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Moderate- vs. high-carbohydrate diets on glucose metabolism and insulin sensitivity during weight maintenance in overweight Indian adults: A pilot randomized parallel group trial

doi: 10.6133/apjcn.202610/PP.0002

Published online: October 2026

Running title: Moderate carbohydrate intake and glycemic regulation

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ABSTRACT

Background and Objectives: Indian adults have a high burden of metabolic abnormalities, possibly related to their diet composition. This pilot study compared moderate vs high-carbohydrate (MC vs HC, 40 vs 60% carbohydrate) diets during a weight maintenance period, following weight loss, on glucose metabolism, insulin sensitivity, body weight and composition, and lipid profile. **Methods and Study Design:** Forty overweight adults (BMI 25–32 kg/m²; 85% female) underwent an initial 12-week energy-restricted weight-loss phase (Phase-1, 5–10% weight-loss) and then were randomized to 12-week trial of MC or HC diets for weight-maintenance. Nineteen completers were randomized (non-blinded, parallel-group) to MC (n = 11) or HC (n = 8) diet arm during Phase-2. Besides weight, outcomes included 1-hour Oral-Glucose-Tolerance-Test (OGTT) profile, body insulin sensitivity and secretion measurements, plasma lipid profile, and Dual-Energy-X-Ray-Absorptiometry (DXA) derived body composition. **Results:** Among 19 completers, body weight and body mass index (BMI), decreased significantly during Phase-1 (mean 5.8%, absolute 4.2 kg, 95%CI: 3.9, 4.6, $p < 0.05$), with significant reductions in waist circumference to height ratio (WHtR), body fat mass index (FMI, kg/m²), mean plasma insulin concentration, and insulin sensitivity improved and plasma lipid profile lowered ($p < 0.05$). At the end of Phase-2, body weight changes (0.4 kg) and FMI were similar in both diet-arms. The MC diet-arm showed a trend (non-significant) of lower 1-hour OGTT glucose-response, lower insulin resistance indices, and better lipid profile. **Conclusions:** Body weight loss and FMI reduction induced by a negative energy balance were later maintained by both MC and HC diets, although the MC diet showed a non-significant trend toward better maintenance of metabolic markers.

Key Words: body composition, glucose metabolism, insulin sensitivity, moderate carbohydrate diet, high carbohydrate diet.

INTRODUCTION

India faces a rapidly rising burden of overweight/obesity, affecting ~ 23% of women and 22% of men.¹ Asian Indians also exhibit a “thin-fat” phenotype with normal body mass index (BMI), but higher fat mass (FM) and low lean mass (LM) than Caucasians, predisposing them to glucose dysregulation, insulin resistance, and hyperlipidemia at lower BMI.²⁻³ Traditional obesity management is grounded in the Energy Balance Model (EBM) which attributes weight gain to caloric excess and often overlooks macronutrient-specific metabolic adaptations that hinder weight maintenance.⁴ Conversely, the Carbohydrate-Insulin Model

(CIM) suggests that high-carbohydrate (CHO) diets induce chronic hyperinsulinemia, fat storage, reduce fat oxidation, and increase hunger, thereby promoting overeating and weight gain.^{5,6}

After weight loss, weight regain is pervasive, with ~30–35% of lost weight regained within a year, and up to 80% within 4–5 years, highlighting the need for sustainable, population-specific strategies.^{7–8} Evidence on macronutrient composition for weight loss and maintenance is mixed and phased dietary interventions (weight loss followed by weight maintenance) remain largely underexplored in India. Effective and sustainable strategies should clearly distinguish between the active weight loss phase accompanying favorable metabolic adaptations, and the weight maintenance phase, which focuses on preventing weight regain over time and the preservation of beneficial metabolic adaptations.

In Western populations, Moderate-CHO (MC) diets (~40% energy) improved metabolic outcomes compared to High-CHO (HC) diets (~55% energy) during weight loss.⁹ Since physiological adaptations such as reduced energy expenditure and increased hunger predispose individuals to weight regain following weight loss in overweight adults, MC diets with low-glycemic-load help counter these effects by improving insulin sensitivity, stabilizing plasma glucose concentration, enhancing satiety, reducing adiposity and preserving lean mass, thereby supporting long-term weight-loss maintenance.^{10–12} Very low-carbohydrate, high-fat or ketogenic diets (<20% carbohydrate) are also effective but persisting adherence and safety concerns suggest that MC diets may be a more sustainable and effective strategy.¹³

Indian diets are typically HC (~60–75% energy), low in fibre, with refined cereals and added sugars.¹⁴ After any weight loss regime, these diets might promote weight regain, but this has not been tested. Hence, the objective of the study was to compare the effect of MC versus HC diets on body weight, body composition, glucose metabolism, insulin sensitivity and lipid profile of overweight South Indian adults, following a successful 3-month weight-loss phase that was based on an energy deficit diet.

MATERIALS AND METHODS

Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Ethics Committee (IEC no. 341/2021). Date of approval: Study was approved on 22nd September 2021.

Study design and participants

The study followed an experimental prospective study design, non-blinded randomized controlled trial (Parallel-group design, 1:1 allocation ratio between MC and HC diet-arm) (trial registration: CTRI/2022/01/039191). Community-dwelling overweight adults aged 25–45 years with a BMI of 25.0–32.0 kg/m² and body weight stable (± 2 kg) over the last 3 months were included. Exclusion criteria included diabetes, hypertension, major endocrine or reproductive disorders, pregnancy/lactation, restrictive diets, dietary supplements, and substance dependence. All assessments were conducted at the Division of Nutrition, St. John's Research Institute after obtaining written informed consent from the participants.

Randomization and blinding

Participants were randomized using a computer-generated block randomization sequence prepared by an independent investigator who was not involved in participant recruitment, intervention delivery, outcome assessment, or data analysis. The randomization sequence was stored in a sealed envelope and was disclosed only at the time of intervention assignment to ensure allocation concealment. Owing to the nature of the dietary intervention, participant blinding was not feasible. However, investigators responsible for outcome assessment and data analysis remained blinded to group allocation throughout the study period.

Intervention

This six-month study was conducted in two phases (Supplementary Figure 1).

Phase 1: Weight-loss phase (12 weeks)

All participants were assigned to a 12-week weight-loss phase aimed at achieving a 5–10% reduction in their initial body weight. During this period, participants were prescribed individualized calorie-restricted diet designed to create an energy deficit and result in weight loss of about 5-10%. Participants who achieved at least a 5% reduction in body weight by the end of this phase were eligible to continue to the next phase. Before starting Phase 2, they underwent a one-week washout period with their regular HC diet.

Phase 2: Weight-maintenance phase (12 weeks)

Participants who successfully completed and achieved the target weight loss of 5-10% in Phase 1 entered a 12-week weight-maintenance phase. They were randomly assigned to one of the two diet-arms according to the randomization schedule generated at the start of the study: a MC diet providing 40% of total energy from CHO or a HC diet providing 60% of

total energy from CHO. Participants were prescribed individualized diets to maintain their body weight, with changes only in the macronutrient (CHO) content.

The study protocol initially included a low-CHO (LC) arm (20% of total energy from CHO). However, within the first week, approximately half of the participants reported gastrointestinal and dermatological symptoms and demonstrated poor adherence to the diet. Following approval from the Institutional Ethics Committee, the CHO intake was increased to $\leq 40\%$ of total energy (the MC diet). The participant tolerance and adherence to this was good and the intervention was continued using the MC diet.

Diets in both phases were planned and supervised by a qualified dietitian and were tailored to each participant's energy requirements. The dietary pattern consisted of three main meals and two snacks per day. The MC diet emphasized low-glycemic-index foods, along with foods rich in fiber, protein, and healthy fats. To support adherence, participants received individualized dietary counseling, structured meal plans, cyclic menus, food exchange lists, and guidance on portion sizes using standardized household measures such as cups, bowls, and spoons.

Participants compliance with the prescribed diet was assessed bimonthly using dietary recalls to evaluate adherence to the assigned macronutrient distribution. During the weight-loss phase, participants were encouraged to engage in physical activity to facilitate weight reduction. During the weight-maintenance phase, participants in both diet groups were instructed to maintain the same level of physical activity achieved during Phase 1.

At the beginning and end of each phase, anthropometry, 1-hour Oral Glucose Tolerance Test (1 hour OGTT), plasma lipid profile, and Dual Energy X-ray Absorptiometry (DXA) derived body composition were measured. Compliance to the diet intervention was monitored using bi-monthly 24-hour dietary recalls on three non-consecutive days, and physical activity was assessed using validated physical activity questionnaires (PAQ).

Anthropometry and body composition

Body weight was measured to the nearest 0.01 kg using a calibrated digital weighing scale (Goldtech, AE038, New Delhi, India) and height to nearest 0.1 cm using a Seca stadiometer (Seca 213, Hamburg, Germany). BMI (kg/m^2) was calculated as weight (kg)/height square (m^2). Waist circumference (WC) (cm) was measured using a non-stretchable tape (Seca 201, Hamburg, Germany) at the narrowest region of the torso located between the lowest rib and the iliac crest, at the end of a normal expiration, with the resulting value divided by height (cm) to determine the waist-to-height ratio (WHtR). Measurements, following standard

protocols and were performed in duplicate by two trained staff (inter-observer coefficient of variation (CV) <1.5%); mean values were used for analysis.¹⁵

Fat Free Mass (FFM), and FM were assessed using whole-body DXA (Lunar Prodigy Advanced PA+301969 GE Medical Systems, USA; software version 16). Precision of this measurement for FM was 2.1%. Fat Mass Index (FMI) and Fat-Free Mass Index (FFMI) were calculated by dividing FM (kg) or FFM (kg) by height square (m²). Scans were performed by a trained technician, with participant wearing light clothing and no metal objects.

Metabolic biomarkers

A fasting blood sample (10mL) was collected at each assessment, to measure plasma glucose (fluoride hexokinase method), serum insulin (FI, electrochemiluminescence immunoassay), and plasma lipid profile (homogenous enzymatic colorimetry assay). All assays were performed in a single accredited laboratory using standard quality control procedures. A 1-hour OGTT was performed with 75g of anhydrous glucose in 250 mL of water; 2 mL blood samples were collected at 30 min and 60 min after ingestion.¹⁶ Total Area Under the Curve (AUC_t) for plasma glucose and serum insulin concentrations during the 1-hour OGTT (0-30 and 30-60 min) was calculated using the trapezoidal rule. Insulin sensitivity was estimated from Matsuda, McAuley, Quantitative Insulin Sensitivity Check Index (QUICKI), and Bennett University indices (BENNETTS), insulin resistance from Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), Hepatic Insulin Resistance Index (HIRI) and β -cell function from insulinogenic and disposition indices (Supplementary Table 1).¹⁷⁻²⁰

Dietary intake and physical activity

Dietary intake was assessed using a 3-day, 24-hour recall (two non-consecutive weekdays and one weekend day), at each visit and supplemented by bi-monthly dietary recall to monitor compliance. Energy and nutrient intakes were calculated using an Indian food nutrient database and the USDA database.²¹⁻²² Physical activity was assessed at the end of each phase using a previously validated questionnaire that captured type, duration, and intensity of activities over 24 hours.²³ Metabolic equivalent (Met) values were assigned to estimate the total daily energy expenditure, from which the Physical Activity Level (PAL) was calculated as the ratio of total daily energy expenditure and the predicted basal metabolic rate. The PAL allowed for categorization of individuals into sedentary (PAL <1.4), moderately active (PAL 1.55–1.6), or heavily active (PAL >1.75).²⁴

Statistical analysis

The primary outcome of the study was the difference in fasting insulin levels between the diet arms at the end of phase 2 and the sample size for the study was based on reported differences in fasting insulin secretion between HC and low-carbohydrate (LC) diets (2.15 ± 0.24 pmol/kg/min vs 1.85 ± 0.19 pmol/kg/min).²⁵ To detect this difference during the maintenance phase after weight loss, 10 participants per diet-arm were required at 5% level of significance with 80% power. Allowing 30% attrition and greater within diet-arm variability, a total of 20 participants per arm ($n = 40$) were recruited for the study.

Descriptive statistics were computed for the entire study sample. Continuous variables were summarized as means (standard deviations (SD)) or medians (interquartile range (IQR)) and categorical variables as frequencies and percentages. Triglyceride values were log-transformed prior to analysis. Changes in the AUC_t insulin sensitivity and resistance, lipid profile, body weight, body composition, and diet were compared from start of Phase-1 to end of Phase-1 using paired t-tests. For Phase-2, Difference-in-Differences analysis were performed to evaluate changes in all measured parameters along with standardized effect size with 95%CI from start to end of Phase, between the MC and HC diet-arms. Sensitivity analyses to assess attrition bias were performed by comparing characteristics of retained and dropout participants using independent sample t-tests and chi-square tests. Statistical significance was set at a two-sided p-value < 0.05 and all analyses were performed using IBM SPSS version 29.0 (Armonk, NY, USA).

RESULTS

Forty participants (mean age 32.5 ± 5.5 years) were enrolled; 85% were female. Most (97.5%) participants had at least a graduate degree, with 62.5% holding a postgraduate degree, nearly all were from upper (45%) and upper-middle (50%) socioeconomic classes. Participants ($n = 40$) were randomly allocated to either the MC diet-arm ($n = 20$) or the HC diet-arm ($n = 20$) at the start of the study.

Upon completion of Phase-1, participants continued in their assigned diet-arms. Within two weeks, 21 participants (52.5%) withdrew for various reasons (Figure 1). There were no significant differences in age, socio-economic status, body weight, and glucose concentration between the retained and dropout participants. The remaining 19 participants who completed Phase-1 proceeded to Phase-2, as per their initial randomization prior to Phase-1 (MC, $n=11$; HC, $n=8$). All 19 participants completed Phase-2.

Table 1 summarizes changes in the indices of insulin sensitivity, resistance, β -cell function, lipid profile, body weight, and composition of all participants at the end of 3 months of Phase-1. Their mean body weight, BMI, WHtR, and FMI decreased by 5.8%, 5.7%, 3.8% and 10.3% respectively ($p < 0.05$). Similarly, mean insulin concentrations also decreased significantly (17.9%, $p < 0.05$). Conversely, insulin sensitivity indices (Matsuda and McAuley) increased significantly by 31.3% and 12.8% respectively ($p < 0.05$). HOMA-IR and HIRI demonstrated a non-significant decreasing trend, while β -cell function indices (insulinogenic and disposition indices) demonstrated a non-significant increasing trend. All lipid parameters decreased significantly ($p < 0.05$).

Table 2 presents the baseline characteristics of participants in the MC and HC diet-arms at the start of the weight maintenance phase-2. Participants randomized to the two diet-arms were comparable across all assessed parameters, with no statistically significant differences observed between the diet-arms ($p > 0.05$).

Table 3 presents the changes in body weight and composition, insulin sensitivity, resistance, β -cell function, and lipid profile within and between the diet-arms at the end of 3 months of Phase-2. Body weight was maintained in both MC (difference between start and end of Phase-2: 0.4 kg; 95% CI: -0.8 to 1.6; $p = 0.503$) and HC diet-arms (0.4 kg; 95% CI: -1.1 to 2.0; $p = 0.522$), along with FMI relative to their values at the end of Phase-1. There were no significant differences in mean glucose and insulin concentrations, insulin sensitivity, resistance, β -cell function, and lipid profile parameters, both within and between diet-arms. However, the MC diet-arm demonstrated more favorable trends in these parameters compared to the HC diet-arm (Table 3).

Figure 2 presents the mean AUCt for glucose and insulin concentrations during the 1-hour OGTT for participants across both study phases. For both glucose and insulin concentrations, the mean AUCt decreased at the end of Phase-1, with Δ change = -733.6 (95% CI: 115.4, 1351.7) mg/dL, $p = 0.055$ and Δ change = -735.5 (95% CI: 18.9, 1452.2) mg/dL, $p = 0.092$ respectively. At the end of Phase-2, there were no significant differences in the AUCt for glucose and insulin within and between the MC and HC diet-arms. However, the MC diet-arm showed a declining trend for both parameters, whereas the HC diet-arm maintained values comparable to those at the end of Phase-1 (Figure 2).

Table 4 presents changes in energy and macronutrient intake across the study phases. At the end of Phase-1, mean energy intake decreased significantly from 1684.9 ± 364.0 kcal/day to 1213.3 ± 257.6 kcal/day ($p < 0.001$). Significant reductions were also observed in the intake of all macronutrients, including protein (Δ change = -12.7 g/day; 95% CI: -22.5, -2.9; $p =$

0.014), fat (Δ change = -9.7 g/day; 95% CI: -17.0 , -2.4 ; $p = 0.012$), and carbohydrate (Δ change = -83.4 g/day; 95% CI: -108.3 , -58.6 ; $p < 0.001$). In contrast, PAL increased significantly from 1.48 ± 0.11 to 1.64 ± 0.15 during this phase ($p < 0.001$).

During phase-2, mean energy intake and PAL remained stable, with no significant changes observed from the beginning to the end of the phase in either diet-arm. However, participants in the MC diet-arm showed significant increases in protein (Δ change = 11.3 g/day; 95% CI: 0.4 , 22.2 ; $p = 0.043$) and fat intake (Δ change = 15.6 g/day; 95% CI: 3.8 , 27.4 ; $p = 0.014$), while carbohydrate intake decreased, although the change was not statistically significant. In the HC diet-arm, carbohydrate intake increased significantly from the start to end of phase-2 (Δ change = 26.3 g/day; 95% CI: 0.9 , 51.7 ; $p < 0.05$).

DISCUSSION

This pilot study examined the effect of MC versus HC diet on the maintenance of body weight, body composition, glucose metabolism, insulin sensitivity and plasma lipid profile, following a 3-month weight-loss phase in overweight South Indian adults. In the weight loss phase (Phase-1), energy restriction led to modest weight loss ($\sim 5.8\%$), with improvements in weight, BMI, WHtR, body composition, glucose and lipid regulation, and insulin sensitivity, including both whole-body and hepatic insulin sensitivity. These findings are consistent with existing evidence showing that short-term energy-restricted diets improve glucose control, insulin sensitivity, and lipid profiles in overweight and obese individuals.²⁶⁻²⁸ Similar to previous studies, we observed reductions in plasma triglycerides and LDL-C concentrations, along with a transient decline of HDL-C during weight loss.²⁹ The metabolic benefits observed in Phase-1 are likely driven by reductions in body fat and improvements in insulin signalling and metabolic function.³⁰

During phase-2 (weight-maintenance), participants in both the MC and HC diet-arms successfully maintained their body weight and body composition. Energy intake remained stable in both groups relative to the end of Phase 1, suggesting that the observed metabolic effects during weight maintenance were primarily attributable to differences in macronutrient composition, particularly carbohydrate intake. The MC diet-arm showed further (but non-significant) favorable trends, including lower insulin resistance (HOMA-IR, HIRI) with preserved insulin sensitivity (Matsuda, McAuley, QUICKI, BENNETTS indices), lower AUCt for plasma glucose and insulin concentrations, and a more favorable plasma lipid profile compared to the HC diet-arm. These observations are consistent with prior evidence indicating that partial replacement of carbohydrates with mono- and polyunsaturated fats

(30% of energy) and protein (15-30% of energy) is associated with non-significant improvements in insulin sensitivity, fat oxidation, and lipid metabolism, particularly in short duration interventions.³¹⁻³² Earlier evidence also suggests limited or no additional benefit of MC intake (~40% energy) over HC diets on glucose and insulin metabolism.³³ The trend in improvements in plasma HDL-C in the MC when compared to HC diet-arm, is consistent with earlier evidence of plasma HDL-C decline during weight loss, but its stability and better preservation on lower-CHO, higher-protein diets.²⁹ Although not statistically significant, these patterns in the present study suggest that MC diets may support better maintenance of metabolic markers during long term weight maintenance in this population.

These trends in the MC diet group may be explained by lower glycemic load attenuating postprandial glucose and insulin excursions, thereby reducing chronic hyperinsulinemia. Lower insulin levels promote lipolysis and fat oxidation by relieving inhibition of hormone-sensitive lipase, while also suppressing hepatic de novo lipogenesis, improving lipid metabolism.^{34,35} Given the pilot nature and small sample size of this study, these physiologically coherent, but non-significant findings and estimates of treatment effect, including standardized effect sizes, are presented as exploratory estimates in order to describe the magnitude and uncertainty of plausible intervention effects and should not be interpreted as definitive evidence of efficacy.

Strengths of this study include comprehensive, longitudinal assessments of glucose metabolism, insulin sensitivity, lipid profile, and body composition using validated methods, enabling evaluation of a weight loss maintenance phase and offering mechanistic insights into the effects of dietary macronutrient composition. The participants showed good compliance to dietary advice during weight-loss phase and adherence to the macronutrient distribution during weight maintenance (>85%) in both the diet-arms, likely due to the frequent in-person and telephonic follow-up in this free-living setting; whether similar adherence can be sustained, without regular monitoring needs further study. Limitations include the small sample size due to attrition during the weight maintenance phase (Phase-2) and the shift to a MC diet rather than the planned LC diet, due to the difficulties for participants. The inclusion of mostly female participants, as male participants showed limited interest in participation or did not meet the inclusion criteria despite efforts to achieve balanced recruitment, limits the generalizability of the findings. Finally, this well-educated, predominantly upper socioeconomic, urban cohort may limit generalizability to the broader South Indian population, including rural and middle/lower-income groups with different dietary patterns and constraints.

In summary, weight maintenance after weight loss appeared to be equally sustained by a MC or HC diet. However, the MC diet showed encouraging and favorable near-significant trends in further improving metabolic health after weight loss. This MC pattern emphasizing whole grains, legumes, unsaturated fats, and fibre is consistent with traditional South Indian dietary practices, which might support its long-term feasibility and cultural acceptability.

SUPPLEMENTARY MATERIALS

All supplementary tables and figures are available upon request from the editorial office, and are also accessible on the journal's webpage (apjcn.qdu.edu.cn).

DISCLOSURE ON THE USE OF AI AND AI-ASSISTED TECHNOLOGIES

The authors declare that no artificial intelligence (AI) tools were used in the writing, analysis, or preparation of this manuscript.

ACKNOWLEDGEMENTS

We thank all the participants for their active participation in this study.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

The study was supported by the Indian Council of Medical Research (F.N. 5/9/1411/2022-Nut.).

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Table 1. Changes in indices of insulin sensitivity, resistance, β -cell function, lipid profile, body weight and composition during Phase-1 (n=19)

Indices	Phase-1 [†]		p-value
	Baseline (n=19)	End (n=19)	
Fasting blood glucose (mg/dL)	87.7 $\pm$ 8.6	84.6 $\pm$ 7.1	0.133
1-hour postprandial blood glucose [‡]	128.3 $\pm$ 31.2	112.0 $\pm$ 26.9	0.107
Fasting insulin (μ IU/mL)	15.2 $\pm$ 6.4	12.7 $\pm$ 5.5	0.130
1-hour postprandial insulin [‡]	124.7 $\pm$ 13.4	90.1 $\pm$ 18.0	0.037*
Insulin sensitivity indices			
Matsuda Index	3.2 $\pm$ 1.4	4.2 $\pm$ 2.3	0.044*
McAuley Index	3.9 $\pm$ 0.8	4.4 $\pm$ 0.7	0.006*
QUICKI	0.33 $\pm$ 0.02	0.34 $\pm$ 0.02	0.096
BENNETTS	1.3 $\pm$ 0.3	1.5 $\pm$ 0.3	0.097
Insulin resistance and β -cell function indices			
HOMAIR	3.4 $\pm$ 1.6	2.7 $\pm$ 1.2	0.099
HIRI	1358.2 $\pm$ 643.3	1081.7 $\pm$ 486.4	0.099
Insulinogenic Index [§]	0.8 $\pm$ 0.4	0.9 $\pm$ 0.5	0.555
Disposition Index [§]	1.7 $\pm$ 0.7	2.2 $\pm$ 1.1	0.160
Lipid profile			
TC (mg/dL)	169.9 $\pm$ 25.6	157.9 $\pm$ 21.6	0.017*
HDL-C (mg/dL)	42.8 $\pm$ 9.0	40.6 $\pm$ 8.6	0.027*
LDL-C (mg/dL)	112.4 $\pm$ 22.9	105.2 $\pm$ 20.5	0.049*
TG (mg/dL) [¶]	101.3 (80.8,116.6)	83.2 (67.8,110.3)	0.012*
Body weight and composition			
Weight (kg)	73.7 $\pm$ 9.6	69.5 $\pm$ 9.4	<0.001*
BMI (kg/m ²)	28.2 $\pm$ 1.9	26.6 $\pm$ 1.8	<0.001*
WHtR	0.53 $\pm$ 0.04	0.51 $\pm$ 0.04	<0.001*
% Fat Mass	41.2 $\pm$ 4.0	39.6 $\pm$ 4.8	0.271
Fat Mass Index (kg/m ²)	11.6 $\pm$ 1.7	10.4 $\pm$ 1.8	0.042*
% Fat Free Mass	58.1 $\pm$ 3.3	60.0 $\pm$ 4.8	0.214
Fat Free Mass Index (kg/m ²)	16.6 $\pm$ 3.6	15.8 $\pm$ 1.2	0.497

OGTT: Oral Glucose Tolerance Test, HOMAIR: Homeostatic Model Assessment of Insulin Resistance, QUICKI: Quantitative Insulin Sensitivity Check Index, BENNETTS: Bennett University, HIRI: Hepatic Insulin Resistance Index, TC: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, TG: Triglycerides, BMI: Body Mass Index, WHtR: Waist Circumference to Height Ratio
 BMI = Weight (kg)/Height (m²), Fat Mass Index: Fat Mass (kg)/Height (m²), Fat Free Mass Index = Fat Free Mass (kg)/Height (m²).

[†]Phase 1: weight-loss phase

[‡]1-hour postprandial glucose and insulin were measured 60 minutes after glucose ingestion during the 1 hour OGTT.

[§]Values are expressed as Median (IQR) and Mean $\pm$ SD elsewhere.

[¶]Triglyceride values were log-transformed for statistical analyses but are reported as Median (IQR) of the untransformed data

*Indicates statistical significance based on a paired-samples t-test (p < 0.05).

Table 2. Baseline characteristics between Moderate Carbohydrate and High Carbohydrate diet-arms at the start of weight maintenance phase (n=19)[†]

Indices	MC (n=11)	HC (n=8)	Mean Difference (95% CI)	p-value
Glucose and insulin response				
Fasting blood glucose (mg/dL)	85.5 ± 7.0	83.1 ± 7.5	-2.384 (-5.28, 10.05)	0.501
1-hour postprandial blood glucose [‡]	112.2 ± 32.8	111.6 ± 16.0	-0.674 (-24.00, 25.34)	0.477
Fasting insulin (μIU/mL)	13.2 ± 6.1	11.6 ± 4.7	-1.593 (-4.15, 7.34)	0.587
1-hour postprandial insulin [‡]	92.4 ± 43.8	86.4 ± 41.2	-5.993 (-37.94, 49.93)	0.387
Lipid Profile				
TC (mg/dL)	157.8 ± 22.5	158 ± 21.8	0.182 (-23.19, 22.83)	0.987
HDL-C (mg/dL)	42.2 ± 9.0	38.1 ± 7.9	-4.068 (-4.56, 12.70)	0.341
LDL-C (mg/dL)	105.3 ± 22.4	105.1 ± 18.8	-0.260 (-20.69, 21.21)	0.98
TG (mg/dL) [§]	81.8 (66.3,85.2)	108.7 (68.3,113.7)	0.147 (-0.56, 0.26)	0.384
Body weight and composition				
Weight (kg)	67.8 ± 8.7	71.7 ± 10.6	3.934 (-13.75, 5.88)	0.385
BMI (kg/m ²)	26.1 ± 1.6	27.2 ± 2.1	1.066 (-2.97, 0.83)	0.222
WHtR	0.50 ± 0.03	0.52 ± 0.05	0.019 (-0.06, 0.03)	0.333
%Fat Mass	39.0 ± 4.3	40.4 ± 5.8	1.378 (-7.67, 4.91)	0.606
Fat Mass Index (kg/m ²)	10.0 ± 1.5	11.0 ± 2.2	0.994 (-3.34, 1.35)	0.309
%Fat Free Mass	60.4 ± 4.3	59.6 ± 5.8	-0.804 (-5.56, 7.17)	0.501
Fat Free Mass Index (kg/m ²)	15.6 ± 1.1	16.1 ± 1.5	0.514 (-2.10, 1.07)	0.451

OGTT: Oral Glucose Tolerance Test, TC: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, TG: Triglycerides, BMI: Body Mass Index.

Values are expressed as Median (IQR) and Mean ± SD elsewhere. P-values were obtained using independent-sample t-test

[†]Given the small sample size of Phase 2 (n=19), $p > 0.05$ indicates that no statistically significant between-group difference was observed within the current sample and should not be interpreted as evidence of complete clinical balance between the diet arms at baseline.

[‡]1-hour postprandial glucose and insulin were measured 60 minutes after glucose ingestion during the 1-hour OGTT.

[§]Triglyceride values were log-transformed for statistical analyses but are reported as Median (IQR) of the untransformed data.

* $p < 0.05$ indicates statistical significance.

Table 3. Changes in indices of insulin sensitivity, resistance, β -cell function, lipid profile, body weight and composition within the diet arms during Phase-2 (n=19)^{†‡§}

Indices	MC (n=11)				HC (n=8)			
	Baseline	End	Mean difference (95%CI)	p-value	Baseline	End	Mean difference (95%CI)	p-value
Fasting blood glucose (mg/dL)	85.5 $\pm$ 7.0	84.1 $\pm$ 6.3	-1.4 (-6.3, 3.4)	0.522	83.1 $\pm$ 7.5	85.4 $\pm$ 10.0	2.3 (-2.4, 6.9)	0.274
1-Hour OGTT blood glucose [¶]	112.2 $\pm$ 32.8	119.0 $\pm$ 27.3	6.8 (-10.8, 24.3)	0.410	111.6 $\pm$ 16.0	111.3 $\pm$ 19.1	-0.3 (-25.9, 25.3)	0.979
Fasting Insulin (μ IU/mL)	13.2 $\pm$ 6.1	11.7 $\pm$ 5.0	-1.5 (-6.1, -3.1)	0.482	11.6 $\pm$ 4.7	13.2 $\pm$ 9.4	1.5 (-5.5, 8.6)	0.601
1-Hour OGTT insulin [¶]	92.4 $\pm$ 43.8	92.6 $\pm$ 55.0	0.2 (-42.5, 42.8)	0.994	86.4 $\pm$ 41.2	104.3 $\pm$ 34.9	17.9 (-25.9, 61.6)	0.357
Matsuda Index	4.4 $\pm$ 2.8	4.7 $\pm$ 2	0.3 (-2, 2.6)	0.755	3.9 $\pm$ 1.2	4.3 $\pm$ 2.7	0.4 (-1.5, 2.2)	0.630
McAuley Index	4.4 $\pm$ 0.8	4.4 $\pm$ 1.1	0 (-0.7, 0.7)	0.937	4.3 $\pm$ 0.6	4.3 $\pm$ 1	0 (-0.5, 0.6)	0.896
QUICKI	0.34 $\pm$ 0.03	0.34 $\pm$ 0.03	0.006 (-0.02, 0.03)	0.573	0.34 $\pm$ 0.02	0.34 $\pm$ 0.03	0.001 (-0.02, 0.02)	0.912
BENNETTS	1.45 $\pm$ 0.4	1.54 $\pm$ 0.4	0.09 (-0.3, 0.4)	0.573	1.47 $\pm$ 0.3	1.53 $\pm$ 0.5	0.05 (-0.2, 0.3)	0.618
HOMA-IR	2.8 $\pm$ 1.3	2.4 $\pm$ 1	-0.4 (-1.4, 0.6)	0.414	2.4 $\pm$ 1.1	2.7 $\pm$ 1.8	0.3 (-1.0, 1.6)	0.567
HIRI	1133.5 $\pm$ 527	977 $\pm$ 402	-156.5 (-565.2, 252.3)	0.414	986.8 $\pm$ 430.1	1113.4 $\pm$ 729	126.7 (-405.5, 658.8)	0.567
Insulinogenic Index	0.9 $\pm$ 0.6	0.5 $\pm$ 0.4	-0.4 (-0.8, 0.0)	0.039	0.7 $\pm$ 0.3	0.7 $\pm$ 0.4	0 (-0.4, 0.3)	0.827
Disposition Index	2.2 $\pm$ 1.2	1.7 $\pm$ 0.2	-0.5 (-1.5, 0.3)	0.193	2.1 $\pm$ 0.8	1.9 $\pm$ 0.4	-0.2 (-0.9, 0.4)	0.432

Indices	Mean DiD (95% CI)	Standardized effect size (95% CI)	p-value
Fasting blood glucose (mg/dL)	-3.0 (-13.2, 7.1)	-0.40 (-1.73, 0.94)	0.547
1-Hour OGTT blood glucose [¶]	9.1 (-26.3, 44.4)	0.34 (-0.99, 1.68)	0.605
Fasting insulin (μ IU/mL)	-6.5 (-43.7, 30.7)	-0.51 (-1.88, 0.86)	0.450
1-Hour OGTT insulin [¶]	-11.0 (-73.6, 51.0)	-0.24 (-1.57, 1.10)	0.723
Matsuda Index	0.1 (-3.1, 3.2)	0.02 (-1.35, 1.39)	0.972
McAuley Index	-0.04 (-1.3, 1.2)	-0.04 (-1.41, 1.33)	0.949
QUICKI	0.01 (-0.03, 0.04)	0.22 (-1.15, 1.59)	0.748
BENNETTS	0.1 (-0.5, 0.6)	0.19 (-1.18, 1.56)	0.766
HOMA-IR	-0.7 (-2.5, 1.0)	-0.55 (-1.92, 0.82)	0.418
HIRI	-284.8 (-991.6, 421.9)	-0.55 (-1.92, 0.82)	0.418
Insulinogenic Index	-0.1 (-1.6, 1.4)	-0.13 (-1.51, 1.25)	0.848
Disposition Index	-0.2 (-1.7, 1.2)	-0.22 (-1.60, 1.16)	0.748

HOMAIR: Homeostatic Model Assessment of Insulin Resistance, QUICKI: Quantitative Insulin Sensitivity Check Index, BENNETTS: Bennett University, HIRI: Hepatic Insulin Resistance Index, TC: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, TG: Triglycerides, BMI: Body Mass Index, MC: Moderate Carbohydrate Diet (<40%), HC: High Carbohydrate Diet (>60%), DiD: Difference-in-Differences

WHtR-Waist Circumference to Height Ratio, BMI = Weight (kg)/Height (m²), Fat Mass Index = Fat Mass (kg)/Height (m²), Fat Free Mass Index = Fat Free Mass (kg)/Height (m²)

[†]Phase 2: weight maintenance phase.

[‡]Values are expressed as Median (IQR) and Mean $\pm$ SD elsewhere. p-values for comparisons within the MC and HC diet arms in phase 2 were obtained using a paired t-test.

[§]Difference from midline to endline is reported as percentage change. DiD is reported for MC when compared to HC diet arm. Mean DiD is reported from log-formed values. Standardized effect size is calculated using Hedges' g method.

[¶]Mean glucose and insulin represent the average concentrations measured over the 1-hour period during the oral glucose tolerance test (OGTT).

^{††}Triglyceride values were log-transformed for statistical analyses but are reported as Median (IQR) of the untransformed data.

Table 3. Changes in indices of insulin sensitivity, resistance, β -cell function, lipid profile, body weight and composition within the diet arms during Phase-2 (n=19)^{†‡§} (cont.)

Indices	MC (n=11)				HC (n=8)			
	Baseline	End	Mean difference (95%CI)	p-value	Baseline	End	Mean difference (95%CI)	p-value
TC (mg/dL)	157.8 $\pm$ 22.5	157.1 $\pm$ 26.9	-0.7 (-13.3, 11.9)	0.9	158 $\pm$ 21.8	164.3 $\pm$ 21.6	6.3 (-6.9, 19.5)	0.288
HDL-C (mg/dL)	42.2 $\pm$ 9	42.6 $\pm$ 8.7	0.4 (-3.8, 4.6)	0.839	38.1 $\pm$ 7.9	40.7 $\pm$ 10.7	2.6 (-1.9, 7.1)	0.211
LDL-C (mg/dL)	105.3 $\pm$ 22.4	102.5 $\pm$ 25.9	-2.9 (-14.7, 8.9)	0.6	105.1 $\pm$ 18.8	110.9 $\pm$ 15.9	5.8 (-0.3, 12)	0.058
TG (mg/dL) ^{††}	81.8 (66.3, 85.2)	99.8 (85.5, 116.2)	13 (3.7, 27.2)	0.107	108.7 (68.3, 113.7)	80.0 (76.7, 104.2)	-2.0 (-18.4, 28.6)	0.832
Weight (kg)	67.8 $\pm$ 8.7	68.2 $\pm$ 9.3	0.4 (-0.8, 1.6)	0.503	71.7 $\pm$ 10.6	72.2 $\pm$ 11.6	0.4 (-1.1, 2.0)	0.522
BMI (kg/m ²)	26.1 $\pm$ 1.6	26.2 $\pm$ 1.4	0.1 (-0.3, 0.6)	0.604	27.2 $\pm$ 2.1	27.3 $\pm$ 2.6	0.2 (-0.4, 0.7)	0.558
WHtR	0.50 $\pm$ 0.03	0.49 $\pm$ 0.03	-0.01 (-0.02, 0.002)	0.116	0.52 $\pm$ 0.05	0.51 $\pm$ 0.06	-0.002 (-0.02, 0.01)	0.758
%Fat Mass	39.0 $\pm$ 4.3	38.5 $\pm$ 5.4	-0.5 (-1.7, 0.7)	0.354	40.4 $\pm$ 5.8	40.9 $\pm$ 4.9	0.5 (-1.3, 2.3)	0.530
Fat Mass Index (kg/m ²)	10.0 $\pm$ 1.5	10.0 $\pm$ 1.6	-0.1 (-0.4, 0.3)	0.612	11.0 $\pm$ 2.2	11.2 $\pm$ 2.3	0.1 (-0.3, 0.5)	0.435
%Fat Free Mass	60.4 $\pm$ 4.3	61.0 $\pm$ 5.6	0.6 (-0.7, 1.9)	0.312	59.6 $\pm$ 5.8	59.1 $\pm$ 4.9	-0.5 (-2.3, 1.4)	0.532
Fat Free Mass Index (kg/m ²)	15.6 $\pm$ 1.1	15.8 $\pm$ 1.4	0.2 (-0.4, 0.8)	0.448	16.1 $\pm$ 1.5	16.0 $\pm$ 1.5	-0.2 (-1.1, 0.8)	0.695

Indices	Mean DiD (95% CI)	Standardized effect size (95% CI)	p-value
TC (mg/dL)	-1.6 (-34.8, 31.6)	-0.06 (-1.40, 1.27)	0.922
HDL-C (mg/dL)	-1.3 (-13.5, 11.0)	-0.14 (-1.47, 1.19)	0.833
LDL-C (mg/dL)	-5.8 (-35.7, 24.1)	-0.26 (-1.59, 1.08)	0.696
TG (mg/dL) ^{††}	0.2 (-0.3, 0.7)	0.50 (-0.84, 1.83)	0.453
Weight (kg)	-0.1 (-13.3, 13.2)	-0.01 (-1.31, 1.30)	0.993
BMI (kg/m ²)	-0.1 (-2.6, 2.5)	-0.02 (-1.33, 1.28)	0.971
WHtR	-0.004 (-0.06, 0.05)	-0.09 (-1.40, 1.22)	0.890
%Fat Mass	-0.4 (-7.6, 6.9)	-0.07 (-1.48, 1.34)	0.922
Fat Mass Index (kg/m ²)	-0.1 (-2.8, 2.7)	-0.02 (-1.44, 1.39)	0.973
%Fat Free Mass	0.5 (-7.1, 8.0)	0.09 (-1.36, 1.54)	0.898
Fat Free Mass Index (kg/m ²)	0.2 (-1.7, 2.1)	0.17 (-1.24, 1.58)	0.808

HOMAIR: Homeostatic Model Assessment of Insulin Resistance, QUICKI: Quantitative Insulin Sensitivity Check Index, BENNETTS: Bennett University, HIRI: Hepatic Insulin Resistance Index, TC: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, TG: Triglycerides, BMI: Body Mass Index, MC: Moderate Carbohydrate Diet (<40%), HC: High Carbohydrate Diet (>60%), DiD: Difference-in-Differences

WHtR-Waist Circumference to Height Ratio, BMI = Weight (kg)/Height (m²), Fat Mass Index = Fat Mass (kg)/Height (m²), Fat Free Mass Index = Fat Free Mass (kg)/Height (m²)

[†]Phase 2: weight maintenance phase.

[‡]Values are expressed as Median (IQR) and Mean $\pm$ SD elsewhere. p-values for comparisons within the MC and HC diet arms in phase 2 were obtained using a paired t-test.

[§]Difference from midline to endline is reported as percentage change. DiD is reported for MC when compared to HC diet arm. Mean DiD is reported from log-formed values. Standardized effect size is calculated using Hedges' g method.

^{*}Mean glucose and insulin represent the average concentrations measured over the 1-hour period during the oral glucose tolerance test (OGTT).

^{††}Triglyceride values were log-transformed for statistical analyses but are reported as Median (IQR) of the untransformed data.

Table 4. Changes in energy and macronutrient intake during the 3 months of weight loss followed by 3-months of weight maintenance[†]

Indices	Phase 1: Weight-loss phase [‡]			
	Whole group (n=19)			
	Baseline	End	Mean difference (95%CI)	p-value
Energy (kcal/day)	1684.9 ± 364	1213.3 ± 257.6	-471.57 (-303.3, -639.8)	<0.001*
Energy (kcal/kg/d)	23.1 ± 5.0	17.6 ± 3.6	-5.5 (-3.1, -7.8)	<0.001*
Protein (g/day)	56.2 ± 19.4	43.5 ± 11.9	-12.7 (-2.9, -22.5)	0.014*
Protein (g/kg/d)	0.7 ± 0.2	0.6 ± 0.2	-0.1 (-0.0, -0.3)	0.049*
Fat (g/day)	56.7 ± 13.8	47.0 ± 14.7	-9.7 (-2.4, -17.0)	0.012*
Carbohydrates (g/day)	238.8 ± 54.6	155.4 ± 26.7	-83.4 (-58.6, -108.3)	<0.001*

Indices	Phase 2: Weight maintenance phase [§]							
	MC (n=11)				HC (n=8)			
	Baseline	End	Mean difference (95%CI)	p-value	Baseline	End	Mean difference (95%CI)	p-value
Energy (kcal/day)	1153.6 ± 231.6	1232.7 ± 241.0	79.1 (-86.4, 244.7)	0.312	1295.5 ± 284.0	1362.6 ± 160.7	67.0 (-87.6, 221.7)	0.340
Energy (kcal/kg/d)	17.1 ± 3.1	18.2 ± 3.2	1.1 (-1.1, 3.4)	0.297	18.2 ± 4.3	19.0 ± 2.0	0.8 (-1.4, 3.0)	0.422
Protein (g/day)	40.9 ± 9.4	52.1 ± 13.9	11.3 (0.4, 22.2)	0.043*	47.2 ± 45.5	45.5 ± 11.2	-1.7 (-9.7, 6.3)	0.631
Protein (g/kg/d)	0.6 ± 0.2	0.8 ± 0.2	0.2 (0.0, 0.3)	0.049*	0.7 ± 0.2	0.6 ± 0.1	0.0 (-0.1, 0.1)	0.615
Fat (g/day)	43.8 ± 11.7	59.4 ± 18.7	15.6 (3.8, 27.4)	0.014*	51.3 ± 18.0	47.9 ± 8.4	3.5 (-14.5, 7.5)	0.481
Carbohydrates (g/day)	150.4 ± 27.8	123.5 ± 30.5	-26.9 (-54.7, 0.9)	0.057	162.3 ± 25.3	188.6 ± 20.1	26.3 (0.9, 51.7)	0.044*

d: day

Values are expressed as Mean ± SD; Difference from baseline to endline at each phase is reported as mean difference with 95% CI; p-values for comparisons were obtained using a paired t-test

[‡]Phase 1: weight-loss phase[§]Phase 2: weight maintenance phase

*p-value <0.05.

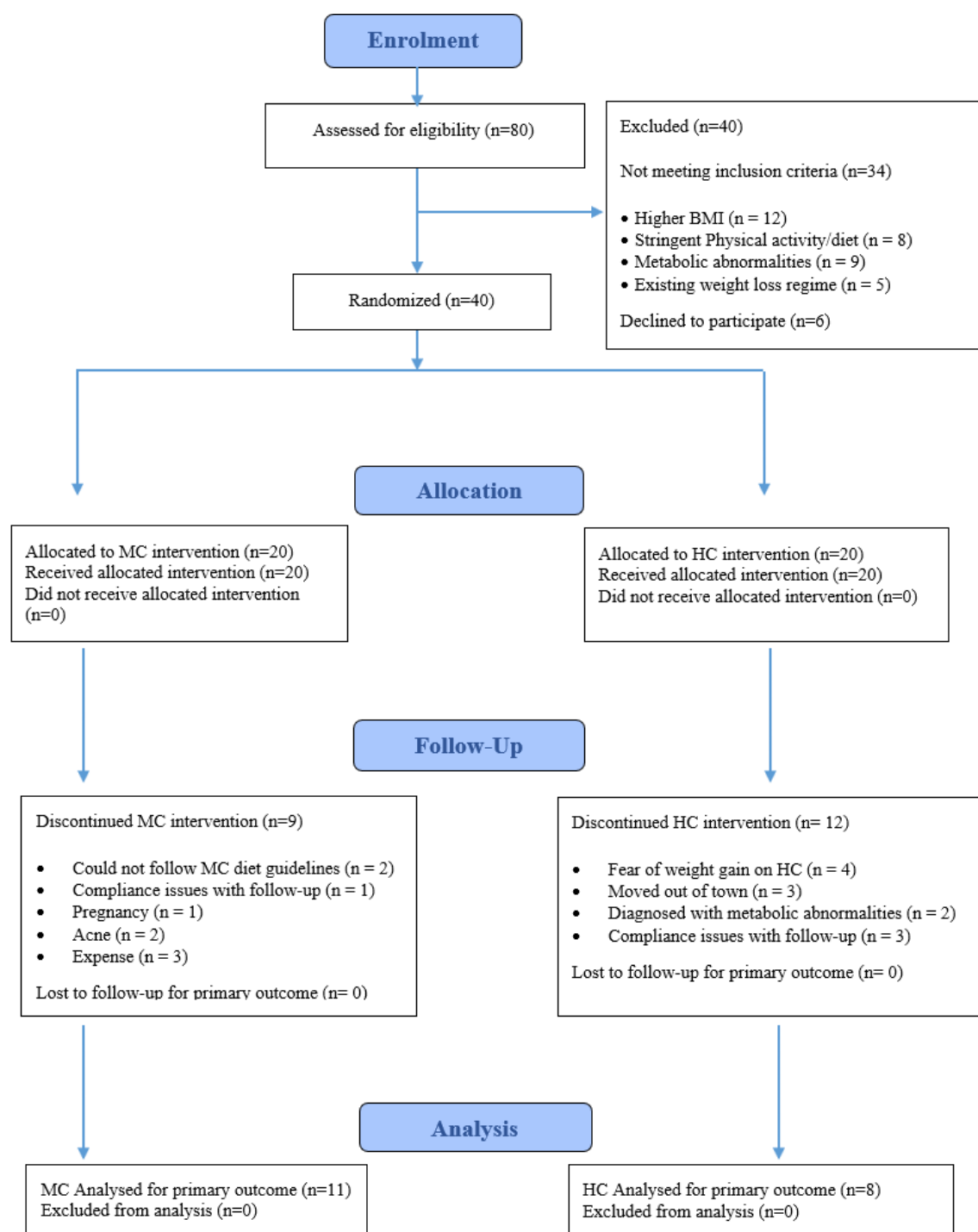


Figure 1. CONSORT flow diagram. MC: Moderate Carbohydrate Diet (<40%), HC: High Carbohydrate Diet (>60%), BMI: Body Mass Index

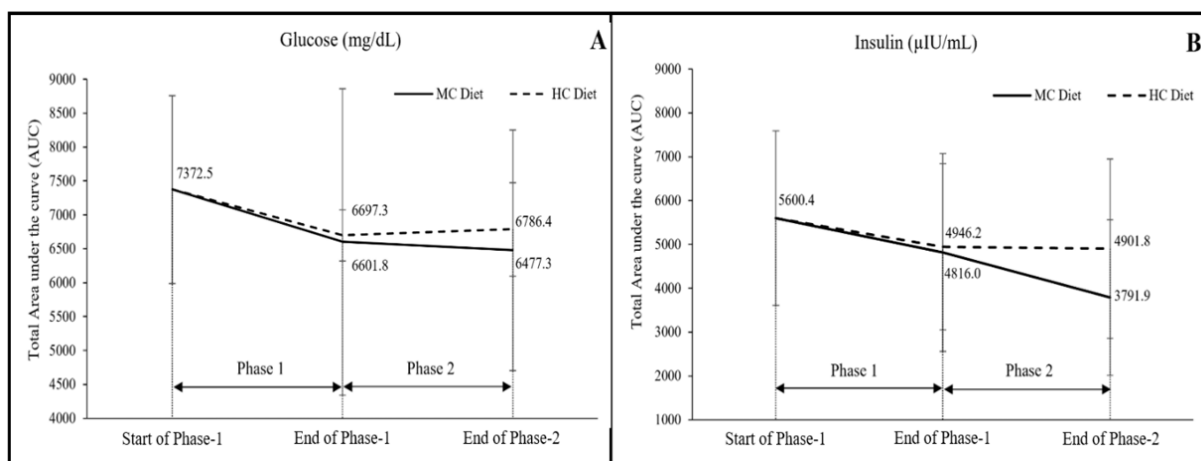
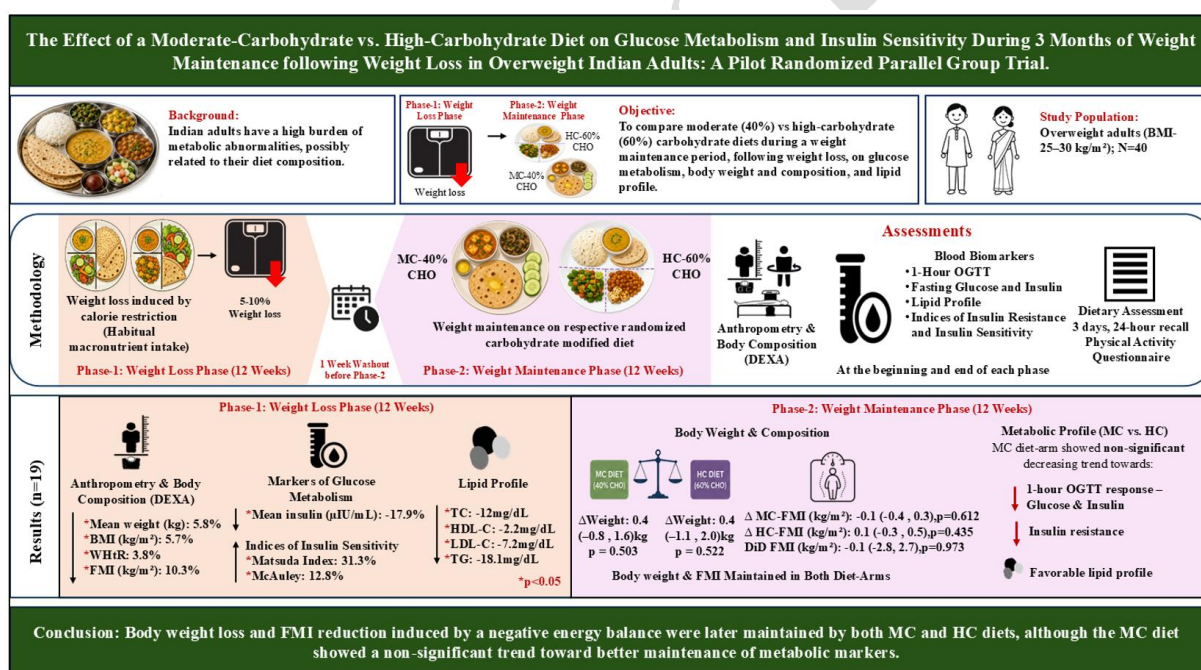


Figure 2. Mean total area under the curve of all participants for glucose and insulin across the phases (n=19). Panel A and Panel B represents the mean AUCt for glucose (mg/dL) insulin (µIU/mL) during the 1-hour OGTT at start of phase-1, end of Phase-1, and end of Phase-2, respectively. The solid line represents MC diet arm and the dashed lines (----) represent the HC diet arm. Error bars indicate standard deviation. Phase 1- weight loss phase, Phase 2 – weight maintenance phase. AUCt: Total area under the curve, OGTT: Oral Glucose Tolerance Test, MC: Moderate Carbohydrate Diet (<40%), HC: High Carbohydrate Diet (>60%).



Graphical abstract. Mean glucose and mean insulin represent the average glucose and insulin concentrations measured during the 1-hour OGTT. Values are expressed as percentage (%) change or mean difference (95% CI). Statistical significance was considered at $p < 0.05$.

BMI: body mass index; CHO: carbohydrate; MC: moderate-carbohydrate; HC: high-carbohydrate; OGTT: oral glucose tolerance test; DEXA: dual-energy X-ray absorptiometry; FMI: fat mass index; FFMI: fat-free mass index; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; DiD: difference-in-difference.