Figure S1. Participant Flow Diagram. *Related to Figure 1.* Screening criteria were applied in increasing order of difficulty to assess; if a candidate failed to meet a criterion, he was excluded, and no further criteria were measured. In particular, candidates whose HbA1c levels were not elevated were excluded from the trial without having their glucose tolerance measured.
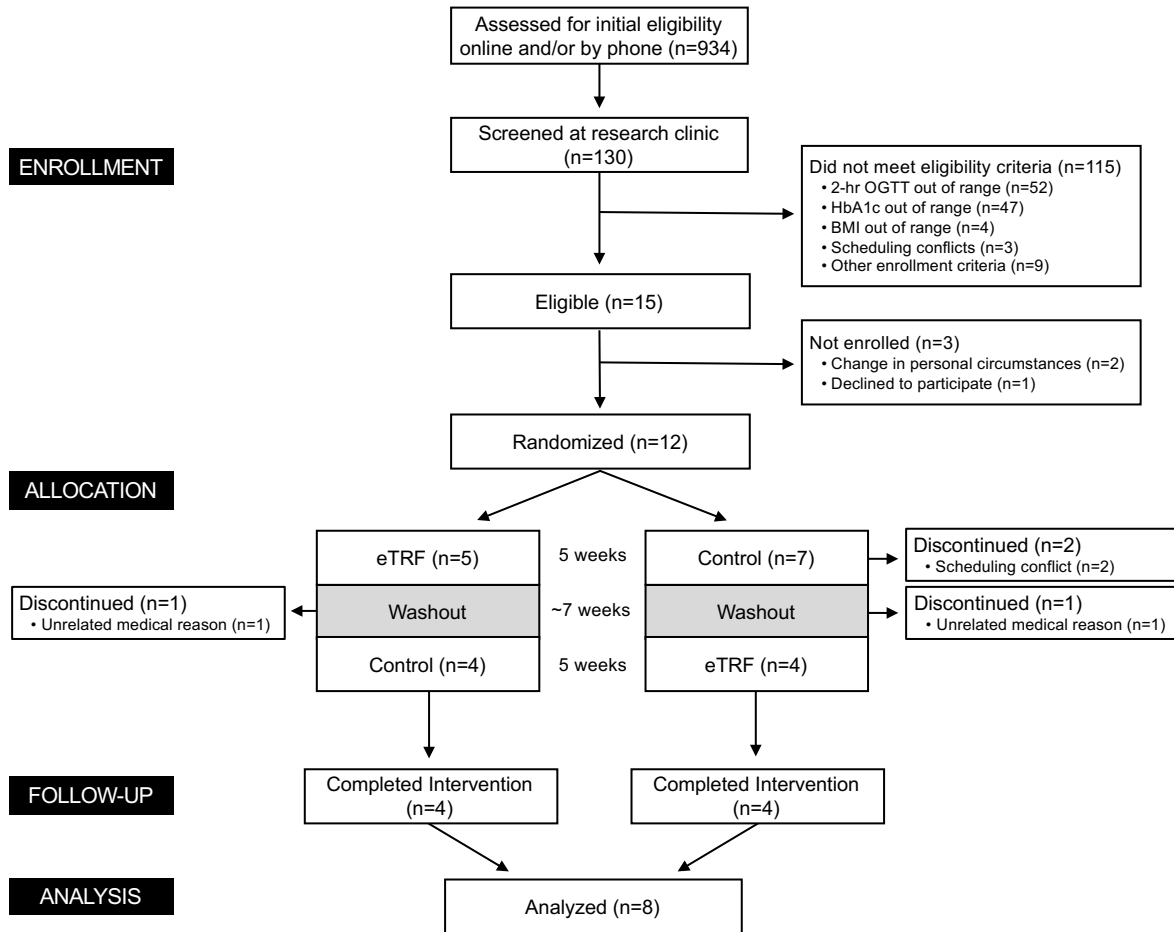
Table S1. **Participant Characteristics at Screening.** *Related to Figure 1*. Data are presented as raw mean ± SD.

Characteristics	Baseline Value
Age (years)	56 ± 9
Race/Ethnic Group (White/Black/Other, n)	6/1/1
Weight (kg)	100.7 ± 18.4
BMI (kg/m^2)	32.2 ± 4.4
Fasting Glucose (mg/dl)	102 ± 9
2-Hour Glucose Tolerance (mg/dl)	154 ± 17
Fasting Insulin (mU/l)[a]	25.1 ± 14.5
Systolic Blood Pressure (mm Hg)	123 ± 8
Diastolic Blood Pressure (mm Hg)	82 ± 7
Heart Rate (beats/min)	70 ± 4
Total Cholesterol (mg/dl)	179 ± 39
LDL Cholesterol (mg/dl)	108 ± 26
HDL Cholesterol (mg/dl)	46 ± 8
Triglycerides (mg/dl)	120 ± 75

[a] *Measured instead at baseline (Day 2) in Arm 1*

Figure S2. Glycemic Control. *Related to Figure 2.* With the exception of fasting glucose, which was slightly lower in the eTRF arm at both (A) baseline and (B) post-intervention, most glucose values were similar between arms. By contrast, (C) insulin levels were higher at baseline in the eTRF arm but (D) were also lower post-intervention in the eTRF arm. These data suggest that five weeks of eTRF does not affect postprandial glucose levels in the morning but does dramatically reduce postprandial insulin levels and that such reductions were long-lived. All data are paired, with n=8 completers in each arm. Data are presented as raw mean $\pm$ SEM. * $p \leq 0.05$
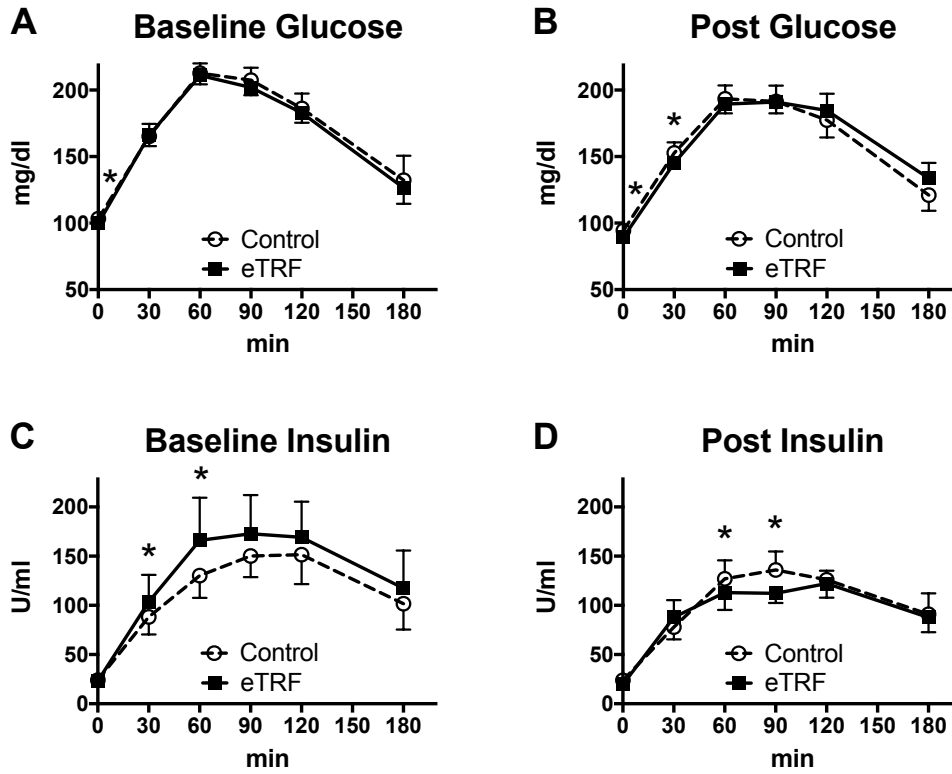
Table S2. **Cardiometabolic Endpoints.** *Related to Figures 2-5.* All data are paired, with n=8 completers in each arm. Baseline values are reported as raw mean ± SD, whereas the treatment effects for eTRF (reported as least squares mean ± SEM) and associated p-values were derived from linear mixed modelling. Endpoints affected by eTRF (p ≤ 0.05) are highlighted in grey.

Endpoint	BASELINE			TREATMENT EFFECT	
	Control	eTRF	p	Δ ± SEM	p
Weight (kg)	101.8 ± 19.6	100.9 ± 18.9	0.01	-0.5 ± 0.3	0.12
Fasting Glucose (mg/dl)	103 ± 9	100 ± 6	0.05	-2 ± 2	0.49
Mean Glucose (mg/dl)	175 ± 22	172 ± 12	0.53	5 ± 5	0.40
Peak Glucose (mg/dl)	218 ± 24	216 ± 15	0.76	-1 ± 8	0.91
Fasting Insulin (mU/l)	24.0 ± 17.8	23.4 ± 13.9	0.72	-3.4 ± 1.6	0.05
Mean Insulin (mU/l)	118 ± 59	138 ± 92	0.13	-26 ± 9	0.01
Peak Insulin (mg/dl)	170 ± 86	189 ± 114	0.25	-35 ± 13	0.01
HOMA-IR	6.2 ± 4.8	5.8 ± 3.5	0.57	-0.84 ± 0.42	0.07
Insulinogenic Index (U/mg)	104 ± 51	113 ± 60	0.31	14 ± 7	0.05
Incremental AUC Ratio (U/mg)	142 ± 81	161 ± 112	0.13	-36 ± 10	0.005
Systolic Blood Pressure (mm Hg)	119 ± 16	125 ± 15	0.08	-11 ± 4	0.03
Diastolic Blood Pressure (mm Hg)	74 ± 11	77 ± 10	0.43	-10 ± 4	0.03
Heart Rate (beats/min)	73 ± 4	70 ± 8	0.17	5 ± 3	0.10
Augmentation Index (%)	30 ± 9	31 ± 12	0.56	-1.4 ± 2.1	0.53
Pulse Wave Velocity (m/s)	8.0 ± 1.8	8.3 ± 1.7	0.48	-0.5 ± 0.4	0.23
Total Cholesterol (mg/dl)	174 ± 33	176 ± 26	0.67	13 ± 5	0.02
LDL Cholesterol (mg/dl)	103 ± 22	106 ± 20	0.65	2 ± 6	0.75
HDL Cholesterol (mg/dl)	43.0 ± 4.6	42.7 ± 4.6	0.77	-0.6 ± 0.9	0.48
Triglycerides (mg/dl)	140 ± 71	140 ± 59	0.98	57 ± 13	0.0007
8-Isoprostane (pg/ml)	78 ± 23	84 ± 22	0.44	-11 ± 5	0.05
Cortisol (μg/dl)	9.2 ± 2.6	10.7 ± 3.6	0.10	-0.1 ± 1.3	0.95
hs-CRP (mg/l)	6.2 ± 6.1	6.5 ± 7.3	0.78	-0.3 ± 1.0	0.77
IL-6 (pg/ml)	1.40 ± 1.20	1.00 ± 0.58	0.10	0.45 ± 0.27	0.12
Active Ghrelin (pg/ml)	78 ± 27	80 ± 22	0.86	-5.7 ± 6.6	0.41
PYY (pg/ml)	81 ± 28	91 ± 36	0.12	-23 ± 7	0.003
Leptin (ng/ml)	27.9 ± 16.4	27.1 ± 17.7	0.42	-0.6 ± 1.0	0.54
Adiponectin (μg/ml)	4.996 ± 2.999	3.928 ± 2.943	0.18	0.408 ± 0.765	0.61
GLP-1 (pmol/l)	5.9 ± 8.8	8.2 ± 10.6	0.09	-1.2 ± 1.0	0.26

Figure S3. Feasibility and Acceptability. *Related to Figure 5*. Participants reported that (A) it took an average of two weeks (range: 2 - 35 days) to adjust to the eTRF eating schedule and that (B) the challenge of eating within 6 hours each day was more difficult than the challenge of fasting for 18 hours per day. (C) On average, participants thought that following an ~8-hour eating period (range: 4-10 hours) would be feasible for most people. (D) Seven out of eight participants said they would be willing to eat dinner earlier based on their experiences in the study, while all eight participants would be willing to eat dinner earlier if it improved their health. All data are paired, with n=8 completers in each arm. Data are presented as raw mean ± SD. * $p \leq 0.05$

A Days It Took to Adjust to eTRF

B Difficulty of Eating vs. Fasting

C Length of Feasible Eating Period

D Willing to Eat Earlier in the Day