

## Adherence to a low-fat vs. low-carbohydrate diet differs by insulin resistance status

Previous research shows diminished weight loss success in insulin-resistant (IR) women assigned to a low-fat (LF) diet compared to those assigned to a low-carbohydrate (LC) diet. These secondary analyses examined the relationship between insulin-resistance status and dietary adherence to either a LF-diet or LC-diet among 81 free-living, overweight/obese women [age =  $41.9 \pm 5.7$  years; body mass index (BMI) =  $32.6 \pm 3.6$  kg/m<sup>2</sup>]. This study found differential adherence by insulin-resistance status only to a LF-diet, not a LC-diet. IR participants were less likely to adhere and lose weight on a LF-diet compared to insulin-sensitive (IS) participants assigned to the same diet. There were no significant differences between IR and IS participants assigned to LC-diet in relative adherence or weight loss. These results suggest that insulin resistance status may affect dietary adherence to weight loss diets, resulting in higher recidivism and diminished weight loss success of IR participants advised to follow LF-diets for weight loss.

**Keywords:** clinical trial, dietary intervention, insulin resistance, randomized trial

Date submitted 12 March 2012; date of first decision 28 April 2012; date of final acceptance 6 July 2012

### Introduction

Clinical trials comparing a spectrum of low to high carbohydrate diets show clinically meaningful weight loss on any reduced calorie diet regardless of macronutrient composition, provided there is adequate adherence to the dietary regimen [1]. These findings suggest that determinants of dietary adherence among individuals need to be further investigated in supporting successful weight loss.

The dominant framework to investigate the determinants of dietary adherence focuses on psychosocial characteristics [2]. Physiological mechanisms that may affect adherence to a specific diet remain underinvestigated. A person's ability to adhere and lose weight on a diet might be influenced by the way in which a diet affects hunger and metabolism [3].

Research illustrates that insulin dynamics, such as insulin-resistance and high insulin secretion, result in diminished weight loss success in women assigned to a low-fat (LF) diet compared to those assigned to a low-carbohydrate (LC) diet [4]. These studies suggest that insulin dynamics might be a physiological mechanism that influences dietary adherence.

To date, no study has investigated whether insulin-resistance status differentially affects dietary adherence to the prescribed macronutrient composition of a diet. This study determines if adherence to a LF-diet vs. LC-diet differs between insulin-resistant (IR) and insulin-sensitive (IS) participants.

### Research Design And Methods

Data for this secondary analysis come from a 1-year randomized clinical trial (the A to Z study [5]), which compared the effectiveness of four diets, representing a spectrum of low to high carbohydrate intake on weight loss. Generally healthy, non-diabetic women ages 25–50 years with a body mass index (BMI) of 27–40 kg/m<sup>2</sup> were recruited. Because these analyses examine the association of insulin-resistance status with adherence to either a LF-diet or LC-diet, only participants assigned to the lowest fat (Ornish: dietary goal  $\leq 10\%$  of energy from fat/day) and the lowest carbohydrate (Atkins: diet goal  $\leq 50$  g carbohydrate/day) diets are included in the analyses.

Blood samples were collected after a minimum 10-hr fast. Total plasma insulin in serum was measured by radioimmunoassay. The entire study population ( $n = 311$ ) was divided into tertiles based on baseline fasting insulin levels ( $< 6.9$ ,  $6.9$ – $10.6$ , and  $> 10.6$   $\mu\text{IU/ml}$ ), which is considered a useful surrogate for assessing relative insulin-resistance vs. sensitivity [6]. The most IR ( $> 10.6$   $\mu\text{IU/ml}$ ) and the most IS-participants ( $< 6.9$   $\mu\text{IU/ml}$ ) – hereafter referred to simply as 'IR' and 'IS' – were included in the final analysis. Individuals with intermediate levels of fasting insulin were excluded to minimize the misclassification involved in dichotomizing the study population [7].

Body weight and height were measured at baseline and 12 months using a calibrated scale and a standard wall-mounted stadiometer. BMI (kg/m<sup>2</sup>) was calculated. Dietary intake at baseline and 12 months were obtained via telephone-administered, 3-day, unannounced, 24-h dietary recalls using Nutrition Data System for Research (v.4.05.33, 4.06.34 and 5.0.35). Dietary adherence was defined as relative adherence to

Correspondence to: Arianna D. McClain, PhD, Stanford Prevention Research Center, Stanford University School of Medicine, 1070 Arastradero Road, Suite 300, Palo Alto, California 94304, USA.  
E-mail: mcclaina@stanford.edu

**Table 1.** Participant characteristics

	Low-fat diet		Low-carbohydrate diet		p-Value
	IR (N = 22)	IS (N = 17)	IR (N = 20)	IS (N = 22)	
Baseline					
Demographics					
Age (years)	40.7 (6.1)	43.0 (5.0)	41.4 (7.2)	42.8 (4.3)	0.51
Education (years)	15.9 (2.5)	16.4 (1.7)	15.8 (2.1)	15.6 (1.8)	0.71
Race/ethnicity, no. (%)					0.38
White	14 (63.6)	15 (88.2)	16 (80)	17 (77.3)	
Black	2 (9.1)	1 (5.9)	0 (0)	2 (9.1)	
Asian/Pacific Islander	3 (13.6)	1 (5.9)	2 (10)	1 (4.6)	
American Indian	2 (9.1)	0 (0)	2 (10)	1 (4.6)	
Other	1 (4.6)	0 (0)	0 (0)	1 (4.6)	
Anthropometrics					
Weight, kg	91.4 (12.1) <sup>a</sup>	84.7 (7.6) <sup>a,b</sup>	92.9 (12.1) <sup>a</sup>	81.9 (12.2) <sup>b</sup>	<0.01
Body mass index, kg/m <sup>2</sup>	34.2 (3.5) <sup>a</sup>	30.8 (2.1) <sup>b</sup>	34.8 (3.0) <sup>a</sup>	30.5 (3.3) <sup>b</sup>	<0.0001
Body fat, %	42.2 (7.0)	39.8 (5.8)	42.0 (5.0)	38.7 (6.9)	0.20
Fasting insulin, µIU/ml	14.5 (4.3) <sup>a</sup>	5.13 (1.0) <sup>b</sup>	17.6 (7.4) <sup>a</sup>	4.9 (1.2) <sup>b</sup>	<0.0001
Dietary intake					
Total energy	1863 (431)	1799 (490)	2043 (580)	1843 (440)	0.42
Carbohydrate (% energy)	49 (8)	49 (5)	47 (11)	43 (13)	0.17
Fat (% energy)	34 (6)	39 (6)	36 (8)	37 (10)	0.58
Protein (% energy)	16 (3)	16 (3)	16 (4)	17 (5)	0.59
12-Month change					
Anthropometrics					
Weight, kg	-2.2 (4.6) <sup>a</sup>	-4.3 (3.7) <sup>a,b</sup>	-6.2 (5.4) <sup>a,b</sup>	-4.9 (4.5) <sup>b</sup>	0.04
Body mass index, kg/m <sup>2</sup>	-0.7 (1.6) <sup>a</sup>	-1.5 (1.3) <sup>a,b</sup>	-2.2 (1.7) <sup>a,b</sup>	-1.8 (1.7) <sup>b</sup>	0.02
Body fat, %	-1.0 (4.7)	-2.7 (4.2)	-2.3 (4.5)	-3.2 (3.8)	0.43
Fasting insulin, µIU/ml	-0.2 (5.0) <sup>a</sup>	-0.3 (2.5) <sup>a</sup>	-5.8 (5.4) <sup>b</sup>	0.1 (2.2) <sup>a</sup>	<0.0001
Dietary intake					
Total energy	-338 (395)	-388 (446)	-324 (645)	-275 (508)	0.92
Carbohydrate (% energy)	1.7 (10.6) <sup>a</sup>	10.4 (9.3) <sup>b</sup>	-12.1 (14.5) <sup>c</sup>	-11.7 (14.7) <sup>c</sup>	<0.0001
Fat (% energy)	-2.7 (9.2) <sup>a</sup>	-11.5 (10.0) <sup>b</sup>	8.9 (11.5) <sup>c</sup>	8.4 (14.0) <sup>c</sup>	<0.0001
Protein (% energy)	3.0 (4.3)	1.8 (2.7)	3.6 (5.5)	4.8 (6.2)	0.28

Analysis of variance was used to compare baseline, mean weight and BMI change from baseline to 12 months across groups; IR, insulin resistant; IS, insulin sensitive; data are presented as mean (SD) unless otherwise noted; data with different superscripts are significantly different.

assigned diet over 12 months, focussing on change in per cent of total energy from fat and carbohydrates relative to baseline.

### Statistical Analysis

A two-way analysis of variance compared baseline demographics, body composition, dietary variables and mean weight change from baseline to 12 months across groups. Analysis of covariance using general linear modelling was conducted for dietary adherence, controlling for diet group and insulin-resistance status. An insulin-resistance status × diet group interaction was also included to assess whether macronutrient intake and insulin-resistance status differed by diet group. Subsequently, *post hoc* Fisher's least significant difference tests examined pairwise comparisons of adherence by insulin-resistance status within each diet group. Data were analysed with SAS (v.9.2) statistical software package (SAS, Cary, NC, USA) and type I error was set at  $\alpha < 0.05$ .

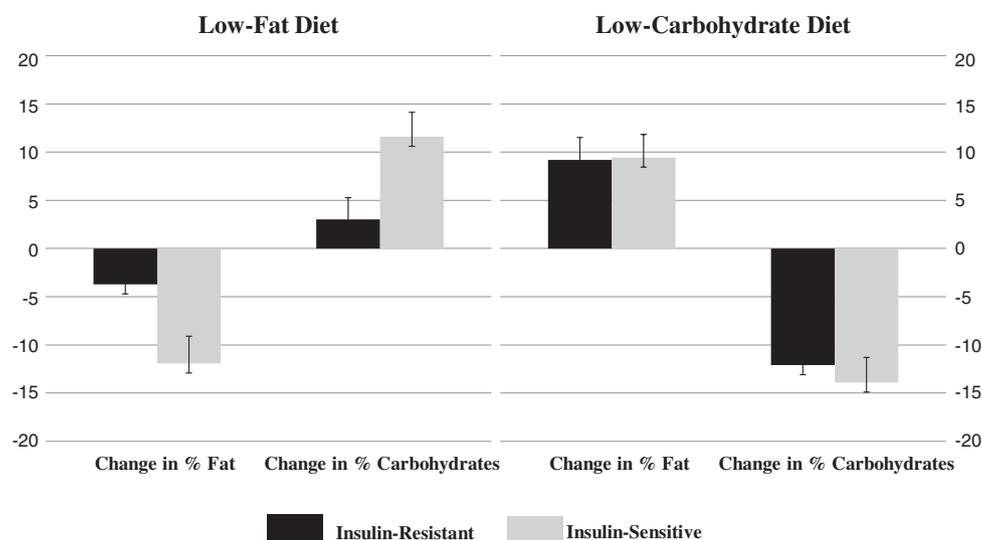
### Results

Table 1 illustrates that at baseline, IR-participants had significantly greater weight, BMI and fasting insulin levels compared to IS-participants. There were no significant differences across groups in energy or macronutrient intake.

At 12 months, weight, BMI and body fat percentage decreased across all groups. IR-women assigned to the LF-diet lost less weight compared to the other groups. The insulin-resistance status × diet group interaction illustrated significant differences in fat and carbohydrate intake by insulin-resistance status in the LF-diet vs. LC-diet group ( $F = 2.94$ ,  $p = 0.08$ ;  $F = 3.99$ ,  $p = 0.049$ , respectively). Among participants assigned to the LF-diet, IR-participants made smaller 12-month changes in fat and carbohydrate intake compared to IS-participants. By 12 months, IR-participants' fat and carbohydrate intake were not significantly different from baseline ( $p = 0.11$ ;  $p = 0.24$ , respectively). Among participants assigned to the LC-diet, there were no significant differences in fat and carbohydrate intake between IR and IS participants ( $p = 0.94$ ;  $p = 0.64$ , respectively) (Figure 1). IR-women assigned to LC-diet significantly improved insulin levels compared to other groups. Changes in insulin were associated with degree of weight loss ( $r = 0.44$ ,  $p < 0.0001$ ).

### Conclusion

These secondary analyses examined the relationship between insulin-resistance and dietary adherence to either a LF-diet or LC-diet and found differential adherence by insulin-resistance



**Figure 1.** Twelve-month change in diet by insulin resistance status in diet groups.

status only to a LF-diet, not a LC-diet. IR-participants were less likely to adhere and lose weight on a LF-diet compared to IS-participants assigned to the same diet. There were no significant differences between IR and IS participants assigned to LC-diet in relative adherence or weight loss.

Dietary adherence to any macronutrient diet is a strong predictor of weight loss success [1]. This analysis suggests that variability in individual weight change observed across dietary weight-loss trials [8,9] might be partially attributable to physiological mechanisms, such as insulin-resistance. Insulin-resistance may predispose individuals to be less successful in adhering to a LF/higher carbohydrate diet resulting in higher rates of recidivism and decreased weight loss success.

The mechanisms responsible for the diminished weight loss success of IR-individuals assigned to LF-diets remain relatively unexplored. LF-diets have been criticized for their potential to substitute fat with unhealthy carbohydrates, such as simple sugars, which might spike insulin levels, resulting in increased hunger [10]. Research also shows that after consuming a LF/high-carbohydrate meal, a rapid absorption of glucose induces a sequence of hormonal and metabolic changes that increases hunger and energy intake in obese subjects [11]. One study showed that women with diabetes (a metabolic disorder characterized by high blood glucose in the context of IR and insulin deficiency) experienced adverse glycaemic effects when assigned to a LF-diet [12]. These studies suggest that IR-participants may feel less satiated and might experience stronger metabolically driven urges after consuming a LF/higher carbohydrate meal compared to IS-participants, which may explain why this population may be less likely to adhere to the assigned diet over time. Future research is needed to fully understand these physiological mechanisms and the effect of macronutrient composition of diets on other metabolic outcomes.

The baseline finding that IR-participants had greater BMIs and weight is consistent with research showing BMI, weight and insulin-resistance are related. Previous studies report

improvements in insulin levels are associated with degree of weight loss [7], consistent with our finding of significant improvements in insulin levels only among IR-participants, who were more likely to lose weight when assigned to a LC-diet.

Overall, these findings suggest dietary recommendations that advise people to follow a LF/high-carbohydrate diet for weight loss may actually undermine the success of IR-individuals. Further investigation is needed to determine if caution should be exercised in recommending a LF-diet for IR adults. It is possible that the growing population of IR adults might be more successful adhering, losing weight and improving insulin levels when prescribed a LC-diet. Future studies are needed to investigate the potential factors, such as insulin-resistance, that impact dietary adherence and recidivism in order to develop more individually tailored interventions for effective behavioural change.

**A. D. McClain<sup>1</sup>, J. J. Otten<sup>1</sup>, E. B. Hekler<sup>2</sup> & C. D. Gardner<sup>1</sup>**

<sup>1</sup>Stanford Prevention Research Center, Stanford University School of Medicine, Palo Alto, CA, USA

<sup>2</sup>School of Nutrition and Health Promotion, Arizona State University, Phoenix, AZ, USA

## Conflict of Interest

This work was supported by NIH grant R21 AT001098, and by Human Health Service grant M01-RR00070, General Clinical Research Centers, National Center for Research Resources and National Institutes of Health. Dr A. D. M. was supported by Public Health Service Training Grant 5 T32 HL 007034 from the National Heart, Lung, and Blood Institute.

Dr C. D. G. received a pilot grant from the R. C. Atkins Foundation in 2007 after the conclusion of the A to Z weight loss study. None of the other authors had a personal or financial conflict of interest.

## References

1. Alhassan S, Kim S, Bersamin A, King AC, Gardner CD. Dietary adherence and weight loss success among overweight women: results from the A to Z weight loss study. *Int J Obes (Lond)* 2008; **32**: 985–991.
2. Webber KH, Tate DF, Ward DS, Bowling JM. Motivation and its relationship to adherence to self-monitoring and weight loss in a 16-week Internet behavioral weight loss intervention. *J Nutr Educ Behav* 2010; **42**: 161–167.
3. Ludwig DS, Ebbeling CB. Weight-loss maintenance--mind over matter? *N Engl J Med* 2010; **363**: 2159–2161.
4. Pittas AG, Roberts SB. Dietary composition and weight loss: can we individualize dietary prescriptions according to insulin sensitivity or secretion status? *Nutr Rev* 2006; **64**: 435–448.
5. Gardner CD, Kiazand A, Alhassan S et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A to Z Weight Loss Study: a randomized trial. *JAMA* 2007; **297**: 969–977.
6. McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. *Ann Intern Med* 2003; **139**: 802–809.
7. Cornier MA, Donahoo WT, Pereira R et al. Insulin sensitivity determines the effectiveness of dietary macronutrient composition on weight loss in obese women. *Obes Res* 2005; **13**: 703–709.
8. Greenberg I, Stampfer MJ, Schwarzfuchs D, Shai I. Adherence and success in long-term weight loss diets: the dietary intervention randomized controlled trial (DIRECT). *J Am Coll Nutr* 2009; **28**: 159–168.
9. Sacks FM, Bray GA, Carey VJ et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *N Engl J Med* 2009; **360**: 859–873.
10. Rodin J. Insulin levels, hunger, and food intake: an example of feedback loops in body weight regulation. *Health Psychol* 1985; **4**: 1–24.
11. Ludwig DS, Majzoub JA, Al-Zahrani A, Dallal GE, Blanco I, Roberts SB. High glycemic index foods, overeating, and obesity. *Pediatrics* 1999; **103**: E26.
12. Shikany JM, Margolis KL, Pettinger M et al. Effects of a low-fat dietary intervention on glucose, insulin, and insulin resistance in the Women's Health Initiative (WHI) Dietary Modification trial. *Am J Clin Nutr* 2011; **94**: 75–85.