

INCREASE MALNUTRITION AWARENESS: CHALLENGE FOR THE FUTURE

CONGRESSO
NAZIONALE

Metabolic effects of early Time Restricted Carbohydrate consumption

Maria Chiara Masoni

SD Dietologia Universitaria, Università di Pisa



Introduction: early Time-Restricted Feeding (eTRF)

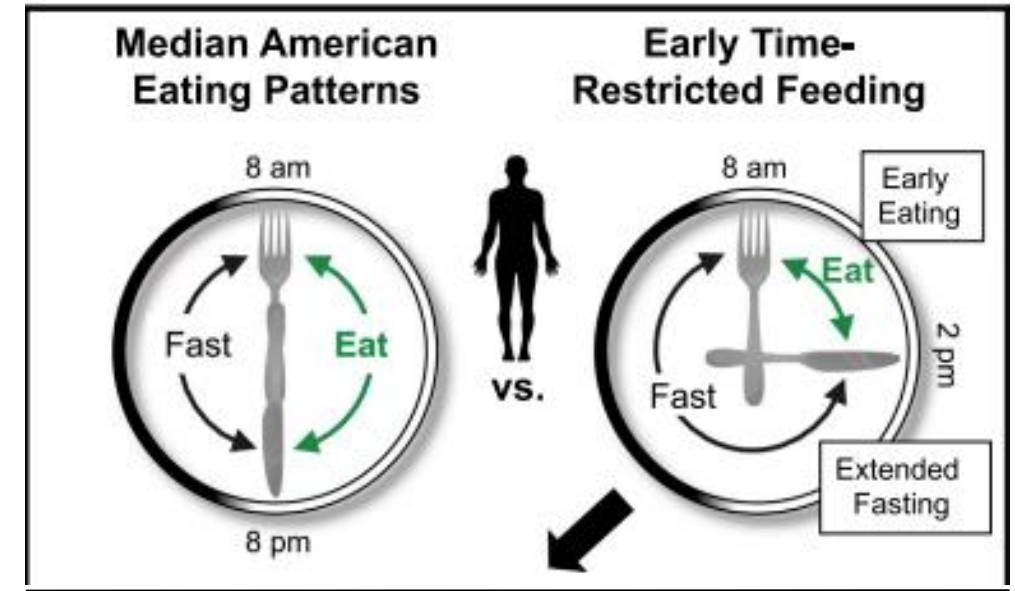
Type 2 Diabetes is a worldwide problem in terms of prevalence and incidence



There is an urgent need for effective nutritional strategies to contain this epidemic chronic disease

Early time-restricted feeding (eTRF) is a popular nutritional strategy

- eTRF is a form of intermittent fasting that involves restricting food consumption early in the day to align with the circadian rhythm and promote ketosis
- In fact, glucose tolerance peaks during daylight and is lower during the night/dark cycle



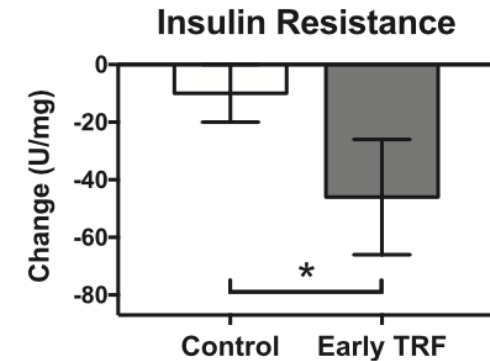
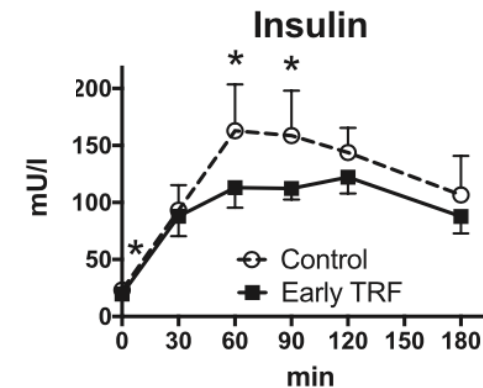
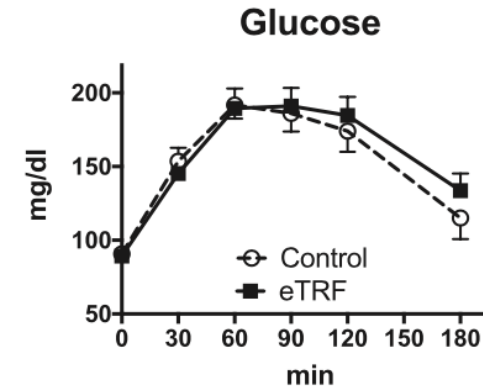
Introduction: early Time-Restricted Feeding (eTRF)

Metabolic effects:

- ↓ Body weight
- ↓ Insulin resistance
- ↑ Glucose tolerance

Limitations:

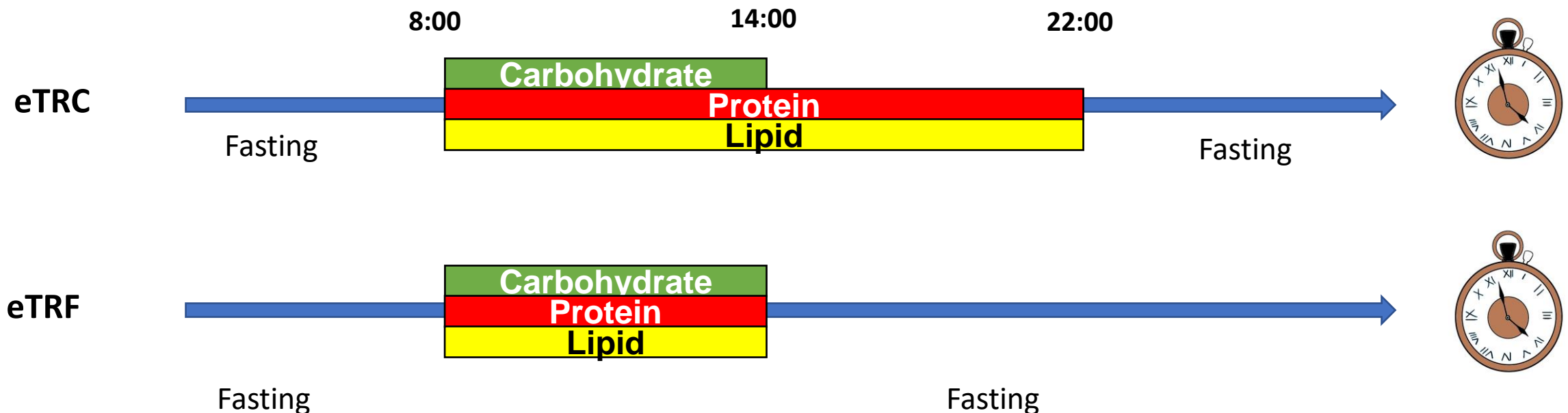
- Incomplete adherence to the diet: fasting is often unfeasible and poorly accepted
- Conflicting evidence in literature



Early Time-Restricted Feeding improves insulin sensitivity, blood pressure and oxidative stress even without weight loss in men with prediabetes
Sutton et al. Cell Metab 2018

Hypothesis: early Time-Restricted Carbohydrate consumption (eTRC)

Restricting the consumption of carbohydrate-rich food in the morning may provide the same cardiometabolic benefits of eTRF while not requiring an absolute daily fast of 16-18 hours



Three weeks of time-restricted eating improves glucose homeostasis in adults with type 2 diabetes but does not improve insulin sensitivity: a randomised crossover trial. Andriessen et al. Diabetologia, 2022

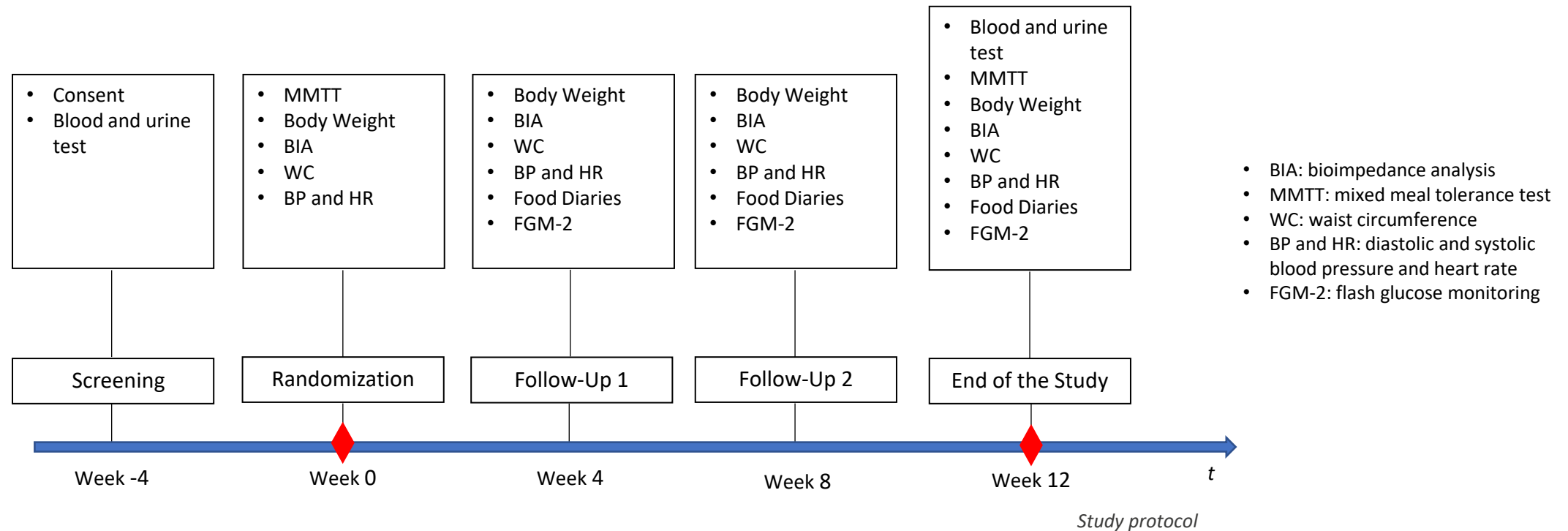
Time-restricted feeding improves blood glucose and insulin sensitivity in overweight patients with type 2 diabetes: a randomised controlled trial. Che et al. Nutrition & Metabolism, 2021

Methods: Study Design

Randomized double-arm clinical trial

Both groups followed a hypocaloric Mediterranean-like diet (50%C, 30%P, 20%F) for 12 weeks

- **eTRC**: early Time-Restricted Carbohydrate consumption
- **Control**: carbohydrates equally distributed during the day



Methods: Food Diary Analysis

- Food diaries were completed 3 days in a row, for two weeks, every month, indicating:
 - Kind of food
 - Raw food weight
 - Cooking method
 - Timing of the meal
- It was checked at every visit
- Caloric intake and macronutrient subdivision were determined by the "CREA" nutritional tables

MACRO NUTRIENTI			
Descrizione Nutriente	Valore per 100 g	Valore per Porzione 80 g	Origine Dato
Acqua (g)	12.2	9.8	A
Energia (kcal)	367	293	C
Energia (kJ)	1534	1226	C
Proteine (g)	9.0	7.2	A
Lipidi (g)	1.9	1.5	A
Colesterolo (mg)	0	0	ZL
Carboidrati disponibili (g)	82.9	66.3	C
Amido (g)	74.4	59.5	A
Zuccheri solubili (g)	1.1	0.9	A
Alcool (g)	0	0	ZL
Fibra totale (g)	1.3	1.0	A



AlimentiNUTrizione
Il gusto di scegliere consapevolmente

COLAZIONE - ORE 8:00
 1 BICCHIERE DI ACQUA APPENA ALZATA
 200 ml LATTE DI SOIA CON CAFFÈ E CANNELLA
 230g FRAGOLE
 37g CORN FLAKES INTEGRALI

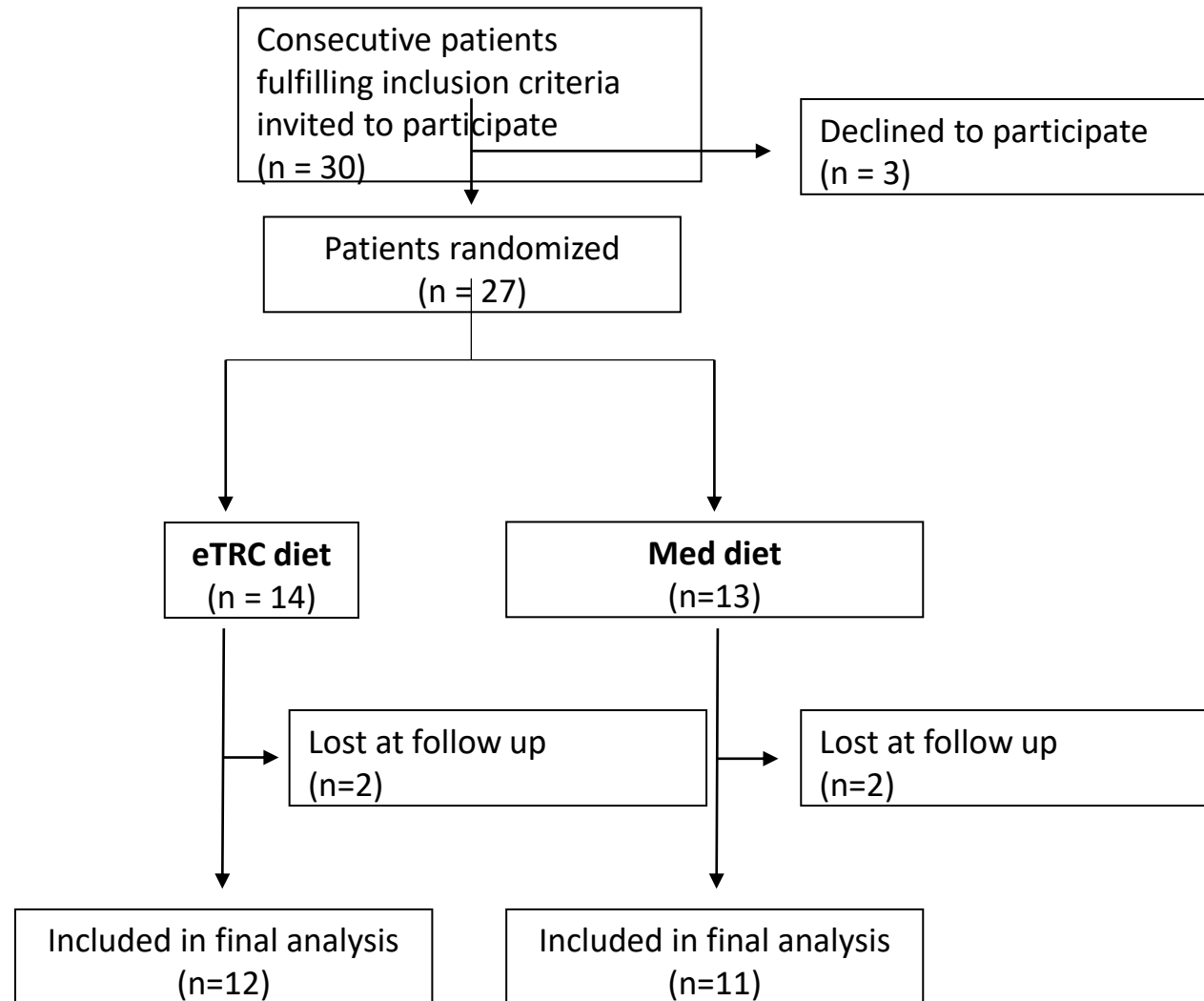
PRANZO - ORE 12:50
 80g PASTA INTEGRALE CON POMODORINI 1 CUCCIAINO DI OLIO E BASILICO
 30g DI PANE AI CEREALI
 1 ARANCIA
 CAFFÈ

CENA - ORE 20:30
 200g PETTO DI POLLO
 250g FUNGHI CHAMPIGNON
 2 CUCCIAINI DI OLIO
 INTUTTO IL GIORNO PIÙ DI 1500 cc DI ACQUA

Mediterranean Diet Pyramid: A proposal for italian people. A systematic review of prospective studies to derive serving sizes. D'Alessandro A et al. Nutrients 2019

Effects of low-carbohydrate versus mediterranean diets on weight loss, glucose metabolism, insulin kinetics and beta-cell function in morbidly obese individuals. Tricò et al. Nutrients, 2021

Results: Study Flowchart



Study flow diagram

Results: Characteristics of study participants

Characteristics	eTRC (n=12)	Control (n=11)	<i>p</i>
Age, years	71.5 [59.5-74.0]	67.0 [63.0-71.0]	0.688
Women (N, %)	5 (41.7)	6 (54.6)	0.684
BMI, kg/m ²	28.2 [26.6-29.4]	30.4 [27-32.8]	0.196
Body Weight	76.9 [67.5-86.5]	82.4 [71.1-94.5]	0.295
Waist Circumference, cm	97.5 [93.3-101.8]	99.0 [96.0-110.0]	0.281
Fat Mass, %	27.8 [25.3-35.8]	34.8 [22.7-44.9]	0.389
Visceral Fat, %	11.5 [8.3-15.0]	12.0 [9.0-17.0]	0.621
Duration of Diabetes, years	6.0 [2.0-10.0]	5.0 [2.0-8.5]	0.730
Alcohol			0.500
Never (N, %)	10 (83.3)	8 (80.0)	
Often (N, %)	0 (0)	1 (10.0)	
Frequently (N, %)	2 (16.7)	1 (10.0)	
Smoking			0.517
Active Smokers (N, %)	0 (0)	1 (10.0)	
Ex-Smokers (N, %)	6 (50.0)	4 (40.0)	
Systolic blood pressure, mmHg	139.0 [127.5-148.5]	130.0 [118.8-156.5]	0.786
Diastolic blood pressure, mmHg	84.5 [78.0-92.5]	80.0 [78.0-86.3]	0.327
Heart Rate, bpm	75.0 [67.0-76.0]	85.0 [58.5-87.0]	0.461

*Data are count (%) or median .
Group differences were tested by
Fisher's exact test or Mann-
Whitney U-test, respectively.*

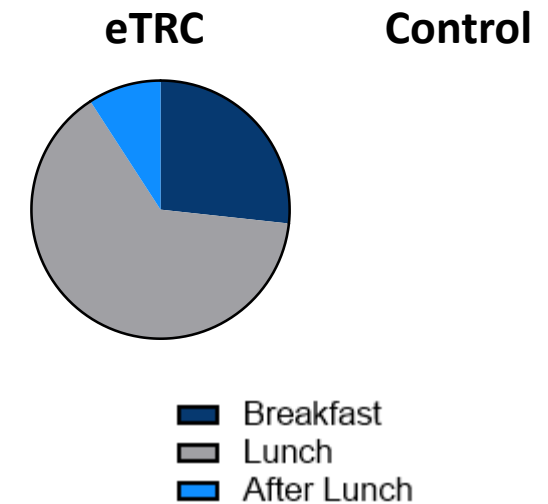
Results: Characteristics of study participants

Characteristics	eTRC (n=12)	Control (n=11)	<i>p</i>
HbA1c, %	6.6 [6.2-6.8]	6.5 [6.5-6.8]	0.755
Fasting plasma glucose, mg/dl	137.0 [102.5-142.5]	118.5 [108.3-143.3]	0.715
Total cholesterol, mg/dl	174.5 [135.5-148]	167 [148-205]	0.712
HDL-cholesterol, mg/dl	55.0 [49.8-64.0]	56.0 [45.0-61.0]	0.902
LDL-cholesterol, mg/dl	104.0 [71.5-133.8]	99.0 [80.0-140.0]	0.622
Triacylglycerol, mg/dl	108.5 [68.5-147.5]	104.0 [83.0-140.0]	0.902
AST, mg/dl	17.0 [16.0-20.0]	22.0 [19.0-27.0]	0.016
ALT, mg/dl	18.0 [13.0-19.8]	23.0 [20.0-38.0]	0.011
Creatinine, mg/dl	0.80 [0.67-0.91]	0.81 [0.68-0.99]	0.782
Medications			
Metformin (N, %)	7 (58.3)	8 (72.7)	0.469
DPP4 (N, %)	0 (0)	2 (18.2)	0.122

*Data are count (%) or median .
Group differences were tested by
Fisher's exact test or Mann-
Whitney U-test, respectively.*

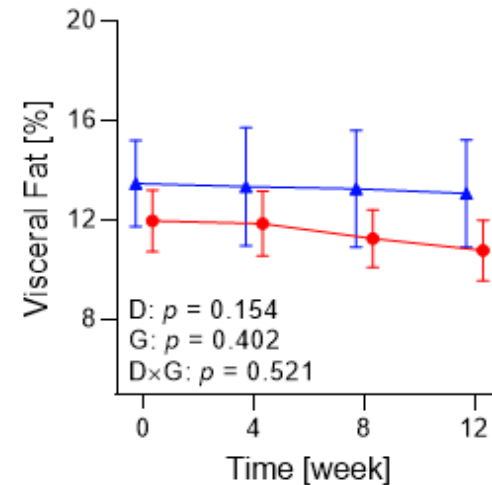
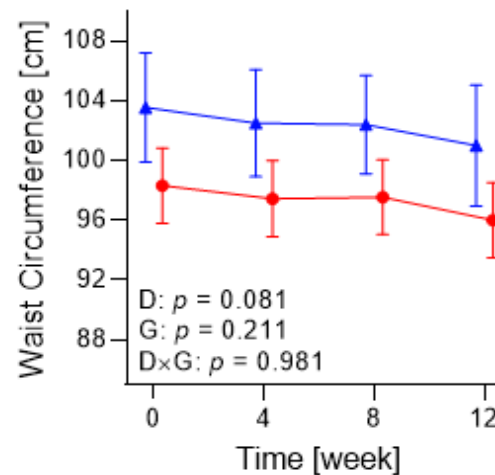
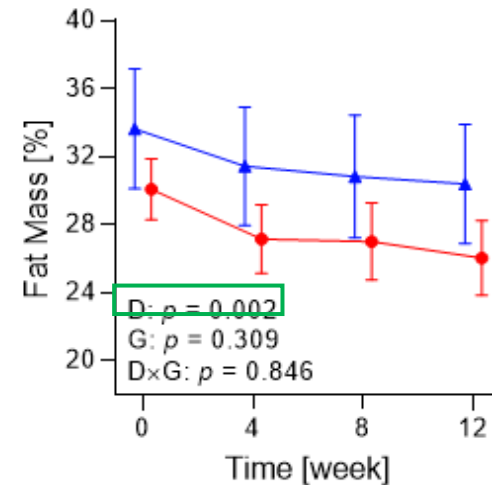
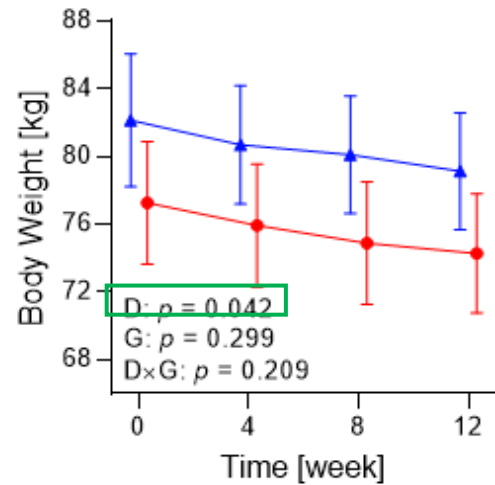
Results: Diet Composition

Characteristics	eTRC (n=12)	Control (n=11)	<i>p</i>
Prescribed diet composition			
Total energy, Kcal	1539 [1300-1759]	1520 [1389-1738]	0.878
Carbohydrates, %	49.0 [48.3-49.8]	50.0 [48.0-50.0]	0.329
Fat, %	28.0 [26.3-30.0]	29.0 [28.0-30.0]	0.609
Protein, %	23.0 [21.0-24.8]	22.0 [20.0-22.0]	0.287
Estimated diet composition			
Total energy, Kcal	1236 [1124-1292]	1253 [1211-1780]	0.196
Carbohydrates, %	44.5 [36.6-52.1]	44.8 [38.2-51.4]	0.644
Protein, %	22.3 [18.9-26.5]	21.4 [18.5-23.4]	0.460
Fat, %	32.0 [27.9-35.3]	29.9 [27.5-35.6]	0.644
Carbohydrates at breakfast, %	25.7 [21.2-33.3]	16.3 [11.4-23.7]	0.008
Carbohydrates at lunch, %	61.7 [51.1-67.6]	57.7 [45.5-62.6]	0.325
Carbohydrates after lunch, %	8.8 [6.4-15.6]	28.1 [24.0-31.1]	0.0026



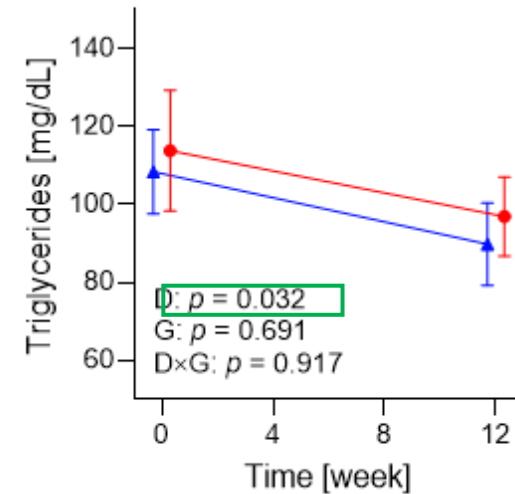
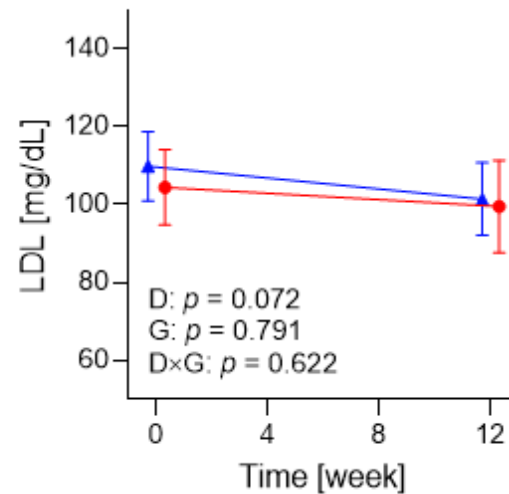
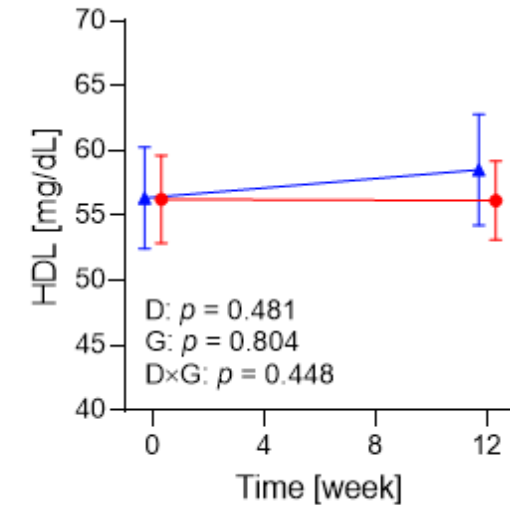
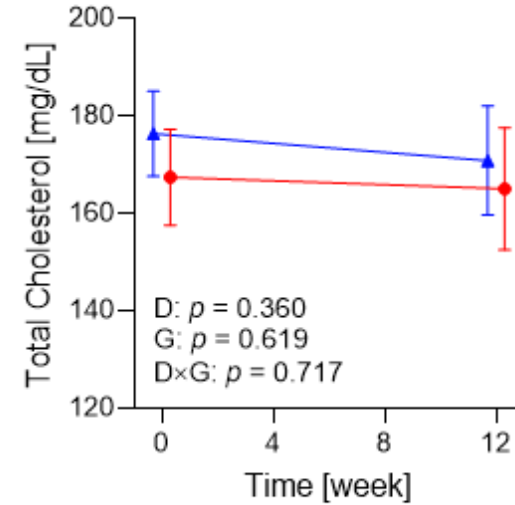
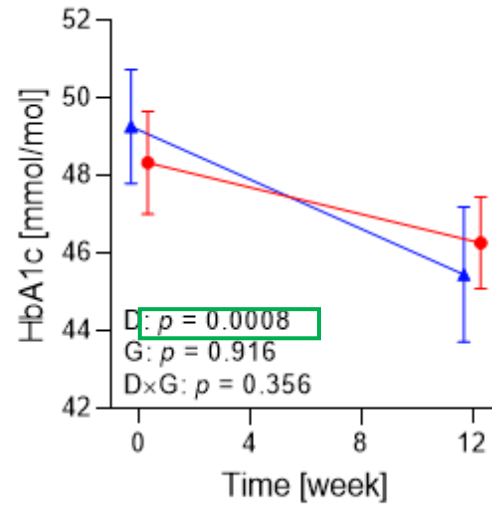
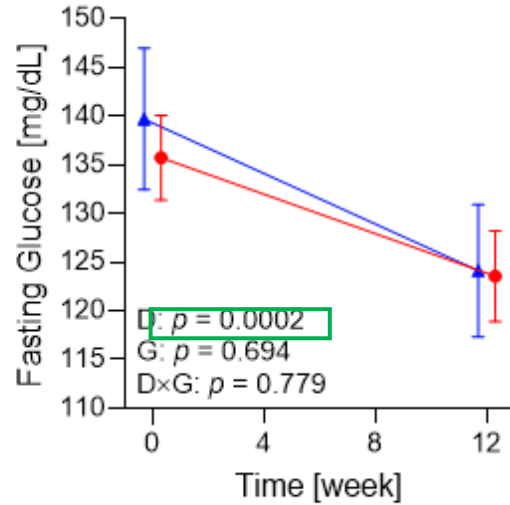
Prescribed and self-reported dietary intake,
Data are median

Results: Body Weight and Composition



Changes in body weight, fat mass, waist circumference, visceral fat in individuals with type 2 diabetes randomly assigned to a 12-week eTRC diet (red circles) or a Mediterranean-style control diet (blue triangles) with matched calorie restriction and macronutrient distribution.

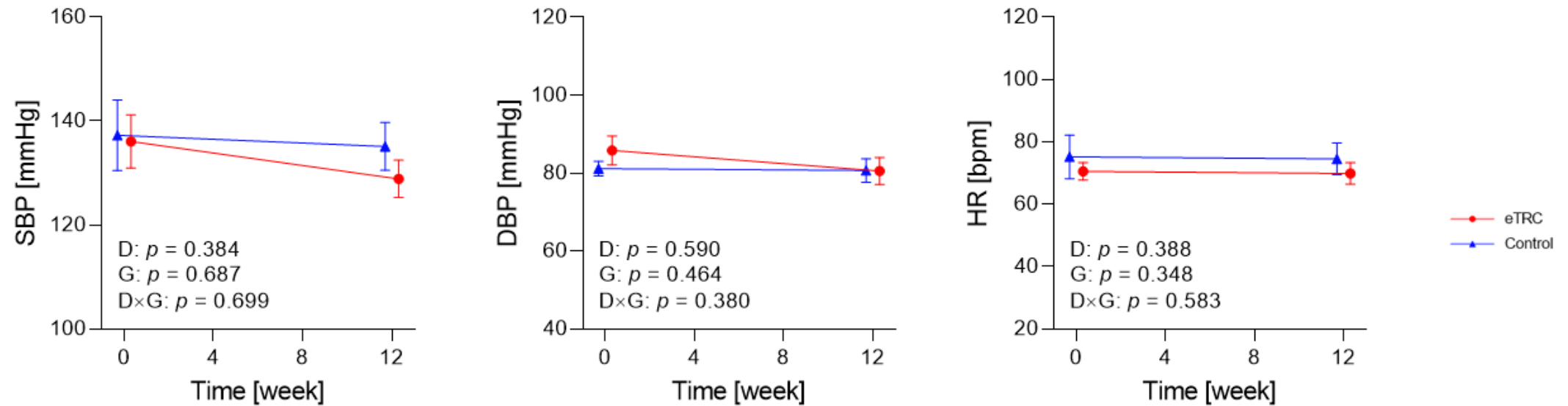
Results: Glucose and lipid metabolism



● eTRC
▲ Control

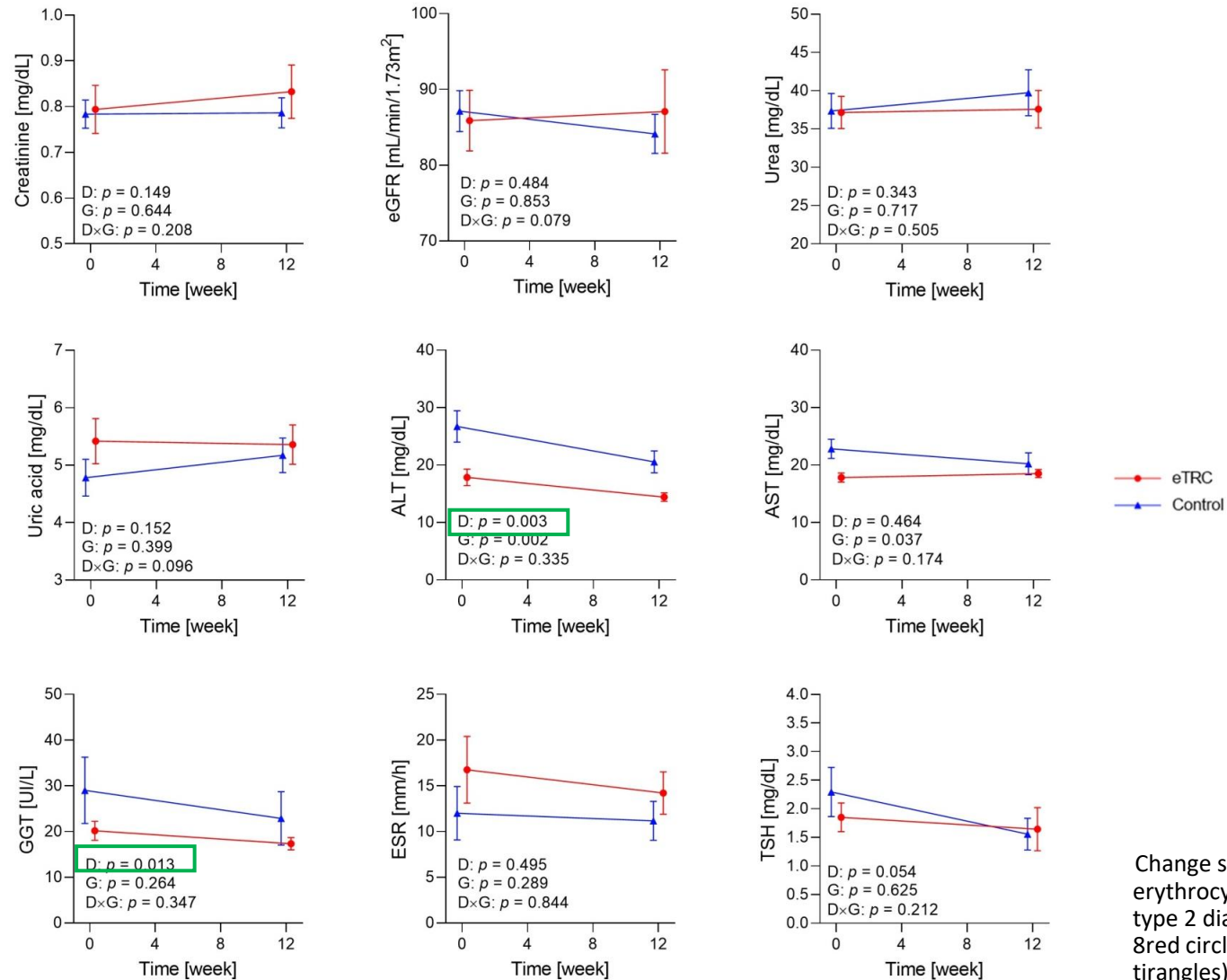
Changes in fasting glucose, HbA1c, total and fractional cholesterol, triglycerides in individuals with type 2 diabetes randomly assigned to a 12-week eTRC diet (red circles) or a Mediterranean-style control diet (blue triangles) with matched calorie restriction and macronutrient distribution.

Results: Blood Pressure and Heart Rate



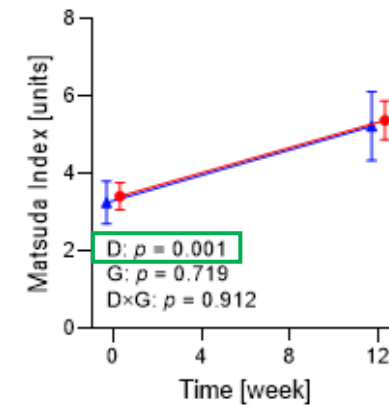
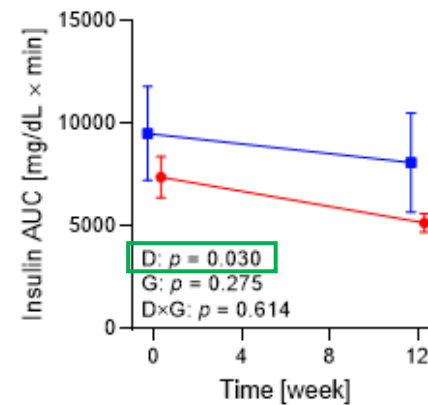
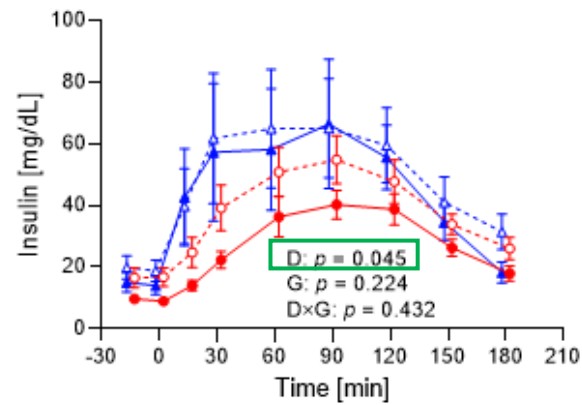
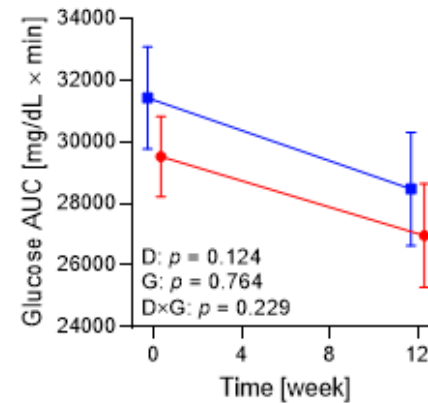
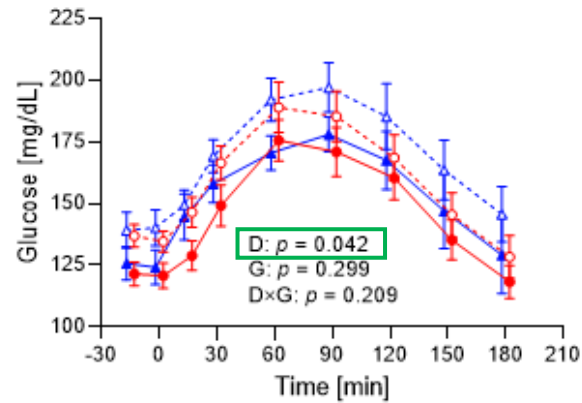
Changes in systolic and diastolic blood pressure and heart rate in individuals with type 2 diabetes randomly assigned to a 12-week eTRC diet (red circles) or a Mediterranean-style control diet (blue triangles) with matched calorie restriction and macronutrient distribution.

Results: Safety Parameters



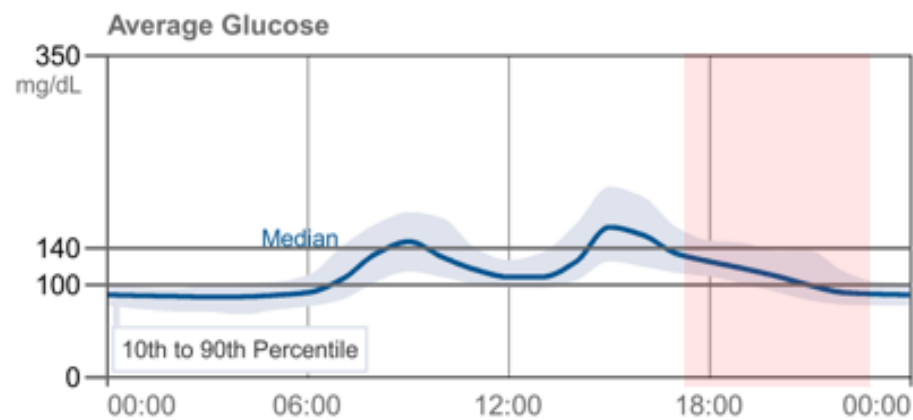
Changes in kidney markers, uric acid, liver markers, erythrocyte sedimentation rate, TSH in individuals with type 2 diabetes randomly assigned to a 12-week eTRC diet (red circles) or a Mediterranean-style control diet (blue triangles) with matched calorie restriction and macronutrient distribution.

Results: Mixed Meal Tolerance Test (MMTT)

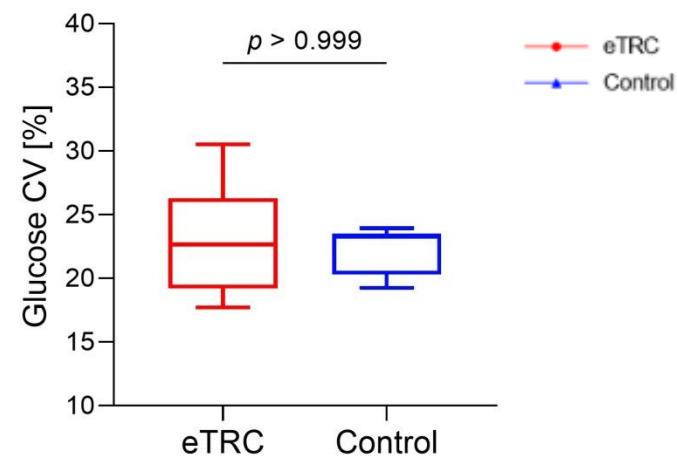
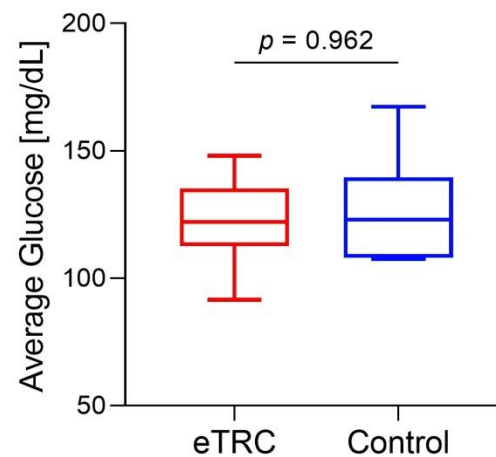
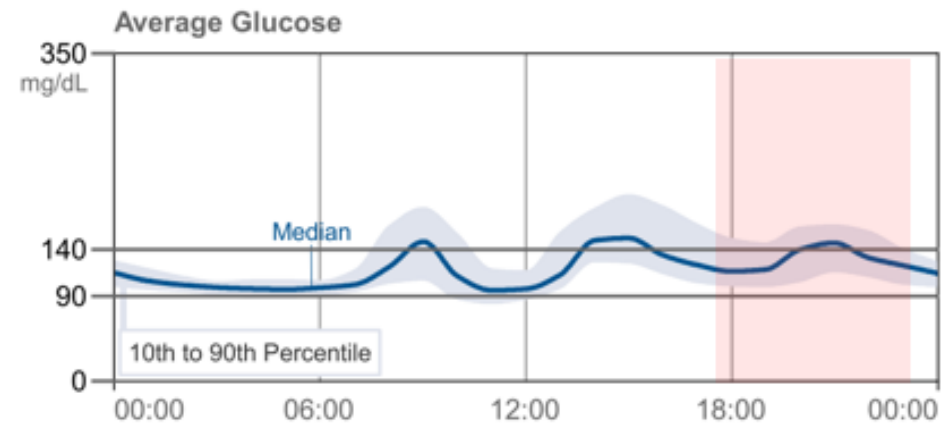


Results: Flash Glucose Monitoring (FGM)

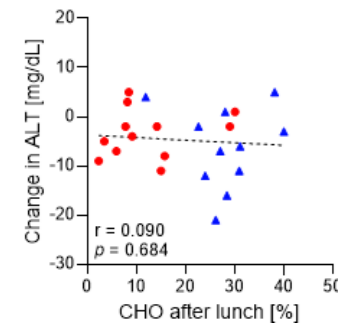
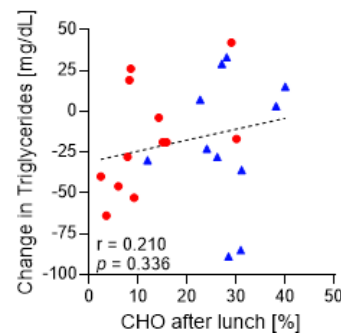
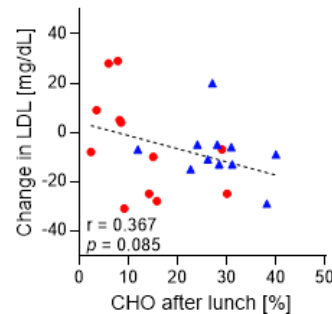
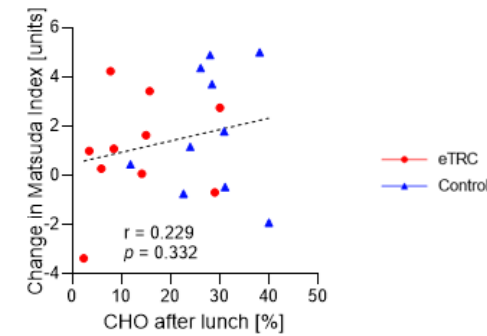
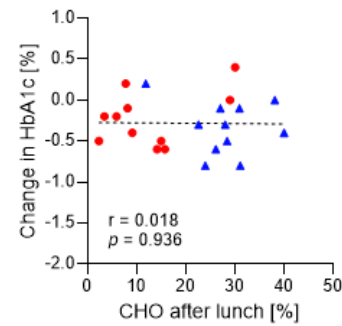
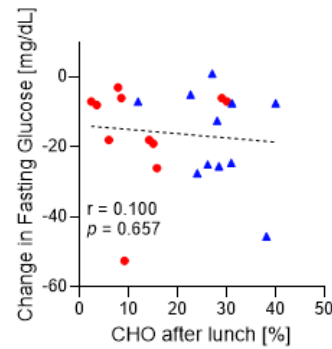
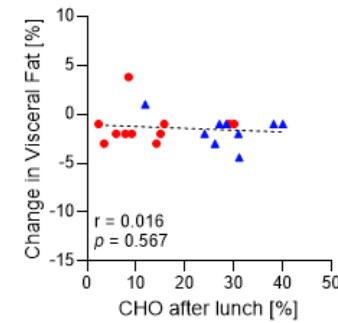
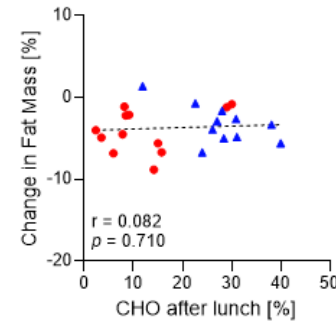
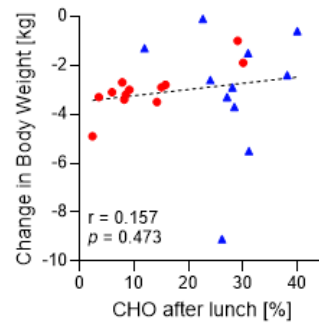
eTRC



Control



Sensitivity Analysis: Correlation Analysis



Correlations between percent carbohydrate intake after lunch during the 12-week intervention and diet-induced changes in body weight, fat mass, visceral fat, fasting glucose, HbA1c, Matsuda index, triglycerides, LDLc, ALT in individuals with type 2 diabetes randomly assigned to a 12-week eTRC (red circles) or a Mediterranean-style control diet (blue triangles) with matched calorie restriction and macronutrient distribution

Summary: Key findings

eTRC and Control experience significant and comparable:

↓ Body weight

↓ Fat mass

↓ Fasting plasma glucose

↓ HbA1c

↓ Insulin resistance

↓ TG

↓ ALT

↓ GGT

*Time restricted eating: a dietary strategy to prevent and treat metabolic disturbances.
Schuppelius et al. Frontiers in Endocrinology 2021*

Conclusions

eTRC can be an effective and safe alternative to a conventional Mediterranean diet, without additional metabolic benefits

Weight loss is extremely important for the management of Type 2 Diabetes

There is no evidence proving that one strategy is better than the others: the most successful strategy for each patient will likely be the one more feasible for the specific individual, allowing for greater and longer adherence
