Supplemental information

Time-restricted eating with or without low-carbohydrate diet reduces visceral fat and improves metabolic syndrome: A randomized trial

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1 **Table S1. Baseline characteristics of participants**

	LCD N = 55	TRE N = 55	Both N = 52	p value
Drug treatment (number, n%)				0.252
Hypotensive drugs	9 (16.4)	12 (21.8)	5 (9.6)	
Lipid-lowering drugs	2 (3.6)	4 (7.3)	0 (0.0)	
Urate-lowering drugs	3 (5.5)	3 (5.5)	5 (9.6)	
Oral hypoglycemic drugs	8 (14.5)	2 (3.6)	4 (7.7)	
Insulin	2 (3.6)	2 (3.6)	1 (1.9)	
Complicating metabolic disease (number, n%)				0.539
Hypertension	12 (21.8)	17 (30.9)	8 (15.4)	
Coronary heart disease	2 (3.6)	2 (3.6)	1 (1.9)	
Arthrolithiasis	4 (7.3)	3 (5.5)	6 (11.5)	
Type 2 diabetes	8 (14.5)	3 (5.5)	6 (11.5)	

2   LCD, low-carbohydrate diet; TRE, time-restricted eating; Both, combination treatment.

3   Differences between treatment arms (LCD, TRE and Both) were tested by Chi-square test.

4   Related to Table 1.

5

6

Table S2. Baseline characteristics of early TRE and late TRE subgroups

	TRE		p value	Both		p value
	eTRE (N = 38)	lTRE (N = 17)		eTRE (N = 32)	lTRE (N = 20)	
Gender male/female	23/15	12/5	0.473	22/10	15/5	0.628
Age (years)	43.7 ± 1.6	41.6 ± 2.9	0.501	40.6 ± 1.6	36.5 ± 1.8	0.095
Meal eating window (hours)	10.3 ± 0.4	10.5 ± 0.4	0.824	10.9 ± 0.3	10.3 ± 0.4	0.118
Daily carbohydrate intake (g)	341 ± 18	365 ± 33	0.499	352 ± 29	375 ± 35	0.607
Weight (kg)	84.2 ± 2.4	85.7 ± 3.6	0.725	84.7 ± 2.3	85.0 ± 3.1	0.935
BMI (kg/m^2)	29.7 ± 0.5	29.2 ± 0.9	0.639	29.1 ± 0.6	28.8 ± 0.8	0.808
Waist circumference (cm)	96.8 ± 1.4	97.0 ± 2.6	0.930	94.8 ± 1.4	94.4 ± 1.5	0.819
Hip circumference (cm)	104.7 ± 1.2	104.1 ± 1.3	0.773	104.1 ± 1.3	104.1 ± 2.1	0.987
Waist-to-hip ratio (WHR)	0.93 ± 0.01	0.95 ± 0.02	0.462	0.91 ± 0.01	0.92 ± 0.02	0.611
Body fat mass (kg)	33.7 ± 1.1	32.3 ± 1.6	0.496	33.3 ± 1.0	31.8 ± 1.5	0.374
Body muscle mass (kg)	31.2 ± 1.1	32.6 ± 1.7	0.477	31.5 ± 1.1	32.7 ± 1.4	0.506
Subcutaneous fat area (SFA, cm^2)	270 ± 11	270 ± 19	0.990	256 ± 10	254 ± 18	0.902
Visceral fat area (VFA, cm^2)	102 ± 6	113 ± 8	0.321	97 ± 5	94 ± 7	0.681
Hemoglobin A1c (HbA1c, %)	5.6 (0.6)	5.7 (0.6)	0.784	5.6 (0.7)	5.6 (1.1)	0.445
Fasting blood glucose (mmol/L)	5.05 (1.16)	5.05 (0.69)	0.579	5.01 (1.05)	5.19 (1.66)	0.735
Fasting insulin (mIU/L)	27.8 (21.1)	32.8 (19.9)	0.344	27.0 (13.9)	30.6 (57.6)	0.337
C-peptide (pg/mL)	1696.1 ± 131.9	1580.0 ± 137.9	0.877	1570.7 ± 84.7	1781.4 ± 185.6	0.250
HOMA-IR	6.70 (6.55)	7.64 (6.58)	0.202	6.79 (4.05)	7.58 (14.00)	0.829
HOMA-IS	0.21 (0.23)	0.14 (0.12)	0.177	0.16 (0.10)	0.16 (0.17)	0.836
QUICKI	0.29 (0.04)	0.29 (0.02)	0.236	0.29 (0.03)	0.29 (0.05)	0.463
Uric acid (UA, μmol/L)	383 ± 15	387 ± 26	0.877	429 ± 23	395 ± 18	0.298
Total cholesterol (mmol/L)	4.67 ± 0.16	4.95 ± 0.20	0.309	4.82 ± 0.18	4.58 ± 0.19	0.384
LDL-c (mmol/L)	2.88 ± 0.14	3.28 ± 0.19	0.108	3.15 ± 0.17	2.85 ± 0.16	0.235
Triglycerides (TG, mmol/L)	2.10 (1.52)	2.31 (1.77)	0.439	1.92 (1.92)	2.43 (3.63)	0.776
HDL-c (mmol/L)	1.11 ± 0.04	1.08 ± 0.05	0.663	1.07 ± 0.04	1.01 ± 0.05	0.378
TG/HDL	1.77 (1.85)	2.24 (1.99)	0.412	1.89 (2.61)	2.32 (4.43)	0.749
Systolic blood pressure (mmHg)	136 ± 3	137 ± 4	0.857	132 ± 3	129 ± 4	0.558
Diastolic blood pressure (mmHg)	86 ± 2	89 ± 3	0.407	86 ± 2	81 ± 2	0.091

2   TRE, time-restricted eating; Both, combination treatment; eTRE, early TRE; lTRE, late TRE;

3   BMI, body mass index; HOMA-IR, homeostasis model assessment insulin resistance; HOMA-

4   IS, homeostatic model assessment of insulin sensitivity; QUICKI, quantitative insulin-sensitivity

5   check index; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein

6   cholesterol. All data are presented as the mean ± standard error of the mean (SEM) for normal

7   distribution or median (interquartile range) for abnormal distribution. Differences between the

8   eTRE and lTRE subgroups were tested by two sample dependent T test or Mann-Whitney U

9   test. Related to Table 1.

10

Table S3. Food intake among participants who completed the intervention

	LCD	TRE	Both	p value for pairwise comparison		
	N = 47	N = 44	N = 44	LCD vs. TRE	LCD vs. Both	TRE vs. Both
Staple food- rice						
Baseline	450 (400)	600 (750)	475 (563)			
Follow-up	200 (300)***	450 (550)	225 (388)***			
△	-250 (475)	0 (413)	-273 (700)	**0.002**	0.424	0.068
Staple food- wheat flour						
Baseline	600 (750)	700 (906)	750 (1088)			
Follow-up	200 (363)***	500 (400)*	150 (213)***			
△	-350 (800)	-100 (1019)	-575 (1050)	0.051	0.350	**0.005**
Staple food- coarse grain and field crop (corn, oat, sorghum, etc.)						
Baseline	150 (300)	50 (369)	100 (309)			
Follow-up	0 (150)**	0 (100)**	0 (94)***			
△	0 (200)	0 (338)	0 (250)	0.789	0.811	0.623
Staple food- tuber vegetable (potato, batata, yam, taro, etc.)						
Baseline	200 (300)	100 (275)	0 (169)			
Follow-up	50 (200)*	0 (150)	0 (150)			
△	-50 (200)	0 (100)	0 (144)	0.287	0.044	0.350
Staple food- starch and derived products (vermicelli, etc.)						
Baseline	0 (100)	0 (100)	50 (150)			
Follow-up	0 (50)	0 (100)	0 (100)			
△	0 (50)	0 (62)	0 (130)	0.664	0.467	0.351
Pastry- bread, cake, cookie, etc.						
Baseline	50 (200)	0 (100)	25 (150)			
Follow-up	0 (50)**	0 (138)	0 (0)**			
△	-50 (150)	0 (100)	0 (100)	**0.020**	0.864	**0.016**
Meat- pork, beef and lamb						
Baseline	350 (300)	350 (588)	350 (550)			
Follow-up	300 (300)	350 (588)	375 (838)**			
△	0 (350)	0 (388)	100 (438)	0.733	**0.006**	**0.004**
Meat- processed meat (bacon, sausage, etc.)						
Baseline	0 (50)	0 (8)	0 (15)			
Follow-up	0 (50)	0 (50)	0 (0)			
△	0 (25)	0 (0)	0 (0)	0.242	0.627	0.437
Meat- animal innards						
Baseline	0 (0)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.120	0.883	0.161
Aquatic product- fish, crab, shrimp, shellfish, molluscs, etc.						
Baseline	50 (150)	100 (200)	0 (50)			
Follow-up	100 (200)	0 (150)*	0 (150)			
△	0 (150)	0 (100)	0 (100)	**0.011**	0.980	**0.009**
Poultry- chicken, duck, pigeon, etc.						

Baseline	100 (200)	50 (150)	0 (138)			
Follow-up	100 (263)	50 (200)	100 (200)			
△	0 (150)	0 (150)	0 (175)	0.358	0.763	0.254
Egg- hen's egg, duck's egg, preserved egg, salted egg, etc.						
Baseline	300 (150)	350 (475)	200 (200)			
Follow-up	350 (200)	350 (313)	290 (356)			
△	0 (325)	-25 (408)	0 (375)	0.178	0.978	0.235
Milk and milk products- milk, yogurt, etc.						
Baseline	540 (1260)	450 (1014)	600 (1038)			
Follow-up	700 (1400)	500 (838)	600 (928)			
△	0 (1200)	0 (434)	0 (838)	0.758	0.582	0.299
Milk and milk products- milk powder, cheese, etc.						
Baseline	0 (0)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.607	0.262	0.642
Beans and legume products- soybean						
Baseline	0 (150)	0 (200)	0 (150)			
Follow-up	0 (250)	0 (100)	0 (100)			
△	0 (175)	0 (100)	0 (164)	0.171	0.763	0.160
Beans and legume products- tofu, soybean curd sheet, soybean curd slab and oily bean curd						
Baseline	100 (150)	100 (200)	33 (100)			
Follow-up	100 (225)	65 (281)	50 (150)			
△	0 (150)	0 (150)	0 (226)	0.438	0.345	0.806
Vegetables- dark vegetables						
Baseline	500 (1200)	650 (738)	613 (1100)			
Follow-up	600 (110)	600 (1113)	700 (1113)			
△	100 (725)	0 (998)	-18 (975)	0.570	0.247	0.613
Vegetables- light vegetables						
Baseline	350 (1200)	350 (1163)	350 (538)			
Follow-up	450 (850)	375 (813)	600 (675)			
△	0 (650)	-50 (653)	120 (838)	0.279	0.352	0.073
Phytocomycetes- mushrooms, seaweed, porphyra, etc.						
Baseline	50 (150)	50 (100)	50 (125)			
Follow-up	100 (225)	0 (100)	100 (200)*			
△	0 (105)	0 (100)	25 (150)	0.299	0.396	0.084
Fruits- apple, pear, peach, cherry, grapefruit, kiwifruit, etc.						
Baseline	350 (950)	350 (675)	450 (694)			
Follow-up	200 (400)*	300 (425)*	200 (388)**			
△	0 (500)	-75 (425)	-200 (613)	0.927	0.368	0.268
Fruits- mango, pineapple, etc.						
Baseline	0 (0)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.824	0.734	0.576
Fruits- watermelon, etc.						

Baseline	0 (50)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.658	0.238	0.105
Nuts- peanut, sunflower seed, walnut, pumpkin seed, etc.						
Baseline	35 (175)	0 (169)	50 (150)			
Follow-up	140 (300)	63 (150)	63 (200)			
△	0 (185)	0 (150)	0 (181)	0.404	0.275	0.799
Alcohol- low-alcohol liquor (≤38°)						
Baseline	0 (0)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.680	0.171	0.100
Alcohol- high-alcohol liquor (＞38°)						
Baseline	0 (0)	0 (50)	0 (0)			
Follow-up	0 (0)	0 (50)	0 (0)			
△	0 (0)	0 (38)	0 (0)	0.321	0.408	0.876
Alcohol- beer						
Baseline	0 (0)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.405	0.514	0.183
Alcohol- fruit wine						
Baseline	0 (0)	0 (0)	0 (0)			
Follow-up	0 (0)	0 (0)	0 (0)			
△	0 (0)	0 (0)	0 (0)	0.169	0.195	0.559

1 LCD, low-carbohydrate diet; TRE, time-restricted eating; Both, combination treatment. All data
2 were presented as the median (interquartile range) for abnormal distribution. Analyses were
3 conducted in participants who completed the intervention. Change scores from baseline were
4 represented by "Δ" in the table. After 3 months of intervention, pairwise comparisons of change
5 scores between the groups (e.g., TRE vs. LCD, TRE vs. Both, LCD vs. Both) were evaluated
6 by Mann-Whitney U test. *p < 0.05, **p < 0.01, ***p < 0.001: significant differences compared
7 with baseline (paired Wilcoxon test). Related to STAR Methods.
8

Table S4. Physical activity analysis among participants who completed the intervention

		LCD N = 47	TRE N = 44	Both N = 44
Intense physical activity time (h/week)	Baseline	0.0 (0.3)	0.0 (0.6)	0.0 (1.0)
	Follow-up	0.0 (0.8)	0.0 (0.5)	0.0 (0.8)
	△	0.0 (0.0)	0.0 (0.0)	0.0 (0.2)
Moderate physical activity time (h/week)	Baseline	0.0 (1.3)	0.0 (0.1)	0.0 (0.5)
	Follow-up	0.0 (1.0)	0.0 (0.0)	0.0 (1.0)
	△	0.0 (0.0)	0.0 (0.0)	0.0 (0.6)
Walking time (h/week)	Baseline	2.3 (3.8)	3.5 (4.0)	3.5 (3.6)
	Follow-up	2.5 (4.8)	2.5 (2.4)	2.6 (4.8)
	△	0.0 (2.3)	0.0 (3.2)	-0.5 (1.5)
Sitting time (h/week)	Baseline	35.0 (31.5)	28.6 (25.7)	33.8 (35.0)
	Follow-up	35.0 (25.7)	35.0 (25.7)	35.0 (34.4)
	△	0.0 (7.0)	0.0 (16.3)	0.0 (16.3)

3 LCD, low-carbohydrate diet; TRE, time-restricted eating Both, combination treatment. All data
4 were presented as the median (interquartile range) for abnormal distribution. Analyses were
5 conducted in participants who completed the intervention. Change scores from baseline were
6 represented by "Δ" in the table. After 3 months of intervention, pairwise comparisons of baseline
7 and change scores between the groups (e.g., TRE vs. LCD, TRE vs. Both, LCD vs. Both) were
8 evaluated by Mann-Whitney U test. The significant difference as compared with baseline were
9 evaluated by paired Wilcoxon test for each group. No significant difference was found either
10 within each group or between groups. Related to STAR Methods.
11

1 **Table S5. Change in primary outcomes between participants with or without more than 50% dietary log records**

	LCD (N = 55)			TRE (N = 55)			Both (N = 52)		
	Records ≥ 50% (N = 19)	Records < 50% (N = 36)	p value	Records ≥ 50% (N = 19)	Records < 50% (N = 36)	p value	Records ≥ 50% (N = 23)	Records < 50% (N = 29)	p value
Days of dietary log (during the first 2 weeks)	14 (5)	1 (2)	<0.001	14 (4)	1 (2)	<0.001	14 (2)	0 (1)	<0.001
△ Weight (kg)	-2.2 ± 0.9	-2.3 ± 0.5	0.908	-3.1 ± 0.7	-3.7 ± 0.7	0.540	-5.4 ± 0.9	-4.9 ± 0.8	0.739
△ Visceral fat area (VFA, cm^2)	-7 ± 7	12 ± 7	0.089	-11 ± 4	-14 ± 7	0.738	-9 ± 5	-10 ± 5	0.842
△ Subcutaneous fat area (SFA, cm^2)	-29 ± 9	-21 ± 6	0.468	-24 ± 13	-24 ±10	0.994	-35 ± 7	-15 ± 13	0.235

2 LCD, low-carbohydrate diet; TRE, time-restricted eating; Both, combination treatment. During the first 2-week of intervention period, when participants were
3 trained for diet schemes, daily dietary log was monitored, analyzed and clustered into two groups based on the record time more than 7 days (≥ 50%) or not (<
4 50%). All data were presented as mean ± standard error of the mean (SEM) for normally distributed variables or the median (interquartile range) for abnormal
5 distribution (Days of dietary log). Change scores from baseline were represented by "Δ" in the table. Analyses were conducted using all participants (intention-
6 to-treat), using a multiple imputation approach for missing data. After 3 months of intervention, pairwise comparisons of change scores between the valid and
7 invalid record subgroups were evaluated by t test or Mann-Whitney U test. Related to STAR Methods.

8

Table S6. Change in body composition and metabolic risk markers after 3 months of the intervention between early TRE and late TRE subgroups.

		TRE		p value	Both		p value
		eTRE (N = 38)	lTRE (N = 17)		eTRE (N = 32)	lTRE (N = 20)	
Days of adherence (days)		61.4 ± 4.0	74.9 ± 2.7	**<u>0.031</u>**	57.0 ± 3.9	58.7 ± 5.3	0.798
Willingness to continue the diet (n/total, %)		29/30 (97)	14/14 (100)	0.490	20/27 (74)	16/17 (94)	0.093
Meal eating window (hours)	Follow-up	6.4 ± 0.4***	6.9 ± 0.3***		6.9 ± 0.5***	6.6 ± 0.5***	
	△	-4.0 ± 0.6	-3.6 ± 0.4	0.715	-4.0 ± 0.5	-3.7 ± 0.7	0.726
Daily carbohydrate intake (g)	Follow-up	315 ± 19	356 ± 26		144 ± 15***	133 ± 14***	
	△	-26 ±18	-9 ± 22	0.564	-207 ± 23	-243 ± 36	0.392
Weight (kg)	1 M Follow-up	81.6 ± 2.7^b	85.7 ± 3.6^b		81.5 ± 2.3^b	83.1 ± 2.9^a	
	1 M △	-2.4 ± 0.4	-2.5 ± 0.7	0.869	-3.1 ± 0.5	-1.9 ± 0.7	0.151
	2 M Follow-up	80.4 ± 2.6^a	83.3 ± 3.2^a		79.7 ± 2.2^b	81.8 ± 2.9^b	
	2 M △	-3.6 ± 0.4	-4.0 ± 0.7	0.599	-4.9± 0.5	-3.2 ± 0.7	**<u>0.040</u>**
	3 M Follow-up	79.9 ± 2.8	84.0 ± 3.5		78.9 ± 2.4	82.4 ± 2.6	
	3 M △	-3.3 ± 0.4	-3.7 ± 0.7	0.606	-5.6 ± 0.5	-4.2 ± 0.7	0.096
BMI (kg/m^2)	Follow-up	28.3 ± 0.5***	27.7 ± 0.5*		27.0 ± 0.6***	27.5 ± 0.7**	
	△	-1.4 ± 0.3	-1.6 ± 0.6	0.781	-2.1 ± 0.3	-1.4 ± 0.4	0.148
Waist circumference (cm)	Follow-up	91.7 ± 1.8***	94.9 ± 2.8		91.0 ± 1.9*	92.0 ± 1.8	
	△	-5.1 ± 1.1	-2.1 ± 2.1	0.167	-3.8 ± 1.5	-2.4 ± 1.9	0.558
Hip circumference (cm)	Follow-up	103.1 ± 1.1	102.9 ± 1.3		101.0 ± 1.4*	100.8 ± 1.5	
	△	-1.7 ± 0.9	-1.2 ± 1.2	0.796	-3.2 ± 1.2	-2.3 ± 1.2	0.621
Waist-to-hip ratio (WHR)	Follow-up	0.89 ± 0.01**	0.92 ± 0.02		0.90 ± 0.01	0.91 ± 0.02	

	△	-0.04 ± 0.01	-0.02 ± 0.02	0.380	-0.01 ± 0.01	-0.00 ± 0.01	0.838
Body fat mass (kg)	Follow-up	32.4 ± 1.1	30.8 ± 1.5		30.5 ± 1.1**	28.5 ± 1.6***	
	△	-1.3 ± 0.8	-1.4 ± 0.7	0.912	-2.8 ± 0.8	-3.2 ± 0.7	0.703
Body muscle mass (kg)	Follow-up	30.6 ± 1.0	32.3 ± 1.5		30.7 ± 1.0*	32.8 ± 1.2	
	△	-0.6 ± 0.3	-0.4 ± 0.3	0.674	-0.8 ± 0.3	0.1 ± 0.4	0.061
Subcutaneous fat area (SFA, cm^2)	Follow-up	251 ± 13*	232 ± 14		227 ± 13*	239 ± 18	
	△	-18 ± 7	-38 ± 21	0.256	-29 ± 11	-15 ± 13	0.394
Visceral fat area (VFA, cm^2)	Follow-up	88 ± 7*	101 ± 8		88 ± 6*	83 ± 7	
	△	-14 ± 6	-12 ± 8	0.872	-9 ± 4	-10 ± 6	0.856
Hemoglobin A1c (HbA1c, %)	Follow-up	5.5 (0.6)	5.6 (0.7)		5.6 (0.7)	5.5 (0.9)	
	△	0.0 (0.3)	-0.1 (0.4)	0.854	-0.1 (0.6)	-0.2 (0.4)	0.502
Fasting blood glucose (mmol/L)	Follow-up	4.77 (1.07)	4.76 (0.94)		4.83 (1.22)	5.23 (1.13)	
	△	-0.15 (1.02)	-0.22 (0.35)	0.863	-0.32 (0.95)	-0.15 (0.82)	0.457
Fasting insulin (mIU/L)	Follow-up	23.9 (21.0)***	29.9 (12.7)*		16.1 (13.4)**	26.4 (34.7)*	
	△	-3.5 (13.2)	-2.2 (13.6)	0.771	-5.3 (11.0)	-5.7 (24.6)	0.880
C-peptide (pg/mL)	Follow-up	1451.1 ± 108.2**	1338.5 ± 96.5		1185.5 ± 74.1***	1568.1 ± 127.1	
	△	-245.0 ± 77.5	-241.5 ± 128.4	0.981	-385.2 ± 76.2	-213.3 ± 126.4	0.221
HOMA-IR	Follow-up	4.68 (4.51)***	6.48 (4.67)**		3.76 (2.33)***	6.78 (5.72)	
	△	-0.84 (4.61)	-2.15 (4.99)	0.548	-2.40 (4.54)	-1.65 (7.53)	0.229
HOMA-IS	Follow-up	0.28 (0.51)***	0.18 (0.25)*		0.31 (0.23)***	0.24 (0.22)	
	△	0.05 (0.33)	0.03 (0.09)	0.629	0.14 (0.21)	0.04 (0.14)	**0.007**
QUICKI	Follow-up	0.31 (0.05)***	0.30 (0.03)*		0.32 (0.03)***	0.30 (0.04)	
	△	0.02 (0.03)	0.01 (0.02)	0.489	0.02 (0.01)	0.01 (0.04)	0.102
Uric acid (UA, µmol/L)	Follow-up	344 ± 16*	347 ± 16*		370 ± 17**	354 ± 18**	

	△	-39 ± 15	-40 ± 18	0.967	-58 ± 19	-41 ± 14	0.511
Total cholesterol (mmol/L)	Follow-up	4.56 ± 0.15	5.30 ± 0.27		4.93 ± 0.20	4.77 ± 0.22	
	△	-0.12 ± 0.21	0.35 ± 0.26	0.201	0.11 ± 0.13	0.19 ± 0.27	0.775
LDL-c (mmol/L)	Follow-up	2.89 ± 0.15	3.69 ± 0.25*		3.42 ± 0.19*	3.17 ± 0.23	
	△	0.01 ± 0.18	0.41 ± 0.19	0.180	0.28 ± 0.12	0.33 ± 0.28	0.847
Triglycerides (TG, mmol/L)	Follow-up	1.53 (1.65)*	1.98 (1.56)*		1.40 (1.25)**	1.30 (1.76)*	
	△	-0.39 (1.33)	-0.30 (1.38)	0.884	-0.51 (1.84)	-0.49 (2.28)	0.707
HDL-c (mmol/L)	Follow-up	1.14 ± 0.04	1.09 ± 0.05		1.15 ± 0.04*	1.13 ± 0.05*	
	△	0.03 ± 0.04	0.01 ± 0.04	0.723	0.07 ± 0.03	0.12 ± 0.04	0.327
TG/HDL-c	Follow-up	1.25 (1.63)	2.01 (1.29)		1.23 (1.08)***	1.63 (1.82)**	
	△	-0.31 (1.48)	-0.30 (2.06)	0.855	-0.54 (2.07)	-0.87 (2.64)	0.707
Systolic blood pressure (mmHg)	Follow-up	136 ± 2	139 ± 3		131 ± 3	132 ± 3	
	△	0 ± 2	2 ± 3	0.590	-1 ± 2	3 ± 3	0.367
Diastolic blood pressure (mmHg)	Follow-up	84 ± 2	88 ± 2		82 ± 2*	76 ± 2	
	△	-2 ± 2	-2 ± 2	0.895	-5 ± 2	-4 ± 2	0.873

1 TRE, time-restricted eating; Both, combination treatment; eTRE, early TRE; lTRE, late TRE; BMI, body mass index; HOMA-IR, homeostasis model assessment
2 of insulin resistance; HOMA-IS, homeostatic model assessment of insulin sensitivity; QUICKI, quantitative insulin-sensitivity check index; LDL-c, low-density
3 lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol. All data were presented as mean ± standard error of the mean (SEM) for normally distributed
4 variables or the median (interquartile range) for abnormal distribution. Change scores from baseline were represented by "Δ" in the table. Analyses were
5 conducted using all participants (intention-to-treat), using a linear mixed model with randomized dietary intervention as factor to correct for the correlations of
6 repeated measurements on changes in body weight, and using a multiple imputation approach for other missing data. After 3 months of intervention, pairwise
7 comparisons of change scores between the eTRE and lTRE subgroups were evaluated by t test or Mann-Whitney U test. [a]$p < 0.05$, [b]$p < 0.001$: significant
8 differences compared with one month before (paired t test); *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$: significant differences compared with baseline (paired t test or
9 paired Wilcoxon test). Related to Table 2.
10
11

Table S7. Suggested Food and Menu List

Go/Green	**Vegetables:**
	Spinach, Cabbage, Red cabbage, Watercress, Lettuce, Stern lettuce, Bok choy, Coriander, Celery, Leeks, Bitter melon, Cucumber, Garlic, Ginger, Spring onions, Onion, Chili pepper, Green bell Pepper, Red bell pepper, Tomato, Eggplant, Cauliflower, Broccoli, Mushroom, Bean sprouts
	Meat:
	Pork, Lean meet, Bacon belly, Pig's Trotters , Pork liver, Spareribs, Beef, Mutton, Chicken, Shrimp, Fish
	Soups: excluding any staple food contained in the soup
	Egg & vegetable soup, Seaweed soup, Sweet & sour soup , Pork thick soup, Fish ball soup, Meat ball soup
	Fruit and nuts: Coconut, Avocado
	Drinks: Mineral water, Soda water
	Local snacks: excluding any staple food contained in the dish
	Vegetable stew with lamb ball, Casserole
	Common vegetarian dishes:
	Scrambled egg with tomato, Stir fried beancurd with sliced pork & pepper, Sauté eggplant with fish flavor, Sauté leek sprouts & eggs, Stir fried green bean, Stir fried bitter melon, Stir fried mixed greens, Stir fried Chinese broccoli, Sauté string bean
	Common meat dishes:
	Stir fried shredded pork with sweet and sour sauce, Sauté diced chicken with hot peppers, Sauté diced chicken with peanuts, Stir fried shrimps with bamboo shoots, Beef curry, Chicken curry, Braised common carp, Steamed fish, Braised prawns with soy sauce, Sauté pork in hot sauce, Braised pork with soy sauce, Boiled salted duck, Braised beef with brown sauce, Roast Beijing duck
Slow down /Yellow < 300 ml/day	**Vegetables: (< 50ml/meal, 150 ml/day)**
	Lima bean, Pea, Radish, Carrot, Lotus root, Yam, Sweet corn, Pump, Potato, Sweet potato
	Staple food: (< 50 ml/meal, 150 ml/day)
	Plain white rice, Fried rice with egg, Sweet potato congee, Rice porridge, Rice noodles
	Fruits and nuts: (< 50 ml/meal, 100 ml/day)
	Apple, Pear, Peach, Apricot, Orange, Lemon, Grape, Strawberry, Mulberry, Nectarine, Cherry, Watermelon, Papaya, Pomegranate, Persimmon, Guava, Kiwi, Lychee, Pomelo, Mangosteen, Longan, Pineapple, Banana, Mango, Durian, Date, Peanut, Chestnut
	Drinks: (< 50 ml/meal, < 100 ml/day)
	Soybean milk
	Local Snack: < 50 ml/meal, < 150 ml/day
	Extra soft tofu, Cold steamed rice noodle, Mutton blood with rice noodles, Honey glutinous rice
	Common meat dishes: (< 50 ml/meal, < 150 ml/day)
	Pork fillets with sweet & sour sauce, Sauté chops with sweet & sour sauce, Crisp fried spareribs
Stop/Red	**Staple food:**
	Clay oven rolls, Fried bread stick, Steamed buns, Boiled dumplings, Steamed dumplings, Sliced noodles, Sesame paste noodles, Shredded pork & pickled mustard green noodles
	Drinks: Coffee with cream and sugar, Juice, Carbonated drinks, Milk shake, Milk tea
	Local Snack:
	Pot Sticker, Beef (lamb) stew of bread, Chinese bread stuffed with cooked pork, Buckwheat noodles with sesame dressing, Sweets, glutinous millet

2

3 **Low carbohydrate diet guide:**
4 - Avoid all sugars and sweeteners such as white sugar, brown sugar, honey, corn syrup,
5 maple syrup
6 - Avoid all artificial sweeteners such as aspartame
7 - Limit all staple and starchy foods
8 - Use olive oil, suet, coconut oil, butter, lard, palm oil, tallow, tea seed oil for cooking.
9 - Avoid using vegetable seed oils such as canola oil for high heat cooking (cold press is
10 acceptable)
11 - Avoid deep fried food
12 - Use konjac to replace staple and starchy food when possible
13
14 **Time-restricted eating guide:**
15 - Most people can fast for a medical procedure such as a fasting blood sugar test. Therefore,
16 it is safe for most people not to eat for 16 hours
17 - When we are busy or occupied, we are less likely to feel hungry
18 - To eat at a certain time is a habit not a necessity

1   - Drink plenty of fluid
2
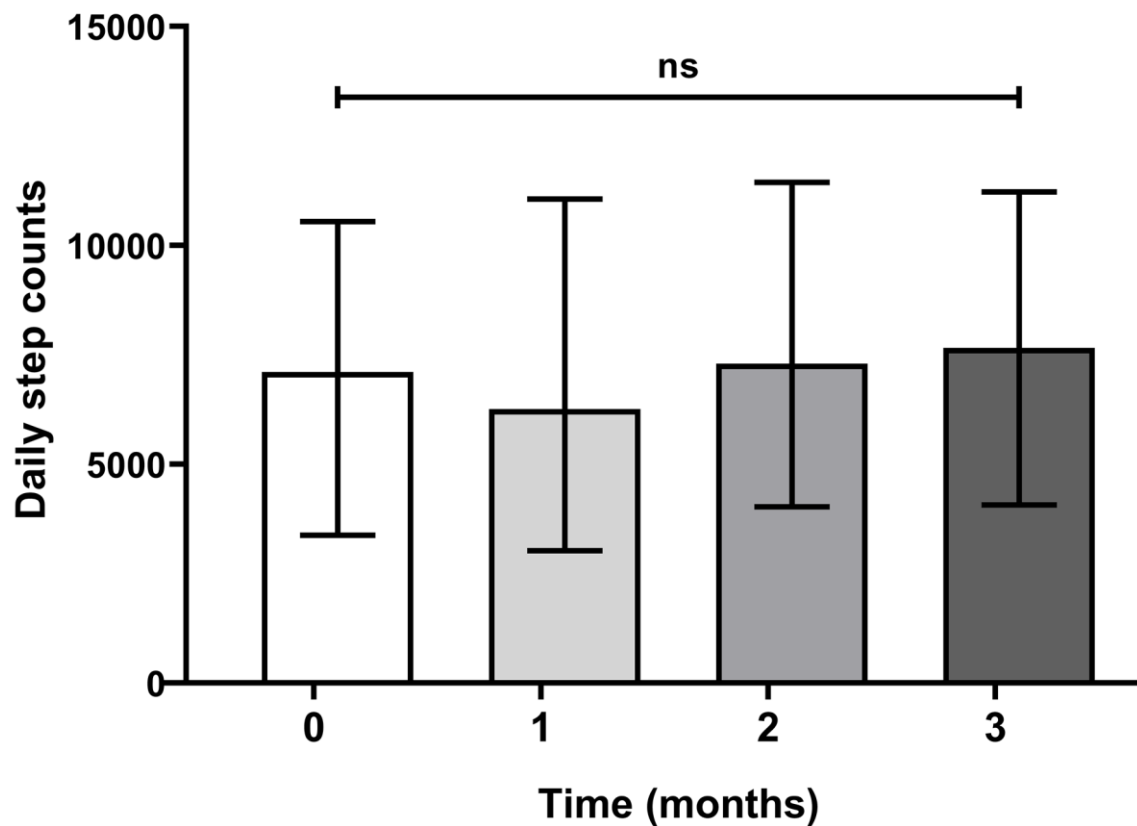3   **Recommended zero calorie beverages:**
4   - Water, mineral water, sparkling water, tea, herbal tea
5   - Absolutely no sweetened drink, especially those with artificial sweeteners
6   Related to STAR Methods.
7

1   **Supplemental figures**

2

3   **Figure S1. The daily step counts during the intervention period**

4   Data from all participates (n = 162) are presented as median (interquartile range, IQR) for abnormally distributed variables. There were no significant differences
5   between baseline, 1-month, 2-month, and 3-month follow-up, which were measured by Wilcoxon test. Related to STAR Methods.
6
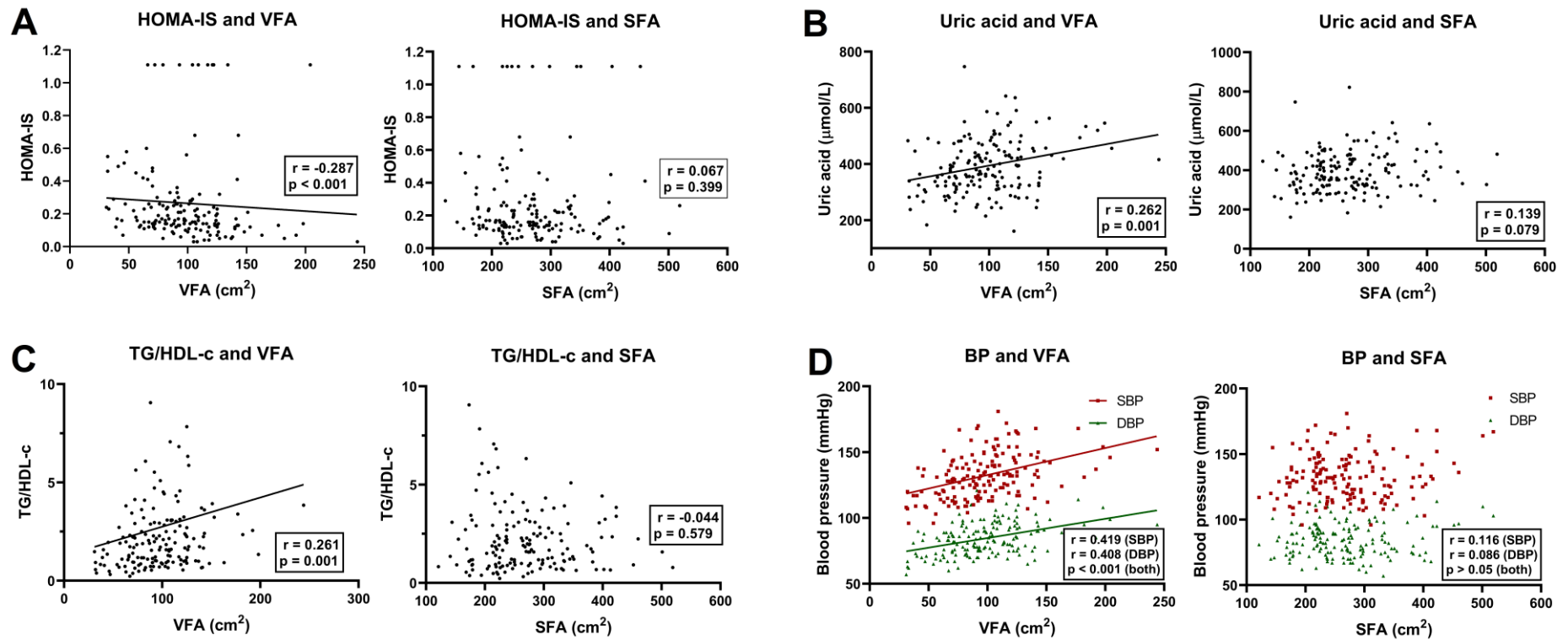
Figure S2. The correlation between metabolic factors and abdominal fat area

The correlation between baseline (A) homeostasis model assessment insulin sensitivity (HOMA-IS), (B) uric acid, (C) the ratio between triglycerides and high-density lipoprotein cholesterol (TG/HDL-c), (D) systolic and diastolic blood pressure (SBP and DBP), and abdominal fat area (visceral fat area, VFA; subcutaneous fat area, SFA). Pearson or Spearman correlations were performed to assess the relationship between abdominal fat area and other metabolic risk factors. Each data point represents an individual participant (n = 162). Related to Figure 3.

Data S1

Food Frequency Questionnaire (FFQ), related to STAR Methods

1. Days of adherence over the past two weeks: ___ days

2. Mean meal time over the past two weeks
First meal started at □□:□□
Second meal started at □□:□□ (leave a blank if skipped)
Third meal ended at □□:□□

3. Food frequency and quantity over the past two weeks
● Staple food
(1) How often and how much did you eat rice?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
(2) How often and how much did you eat wheat flour?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
(3) How often and how much did you eat coarse grain and field crop (corn, oat, sorghum, etc.)?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
(4) How often and how much did you eat tuber vegetable (potato, batata, yam, taro, etc.)?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
(5) How often and how much did you eat starch and derived products (vermicelli, etc.)?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
● Pastry
(1) How often and how much did you eat bread, cake, cookie, etc.?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
● Meat
(1) How often and how much did you eat pork, beef and lamb?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
(2) How often and how much did you eat processed meat (bacon, sausage, etc.?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
(3) How often and how much did you eat animal innards?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.
● Aquatic product
(1) How often and how much did you eat fish, crab, shrimp, shellfish, molluscs, etc.?
    A Never
    B ___ times a day, and ___ g each time.
    C ___ times a week, and ___ g each time.

1   ● Poultry
2   (1) How often and how much did you eat chicken, duck, pigeon, etc.?
3   A Never
4   B ＿＿ times a day, and ＿ g each time.
5   C ＿＿ times a week, and ＿ g each time.
6   ● Egg
7   (1) How often and how much did you eat hen's egg, duck's egg, preserved egg, salted egg,
8   etc.?
9   A Never
10   B ＿＿ times a day, and ＿ g each time.
11   C ＿＿ times a week, and ＿ g each time.
12   ● Milk and milk products?
13   (1) How often and how much did you eat milk, yogurt, etc.?
14   A Never
15   B ＿＿ times a day, and ＿ ml each time.
16   C ＿＿ times a week, and ＿ ml each time.
17   (2) How often and how much did you eat milk powder, cheese, etc.?
18   A Never
19   B ＿＿ times a day, and ＿ ml each time.
20   C ＿＿ times a week, and ＿ ml each time.
21   ● Beans and legume products
22   (1) How often and how much did you eat soybean?
23   A Never
24   B ＿＿ times a day, and ＿ g each time.
25   C ＿＿ times a week, and ＿ g each time.
26   (2) How often and how much did you eat tofu, soybean curd sheet, soybean curd slab and
27   oily bean curd?
28   A Never
29   B ＿＿ times a day, and ＿ g each time.
30   C ＿＿ times a week, and ＿ g each time.
31   ● Vegetables
32   (1) How often and how much did you eat dark vegetables?
33   A Never
34   B ＿＿ times a day, and ＿ g each time.
35   C ＿＿ times a week, and ＿ g each time.
36   (2) How often and how much did you eat light vegetables?
37   A Never
38   B ＿＿ times a day, and ＿ g each time.
39   C ＿＿ times a week, and ＿ g each time.
40   ● Phytocomycetes
41   (1) How often and how much did you eat mushrooms, seaweed, porphyra, etc.?
42   A Never
43   B ＿＿ times a day, and ＿ g each time.
44   C ＿＿ times a week, and ＿ g each time.
45   ● Fruits
46   (1) How often and how much did you eat apple, pear, peach, cherry, grapefruit, kiwifruit,
47   etc.?
48   A Never
49   B ＿＿ times a day, and ＿ g each time.
50   C ＿＿ times a week, and ＿ g each time.
51   (2) How often and how much did you eat mango, pineapple, etc.?
52   A Never
53   B ＿＿ times a day, and ＿ g each time.
54   C ＿＿ times a week, and ＿ g each time.
55   (3) How often and how much did you eat watermelon, etc.?
56   A Never
57   B ＿＿ times a day, and ＿ g each time.

C ____ times a week, and ___ g each time.
● Nuts
(1) How often and how much did you eat peanut, sunflower seed, walnut, pumpkin seed, etc.?
    A Never
    B ____ times a day, and ___ g each time.
    C ____ times a week, and ___ g each time.
● Alcohol
(1) How often and how much did you drink low-alcohol liquor (≤38%)?
    A Never
    B ____ times a day, and ___ ml each time.
    C ____ times a week, and ___ ml each time.
(2) How often and how much did you drink high-alcohol liquor (>38%)?
    A Never
    B ____ times a day, and ___ ml each time.
    C ____ times a week, and ___ ml each time.
(3) How often and how much did you drink beer?
    A Never
    B ____ times a day, and ___ ml each time.
    C ____ times a week, and ___ ml each time.
(4) How often and how much did you drink yellow rice wine?
    A Never
    B ____ times a day, and ___ ml each time.
    C ____ times a week, and ___ ml each time.
(5) How often and how much did you drink fruit wine?
    A Never
    B ____ times a day, and ___ ml each time.
    C ____ times a week, and ___ ml each time.

1　**Data S2**

2

3　**Trial protocol, related to STAR Methods**

4　This is a randomized, open-label, single-centre, clinical trial to evaluate the weight loss efficacy

5　and improvement of metabolic parameters by low-carbohydrate diet (LCD), time-restricted

6　feeding (TRF), and their combination in adults with MetS. This study is conducted with approval

7　from the Institutional Review Board at the First Affiliated Hospital of Xi'an Jiaotong University,

8　Xi'an, China (No: XJTUAF2020LSK-003). The trial is registered as ClinicalTrials.gov, number

9　NCT04475822.

10　**Sample size calculation**

11　The study is powered to detect the primary outcome of percentage reduction in body weight.

12　For the sample size calculation, we estimate that the LCD-treated group (A) would lose 5%

13　body weight and that the group treated with combination diet (C) would lose 10% body weight

14　over 3 months. We calculate that n=26 participants per group would provide 80% power to

15　detect a significant difference of 5% in body weight between the A and C groups by 3 month

16　using a 2-tailed independent-samples t test with α=0.05. We anticipate a dropout rate of 20%.

17　Thus, we initially aim to recruit 99 participants (n=33 per group), assuming that 78 participants

18　(n=26 per group) would complete the trial. We finally decided to increase the number of recruits

19　to 165 because of concerns about the high dropout, but also to increase the strength of statistics.

20　**Recruitment**

21　Participants are recruited between July 2020 and September 2020 from Xi'an via emails, flyers,

22　social media, and website advertisements and are diagnosed with metabolic syndrome (using

23　AHA/National Heart, Lung, and Blood Institute cutoff points for waist circumference). All

24　participants should provide written informed consent.

25　Inclusion criteria

26　(1) Diagnosed with metabolic syndrome (i.e., more than 3 abnormal findings out of 5):

27　a. Waist circumference ≥ 90 cm (men) or ≥ 80 cm (women).

28　b. Elevated TG (use of medications for elevated TG is an alternate indicator) ≥ 150 mg/dL (1.7

29　mmol/L).

30　c. Reduced HDL-c (use of medications for reduced HDL-c is an alternate indicator) < 40 mg/dL

31　(1.0 mmol/L) in males < 50 mg/dL (1.3 mmol/L) in females.

32　d. Elevated blood pressure (use of hypoglycemic medications is an alternate indicator). SBP ≥

33　130 and/or DBP ≥ 85 mmHg.

34　e. Elevated FBG (used of hypoglycemic medications is an alternate indicator) ≥ 100 mg/dL (5.6

35　mmol/L).

36　(2) Age from 18 to 65 years.

37　(3) Stable weight (change ≤ 10% current body weight) for 3 months prior to the study.

38　(4) If participants were on hypoglycemic medications, hypotensive medications, lipid-lowering

39　medications and cardiovascular medications, dose adjustment was not permitted during the 3-

40　month intervention.

41　Exclusion criteria

42　1) Pregnant or breast-feeding.

1   2) Night shift workers.

2   3) History of major diseases or related diseases, such as inflammatory disease, rheumatologic
3   disease, adrenal disease, malignancy, type 1 diabetes, cirrhosis, chronic kidney disease,
4   acquired immunodeficiency syndrome, eating disorder, uncontrolled psychiatric disorder and
5   major adverse cardiovascular event.

6   4) Current participate in other weight-management program, current on a prescribed diet for
7   special disease or current on any drugs that effect appetite.

8   5) History of weight-loss surgery.

9   **Randomisation and masking**

10 Participants are randomly divided into LCD, TRF and a combination group at a ratio of 1:1:1
11 (the formal study is preceded by basic assessment and a two-week window period). Block
12 randomization is performed by a computer-generated random number list prepared by an
13 investigator with no clinical involvement in the trial. After the research nurse obtains the patient's
14 consent, she telephones a clinician who is independent of the recruitment process for allocation
15 consignment.

16 **Procedures**

17 Before commencing the study, all participants are asked to maintain a consistent diet, exercise
18 and lifestyle during a two-week window period to keep their weight stable. During the 3-months
19 intervention period, the LCD group is instructed to eat a low-carbohydrate diet (carbohydrates
20 <130 g/day or <26% total energy, according to the ADA definition of 130 g/day as recommended
21 minimum). The 8h TRF group is instructed to eat *ad libitum* from 8 am to 4 pm daily and fasting
22 from 4 pm to 8 am or to eat *ad libitum* from 12 am to 8 pm daily and fasting from 8 pm to 12 am
23 (16h fast). During the 8h feeding windows, there are no restrictions on the types or quantities
24 of foods consumed, and the fasting guide is provided in the supplemental materials. Likewise,
25 the combination group is instructed to eat a LCD in the same 8h feeding windows as the TRF
26 group. Moreover, participants are not required to monitor their caloric intake during this *ad*
27 *libitum* feeding period. During the fasting period, participants are encouraged to drink plenty of
28 water and are permitted to consume energy-free beverages, such as black tea and sparkling
29 water.

30 The study is conducted with the help of the internet hospital application (app) of the First
31 Affiliated Hospital of Xi'an Jiaotong University, named "Smart Hospital", which is a new
32 approach to provide health services, outpatient service in particular, through the internet
33 technology. All participants could contact clinicians at any time and any place though online
34 communication and receive diet guides and questionnaires through the app. According to a
35 previously defined method providing quantitative information on macronutrient composition of
36 the diet, compliance with the dietary intervention is evaluated by the same dietician every other
37 week through diet questionnaires. All subjects are asked to maintain their usual physical activity
38 throughout the study, which is supervised by our own custom-made sport bracelet.

39 **Outcomes**

40 The primary outcome of the study is change in body weight and abdominal fat area, and the
41 secondary outcomes are body composition, glycemic control, plasma lipids, uric acid (UA),
42 blood pressure and diet adherence.

43 Body weight is assessed every month at the research center with the participants without shoes
44 and in light clothing using a digital scale (OMRON MEDICAL Beijing Co., Ltd. HNH-318) to the
45 nearest 0.1 kg. Height is assessed during the screening visit using a wall-mounted stadiometer

(OMRON MEDICAL Beijing Co., Ltd. HNH-318) to the nearest 0.1 cm. Abdominal fat area (visceral fat area, VFA; subcutaneous fat area, SFA) is measured at baseline and after 3 months using bioelectrical impedance analysis (OMRON MEDICAL Beijing Co., Ltd. DUALSCAN, HDS-2000) to the nearest 1 cm^2, and body composition (body fat mass and body muscle mass) is measured at baseline and month 3 using the direct segmental multifrequency bioelectrical impedance analysis method DSM-BIA (InBody H20) to the nearest 0.1 kg.

Blood samples are collected after a 12h fast at week 1 (before starting the intervention) and at month 3, between 7:40 and 9:00 am. All blood draws are performed at the physical examination center of the First Affiliated Hospital of Xi'an Jiaotong University. Blood is centrifuged for 20 min at 520g and 4°C to separate plasma from red cells and stored at -80°C until analysis. Hemoglobin A1c (HbA1c) is measured on an automatic HbA1c analyzer (TOSOH BIOSCIENCE, Inc.; HLC-723G8) to the nearest 0.1%. FBG, UA, total cholesterol, TG, HDL-c, and LDL-c are measured on an automatic biochemistry analyzer (HITACHI, Inc.; LAbOSPECT, 008AS) using standard reagents to the nearest 0.01 mmol/L, 1 µmol/L, 0.01 mmol/L, 0.01 mmol/L, 0.01 mmol/L and 0.01 mmol/L, respectively.

Fasting insulin and C-peptide are measured by immunoassay with fluorescent detection on a Luminex instrument (EMD Millipore Corporation; HMHEMAG-34K) to the nearest 0.1 pg/mL. Insulin resistance (IR) and insulin sensitivity (IS) is calculated using the homeostasis model assessment (HOMA) method by applying the following formula: [HOMA-IR=fasting insulin (mIU/L) × fasting glucose (mg/dL)/405], [HOMA-IS=1/HOMA-IR]. Quantitative insulin-sensitivity check index (QUICKI)=1/[log (fasting insulin level, in microunits per milliliter) + log (fasting glucose level, in milligrams per deciliter)]. Blood pressure is measured in triplicate using a digital automatic blood pressure (Omron HBP-9020, Kyoto, Japan) to the nearest 1 mmHg with the participant in a seated position after a 10-min rest.

Neurological issues (dizziness, headache, fatigue, and irritability) and gastrointestinal issues (nausea, diarrhea, constipation, and dry mouth) are assessed by a telephone interview at baseline and every other week during the intervention period.

Statistical Analysis Plan

Statistical analyses are performed using SPSS v.25.0 for Windows. A two-tailed p value of less than 0.05 is considered statistically significant. Tests for normality are conducted. All data are presented as the mean ± standard deviation (SD) for normally distributed variables or median (interquartile range, IQR) for abnormally distributed variables. At baseline, differences between treatment arms (LCD, TRF and combination) are tested by one-way ANOVA or Kruskal-Wallis H test, with an LSD post hoc test (continuous variables) or McNemar test (categorical variables). Pearson and Spearman correlations are performed to assess the relationship between abdominal fat area and other metabolic risk factors. The significant difference between baseline and 3-month follow-up is measured by paired T test or Wilcoxon test in each group. At month 3, differences across treatment arms (LCD, TRF and combination) are evaluated as change scores (from baseline to month 3) using one-way ANOVA or Kruskal-Wallis H test, with an LSD post hoc test (continuous variables) or McNemar test (categorical variables).