6–18.4)	19.0 (18.7–19.3)	21.2 (20.8–21.7)	<0.001
hsCRP (mg/L)	4.8 (3.2–6.5)	2.0 (0.9–3.1)	2.9 (1.6–4.1)	2.1 (1.1–3.0)	2.0 (0.6–3.4)	<0.001
HOMA-IR	1.02 (0.99–1.06)	1.19 (1.17–1.22)	1.30 (1.28–1.33)	1.42 (1.41–1.44)	1.68 (1.65–1.71)	<0.001

CI, confidence intervals; ALT, alanine aminotransferase; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein-cholesterol; hsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance.

<sup>a</sup>Adjusted for age and sex. Data are expressed as age- and sex-adjusted means (95% CI).

<sup>b</sup>The negative numbers in each weight change category, expressed with a “-“ sign before each number, refer to weight loss during follow-up.



**Supplemental Table 5.** Estimated<sup>a</sup> mean values (95% CI) and adjusted<sup>a</sup> proportion (95% CI) of baseline characteristics according to BMI categories among metabolically healthy overweight or obese individuals (n = 14,779)

Characteristics	BMI Categories			P for trend
	23.0 to 24.9	25.0 to 29.9	≥30.0%	
Number	10,477	4,209	93	
Age (years)	36.5 (36.4-36.6)	36.4 (36.2-36.6)	34.2 (32.9-35.4)	0.057
Male (%)	53.2 (52.2-54.1)	56.4 (54.9-57.9)	31.9 (22.6-41.2)	0.030
Current smoker (%)	16.5 (15.8-17.2)	17.0 (15.9-18.1)	17.9 (8.7-27.2)	0.420
Alcohol intake (%) <sup>b</sup>	31.8 (30.9-32.6)	32.4 (31.2-33.7)	37.2 (27.6-46.8)	0.254
HEPA (%)	18.3 (17.6-19.0)	20.1 (18.9-21.3)	20.0 (11.6-28.4)	0.012
High education level (%) <sup>c</sup>	87.1 (86.4-87.7)	84.9 (83.8-86.0)	72.5 (63.9-81.2)	<0.001
Weight change for the past year				
Stable	58.6 (57.7-59.6)	45.7 (44.2-47.3)	34.2 (23.8-44.5)	<0.001
Weight loss	8.9 (8.4-9.5)	9.0 (8.1-9.9)	14.8 (7.1-22.5)	0.548
Weight gain	32.4 (31.5-33.4)	45.3 (43.8-46.8)	49.5 (39.2-59.9)	<0.001
Weight change from visit 1 to visit 2 (kg)	0.5 (0.5-0.6)	0.1 (-0.0-0.2)	0.7 (-0.0-1.4)	<0.001

Systolic BP (mmHg)	106.3 (106.2-106.5)	108.4 (108.2-108.7)	111.0 (109.3-112.7)	<0.001
Diastolic BP (mmHg)	66.8 (66.7-66.9)	67.8 (67.6-68.0)	69.4 (68.0-70.8)	<0.001
Glucose (mg/dL)	90.2 (90.1-90.3)	90.3 (90.1-90.4)	90.5 (89.4-91.7)	0.199
Total cholesterol (mg/dL)	191.3 (190.7-191.8)	194.3 (193.4-195.2)	195.9 (190.0-201.9)	<0.001
LDL-C (mg/dL)	116.9 (116.4-117.4)	120.6 (119.8-121.4)	121.1 (115.7-126.6)	<0.001
HDL-C (mg/dL)	64.0 (63.8-64.2)	62.6 (62.3-63.0)	62.3 (60.1-64.4)	<0.001
Triglycerides (mg/dl)	77.3 (76.8-77.8)	81.5 (80.7-82.2)	83.5 (78.3-88.7)	<0.001
ALT (U/l)	17.8 (17.6-17.9)	19.5 (19.3-19.8)	21.8 (20.1-23.5)	<0.001
hsCRP (mg/L)	0.87 (0.82-0.92)	1.08 (0.99-1.16)	1.82 (1.27-2.38)	<0.001
HOMA-IR	1.07 (1.06-1.08)	1.19 (1.18-1.21)	1.47 (1.37-1.57)	<0.001
Total energy intake (kcal/d) <sup>d</sup>	1,630.9 (1,615.7-1,646.1)	1,640.1 (1,616.1-1,664.1)	1,518.8 (1,355.6-1,682.1)	<0.001

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ALT, alanine aminotransferase; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; HEPA, health-enhancing physically active; hsCRP, high-sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol.

<sup>a</sup>Adjusted for age and sex. Data are expressed as age- and sex-adjusted mean (95% CI), and age- and sex-adjusted proportions (95% CI).

<sup>b</sup> ≥10 g/d; <sup>c</sup> ≥ College graduate; <sup>d</sup>Among 10,556 participants with plausible estimated energy intake levels (within three standard

deviations from the log-transformed mean energy intake).

**Supplementary Table 6.** Development of hepatic steatosis and hepatic steatosis plus intermediate or high probability of advanced fibrosis by weight change category among metabolically healthy overweight or obese individuals according to BMI category

Weight change category <sup>a</sup>	Multivariable-adjusted HR <sup>b</sup> (95% CI)		
	Hepatic steatosis	Hepatic steatosis plus	
		intermediate / high probability of advanced	
		fibrosis	
		Based on FIB-4	Based on NFS
<b>BMI&lt;25 (kg/m<sup>2</sup>)</b>			
>-5.0%	0.51 (0.41-0.64)	0.20 (0.05-0.85)	0.22 (0.07-0.73)
- 1.0% to -5.0%	0.82 (0.72-0.94)	0.83 (0.51-1.38)	0.78 (0.50-1.23)
-0.9% to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1.0% to 5.0%	1.22 (1.08-1.37)	0.72 (0.44-1.17)	1.09 (0.73-1.63)
>5.0%	1.43 (1.25-1.65)	0.62 (0.28-1.36)	1.20 (0.70-2.04)
<i>P</i> for trend	< 0.001	0.810	0.002
<b>BMI≥25 (kg/m<sup>2</sup>)</b>			
>-5.0%	0.49 (0.39-0.62)	0.41 (0.09-1.86)	0.43 (0.18-1.04)
- 1.0% to -5.0%	0.83 (0.70-0.98)	1.36 (0.63-2.95)	0.87 (0.51-1.48)
-0.9% to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1.0% to 5.0%	1.20 (1.03-1.40)	1.96 (0.95-4.06)	1.34 (0.83-2.16)
>5.0%	1.53 (1.28-1.83)	1.89 (0.74-4.83)	1.79 (1.01-3.18)
<i>P</i> for trend	< 0.001	0.019	< 0.001
<i>P</i> for interaction	0.931	0.184	0.815

HR, hazard ratio; CI, confidence interval; FIB-4, Fibrosis-4; NFS, non-alcoholic fatty liver disease fibrosis score; BMI, body mass index.

<sup>a</sup>The negative numbers in each weight change category, expressed with a “-“ sign before each number, refer to weight loss during follow-up.

<sup>b</sup>Estimated from parametric proportional hazard models. The multivariable model was adjusted for age, sex, center, year of screening exam, educational level, smoking status, alcohol intake, physical activity, and total energy intake.

**Supplementary Table 7.** Development of hepatic steatosis and hepatic steatosis plus intermediate or high probability of advanced fibrosis by weight change category among metabolically healthy overweight or obese participants who were weight stable during the previous year (n = 7,206)

Weight change category <sup>a</sup>	Multivariable-adjusted HR <sup>b</sup> (95% CI)		
	Hepatic steatosis	Hepatic steatosis plus	
		intermediate / high probability of advanced	
		fibrosis	
		Based on FIB-4	Based on NFS
>-5.0%	0.46 (0.36-0.60)	0.33 (0.08-1.38)	0.47 (0.18-1.20)
- 1.0% to -5.0%	0.77 (0.66-0.89)	0.97 (0.55-1.69)	0.98 (0.62-1.55)
-0.9% to 0.9%	1.00 (reference)	1.00 (reference)	1.00 (reference)
1.0% to 5.0%	1.18 (1.04-1.34)	1.11 (0.65-1.88)	1.28 (0.85-1.94)
>5.0%	1.45 (1.23-1.71)	1.11 (0.47-2.62)	1.48 (0.82-2.68)
<i>P</i> for trend	< 0.001	0.180	0.010

HR, hazard ratio; CI, confidence interval; FIB-4, Fibrosis-4; NFS, non-alcoholic fatty liver disease fibrosis score.

<sup>a</sup>The negative numbers in each weight change category, expressed with a “-“ sign before each number, refer to weight loss during follow-up.

<sup>b</sup>Estimated from parametric proportional hazard models. The multivariable model was adjusted for age, sex, center, year of screening exam, educational level, smoking status, alcohol intake, physical activity, and total energy intake.