Supplementary Online Content

Pavlou V, Cienfuegos S, Lin S, et al. Efficacy of time-restricted eating in adults with type 2 diabetes: a randomized clinical trial. *JAMA Netw Open*. 2023;6(10):e2339337. doi:10.1001/jamanetworkopen.2023.39337

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Medication Use at Baseline and Month 6

	Time restricted eating		Daily calorie restriction		Control	
	Baseline (n = 25)	**Month 6 (n = 23)**	**Baseline (n = 25)**	**Month 6 (n = 22)**	**Baseline (n = 25)**	**Month 6 (n = 24)**
Diabetes medications, no. (%)						
Oral hypoglycemic agents (OHA)						
Metformin	21 (84%)	17 (74%)	19 (76%)	16 (73%)	21 (84%)	20 (83%)
DPP-4 Inhibitors	0 (0%)	1 (4%)	4 (16%)	4 (18%)	1 (4%)	0 (0%)
SGLT2 inhibitors	9 (36%)	7 (30%)	1 (4%)	2 (9%)	5 (20%)	5 (21%)
GLP-1 agonists	8 (32%)	8 (35%)	5 (20%)	5 (23%)	6 (24%)	10 (42%)
Sulfonylureas	2 (8%)	1 (4%)	7 (28%)	6 (27%)	2 (8%)	2 (8%)
Insulin	13 (52%)	12 (52%)	4 (16%)	4 (18%)	9 (36%)	8 (33%)

Data are expressed as the number and percent of participants using diabetes medications at baseline and month 6.

eTable 2. Multiple Imputation Sensitivity Analysis Results

Variables	N	Difference between groups (95% CI)		
		TRE vs CR	TRE vs CON	CR vs CON
Body weight				
Weight change (%)	75	-1.476 (-3.854 to 0.902) p=0.217	-3.241 (-5.609 to -0.872) p=0.008	-1.764 (-3.695 to 0.166) p=0.072
Body weight (kg)	75	-1.555 (-4.161 to 1.052) p=0.235	-3.149 (-5.806 to -0.492) p=0.021	-1.594 (-3.736 to 0.548) p=0.141
Glycemic control				
HbA1c (%)	72	0.12 (-0.57 to 0.81)	-0.84 (-1.56 to -0.13)	-0.97 (-1.66 to -0.27)
Time in range (%)	67	-7.67 (-19.06 to 3.72)	10.13 (-8.85 to 29.10)	17.80 (-0.69 to 36.28)
Mean glucose (mg/dl)	67	8.57 (-11.83 to 28.97)	-32.18 (-72.30 to 7.94)	-40.75 (-78.69 to -2.82)
Medication effect score				
Oral hypoglycemic agents	75	-0.18 (-0.40 to 0.05)	-0.16 (-0.39 to 0.08)	0.02 (-0.24 to 0.27)
Insulin	75	0.00 (-0.08 to 0.08)	-0.02 (-0.10 to 0.06)	-0.02 (-0.05 to 0.02)
Body composition				
Fat mass (kg)	71	-0.51 (-2.40 to 1.38)	-2.28 (-4.16 to -0.40)	-1.77 (-3.47 to -0.07)
Lean mass (kg)	71	-1.77 (-4.90 to 1.37)	-1.78 (-4.96 to 1.39)	-0.02 (-1.22 to 1.18)
Visceral fat mass (kg)	70	0.04 (-0.19 to 0.27)	-0.07 (-0.29 to 0.15)	-0.11 (-0.30 to 0.07)
Waist circumference (cm)	74	0.03 (-2.55 to 2.61)	-3.11 (-5.35 to -0.88)	-3.14 (-5.33 to -0.95)
BMI (kg/m^2)	75	-0.68 (-1.57 to 0.22)	-1.22 (-2.20 to -0.25)	-0.55 (-1.29 to 0.19)
Blood pressure, heart rate				
Systolic BP (mm Hg)	75	-0.66 (-7.68 to 6.35)	-5.34 (-13.04 to 2.36)	-4.68 (-12.52 to 3.16)
Diastolic BP (mm Hg)	75	-1.04 (-5.63 to 3.55)	-2.83 (-7.84 to 2.18)	-1.79 (-6.13 to 2.55)
Heart rate (bpm)	75	-0.64 (-6.38 to 5.09)	-1.03 (-7.97 to 5.90)	-0.39 (-7.26 to 6.49)
Plasma lipids				
Total cholesterol (mg/dl)	71	5.95 (-10.57 to 22.47)	-1.11 (-18.55 to 16.34)	-7.06 (-26.24 to 12.13)
LDL cholesterol (mg/dl)	71	2.94 (-10.93 to 16.82)	2.26 (-12.53 to 17.04)	-0.69 (-16.71 to 15.34)
HDL cholesterol (mg/dl)	71	2.86 (-0.91 to 6.63)	1.07 (-3.23 to 5.38)	-1.79 (-6.68 to 3.11)
Triglycerides (mg/dl)	71	-0.29 (-28.13 to 27.54)	-19.91 (-50.29 to 10.46)	-19.62 (-49.34 to 10.09)

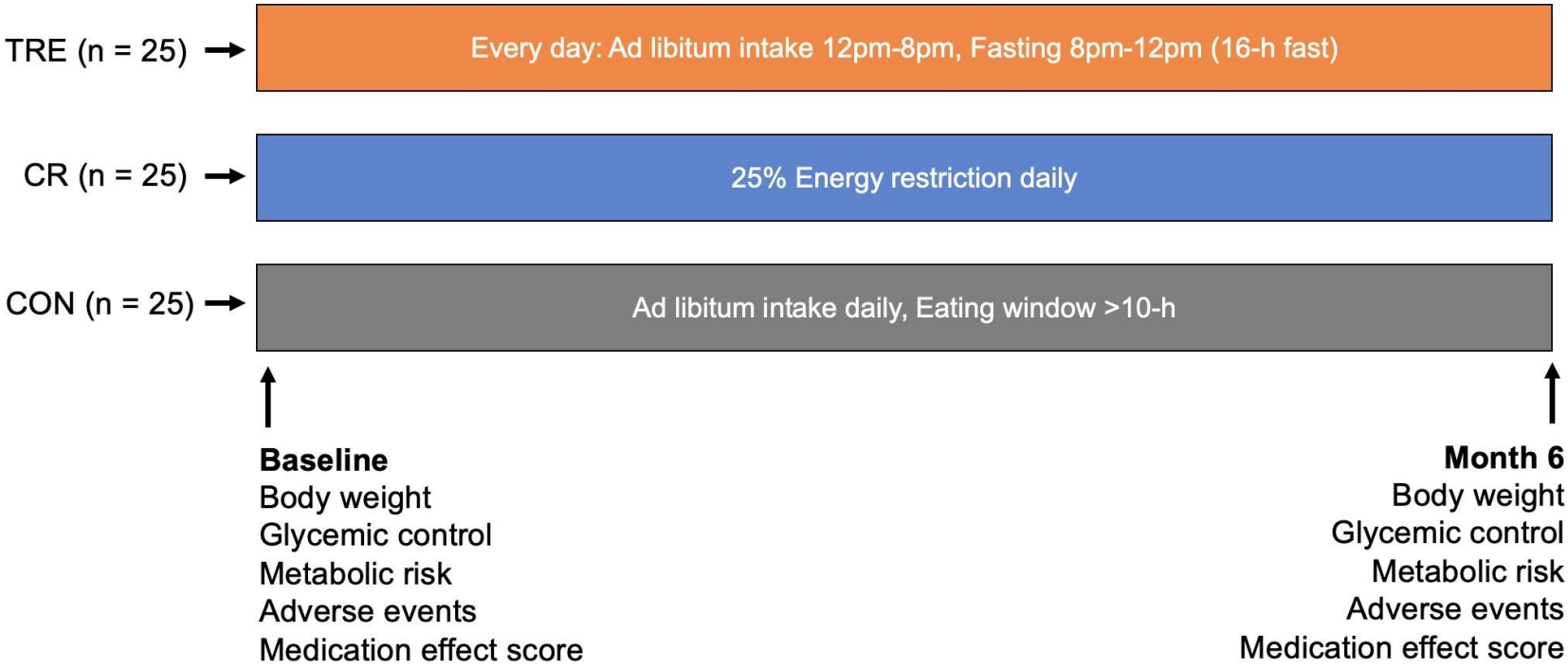
Data were included for 75 participants; missing values of the outcome at non-baseline time points were imputed using multiple imputation by chained equations with predictive mean matching and 30 imputed datasets in these sensitivity analyses. Multiple imputation can incorporate observed data not otherwise accounted for in the model (e.g., using baseline insulin levels to impute missing time in euglycemic range) to estimate multiple values for each missing data point to account for sampling variability. Abbreviations: BP: Blood pressure; CON: control group, CR: Calorie restriction group, HbA1c: Glycated hemoglobin, TRE: Time restricted eating group.

eTable 3. Adverse Events During the Intervention

	Time restricted eating (n =25)	Calorie restriction (n =25)	Control (n =25)	
	No. (%) participants			P-value
Glycemic adverse events				
Diabetic ketoacidosis	0 (0)	0 (0)	0 (0)	1.000
Hypoglycemia	10 (40)	11 (44)	14 (56)	0.498
Hyperglycemia	21 (84)	20 (80)	22 (88)	0.743
Gastrointestinal adverse events				
Nausea	12 (48)	14 (56)	10 (40)	0.527
Vomiting	4 (16)	4 (16)	2 (8)	0.630
Diarrhea	13 (52)	17 (68)	18 (72)	0.297
Constipation	17 (68)	20 (80)	15 (60)	0.304
Other adverse events				
Headache	15 (60)	18 (72)	16 (64)	0.662
Dizziness	13 (52)	16 (64)	12 (48)	0.497
Fatigue	17 (68)	21 (84)	20 (80)	0.372
Irritability	15 (60)	13 (52)	12 (48)	0.687
Halitosis	7 (28)	7 (28)	8 (32)	1.000
Dry mouth	15 (60)	14 (56)	18 (72)	0.477

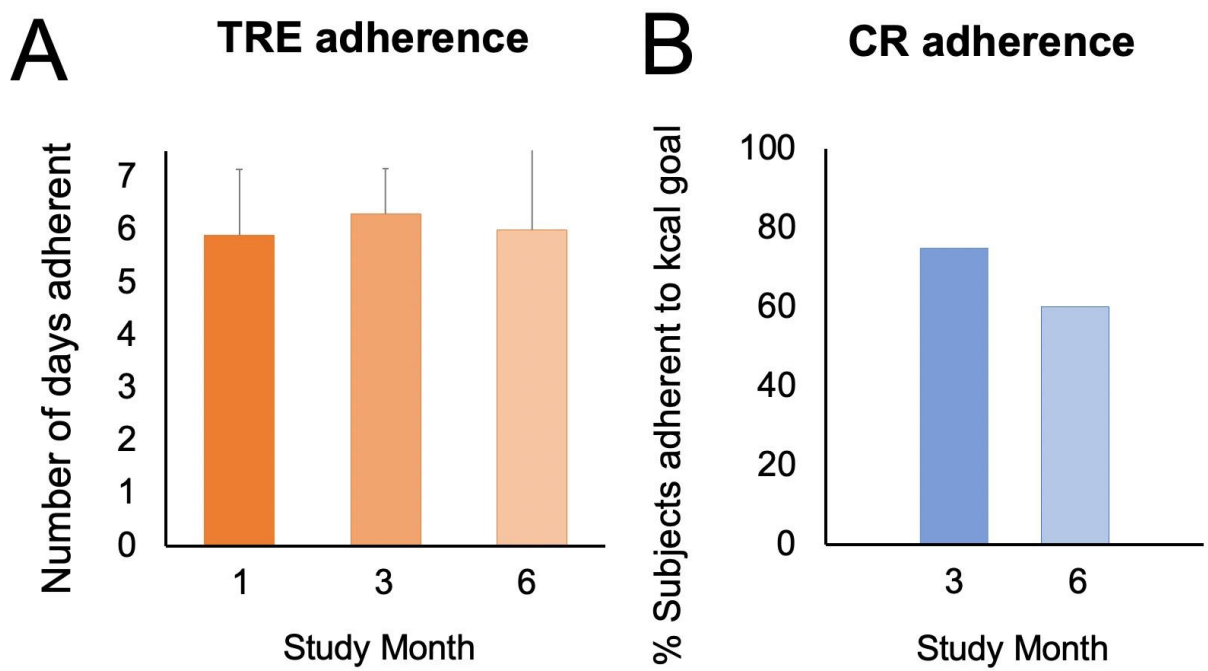
Data are expressed as the number of participants with at least one adverse event that occurred over the course of the 6-month trial. Participants may have experienced an adverse event at more than one time point.

eFigure 1. Experimental Design



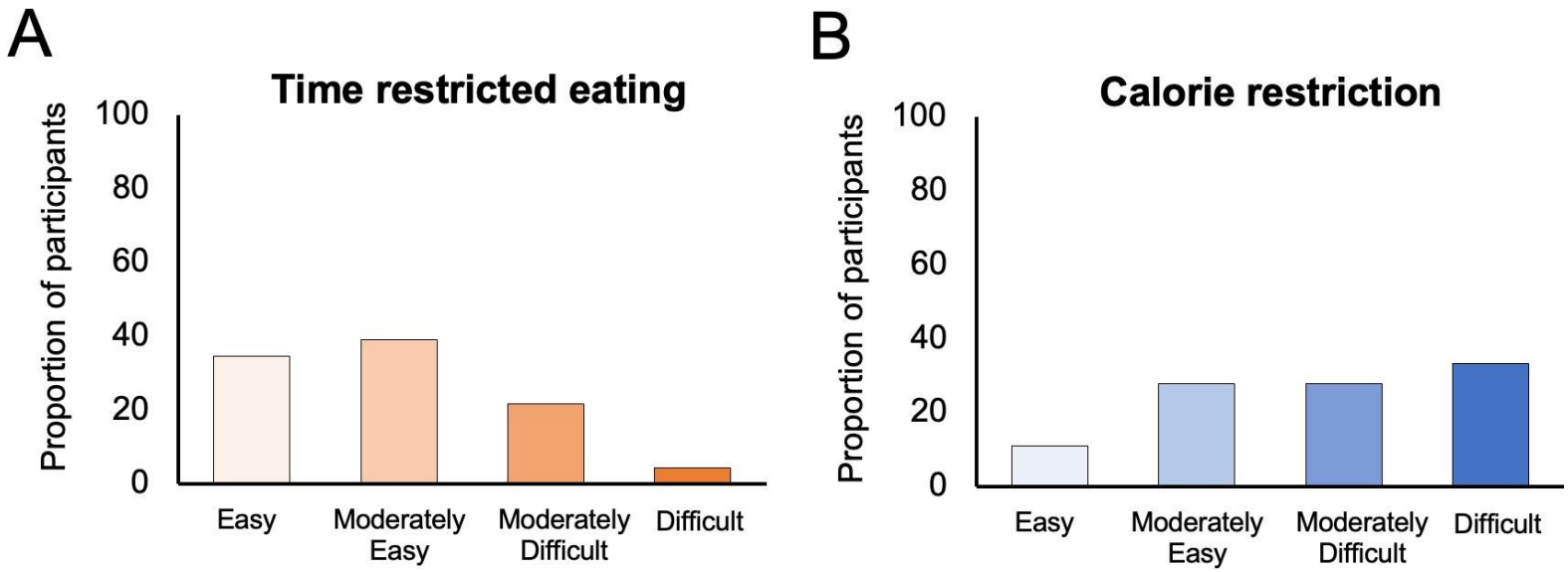
Abbreviations: CON: control group, CR: Calorie restriction group, TRE: Time restricted eating group.

eFigure 2. Adherence to the Diet Interventions



A. Adherence to the time restricted eating (TRE) intervention. Data are expressed as mean (SD) days per week that participants reported being adherent with the 12:00 pm to 8:00 pm eating window; only observed values included. A total of 21/25 TRE participants returned all adherence logs. **B.** Adherence to the daily calorie restriction (CR) intervention. Data are expressed as the proportion of participants whose actual energy intake, determined via food recalls, was within 200 kcal of their prescribed daily energy goal; only observed values included. A total of 20/25 CR participants returned all food records. Abbreviations: CR: Calorie restriction group, TRE: Time restricted eating group.

eFigure 3. Difficulty in Adhering to the Time-Restricted Eating vs Calorie Restriction Intervention



A. Data are expressed as the proportion of time restricted eating participants who reported finding their assigned diet intervention easy, moderately easy, moderately difficult, or difficult to adhere to. A total of 23/25 TRE participants returned the survey. **B.** Data are expressed as the proportion of calorie restriction participants who reported finding their assigned diet intervention easy, moderately easy, moderately difficult, or difficult to adhere to. A total of 19/25 CR participants returned the

survey. TRE participants reported finding their diet intervention easier to adhere to, when compared CR participants.