

Protein Ingestion as a Dietary Strategy for Managing Caloric Intake in Healthy

Adults

by

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A Dissertation Presented in Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy

Approved November 2012 by the
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December 2012

ABSTRACT

It is widely recognized that dietary protein induces greater satiety compared to carbohydrate and fat. Two separate trials were conducted to assess the use of protein as a dietary approach to manage energy intake (EI). The first, crossover trial, examined 24-hour EI after consuming a high protein bar (HP) vs. a high carbohydrate (HC) bar upon awakening on two separate days and a control, no bar day. Of the 54 participants who entered the trial, 37 subjects completed the study in its entirety. Results showed there was no significant difference in mean EI between the intervention days when the bars were consumed and the control day. The subjects consumed 1752 ± 99 kcal on the control day, and 1846 ± 75 and 1891 ± 110 kcal on the days the HP and HC bars were consumed, respectively ($P=0.591$). However, compared to the control day, snack bar ingestion was significantly related to an increase in EI for the subjects who self-reported high weekly physical activity levels ($n=11$) (+22%; $P=0.038$ and +45%; $P=0.030$, HP and HC bars, respectively). These data suggest that individuals who have moderate to low physical activity levels compensate for the ingestion of energy bars (regardless of protein content) over a 24-hour period. The second parallel-arm, pilot trial examined the effect of 6 g daily gelatin ingestion vs. control on EI and weight change in healthy, overweight and obese women who initiated a walking program. Of the 37 women who entered the trial, 28 completed the six week trial. The results showed activity level (steps/d) increased in both groups (+ 22%, $P=0.022$). There was a significant group difference in mean EI at week 6 vs. baseline (-174 ± 612 kcal/d and $+197 \pm 320$ kcal/d, $P=0.001$; gelatin and control groups, respectively). However, there was no significant between group difference for changes in

weight, percent body fat and waist circumference. Those subjects having baseline Disinhibition scores of ≥ 12 gained significantly more weight throughout the study vs. those scoring < 12 ($P=0.004$). These results indicate that daily gelatin ingestion may be a practical strategy for controlling EI among overweight and obese women initiating an exercise program.

DEDICATION

I dedicate this work to my family and friends who stuck by me, through thick and thin, with their utmost support during this process.

ACKNOWLEDGMENTS

I would like to express my ardent appreciation to my committee chairperson and nutritional guru, Dr. Carol Johnston, for her innovation, leadership, assistance, and above all for her enthusiasm and support throughout my doctoral tenure.

In addition, I would like to extend my sincere gratitude to my committee members for their participation; Dr. Pamela Swan, for her thoughtful insights regarding the topic of obesity; Dr. Glenn Gaesser, also for his understanding of the obesity conundrum; Dr. Sandra Mayol-Kreisor, for her enthusiasm and for teaching me how to be a teacher; and finally to Dr. Christy Appel, for being a great role model as a student and for showing me what I can aspire to be.

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Chapter 1

SUMMARY OF RESEARCH

Worldwide, overweight and obesity rates have drastically increased over the past few decades. In the United States, this upsurge has coincided with a number of factors including food that is widely available, and typically large portion sizes. Currently, enticing, low-priced, salty, high-fat, and extensively processed food is seemingly obtainable everywhere. For instance, greasy snacks and sugary beverages are abundantly available at gas stations, and vending machines located at work and in schools offer a multitude of low nutritional quality food and drink items. It is noteworthy that increased calorie consumption and not decreased energy expenditure (EI) is largely accepted as the culprit for the current, elevated obesity rates.

The review of literature in this document (Chapter 4) examines the physiological reasons individuals have difficulty losing weight and sustaining weight loss. For example, orexigenic human brain neurotransmitters, which promote food consumption and decreased energy expenditure, are unregulated during times of decreased food intake. In addition, the increased level of stress that our culture now experiences promotes elevated cortisol levels, which in turn, produces an increased desire for high fat, sugary foods and visceral fat deposition. Thus, it is desirable to find simple strategies individuals could use to help decrease hunger and the craving to eat.

Of the three macronutrients, protein is known to be the most satiating. The first study in this dissertation, found in Chapter 2, was done to determine if consuming high protein nutrition bars would produce a decrease in 24-hour calorie consumption compared to a high carbohydrate bar or a control day.

Although there was no difference in daily calorie intake between the two bars, consumption of neither bar resulted in an increase in 24-hour calorie consumption, except in those who self-reported high, weekly activity levels.

The trial reported in Chapter 3 was done to determine if gelatin, an incomplete protein, would help overweight/obese women lose weight when undertaking a walking program. This is important because many women who start exercising actually gain weight even though weight loss is the desired goal. This six-week, parallel-arm trial showed that those women who ingested gelatin on a daily basis while initiating a walking program had a mean decrease in energy intake vs. the control group, although neither group experienced a mean weight change over that time period. Therefore, this trial gives evidence that daily consumption of gelatin may indeed be a simple weight loss strategy for overweight and obese women who begin an exercise regimen.

Finally, weight loss attained through calorie restriction and exercise often results in high recidivism rates. In addition, weight cycling can have detrimental health consequences. Thus, it is important to note that being aerobically fit and leading a healthy lifestyle at any size may have an even more important role vs. body weight per se when considering health indices.

Chapter 2

INGESTION OF NUTRITION BARS HIGH IN PROTEIN OR CARBOHYDRATE DO NOT IMPACT 24-H ENERGY INTAKES IN HEALTHY YOUNG ADULTS

Sales of nutrition bars, both as snacks and as meal replacements, jumped from \$200 million in 1997 to nearly \$1.7 billion in 2010 (Rigik, 2011). Although initially marketed to serious athletes, a wide range of consumers now purchase nutrition bars regularly not only to satisfy immediate hunger but also because they are perceived as a source of nutrients or as a healthy mini-meal (Wyatt, 2010). Concern that consumption of nutrition bars may lead to unhealthy dietary patterns and contribute to obesity risk has been raised (Kalergis, 2009), but few studies have addressed this issue.

Chow et al. (2007) demonstrated that consumption of cereal bars high in viscous fibers was associated with greater ratings of fullness for up to 3 hours as compared to cereal bars low in viscous fiber. Others have shown that the mid-morning ingestion of nutrition bars high in protein and fiber, as compared to nutrition bars high in fat and refined carbohydrate, significantly reduced energy intake at the lunch meal (Williams, Noakes, Keogh, Foster, & Clifton, 2006). Several trials have observed reduced postprandial glycemic responses following the ingestion of nutrition bars high in protein versus nutrition bars high in carbohydrate (Williams et al., 2006; Hertzler & Kim, 2003; Miller, Gabbay, Dillon, Apgar, & Miller, 2006).

Although the macronutrient composition of snack bars appears to impact satiety and energy intakes in the short-term, it is not known whether these changes extend over a 24-h period and influence daily energy intakes. The objective of this crossover trial was to assess 24-h energy intakes in free-living

college students ingesting nutrition bars high in protein or high in carbohydrates for the breakfast meal.

METHODS

Volunteers were recruited from a campus population using classroom announcements. Fifty-four healthy college students expressed interest in the study and met the inclusion criteria (not pregnant or lactating, not currently dieting, and not taking prescription medications). Written informed consent was obtained from participants, and the study was approved by the Arizona State University Institutional Review Board.

Participants completed a short health history questionnaire that included questions on medication use, dieting history, current health status, body weight, and height. Leisure-time physical activity was estimated for the past week using a validated screener that captured vigorous, moderate, and mild exercise (Godin & Shephard, 1985). Total physical activity was calculated by multiplying the number of exercise and walking episodes by the intensity index expressed in metabolic equivalent (MET) values (9, 5, and 3 METS for vigorous, moderate, and mild exercise respectively). [1 MET corresponds to an energy expenditure of $1 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$.]

In the first week of the trial, participants completed a baseline 24-hour dietary recall during a weekday without intervention using the automated, self-administered 24-h dietary recall (ASA24) system, an interactive website developed by the National Cancer Institute. The ASA24 is a modified version of the interviewer-administered Automated Multiple Pass Method 24-hour recall developed by the U.S. Department of Agriculture and employs multi-level food

probes to estimate food types and amounts (Zimmerman et al., 2009). All participants received basic verbal training on how to use the website.

One-week-to-the-day after entering the baseline dietary data, participants were randomly assigned to consume one of two test foods: a high-protein (HP) bar (280 kcal, 30 grams (g), protein, 7 g fat, and 1 fiber; Premier protein bar, Premier Nutrition® Inc. Carlsbad, CA USA) or two high-carbohydrate (HC) bars (260 kcal, 4 g protein, 6 g fat, and 4 g fiber; Nutri-Grain® cereal bars, Kellogg's, Battle Creek, MI USA). The HP bars consisted of a blend of protein from soy protein isolate, whey protein concentrate, whey protein hydrolysate with additional protein from hydrolyzed gelatin. The two main ingredients of the HC bars were whole grain oats and enriched flour.

The bar(s) were consumed within one hour of waking. The participants were instructed not to consume any other calorie-containing food or beverage at that time, and to refrain from eating or drinking calorie-containing foods or beverages for one hour after consumption of the bar(s). For the remainder of the day, subjects were instructed to follow their normal eating regimen. One week later, the alternate bar was consumed following the same instructions. On the days the bars were consumed, participants completed a 24-hour dietary recall using ASA24 as described above.

Statistical analyses. Data are reported as mean \pm SE, and statistical analysis was completed using Statistical Package for the Social Sciences (SPSS V19, IBM Corporation, Somers, NY) with significance set at $P\leq 0.05$. Data were assessed for normality, and univariate and repeated measures ANOVA were conducted to compare daily calorie intake on the control day and the days when the bar(s) were consumed. Utilizing a standard deviation for the change in 24-h

energy intakes for subjects from a recent pilot trial in a similar population sample (580 kcal), 45 participants were required to detect a treatment difference of 250 kcal with an 80% probability in this crossover trial.

RESULTS

Of the 54 randomized participants, 39 completed the study in its entirety (7 males; 32 females). Reasons cited for not completing the study included dislike of the intervention foods and difficulty using the ASA24 program. Gender, body weight, and BMI did not differ significantly between the completers and non-completers; however, the non-completers were younger than the completers, 21.8 ± 0.7 versus 25.6 ± 1.0 y [$F(1,52)=4.9$, $P = 0.004$]. Two of the completers reported high 24-h energy intakes (>3 SD above the mean; 1 male, 1 female), and these individuals were removed from all subsequent data analyses. For the 37 participants entered into the analyses, age ranged from 19 to 49 y (25.7 ± 1.1 y) and weight ranged from 46.4 to 106.8 kg (85.0 ± 7.3 and 62.7 ± 2.3 kg for the men and women respectively); and although none of the participants were classified as obese ($\text{BMI} \geq 30.0 \text{ kg/m}^2$), 34% of the sample was overweight ($\text{BMI} > 24.9 - < 29.9 \text{ kg/m}^2$). Two of the participants (6% of the sample) indicated that they currently smoked cigarettes.

Daily energy intakes assessed on the same weekday during the 3-wk study did not differ significantly; mean 24-h energy intakes ranged from 1752 ± 99 kcal for the non-intervention day to 1846 ± 75 and 1891 ± 110 kcal for the days the HP and HC bars were consumed respectively [$F(2,35)=0.5$, $P = 0.591$] (Figure 1A). Age and BMI were not significantly related to 24-h energy intakes on the days the nutrition bars were consumed. Although not statistically different, overweight participants ($n = 13$) consumed an additional 370 ± 117 to 447 ± 204

kcal on the days the HP and HC bars were consumed relative to the control day whereas normal weight participants consumed -16 ± 149 kcal and $+4\pm 177$ kcal under the same circumstances, respectively [$F(2,33)=1.7$, $P = 0.194$].

Physical activity levels were correlated with energy intakes on the days the nutrition bars were consumed. To examine this relationship further, MET tertiles were used to divide the sample into two groups: high physical activity

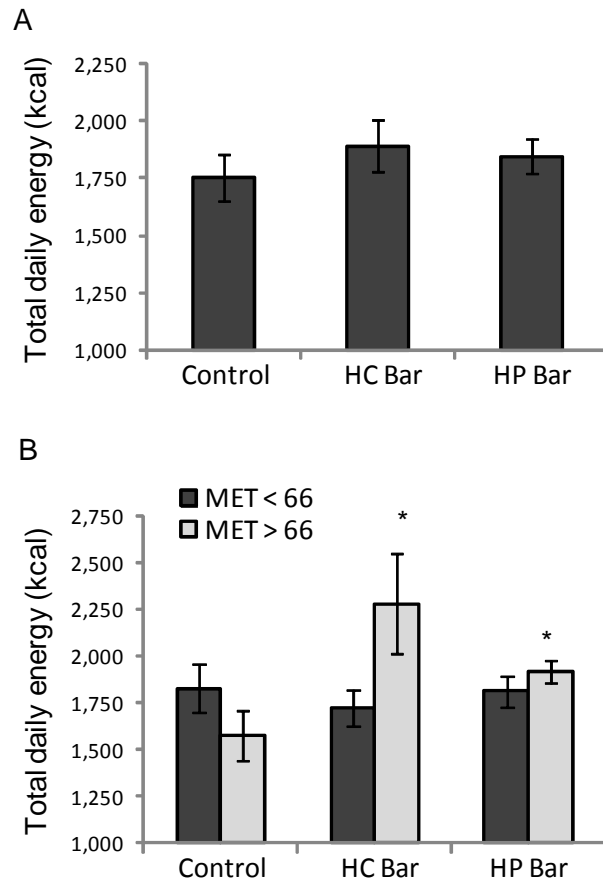


Figure 1. Study participant's 24-hour energy intakes. ($P = 0.591$, repeated measures ANOVA) [A]. For participants who were more physically active (MET >66; $n = 11$), daily energy intakes increased significantly compared to the control day for the HC bar day (+45%; $P = 0.030$) and for the HP bar day (+22%; $P = 0.038$) [B].

(top MET tertile; MET scores >66) and moderate-to-low physical activity (bottom two tertiles; MET scores <66). In the individuals who were more physically active ($n = 11$), daily energy intakes increased significantly compared to the control day

for the HC bar day (+45% or +709±281 kcal) [F(1,10)=6.4, P = 0.030] and for the HP bar day (+22% or 346±145 kcal) [F(1,10)=5.7, P = 0.038] (Fig. 1B). Daily energy intakes did not differ across the test days for those with low to moderate physical activity (-103±130 kcal and -13±139 kcal for the HC and HP bar days respectively) (Fig. 1B).

Carbohydrate intakes (g/d or %energy) were significantly increased in participants for the day the HC bar was ingested (Table 1). Similarly, protein intakes (g/d or %energy) increased in participants for the day the HP bar was ingested (Table1). Fiber (g) and iron (mg) intakes did not differ between treatment days; however, calcium (mg) intakes were significantly increased (+35) for the day the HC bar was consumed compared to the control day (Table1)

Table 1.
Energy and nutrient intake comparisons for each treatment
(CON,control; HC, high carbohydrate bar; HP, high protein bar)¹

	CON	HC	HP	F	P value
Energy, kcal/d	1752±99	1891±110	1846±75	(2,35)=0.5	0.591
Protein, g/d	69±5 ^a	73±6 ^a	93±5 ^b	(2,35)=9.2	0.001
Protein, %energy	15.9±1.0 ^a	15.0±0.8 ^a	20.5±0.8 ^b	(2,35)=21.1	<0.001
Fat, g/d	63±5	67±6	68±5	(2,35)=0.3	0.759
Fat, %energy	32.4±1.4	30.9±1.2	32.5±1.3	(2,35)=0.9	0.406
Carbohydrate, g/d	232±16 ^{ab}	256±14 ^a	217±13 ^b	(2,35)=3.2	0.051
Carbohydrate, %energy	53.1±1.9 ^a	55.1±1.4 ^a	46.9±1.7 ^b	(2,35)=11.8	<0.001
Fiber, g/d	21±2	21±2	20±3	(2,35)=0.1	0.942
Calcium, mg/d	864±76 ^a	1166±75 ^b	896±82 ^a	(2,35)=7.9	0.001
Iron, mg/d	14±1	15±1	16±1	(2,35)=0.6	0.531

¹n = 37; P value for repeated measures ANOVA; values with different superscripts differ significantly.

DISCUSSION

Although nutrition bar ingestion has been demonstrated to raise satiety and reduce food intake in the short term (0-4 h post-meal) (Chow et al., 2007;

Williams et al., 2006), the data reported herein suggest that energy intakes across 24 hours are not reduced when nutrition bars, either HP or HC, are added to the diet. Overall, participants adjusted caloric intakes following the ingestion of energy-dense nutrition bars such that 24-h energy intakes did not differ between the control, HP, or HC treatments. These results imply that the reported reductions in hunger and energy intakes in the immediate hours following ingestion of satiating snacks may be cancelled by food intake later in the day and that 24-h surveillance may be necessary to determine the impact of food intake on satiation. Indeed, McKiernan, Hollis, & Mattes (2008) concluded that single meal feeding trials may not be appropriate for assessing compensatory responses since the adults in their trials regulated energy intake over a 24-h period more precisely than at individual eating occasions.

BMI was not related to the change in energy intakes noted on the days the HP or HC treatments were consumed; however, overweight participants (BMI >24.9 – <29.9 kg/m²) did not compensate for the energy in the nutrition bars as accurately as the lean participants. Others have documented that lean individuals properly adjust energy intakes throughout the day to compensate for energy from added snacks (Whybrow, Mayer, Kirk, Mazlan, & Stubbs 2007; Viskaal-van Dongen et al. 2010; Potier et al. 2009), but less is known regarding the compensatory capacity of overweight individuals. Ebbeling et al. (2004) reported that overweight adolescents were more likely to increase 24-h energy intakes on days 'extra large' fast food meals were consumed as compared to their lean counterparts (+409 kcal versus -47 kcal, respectively). However, Whybrow et al. (2007) reported that both lean and overweight subjects compensated to a similar degree during a mandatory 2-week snacking

intervention. Although the consumption of nutrition bars does not appear to contribute to the obesogenic environment of lean adults, more research is necessary to confirm these results and to examine the influence of weight status on compensatory responses.

Regular consumption of nutrition bars may impact the macronutrient and/or micronutrient profile of the diet. On days HP bars were consumed, protein intake increased an average of 35%; whereas, on the days HC bars were consumed, carbohydrate intake increased 10%. Calcium intakes increased 35% on days HC bars were consumed. Thus, energy dense nutrition bars formulated to address nutrient concerns of young adults and marketed to this demographic may improve nutritional health. Nutrition bars represent the most rapidly increasing sales market for snack foods, and annual total sales volume for nutrition bars increased 5.6% in 2010 as compared to the industry average of -0.6% (Wyatt, 2010). Consumers perceive nutrition bars as healthy, nutritious snacks or meal-replacements; yet, the rise in sales of nutrition bars over the past several decades has paralleled the rise in obesity. Only one known trial has investigated the impact of daily nutrition bar ingestion on body weight over time. Zaveri & Drummond (2009) observed no change in body weight or energy intakes over a 12-week period in overweight adult men instructed to consume cereal bars (n = 14; 227 kcal) or almonds (n = 18; 343 kcal) as snacks each day. However, physical activity levels were not controlled in this trial and all participants received healthy eating advice, factors that may have impacted energy intakes.

It is noteworthy that close examination of the data revealed that individuals with high leisure time physical activity levels reported 24-h energy

intakes that were significantly elevated on days that nutrition bars were consumed. These data imply that appropriate energy compensation may not occur under conditions of high physical activity. Although controversial, some experts claim that exercise may lead to excess food consumption, a phenomenon linked to desires for self-reward or to misjudgments regarding energy deficits from the exercise bout (Blundell & King, 1998; Westerterp, 2010). Interestingly, there is evidence that simply thinking about exercise can lead to increased food consumption in adults (Werle, Wansink, & Payne, 2011). However, in well-controlled experimental human trials with prescribed exercise bouts, energy intakes did not change over 1-2 weeks resulting in negative energy balances (Stubbs et al., 2002; Whybrow et al., 2008; Woo & Pi-Sunyer, 1985).

The attrition rate in this trial was high, 28%; however, body weight and weight status did not differ between the completers and non-completers. Self-reporting of dietary intakes and the single day treatment duration are limitations, but the crossover nature of the study reduced confounding covariates. Participants were free-living and their eating environments were not disturbed or manipulated strengthening the external validity.

In summary, energy-dense nutrition bars are a rapidly growing consumer market and may represent a unique opportunity to favorably influence nutrient status of young, lean adults without promoting excessive energy intakes. The secondary observations that overweight and/or physically active individuals may not compensate for the energy in these snacks, however, is an area of concern that should be examined carefully in future trials.

REFERENCES

- Blundell, J. E. & King, N. A. (1998). Effects of exercise on appetite control: loose coupling between energy expenditure and energy intake. *International Journal of Obesity and Related Metabolic Disorders*, 22, S22-29.
- Chow, J., Choe, Y. S., Noss, M. J., Robinson, K. J., Dugle, J. E., Acosta, S. H. & Garleb, K. A. (2007). Effect of a viscous fiber-containing nutrition bar on satiety of patients with type 2 diabetes. *Diabetes Research and Clinical Practice*, 76(3), 335-340.
- Ebbeling, C.B., Sinclair, K.B., Pereira, M.A., Garcia-Lago, E., Feldman, H.A. & Ludwig, D.S. (2004). Compensation for energy intake from fast food among overweight and lean adolescents. *Journal of the American Medical Association*, 291(23), 2828-2833.
- Godin, G. & Shephard, R. J. (1985). A simple method to assess exercise behavior in the community. *Canadian Journal of Applied Sport Sciences*, 10(3), 141-146.
- Hertzler, S. R. & Kim, Y. (2003). Glycemic and insulinemic responses to energy bars of differing macronutrient composition in healthy adults. *Medical Science Monitor*, 9(2), CR84-90.
- Kalergis, M. & Macdonald, A. (2009). Discretionary food fortification: implications of consumer attitudes. *Canadian Journal of Dietary Practices and Research*, 70(4), e26-31.
- McKiernan, F., Hollis, J.H. & Mattes, R.D. (2008). Short-term dietary compensation in free-living adults. *Physiology and Behavior*, 93(4-5), 975-983.
- Miller, C. K., Gabbay, R. A., Dillon, J., Apgar, J. & Miller, D. (2006). The effect of three snack bars on glycemic response in healthy adults. *Journal of the American Dietetic Association*, 106(5), 745-748.
- Potier, M., Fromentin, G., Calvez, J., Benamouzig, R., Martin-Rouas, C., Pichon, L., Tomé, D. & Marsset-Baglieri, A. (2009). A high-protein, moderate-energy, regular cheesy snack is energetically compensated in human subjects. *British Journal of Nutrition*, 102(4), 625-631.
- Rigik, E. (2011). Forecasting snack bar sales. Convenience Store Decisions. <http://www.csdecisions.com/2011/05/27/forecasting-snack-bar-sales/>. Accessed June 13.
- Stubbs, R. J., Sepp, A., Hughes, D. A., Johnstone, A. M., Horgan, G. W., King, N. & Blundell, J. (2002). The effect of graded levels of exercise on energy intake and balance in free-living men, consuming their normal diet. *European Journal of Clinical Nutrition*, 56(2), 129-140.

- Viskaal-van Dongen, M., Kok, F. J. & de Graaf, C. (2010). Effects of snack consumption for 8 weeks on energy intake and body weight. *International Journal of Obesity*, 34(2), 319-326.
- Werle, C. O., Wansink, B. & Payne, C. R. (2011). Just thinking about exercise makes me serve more food. Physical activity and calorie compensation. *Appetite*, 56(2), 332-335.
- Westerterp, K. R. (2010). Physical activity, food intake, and body weight regulation: insights from doubly labeled water studies. *Nutrition Reviews*, 68(3), 148-154.
- Whybrow, S., Mayer, C., Kirk, T.R., Mazlan, N. & Stubbs R.J. (2007). Effects of two weeks' mandatory snack consumption on energy intake and energy balance. *Obesity*, 15(3), 673-685.
- Whybrow, S., Hughes, D. A., Ritz, P., Johnstone, A. M., Horgan, G. W., King, N., Blundell, J. E. & Stubbs R. J. (2008). The effect of an incremental increase in exercise on appetite, eating behavior and energy balance in lean men and women feeding ad libitum. *British Journal of Nutrition*, 100(5), 1109-1115.
- Williams, G., Noakes, M., Keogh, J., Foster, P. & Clifton, P. (2006). High protein high fibre snack bars reduce food intake and improve short term glucose and insulin profiles compared with high fat snack bars. *Asia Pacific Journal of Clinical Nutrition*, 15(4), 443-450.
- Woo, R. & Pi-Sunyer, F. X. (1985). Effect of increased physical activity on voluntary intake in lean women. *Metabolism*, 34(9), 836-841.
- Wyatt, S.L. (2011). State of the snack industry 2010. SymphonyIRI Group. <http://www.symphonyiri.com/Portals/0/SNAXPO-2011.pdf> . Accessed June 23.
- Zaveri, S. & Drummond, S. (2009). The effect of including a conventional snack (cereal bar) and a nonconventional snack (almonds) on hunger, eating frequency, dietary intake and body weight. *Journal of Human Nutrition and Dietetics*, 22(5), 461-468.
- Zimmerman, T. P., Hull, S. G., McNutt, S., Mittl, B., Islam, N., Guenther, P. M., Thompson F. E., Potischman, N. A. & Subar, A. F. (2009). Challenges in converting an interviewer-administered food probe database to self-administration in the National Cancer Institute Automated Self-administered 24-Hour Recall (ASA24). *Journal of Food Composition and Analysis*, 22(supplement 1), S48-S51.

Chapter 3

EFFECT OF DAILY SUPPLEMENTAL GELATIN INGESTION ON CALORIE INTAKE IN OVERWEIGHT AND OBESE WOMEN INITIATING A WALKING PROGRAM

Although the rate of increased obesity in the US has seemingly tapered off over the past decade (Flegal, Carroll, Ogden, & Curtin, 2010), it is estimated that world-wide approximately 1.46 billion adults have a BMI of 25 kg/m² or more, and of these, 497 million are obese (BMI \geq 30 kg/m²) (Finucane et al., 2011). The costs of obesity-related conditions are high, both from the standpoint of physical wellbeing (Haslam & James, 2005) and also from the steep economic burden derived directly from health care costs of an estimated \$147 billion per year in the US alone (Finkelstein, Trogon, Cohen, & Dietz, 2009). Obesity also indirectly impacts increased expenses including absenteeism and presenteeism (Finkelstein, DiBonaventura, Burgess, & Hale, 2010), disability, worker's compensation and premature mortality (Trogon, Finkelstein, Hylands, Dellea, & Kamal-Bahl, 2008).

While the causes of obesity are multi-factorial (Zinn, 2010) adopting a lower calorie diet and/or increasing regular exercise continue to be the established treatment (Macfarlane & Thomas, 2010). Undoubtedly exercise, even with little or no weight loss, has been shown to be beneficial in improving many health parameters related to obesity including improved blood lipid profile (Balducci et al., 2010; Cornelissen & Fagard, 2005; Couillard et al., 2001), glucose tolerance indices (Balducci et al., 2010; Ferrara, Goldberg, Ortmeyer, & Ryan, 2006; Roumen et al., 2008; Sigal et al., 2007; Smeets, Soenen, Luscombe-Marsh, Ueland, & Westerterp-Plantenga, 2008) and endothelial cell

function (De Filippis et al., 2006; Mestek et al., 2010) and decreased blood pressure (Balducci et al., 2010; King, Hopkins, Caudwell, Stubbs, & Blundell, 2008). Although studies have shown weight control can be achieved through exercise (Donnelly et al., 2003; Rampersaud et al., 2008), it is generally accepted that decreased caloric intake plays a much more salient role in weight reduction (Keim, Canty, Barbieri, & Wu, 1996; King et al., 2007; Macfarlane & Thomas, 2010). For instance, a recent longitudinal study found women of Nigeria and African American women had similar average daily energy expenditure and physical activity levels after adjusting for body size, but their mean BMI varied greatly (23 kg/m² vs. 31 kg/m², respectively) (Luke et al., 2009); thus, suggesting that nutrient intake primarily dictates body weight. In addition, many intervention trials show poor weight loss results while on weight reducing programs based exclusively on exercise (Franz et al., 2007; Miller, Kocaja, & Hamilton, 1997). Interestingly, a meta-analysis of 16 aerobic exercise trials involving women found they have an even harder time losing weight after initiating an exercise regimen without making dietary changes compared to men (Ballor & Keeseey, 1991). A recent, supervised, 16-month exercise trial of 71 men and women resulted in a decrease in BMI by an average of 1.6 units for men, but there was no overall weight change in females owing to the fact that approximately half of the women in the study gained weight (Donnelly et al., 2003; Donnelly & Smith, 2005). An additional, tightly controlled intervention study of 411 postmenopausal women examining the effects of different doses of exercise showed nearly a quarter of the women gained weight between baseline and 6 months (Church et al., 2009).

The concept of reduced effectiveness when relying on exercise as the sole mode of weight loss has been extensively reviewed (King et al., 2007; Stiegler & Cunliffe, 2006) and has been attributed to a set of compensatory adaptations that involve both autonomic and volitional responses. Autonomic responses are compulsory and include metabolic adaptations such as decreased resting and non-resting metabolic rate and behavioral changes such as reduced spontaneous activity due to fatigue. Volitional responses are solely behavioral and include increased energy intake and non-compliance to the exercise regimen (King et al., 2007).

In addition, the term “compensation” has been used to describe the disparity between predicted and actual weight loss based on caloric expenditure (Blundell, Stubbs, Hughes, Whybrow, & King, 2003; King et al., 2008). It appears that compensation is largely a result of the behavioral response of increasing energy intake after exercising. For instance, in an acute exercise study of 22 healthy female subjects (BMI between 20-25kg/m²) who took part in one bout of high intensity exercise found that 11 of the 22 participants compensated by eating up to 600 calories more on the exercise day compared to the non-exercise control day (Finlayson, Bryant, Blundell, & King, 2009). A separate, 12-week study of 35 overweight and obese sedentary men and women found that non-compensators lost an average of 6.3kg while decreasing their energy intake (EI) by an average of 130 kcal/d; however, compensators only lost an average of 1.5 kg and their energy intake increased by a mean of 268 kcal/d (King et al., 2008). Additionally, a crossover study conducted at Arizona State University found that amongst young adults who are highly active, ingestion of either a high protein or high carbohydrate breakfast bar lead to increased energy intake throughout the

day compared to the control day (Trier & Johnston, 2012). In fact, it has been shown that just contemplating exercise can result in increased energy intake (Werle, Wansink, & Payne, 2011). King et al. (2009) conducted a 12-week supervised exercise study of 58 overweight and obese men and women that induced a 2,500 kcal/week energy deficit to assess the effect of chronic exercise on appetite regulation. Interestingly, they found that exercise improved post-meal ingestion satiety after breakfast in all individuals, but increased the general drive to eat throughout the remainder of the day for those who did not lose weight while on the prolonged exercise regimen.

It is unknown why some women have a hyperphagic response to exercise while others do not. The Three Factor Eating Questionnaire (TFEQ) measures Disinhibition, Hunger, and Restraint (Stunkard & Messick, 1985). Disinhibition refers to the tendency to eat opportunistically in response to stress, social situations involving food, and the availability of highly palatable food (Bryant, King, & Blundell, 2008). It has been suggested that women who score higher for Disinhibition (Keim et al., 1996) and those who score high in Restraint and are dieting (Visona & George, 2002), spontaneously increase energy intake with exercise initiation.

Given the prospect that exercise can induce compensatory caloric ingestion for a large percentage of individuals, it is highly desirable to uncover dietary manipulations that maximize satiety leading to decreased EI while undertaking a new exercise regimen. To this end it is widely recognized that higher protein diets improve satiety (Lejeune, Westerterp, Adam, Luscombe-Marsh, & Westerterp-Plantenga, 2006; Poppitt, McCormack, & Buffenstein, 1998; Smeets et al., 2008; Weigle et al., 2005). It is also recognized certain types of

proteins may confer a more satiating effect than others (Veldhorst et al., 2008; Veldhorst et al., 2009a). It has been hypothesized that the increased satiety effect of incomplete protein ingestion may be due to the area of the brain called the anterior piriform cortex, which is instrumental in rejecting a diet of incomplete protein intake (Gietzen & Aja, 2012). When rats are exposed to a lysine deficient diet, they are able to locate and consume a bitter solution containing lysine in preference over 15 other bottles of solution (Mori, Kawanda, Ono & Torii, 1991).

Gelatin, which consists of a mix of peptides and protein derived from bovine hides, bones and pig skin, is an incomplete protein because it is devoid of the essential amino acid tryptophan and the amount of methionine and histidine it contains is limited (Cole, 2000). There is a dearth of published research examining the effect of gelatin on satiety and EI but two published studies do indicate that the ingestion of gelatin confers a higher degree of satiation (Hochstenbach-Waelen, Westerterp-Plantenga, Veldhorst, & Westerterp, 2009) and leads to decreased EI compared to other, complete protein sources (Veldhorst et al., 2009b). In a single-blinded, randomized crossover study, 34 lean, healthy men and women were tested to examine the satiating effect of gelatin vs. the complete protein casein (Hochstenbach-Waelen et al., 2009). They found that a full day diet of 10% energy derived from gelatin resulted in an overall 44% decrease in appetite rating throughout the day. A separate study compared satiety and EI resulting from a breakfast containing a mean of 14 g of five sources of proteins: alpha-lactalbumin, gelatin, casein, soy, and whey. The results indicated there was a 20% decrease in subsequent caloric intake at the next meal served three hours later for those who ingested gelatin and alpha-lactalbumin compared to casein, soy or whey (Veldhorst et al., 2009b). Data

from a 2010 cross-over, pilot trial at Arizona State University found that at breakfast, ingestion of 4 grams of protein from gelatin resulted in significantly reduced energy intake of 400 kcal throughout the day compared to the ingestion of 4 grams of protein from algae or the control day (0 g protein). However, it is important to note that no study has been published showing the effect of gelatin ingestion on daily caloric intake when initiating an exercise regimen. If gelatin ingestion were able to reduce daily caloric intake among exercising women, this would be a simple, cost-effective strategy to help thwart the incidence of weight stability or weight gain that coincides with exercise initiation when exercise induced weight loss is the desired outcome. Thus, it would be highly beneficial to determine the long-term effects on weight status from gelatin ingestion during an exercise program in previously sedentary women. The purpose of this study was to assess the influence of daily gelatin ingestion while partaking in an exercise program in offsetting EI compensation due to increased physical activity. It is also anticipated that those subjects who are the most resistant to weight loss will have higher baseline Disinhibition scores as measured by the TFEQ.

The primary hypothesis of this research study is that daily gelatin ingestion, vs. placebo, will result in decreased calorie intake in healthy, overweight/obese women initiating a walking program.

The secondary hypothesis is that daily gelatin ingestion, vs. placebo, will result in greater weight loss in healthy, overweight/obese women initiating a walking program.

The tertiary hypothesis is that women who score higher for Disinhibition eating behavior traits will have either weight gain or little to no weight loss compared to those who score lower.

METHODS

Subjects. Only women were recruited for this study because research shows women have difficulty losing weight through exercise alone compared to men (Ballor & Keeseey, 1991; Church et al., 2009; Donnelly et al., 2003). The target sample was set at 70 participants for this parallel arm trial, a sample size that was calculated to provide an 80% power to detect a difference in energy intake. The subjects were screened and excluded for the following conditions: <20 or >59 years of age, BMI <25.0 or >45.9, recent weight change over the past 3 months of > 5 lbs., being physically active (moderate exercise of more than 2 times/week), pregnancy or lactation within the last year, unable to walk at a moderately intense pace, following a special diet including vegetarian or Kosher, gastric bypass or any type of GI surgery or conditions, and use of medications affecting appetite or metabolism (i.e. thyroid agents or corticosteroids etc.). In addition, all subjects were generally of good health. Further screening measurements included body weight and height and answering no to all questions on Physical Activity Readiness Questionnaire (PAR-Q), which is a screening tool used to identify any possible health risks of exercising.

Recruiting and retention. The subjects were recruited from an accessible sample at Arizona State University, Phoenix, AZ. Recruitment started in November, 2010 and ended in January, 2011. Targeted subjects, as advertised for, were those who have difficulty losing weight and a BMI between 25 and 45.9 kg/m², and requiring a doctor's note for those having a BMI >40 (<46) clearing them for participation in the study. Advertisement was done through Blackboard announcements, email list serves, flyers, and by word of mouth at ASU. In attempt to retain the maximum amount of subjects, those who

completed the 4 and 6-week portion of the study received a \$10.00 retail gift card at those visits. In addition, regular email reminders were sent. Participants were provided with the researchers' email addresses to ask questions or relay concerns that arose throughout the study. Written informed consent, approved by the Arizona State University Office of Research Integrity and Assurance, was obtained from the subjects prior to entering the study.

Study design. In this 6-week, single-blinded, randomized, parallel arm trial, 37 female subjects were assigned to one of two groups; a “gelatin” group (n = 19) or a control group (n = 18). The gelatin group consumed 1 tablespoon of Knox® gelatin powder per day (Kraft Foods Global Inc., Northfield, IL, USA) which is equal to 6 g protein. The control group consumed 1 teaspoon casein powder (General Nutrition Corporation, Pittsburgh, PA, USA) per day, providing 1.25 g protein (Table 2). They were instructed to mix the powder in 8 fl. oz. of cold water or another, self-selected cold beverage within one hour upon awakening. In addition, all subjects commenced an exercise regimen, which consisted of wearing a pedometer (OMRON HJ720ITC, HRM USA, INC. PA, USU) on either hip or mid back everyday throughout the study. This brand of

Table 2.
Nutritional composition of trial supplements.

Supplement	Amount	Calories	PRO ¹ (g)	CHO ² (g)	Fat(g)
Casein ³ (Control)	1 teaspoon	7.5	1.25	0.5	0.05
Gelatin ⁴	1 tablespoon	23.4	6.0 ⁵	0.0	0.0

¹Protein.

²Carbohydrate.

³Source: Nutrient data for this listing was extrapolated from the nutrition label on the package.

⁴Source: Nutrient data for this listing was provided by USDA SR-25.

⁵Incomplete Protein (devoid of tryptophan).

pedometer features dual piezoelectric sensors and was chosen because it has been shown to provide both valid and reliable tracking of steps (Holbrook,

Barreira, & Kang, 2009) and for its computer downloading capability and 41-day storable memory. The exercise goal for the subjects was to reach or exceed 10,000 steps per day. This amount of walking signifies the stage that would categorize an individual as being “active” and is an attainable goal that has been shown to result in beneficial health parameters (Tudor-Locke & Bassett, 2004).

Procedures. Participants met with the investigators for a total of 5 meetings. A schematic plan of the trial is displayed in Figure 2. The initial meeting involved a pre-trial screening and participant consent. At this time body composition was measured using bioimpedance (Tanita, UM-018 Digital Scales, Tanita Corp., Tokyo, Japan). A stadiometer was used to measure height and a

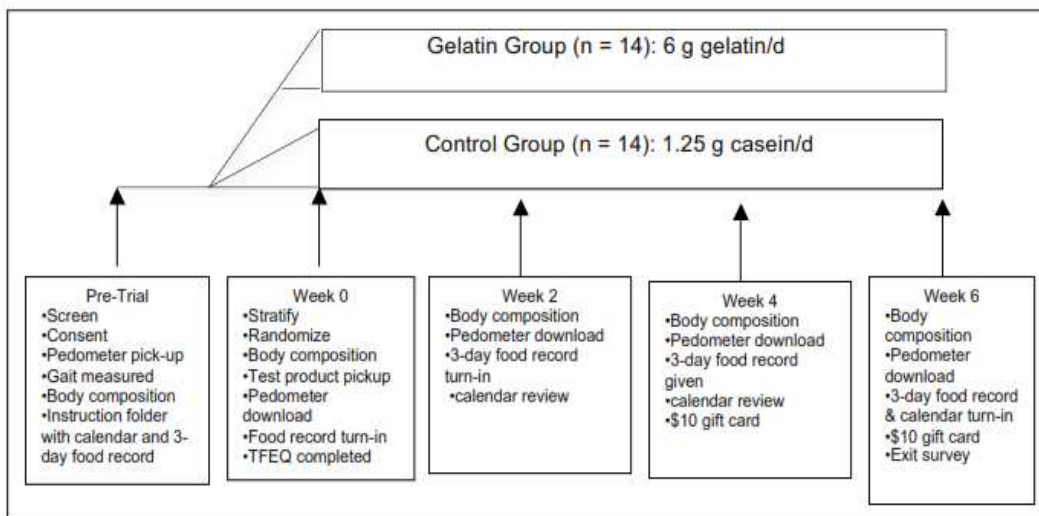


Figure 2. Gelatin trial timeline.

flexible tension tape was used to measure waist circumference at the umbilicus. Average gait length was measured and this data was programmed into the pedometer supplied to the participants to be worn for one week prior to starting the exercise program to attain a baseline activity level. Subjects also received a calendar to track their daily steps and to note daily consumption of the powder (gelatin or casein) throughout the study. For the baseline assessments (3-day

average calorie intake and physical activity), subjects were instructed to continue their regular daily activity and eating patterns. A blank, 3-day food diary was provided and the subjects were instructed to fill out the records on three consecutive days including one weekend and two week days and the three day average was used to assess the subject's routine nutrient intake.

They were advised to fill out the record in detail describing the type and amount of each item consumed as accurately as possible. The food records were analyzed using The Food Processor© Nutrition Analysis Software from ESHA Research, Salem, Oregon.

From the screening information, the subjects were stratified by age, BMI and weight, and randomized to their experimental group. At the second meeting, approximately six days later, body composition was re-measured, baseline pedometer data was downloaded, and the subjects received their test product and written and verbal instructions for consuming the product. In addition, the TFEQ was administered and the subjects were counseled to increase their daily steps by 500 steps every day until they reached at least 10,000 steps/d. They were initially advised to walk at a brisk pace ½ mile in the morning and ½ mile in the evening and to increase the mileage over a 2 week period until they reached a goal of walking 2 miles/d purposefully in < 40 minutes, estimated to equal 4,000-5,000 steps/d of moderate aerobic exercise (Ainsworth et al., 2000). Two weeks later, the subjects returned to the research unit. At this time, body composition was measured, pedometer information was downloaded, and their 3-day diet record and the daily step and the powder consumption-tracking calendar were reviewed. The two-week procedures were duplicated at the four- and six-week meetings (but no food diary was turned in at week four) and during

the sixth and final meeting an exit survey was filled out by each subject. In addition, the subjects received a \$10 gift card at both the four and six week visits.

Statistical analyses. The sample size for this study was based on a previous study in this lab with a similar intervention and outcome measures. An attrition rate of 30% was anticipated, and an enrollment of 70 subjects was targeted. Other studies have used sample sizes in this range ($n = 45$, $n = 70$, respectively) (Georg Jensen, Kristensen, & Astrup, 2012; Zaveri & Drummond, 2009) to examine weight loss and dietary intake using protein based food interventions. Only 37 women were enrolled in this trial and 28 subjects completed the trial in its entirety. Hence, this study is underpowered.

Statistical analyses were completed using Statistical Package for the Social Sciences (SPSS V19, IBM Corporation, Somers, NY). Normality testing showed all data were normally distributed; thus, parametric testing was used for all data analyses. Comparison of baseline characteristics for the two study groups was done using independent-samples t-tests. Pearson correlation coefficient was used to explore the relationship between variables. Changes in dependent variables were analyzed using multivariate general linear model for repeated measures (ANOVA) and paired samples t-tests. Three-day diet records at all three time points and baseline pedometer data were not available for all participants, which resulted in reduced sample sizes for these analyses ($n = 21$ and $n = 27$, respectively). Additionally, some daily pedometer data were missing or step counts were $< 1,000$, and the mean data were calculated omitting these days, leaving 92% of the trial days available for analysis. Restraint, Disinhibition, and Hunger scores were grouped into tertiles by visual binning; cut-points were set at equal percentiles based on scanned cases. Data are presented as mean

±SD and significance was set at $P < 0.05$. To reduce assessment bias when analyzing the 3-day food records, an extensive default food code list encompassing over 450 foods and beverages was used when an item could not confidently be assigned a specific code. Standard USDA serving sizes were used when serving amounts were not indicated.

RESULTS

A CONSORT (Moher et al., 2010) diagram describes the recruitment, enrollment and retention of participants (Figure 3). Of the 37 women enrolled in the study, three did not start the study and an additional six left the study prior to

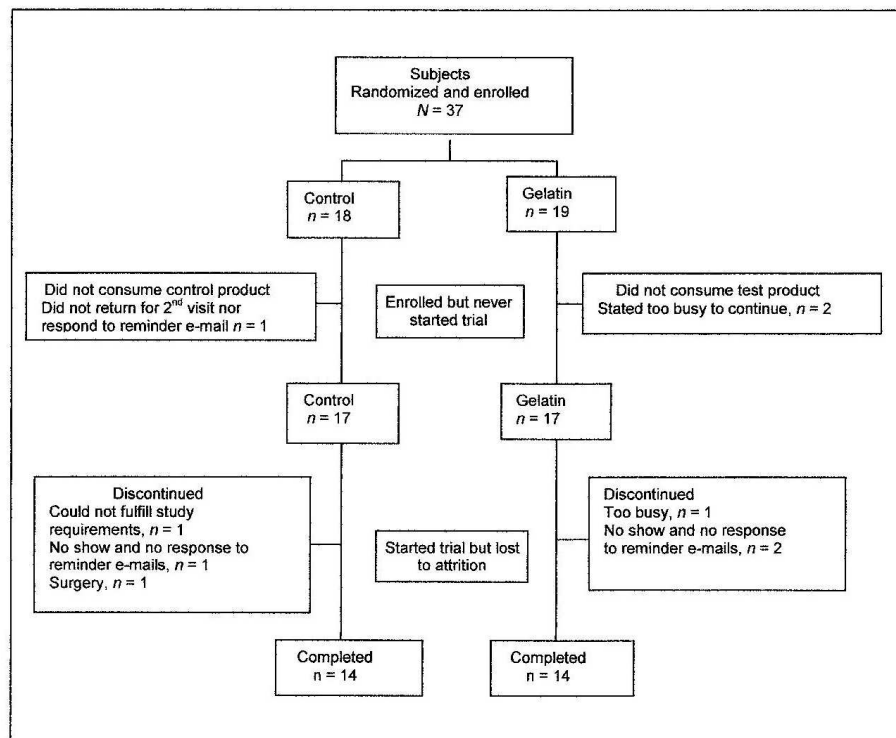


Figure 3. Flow of study participants.

completion; therefore, 28 participants (76%) completed the six-week trial in its entirety. There were no significant differences by age ($P = 0.711$), weight ($P = 0.903$), BMI ($P = 0.446$), body fat % ($P = 0.742$), or waist circumference ($P = 0.359$) between those who remained in the trial compared to those who did not

complete the trial. Baseline characteristics of the subjects completing the study did not vary by group (Table 3). In addition, one subject smoked cigarettes (1 pack/d, control group), two subjects were African-American (1 control, 1 gelatin), five subjects were Hispanic (3 control, 2 gelatin), and one subject was Asian-American (gelatin). Self-reported daily compliance of test product ingestion was 88.1 ± 7.4 and $87.6 \pm 16.1\%$ ($P = 0.929$) throughout the 6-week trial for the control and gelatin groups, respectively. Although compliance was high, 14% of the control (casein) subjects and 57% of the gelatin subjects reported dislike of the drink. Table 4 summarizes the mean difference in

Table 3.
Characteristics of subjects in the supplement groups at baseline.¹

Characteristic	Control (n = 14)	Gelatin (n = 14)	<i>P</i> value ²
Age (yr)	36.9 ± 10.7	36.7 ± 9.5	0.956
Weight (lbs)	173.9 ± 28.5	178.2 ± 21.8	0.652
Height (in)	63.7 ± 2.1	64.1 ± 1.9	0.550
BMI (kg/m ²)	30.1 ± 5.0	30.5 ± 3.9	0.835
Body Fat (%)	40.0 ± 5.7	41.3 ± 4.9	0.507
Waist Circumference (in)	34.8 ± 4.1	35.0 ± 3.6	0.924
Activity (steps/d)	6365 ± 1281 ³	6286 ± 2507	0.920
Energy intake (kcal, 3 d average)	1784 ± 532	1743 ± 487	0.835
Restraint Score (0–21) ⁴	8.2 ± 5.4 ³	9.0 ± 3.7	0.636
Disinhibition Score (0–16) ⁴	7.7 ± 2.7 ³	9.9 ± 4.0	0.118
Hunger Score (0–14) ⁴	7.4 ± 2.0 ³	5.9 ± 3.2	0.169

¹ Values are mean ± SD.

² Independent *t*-test.

³ n = 13.

⁴ Test range.

outcome variables across time and between groups throughout the trial period. There was a statistically significant time effect for mean step count across time; both groups together increased daily step count by +22% from baseline through week six after controlling for age, although there was no difference in increase by

group. The trial average step counts were 7518 ± 1889 and 7923 ± 2061 steps for the control and gelatin groups, respectively ($P = 0.493$). One-half of all

Table 4.
Comparison of outcome measures by time effect and interaction.¹

	Control n = 14	Gelatin n = 14	P value Time effect	P value Interaction
Energy intake ² (kcal, 3 d average)				
Baseline	1747 ± 508	1761 ± 575		
Week 1	1882 ± 508	1922 ± 277	0.643	0.011
Week 6	1944 ± 503	1587 ± 281		
Activity (steps/d) ³				
Baseline	6365 ± 1281	6286 ± 2507		
Trial average	7518 ± 1889	7923 ± 2061	0.022	0.493
BMI (kg/m ²)				
Baseline	30.1 ± 5.0	30.5 ± 3.9		
Week 6	30.1 ± 4.7	30.6 ± 4.0	0.786	0.528
Weight (lbs)				
Baseline	173.9 ± 28.5	178.2 ± 21.8		
Week 6	173.6 ± 28.3	179.0 ± 22.8	0.194	0.268
Body Fat (%)				
Baseline	40.0 ± 5.7	41.3 ± 4.9		
Week 6	39.5 ± 5.7	41.1 ± 4.6	0.339	0.713
Waist circumference (in)				
Baseline	34.8 ± 4.1	35.0 ± 3.6	0.388	0.705
Week 6	34.4 ± 4.3	34.6 ± 3.6		

¹ Means ± SD. P values for repeated measures ANOVA controlling for any confounding variables as discussed in the text.

² Reduced sample size: n = 11 and n = 10 for the control and gelatin groups, respectively.

³ Reduced sample size: n = 13 and n = 14 for the control and gelatin groups, respectively.

subjects reported the step goal (10,000 steps/d) was “challenging” and “not easy to reach.” After controlling for baseline weight, Restraint score and Hunger score, there was a statistically significant between group difference in mean calorie intake from baseline to week six such that the control group had a mean increase in calorie intake from baseline by $+197 \pm 320$ kcal/d, whereas the gelatin group decreased energy intake by -174 ± 612 Kcal/d (Table 4). Further analysis using Independent *t*-test shows no significant between group difference

in calorie intake at week 1 ($P = 0.623$) but by week 6 the difference between the groups reached significance ($P = 0.043$). Paired t -test indicated that after initiation of the walking program, the control group had a significant increase in mean calorie consumption from baseline vs. week 6 ($P = 0.038$); conversely, the gelatin group had a mean calorie decrease from week 1 vs. week 6 ($P = 0.011$). Additionally, there was no significant change in BMI (controlling for Restraint and

Table 5.
Associations¹ between changes in outcome measures and baseline TFEQ scores.

Characteristic		Step Change	Weight Change	Body Fat Change	Waist Change	Restraint Score	Dis-inhibition Score	Hunger Score
Calorie Change	r	.154	-.290	.119	.010	.369	-.124	-.326
	Sig. (2-tailed)	.455	.179	.588	.653	.091	.581	.139
	N	22	23	23	23	22	22	22
Step Change	r	–	.108	.184	-.056	-.107	-.159	-.366
	Sig. (2-tailed)		.591	.358	.783	.597	.427	.061
	N		27	.27	27	27	27	27
Weight Change	r		–	-.031	.078	-.075	.261	.110
	Sig. (2-tailed)			.877	.694	.710	.188	.586
	N			28	28	27	27	27
Body Fat Change	r			–	-.192	.422	-.205	-.290
	Sig. (2-tailed)				.328	.028	.306	.143
	N				28	27	27	27
Waist Change	r				–	-.006	-.157	-.038
	Sig. (2-tailed)					.978	.435	.852
	N					27	27	27
Restraint Score	r					–	-.105	-.329
	Sig. (2-tailed)						.602	.094
	N						27	27
Dis-inhibition Score	r						–	.254
	Sig. (2-tailed)							.201
	N							27

¹ Pearson product-moment correlation coefficient.

Disinhibition scores), weight (controlling for baseline mean calorie intake and Restraint score), percent body fat (controlling for Restraint and Disinhibition scores) or waist circumference (controlling for Restraint scores).

An analysis of correlations between change in outcome variables and baseline TFEQ scores shows the only relationship that reached significance was

the negative relationship between percent body fat change and Restraint score ($P = 0.028$) (Table 5). There was also a trend toward significance in the negative association between step change and Hunger score. Table 6 describes the

Table 6.
Association of Restraint, Disinhibition, and Hunger scores vs. baseline weight and weight change.¹

	Weight (lbs) Baseline	Weight (lbs) Week 6	<i>P</i> value Time effect	<i>P</i> value Interaction
Restraint Score				
≤7 (n = 11)	189.4 ± 21.8	189.4 ± 22.4		
8 – 10 (n = 8)	177.0 ± 25.5	178.0 ± 26.8	0.532	0.746
≥11 (n = 8)	161.2 ± 18.9*	161.3 ± 17.7		
Disinhibition Score				
≤7 (n = 9)	165.1 ± 19.7**	165.0 ± 20.2		
8 – 11 (n = 12)	180.6 ± 28.4	180.0 ± 27.8	0.098	0.004
≥12 (n = 6)	189.3 ± 15.3	192.7 ± 16.2***		
Hunger Score				
≤5 (n = 11)	172.1 ± 25.1	172.8 ± 25.7		
6 – 7 (n = 7)	185.8 ± 26.7	184.5 ± 26.7	0.759	0.211
≥8 (n = 9)	177.3 ± 22.6	178.3 ± 23.7		

¹Means ± SD; *P* values for repeated measures ANOVA

*Significantly different from lower tertiles at baseline, $P < 0.05$

**Trended different from highest disinhibition tertile at baseline, $P = 0.06$

***Greater change from baseline vs. ≤7 and 8 – 11 tertiles, $P = 0.034$

relationship between the TFEQ scores and weight. Although Restraint and Hunger scores were not associated with baseline weight or weight change during the trial, subjects having Disinhibition scores in the highest tertile (≥12) tended to weigh more than those who scored in the lowest tertile (≤ 7) at baseline. In addition, there was no mean weight change for those in the two lowest Disinhibition tertiles, while those scoring in the highest had a significant increase in weight of an average of 3.3 ± 1.9 lbs. (Figure 4).

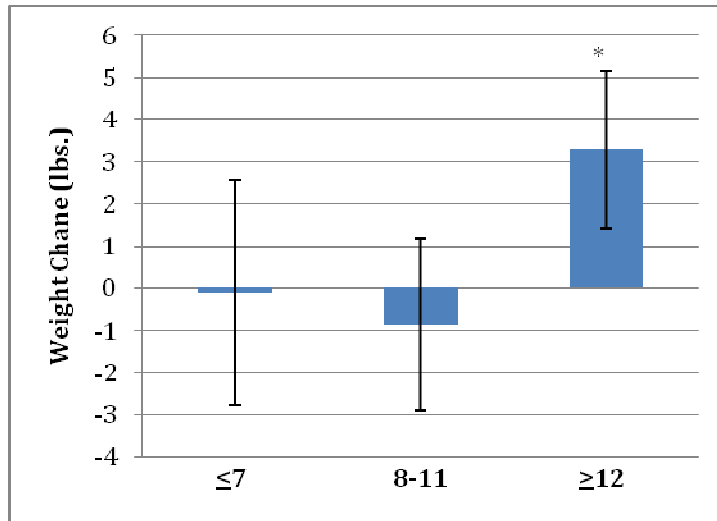


Figure 4. Weight change by Disinhibition tertiles. (Means \pm SD)
 *Significantly different from the two lower tertiles ($P = 0.004$)

DISCUSSION

This trial investigated whether females supplementing their diets with daily ingestion of 6 g gelatin while undertaking a walking program can aid in suppressing calorie intake and promote weight loss compared to a control group. The results show that while both groups initially increased their calorie intake when starting an exercise program (baseline to week 1), this increase was attenuated in the gelatin group at week 6 such that by the end of the trial, the control group ate more calories vs. baseline while the gelatin group decreased their calorie intake over the same time period. Thus, it does appear that gelatin may have satiating power, leading to decreased calorie intake while increasing physical activity on an ad libitum diet. Nevertheless, there was no reduction in weight, waist circumference, and percent body fat after six weeks of increased activity. Additional health parameters including blood lipid profiles, blood pressure and endothelial cell function were not measured; however, future

studies may want to pursue this line of investigation to see if even a modest increase in daily steps as seen in this trial would improve these health indicators.

Different theories examine how protein influences calorie intake. For instance, Mellinkoff, Frankland, Boyle, & Greipel (1956) originally conceptualized the aminostatic hypothesis; specifically, that amino acid concentration has an independent effect and is inversely correlated to appetite. Additionally, it has been theorized that the satiation properties of high protein foods could be due to the particular type of amino acid found in the food such that certain amino acids may confer a higher degree of satiety than others. For instance, there is emerging evidence that the branch chain amino acid leucine acts as an important amino acid signal to suppress food intake through its explicit action on AgRP gene expression within the hypothalamus (Blouet, Jo, Li, & Schwartz, 2009; Cota et al., 2006; Morrison, Xi, White, Ye, & Martin, 2007). Additionally, different protein sources have also shown differential potential for increased satiety and subsequent EI. In concordance with the “fast and slow protein” premise (Boirie et al., 1997), Hall, Millward, Long, & Morgan (2003) found that a 48 g/400 kcal liquid whey protein preload significantly increased amino acid concentration by 28% at three hours after ingestion compared to a similar casein preload. The authors postulated that the faster rate of digestion from whey compared to casein (the gastric emptying rate of casein is decreased due to curd formation from the acidic environment) caused the higher amino acid concentration and an increase in satiety and subsequent decreased EI compared to casein. In contrast, a different trial (Abou-Samra, Keersmaekers, Brienza, Mukherjee, & Mace, 2011) found a 20 g protein preload of casein or pea protein significantly decreased calorie intake at a subsequent meal 30 minutes after ingestion vs. a water

control, but whey protein and egg albumin did not. Moreover, Veldhorst et al. (2009a) found no significant difference in EI at lunch after ingestion of either a 10% or 25% iso-caloric custard breakfast of either casein, whey or soy protein. Thus, drawing consistent conclusions regarding differences in EI resulting from various protein sources remains challenging.

In the present study, a decreased mean daily EI was accompanied by gelatin consumption, which is an incomplete protein, lacking in tryptophan. This finding supports the concept that the brain has the ability to recognize a diet deficient in a particular essential amino acid leading to decreased EI (Fromentin, Feurte, Nicolaidis, & Norgren, 2000; Gietzen & Aja, 2012). This result is in agreement with short-term studies showing that gelatin intake may have an inhibitory effect on appetite and subsequent food intake (Hochstenbach-Waelen et al., 2009; Veldhorst et al., 2009b). To the best of current knowledge, there is only one long-term (8 week) study examining the effect of gelatin combined with milk protein compared to milk protein alone as meal replacements during a weight reduction trial (Hochstenbach-Waelen, Soenen, Westerterp, & Westerterp-Plantenga, 2011). These authors found gelatin did not improve weight loss compared to the control, milk only groups. However, since the caloric intake was restricted in all subjects in each dietary intervention group, spontaneous weight loss due to increased satiety could not be determined.

An alternative theory for explaining the decrease in EI in the gelatin group is that the viscous properties of hydrocolloid foods, as seen with the consumption of certain dietary fibers such as guar gum and pectin, may provide increased satiation efficacy. For instance, a cross-over trial (Solah et al., 2010) investigating the satiety effects of viscosity/gel strength and protein level found

that when comparing either a high- or low-viscosity, low-protein, alginate-based drink (≈ 2 g Pro/serving), four hours after consumption the high-viscosity drink conferred significantly lower Hunger scores ($P < 0.05$) on a visual analogue scale (VAS). However, when these researchers compared a high-viscosity, low-protein alginate-based drink (≈ 2 g Pro/serving), to a low-viscosity, high-protein, whey based drink (≈ 30 g Pro/serving), the high-viscosity, low-protein drink lead to decreased VAS Hunger scores after 4 hours of ingestion ($P < 0.05$). Thus, the authors concluded that viscosity level may play a more salient roll in hunger suppression than the amount of protein a product contains. After heating in liquid, gelatin gels at $<35^{\circ}\text{C}$. Nevertheless, the subjects in this trial drank the gelatin prior to the gelling process; therefore, the rheological behavior of gelatin and its impact on digestion was not studied, precluding any conclusions to be drawn regarding the potential satiety effects of gelatin as related to the extent of viscosity, gastric distention, and the speed of gastric emptying that gelatin may confer.

Be it due to the amount and/or type of protein or some other physiological factor, the results of the current study do show that there was an unprompted decrease in calorie consumption in the gelatin group compared to the control group, although this did not translate to any sort of expected weight reduction at six weeks. Possibilities for this discrepancy between decreased calorie intake and lack of weight loss could be due low sample size of the study. A power analysis shows that for a parallel study design, 4524 subjects would be needed to show a 2 lb. weight change based on a standard deviation of 24 lbs. at a power of 80% to detect a difference. Another explanation could be that the decrease in daily calorie intake in the gelatin group was small (<200 kcal/d); thus,

weight loss may have been actualized were the study to go longer with a sustained decrease in daily EI.

The primary finding in this study regarding the results from the TFEQ responses and weight change confirmed that higher Disinhibition scores at baseline were a predictor for increased baseline weight and potential for weight gain. At baseline, those with higher restraint scores weighed less, but baseline Restraint scores did not impact weight change throughout the trial. Hunger scores did not appear to be predictive of neither baseline weight nor weight change. It has been postulated that elevated Restraint and Disinhibition scores may co-occur because high dietary Restraint scores may be a result of dieting in response to increased weight gain ostensibly related to Disinhibition (Johnson, Pratt, & Wardle, 2012). However, results from this trial did not show a significant correlation between Disinhibition and Restraint scores. Several studies have shown that increased Disinhibition scores are highly predictive of increased BMI levels and a propensity toward weight gain over time (Bellisle et al., 2004; Dykes, Brunner, Martikainen, & Wardle, 2004; Hays et al., 2002; Hays & Roberts, 2008; Williamson et al., 1995). Interestingly, a recent 12-week, supervised, exercise induced weight loss study showed higher baseline Disinhibition scores coincided with greater decreases in BMI and decreased Disinhibition scores overtime (Bryant, Caudwell, Hopkins, King, & Blundell, 2012). The authors postulate that their contrary findings may be explained by the singular mode of intervention compared to other trials that use multiple components including diet, exercise and behavioral components, and individuals with higher initial Disinhibition scores may benefit more from mandatory, supervised and structured exercise sessions. Indeed, in the present study, free-living subjects were merely

encouraged to increase exercise over 6 weeks and those with high Disinhibition scores had an increase in weight overtime which is in congruence with most other studies showing a clear-cut correlation between increased propensity for weight gain and higher Disinhibition scores. Thus, it appears that the TFEQ may be an appropriate tool that could help identify those who may benefit most from an exercise program that is regulated and compulsory, thereby improving chances of success when exercise induced weight loss is the goal.

Limitations. Based on the pre-study power calculation, this study was underpowered as only 28 finished the trial, reducing the power to 42%. It was calculated that 70 individuals were needed for 80% power to detect a difference in energy ingestion between groups. Additional limitations include issues surrounding the reliance of food records to accurately reflect EI and bias toward underreporting, especially in obese populations (Trabulsi & Schoeller, 2001). However, given that the groups were comparable in baseline characteristics, one would anticipate the susceptibility to underreporting EI to be of equal magnitude for each arm. Subject compliance to physical activity was assessed by average daily step count, but the pedometers used did not provide information on exercise intensity and this limited interpretation of the daily activity data. Finally, the full duration of the study was 6 weeks. Therefore, longer-term compliance and the effects of the exercise program and gelatin ingestion on caloric intake and weight status cannot be determined.

In conclusion, the result of this trial, showing that weight loss was not realized although activity level increased throughout the study compared to baseline is in agreement with previous studies showing that increased physical activity without intentional calorie restriction may be a less effective as a method

of weight reduction. However, it is noteworthy that the initial hyperphagic response with increased exercise in both groups during the first week of the trial was abated for those ingesting gelatin, although, the root cause for decreased EI which coincided with gelatin consumption remains unclear.

REFERENCES

- Abou-Samra, R., Keersmaekers, L., Brienza, D., Mukherjee, R., & Mace, K. (2011). Effect of different protein sources on satiation and short-term satiety when consumed as a starter. *Nutrition Journal*, *10*, 139.
- Ainsworth, B., Haskell, W., Whitt, M., Irwin, M., Swartz, A., Strath, S., et al. (2000). Compendium of physical activities: An update of activity codes and MET intensities RID B-7154-2011. *Medicine and Science in Sports and Exercise*, *32*(9), S498-S516.
- Balducci, S., Zanuso, S., Nicolucci, A., De Feo, P., Cavallo, S., Cardelli, P., et al. (2010). Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: A randomized controlled trial: The Italian diabetes and exercise study (IDES). *Archives of Internal Medicine*, *170*(20), 1794-1803.
- Ballor, D., & Keeseey, R. (1991). A metaanalysis of the factors affecting exercise-induced changes in body-mass, fat mass and fat-free mass in males and females. *International Journal of Obesity*, *15*(11), 717-726.
- Bellisle, F., Clement, K., Le Barzic, M., Le Gall, A., Guy-Grand, B., & Basdevant, A. (2004). The eating inventory and body adiposity from leanness to massive obesity: A study of 2509 adults. *Obesity Research*, *12*(12), 2023-2030.
- Blouet, C., Jo, Y. H., Li, X., & Schwartz, G. J. (2009). Mediobasal hypothalamic leucine sensing regulates food intake through activation of a hypothalamus-brainstem circuit. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *29*(26), 8302-8311.
- Blundell, J. E., Stubbs, R. J., Hughes, D. A., Whybrow, S., & King, N. A. (2003). Cross talk between physical activity and appetite control: Does physical activity stimulate appetite? *The Proceedings of the Nutrition Society*, *62*(3), 651-661.
- Boirie, Y., Dangin, M., Gachon, P., Vasson, M. P., Maubois, J. L., & Beaufrere, B. (1997). Slow and fast dietary proteins differently modulate postprandial protein accretion. *Proceedings of the National Academy of Sciences of the United States of America*, *94*(26), 14930-14935.

- Bryant, E. J., Caudwell, P., Hopkins, M. E., King, N. A., & Blundell, J. E. (2012). Psycho-markers of weight loss: the roles of TFEQ disinhibition and restraint in exercise-induced weight management. *Appetite*, *58*(1), 234-241.
- Bryant, E. J., King, N. A., & Blundell, J. E. (2008). Disinhibition: Its effects on appetite and weight regulation. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, *9*(5), 409-419.
- Church, T. S., Martin, C. K., Thompson, A. M., Earnest, C. P., Mikus, C. R., & Blair, S. N. (2009). Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *Plos One*, *4*(2), e4515.
- Cole, C. (Ed.). (2000). *Encyclopedia of food science and technology*, 2nd edition. (1183-1188.). New York: John Wiley & Sons.
- Cornelissen, V. A., & Fagard, R. H. (2005). Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension*, *46*(4), 667-675.
- Cota, D., Proulx, K., Smith, K. A., Kozma, S. C., Thomas, G., Woods, S. C., et al. (2006). Hypothalamic mTOR signaling regulates food intake. *Science (New York, N.Y.)*, *312*(5775), 927-930.
- Couillard, C., Despres, J. P., Lamarche, B., Bergeron, J., Gagnon, J., Leon, A. S., et al. (2001). Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: Evidence from men of the health, risk factors, exercise training and genetics (HERITAGE) family study. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *21*(7), 1226-1232.
- De Filippis, E., Cusi, K., Ocampo, G., Berria, R., Buck, S., Consoli, A., et al. (2006). Exercise-induced improvement in vasodilatory function accompanies increased insulin sensitivity in obesity and type 2 diabetes mellitus. *The Journal of Clinical Endocrinology and Metabolism*, *91*(12), 4903-4910.
- Donnelly, J., Hill, J., Jacobsen, D., Potteiger, J., Sullivan, D., Johnson, S., et al. (2003). Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women - the midwest exercise trial. *Archives of Internal Medicine*, *163*(11), 1343-1350.
- Donnelly, J., & Smith, B. (2005). Is exercise effective for weight loss with ad libitum diet? energy balance, compensation, and gender differences. *Exercise and Sport Sciences Reviews*, *33*(4), 169-174.
- Dykes, J., Brunner, E. J., Martikainen, P. T., & Wardle, J. (2004). Socioeconomic gradient in body size and obesity among women: The role of dietary restraint, disinhibition and hunger in the whitehall II study. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, *28*(2), 262-268.

- Ferrara, C. M., Goldberg, A. P., Ortmeyer, H. K., & Ryan, A. S. (2006). Effects of aerobic and resistive exercise training on glucose disposal and skeletal muscle metabolism in older men. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 61(5), 480-487.
- Finkelstein, E. A., DiBonaventura, M. d., Burgess, S. M., & Hale, B. C. (2010). The costs of obesity in the workplace. *Journal of Occupational and Environmental Medicine*, 52(10), 971-976.
- Finkelstein, E. A., Trogdon, J. G., Cohen, J. W., & Dietz, W. (2009). Annual medical spending attributable to obesity: Payer- and service-specific estimates. *Health Affairs*, 28(5), W822-W831.
- Finlayson, G., Bryant, E., Blundell, J. E., & King, N. A. (2009). Acute compensatory eating following exercise is associated with implicit hedonic wanting for food. *Physiology & Behavior*, 97(1), 62-67.
- Finucane, M. M., Stevens, G. A., Cowan, M. J., Danaei, G., Lin, J. K., Paciorek, C. J., et al. (2011). National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *The Lancet*, 377(9765), 557-567.
- Flegal, K. M., Carroll, M. D., Ogden, C. L., & Curtin, L. R. (2010). Prevalence and trends in obesity among US adults, 1999-2008. *JAMA : The Journal of the American Medical Association*, 303(3), 235-241.
- Franz, M. J., VanWormer, J. J., Crain, A. L., Boucher, J. L., Histon, T., Caplan, W., et al. (2007). Weight-loss outcomes: A systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *Journal of the American Dietetic Association*, 107(10), 1755-1767.
- Fromentin, G., Feurte, S., Nicolaidis, S., & Norgren, R. (2000). Parabrachial lesions disrupt responses of rats to amino acid devoid diets, to protein-free diets, but not to high-protein diets. *Physiology & Behavior*, 70(3-4), 381-389.
- Georg Jensen, M., Kristensen, M., & Astrup, A. (2012). Effect of alginate supplementation on weight loss in obese subjects completing a 12-wk energy-restricted diet: A randomized controlled trial. *The American Journal of Clinical Nutrition*, 96(1), 5-13.
- Gietzen, D. W., & Aja, S. M. (2012). The brain's response to an essential amino acid-deficient diet and the circuitous route to a better meal. *Molecular Neurobiology*, 46(2), 332-348.
- Hall, W. L., Millward, D. J., Long, S. J., & Morgan, L. M. (2003). Casein and whey exert different effects on plasma amino acid profiles, gastrointestinal hormone secretion and appetite. *The British Journal of Nutrition*, 89(2), 239-248.

- Haslam, D., & James, W. (2005). Obesity. *Lancet*, 366(9492), 1197-1209.
- Hays, N. P., Bathalon, G. P., McCrory, M. A., Roubenoff, R., Lipman, R., & Roberts, S. B. (2002). Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. *The American Journal of Clinical Nutrition*, 75(3), 476-483.
- Hays, N. P., & Roberts, S. B. (2008). Aspects of eating behaviors "disinhibition" and "restraint" are related to weight gain and BMI in women. *Obesity (Silver Spring, Md.)*, 16(1), 52-58.
- Hochstenbach-Waelen, A., Westerterp-Plantenga, M. S., Veldhorst, M. A., & Westerterp, K. R. (2009). Single-protein casein and gelatin diets affect energy expenditure similarly but substrate balance and appetite differently in adults. *The Journal of Nutrition*, 139(12), 2285-2292.
- Hochstenbach-Waelen, A., Soenen, S., Westerterp, K. R., & Westerterp-Plantenga, M. S. (2011). Effects of a supra-sustained gelatin-milk protein diet compared with (supra-)sustained milk protein diets on body-weight loss. *British Journal of Nutrition*, 105(9), 1388-1398.
- Holbrook, E. A., Barreira, T. V., & Kang, M. (2009). Validity and reliability of omron pedometers for prescribed and self-paced walking. *Medicine and Science in Sports and Exercise*, 41(3), 670-674.
- Johnson, F., Pratt, M., & Wardle, J. (2012). Dietary restraint and self-regulation in eating behavior. *International Journal of Obesity (2005)*, 36(5), 665-674.
- Keim, N. L., Canty, D. J., Barbieri, T. F., & Wu, M. M. (1996). Effect of exercise and dietary restraint on energy intake of reduced-obese women. *Appetite*, 26(1), 55-70.
- King, N. A., Caudwell, P., Hopkins, M., Byrne, N. M., Colley, R., Hills, A. P., et al. (2007). Metabolic and behavioral compensatory responses to exercise interventions: Barriers to weight loss. *Obesity (Silver Spring, Md.)*, 15(6), 1373-1383.
- King, N. A., Caudwell, P. P., Hopkins, M., Stubbs, J. R., Naslund, E., & Blundell, J. E. (2009). Dual-process action of exercise on appetite control: Increase in orexigenic drive but improvement in meal-induced satiety. *The American Journal of Clinical Nutrition*, 90(4), 921-927.
- King, N. A., Hopkins, M., Caudwell, P., Stubbs, R. J., & Blundell, J. E. (2008). Individual variability following 12 weeks of supervised exercise: Identification and characterization of compensation for exercise-induced weight loss. *International Journal of Obesity (2005)*, 32(1), 177-184.

- Lejeune, M., Westerterp, K., Adam, T., Luscombe-Marsh, N., & Westerterp-Plantenga, M. (2006). Ghrelin and glucagon-like peptide 1 concentrations, 24-h satiety, and energy and substrate metabolism during a high-protein diet and measured in a respiration chamber RID A-5371-2010. *American Journal of Clinical Nutrition*, 83(1), 89-94.
- Luke, A., Dugas, L. R., Ebersole, K., Durazo-Arvizu, R. A., Cao, G., Schoeller, D. A., et al. (2009). Energy expenditure does not predict weight change in either nigerian or african american women. *American Journal of Clinical Nutrition*, 89(1), 169-176.
- Macfarlane, D. J., & Thomas, G. N. (2010). Exercise and diet in weight management: Updating what works. *British Journal of Sports Medicine*, 44(16), 1197-1201.
- Mellinkoff, S. M., Frankland, M., Boyle, D., & Greipel, M. (1956). Relationship between serum amino acid concentration and fluctuations in appetite. *Journal of Applied Physiology*, 8(5), 535-538.
- Mestek, M. L., Westby, C. M., Van Guilder, G. P., Greiner, J. J., Stauffer, B. L., & DeSouza, C. A. (2010). Regular aerobic exercise, without weight loss, improves endothelium-dependent vasodilation in overweight and obese adults. *Obesity (Silver Spring, Md.)*, 18(8), 1667-1669.
- Miller, W. C., Koceja, D. M., & Hamilton, E. J. (1997). A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 21(10), 941-947.
- Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gotzsche, P. C., Devereaux, P. J., et al. (2010). CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *Journal of Clinical Epidemiology*, 63(8), e1-37.
- Mori, M., Kawada, T., Ono, T., & Torii, K. (1991). Taste preference and protein nutrition and L-amino acid homeostasis in male sprague-dawley rats. *Physiology & Behavior*, 49(5), 987-995.
- Morrison, C. D., Xi, X., White, C. L., Ye, J., & Martin, R. J. (2007). Amino acids inhibit agrp gene expression via an mTOR-dependent mechanism. *American Journal of Physiology. Endocrinology and Metabolism*, 293(1), E165-71.
- Poppitt, S. D., McCormack, D., & Buffenstein, R. (1998). Short-term effects of macronutrient preloads on appetite and energy intake in lean women. *Physiology & Behavior*, 64(3), 279-285.

- Rampersaud, E., Mitchell, B. D., Pollin, T. I., Fu, M., Shen, H., O'Connell, J. R., et al. (2008). Physical activity and the association of common FTO gene variants with body mass index and obesity. *Archives of Internal Medicine*, 168(16), 1791-1797.
- Roumen, C., Corpeleijn, E., Feskens, E. J., Mensink, M., Saris, W. H., & Blaak, E. E. (2008). Impact of 3-year lifestyle intervention on postprandial glucose metabolism: The SLIM study. *Diabetic Medicine : A Journal of the British Diabetic Association*, 25(5), 597-605.
- Sigal, R. J., Kenny, G. P., Boule, N. G., Wells, G. A., Prud'homme, D., Fortier, M., et al. (2007). Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: A randomized trial. *Annals of Internal Medicine*, 147(6), 357-369.
- Smeets, A. J., Soenen, S., Luscombe-Marsh, N. D., Ueland, O., & Westerterp-Plantenga, M. S. (2008). Energy expenditure, satiety, and plasma ghrelin, glucagon-like peptide 1, and peptide tyrosine-tyrosine concentrations following a single high-protein lunch. *Journal of Nutrition*, 138(4), 698-702.
- Solah, V. A., Kerr, D. A., Adikara, C. D., Meng, X., Binns, C. W., Zhu, K., et al. (2010). Differences in satiety effects of alginate- and whey protein-based foods. *Appetite*, 54(3), 485-491.
- Stiegler, P., & Cunliffe, A. (2006). The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports Medicine (Auckland, N.Z.)*, 36(3), 239-262.
- Stunkard, A. J., & Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of Psychosomatic Research*, 29(1), 71-83.
- Trabulsi, J., & Schoeller, D. A. (2001). Evaluation of dietary assessment instruments against doubly labeled water, a biomarker of habitual energy intake. *American Journal of Physiology. Endocrinology and Metabolism*, 281(5), E891-9.
- Trier, C. M., & Johnston, C. S. (2012). Ingestion of nutrition bars high in protein or carbohydrate does not impact 24-h energy intakes in healthy young adults. *Appetite*, 59(3), 778-781.
- Trogdon, J. G., Finkelstein, E. A., Hylands, T., Dellea, P. S., & Kamal-Bahl, S. J. (2008). Indirect costs of obesity: A review of the current literature. *Obesity Reviews*, 9(5), 489-500.
- Tudor-Locke, C., & Bassett, D. R., Jr. (2004). How many steps/day are enough? preliminary pedometer indices for public health. *Sports*, 34(1), 1-8.

- Veldhorst, M., Smeets, A., Soenen, S., Hochstenbach-Waelen, A., Hursel, R., Diepvens, K., et al. (2008). Protein-induced satiety: Effects and mechanisms of different proteins. *Physiology & Behavior*, *94*(2), 300-307.
- Veldhorst, M. A., Nieuwenhuizen, A. G., Hochstenbach-Waelen, A., van Vught, A. J., Westerterp, K. R., Engelen, M. P., et al. (2009a). Dose-dependent satiating effect of whey relative to casein or soy. *Physiology & Behavior*, *96*(4-5), 675-682.
- Veldhorst, M. A. B., Nieuwenhuizen, A. G., Hochstenbach-Waelen, A., Westerterp, K. R., Engelen, M. P. K. J., Brummer, R. M., et al. (2009b). A breakfast with alpha-lactalbumin, gelatin, or gelatin plus TRP lowers energy intake at lunch compared with a breakfast with casein, soy, whey, or whey-GMP. *Clinical Nutrition*, *28*(2), 147-155.
- Visona, C., & George, V. A. (2002). Impact of dieting status and dietary restraint on postexercise energy intake in overweight women. *Obesity Research*, *10*(12), 1251-1258.
- Weigle, D., Breen, P., Matthys, C., Callahan, H., Meeuws, K., Burden, V., et al. (2005). A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. *American Journal of Clinical Nutrition*, *82*(1), 41-48.
- Werle, C. O., Wansink, B., & Payne, C. R. (2011). Just thinking about exercise makes me serve more food. physical activity and calorie compensation. *Appetite*, *56*(2), 332-335.
- Williamson, D. A., Lawson, O. J., Brooks, E. R., Wozniak, P. J., Ryan, D. H., Bray, G. A., et al. (1995). Association of body mass with dietary restraint and disinhibition. *Appetite*, *25*(1), 31-41.
- Zaveri, S., & Drummond, S. (2009). The effect of including a conventional snack (cereal bar) and a nonconventional snack (almonds) on hunger, eating frequency, dietary intake and body weight. *Journal of Human Nutrition and Dietetics : The Official Journal of the British Dietetic Association*, *22*(5), 461-468.
- Zinn, A. R. (2010). Unconventional wisdom about the obesity epidemic. *The American Journal of the Medical Sciences*, *340*(6), 481-491.

Chapter 4

REVIEW OF LITERATURE

The high prevalence of obesity in the US, which has been hovering around 30 to 35% for the past 10 years, (Flegal, Carroll, Ogden, & Curtin, 2010) has drawn national attention and concern. The causes of obesity are multifactorial and include genetic, epigenetic, and environmental components. The rise in obesity from approximately 15% in the late 70's to its current rate has coincided with drastic changes in lifestyle; from active to sedentary and from home cooked meals to fast food diets with amplified portions. Even the average diameter of plates sold in the US has increased from 8.6 inches in the 60's to 12 inches at present (Bogusky A, 2008). Although some people have the genetic capacity to resist weight gain no matter how much they eat, most individuals do not fall into that category. In addition, weight cycling has become a byproduct of this unwanted weight gain as people who struggle to lose weight have an even harder time maintaining weight loss (Svetkey et al., 2008). Moreover, weight cycling comes with its own risks including high blood pressure, unfavorable blood lipid levels, and increased visceral fat accumulation and risk for diabetes mellitus (DM).

Finding ways to alleviate this predicament has triggered health care providers, governmental agencies, and the food and supplement industries to investigate the causes of obesity and provide solutions for weight management. To this end, dietitians and nutrition experts have done extensive research on dietary strategies to help individuals to better control their weight. These tactics include different dietary approaches such as: low energy dense, high protein, low dietary n-6/n-3 ratio, low glycemic index, high fiber, and meal replacement diets.

However, for most, these strategies aimed at losing and maintaining weight loss have been less than fruitful. Thus, it is important to continue to conduct research regarding diet, exercise, and weight loss. The following review of the literature provides background information regarding research that focuses on weight management.

PHYSIOLOGICAL MECHANISMS FOR CONTROL OF SATIETY AND HUNGER IN HUMANS

With the discovery of more than 20 hormones that have been associated with food intake, the comprehension of the control of food intake has become progressively more complex. Ultimately, the brain is the key factor in determining the homeostasis of food intake and body weight by orchestrating complex neuropathways. Specifically, from peptides located inside the brain and after peripheral hormones and peptides cross the blood brain barrier, the hypothalamic nuclei and neuronal circuits are elaborately engaged in the control of appetite (Suzuki, Simpson, Minnion, Shillito, & Bloom, 2010).

Hypothalamic regulation of hunger and satiety. Minute signaling proteins that originate in the arcuate nucleus (ARC) of the hypothalamus act as neurotransmitters or neuromodulators in the paraventricular nucleus (PVN). Two of these are orexigenic or appetite stimulating and include neuropeptide Y (NPY) and agouti-related peptide (AgRP) and two are anorexigenic or appetite suppressing and include cocaine- and amphetamine-regulated transcript (CART), and neuron pro-opiomelanocortin (POMC) (Wernette, White, & Zizza, 2011). In addition, anorexigenic Alpha-melanocyt-stimulating hormone (α -MSH) is produced by POMC (Boston, Blaydon, Varnerin, & Cone, 1997).

NPY is one of the most broadly disseminated peptide in both the central and peripheral nervous systems and it exerts strong orexigenic effects. NPY and

AgRP signaling is decreased during positive energy balance because insulin and leptin impede its expression while growth hormone, ghrelin, and glucocorticoids such as cortisol promote it (L. Zhang, Bijker, & Herzog, 2011). When rats are injected with NPY and are given the same amount of food as control-matched rats, excessive fat gain continues (Fekete et al., 2001); thus, indicating that NPY also impacts energy expenditure which may play a significant part in NPY's ability to trigger weight gain. Additionally, NPY activity intensifies as a result of reduced energy intake during weight loss and maintenance stimulating increased hunger and food intake and decreased daily energy expenditure. Therefore, the persistent increase in NPY expression during weight maintenance after weight loss may explain, at least in part, the high relapse rate from energy restricted dieting (Yu, Deng, & Huang, 2009).

As previously mentioned, appetite suppressing hormones, produced by anorexic neurons of the ARC include cocaine- and amphetamine-regulated transcript (CART) and pro-opiomelanocortin (POMC) which produces alpha-melanocyt-stimulating hormone (α -MSH). The importance of the CART neuropeptide was established in 1995. Endogenous CART peptides are undoubtedly involved as central components in control of eating behavior and it has been indicated that they function as physiological satiety factors and may have both functional and anatomical interactions with the neuropeptide Y system. Interestingly, they are also most likely involved with development of sensory processing, reward and reinforcement, and stress (Lambert et al., 1998). α -MSH acts on melanocortin-4 receptors (MC4R) in the PVN to impede energy intake and enhance energy expenditure. It has been shown that more than 70 mutations of MC4R in humans influence fat mass and account for six percent of

severe, early onset obesity (Tao, 2005). Intriguingly, orexigenic AgRP blocks the inhibition of energy intake by acting as an antagonist to melanocortin receptors (MC3R and MC4R) in the PVN; thus, the activation of AgRP not only increases energy intake, but also blocks the action of anorexic neuropeptide α -MSH. Additionally, NPY has its orexigenic effect not only by activating hypothalamic Y1 receptor and Y5 receptor, but also by inhibiting POMC neurons in the ARC (Roseberry, Liu, Jackson, Cai, & Friedman, 2004).

In addition to the PVN receiving signaling messages from POMC/CART and NPY/AgRP which originate in the ARC, it also processes signals from other anorectic hormones that are derived from within the PVN itself. These include corticotrophin-releasing hormone and thyrotropin-releasing hormone. Additionally, the lateral hypothalamic area (LHA), which is considered the hypothalamic hunger center, contains the orexigenic hormones, melanin-concentrating hormone and orexin (Wynne, Stanley, McGowan, & Bloom, 2005). Likewise, the ventromedial hypothalamic nucleus (VMN) is known as the satiety center. It has been established that this is where, through the signaling of MC4R, brain-derived neurotrophic factor (BDNF) profoundly represses the intake of food.

Additional signals that are involved in the regulation of satiety originate from the gastrointestinal tract, pancreas, and adipose tissue, and are transmitted to the brain through nervous system pathways, peptides and hormones. While gut peptides control food intake via a meal-to-meal manner, long-term management of energy regulation comes from the action of leptin and insulin derived from adipose tissue the pancreatic β , respectively (Suzuki et al., 2010).

Gut hormone regulation of hunger and satiety. Proglucagon, which is expressed in the pancreatic L-cells of the small intestine and the nucleus of the tractus solitarius (NTS) of the brainstem, is a precursor polypeptide that generates four structurally associated proglucagon-derived peptides (PGDPs) including: glucagon-like peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2), oxyntomodulin (OXM), and glucagon. The pancreas mainly produces glucagon while the brain and intestines generate OXM and GLP-1. GLP-1 is produced predominantly in the ileum and colon. There are two known organs where GLP-1 receptors (GLP1R) are found, one is the pancreas where GLP-1 acts as a potent incretin (a substance that escalates the amount of insulin produced and inhibits the gastric emptying rate after eating); thus, GLP-1 levels rise after a meal and fall during the fasted state. The second GLP1R is expressed in the brain and acts to decrease appetite and food intake and suppresses glucagon production (Drucker, 2005). Interestingly, it has been shown that GLP-1R agonism, by a synthetic, GLP-1 mimetic that is DPP-4 resistant (DPP-4 is the enzyme that breaks down GLP-1), can enhance glycemic control in people with Type II DM, with a concurrent decrease in body weight (Cvetkovic & Plosker, 2007; Gutniak, Orskov, Holst, Ahren, & Efendic, 1992). Like GLP-1, OXM is released in the small intestine and in the relative amount of the calorie content of ingested food. It has been shown that OXM elevates energy expenditure and decreases food intake. It is thought that the OXM peptide hormone utilizes the same receptor as GLP-1; however, OXM has 50% less binding capacity as GLP-1 to GLP1R (Suzuki et al., 2010). Glucagon, also a product of proglucagon, is produced by the pancreatic α cells. It is secreted in response to hypoglycemia and triggers liver

gluconeogenesis. It has been reported that the provision of exogenous glucagon in rats can spontaneously reduce meal size (Geary, Le Sauter, & Noh, 1993).

Peptide tyrosine tyrosine (PYY) belongs to the family of the PY peptides which also includes pancreatic polypeptide (PP) and NPY. These are known as the PP-family due to the similar amino acid sequence of PYY (70%) and PY (50%) to NPY. Like GLP-1 and OXM, PYY is secreted from the L-cells of the gut. PYY is an anorexigenic peptide; thus, concentration increases rapidly post-meal ingestion and in proportion to the caloric load. Although PYY binds to other Y receptors in the hypothalamus, it has the highest affinity to Y2R (Adrian et al., 1985). In addition to the anorectic effects of PYY, it also has been shown to escalate energy expenditure. PYY levels rise instantly after food ingestion; however, obese people have been shown to have a blunted increase of PYY (Ashby & Bloom, 2007). PP is released from the pancreatic F-cells. Like PYY, PP levels rise rapidly after a meal has been shown to decrease food intake via the Y4R in the hypothalamus and brainstem.

Amylin, also known as islet amyloid polypeptide, is co-secreted with insulin from the β cells of the pancreas in response to food ingestion. The anorectic effects of amylin are due to both central and peripheral mechanisms and circuitously by impeding gastric emptying. The central mechanism of action appears to be due to its inhibition of NPY and also by its link to the serotonergic, histaminergic, and dopaminergic system (Reda, Geliebter, & Pi-Sunyer, 2002).

Cholecystokinin (CCK) is secreted by the duodenum. It has been well recognized as an anorexigenic hormone that works in conjunction with ghrelin to mediate food intake. In addition, CCK works synergistically with amylin, leptin, and GLP-1 to enhance the satiety signaling effect (Stengel & Tache, 2011).

Ghrelin is an acylated peptide and the only known hormone originating from the gut that is orexigenic. More than ninety percent of ghrelin is secreted by the stomach, duodenum, and parts of the gastrointestinal tract (Somogyi et al., 2011). It was first reported in 1999, when it was isolated from rat gut and first identified as stimulator for growth hormone released in the pituitary (Kojima et al., 1999). Ghrelin levels rise during fasting and fall rapidly during the fed state. Injections of ghrelin in both the peripheral and central nervous system result in increased energy intake and weight and decrease lipid utilization (Nakazato et al., 2001). Ghrelin has been shown to increase c-fos activity in the ARC NPY/AgRP neurons with peripheral administration and the effect of ghrelin is eliminated with the ablation of these neurons. In addition to appetite control, it has been established that ghrelin promotes lipogenesis and suppresses adipose tissue degradation resulting in rises in body weight and adiposity (Somogyi et al., 2011). Cummings et al. (2002) found a 24% increase of 24-hour ghrelin concentration with a 17% diet stimulated weight loss ($P = 0.006$), but post-gastric bypass patients have 77% lower ghrelin levels compared to normal weight controls ($P < 0.001$). They also found that after gastric bypass, the usual flux of ghrelin levels before and after a meal and diurnal rhythm levels were also absent.

Adipocyte and pancreatic regulation of hunger and satiety. Initially, obese gene coding for leptin was discovered in white adipose tissue in 1994 (Y. Zhang et al., 1994). Leptin is synthesized in adipose tissue in the amount relative to adipose tissue mass (Considine et al., 1996). It is secreted in a diurnal pattern and it is found to hit its peak level at night; thus, levels do not change acutely with ingestion of a meal (Schoeller, Cella, Sinha, & Caro, 1997). Leptin crosses the blood brain barrier where it exerts its anorectic effect by activating

POMC/CART neurons and inhibiting NPY/AgRP neurons. Although it has been shown that leptin administration in leptin-deficient *ob/ob* mice can reverse hyperphagia and obesity (Halaas et al., 1995), human obesity, which is frequently correlated with elevated leptin levels, does not respond to exogenous administration (Suzuki et al., 2010). Like leptin, insulin is anorectic and is excreted in the amount relative to adipose tissue mass. The β cells of the pancreas synthesize insulin and levels rise sharply after food ingestion. Insulin crosses the blood brain barrier and acts on the ARC where it restricts the fasting-induced mRNA NPY expression and boosts mRNA POMC levels (Benoit et al., 2002; Schwartz et al., 1992).

SUBJECTIVE AND OBJECTIVE MEASUREMENTS OF SATIETY

One of the most commonly used tools to subjectively measure satiety is the visual analogue scale (VAS). The VAS consists of a 100 mm line anchored by two end-points that indicate motivation to eat. For example, a bipolar VAS consists of two end-points labeled at the top with “Extremely Hungry” and at the bottom “Extremely Full”. A unipolar scale would be labeled “Extremely Hungry” at the top and “Not at all Hungry” at the bottom (Merrill, Kramer, Cardello, & Schutz, 2002). The Eating Inventory (originally known as the Three-Factor Eating Questionnaire), designed by Stunkard & Messick (1985), is another primary tool used to assess perceived Hunger, Disinhibition (lack of control of food consumption), and Restraint (deliberate control of food intake). Studies have shown that weight loss is significantly correlated with increased Restraint scores and decreased Disinhibition and Hunger scores (Foster et al., 1998). In a large population based study, Hainer et al. (2006) found Restraint and Hunger

scores were significantly associated with those who have diabetes but found no correlation between Restraint scores and BMI in women.

Objective measurements of satiety include measuring the previously mentioned peptides and hormones involved in the satiety cascade such as CCK, PYY, GLP-1, ghrelin, and insulin. In addition, blood glucose levels act as a short-term biomarker for satiety (de Graaf, Blom, Smeets, Stafleu, & Hendriks, 2004). Measuring levels of these peptides and hormones is used extensively in the preload test condition. In addition to these conventional objective measures of satiety, the use of *fMRI* to investigate brain responses to visual food cues is now being practiced (Y. Zhang, von Deneen, Tian, Gold, & Liu, 2011).

The use of preloads to assess satiety. The preload experimental study design is used to determine the control of food intake on the next meal eaten; thus, the satiety effects of the nutritional properties contained in the preload can be assessed. To be clear, satiety refers to the post-ingestion effect a type food can produce and usually refers to the resulting magnitude of the drive, either time delay or amount eaten, for the next meal. Thus, the outcome measure can be either the spontaneous time delay or the calorie intake at the next meal. Satiation refers to the processes involved that lead to the termination of a meal or the feeling of being comfortably full (de Graaf et al., 2004; Rolls & Hammer, 1995).

This type of preload-test meal protocol measures short-term control of food intake and the use of it has become wide spread due its perceived simplicity. The repeated measure, within subject study design is thought to be the optimal method to determine the satiety effects of the preload. However, one drawback of the pre-load study design it that it is predisposed to Type 2 errors.

Therefore, special care should be given when selecting the sample size, along with assuring that physical activity, antecedent energy deficit and post-preload meal composition are all recorded. Furthermore, usually the subjects are not told of the satiating effects the preloads are expected to confer, but this information would be very relevant in free living conditions (Blundell et al., 2010). Compared to buffet style, the single course method can lead to better assessment of the effectiveness of the preload because a high variety in food selection increases food intake, and the single course method is more reflective of the real life situations most people experience, unless the goal of the study is to test food preference rather than energy intake (Hetherington, Foster, Newman, Anderson, & Norton, 2006). Further, the time delay between the preload and the test meal has proved to be an issue. For instance, G. Anderson & Moore (2004) found a significant decrease in EI after ingestion of a 50 g liquid whey preload at 1 hour post-treatment compared to the control treatment (water), but when repeating this study on a different day, no difference between the preload and the water control was seen after a 2 hour time lapse. In addition, volume, energy content, energy density, viscosity and palatability of the preload can all be confounding factors. The two main preload study types include those done short-term under supervised conditions; thus, increasing internal validity, and those done long-term on free-living subjects, which increases external validity; however, only the short-term studies have been extensively published.

Most preload of the published pre-load studies have investigated the satiating effects of protein (PRO) to carbohydrate (CHO) and fat. Of the 13 reported studies analyzing the effects of liquid beverages either high in PRO or CHO, six reported reduced energy intake at the next meal with the high PRO

preload. The remaining studies resulted in no difference between PRO and CHO (Poppitt et al., 2011).

One, recent, well designed preload study compared the satiating effects of PRO, CHO and fat in 60 lean (BMI \leq 25) men and women, 18 to 60 years, on four separate occasions including a control day (Potier et al., 2010). The preload was a 245 kcal hot chocolate drink that contained 50 g whey PRO, 50 g maltodextrin, or 22.3 g of a 50% palm and 50% soy oil blend, that had the same palatability, viscosity, energy density and volume. The results showed the only difference in EI was at the test lunch; subjects consuming the CHO preload ate the least and their intake was significantly less compared to the fat preload; the fat preload resulted in the highest caloric intake at lunch. In addition, there was no difference in EI when the test meal was eaten immediately after consumption of the preload compared to a one-hour time lapse. Of interest is that energy intake for the entire day was greater on the day the preload was administered compared to the control day and this difference reached significance on the day the fat preload was ingested compared to the control day ($P < 0.05$). Although not statistically significant, the CHO preload test day resulted in the least daily calories consumed compared to the PRO and fat preload days. Thus, the participants in the study did not fully compensate for the preload calories throughout the entire day.

Examples of studies using solid preloads, include one conducted using 15 healthy, young male subjects (Fischer, Colombani, & Wenk, 2004). They were tested in a cross-over fashion on three separate occasions to assess the effect of PRO, fat and a med/high glycemic index CHO, on satiety, energy intake and metabolic indices. The subjects were provided pre-test day evening meals and

avoided alcohol and caffeine. The preloads consisted of isocaloric, 400 kcal emulsions in a cream form of just one specific macronutrient, that were equivalent in volume, color, texture and taste. The results showed that, despite the increased hunger rating the fat preloads conferred compared to PRO and CHO, the energy intake at the following buffet style lunch was not different between the groups. In addition, intake, for CHO, PRO or fat intake as percentages of total calories was similar at the lunch meal. In evaluating these results, the authors explore the possibility that the 4-hour time delay until lunch was served was too long, the buffet style venue was inappropriate, and the subject selection of young healthy males, notorious for voracious appetites, may have been inappropriate.

A second, crossover design study examined the satiety effects of PRO, CHO, fat, and alcohol preloads in 12 lean women (BMI < 25kg/m²) (Poppitt, McCormack, & Buffenstein, 1998). This preload design was interesting because the preload (~240 kcal beverage) was fed along with a fish and potato pie (~240 kcal), and the test meal was served 90 minutes later, plate style and in surplus of expected consumption. They found the subjects who ate the PRO preload reported a higher level of satiety and ate significantly less at the test meal ($F = 3.11$, $P < 0.05$) compared to the other macronutrients; increased intakes were 12.3%, 14.2%, and 20.8% higher for CHO, fat and alcohol, respectively.

Overall, the results of the studies examining short-term satiety and EI effects of PRO, CHO and fat are mixed, but seem to favor PRO, and to a lesser extent CHO, over fat as most effective in suppressing appetite. Reasons for the inconsistent results include the form of the preload (either liquid or solid), (Pan & Hu, 2011), or the source of PRO (whey, egg albumin, soy etc). (G. Anderson &

Moore, 2004), CHO (maltodextrins, glucose, sucrose etc.) or fat (LC, MUFA etc) (French, 2004).

There have been many preload design studies investigating the effects of either dietary or functional fiber on subsequent EI (Wanders et al., 2011). For instance, a study by Monsivias, Carter, Christiansen, Perrigue, & Drewnowski (2011) of 38 men and women, compared the satiating effect of ~12 g of resistant starch 60, soluble fiber dextrin, polydextrose, and soluble corn fiber to two control preloads of either an isocaloric, low-fiber or a low-calorie, low-fiber preload. They found only dextrin was associated with significantly reduced EI relative to the isocaloric non-fiber control at the next test meal (mean decrease of -72 kcal, $P = 0.023$). Perrigue, Monsivais, & Drewnowski (2009) conducted a preload study with 28 men and women, examining the effects of 6 g inulin. The inulin was incorporated into either a high-calorie yogurt (440 kcal; 0.9 Kcal/g) or a low-calorie yogurt (180 kcal; 0.4 Kcal/g) beverage, and both yogurts without inulin. All 4 yogurts were compared to an equal volume of 180 kcal orange juice and a no beverage control day. The test meal was served 120 min. post-preload administration. The results showed that, among the four yogurt drinks, there was no statistical difference in suppressing test-meal energy intake. However, the combined calories from the test meal and either the low-calorie, no-fiber and low-calorie with fiber yogurts, and orange juice performed similarly, and combined calorie intake was significantly lower than with the high calorie yogurt treatments ($P < 0.05$), but overall calorie intake (preload plus test meal) was significantly lower for the no beverage treatment compared to all other treatments ($P < 0.05$). Another study (King, Craig, Pepper, & Blundell, 2005) examined the effect of polydextrose and xylitol containing yogurts compared to a sucrose containing

control yogurt in a free living design of 8 young males and females, of over the course of 10 days for each treatment. After eating a fixed breakfast, EI at lunch was tested at the research unit on the 1st (baseline) and 10th day for each treatment with a 90 min. lapse between the pre-load and test meal. The results showed the only significant difference in test-meal EI was between the polydextrose vs. control ($P = 0.002$), when the discrepancy for the energy content of the preload was taken into consideration. Freeland, Anderson, & Wolever (2009) compared insoluble wheat bran fiber preloads of high-fiber (44 g) and low-fiber (1 g) cereal, both with and without the addition of 41g glucose in 16 lean, young males. The findings showed that 60 minutes after ingestion, the high fiber cereal without glucose significantly decreased total energy intake (preload plus test meal) compared to the low-fiber cereal with or without glucose ($P = 0.02$). However, when repeating this protocol with 16 similar test subjects, there was no difference found in total energy consumption (preload plus test meal) between the groups 2 hours past preload ingestion. In a separate crossover study, Kristensen et al. (2010) recruited 20 men and women to test the effect of isocaloric, whole grain bread (11.7g fiber) or pasta (5.0g fiber) and refined grain bread (3.6g fiber) or pasta (2.2g fiber) at breakfast on EI at lunch three hours later. The results showed, with a sufficient time lapse, there was no difference in EI at the subsequent lunch meal. However, the authors comment they believed this may be due to a Type II error resulting from the small sample size and large inter-individual variations in energy intake at the test meal. The inconsistent results from the previously mentioned studies illustrate the difficulty in drawing any unambiguous conclusions regarding high fiber diets, either functional or naturally occurring, and their ability to impact energy intake. This is probably due

to the wide variation of physiochemical properties (viscosity, gelling capacity, fermentability, etc.) found in assorted fibers that may influence appetite and calorie intake differently (Boers, 2009).

The effect of energy density on calorie intake has also been studied in the context of meal preloading. Barbara Rolls is one of the leading researchers in the field of the effect of energy density on energy intake. In one of her early preload studies (Rolls et al., 1998), the satiety effect of incrementally decreasing the energy density of a 300, 450, or 600 ml, milk-based preload, all containing 499 kcals vs. a no-preload control day was assessed in 20 lean men. The drinks were equal in macronutrient content and consumed 30 min. prior to the buffet style lunch and a buffet style dinner >4 hours after the lunch meal. The results showed the 600 ml pre-load was superior in suppressing EI at the following lunch and dinner compared to the lowest energy dense drink ($P \leq 0.022$). Also, compared to the no preload day, the 600 ml preload conferred an average decrease of 318 calories (NS) including the preload, lunch and dinner calories,. A separate crossover study by the same researcher (Rolls, Bell, & Thorwart, 1999) examined the effect of energy density on EI in 24 lean women. The three, 270 calorie preloads treatments consisted of either incorporating and extra 10.2 ounces of water into casserole ingredients to make a soup, serving the casserole containing 1 oz. water with water served separately as a 12.5 oz. beverage, and the same casserole with no water served as a beverage. These three interventions were compared to a no preload treatment on 4 separate days, 17 minutes prior to lunch. They found the subjects ate ~27% less calories at lunch ($P < 0.05$), and felt fuller after consuming the soup compared to the two other preloads. And compared to the no preload day, when the subjects consumed the

soup preload they ingested an average of 355 calories less for lunch (NS), thus fully compensating for the preload calories. However, there was no difference among the four groups for calorie intake when the preload plus lunch and dinner intake was calculated vs. the no preload day. Hence, it appears that incorporating water into the food to reduce energy density, such as in soup, has an acute impact on EI compared to serving a casserole with or without a water beverage, but the effect is not sustained throughout the day.

An additional, recent crossover, preload trial (Blatt, Williams, Roe, & Rolls, 2012) examined the effect of an entire day of pre-portioned solid entrees, containing reduced energy density (64%) and/or energy content (64%, 1 kcal/g) compared to a standard control (100%, 1.6 kcal/g) on subsequent, ad libitum intake from food served after each meal. Sixty-eight weight stable ($\leq \pm 4.5$ kg over the last 6 months) men and women consumed the meals during a weekday for 4 consecutive weeks; the women's entrees contained 30% fewer calories than the men's. They found that for men, decreased energy density (equal calories, larger portion) and energy content (smaller portion) entrees resulted in reduced discretionary calorie intake ($P = 0.003$), but the decrease in total daily calorie intake was greatest on the day when the concurrently reduced energy content- and density entrees were consumed (-445 ± 47 kcal/d, $P < 0.0001$). For women, the pattern was similar, with the entrees having a combined reduction in energy density and content conferring the greatest reduction in daily energy intake (-289 ± 35 kcal/d, $P < 0.0001$). Thus, it appears the low-energy density diet strategy for decreasing spontaneous calorie intake is enhanced when decreased portion sizes are offered. Additionally, the effect is acute rather than

sustained indicating that this type of eating pattern must be maintained throughout the day in order to be effective.

Lastly, the effect of glycemic index (GI) and subsequent EI has also been researched. Soenen & Westerterp-Plantenga (2007) analyzed the effect of isoenergetic, 800ml drinks (~360 kcals), including high-fructose corn syrup, sucrose, whole milk, and a diet-drink control preload on subsequent EI 50 min. past preload ingestion in 30 lean men and women. The study showed that there was no difference between test treatments and EI at the test-meal. These results were in agreement with a preload study by Almiron-Roig and Drewnowski, (2003) that included 32 men and women. They found no significant difference in EI 135 min. after the ingestion of 248 kcal, 20-oz beverages of cola, 1% milk or orange juice. An additional, a crossover study of 8 subjects (G. Anderson, Catherine, Woodend, & Wolever, 2002) found no significant difference in subsequent EI at 60 min. past the treatment when comparing four, 300 kcal, 200 ml drinks that conferred increasing GI response levels from low to high: 80% fructose-20% glucose drink (low GI), 100% sucrose, 100% polycose and 100% glucose (high GI), to a sucralose control. Interestingly, they reported an inverse relationship in the high vs. low glycemic-index preloads and EI at the subsequent test meal which supports the glucostatic theory for food intake regulation which postulates that an increase of blood glucose activates satiety peptides and thus the termination of eating (Mayer, 1953). In conclusion, these three studies refute the idea that consumption of high-glycemic-index drinks promote increased energy intake (Ludwig, 2000; Roberts, 2000) at least when a meal is consumed 50-135 minutes after a 250-360 kcal preload is consumed.

BIOLOGICAL INFLUENCES OF WEIGHT REGULATION

The role of genetics. The effect of biology and genetics on the impact of obesity rates are made clear when examining twin studies. For instance Bouchard et al. (1990) overfed 12 pairs of young, male identical twins for a 100 day period to examine the genetic factors that may lead to divergent weight gain patterns. After overfeeding by 1,000 calories six days of the week, the researchers found a mean increase of 8.1 kg, with a range of 4.3 to 13.3 kg, and these data were not randomly distributed. Moreover, they found a substantial variability in weight gain between twin- but not within twin pairs. In addition, they found the accumulation of visceral fat was not predicted from the increase in body mass or body fat increases, thus showing that different sites of fat deposition are genetically determined as well.

Also, Levine, Eberhardt, & Jensen (1999) described the genetic propensity to increase nonexercise activity thermogenesis (NEAT) as being a major determinant of weight gain when overfeeding 1,000 calories/day for 8 weeks. They found that with overfeeding, differences in the predisposition to increase NEAT was the primary mediator to resist fat deposition. Later, Levine et al. (2005) studied posture allocation in relation to obesity and found that mildly obese subjects tend to sit 164 min longer per day than their lean counterparts and that body movement was negatively correlated with fat mass; thus, the obese subjects would have expended an average of 352 extra calories/day if they would have had the same posture allocation as the lean subjects.

In addition to the twin studies supporting the idea of biology playing a key role in the development of obesity, “the thrifty gene” hypothesis was proposed by geneticist J.V. Neel (1962). The thrifty gene allows people to economically gather

and metabolise food resulting in efficient adipose tissue deposition during times of plentiful food supplies. This would be beneficial for our hunter-gatherer ancestors because they would have better survival rates during times of scarcity. However, since times of famine are not typically experienced with our modern food supply, wide-spread obesity rates have resulted. Nevertheless, this theory has been disputed due to the fact that during times of famine, too few individuals die of starvation, and the loss of the most vulnerable, including the very young and old, would not impact the genetic passing of the thrifty gene.

Genetic differences related to biochemical parameters include Neuropeptide Y (NPY), and the fat mass and obesity associated gene (FTO) variants. NPY is an orexigenic peptide found paraventricular nucleus (PVN). In a large correlational study, van Rossum, Pijl, Adan, Hoebee, & Seidell (2006), found that for young males, but not females, the NPY Leu7Pro polymorphism was associated with higher BMI, and they had a 3.3 odds ratio (OR) for increased risk of being overweight at baseline compared to non-carriers of the allele. Regarding the FTO gene variant and obesity, Rampersaud et al. (2008) found that twenty-six FTO single nucleotide polymorphisms (SNPs) were associated with increased BMI, and their findings confirmed previous studies showed there was a correlation between the most frequent FTO SNP's and greater BMI. Interestingly, they found for those having the susceptible FTO genotypes, expending an additional 980 kcals/day for men and 860 kcals/day for women negated the expression of the SNPs. An additional review article; (Qi & Cho, 2008) describes a large number of both correlational and intervention studies identifying diet and lifestyle interactions with a plethora of gene variations and an increased risk of obesity.

The set point theory. The “set point theory” stems from the observation that over a wide variety of EI, body weight is sustained much more steadily than one would expect over the long term (Farias, Cuevas, & Rodriguez, 2011). In addition, the propensity to regain weight back after weight loss may be due to the homeostatic adaptations to maintain fixed fat stores and body weight (Bennett, 1995). This theory can be affirmed by analyzing the results of the studies that show the change in metabolic rate after weight gain or loss. For instance, Leibel, Rosenbaum, & Hirsch (1995) measured 24-hour total, resting and non-resting energy expenditure in obese and non-obese subjects after gaining 10% or losing 10% or 20% of their baseline body weight. They concluded that subjects would need to consume an average of 500 calories more than predicted to maintain their weight gain and 300 calories less than predicted to maintain a 10% or 20% weight loss. They also found that non-resting energy expenditure (EE) was affected the most for both weight gain and weight loss. In addition, Rosenbaum, Hirsch, Gallagher, & Leibel (2008) compared the EE of obese and lean subjects of usual weight to those maintaining a recent weight loss (5-8 weeks) of $\geq 10\%$ and those who had lost weight of $\geq 10\%$ and sustained the weight loss for over 1 year. They found that for both recent and at 1 year of sustained weight loss, EE was significantly lower than the controls that were matched for usual weight, mostly due to decreased non-resting EE.

Some of the adaptive effect may be due to increased NPY activity that accompanies decreased energy intake during weight loss dieting results in increased appetite and food intake and decreased daily EE. Therefore, the persistent increase in NPY expression during weight maintenance after weight

loss may, in part, explain the high relapse rate from energy restricted dieting (Yu et al., 2009).

Additional data shows there is research, although somewhat limited, that people can lose weight and keep it off, but with substantial effort. For instance, Klem, Wing, McGuire, Seagle, & Hill (1997) reported data from the Nation Weight Control Registry. This data base was developed for individuals who have successfully kept off over 30 lbs for ≥ 1 year. They found that great strides were made to maintain weight loss, and portion control was vital. Of the individuals who did manage to maintain weight loss, 44% counted calories and limited their quantity of food intake. In addition, they expended an average of 2,827 kcal per week doing physical activity.

Epidemiological data (Flegal et al., 2010) shows a now seemingly permanent increase in the average weight of the US population that took place from 1980 through early 2000's, triggered by changes in lifestyle patterns and the obesogenic environment, including increased portions, decreased exercise and high stress levels. Ostensibly, this lasting increase in weight would defy the set-point theory. However, it is possible that the set-point theory is not disproved by the average 20 lb. increase in weight over the past 20 years, but that the set-point can change over time. The average 20 lb. weight gain could simply be a result of people hitting the top of their biological weight range, due to the high availability of food and sedentary lifestyles many Americans lead.

Adaptive thermogenesis. For some people it appears that being overweight is a natural state and, after weight loss, their metabolic rate is decreased to a level that is much greater than would be expected. This phenomenon is referred to as adaptive thermogenesis and can be depicted by

several studies. For instance, Keeseey (1993) reported that for obese rats, when body weight was reduced by caloric restriction, a 14.9% weight loss resulted in a resting metabolic rate (RMR) decrease of 24.6%. As previously mentioned, Leibel et al. (1995) found that a 10% weight loss in obese (BMI > 28.0) and non-obese individuals results in a reduced average resting energy expenditure of -4 (obese) and -3 (non-obese) kcal/kg fat free mass (FFM) and a non-resting energy expenditure of -3 kcal/kg FFM for both obese and non-obese subjects. In addition, the results for observed – predicted energy expenditure was significantly lower ($P < 0.05$) for total and non-resting for both obese and non-obese subjects. Further, Goldsmith et al. (2010) found greater skeletal muscle work efficiency with weight loss due to the change in cytochrome oxidase/phosphofructokinase enzyme activity when energy is expended at levels similar to those of daily activity. Finally, Tremblay and Jean-Philippe (2009) found that adaptive thermogenesis with initial weight loss resulted in resistance to further weight loss in men. Specifically, at a weight plateau, they showed that diminished thermogenesis at rest represented 30.9% of the compensation of energy balance. Thus, adaptive thermogenesis appears to be a sizable explanation for the weight regain that many people experience after going off a weight loss diet.

Weight perturbations. The effect of weight perturbations on weight regulation can be exemplified when evaluating weight cycling (also called yo-yo dieting) which is a term used to describe a pattern of gaining and losing weight. Weight cycling can be a result of intentional or unintentional weight loss, or as a consequence of seasonal weight fluctuations as seen in athletes for the purpose of making a certain weight for performance. Unintentional weight cycling may be

due to intermittent food availability, or recurrent chronic diseases with episodic remissions. There is no standard definition for weight cycling, but severe weight cycling can be described as a weight loss and regain of ≥ 5 kg at least three times, while mild weight cycling would be equal to loss and regain of < 5 kg once or twice. It is probable that various factors influence the consequences of weight cycling including length and amplitude of the cycle as well as the number of cycles.

Diaz, Mainous, & Everett (2005) evaluated population-based data ($n = 8479$) from the National Health and Nutrition Examination Survey (NHANES) and NHANES I epidemiologic follow-up study. They specifically considered individuals who experienced weight fluctuation, defined as the sum of deviations > 5.04 BMI units but having < 3.0 BMI unit variation from baseline, for the duration of almost 20 years. After eliminating those with debilitations or poor health, those with weight fluctuations had a 1.83 increased relative risk (RR) for all cause mortality compared a 1.35 RR in weight stable, obese individuals. Weight cycling has also been related to renal cancer from the data of 140,057 females, 50 to 79 years, enlisted the Women's Health Initiative trial (Luo et al., 2007). Weight cycling was categorized by the number of times weight went up and down more than 10 lbs. excluding pregnancy or illness. This correlational data showed that, after correcting for total energy intake, smoking, age, oral contraceptive use, hypertension (HTN), and waist-hip ratio, compared to the weight stable women, those who weight cycled more than 10 times had an increased RR of 2.6 for renal cell carcinoma.

When examining the weight cycling effect from the Women's Ischemia Syndrome Evaluation study of 485 women with cardiovascular disease (CVD),

Olson et al. (2000) found weight cycling was associated with a 7% decrease in high density lipoprotein cholesterol (HDL-C). And for those who weight cycled the most the effect was stronger.

Guagnano et al. (2000) compared 258 obese women with or without HTN and found that in obese women, weight cycling (a loss of at least 4.5 kg per cycle at least 5 times in the last 5 years due to dieting) had a significant increase in the chance of having HTN and increased waist circumference compared to controls.

In a single-arm trial (Kajioka, Tsuzuku, Shimokata, & Sato, 2002) lean, young women were prescribed a < 1,200 kcal/d diet to lose > 4 kg over 30 days, then regain \geq the lost weight over the next 14 days eating ad libitum, and once again to lose > 4 kg over the final 30 days. At 180 days, after 106 days eating ad libitum and returning to their approximate baseline weight, resulted in the women having significant increases in triglyceride levels, both systolic and diastolic blood pressure, and significantly lower resting metabolic rate and lean body mass levels. In a review article, Montani, Viecelli, Prevot, & Dulloo (2006) propose that although the metabolic pathways for increased CVD mortality from weight cycling are not fully understood, enhanced weight gain, total body and visceral fat accumulation, alteration in the composition of tissue lipids, insulin resistance and type 2 diabetes, dyslipidemia, and hypertension to be the primary risk factors for weight regain after weight loss.

THE EFFECT OF MACRONUTRIENTS ON SATIETY AND CALORIE INTAKE

Glycemic index and glycemic load. Jenkins et al. (1981) proposed the idea of the glycemic index (GI). It has been formally defined as a measurement of the incremental area under the curve for blood glucose response after ingestion a test food containing 50 g of digestible carbohydrates divided by the

area under the curve after ingesting 50 g of glucose. Thus, foods can be ranked according to their GI value. Glycemic load (GL) is determined by multiplying the glycemic index value of a food by the grams of digestible carbohydrates the food contains divided by 100. One of the main interests of GI in relation to weight control stems from the idea that low GI foods may confer potential benefits by decreasing food intake through increased satiety (Ludwig, 2000). A recent review article assessed the data from clinical trials with the aim of determining the effectiveness of low GI diets. Niwano et al. (2009) concluded that data from short term studies (1-3 days) support the hypothesis that satiety was prolonged when low-GI foods were ingested, but for long term studies, there is no conclusive evidence that low GI-foods are a valid predictor of neither leptin or ghrelin status, nor of satiety or hunger. Interestingly, they pointed out that this may be related to the greater ability of high-GI foods to suppress ghrelin levels and that ingestion of low-GI food may not inevitably confer a rise in satiety level due to attenuated stimulation of ghrelin and insulin modulated leptin release.

In addition to satiety, weight status in relation to GI and GL has been extensively evaluated but the reported outcomes are conflicting and the topic has triggered controversy in the public health and scientific arena. Those who support eating a low-GI diet for management of obesity include Brand-Miller, McMillan-Price, Steinbeck, & Caterson (2009). These researchers attribute the benefit of a low-GI diet to lower post-parandial insulin levels which may change substrate utilization by shifting metabolism to enhance fat- over carbohydrate oxidation and by the promotion of satiety that low-fat, low GI foods yield due to slower absorption and digestion rates. A recent meta-analysis (Thomas, Elliott, & Baur, 2007) of 202 subjects pooled from six randomized controlled trials

(Bouche et al., 2002; Ebbeling, Leidig, Sinclair, Hangen, & Ludwig, 2003; Ebbeling et al., 2005; McMillan-Price et al., 2006; Slabber, Barnard, Kuyl, Dannhauser, & Schall, 1994; Sloth et al., 2004) ranging from five weeks to six months found that the subjects on the low- GI or GL diets lost an average of 1 kg more than those on control diets (calorie restricted, low-fat or other) and the low GI/GL dieters had improved blood lipid profiles compared to the control groups. They also emphasized that for the studies where all the participants were obese (Ebbeling et al., 2003; Slabber et al., 1994) the average weight loss was even greater (-4.2 kg vs. -1.1 BMI units, low GI diets vs. control, respectively).

A recent, well designed, randomized controlled trial (RCT) that was not considered for the aforementioned meta-analysis (Das et al., 2007), resulted in contradictory findings. These researchers designated 34 overweight participants to either a high-GL (60% CHO, 20% PRO, 20% fat), or low-GL (40% CHO, 30% PRO and 30% fat) diet with a 30% caloric restriction (CR) for both groups, in which all food was provided for the first 6 months of the trial. After 6 months both groups lost 9% to 10% body weight and there was no difference between the groups. For the next 6 months the 30% CR diets were self-selected but the participants were instructed to follow their previous regimen. At one year past baseline, both groups lost ~8% body weight. In addition, they found no differences in body fat, RMR, or perceived hunger or satiety between the two groups. In concurrence with this study, a recent report (Howlett & Ashwell, 2008) from The European Branch of the International Life Sciences Institute workshop, which debated the notion that decreased GI and/or GL intake is beneficial for weight loss, concluded there are negligible data backing the position that a low GI/GL diet is an advantageous weight loss strategy. An additional review article

(Gaesser, 2007) reported results from a large majority of the intervention and all epidemiological data showed no negative consequence from high GI diets on BMI status. Interestingly, it was found from the epidemiological studies that high GI intake was either not associated with or had an inverse relation to BMI. As for public health recommendations, currently the Academy of Nutrition and Dietetics position states “A low glycemic index diet is not recommended for weight loss or weight maintenance as part of a comprehensive weight management program, since it has not been shown to be effective in these areas (Seagle, Strain, Makris, Reeves, & American Dietetic Association, 2009).”

Dietary fiber. Dietary fiber is defined as an assortment of plant based substance impervious to digestive enzymes in humans and most animals (Burton-Freeman, 2000). Basically, fibers have been categorized as either water soluble fiber, such as beta-glucans found in barley and oatmeal and fermented in the colon, or water insoluble fiber, which consist of the undissolvable parts of plant walls found mostly in whole grains and vegetables. Possibilities as to why a high fiber diet may be conducive to weight loss include: the influence of food volume and energy density (Rolls, 2009), increased satiety (Cani, Dewever, & Delzenne, 2004; Sanchez, Miguel, & Aleixandre, 2012), slowed gastric emptying and decreased absorption, hampered glycemic response (Jonnalagadda et al., 2011), increased chewing (Li et al., 2011), or simply that individuals who eat high fiber diets are prone to be more health conscious.

Several review articles analyzing epidemiological data report that, particularly from whole grain consumption, there is an inverse relationship between high dietary fiber intake and BMI (J. Anderson et al., 2009; Jonnalagadda et al., 2011; Williams, Grafenauer, & O'Shea, 2008). Moreover, an

additional systematic review found that higher viscous fibers were more effective in reducing appetite and energy intake compared to lower viscous fibers (Wanders et al., 2011). Howarth, Huang, Roberts, & McCrory (2005) analyzed data from participants in the Continuing Survey of Food Intakes by Individuals (CSFI) I and found for women, mean BMI is increased with low fiber intake but decreased incrementally as dietary fiber intake increased as long as dietary fat intake fell below 35%. NHANES data from 1999-2004 showed an inverse relationship between increased fiber intake and BMI status (O'Neil, Zanovec, Cho, & Nicklas, 2010). Howarth et al. (2001) reviewed 22 qualifying RCTs of greater than 4 weeks duration published between 1959 and 1993. They found in 14 of the 22 studies analyzed, higher fiber intake (either mixed, soluble or insoluble fiber) resulted in significantly greater weight loss relative to the low fiber controls. The 12 ad libitum trials reviewed seemed to confer greater weight loss compared to fixed calorie diets (-1.9 kg vs. -1.3 kg, respectively). C. Smith & Tucker (2011) identified four, more contemporary trials published between 2003 and 2008, in which weight change in relation to cereal fiber intake was an endpoint (Behall, Scholfield, & Hallfrisch, 2004; Howarth et al., 2003; Lee et al., 2006; Queenan et al., 2007). Two of the three short-term trials reviewed (3-6 weeks in length) found no change in weight; however, the 48-week trial showed ingestion of 20 extra grams of fiber/d correlated with greater adherence to a 30% calorie reduced diet ($r=.69$, $P < 0.001$), decreased BMI ($r=.38$, $P = 0.04$) and an increased level of satisfaction with the quantity of food ingested ($r=.59$, $P = 0.002$) compared the controls at 48 weeks (Gilhooly et al., 2008).

Thus, evidence shows that increased dietary fiber either has no effect, or that increased fiber intake may promote weight stability and/or help with weight

loss. A position paper from the Academy of Nutrition and Dietetics states, “Based on current data, dietary fiber intake from whole foods or supplements may have some benefit in terms of weight loss and other health outcomes. Benefits may occur with intakes of 20 to 27 g/day from whole foods or up to 20 g fiber per day from supplements (Anonymous, 2008).” However, according to the “Dietary Guidelines for America, 2010”, the average intake of fiber is 15 g/day, which is far below the recommended AI of 25 g/day for women and 38 g/d for men. To achieve this they recommend limiting ingestion of refined grains and increasing the consumption of fruit, vegetables, and whole grains (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2010).

Energy density. The consumption of decreased energy-dense (ED) foods has been touted as an effective way to curb calorie intake without counting calories (Rolls & Bell, 2000). At 1.5–2.5 kcal/g, fiber is the least ED food, followed by PRO and CHO which both contribute 4 kcal/g, alcohol (7 kcal/g) and fat which has the highest ED of 9 kcal/g. Hence, energy from food and drinks ranges from 0 kcal/g (water and non-calorie drinks) to 9 kcal/g. Consequently, foods high in fat tend to have high ED, while foods high in water content are more likely to have lower ED. Moreover, the consumption of low ED foods containing fewer calories per gram may reduce energy intake due to the fact that people are inclined to eat a fairly constant weight of food over the a few days’ duration (Bell & Rolls, 2001). Thus, a low ED ad libitum diet would be low in fat and refined carbohydrates, high in fruits, vegetables, and moderate in low-fat dairy and low-fat meat. Ledikwe et al. (2007) analyzed data from the PRIMIER trial and found the subjects consuming the diet with the lowest ED tertile had a

significantly ($P < 0.05$) greater decrease in average weight (-5.9 kg) compared to those in the highest ED tertile (-2.4 kg) and waist circumference (-5.7 cm vs. -2.3, low ED vs. high ED, respectively) after the 6 month intervention. In addition, Savage, Marini, & Birch (2008) studied the long-term effect of a low ED diet in 186 young women over 6 years. ED was calculated from three randomly selected 24-hour dietary recalls every two years at four time points throughout the study. Again, the women following a higher ED diet pattern (≥ 1.85 kcal/g) gained an average of 6.4 ± 6.5 kg over six years, while those consuming lower ED diets (< 1.5 kcal/g) only gained of 2.5 ± 6.8 kg ($P < 0.05$).

Eating a low ED diet permits individuals to eat fewer calories but a higher volume, which may promote satiety. However, fundamental physiological and/or psychological processes by which reduced ED and increased volume effects satiety are probably multifaceted and still not well understood. Further studies could provide greater understanding of how ED impacts energy intake (Rolls, 2009). Nevertheless, the research substantiates that this type of dietary pattern seems promising as an enduring method of weight management.

Protein. Over the past few decades, there has been a plethora of investigations addressing the effect of macronutrient intake on satiety and control of energy intake. It has been reported that the hierarchy of satiety for macronutrient intake is that protein (PRO) confers the highest level, followed by carbohydrate (CHO) and then fat (Marmonier, Chapelot, & Louis-Sylvestre, 2000; Stubbs & Whybrow, 2004; Weigle et al., 2005). Thus, one dietary paradigm for weight control is that diets moderately higher in protein (30%-40%) are more advantageous. Additional reasons for the positive effect higher protein diets may confer include an increase in diet induced thermogenesis, enhanced energy

expenditure (Raben, Agerholm-Larsen, Flint, Holst, & Astrup, 2003) and increased retention of lean body mass (Layman, 2009). Interestingly, it has recently been hypothesized (Devkota & Layman, 2010) that the increased lean body mass effects may at least be partially due to the increased amount of leucine levels found in high protein foods, which stimulates increased protein synthesis by stimulating mammalian target of rapamycin (mTOR) dependent translation initiation (Kimball & Jefferson, 2001).

A comprehensive meta-analysis (Krieger, Sitren, Daniels, & Langkamp-Henken, 2006) analyzing 87 studies found that PRO intake of >1.05g/kg/d was associated with an additional 1.2 kg fat-free mass retention in diets lasting >12 weeks, but the level of PRO intake made no differences in body mass or fat mass reductions. One recent, long term, well designed RCT lasting 4 months followed by a 8 month maintenance period (Layman et al., 2009) consisted of overweight and obese subjects (n = 130) following a calorie deficit diet of -500 kcal/d and randomized to either a 1.6 g/kg/day PRO or 0.8 g/kg/day diet with both supplying 30% of calories from fat, and the remainder from CHO. After 4 months, weight loss was similar between the groups (~7.5 Kg); however, the high PRO group lost 22% more fat mass. And for those achieving >10% weight loss at 12 months, there was a significant difference in weight loss between the high PRO group (avg. -16.5 kg, n = 20) vs. the low PRO group (avg.-12.3, n = 14). In addition, the PRO diet enhanced blood lipids with respect to atherogenic dyslipidemia; the high PRO group had decreased triglycerides (TG) and increased HDL-C levels ($P < 0.01$) at both 4 and 12 months. In light of the improved body composition that the higher protein diet conferred, the authors postulated that the current RDA for protein is based on young healthy adults with

sufficient energy intake and increased PRO intake may be warranted during weight loss diets.

Although high PRO diets have proven to be effective in the short-term (≤ 6 -months) (Johnston, Tjonn, & Swan, 2004; Skov, Toubro, Ronn, Holm, & Astrup, 1999) long-term adherence to any type of diet has proven to be difficult for most people. For instance, a trial exploring diets differing in macronutrient content (Dansinger, Gleason, Griffith, Selker, & Schaefer, 2005) included 160 participants who were randomized to adhere to one of 4 popular diets including the Adkins, Ornish, Weight Watchers, and Zone diets for 1 year. The results showed those following the Adkins diet lost the least amount of weight (-2.1 kg) at 12 months, although there was no statistical difference in weight loss among the groups ($P = 0.4$). However, adherence to diet they were prescribed to was a strong predictor of weight loss ($r = 0.06$; $P < 0.001$). Additionally, there was no between group difference for diet adherence which decreased over time for all diet types, and on a 1 – 10 point scale and only 25% of the subjects maintained a mean adherence level of 6 throughout the trial.

Furthermore, Sacks et al. (2009) compared the long-term effects of different macronutrient levels on body weight. These diets, randomly distributed between the 811 participants of between 201-204 per group, included med- and high-PRO, low- and high-fat, and a CHO spread of between 35% and 65% total calories. Specifically, the nutrient goals for percent fat/protein/carbohydrates for the four diet groups were: G1) 20/15/65; G2) 20/25/55; G3) 40/15/45 and G4) 40/25/35. They were each prescribed a caloric deficit of 750 kcal/day below estimated total energy expenditure. Daily meal plans and individual and group counseling sessions were provided. Eighty percent of the participants completed

the 2-year study. They found no difference in weight loss between the low and high fat, or medium and high protein diet groups. Likewise, weight loss across the various CHO levels was also similar. At 6 months the average weight loss was between 6 and 7 kg and between 3 and 5 kg at 2 years. Again, there was not a significant difference in actual macronutrient intake between the low-fat, high-protein and low-fat, average-protein diets at both 6 months and 2 years.

Thus, it appears that although high protein diets confer theoretical advantages for dietary adherence and metabolic factors involved in weight loss, data from longer trials show that study participants struggle to adhere to dietary restrictions of any kind. Ostensibly, the desire to lose weight, as assessed by sustained adherence to the diet, may be the most salient determinate of weight loss in these weight loss trials. Finally, from a practical standpoint, it may be that randomization of the subjects into a particular arm of a weight loss trial that includes macronutrient manipulation may be counterproductive in that different people may do better on one type of diet as opposed to another according to dietary preference.

DHA and EPA. It is generally accepted that long-chain polyunsaturated fatty acids (LC-PUFAs) of the omega-3 (n-3) series, docosahexaenoic acid (DHA; 22:6n-3) and eicosapentaenoic acid (EPA; 20:5n-3), have beneficial cardiovascular effects specifically by lowering plasma TGs while increasing HDL-C, preventing arrhythmia, and exerting anti-inflammatory and BP lowering effects (Flachs, Rossmeisl, Bryhn, & Kopecky, 2009). More recently, EPA and DHA have been studied for their ability to thwart the progression of obesity. Humans and animals (including fish) are unable to synthesize n-3 fatty acids; thus, they are considered essential fatty acids. The main source of n-3 fatty acid in the

human diet is from α -linolenic acid (18:3n-3). α -Linolenic acid (not to be confused with linoleic acid, a n-6 fatty acid) is found in high amounts in canola oil, soybeans, walnuts, flaxseed and green vegetables. It used to be thought the main biochemical purpose of α -linolenic acid was that of the precursor to DHA and EPA. However it is now known the conversion rate of α -linolenic acid to EPA and DHA is approximately 5%, depending on the amount of n-6 (omega-6) fatty acids and LC-PUFAs in the diet, deeming it a poor source of EPA and DHA (Brenna, 2002). EPA and DHA are mainly found in marine phytoplankton, which is the source for fatty fish and why fish contain high amounts of DHA and EPA. The ratio of n-6 to n-3 fatty acids was much lower in our ancestor's hunter-gather diets. Specifically, it has increased from an estimated 1-4:1 to a whopping 11:1 in affluent western societies (Eaton, Eaton, Konner, & Shostak, 1996). This is important because n-6 fatty acids compete for the same metabolic pathways as the EPA and DHA, and both produce eicosanoids, which are the mediators and regulators of inflammation, with eicosanoids derived from n-6 fatty acid generally acting as pro-inflammatory agents, while eicosanoids derived from n-3 fatty acids are anti-inflammatory (Calder, 2009).

Although the anti-obesity effects of these n-3 fatty acids in animal studies has been well documented, small cohorts of human studies only show moderate fat lowering effects. The mechanism of action is thought to be at the cellular level and not due to and change in calorie intake or exercise effects. Moreover, the eicosanoids derived from EPA and DHA induce peroxisome proliferator-activated receptor (PPAR- α) activity. In turn, PPAR- α acts as a central player in intracellular lipid metabolism by modulating the expression of proteins required

for the transport and oxidation of free fatty acids (van Raalte, Li, Pritchard, & Wasan, 2004).

Mice studies have shown that adipose tissue deposition is less effective from long chain (LC) n-3 PUFAs compared to other types of fat. For instance, Hun et al. (1999) found in KK-Ay mice fed perilla oil, soybean oil or lard with or without the addition of 30% EPA/DHA, there were significant decreases in visceral fat ($P < 0.05$) and lower leptin ($P < 0.001$) levels, but no difference in energy intake or body weight in the groups given each type of oil with fish oil added, compared to the no EPA/DHA controls. Flachs et al. (2005) investigated the effects of a high-fat diet, with 15% of dietary oil replaced by EPA and DHA on C57BL/6J mice. Their results showed, with no difference in food consumption, a decrease on body weight gain by 22% and epididymal fat gain was 24% lower, but no difference in dorsolombar fat compared to the chow high fat diet not containing EPA and DHA. They also found a suppression of lipogenesis in adipocytes and an upregulation of mitochondrial biogenesis causing increased β -oxidation, which resulted in the prevention of fat accumulation specifically favoring a decrease in abdominal fat. Interestingly, Ruzickova et al. (2004) found that of the n-3's, DHA may play a stronger role on the protective outcome of decreased fat cell accumulation as a consequence, in part, from the suppression of fat cell production without a decrease in food consumption. However, extrapolating their data to humans, daily intake of EPA/DHA would need to be 11g/day, which is much higher than the current dietary guidelines called for by the American Heart Association (2010) of 250-500mg/day.

Although the mice models are robust and promising, the results from the human studies examining fish oils and body composition are limited with mixed

results. One of the first studies done in this area was a cross-over design of six healthy adults fed a diet with or without 6 g/day fish oil over three consecutive weeks in a metabolic unit (Couet, Delarue, Ritz, Antoine, & Lamisse, 1997). The control period of 3 weeks on a low EPA/DHA diet was started first for all subjects due to the prolonged effects of n-3 PUFAs on membrane phospholipid composition. They found that although there was no reduction in body weight, there was a significant decrease in fat mass ($P = 0.02$) and a significant increase in fat oxidation ($P = 0.03$) and resting metabolic rate ($P = 0.045$) when the subjects consumed the fish oil supplemented diet.

An additional, human RCT published in 2006 examined the effect of a very low calorie diet (VLCD) with and without LC n-3 PUFA for three weeks in 20 severely obese women weighing over 100 kg (Kunesova et al., 2006). The VLCD consisted of ≈ 521 kcal/d for 3 weeks and an n-3 supplement, which was comprised of 2.8 g/day EPA and DHA at a 2:1 ratio vs. a no supplement control ($n = 10$ per group). Daily semi-quantitative measurements of urine ketone bodies were evaluated to ensure adherence to the diet. The results showed higher decreases in BMI (2.82 ± 0.62 vs. 2.22 ± 0.74 , $P < 0.05$), weight ($7.55 \text{ kg} \pm 1.77$ vs. $6.07 \text{ kg} \pm 2.16$ kg, NS), hip circumference ($4.8 \text{ cm} \pm 1.81$ vs. $2.5 \text{ cm} \pm 2.51$ cm, $P < 0.05$) and waist circumference ($5.5 \text{ cm} \pm 1.71$ vs. $3.3 \text{ cm} \pm 4.1$, NS) in the n-3 group as compared to the control group, respectively. They also found a significant negative correlation between BMI change and phospholipid docosahexaenoic acid change ($r = -0.595$, $P < 0.008$). The outcome of this study indicates that LC n-3 PUFA enhanced weight loss in obese females treated with a VLCD and that DHA appears to be a moderating factor.

Another human investigation on the effects of EPA and DHA on weight loss in 93 overweight or obese (BMI ≥ 27 kg/m²), insulin-resistant women was published in 2006 (Krebs et al., 2006). The subjects were randomly divided into three groups: a weight-loss program with 1.3 g/day EPA and 2.9 g/day DHA (n = 35); a weight-loss program with placebo oil (n = 32); and a control group consisting of placebo oil only and no weight loss program (n = 26). The study was designed to induce a 10% weight loss by consuming \approx 800-900kcal/day from a skim-milk drink for five weeks followed by a gradual introduction of solid foods so that at 12 weeks, the subjects would be consuming \approx 2500 kcal/day to achieve weight maintenance. The results found no difference in weight loss, fat mass or waist circumference between the fish oil and placebo oil groups at anytime throughout the study. However, they did find a decrease in triglycerides ($P < 0.01$), and increases in HDL-C ($P < 0.001$) and adiponectin ($P < 0.001$) in the fish oil group.

Kratz, Callahan, Yang, Matthys, & Weigle (2009) examined the effect of diets with or without LC n-3 PUFA supplementation in 26 overweight or moderately obese (BMI between 28-33 kg/m²) men and women vs. a control group. All subjects consumed the isoenergetic lead-in diet, calculated to maintain weight within 1 kg, for 2 weeks without LC n-3 PUFA supplementation. After 2 weeks the experimental group consumed 1.4% of energy from EPA and DHA derived from fish oil and 2.2% of energy from plant based α -linolenic acid (n = 13), while the control group consumed no fish oil and 0.5% of energy from α -linolenic acid (n = 13) for 12 weeks on an ad libitum diet. All meals were provided by the research unit. After the 16 weeks they found no difference in weight loss in the n-3 PUFA group compared to the controls (-2.8 \pm 3.7 vs. -

3.5±3.7, respectively, NS). Additionally, no differences between the two groups were found in regard to appetite levels, food intake, resting energy expenditure, plasma leptin levels or fasting ghrelin levels. Results of this study, showing no impact of LC n-3 PUFA supplementation may be due to the lower intake of the fish oil (≈ 4.1 g/day) compared to the previous study (6g/day).

Kabir et al. (2007) examined the effects of 2 months daily intake of EPA (1.08 g/day) and DHA (0.72 g/day) from fish oil vs. control (paraffin), on adiposity and insulin sensitivity in 27 post-menopausal women with type 2 diabetes mellitus (T2DM). Both groups consumed ad libitum diets. There was no significant change in body weight between treatment arms, however, the fish oil group had significant reduction in percent body fat (-4.6%, $P = 0.02$), trunk fat (-5.6%, $P = 0.04$) and subcutaneous abdominal adipose tissue diameter (-6.3%, $P = 0.002$) vs. the control group. However, physical activity was not controlled for.

Hill, Buckley, Murphy, & Howe (2007) studied the effects of 12-weeks of daily tuna fish oil (FO) supplementation containing 260 mg DHA and 60 mg EPA vs. sunflower oil (SO) with or without exercise in 65 overweight/obese men and women with CVD risk factors. The unsupervised exercise consisted of walking for 45 min., 3 days/ week at 75% estimated maximum heart rate. Mean caloric intake at baseline and throughout the trial was not significantly different between the groups. However, only the FO with exercise group experienced a significant but modest mean decrease in BMI (-1.7%, $P < 0.05$) or percent body fat (-2.8%, $P \leq 0.05$) vs. the FO without exercise and SO with and without exercise groups.

An additional randomized trial (Thorsdottir et al., 2007) investigated the effect of diets consisting of lean fish (LF), fatty fish (FF) and fish oil (FO) supplements vs. sunflower oil with no fish (C), on weight loss in 278 men and

women while on calorie restricted diets (-30% reduced from estimated total energy expenditure) for 8 weeks. They found the men on the fish or fish capsule diets had lost more weight than controls (C= -5.3kg, FO= -6.7kg, FF = -7.0kg, LF -6.5kg, $P < 0.05$). Waist circumference was also significantly reduced in the fish groups compared to controls ($P < 0.05$). However, for women, weight loss was similar between all diet groups.

A separate study (Noreen et al., 2010) assessed the effect of fish oil capsules on cortisol levels, body composition and RMR in 44 women and men. Baseline measurements were taken and the subjects were randomized to receive either fish oil (4g) or safflower oil (4 g) capsules, added to their normal, ad libitum diet for six weeks. As expected, there was no change in weight between the groups at six weeks; however, in the fish oil vs. safflower oil groups respectively, there was a small but significant mean increase in fat free mass ($+0.5 \pm 0.05$ kg vs. -0.1 ± 1.2 kg, $P = 0.03$), and decrease in fat mass (-0.5 ± 1.3 kg vs. $+0.2 \pm 1.2$ kg, $P = 0.04$). They also found the fish oil group had decreased cortisol levels at six weeks compared to baseline, but there was no difference between the two groups.

To date, the latest published investigation, exploring the possible advantages of EPA and DHA for weight loss in humans, was published in 2011 (DeFina, Marcoux, Devers, Cleaver, & Willis, 2011). In this randomized, placebo controlled trial, 128 overweight and obese subjects (BMI 26-40 kg/m²) were equally divided to receive either a daily dose of 5g EPA & 1g DHA or an isocaloric placebo consisting of a 1:1 ratio of soy and corn oil for 6 months to determine if the addition of omega 3 FA's would have an enhanced benefit while on a weight loss diet. Both groups followed a calorie restricted diet and

exercised 150 min/week at 50-85% VO_2 max plus resistance training twice per week. Each group lost an average of 5% body weight and decreases in body fat, waist circumferences and resting metabolic rate/kg were also similar between the groups. Thus, this study showed no enhanced benefit for weight loss with intake of EPA and DHA compared to soy and corn oil supplementation during a lifestyle intervention trial.

Overall, although beneficial results regarding fish and weight loss were found in animal studies, the small amount of published human studies show less inspiring support for the use of fish or fish oil for improved weight management or body composition. This could be due to the differences in type, amount and duration of n-3 supplementation. In addition, the heterogeneity in study participants and trial design further complicate interpreting the results. Obviously, more studies that address these issues are needed.

PARTIAL MEAL REPLACEMENT DIETS AS A STRATEGY FOR BODY WEIGHT CONTROL

The fundamental principle of a partial meal replacement (MR) is to substitute either one or two meals/day with a low-calorie, nutrient fortified, portion-controlled alternative, along with conventional low-calorie meal(s), resulting in a daily calorie intake between 800 and 1,600 kcal/day (Heymsfield, van Mierlo, van der Knaap, Heo, & Frier, 2003). MRs come in all shapes and forms including, shakes, bars, cookies, soups and drinks with brand names such as Slim-Fast, Medifast, OPTIFAST, and Celebrity Slim being amongst some of the most popular. Commercially available MRs typically cost from \$0.50 (milk added by consumer) to >\$3.00 each (Hamdy & Zwiefelhofer, 2010).

The success of MRs is founded on the premise that the copious amount of extremely appetizing, calorie dense food available in our modern-day society promotes weight gain in those who are unable to perceive and regulate the amount of food they eat. In addition, obese individuals habitually underestimate their caloric consumption by 40% to 50% when ingesting a standard diet (Lichtman et al., 1992). For these individuals, calorie-controlled MRs can provide a structured, simple method to achieve a negative energy balance, compared to a self-selected, reduced calorie, mixed-food plan by enhancing compliance and thus a “healthy” BMI can be achieved (Heymsfield, 2010).

One of the most successful MR trials (Ditschuneit, Flechtner-Mors, Johnson, & Adler, 1999) consisted of 110 subjects, randomized to a reduced calorie diet (RCD) of 1,200-1,500 kcal/d or an isocaloric diet with two of the meals replaced with MR shakes, plus 2 MR snacks. At 3 months the MR group lost an average of $11.3 \pm 6.8\%$ of their initial body weight compared to a $5.9 \pm 5.0\%$ weight loss in the RCD group ($P < 0.0001$). After 3 months, all subjects were prescribed the same diet and told replace one meal per day and one snack with a meal/snack replacement product, and after 4 years, data from 75% of the subjects was analyzed (Flechtner-Mors, Ditschuneit, Johnson, Suchard, & Adler, 2000). The results showed that through 4 years of weight maintenance, the MR group lost more weight from baseline than the RCD group ($8.4 \pm 0.8\%$ vs. $3.2 \pm 0.8\%$, respectively, significance not reported).

A meta- and pooling analysis was published in 2003 examining the safety and efficacy of meal replacement diets (MRDs) (Heymsfield et al., 2003). These researchers critically evaluated the available published MR research studies between 1960 and 2001. Unfortunately, of the 276 RCTs detected and screened

for retrieval, only 30 were identified for further examination. And, of those 30, only six met the predefined criteria of randomized, parallel design, lasting at least three months with subjects ≥ 18 years of age and a BMI ≥ 25 . In addition, the suggested calorie intake for the MRD and reduced calorie diet (RCD) was equal, with two meals per day being replaced by a MR during the weight loss phase, and during the weight maintenance phase only one MR per day was used. Four of the selected trials lasted 1 year, another lasted 51 months and one lasted only 3 months. Pooling the six data sets resulted in a total of 249 MR-treated subjects and 238 control subjects. Seventy-five percent of the subjects were female, and at baseline the subjects had a mean BMI of 31, their average age was 46.1 years, and 32% had non-insulin dependent diabetes mellitus. The drop-out rate was similar between the MR and RCD groups (16% vs. 19% respectively, $P = 0.407$) at 3 months, but it was significantly higher in the RCD group at one year (47% vs. 64%, $P < 0.001$). Although both groups in all six studies experienced a significant amount of weight reduction at three months ($P < 0.001$), in three of the six studies, weight loss was significantly greater in the MR groups ($r = 0.469$ to $P < 0.001$). In particular, the meta-analysis results showed an average weight loss of 6.3kg in the MR-treated subjects compared to 3.4kg in the RCD groups. Overall, depending on the duration of the study, follow-up evaluation of the subjects revealed an average weight loss of ≈ 7 -8% in the MR group and ≈ 3 -7% for the RCD group.

More current reports have confirmed the usefulness of the MR plan for weight maintenance. Vazquez et al. (2009) enrolled 62 subjects who had lost at least 5% of their body weight solely through dieting for 6 months by reducing daily caloric intake by 400-500 kcal/d from estimated energy expenditure. The

subjects were then randomized into two equal groups and both groups were encouraged to continue their low-calorie diet, but the MR subjects were provided with MRs and told to consume one per day as a replacement for any meal. At 6 months, with only a 13% drop-out rate, the results showed the subjects randomized to the MR group lost an additional 3.2 kg vs. a 1.3 kg weight loss average for the RC group ($P = 0.03$). In addition, 83.9% either maintained or lost more weight in the MR group, but only 58.1% of the RC subjects were able to do so ($P = 0.025$).

In contrast, several randomized controlled trials (RCT) have resulted in the MR diet having no long-term advantage over a control diet. For instance a MR study was done with volunteers attending the US Army's "Weight to Stay" program at Fort Bragg, NC (T. Smith et al., 2010). In this parallel arm study, 113 subjects were randomized to follow the traditional "Weight to Stay" plan, which consisted of diet and exercise education, or to receive 2 MRs/day and supplementary dietary education in addition to the information provided at the "Weight to Stay" plan meetings. The diets lasted until the subjects met the Army's standards for percent body fat or for six months if they were unable to meet the standards. The results showed there was an extremely high attrition rate in both groups, and only 46 subjects (41%) completed the study, which was attributed to geographical relocation. Both groups achieved a decrease in BMI of ~1 unit and there was no difference in % body fat or % FFM between the groups.

Noakes, Foster, Keogh, & Clifton (2004) studied the effectiveness of a MR vs. a RCD diet for 6 months in 66 subjects not having a BMI < 27 or > 40. The subjects were randomized into two groups of 33 each and both were restricted to ~1,430 kcal/d, but the MR group replaced breakfast and lunch with a

MR and ate a low-fat dinner and at least 5 fruits of vegetables/d. The retention rate at 6 months was 79% for the MR group and 88% in the RCD group. Both diets were equally effective; each group lost ~6.3% body weight at 3 months and ~9.1% at 6 months. BMI and anthropometric data was not reported. The authors concluded that a MR diet is just as effective as a reduced calorie diet, but when assessing the subject's attitude toward the diet using a nutrition quality of life survey, the MR group scored significantly higher ($P < 0.01$).

A trial by Davis et al. (2010) of 90 adult subjects with a BMI ≥ 30 and ≤ 50 were equally randomized to two groups consisting of either MR or a RCD. During the initial 16 week phase, the MR group consumed 5 MRs/d, each containing ~ 100 kcals and 5-7 oz. lean meat, 1-1/2 cup non-starchy vegetables and 2 fat servings to provide a total 800-1,000 kcal/day. The RCD group was restricted to a low-fat diet consisting of 1,000 kcal/d from low-fat protein, dairy, grains and fruits and vegetables. During the 24-week maintenance phase, both groups increased their caloric intake to reach levels estimated individually using the Mifflin-St. Jeor equation for total daily energy requirements; however, the MR group continued using 5 MRs/d supplemented with food. At week 40, the retention rate was 58% for MR and 44% for RCD subjects. The MR group had greater weight loss vs. the control group; 12.3% vs. 6.7%, respectively ($P = 0.001$) at 16 weeks. However, after the 24-week maintenance phase, average weight regain was significantly greater in the MR group (4.8kg vs. 0.8kg, $P = 0.027$). Therefore, BMI reduction for both groups was similar at 40 weeks (MR, -2.9 BMI units, and RCD, -2.8 BMI units, $P = 0.18$).

In a study of subjects having Type 2 diabetics, Cheskin et al. (2008) recruited 119 adults with a BMI between 25 and 40 and randomly assigned them

to a to a RCD group or a isocaloric MRD group for 34 weeks. All subjects were prescribed a 25% RCD (individually determined using the Harris-Benedict equation for estimated energy expenditure) but the MRD consisted of 50% to 60% of caloric intake from MRs. Both groups received group education regarding diet and exercise throughout the study. At 34-weeks both groups then transitioned to a 10% RCD based on their current weight for the 52-week weight maintenance phase. The MR group continued to use the MRs for half of the 52 weeks. The dropout rate was high (57% MR and 29% RCD remained), but for those completing the study at 34 weeks, BMI was significantly reduced in both groups but average weight reduction was higher in the MR group vs. controls (7% vs. 4%, $P = 0.039$). At 86 weeks, there were appreciable drop-out rates in both groups with 29% MR and 14% RCD remaining in the study; however, significantly more dropped out of the RCD group $P = 0.02$. Both groups maintained significant weight loss but there was no difference in BMI between the groups with both maintaining an average overall decrease of about 2 BMI units.

The Look AHEAD study is a large, ongoing weight management study examining 5145 diabetic patients for ten years, who were randomly assigned to either the MR strategy in the intensive lifestyle intervention group (ILI) or no MR in the standard diabetes support and education (DSE) group (Wadden et al., 2009). They found the number of MRs consumed in the first six months was significantly related to weight loss attainment ($r = 0.32$, $P < 0.001$) and the association continued at week 52 ($r = 0.30$, $P < 0.001$). In addition, subjects in the highest quartile of MR consumption (average of 608 MRs/year) had a four times

increased chance of attaining a weight loss goal of 7% compared to participants in the lowest quartile of MR consumption (average of 117 MRs/year).

Finally, in a recent 12-month trial, 113 obese children between 13 and 17 years of age and with a BMI between 28-50 were recruited and randomized to receive a conventional diet (CD) of between 1,300 – 1,500 kcal/d or a isocaloric MR diet which consisted of 3 MRs/d (~250 kcal each) along with a frozen entre (225-300kcal/each) and 5 servings of fruit and vegetables/day (Berkowitz et al., 2011). After 4 months, half the MR group was transitioned to a conventional diet and half continued taking 2 MR/d, one frozen entre/d, a self-selected breakfast, and 5 fruits and vegetables/d, with the goal of all three diet groups achieving a caloric intake of 1,300 - 1,500 kcal/d and 30 minutes of physical activity/d for the next 8 months. All groups attended a lifestyle modification program with their families throughout the study. The results showed that at 4 months, the overall retention rate was 90%, and not significantly different (NS) between groups; the MR group had a significantly larger decrease in BMI units compared to the control group (-2.3 vs. -1.3 respectively, $P = 0.01$). At 12 months the overall retention rate was 67% (NS between groups). However, all groups regained some of their weight, and the MR groups regained more than the controls; + ~1.0 BMI unit for the continued MR and MR/CD groups vs. +0.35 for the control group, and there was no significant differences between the groups in overall average BMI reduction from baseline, which was -1.3, - 1.3 and -0.96 for the MR, MR/CD and CD groups, respectively. The weight regain from 5-12 months in the MR group coincided with a significant reduction in MR use, and the subjects reported consuming the MRs only 1.6 days/week on average at 12 months.

Overall, the MRDs typically performed better in the short term, but over longer periods of use, the advantage tended to diminish. This may be due to taste fatigue or non-compliance. However, retention rates tended to be higher for the MR subjects. Heymsfield et al. (2003) found at one year, retention rates in the MR groups were significantly higher in their meta-analysis. Of concern is that the dependence on the use MRs as a diet strategy inhibits individuals from learning how to make wise food choices. In addition, it is becoming increasingly apparent that whole foods contain countless healthful substances, including polyphenols, antioxidants, fiber and prebiotics typically not found in MRs. As for the Academy of Nutrition and Dietetics stance on meal replacements, they state that using them can be an effective diet strategy for those who have difficulty with portion control (Seagle, Strain, Makris, Reeves, & American Dietetic Association, 2009).

IMPROVED WEIGHT RELATED HEALTH OUTCOMES WITHOUT WEIGHT LOSS

The commonly used statistics that indicate that kills comes from correlational data to develop the relative risk relationship between BMI and death rate (Allison, Fontaine, Manson, Stevens, & VanItallie, 1999; Mokdad, Marks, Stroup, & Gerberding, 2004; Pischon, Nothlings, & Boeing, 2008). Obviously, this correlational data does not meet Hill's criteria for establishing a causal relationship. Additionally, this type of analysis does not take into account lifestyle patterns such as diet and exercise. Campos, Saguy, Ernsberger, Oliver, & Gaesser (2006) pointed out in their review article that the view that "obesity kills" is, at best, only weakly supported by the epidemiological literature. Specifically, the relative risk for premature mortality among individuals in the overweight category (BMI 25-25.9) is actually lower than for people in the normal weight

category, showing that being overweight may actually be protective (Flegal, Graubard, Williamson, & Gail, 2005).

Accordingly, Gruberg et al. (2002) coined the term “obesity paradox”, noting that overweight and obese patients who were post-op for coronary occlusion surgery had decreased mortality rates compared to normal weight patients. Since then, McAuley & Blair (2011) have identified additional paradoxes including “Fat but Fit”, meaning fit, overweight or obese individuals are not at higher risk for mortality, and “Healthy Obesity”, because most obese adults have normal cardiometabolic risk factors. To that end, epidemiological data has been published to support this paradigm. Wildman et al. (Wildman et al., 2008) examined the association between cardiometabolic risk factors and BMI, from NHANES 1999-2004 data. This included a sample of 5440 participants having blood samples, and lifestyle and anthropometric data. Their results showed that approximately 30% of obese, and 50% of overweight men and women have only one or fewer cardiometabolic risk factors, and that of the normal weight men and women, 25% had two or more cardiometabolic risk factors. Thus, extending the hypothesis that BMI is not a good indicator of cardiovascular disease. In addition, Fogelholm (2010) conducted a meta-analysis of eleven qualifying studies examining the health risks of poor cardio-respiratory fitness or physical inactivity in normal weight individuals vs. good cardio-respiratory fitness in obese in people. The data from this research showed that for all-cause mortality (9 studies) and cardiovascular disease mortality (10 studies), having a high level of aerobic fitness with a high BMI was more favorable compared to having a normal BMI and poor aerobic fitness. In addition, Ross and Janizewski (2008) reviewed 29 studies that reported body

composition, metabolic parameters and fitness levels from both randomized and nonrandomized trials examining the impact of exercise on waist circumference and cardio-metabolic fitness. They found in a vast majority of the studies that short-term regular exercise, even with little or no weight reduction, improved cardiometabolic risk factors. These risk factors included: insulin sensitivity, fasting glucose, hemoglobinA1c, TG, HDL-C, total cholesterol, and waist circumference. In addition, information from a review article examining blood pressure and physical activity found a particularly low association between BMI and diastolic and systolic blood pressure (Fagard, 1999).

Although the leading cause of death in the US is from cardiovascular disease, it is closely followed by cancer (Kochanek, Jiaquan, Murphy, Minino, & Hsiang-Ching, 2011). One study (Farrell, Cortese, LaMonte, & Blair, 2007) examined data from the Aerobic Center Longitudinal Study, consisting of 38,410 men over 30 years old and followed for an average of 17.2 ± 7.9 years. They found that increased levels of cardiorespiratory fitness were associated with decreased cancer mortality risk across all waist circumference, BMI and percent body fat quintiles. And, when cardiorespiratory fitness was added as a covariate (along with age, examination year, smoking status, and chronic illness at baseline), the body fat percent association to cancer mortality risk did not persist ($P = 0.81$) and the risk was diminished with increased waist circumference ($P = 0.09$). Additionally, increased risk only continued to remain within the highest BMI quintile of ≥ 29.80 (1.40, 1.13 – 1.50, $P < 0.01$).

In a different epidemiological study that supports these findings, 141 published articles were reviewed to determine the association between cancer risk and incremental increases in BMI (Renehan, Tyson, Egger, Heller, &

Zwahlen, 2008). The results showed that although some types of cancer such as oesophageal adenocarcinoma are associated with higher risk of obesity, most of the more common types of cancer are not, and in fact having a higher BMI was found to be associated with lower rates of lung and oesophageal squamous cancer.

Intervention studies have examined the role of physical activity and diet with and without weight loss in reducing the progression of DM and CVD incidence. For instance, Cornelissen & Fagard (2005) conducted a meta-analysis of 72 trials, comparing 105 study groups and included 3936 participants. These trials examined the effect of endurance training of at least four weeks duration on blood pressure (BP) status. They found that in hypertensive individuals, exercise training increased VO_2 max by an average of 4.4 ml/kg/minutes, which coincided decreased average systolic BP (-6.9 mmHg) and diastolic BP (-4.9 mmHg) but with only negligible decreases in body weight (-1.1 kg) and body fat (-0.79%). Mestek et al. (2010) examined the effects of exercise on forearm blood flow. Twenty overweight and obese adults were tested at baseline and after 3 months of aerobic training, which consisted of exercising 40-50 min/day, 5-7 days/week at 60-75% maximum heart rate as assessed by exercise testing. The data showed that at 3 months, there were no changes in body weight, but endothelium-dependent vasodilation improved by 35% ($P < 0.01$).

In a separate study (King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE, 2009) 58 sedentary, overweight men and women were recruited for a exercise induced weight loss trial lasting 12 weeks. Interestingly, 45% of the subjects lost an average of only -0.9 kg, which was much less than expected.

Despite the small weight loss, they still experienced significant improvements in VO₂max, BP, waist circumference, and resting heart rate (HR).

A 6-month study of 22 middle aged, overweight and obese men (Ferrara, Goldberg, Ortmeyer, & Ryan, 2006), who were randomized to either aerobic training (45-50 min/d) or resistance training (both upper and lower body) was designed to determine the differing effects of these two types of exercise on glucose disposal. Although there was negligible weight change in either group, both types of exercise increased glucose disposal, as assessed by euglycemic–hyperinsulinemic clamp, to a similar degree (20-25%, $P < 0.05$). Additionally, the aerobic group had an increased glycogen synthase activity over baseline of $280 \pm 59\%$, ($P < 0.05$), although resistance training did not confer this benefit.

The Study on Lifestyle Intervention and Impaired Glucose Tolerance Maastricht (SLIM) (Roumen et al., 2008) was a 3-year, randomized, parallel-arm diet and exercise intervention consisting of 106 subject completers with impaired glucose tolerance. The intervention group was given individual nutrition advice and exercise recommendations consisting of increased physical activity by 30 min/d, 5 days/week and the control group was given only brief advice regarding the benefits of a healthy diet and regular exercise. After 3 years, the participants in the diet and exercise group had lost only 1.08 kg, but had a 58% reduced risk for developing diabetes mellitus (DM) ($P = 0.025$) and significantly reduced 2-hour plasma glucose levels vs. controls ($P = 0.023$).

The Diabetes, Aerobic and Resistance Exercise (DARE) study consisted of 251 inactive men and women, 39-70 years with T2DM (Sigal et al., 2007). They were randomized to 1 of 3 exercise groups (3 times/week): aerobic exercise consisting of 45 minutes per session at 75% maximal heart rate,

resistance training on weight machines consisting of 7 different exercises, including 2 to 3 sets of each exercise at the maximum weight that could be lifted 7 to 9 times, or a combination of the full aerobic and resistance training routines, and a control, non-exercise group for 6 months. With negligible weight change, the results indicated that compared to the control group, %Hemoglobin A_{1c} was significantly lower in both the aerobic (-0.51, $P < 0.007$) and resistance (-0.38, $P < 0.038$) groups, and the combined aerobic and resistance group had even lower levels compared to the other two groups.

The Italian Diabetes and Exercise Study (IDES) was a one year study of 560 overweight or obese, sedentary men and women averaging 58 years with T2DM and metabolic syndrome (Balducci et al., 2010). All subjects were prescribed a diet to achieve a negative energy balance of 500 kcal/day of estimated calorie expenditure, and divided into 2 groups of either 2 sessions/week to total 150 min/week of supervised, aerobic and resistance exercise or a control group that received individual counseling in achieving physical activity goals every 3 months. At the end of the 1 year trial, the subjects lost an average of 0.9 and 0.2 BMI units, exercise and control groups, respectively; however, the exercise group had a decrease in %Hemoglobin A_{1c} of -0.42 vs. a -0.13 decrease in the control group ($P < 0.001$). The exercise group also had significantly greater decreases in systolic (-4.2 mmHg, $P < 0.002$) and diastolic (-1.7 mmHg, $P = 0.03$) BP and LDL-C (-9.6 mg/dL, $P = 0.003$) and a significantly greater increase in HDL-C (3.7 mg/dL, $P < 0.001$) vs. controls.

The Health Risk Factors, Exercise Training & Genetics Family (HERITAGE) study (Couillard et al., 2001) consisted of 200 sedentary males (79 fathers and 121 sons), who were divided into 4 groups of those with either 1)

normal lipids, 2) isolated high TGs, 3) isolated low HDL-C or, 4) a combination of increased TGs and decreased HDL-C levels. All subjects were put on a supervised training program that consisted of 50 minutes, 1-4 times/week, to total 60 aerobic exercise sessions in 20 weeks and reach a goal heart rate associated with 75% VO₂max. Despite the combined high TG/low HDL-C group only having a negligible mean weight change of -0.3 ± 0.6 BMI units at the end of the study, they had significantly increased HDL-C (+4.9%), apoA-I (+3.7%), and a significantly decreased ratio of total/HDL-C (-9%). In addition, both of the groups with high initial TG levels had significantly reduced TG levels by ~ 15% with the high isolated high TG only group although they lost only 0.1 ± 0.6 BMI units.

Finally, a 2006 meta-analysis (Snowling & Hopkins, 2006) of 27 qualifying studies which included a total of 1003 subjects with T2DM, examined the effect 5 to 104 weeks of aerobic, resistance or a combination of both types of exercise on glucose control and CVD risk factors. They found trivial to small changes in body mass of -0.09 kg in the aerobic group, +0.03 kg in the resistance group and -0.32 in the combined exercise group; however, there were significant improvements in %Hemoglobin A_{1c} and insulin sensitivity in all groups. In addition, both the aerobic and combined exercise groups had small improvements in fasting and postprandial glucose levels and small to moderate improvements in systolic and diastolic BP.

Intervention studies have also shown that dietary improvements without concurrent weight loss can improve cardiovascular parameters as well as those related to DM. For instance, the Prevencio'n con Dieta Mediterra'nea (PREDIMED) study (Estruch et al., 2006), was a large randomized, parallel trial, 772 subjects at high DM risk. The percentage of subjects had the following risk

factors: DM (55%) and/or ≥ 3 CVD risk factors including current smoking (17%), BP $>140/90$ mmHg (79%) or HTN treatment, dislipidemia (67%) including LDL-C ≥ 160 mg/dL or hypolipidemic drug treatment and/or HDL-C ≤ 40 mg/dL, BMI ≥ 25 kg/m² (90%), or family history of CHD (23%). The subjects were partitioned to consume either a low-fat diet (control), or a Mediterranean diet high in either virgin olive oil (VOO) or mixed nuts (walnuts, hazelnuts and almonds) for 3 months. All three groups lost a negligible amount of weight, which translated to a loss of between -0.09 and -0.21 BMI units, and estimated physical activity levels at baseline and at 3 months were similar among 3 groups. However, both the VOO and nut groups had significant reductions in systolic (-1.7 to -5.9 mmHg) and diastolic (-1.6 to -2.6 mmHg) BP and fasting blood glucose (-5.4 to -7.1 mg/dL), fasting insulin (-16.7 to -20.4 pmol/L) and HOMA-IR (-0.91 to -1.1) and significantly increased HDL-C levels (1.6 to 2.9) compared to the low-fat group. They also found significantly decreased triglyceride levels in the nut group (-13.0 mg/dL), when compared to the low-fat group. Inflammatory biomarkers including, ICAM-1, VCAM-1, and interleukin-6 dropped significantly in both the nut and VOO groups, but these levels increased in the low-fat group. In addition, CRP levels dropped in the VOO group compared to the nut and low-fat groups. In a subsequent report, a subset of 418 non-diabetic older adults (55-80y) having at least 3 CVD risk factors from the PREDIMED trial were randomly assigned to the same dietary groups as previously mentioned (Salas-Salvado et al., 2011). Although there were no significant changes in physical activity and weight, the pooled nut and VOO groups had a 52% reduced incidence of diabetes after following the diet for 4 years without significant changes in weight or PA levels. The hazard ratio (95% CI) for the multivariate adjusted model was 0.49 (0.25-

0.97). Interestingly, they also found an inverse relationship between those that had the highest compliance to the diet had the lowest incidence of diabetes. And a different analysis of a weight stable subset of 112 subjects in the PREDIMED trial (Mena et al., 2009) who had DM or ≥ 3 CVD risk factors and no change in PA level from baseline, found significant decreases in CD49d, CD40, ICAM-1 and IL-6 for those subjects in either the VOO or nut groups ($P < 0.05$) vs. controls. The VOO group also had significant decreases in VCAM-1 and CRP ($P < 0.05$).

In 1997, a landmark study (Appel et al., 1997), the Dietary Approaches to Stop Hypertension (DASH) trial, was published in the New England Journal of Medicine. This trial enrolled 459 subjects with systolic BP < 160 mmHg and diastolic BP of 80 to 95 mmHg. After a 3-week run in phase consisting of a diet low in fruits, vegetables and dairy, and with fat intake equal to that of a typical American diet, the subjects were randomized to receive one of three diets prepared by the research unit for 8 weeks: 1) a diet high in fruits and vegetables, 2) a combination diet high in fruits and vegetable plus low-fat dairy and low in fat and saturated fat, or 3) a control diet low in potassium, magnesium, calcium and fiber with macronutrient intake comparable to average US intake. All diets contained ~ 3 grams sodium and body weight was held stable. Although both diets had significant decreases in systolic BP vs. the control group, the combination diet proved to have a greater effect (-5.5 mmHg, $P < 0.001$) compared to the high fruit and vegetable diet (-2.8 mmHg, $P < 0.001$). Likewise, the combination group had a significantly lower diastolic BP level of -3.0 mmHg ($P < 0.001$) more than the control diet. And, although the high fruit and vegetable diet conferred a greater reduction in diastolic BP of -1.1 mmHg compared to controls, this reduction did not achieve significance ($P = 0.07$). Interestingly, the

researchers reported the decreases in BP were achieved within the first two weeks of the experimental diets and were sustained throughout the next 6 weeks of the study.

A follow-up, cross-over study was conducted in an attempt to further study the underlying effects that potassium, magnesium and fiber found in the DASH diet on BP (Al-Solaiman et al., 2010). In this study, a total of 30 subjects were enrolled including 15 lean ($BMI < 25 \text{ kg/m}^2$) normotensive, low CVD risk subjects and 15 abdominally obese ($WC > 40''$ for men and $>35''$ for women), hypertensive individuals with at least one other metabolic syndrome criteria risk factor. After a 3 week run in diet consisting of low fruit (1-2 servings/d), vegetables (1-2 servings/d), and fiber (9g/d), the subjects were randomized to consume either a diet high in fruits (5-6 servings/d), vegetables (3-4 servings/d) and fiber (31g/d) (DASH) or the run in diet with potassium citrate or potassium chloride, magnesium oxide and metamucil supplements to achieve levels equal to those of the DASH diet. Both diets consisted of 50%CHO/35%fat/15%PRO, 3 grams sodium, 700mg calcium, and 2000 kcal per day. Despite no significant weight change throughout the study, after 3 weeks on the DASH diet, the abdominally obese subjects had lower systolic and diastolic BP than either the supplemented or run in diet ($P < 0.01$). They also had significantly lower systolic BP level on the fruit and vegetable diet compared to the supplemented group ($P < 0.05$), but there were no differences in BP between the run in and supplemented diet groups. However, the lean, normotensive subjects had no significant difference in either systolic or diastolic BP between all three diets. Markers of endothelial function, including small ($P < 0.01$) and large ($P < 0.05$) artery elasticity and aortic-elasticity index (AIX), ($P < 0.001$) were all significantly

improved on the DASH diet in the abdominally obese groups compared to the run in diet, whereas the supplemented group only had improvements in AIX ($P < 0.001$). Additionally, the DASH diet resulted in a significant improvement in AIX compared to the run in diet ($P < 0.05$) in normotensive, lean subjects. The authors concluded that the higher levels of vitamins C, E, and folate, and arginine and lycopene found in the DASH diet compared to the supplemented diet may have been responsible for the added benefit of consuming whole fruits and vegetables and dietary fiber rather than supplements.

A 2005 meta-analysis of 24 qualifying randomized, controlled trials consisting of 1404 subjects was conducted to examine the effect of dietary fiber supplementation of between 3.5 and 42.6 g/day on BP status (Streppel, Arends, van 't Veer, Grobbee, & Geleijnse, 2005). Despite an overall average weight loss of only -0.39 kg ($P = 0.13$), they found a significant decrease in diastolic BP (-1.26 mmHg; 95% CI, -2.04 to -0.48) in the weighted analysis. An additional meta-analysis of 67 controlled trials which included a total of 2990 subjects examined the effect of soluble fiber supplementation (oat, psyllium, pectin or guar gum), which lasted an average of 49 days with a mean intake of 9.5 g/d, on serum lipid levels (Brown, Rosner, Willett, & Sacks, 1999). The subjects in the intervention, high-fiber groups only lost an average of -0.9 kg, whereas the control, low-fiber diet groups lost a mean of -0.64 kg. When examining the practical dose of between 2 and 10 grams of soluble fiber supplementation, psyllium had the greatest LDL-C lowering effect of -2.55 mg/dL (95% CI, -5.64 to -0.54). In addition, all soluble fiber types combined showed a decrease in LDL-C cholesterol of -2.20 mg/dL (95% CI, -2.71 – 1.70) with negligible change in HDL-C and TGs. Thus, it appears that although the decreases in LDL-C are small,

soluble fiber consumption proves to be an addition dietary tool to confer positive health benefits with little or no weight change. Hence, the FDA allows manufactures to label products with a qualified health claim that states there may be a reduced risk of CVD resulting from regular consumption of soluble fiber when it is a part of a diet low in cholesterol and saturated fat (Food and Drug Administration, 2009)

The fact that intervention studies show improved parameters in cardiovascular and diabetic risk factors without weight loss is encouraging because successful weight loss maintenance, which has been reported to be between 5-20%, is extremely low (Crawford, Jeffery, & French, 2000; Wing & Phelan, 2005). Finally, the data show that, not obesity per se, but poor dietary habits and low levels of fitness are more likely predictive of higher rates of CVD, DM and most cancers. And because it has been shown that with intentional weight loss there is a subsequent low rate of weight loss maintenance, and the accompanying weight regain comes with a price, it may be wise to place a much higher priority on diet and exercise either with or without weight loss to successfully ameliorate many of the negative physiological health parameters related to obesity.

REFERENCES

- Anonymous. (2008). Position of the american dietetic association: Health implications of dietary fiber. *Journal of the American Dietetic Association*, 108(10), 1716-1731.
- Adrian, T. E., Ferri, G. L., Bacarese-Hamilton, A. J., Fuessl, H. S., Polak, J. M., & Bloom, S. R. (1985). Human distribution and release of a putative new gut hormone, peptide YY. *Gastroenterology*, 89(5), 1070-1077.
- Allison, D. B., Fontaine, K. R., Manson, J. E., Stevens, J., & VanItallie, T. B. (1999). Annual deaths attributable to obesity in the united states. *JAMA : The Journal of the American Medical Association*, 282(16), 1530-1538.

- Almiron-Roig, E., & Drewnowski, A. (2003). Hunger, thirst, and energy intakes following consumption of caloric beverages. *Physiology & Behavior*, 79(4-5), 767-773.
- Al-Solaiman, Y., Jesri, A., Mountford, W. K., Lackland, D. T., Zhao, Y., & Egan, B. M. (2010). DASH lowers blood pressure in obese hypertensives beyond potassium, magnesium and fibre. *Journal of Human Hypertension*, 24(4), 237-246.
- American Heart Association. (2012). Retrieved May 13 from <http://www.cnpp.usda.gov/publications/dietaryguidelines/2010/meeting2/commitmentattachments/aha-220e.pdf>
- Anderson, G. H., Catherine, N. L., Woodend, D. M., & Wolever, T. M. (2002). Inverse association between the effect of carbohydrates on blood glucose and subsequent short-term food intake in young men. *The American Journal of Clinical Nutrition*, 76(5), 1023-1030.
- Anderson, G. H., & Moore, S. E. (2004). Dietary proteins in the regulation of food intake and body weight in humans. *The Journal of Nutrition*, 134(4), 974S-98S.
- Anderson, J. W., Baird, P., Davis, R. H., Jr, Ferreri, S., Knudtson, M., Koraym, A., et al. (2009). Health benefits of dietary fiber. *Nutrition Reviews*, 67(4), 188-205.
- Appel, L. J., Moore, T. J., Obarzanek, E., Vollmer, W. M., Svetkey, L. P., Sacks, F. M., et al. (1997). A clinical trial of the effects of dietary patterns on blood pressure. DASH collaborative research group. *The New England Journal of Medicine*, 336(16), 1117-1124.
- Ashby, D., & Bloom, S. R. (2007). Recent progress in PYY research--an update report for 8th NPY meeting. *Peptides*, 28(2), 198-202.
- Balducci, S., Zanuso, S., Nicolucci, A., De Feo, P., Cavallo, S., Cardelli, P., et al. (2010). Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: A randomized controlled trial: The Italian diabetes and exercise study (IDES). *Archives of Internal Medicine*, 170(20), 1794-1803.
- Behall, K. M., Scholfield, D. J., & Hallfrisch, J. (2004). Lipids significantly reduced by diets containing barley in moderately hypercholesterolemic men. *Journal of the American College of Nutrition*, 23(1), 55-62.
- Bell, E. A., & Rolls, B. J. (2001). Energy density of foods affects energy intake across multiple levels of fat content in lean and obese women. *The American Journal of Clinical Nutrition*, 73(6), 1010-1018.
- Bennett, W. I. (1995). Beyond overeating. *The New England Journal of Medicine*, 332(10), 673-674.

- Benoit, S. C., Air, E. L., Coolen, L. M., Strauss, R., Jackman, A., Clegg, D. J., et al. (2002). The catabolic action of insulin in the brain is mediated by melanocortins. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 22(20), 9048-9052.
- Berkowitz, R. I., Wadden, T. A., Gehrman, C. A., Bishop-Gilyard, C. T., Moore, R. H., Womble, L. G., et al. (2011). Meal replacements in the treatment of adolescent obesity: A randomized controlled trial. *Obesity (Silver Spring, Md.)*, 19(6), 1193-1199.
- Blatt, A. D., Williams, R. A., Roe, L. S., & Rolls, B. J. (2012). Effects of energy content and energy density of pre-portioned entrees on energy intake. *Obesity (Silver Spring, Md.)*,
- Blundell, J., de Graaf, C., Hulshof, T., Jebb, S., Livingstone, B., Lluch, A., et al. (2010). Appetite control: Methodological aspects of the evaluation of foods. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 11(3), 251-270.
- Boers, H. (2009). All fibres are equal, but some fibres are more equal than others. *Agro Food Industry Hi-Tech*, 20(3), 13-16.
- Bogusky A. (2008). *B the 9-inch diet*. (1st edition ed.). Brooklyn, NY: powerHouse Books.
- Boston, B. A., Blaydon, K. M., Varnerin, J., & Cone, R. D. (1997). Independent and additive effects of central POMC and leptin pathways on murine obesity. *Science (New York, N.Y.)*, 278(5343), 1641-1644.
- Bouchard, C., Tremblay, A., Despres, J. P., Nadeau, A., Lupien, P. J., Theriault, G., et al. (1990). The response to long-term overfeeding in identical twins. *The New England Journal of Medicine*, 322(21), 1477-1482.
- Bouche, C., Rizkalla, S. W., Luo, J., Vidal, H., Veronese, A., Pacher, N., et al. (2002). Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. *Diabetes Care*, 25(5), 822-828.
- Brand-Miller, J., McMillan-Price, J., Steinbeck, K., & Caterson, I. (2009). Dietary glycemic index: Health implications. *Journal of the American College of Nutrition*, 28 Suppl, 446S-449S.
- Brenna, J. T. (2002). Efficiency of conversion of alpha-linolenic acid to long chain n-3 fatty acids in man. *Current Opinion in Clinical Nutrition and Metabolic Care*, 5(2), 127-132.
- Brown, L., Rosner, B., Willett, W. W., & Sacks, F. M. (1999). Cholesterol-lowering effects of dietary fiber: A meta-analysis. *The American Journal of Clinical Nutrition*, 69(1), 30-42.

- Burton-Freeman, B. (2000). Dietary fiber and energy regulation. *The Journal of Nutrition*, 130(2S Suppl), 272S-275S.
- Calder, P. C. (2009). Polyunsaturated fatty acids and inflammatory processes: New twists in an old tale. *Biochimie*, 91(6), 791-795.
- Campos, P., Saguy, A., Ernsberger, P., Oliver, E., & Gaesser, G. (2006). The epidemiology of overweight and obesity: Public health crisis or moral panic? *International Journal of Epidemiology*, 35(1), 55-60.
- Cani, P. D., Dewever, C., & Delzenne, N. M. (2004). Inulin-type fructans modulate gastrointestinal peptides involved in appetite regulation (glucagon-like peptide-1 and ghrelin) in rats. *The British Journal of Nutrition*, 92(3), 521-526.
- Cheskin, L. J., Mitchell, A. M., Jhaveri, A. D., Mitola, A. H., Davis, L. M., Lewis, R. A., et al. (2008). Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: A controlled clinical trial. *The Diabetes Educator*, 34(1), 118-127.
- Considine, R. V., Sinha, M. K., Heiman, M. L., Kriauciunas, A., Stephens, T. W., Nyce, M. R., et al. (1996). Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *The New England Journal of Medicine*, 334(5), 292-295.
- Cornelissen, V. A., & Fagard, R. H. (2005). Effect of resistance training on resting blood pressure: A meta-analysis of randomized controlled trials. *Journal of Hypertension*, 23(2), 251-259.
- Couet, C., Delarue, J., Ritz, P., Antoine, J. M., & Lamisse, F. (1997). Effect of dietary fish oil on body fat mass and basal fat oxidation in healthy adults. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 21(8), 637-643.
- Couillard, C., Despres, J. P., Lamarche, B., Bergeron, J., Gagnon, J., Leon, A. S., et al. (2001). Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: Evidence from men of the health, risk factors, exercise training and genetics (HERITAGE) family study. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 21(7), 1226-1232.
- Crawford, D., Jeffery, R. W., & French, S. A. (2000). Can anyone successfully control their weight? findings of a three year community-based study of men and women. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 24(9), 1107-1110.
- Cummings, D. E., Weigle, D. S., Frayo, R. S., Breen, P. A., Ma, M. K., Dellinger, E. P., et al. (2002). Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *The New England Journal of Medicine*, 346(21), 1623-1630.

- Cvetkovic, R. S., & Plosker, G. L. (2007). Exenatide: A review of its use in patients with type 2 diabetes mellitus (as an adjunct to metformin and/or a sulfonylurea). *Drugs*, 67(6), 935-954.
- Dansinger, M. L., Gleason, J. A., Griffith, J. L., Selker, H. P., & Schaefer, E. J. (2005). Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: A randomized trial. *JAMA : The Journal of the American Medical Association*, 293(1), 43-53.
- Das, S. K., Gilhooly, C. H., Golden, J. K., Pittas, A. G., Fuss, P. J., Cheatham, R. A., et al. (2007). Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: A 1-y randomized controlled trial. *The American Journal of Clinical Nutrition*, 85(4), 1023-1030.
- Davis, L. M., Coleman, C., Kiel, J., Rampolla, J., Hutchison, T., Ford, L., et al. (2010). Efficacy of a meal replacement diet plan compared to a food-based diet plan after a period of weight loss and weight maintenance: A randomized controlled trial. *Nutrition Journal*, 9, 11.
- de Graaf, C., Blom, W. A., Smeets, P. A., Stafleu, A., & Hendriks, H. F. (2004). Biomarkers of satiation and satiety. *The American Journal of Clinical Nutrition*, 79(6), 946-961.
- DeFina, L. F., Marcoux, L. G., Devers, S. M., Cleaver, J. P., & Willis, B. L. (2011). Effects of omega-3 supplementation in combination with diet and exercise on weight loss and body composition. *American Journal of Clinical Nutrition*, 93(2), 455-462.
- Devkota, S., & Layman, D. K. (2010). Protein metabolic roles in treatment of obesity. *Current Opinion in Clinical Nutrition and Metabolic Care*, 13(4), 403-407.
- Diaz, V. A., Mainous, A. G., 3rd, & Everett, C. J. (2005). The association between weight fluctuation and mortality: Results from a population-based cohort study. *Journal of Community Health*, 30(3), 153-165.
- Ditschuneit, H. H., Flechtner-Mors, M., Johnson, T. D., & Adler, G. (1999). Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *The American Journal of Clinical Nutrition*, 69(2), 198-204.
- Drucker, D. J. (2005). Biologic actions and therapeutic potential of the proglucagon-derived peptides. *Nature Clinical Practice. Endocrinology & Metabolism*, 1(1), 22-31.
- Eaton, S. B., Eaton, S. B., 3rd, Konner, M. J., & Shostak, M. (1996). An evolutionary perspective enhances understanding of human nutritional requirements. *The Journal of Nutrition*, 126(6), 1732-1740.

- Ebbeling, C. B., Leidig, M. M., Sinclair, K. B., Hangen, J. P., & Ludwig, D. S. (2003). A reduced-glycemic load diet in the treatment of adolescent obesity. *Archives of Pediatrics & Adolescent Medicine*, 157(8), 773-779.
- Ebbeling, C. B., Leidig, M. M., Sinclair, K. B., Seger-Shippe, L. G., Feldman, H. A., & Ludwig, D. S. (2005). Effects of an ad libitum low-glycemic load diet on cardiovascular disease risk factors in obese young adults. *The American Journal of Clinical Nutrition*, 81(5), 976-982.
- Estruch, R., Martinez-Gonzalez, M. A., Corella, D., Salas-Salvado, J., Ruiz-Gutierrez, V., Covas, M. I., et al. (2006). Effects of a mediterranean-style diet on cardiovascular risk factors: A randomized trial. *Annals of Internal Medicine*, 145(1), 1-11.
- Fagard, R. H. (1999). Physical activity in the prevention and treatment of hypertension in the obese. *Medicine and Science in Sports and Exercise*, 31(11 Suppl), S624-30.
- Farias, M. M., Cuevas, A. M., & Rodriguez, F. (2011). Set-point theory and obesity. *Metabolic Syndrome and Related Disorders*, 9(2), 85-89.
- Farrell, S. W., Cortese, G. M., LaMonte, M. J., & Blair, S. N. (2007). Cardiorespiratory fitness, different measures of adiposity, and cancer mortality in men. *Obesity (Silver Spring, Md.)*, 15(12), 3140-3149.
- Fekete, C., Kelly, J., Mihaly, E., Sarkar, S., Rand, W. M., Legradi, G., et al. (2001). Neuropeptide Y has a central inhibitory action on the hypothalamic-pituitary-thyroid axis. *Endocrinology*, 142(6), 2606-2613.
- Ferrara, C. M., Goldberg, A. P., Ortmeyer, H. K., & Ryan, A. S. (2006). Effects of aerobic and resistive exercise training on glucose disposal and skeletal muscle metabolism in older men. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 61(5), 480-487.
- Fischer, K., Colombani, P. C., & Wenk, C. (2004). Metabolic and cognitive coefficients in the development of hunger sensations after pure macronutrient ingestion in the morning. *Appetite*, 42(1), 49-61.
- Flachs, P., Horakova, O., Brauner, P., Rossmeisl, M., Pecina, P., Franssen-van Hal, N., et al. (2005). Polyunsaturated fatty acids of marine origin upregulate mitochondrial biogenesis and induce beta-oxidation in white fat. *Diabetologia*, 48(11), 2365-2375.
- Flachs, P., Rossmeisl, M., Bryhn, M., & Kopecky, J. (2009). Cellular and molecular effects of n-3 polyunsaturated fatty acids on adipose tissue biology and metabolism. *Clinical Science (London, England : 1979)*, 116(1), 1-16.

- Flechtner-Mors, M., Ditschuneit, H. H., Johnson, T. D., Suchard, M. A., & Adler, G. (2000). Metabolic and weight loss effects of long-term dietary intervention in obese patients: Four-year results. *Obesity Research*, 8(5), 399-402.
- Flegal, K. M., Carroll, M. D., Ogden, C. L., & Curtin, L. R. (2010). Prevalence and trends in obesity among US adults, 1999-2008. *JAMA : The Journal of the American Medical Association*, 303(3), 235-241.
- Flegal, K. M., Graubard, B. I., Williamson, D. F., & Gail, M. H. (2005). Excess deaths associated with underweight, overweight, and obesity. *JAMA : The Journal of the American Medical Association*, 293(15), 1861-1867.
- Fogelholm, M. (2010). Physical activity, fitness and fatness: Relations to mortality, morbidity and disease risk factors. A systematic review. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 11(3), 202-221.
- Food and Drug Administration. (2009). *Guidance for industry: A food labeling guide*. Retrieved 06/01, 2012, from <http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/UCM265446.pdf>
- Foster, G. D., Wadden, T. A., Swain, R. M., Stunkard, A. J., Platte, P., & Vogt, R. A. (1998). The eating inventory in obese women: Clinical correlates and relationship to weight loss. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 22(8), 778-785.
- Freeland, K. R., Anderson, G. H., & Wolever, T. M. (2009). Acute effects of dietary fibre and glycaemic carbohydrate on appetite and food intake in healthy males. *Appetite*, 52(1), 58-64.
- French, S. (2004). Effects of dietary fat and carbohydrate on appetite vary depending upon site and structure. *The British Journal of Nutrition*, 92 Suppl 1, S23-6.
- Gaesser, G. A. (2007). Exercise for prevention and treatment of cardiovascular disease, type 2 diabetes, and metabolic syndrome. *Current Diabetes Reports*, 7(1), 14-19.
- Geary, N., Le Sauter, J., & Noh, U. (1993). Glucagon acts in the liver to control spontaneous meal size in rats. *The American Journal of Physiology*, 264(1 Pt 2), R116-22.
- Gilhooly, C. H., Das, S. K., Golden, J. K., McCrory, M. A., Rochon, J., DeLany, J. P., et al. (2008). Use of cereal fiber to facilitate adherence to a human caloric restriction program. *Aging Clinical and Experimental Research*, 20(6), 513-520.

- Goldsmith, R., Joannisse, D. R., Gallagher, D., Pavlovich, K., Shamoan, E., Leibel, R. L., et al. (2010). Effects of experimental weight perturbation on skeletal muscle work efficiency, fuel utilization, and biochemistry in human subjects. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, 298(1), R79-88.
- Gruberg, L., Weissman, N. J., Waksman, R., Fuchs, S., Deible, R., Pinnow, E. E., et al. (2002). The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: The obesity paradox? *Journal of the American College of Cardiology*, 39(4), 578-584.
- Guagnano, M. T., Ballone, E., Pace-Palitti, V., Vecchia, R. D., D'Orazio, N., Manigrasso, M. R., et al. (2000). Risk factors for hypertension in obese women. the role of weight cycling. *European Journal of Clinical Nutrition*, 54(4), 356-360.
- Gutniak, M., Orskov, C., Holst, J. J., Ahren, B., & Efendic, S. (1992). Antidiabetogenic effect of glucagon-like peptide-1 (7-36)amide in normal subjects and patients with diabetes mellitus. *The New England Journal of Medicine*, 326(20), 1316-1322.
- Hainer, V., Kunesova, M., Bellisle, F., Parizkova, J., Braunerova, R., Wagenknecht, M., et al. (2006). The eating inventory, body adiposity and prevalence of diseases in a quota sample of czech adults. *International Journal of Obesity (2005)*, 30(5), 830-836.
- Halaas, J. L., Gajiwala, K. S., Maffei, M., Cohen, S. L., Chait, B. T., Rabinowitz, D., et al. (1995). Weight-reducing effects of the plasma protein encoded by the obese gene. *Science (New York, N.Y.)*, 269(5223), 543-546.
- Hamdy, O., & Zwiefelhofer, D. (2010). Weight management using a meal replacement strategy in type 2 diabetes. *Current Diabetes Reports*, 10(2), 159-164.
- Hetherington, M. M., Foster, R., Newman, T., Anderson, A. S., & Norton, G. (2006). Understanding variety: Tasting different foods delays satiation. *Physiology & Behavior*, 87(2), 263-271.
- Heymsfield, S. B. (2010). Meal replacements and energy balance. *Physiology & Behavior*, 100(1), 90-94.
- Heymsfield, S. B., van Mierlo, C. A., van der Knaap, H. C., Heo, M., & Frier, H. I. (2003). Weight management using a meal replacement strategy: Meta and pooling analysis from six studies. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 27(5), 537-549.

- Hill, A. M., Buckley, J. D., Murphy, K. J., & Howe, P. R. (2007). Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors. *The American Journal of Clinical Nutrition*, 85(5), 1267-1274.
- Howarth, N. C., Huang, T. T., Roberts, S. B., & McCrory, M. A. (2005). Dietary fiber and fat are associated with excess weight in young and middle-aged US adults. *Journal of the American Dietetic Association*, 105(9), 1365-1372.
- Howarth, N. C., Saltzman, E., McCrory, M. A., Greenberg, A. S., Dwyer, J., Ausman, L., et al. (2003). Fermentable and nonfermentable fiber supplements did not alter hunger, satiety or body weight in a pilot study of men and women consuming self-selected diets. *The Journal of Nutrition*, 133(10), 3141-3144.
- Howarth, N.C., Saltzman, E., Roberts, S.B., (2001). Dietary Fiber and Weight Regulation. *Nutrition Reviews*, 59(5), 129-139.
- Howlett, J., & Ashwell, M. (2008). Glycemic response and health: Summary of a workshop. *The American Journal of Clinical Nutrition*, 87(1), 212S-216S.
- Hun, C. S., Hasegawa, K., Kawabata, T., Kato, M., Shimokawa, T., & Kagawa, Y. (1999). Increased uncoupling protein2 mRNA in white adipose tissue, and decrease in leptin, visceral fat, blood glucose, and cholesterol in KK-ay mice fed with eicosapentaenoic and docosahexaenoic acids in addition to linolenic acid. *Biochemical and Biophysical Research Communications*, 259(1), 85-90.
- Jenkins, D. J., Wolever, T. M., Taylor, R. H., Barker, H., Fielden, H., Baldwin, J. M., et al. (1981). Glycemic index of foods: A physiological basis for carbohydrate exchange. *The American Journal of Clinical Nutrition*, 34(3), 362-366.
- Johnston, C. S., Tjonn, S. L., & Swan, P. D. (2004). High-protein, low-fat diets are effective for weight loss and favorably alter biomarkers in healthy adults. *The Journal of Nutrition*, 134(3), 586-591.
- Jonnalagadda, S. S., Harnack, L., Liu, R. H., McKeown, N., Seal, C., Liu, S., et al. (2011). Putting the whole grain puzzle together: Health benefits associated with whole grains--summary of american society for nutrition 2010 satellite symposium. *The Journal of Nutrition*, 141(5), 1011S-22S.
- Kabir, M., Skurnik, G., Naour, N., Pechtner, V., Meugnier, E., Rome, S., et al. (2007). Treatment for 2 mo with n 3 polyunsaturated fatty acids reduces adiposity and some atherogenic factors but does not improve insulin sensitivity in women with type 2 diabetes: A randomized controlled study. *The American Journal of Clinical Nutrition*, 86(6), 1670-1679.

- Kajioka, T., Tsuzuku, S., Shimokata, H., & Sato, Y. (2002). Effects of intentional weight cycling on non-obese young women. *Metabolism: Clinical and Experimental*, 51(2), 149-154.
- Keeseey, R. E. (1993). Physiological regulation of body energy: Implications for obesity. In A. J. Stunkard, & T. A. Wadden (Eds.), *Obesity: Theory and therapy* (2nd ed., pp. 77). New York: Raven Press.
- Kimball, S., & Jefferson, L. (2001). Regulation of protein synthesis by branched-chain amino acids. *Current Opinion in Clinical Nutrition and Metabolic Care*, 4(1), 39-43.
- King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE. (2009). Beneficial effects of exercise: Shifting the focus from body weight to other markers of health. *Br J Sports Med*, 43, 924-927.
- King, N. A., Craig, S. A., Pepper, T., & Blundell, J. E. (2005). Evaluation of the independent and combined effects of xylitol and polydextrose consumed as a snack on hunger and energy intake over 10 d. *The British Journal of Nutrition*, 93(6), 911-915.
- Klem, M. L., Wing, R. R., McGuire, M. T., Seagle, H. M., & Hill, J. O. (1997). A descriptive study of individuals successful at long-term maintenance of substantial weight loss. *The American Journal of Clinical Nutrition*, 66(2), 239-246.
- Kochanek, K., Jiaquan, X., Murphy, S., Minino, A. & Hsiang-Ching, K. (2011). *National vital statistics reports, deaths: Preliminary data for 2009*. Retrieved 6/10, 2011, from http://www.cdc.gov/nchs/data/nvsr/nvsr59/nvsr59_04.pdf
- Kojima, M., Hosoda, H., Date, Y., Nakazato, M., Matsuo, H., & Kangawa, K. (1999). Ghrelin is a growth-hormone-releasing acylated peptide from stomach. *Nature*, 402(6762), 656-660.
- Kratz, M., Callahan, H. S., Yang, P. Y., Matthys, C. C., & Weigle, D. S. (2009). Dietary n-3-polyunsaturated fatty acids and energy balance in overweight or moderately obese men and women: A randomized controlled trial. *Nutrition & Metabolism*, 6, 24.
- Krebs, J. D., Browning, L. M., McLean, N. K., Rothwell, J. L., Mishra, G. D., Moore, C. S., et al. (2006). Additive benefits of long-chain n-3 polyunsaturated fatty acids and weight-loss in the management of cardiovascular disease risk in overweight hyperinsulinaemic women. *International Journal of Obesity* (2005), 30(10), 1535-1544.
- Krieger, J. W., Sitren, H. S., Daniels, M. J., & Langkamp-Henken, B. (2006). Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: A meta-regression 1. *The American Journal of Clinical Nutrition*, 83(2), 260-274.

- Kristensen, M., Jensen, M. G., Riboldi, G., Petronio, M., Bugel, S., Toubro, S., et al. (2010). Wholegrain vs. refined wheat bread and pasta. effect on postprandial glycemia, appetite, and subsequent ad libitum energy intake in young healthy adults. *Appetite*, 54(1), 163-169.
- Kunesova, M., Braunerova, R., Hlavaty, P., Tvrzicka, E., Stankova, B., Skrha, J., et al. (2006). The influence of n-3 polyunsaturated fatty acids and very low calorie diet during a short-term weight reducing regimen on weight loss and serum fatty acid composition in severely obese women. *Physiological Research / Academia Scientiarum Bohemoslovaca*, 55(1), 63-72.
- Lambert, P. D., Couceyro, P. R., McGirr, K. M., Dall Vechia, S. E., Smith, Y., & Kuhar, M. J. (1998). CART peptides in the central control of feeding and interactions with neuropeptide Y. *Synapse (New York, N.Y.)*, 29(4), 293-298.
- Layman, D. K. (2009). Dietary guidelines should reflect new understandings about adult protein needs. *Nutrition & Metabolism*, 6, 12.
- Layman, D. K., Evans, E. M., Erickson, D., Seyler, J., Weber, J., Bagshaw, D., et al. (2009). A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *The Journal of Nutrition*, 139(3), 514-521.
- Ledikwe, J. H., Rolls, B. J., Smiciklas-Wright, H., Mitchell, D. C., Ard, J. D., Champagne, C., et al. (2007). Reductions in dietary energy density are associated with weight loss in overweight and obese participants in the PREMIER trial. *The American Journal of Clinical Nutrition*, 85(5), 1212-1221.
- Lee, K. W., Song, K. E., Lee, H. S., Kim, Y. K., Lee, S. W., Kim, D. J., et al. (2006). The effects of goami no. 2 rice, a natural fiber-rich rice, on body weight and lipid metabolism. *Obesity (Silver Spring, Md.)*, 14(3), 423-430.
- Leibel, R. L., Rosenbaum, M., & Hirsch, J. (1995). Changes in energy expenditure resulting from altered body weight. *The New England Journal of Medicine*, 332(10), 621-628.
- Levine, J. A., Eberhardt, N. L., & Jensen, M. D. (1999). Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science (New York, N.Y.)*, 283(5399), 212-214.
- Levine, J. A., Lanningham-Foster, L. M., McCrady, S. K., Krizan, A. C., Olson, L. R., Kane, P. H., et al. (2005). Interindividual variation in posture allocation: Possible role in human obesity. *Science (New York, N.Y.)*, 307(5709), 584-586.
- Li, J., Zhang, N., Hu, L., Li, Z., Li, R., Li, C., et al. (2011). Improvement in chewing activity reduces energy intake in one meal and modulates plasma gut hormone concentrations in obese and lean young chinese men. *The American Journal of Clinical Nutrition*, 94(3), 709-716.

- Lichtman, S. W., Pisarska, K., Berman, E. R., Pestone, M., Dowling, H., Offenbacher, E., et al. (1992). Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *The New England Journal of Medicine*, 327(27), 1893-1898.
- Ludwig, D. S. (2000). Dietary glycemic index and obesity. *The Journal of Nutrition*, 130(2S Suppl), 280S-283S.
- Luo, J., Margolis, K. L., Adami, H. O., Lopez, A. M., Lessin, L., Ye, W., et al. (2007). Body size, weight cycling, and risk of renal cell carcinoma among postmenopausal women: The women's health initiative (united states). *American Journal of Epidemiology*, 166(7), 752-759.
- Marmonier, C., Chapelot, D., & Louis-Sylvestre, J. (2000). Effects of macronutrient content and energy density of snacks consumed in a satiety state on the onset of the next meal. *Appetite*, 34(2), 161-168.
- Mayer, J. (1953). Glucostatic mechanism of regulation of food intake. *The New England Journal of Medicine*, 249(1), 13-16.
- McAuley, P. A., & Blair, S. N. (2011). Obesity paradoxes. *Journal of Sports Sciences*, 29(8), 773-782.
- McMillan-Price, J., Petocz, P., Atkinson, F., O'Neill, K., Samman, S., Steinbeck, K., et al. (2006). Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: A randomized controlled trial. *Archives of Internal Medicine*, 166(14), 1466-1475.
- Mena, M. P., Sacanella, E., Vazquez-Agell, M., Morales, M., Fito, M., Escoda, R., et al. (2009). Inhibition of circulating immune cell activation: A molecular antiinflammatory effect of the mediterranean diet. *The American Journal of Clinical Nutrition*, 89(1), 248-256.
- Merrill, E. P., Kramer, F. M., Cardello, A., & Schutz, H. (2002). A comparison of satiety measures. *Appetite*, 39(2), 181-183.
- Mestek, M. L., Westby, C. M., Van Guilder, G. P., Greiner, J. J., Stauffer, B. L., & DeSouza, C. A. (2010). Regular aerobic exercise, without weight loss, improves endothelium-dependent vasodilation in overweight and obese adults. *Obesity (Silver Spring, Md.)*, 18(8), 1667-1669.
- Mokdad, A. H., Marks, J. S., Stroup, D. F., & Gerberding, J. L. (2004). Actual causes of death in the united states, 2000. *JAMA : The Journal of the American Medical Association*, 291(10), 1238-1245.
- Monsivais, P., Carter, B. E., Christiansen, M., Perrigue, M. M., & Drewnowski, A. (2011). Soluble fiber dextrin enhances the satiating power of beverages. *Appetite*, 56(1), 9-14.

- Montani, J. P., Viecegli, A. K., Prevot, A., & Dulloo, A. G. (2006). Weight cycling during growth and beyond as a risk factor for later cardiovascular diseases: The 'repeated overshoot' theory. *International Journal of Obesity (2005)*, 30 Suppl 4, S58-66.
- Nakazato, M., Murakami, N., Date, Y., Kojima, M., Matsuo, H., Kangawa, K., et al. (2001). A role for ghrelin in the central regulation of feeding. *Nature*, 409(6817), 194-198.
- Neel, J. V. (1962). Diabetes mellitus: A "thrifty" genotype rendered detrimental by "progress"? *American Journal of Human Genetics*, 14, 353-362.
- Niwano, Y., Adachi, T., Kashimura, J., Sakata, T., Sasaki, H., Sekine, K., et al. (2009). Is glycemic index of food a feasible predictor of appetite, hunger, and satiety? *Journal of Nutritional Science and Vitaminology*, 55(3), 201-207.
- Noakes, M., Foster, P. R., Keogh, J. B., & Clifton, P. M. (2004). Meal replacements are as effective as structured weight-loss diets for treating obesity in adults with features of metabolic syndrome. *The Journal of Nutrition*, 134(8), 1894-1899.
- Noreen, E. E., Sass, M. J., Crowe, M. L., Pabon, V. A., Brandauer, J., & Averill, L. K. (2010). Effects of supplemental fish oil on resting metabolic rate, body composition, and salivary cortisol in healthy adults. *Journal of the International Society of Sports Nutrition*, 7, 31.
- Olson, M. B., Kelsey, S. F., Bittner, V., Reis, S. E., Reichek, N., Handberg, E. M., et al. (2000). Weight cycling and high-density lipoprotein cholesterol in women: Evidence of an adverse effect: A report from the NHLBI-sponsored WISE study. women's ischemia syndrome evaluation study group. *Journal of the American College of Cardiology*, 36(5), 1565-1571.
- O'Neil, C. E., Zanovec, M., Cho, S. S., & Nicklas, T. A. (2010). Whole grain and fiber consumption are associated with lower body weight measures in US adults: National health and nutrition examination survey 1999-2004. *Nutrition Research (New York, N.Y.)*, 30(12), 815-822.
- Pan, A., & Hu, F. B. (2011). Effects of carbohydrates on satiety: Differences between liquid and solid food. *Current Opinion in Clinical Nutrition and Metabolic Care*, 14(4), 385-390.
- Perrigue, M. M., Monsivais, P., & Drewnowski, A. (2009). Added soluble fiber enhances the satiating power of low-energy-density liquid yogurts. *Journal of the American Dietetic Association*, 109(11), 1862-1868.
- Pischon, T., Nothlings, U., & Boeing, H. (2008). Obesity and cancer. *The Proceedings of the Nutrition Society*, 67(2), 128-145.

- Poppitt, S. D., McCormack, D., & Buffenstein, R. (1998). Short-term effects of macronutrient preloads on appetite and energy intake in lean women. *Physiology & Behavior*, 64(3), 279-285.
- Poppitt, S. D., Proctor, J., McGill, A. T., Wiessing, K. R., Falk, S., Xin, L., et al. (2011). Low-dose whey protein-enriched water beverages alter satiety in a study of overweight women. *Appetite*, 56(2), 456-464.
- Potier, M., Fromentin, G., Lesdema, A., Benamouzig, R., Tome, D., & Marsset-Baglieri, A. (2010). The satiety effect of disguised liquid preloads administered acutely and differing only in their nutrient content tended to be weaker for lipids but did not differ between proteins and carbohydrates in human subjects. *The British Journal of Nutrition*, 104(9), 1406-1414.
- Qi, L., & Cho, Y. A. (2008). Gene-environment interaction and obesity. *Nutrition Reviews*, 66(12), 684-694.
- Queenan, K. M., Stewart, M. L., Smith, K. N., Thomas, W., Fulcher, R. G., & Slavin, J. L. (2007). Concentrated oat beta-glucan, a fermentable fiber, lowers serum cholesterol in hypercholesterolemic adults in a randomized controlled trial. *Nutrition Journal*, 6, 6.
- Raben, A., Agerholm-Larsen, L., Flint, A., Holst, J. J., & Astrup, A. (2003). Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. *The American Journal of Clinical Nutrition*, 77(1), 91-100.
- Rampersaud, E., Mitchell, B. D., Pollin, T. I., Fu, M., Shen, H., O'Connell, J. R., et al. (2008). Physical activity and the association of common FTO gene variants with body mass index and obesity. *Archives of Internal Medicine*, 168(16), 1791-1797.
- Reda, T. K., Geliebter, A., & Pi-Sunyer, F. X. (2002). Amylin, food intake, and obesity. *Obesity Research*, 10(10), 1087-1091.
- Rehnan, A. G., Tyson, M., Egger, M., Heller, R. F., & Zwiahlen, M. (2008). Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. *Lancet*, 371(9612), 569-578.
- Roberts, S. B. (2000). High-glycemic index foods, hunger, and obesity: Is there a connection? *Nutrition Reviews*, 58(6), 163-169.
- Rolls, B. J. (2009). The relationship between dietary energy density and energy intake. *Physiology & Behavior*, 97(5), 609-615.
- Rolls, B. J., & Bell, E. A. (2000). Dietary approaches to the treatment of obesity. *The Medical Clinics of North America*, 84(2), 401-18, vi.

- Rolls, B. J., Bell, E. A., & Thorwart, M. L. (1999). Water incorporated into a food but not served with a food decreases energy intake in lean women. *The American Journal of Clinical Nutrition*, 70(4), 448-455.
- Rolls, B. J., Castellanos, V. H., Halford, J. C., Kilara, A., Panyam, D., Pelkman, C. L., et al. (1998). Volume of food consumed affects satiety in men. *The American Journal of Clinical Nutrition*, 67(6), 1170-1177.
- Rolls, B. J., & Hammer, V. A. (1995). Fat, carbohydrate, and the regulation of energy intake. *The American Journal of Clinical Nutrition*, 62(5 Suppl), 1086S-1095S.
- Roseberry, A. G., Liu, H., Jackson, A. C., Cai, X., & Friedman, J. M. (2004). Neuropeptide Y-mediated inhibition of proopiomelanocortin neurons in the arcuate nucleus shows enhanced desensitization in ob/ob mice. *Neuron*, 41(5), 711-722.
- Rosenbaum, M., Hirsch, J., Gallagher, D. A., & Leibel, R. L. (2008). Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. *The American Journal of Clinical Nutrition*, 88(4), 906-912.
- Ross R., & Janiszewski, P.M. (2008). Is weight loss the optimal target for obesity-related cardiovascular disease risk reduction? *Can J Cardiol*, 24 (Suppl D), 25D-31D.
- Roumen, C., Corpeleijn, E., Feskens, E. J., Mensink, M., Saris, W. H., & Blaak, E. E. (2008). Impact of 3-year lifestyle intervention on postprandial glucose metabolism: The SLIM study. *Diabetic Medicine : A Journal of the British Diabetic Association*, 25(5), 597-605.
- Ruzickova, J., Rossmeisl, M., Prazak, T., Flachs, P., Sponarova, J., Veck, M., et al. (2004). Omega-3 PUFA of marine origin limit diet-induced obesity in mice by reducing cellularity of adipose tissue. *Lipids*, 39(12), 1177-1185.
- Sacks, F. M., Bray, G. A., Carey, V. J., Smith, S. R., Ryan, D. H., Anton, S. D., et al. (2009). Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *The New England Journal of Medicine*, 360(9), 859-873.
- Salas-Salvado, J., Bullo, M., Babio, N., Martinez-Gonzalez, M. A., Ibarrola-Jurado, N., Basora, J., et al. (2011). Reduction in the incidence of type 2 diabetes with the mediterranean diet: Results of the PREDIMED-reus nutrition intervention randomized trial. *Diabetes Care*, 34(1), 14-19.
- Sanchez, D., Miguel, M., & Aleixandre, A. (2012). Dietary fiber, gut peptides, and adipocytokines. *Journal of Medicinal Food*, 15(3), 223-230.

- Savage, J. S., Marini, M., & Birch, L. L. (2008). Dietary energy density predicts women's weight change over 6 y. *The American Journal of Clinical Nutrition*, 88(3), 677-684.
- Schoeller, D. A., Cella, L. K., Sinha, M. K., & Caro, J. F. (1997). Entrainment of the diurnal rhythm of plasma leptin to meal timing. *The Journal of Clinical Investigation*, 100(7), 1882-1887.
- Schwartz, M. W., Sipols, A. J., Marks, J. L., Sanacora, G., White, J. D., Scheurink, A., et al. (1992). Inhibition of hypothalamic neuropeptide Y gene expression by insulin. *Endocrinology*, 130(6), 3608-3616.
- Seagle, H. M., Strain, G. W., Makris, A., Reeves, R. S., & American Dietetic Association. (2009). Position of the american dietetic association: Weight management. *Journal of the American Dietetic Association*, 109(2), 330-346.
- Sigal, R. J., Kenny, G. P., Boule, N. G., Wells, G. A., Prud'homme, D., Fortier, M., et al. (2007). Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: A randomized trial. *Annals of Internal Medicine*, 147(6), 357-369.
- Skov, A. R., Toubro, S., Ronn, B., Holm, L., & Astrup, A. (1999). Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 23(5), 528-536.
- Slabber, M., Barnard, H. C., Kuyl, J. M., Dannhauser, A., & Schall, R. (1994). Effects of a low-insulin-response, energy-restricted diet on weight loss and plasma insulin concentrations in hyperinsulinemic obese females. *The American Journal of Clinical Nutrition*, 60(1), 48-53.
- Sloth, B., Krog-Mikkelsen, I., Flint, A., Tetens, I., Bjorck, I., Vinoy, S., et al. (2004). No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet. *The American Journal of Clinical Nutrition*, 80(2), 337-347.
- Smith, C. E., & Tucker, K. L. (2011). Health benefits of cereal fibre: A review of clinical trials. *Nutrition Research Reviews*, , 1-14.
- Smith, T. J., Sigrist, L. D., Bathalon, G. P., McGraw, S., Karl, J. P., & Young, A. J. (2010). Efficacy of a meal-replacement program for promoting blood lipid changes and weight and body fat loss in US army soldiers. *Journal of the American Dietetic Association*, 110(2), 268-273.
- Snowling, N. J., & Hopkins, W. G. (2006). Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: A meta-analysis. *Diabetes Care*, 29(11), 2518-2527.

- Soenen, S., & Westerterp-Plantenga, M. S. (2007). No differences in satiety or energy intake after high-fructose corn syrup, sucrose, or milk preloads. *The American Journal of Clinical Nutrition*, 86(6), 1586-1594.
- Somogyi, V., Gyorffy, A., Scalise, T. J., Kiss, D. S., Goszleth, G., Bartha, T., et al. (2011). Endocrine factors in the hypothalamic regulation of food intake in females: A review of the physiological roles and interactions of ghrelin, leptin, thyroid hormones, oestrogen and insulin. *Nutrition Research Reviews*, , 1-23.
- Stengel, A., & Tache, Y. (2011). Interaction between gastric and upper small intestinal hormones in the regulation of hunger and satiety: Ghrelin and cholecystokinin take the central stage. *Current Protein & Peptide Science*, 12(4), 293-304.
- Streppel, M. T., Arends, L. R., van 't Veer, P., Grobbee, D. E., & Geleijnse, J. M. (2005). Dietary fiber and blood pressure: A meta-analysis of randomized placebo-controlled trials. *Archives of Internal Medicine*, 165(2), 150-156.
- Stubbs, R., & Whybrow, S. (2004). Energy density, diet composition and palatability: Influences on overall food energy intake in humans. *Physiology & Behavior*, 81(5), 755-764.
- Stunkard, A. J., & Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of Psychosomatic Research*, 29(1), 71-83.
- Suzuki, K., Simpson, K. A., Minnion, J. S., Shillito, J. C., & Bloom, S. R. (2010). The role of gut hormones and the hypothalamus in appetite regulation. *Endocrine Journal*, 57(5), 359-372.
- Svetkey, L. P., Stevens, V. J., Brantley, P. J., Appel, L. J., Hollis, J. F., Loria, C. M., et al. (2008). Comparison of strategies for sustaining weight loss: The weight loss maintenance randomized controlled trial. *JAMA : The Journal of the American Medical Association*, 299(10), 1139-1148.
- Tao, Y. X. (2005). Molecular mechanisms of the neural melanocortin receptor dysfunction in severe early onset obesity. *Molecular and Cellular Endocrinology*, 239(1-2), 1-14.
- Thomas, D. E., Elliott, E. J., & Baur, L. (2007). Low glycaemic index or low glycaemic load diets for overweight and obesity. *Cochrane Database of Systematic Reviews (Online)*, (3)(3), CD005105.
- Thorsdottir, I., Tomasson, H., Gunnarsdottir, I., Gisladdottir, E., Kiely, M., Parra, M. D., et al. (2007). Randomized trial of weight-loss-diets for young adults varying in fish and fish oil content. *International Journal of Obesity (2005)*, 31(10), 1560-1566.

- Tremblay, A., & Chaput, J. P. (2009). Adaptive reduction in thermogenesis and resistance to lose fat in obese men. *The British Journal of Nutrition*, 102(4), 488-492.
- U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2011). *Dietary guidelines for Americans 2010*. Retrieved May 15, from <http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/PolicyDoc.pdf>
- van Raalte, D. H., Li, M., Pritchard, P. H., & Wasan, K. M. (2004). Peroxisome proliferator-activated receptor (PPAR)-alpha: A pharmacological target with a promising future. *Pharmaceutical Research*, 21(9), 1531-1538.
- van Rossum, C. T., Pijl, H., Adan, R. A., Hoebee, B., & Seidell, J. C. (2006). Polymorphisms in the NPY and AGRP genes and body fatness in dutch adults. *International Journal of Obesity (2005)*, 30(10), 1522-1528.
- Vazquez, C., Montagna, C., Alcaraz, F., Balsa, J. A., Zamarron, I., Arrieta, F., et al. (2009). Meal replacement with a low-calorie diet formula in weight loss maintenance after weight loss induction with diet alone. *European Journal of Clinical Nutrition*, 63(10), 1226-1232.
- Wadden, T. A., West, D. S., Neiberg, R. H., Wing, R. R., Ryan, D. H., Johnson, K. C., et al. (2009). One-year weight losses in the look AHEAD study: Factors associated with success. *Obesity (Silver Spring, Md.)*, 17(4), 713-722.
- Wanders, A. J., van den Borne, J. J., de Graaf, C., Hulshof, T., Jonathan, M. C., Kristensen, M., et al. (2011). Effects of dietary fibre on subjective appetite, energy intake and body weight: A systematic review of randomized controlled trials. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 12(9), 724-739.
- Weigle, D., Breen, P., Matthys, C., Callahan, H., Meeuws, K., Burden, V., et al. (2005). A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. *American Journal of Clinical Nutrition*, 82(1), 41-48.
- Wernette, C. M., White, B. D., & Zizza, C. A. (2011). Signaling proteins that influence energy intake may affect unintentional weight loss in elderly persons. *Journal of the American Dietetic Association*, 111(6), 864-873.
- Wildman, R. P., Muntner, P., Reynolds, K., McGinn, A. P., Rajpathak, S., Wylie-Rosett, J., et al. (2008). The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: Prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). *Archives of Internal Medicine*, 168(15), 1617-1624.

- Williams, P. G., Grafenauer, S. J., & O'Shea, J. E. (2008). Cereal grains, legumes, and weight management: A comprehensive review of the scientific evidence. *Nutrition Reviews*, 66(4), 171-182.
- Wing, R. R., & Phelan, S. (2005). Long-term weight loss maintenance. *The American Journal of Clinical Nutrition*, 82(1 Suppl), 222S-225S.
- Wynne, K., Stanley, S., McGowan, B., & Bloom, S. (2005). Appetite control. *The Journal of Endocrinology*, 184(2), 291-318.
- Yu, Y., Deng, C., & Huang, X. F. (2009). Obese reversal by a chronic energy restricted diet leaves an increased arc NPY/AgRP, but no alteration in POMC/CART, mRNA expression in diet-induced obese mice. *Behavioural Brain Research*, 205(1), 50-56.
- Zhang, L., Bijker, M. S., & Herzog, H. (2011). The neuropeptide Y system: Pathophysiological and therapeutic implications in obesity and cancer. *Pharmacology & Therapeutics*, 131(1), 91-113.
- Zhang, Y., Proenca, R., Maffei, M., Barone, M., Leopold, L., & Friedman, J. M. (1994). Positional cloning of the mouse obese gene and its human homologue. *Nature*, 372(6505), 425-432.
- Zhang, Y., von Deneen, K. M., Tian, J., Gold, M. S., & Liu, Y. (2011). Food addiction and neuroimaging. *Current Pharmaceutical Design*, 17(12), 1149-1157.

REFERENCES

- Anonymous. (2008). Position of the American Dietetic Association: Health implications of dietary fiber. *Journal of the American Dietetic Association*, 108(10), 1716-1731.
- Abou-Samra, R., Keersmaekers, L., Brienza, D., Mukherjee, R., & Mace, K. (2011). Effect of different protein sources on satiation and short-term satiety when consumed as a starter. *Nutrition Journal*, 10, 139.
- Adrian, T. E., Ferri, G. L., Bacarese-Hamilton, A. J., Fuesl, H. S., Polak, J. M., & Bloom, S. R. (1985). Human distribution and release of a putative new gut hormone, peptide YY. *Gastroenterology*, 89(5), 1070-1077.
- Ainsworth, B., Haskell, W., Whitt, M., Irwin, M., Swartz, A., Strath, S., et al. (2000). Compendium of physical activities: An update of activity codes and MET intensities RID B-7154-2011. *Medicine and Science in Sports and Exercise*, 32(9), S498-S516.
- Allison, D. B., Fontaine, K. R., Manson, J. E., Stevens, J., & VanItallie, T. B. (1999). Annual deaths attributable to obesity in the United States. *JAMA : The Journal of the American Medical Association*, 282(16), 1530-1538.
- Almiron-Roig, E., & Drewnowski, A. (2003). Hunger, thirst, and energy intakes following consumption of caloric beverages. *Physiology & Behavior*, 79(4-5), 767-773.
- Al-Solaiman, Y., Jesri, A., Mountford, W. K., Lackland, D. T., Zhao, Y., & Egan, B. M. (2010). DASH lowers blood pressure in obese hypertensives beyond potassium, magnesium and fibre. *Journal of Human Hypertension*, 24(4), 237-246.
- American Heart Association. (2012). Retrieved May 13, from <http://www.cnpp.usda.gov/publications/dietaryguidelines/2010/meeting2/commitments/aha-220e.pdf>
- Anderson, G. H., Catherine, N. L., Woodend, D. M., & Wolever, T. M. (2002). Inverse association between the effect of carbohydrates on blood glucose and subsequent short-term food intake in young men. *The American Journal of Clinical Nutrition*, 76(5), 1023-1030.
- Anderson, G. H., & Moore, S. E. (2004). Dietary proteins in the regulation of food intake and body weight in humans. *The Journal of Nutrition*, 134(4), 974S-9S.
- Anderson, J. W., Baird, P., Davis, R. H., Jr, Ferreri, S., Knudtson, M., Koraym, A., et al. (2009). Health benefits of dietary fiber. *Nutrition Reviews*, 67(4), 188-205.

- Appel, L. J., Moore, T. J., Obarzanek, E., Vollmer, W. M., Svetkey, L. P., Sacks, F. M., et al. (1997). A clinical trial of the effects of dietary patterns on blood pressure. DASH collaborative research group. *The New England Journal of Medicine*, 336(16), 1117-1124.
- Ashby, D., & Bloom, S. R. (2007). Recent progress in PYY research--an update report for 8th NPY meeting. *Peptides*, 28(2), 198-202.
- Balducci, S., Zanuso, S., Nicolucci, A., De Feo, P., Cavallo, S., Cardelli, P., et al. (2010). Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with type 2 diabetes mellitus: A randomized controlled trial: The Italian diabetes and exercise study (IDES). *Archives of Internal Medicine*, 170(20), 1794-1803.
- Ballor, D., & Keeseey, R. (1991). A metaanalysis of the factors affecting exercise-induced changes in body-mass, fat mass and fat-free mass in males and females. *International Journal of Obesity*, 15(11), 717-726.
- Behall, K. M., Scholfield, D. J., & Hallfrisch, J. (2004). Lipids significantly reduced by diets containing barley in moderately hypercholesterolemic men. *Journal of the American College of Nutrition*, 23(1), 55-62.
- Bell, E. A., & Rolls, B. J. (2001). Energy density of foods affects energy intake across multiple levels of fat content in lean and obese women. *The American Journal of Clinical Nutrition*, 73(6), 1010-1018.
- Bellisle, F., Clement, K., Le Barzic, M., Le Gall, A., Guy-Grand, B., & Basdevant, A. (2004). The eating inventory and body adiposity from leanness to massive obesity: A study of 2509 adults. *Obesity Research*, 12(12), 2023-2030.
- Bennett, W. I. (1995). Beyond overeating. *The New England Journal of Medicine*, 332(10), 673-674.
- Benoit, S. C., Air, E. L., Coolen, L. M., Strauss, R., Jackman, A., Clegg, D. J., et al. (2002). The catabolic action of insulin in the brain is mediated by melanocortins. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 22(20), 9048-9052.
- Berkowitz, R. I., Wadden, T. A., Gehrman, C. A., Bishop-Gilyard, C. T., Moore, R. H., Womble, L. G., et al. (2011). Meal replacements in the treatment of adolescent obesity: A randomized controlled trial. *Obesity (Silver Spring, Md.)*, 19(6), 1193-1199.
- Blatt, A. D., Williams, R. A., Roe, L. S., & Rolls, B. J. (2012). Effects of energy content and energy density of pre-portioned entrees on energy intake. *Obesity (Silver Spring, Md.)*, 20(10), 2010-2018.

- Blouet, C., Jo, Y. H., Li, X., & Schwartz, G. J. (2009). Mediobasal hypothalamic leucine sensing regulates food intake through activation of a hypothalamus-brainstem circuit. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 29(26), 8302-8311.
- Blundell, J. E. & King, N. A. (1998). Effects of exercise on appetite control: loose coupling between energy expenditure and energy intake. *International Journal of Obesity and Related Metabolic Disorders*, 22, S22-29.
- Blundell, J., de Graaf, C., Hulshof, T., Jebb, S., Livingstone, B., Lluich, A., et al. (2010). Appetite control: Methodological aspects of the evaluation of foods. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 11(3), 251-270.
- Blundell, J. E., Stubbs, R. J., Hughes, D. A., Whybrow, S., & King, N. A. (2003). Cross talk between physical activity and appetite control: Does physical activity stimulate appetite? *The Proceedings of the Nutrition Society*, 62(3), 651-661.
- Boers, H. (2009). All fibres are equal, but some fibres are more equal than others. *Agro Food Industry Hi-Tech*, 20(3), 13-16.
- Bogusky A. (2008). *Be the 9-inch diet*. (1st edition ed.). Brooklyn, NY: powerHouse Books.
- Boirie, Y., Dangin, M., Gachon, P., Vasson, M. P., Maubois, J. L., & Beaufrere, B. (1997). Slow and fast dietary proteins differently modulate postprandial protein accretion. *Proceedings of the National Academy of Sciences of the United States of America*, 94(26), 14930-14935.
- Boston, B. A., Blaydon, K. M., Varnerin, J., & Cone, R. D. (1997). Independent and additive effects of central POMC and leptin pathways on murine obesity. *Science (New York, N.Y.)*, 278(5343), 1641-1644.
- Bouchard, C., Tremblay, A., Despres, J. P., Nadeau, A., Lupien, P. J., Theriault, G., et al. (1990). The response to long-term overfeeding in identical twins. *The New England Journal of Medicine*, 322(21), 1477-1482.
- Bouche, C., Rizkalla, S. W., Luo, J., Vidal, H., Veronese, A., Pacher, N., et al. (2002). Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men. *Diabetes Care*, 25(5), 822-828.
- Brand-Miller, J., McMillan-Price, J., Steinbeck, K., & Caterson, I. (2009). Dietary glycemic index: Health implications. *Journal of the American College of Nutrition*, 28 Suppl, 446S-449S.
- Brenna, J. T. (2002). Efficiency of conversion of alpha-linolenic acid to long chain n-3 fatty acids in man. *Current Opinion in Clinical Nutrition and Metabolic Care*, 5(2), 127-132.

- Brown, L., Rosner, B., Willett, W. W., & Sacks, F. M. (1999). Cholesterol-lowering effects of dietary fiber: A meta-analysis. *The American Journal of Clinical Nutrition*, 69(1), 30-42.
- Bryant, E. J., Caudwell, P., Hopkins, M. E., King, N. A., & Blundell, J. E. (2012). Psycho-markers of weight loss: the roles of TFEQ disinhibition and restraint in exercise-induced weight management. *Appetite*, 58(1), 234-241.
- Bryant, E. J., King, N. A., & Blundell, J. E. (2008). Disinhibition: Its effects on appetite and weight regulation. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 9(5), 409-419.
- Burton-Freeman, B. (2000). Dietary fiber and energy regulation. *The Journal of Nutrition*, 130(2S Suppl), 272S-275S.
- Calder, P. C. (2009). Polyunsaturated fatty acids and inflammatory processes: New twists in an old tale. *Biochimie*, 91(6), 791-795.
- Campos, P., Saguy, A., Ernsberger, P., Oliver, E., & Gaesser, G. (2006). The epidemiology of overweight and obesity: Public health crisis or moral panic? *International Journal of Epidemiology*, 35(1), 55-60.
- Cani, P. D., Dewever, C., & Delzenne, N. M. (2004). Inulin-type fructans modulate gastrointestinal peptides involved in appetite regulation (glucagon-like peptide-1 and ghrelin) in rats. *The British Journal of Nutrition*, 92(3), 521-526.
- Cheskin, L. J., Mitchell, A. M., Jhaveri, A. D., Mitola, A. H., Davis, L. M., Lewis, R. A., et al. (2008). Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: A controlled clinical trial. *The Diabetes Educator*, 34(1), 118-127.
- Chow, J., Choe, Y. S., Noss, M. J., Robinson, K. J., Dugle, J. E., Acosta, S. H. & Garleb, K. A. (2007). Effect of a viscous fiber-containing nutrition bar on satiety of patients with type 2 diabetes. *Diabetes Research and Clinical Practice*, 76(3), 335-340.
- Church, T. S., Martin, C. K., Thompson, A. M., Earnest, C. P., Mikus, C. R., & Blair, S. N. (2009). Changes in weight, waist circumference and compensatory responses with different doses of exercise among sedentary, overweight postmenopausal women. *Plos One*, 4(2), e4515.
- Cole, C. (Ed.). (2000). *Reference: Cole, CGB. gelatin. frederick J francis, editor. encyclopedia of food science and technology, 2nd edition. 4 vols. new york: John wiley & sons, 2000. 1183-1188.* John Wiley & Sons: New York.
- Considine, R. V., Sinha, M. K., Heiman, M. L., Kriauciunas, A., Stephens, T. W., Nyce, M. R., et al. (1996). Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *The New England Journal of Medicine*, 334(5), 292-295.

- Cornelissen, V. A., & Fagard, R. H. (2005a). Effect of resistance training on resting blood pressure: A meta-analysis of randomized controlled trials. *Journal of Hypertension*, 23(2), 251-259.
- Cornelissen, V. A., & Fagard, R. H. (2005b). Effects of endurance training on blood pressure, blood pressure-regulating mechanisms, and cardiovascular risk factors. *Hypertension*, 46(4), 667-675.
- Cota, D., Proulx, K., Smith, K. A., Kozma, S. C., Thomas, G., Woods, S. C., et al. (2006). Hypothalamic mTOR signaling regulates food intake. *Science (New York, N.Y.)*, 312(5775), 927-930.
- Couet, C., Delarue, J., Ritz, P., Antoine, J. M., & Lamisse, F. (1997). Effect of dietary fish oil on body fat mass and basal fat oxidation in healthy adults. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 21(8), 637-643.
- Couillard, C., Despres, J. P., Lamarche, B., Bergeron, J., Gagnon, J., Leon, A. S., et al. (2001). Effects of endurance exercise training on plasma HDL cholesterol levels depend on levels of triglycerides: Evidence from men of the health, risk factors, exercise training and genetics (HERITAGE) family study. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 21(7), 1226-1232.
- Crawford, D., Jeffery, R. W., & French, S. A. (2000). Can anyone successfully control their weight? findings of a three year community-based study of men and women. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 24(9), 1107-1110.
- Cummings, D. E., Weigle, D. S., Frayo, R. S., Breen, P. A., Ma, M. K., Dellinger, E. P., et al. (2002). Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *The New England Journal of Medicine*, 346(21), 1623-1630.
- Cvetkovic, R. S., & Plosker, G. L. (2007). Exenatide: A review of its use in patients with type 2 diabetes mellitus (as an adjunct to metformin and/or a sulfonylurea). *Drugs*, 67(6), 935-954.
- Dansinger, M. L., Gleason, J. A., Griffith, J. L., Selker, H. P., & Schaefer, E. J. (2005). Comparison of the atkins, ornish, weight watchers, and zone diets for weight loss and heart disease risk reduction: A randomized trial. *JAMA : The Journal of the American Medical Association*, 293(1), 43-53.
- Das, S. K., Gilhooly, C. H., Golden, J. K., Pittas, A. G., Fuss, P. J., Cheatham, R. A., et al. (2007). Long-term effects of 2 energy-restricted diets differing in glycemic load on dietary adherence, body composition, and metabolism in CALERIE: A 1-y randomized controlled trial. *The American Journal of Clinical Nutrition*, 85(4), 1023-1030.

- Davis, L. M., Coleman, C., Kiel, J., Rampolla, J., Hutchisen, T., Ford, L., et al. (2010). Efficacy of a meal replacement diet plan compared to a food-based diet plan after a period of weight loss and weight maintenance: A randomized controlled trial. *Nutrition Journal*, 9, 11.
- De Filippis, E., Cusi, K., Ocampo, G., Berria, R., Buck, S., Consoli, A., et al. (2006). Exercise-induced improvement in vasodilatory function accompanies increased insulin sensitivity in obesity and type 2 diabetes mellitus. *The Journal of Clinical Endocrinology and Metabolism*, 91(12), 4903-4910.
- de Graaf, C., Blom, W. A., Smeets, P. A., Stafleu, A., & Hendriks, H. F. (2004). Biomarkers of satiation and satiety. *The American Journal of Clinical Nutrition*, 79(6), 946-961.
- DeFina, L. F., Marcoux, L. G., Devers, S. M., Cleaver, J. P., & Willis, B. L. (2011). Effects of omega-3 supplementation in combination with diet and exercise on weight loss and body composition. *American Journal of Clinical Nutrition*, 93(2), 455-462.
- Devkota, S., & Layman, D. K. (2010). Protein metabolic roles in treatment of obesity. *Current Opinion in Clinical Nutrition and Metabolic Care*, 13(4), 403-407.
- Diaz, V. A., Mainous, A. G., 3rd, & Everett, C. J. (2005). The association between weight fluctuation and mortality: Results from a population-based cohort study. *Journal of Community Health*, 30(3), 153-165.
- Ditschuneit, H. H., Flechtner-Mors, M., Johnson, T. D., & Adler, G. (1999). Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *The American Journal of Clinical Nutrition*, 69(2), 198-204.
- Donnelly, J., Hill, J., Jacobsen, D., Potteiger, J., Sullivan, D., Johnson, S., et al. (2003). Effects of a 16-month randomized controlled exercise trial on body weight and composition in young, overweight men and women - the midwest exercise trial. *Archives of Internal Medicine*, 163(11), 1343-1350.
- Donnelly, J., & Smith, B. (2005). Is exercise effective for weight loss with ad libitum diet? energy balance, compensation, and gender differences. *Exercise and Sport Sciences Reviews*, 33(4), 169-174.
- Drucker, D. J. (2005). Biologic actions and therapeutic potential of the proglucagon-derived peptides. *Nature Clinical Practice. Endocrinology & Metabolism*, 1(1), 22-31.
- Dykes, J., Brunner, E. J., Martikainen, P. T., & Wardle, J. (2004). Socioeconomic gradient in body size and obesity among women: The role of dietary restraint, disinhibition and hunger in the whitehall II study. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 28(2), 262-268.

- Eaton, S. B., Eaton, S. B., 3rd, Konner, M. J., & Shostak, M. (1996). An evolutionary perspective enhances understanding of human nutritional requirements. *The Journal of Nutrition*, 126(6), 1732-1740.
- Ebbeling, C.B., Sinclair, K.B., Pereira, M.A., Garcia-Lago, E., Feldman, H.A. & Ludwig, D.S. (2004). Compensation for energy intake from fast food among overweight and lean adolescents. *Journal of the American Medical Association*, 291(23), 2828-2833.
- Ebbeling, C. B., Leidig, M. M., Sinclair, K. B., Hangen, J. P., & Ludwig, D. S. (2003). A reduced-glycemic load diet in the treatment of adolescent obesity. *Archives of Pediatrics & Adolescent Medicine*, 157(8), 773-779.
- Ebbeling, C. B., Leidig, M. M., Sinclair, K. B., Seger-Shippe, L. G., Feldman, H. A., & Ludwig, D. S. (2005). Effects of an ad libitum low-glycemic load diet on cardiovascular disease risk factors in obese young adults. *The American Journal of Clinical Nutrition*, 81(5), 976-982.
- Estruch, R., Martinez-Gonzalez, M. A., Corella, D., Salas-Salvado, J., Ruiz-Gutierrez, V., Covas, M. I., et al. (2006). Effects of a mediterranean-style diet on cardiovascular risk factors: A randomized trial. *Annals of Internal Medicine*, 145(1), 1-11.
- Fagard, R. H. (1999). Physical activity in the prevention and treatment of hypertension in the obese. *Medicine and Science in Sports and Exercise*, 31(11 Suppl), S624-30.
- Farias, M. M., Cuevas, A. M., & Rodriguez, F. (2011). Set-point theory and obesity. *Metabolic Syndrome and Related Disorders*, 9(2), 85-89.
- Farrell, S. W., Cortese, G. M., LaMonte, M. J., & Blair, S. N. (2007). Cardiorespiratory fitness, different measures of adiposity, and cancer mortality in men. *Obesity (Silver Spring, Md.)*, 15(12), 3140-3149.
- Fekete, C., Kelly, J., Mihaly, E., Sarkar, S., Rand, W. M., Legradi, G., et al. (2001). Neuropeptide Y has a central inhibitory action on the hypothalamic-pituitary-thyroid axis. *Endocrinology*, 142(6), 2606-2613.
- Ferrara, C. M., Goldberg, A. P., Ortmeyer, H. K., & Ryan, A. S. (2006). Effects of aerobic and resistive exercise training on glucose disposal and skeletal muscle metabolism in older men. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 61(5), 480-487.
- Finkelstein, E. A., DiBonaventura, M. d., Burgess, S. M., & Hale, B. C. (2010). The costs of obesity in the workplace. *Journal of Occupational and Environmental Medicine*, 52(10), 971-976.
- Finkelstein, E. A., Trogon, J. G., Cohen, J. W., & Dietz, W. (2009). Annual medical spending attributable to obesity: Payer- and service-specific estimates. *Health Affairs*, 28(5), W822-W831.

- Finlayson, G., Bryant, E., Blundell, J. E., & King, N. A. (2009). Acute compensatory eating following exercise is associated with implicit hedonic wanting for food. *Physiology & Behavior*, 97(1), 62-67.
- Finucane, M. M., Stevens, G. A., Cowan, M. J., Danaei, G., Lin, J. K., Paciorek, C. J., et al. (2011). National, regional, and global trends in body-mass index since 1980: Systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *The Lancet*, 377(9765), 557-567.
- Fischer, K., Colombani, P. C., & Wenk, C. (2004). Metabolic and cognitive coefficients in the development of hunger sensations after pure macronutrient ingestion in the morning. *Appetite*, 42(1), 49-61.
- Flachs, P., Horakova, O., Brauner, P., Rossmeisl, M., Pecina, P., Franssen-van Hal, N., et al. (2005). Polyunsaturated fatty acids of marine origin upregulate mitochondrial biogenesis and induce beta-oxidation in white fat. *Diabetologia*, 48(11), 2365-2375.
- Flachs, P., Rossmeisl, M., Bryhn, M., & Kopecky, J. (2009). Cellular and molecular effects of n-3 polyunsaturated fatty acids on adipose tissue biology and metabolism. *Clinical Science (London, England : 1979)*, 116(1), 1-16.
- Flechtner-Mors, M., Ditschuneit, H. H., Johnson, T. D., Suchard, M. A., & Adler, G. (2000). Metabolic and weight loss effects of long-term dietary intervention in obese patients: Four-year results. *Obesity Research*, 8(5), 399-402.
- Flegal, K. M., Carroll, M. D., Ogden, C. L., & Curtin, L. R. (2010). Prevalence and trends in obesity among US adults, 1999-2008. *JAMA : The Journal of the American Medical Association*, 303(3), 235-241.
- Flegal, K. M., Graubard, B. I., Williamson, D. F., & Gail, M. H. (2005). Excess deaths associated with underweight, overweight, and obesity. *JAMA : The Journal of the American Medical Association*, 293(15), 1861-1867.
- Fogelholm, M. (2010). Physical activity, fitness and fatness: Relations to mortality, morbidity and disease risk factors. A systematic review. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 11(3), 202-221.
- Food and Drug Administration. (2009). *Guidance for industry: A food labeling guide*. Retrieved 06/01, 2012, from <http://www.fda.gov/downloads/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodLabelingNutrition/FoodLabelingGuide/UCM265446.pdf>

- Foster, G. D., Wadden, T. A., Swain, R. M., Stunkard, A. J., Platte, P., & Vogt, R. A. (1998). The eating inventory in obese women: Clinical correlates and relationship to weight loss. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 22(8), 778-785.
- Franz, M. J., VanWormer, J. J., Crain, A. L., Boucher, J. L., Histon, T., Caplan, W., et al. (2007). Weight-loss outcomes: A systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. *Journal of the American Dietetic Association*, 107(10), 1755-1767.
- Freeland, K. R., Anderson, G. H., & Wolever, T. M. (2009). Acute effects of dietary fibre and glycaemic carbohydrate on appetite and food intake in healthy males. *Appetite*, 52(1), 58-64.
- French, S. (2004). Effects of dietary fat and carbohydrate on appetite vary depending upon site and structure. *The British Journal of Nutrition*, 92 Suppl 1, S23-6.
- Fromentin, G., Feurte, S., Nicolaidis, S., & Norgren, R. (2000). Parabrachial lesions disrupt responses of rats to amino acid devoid diets, to protein-free diets, but not to high-protein diets. *Physiology & Behavior*, 70(3-4), 381-389.
- Gaesser, G. A. (2007). Exercise for prevention and treatment of cardiovascular disease, type 2 diabetes, and metabolic syndrome. *Current Diabetes Reports*, 7(1), 14-19.
- Geary, N., Le Sauter, J., & Noh, U. (1993). Glucagon acts in the liver to control spontaneous meal size in rats. *The American Journal of Physiology*, 264(1 Pt 2), R116-22.
- Georg Jensen, M., Kristensen, M., & Astrup, A. (2012). Effect of alginate supplementation on weight loss in obese subjects completing a 12-wk energy-restricted diet: A randomized controlled trial. *The American Journal of Clinical Nutrition*, 96(1), 5-13.
- Gietzen, D. W., & Aja, S. M. (2012). The brain's response to an essential amino acid-deficient diet and the circuitous route to a better meal. *Molecular Neurobiology*, 46(2), 332-348.
- Gilhooly, C. H., Das, S. K., Golden, J. K., McCrory, M. A., Rochon, J., DeLany, J. P., et al. (2008). Use of cereal fiber to facilitate adherence to a human caloric restriction program. *Aging Clinical and Experimental Research*, 20(6), 513-520.
- Godin, G. & Shephard, R. J. (1985). A simple method to assess exercise behavior in the community. *Canadian Journal of Applied Sport Sciences*, 10(3), 141-146.

- Goldsmith, R., Joannisse, D. R., Gallagher, D., Pavlovich, K., Shamoan, E., Leibel, R. L., et al. (2010). Effects of experimental weight perturbation on skeletal muscle work efficiency, fuel utilization, and biochemistry in human subjects. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, 298(1), R79-88.
- Gruberg, L., Weissman, N. J., Waksman, R., Fuchs, S., Deible, R., Pinnow, E. E., et al. (2002). The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: The obesity paradox? *Journal of the American College of Cardiology*, 39(4), 578-584.
- Guagnano, M. T., Ballone, E., Pace-Palitti, V., Vecchia, R. D., D'Orazio, N., Manigrasso, M. R., et al. (2000). Risk factors for hypertension in obese women. the role of weight cycling. *European Journal of Clinical Nutrition*, 54(4), 356-360.
- Gutniak, M., Orskov, C., Holst, J. J., Ahren, B., & Efendic, S. (1992). Antidiabetogenic effect of glucagon-like peptide-1 (7-36)amide in normal subjects and patients with diabetes mellitus. *The New England Journal of Medicine*, 326(20), 1316-1322.
- Hainer, V., Kunesova, M., Bellisle, F., Parizkova, J., Braunerova, R., Wagenknecht, M., et al. (2006). The eating inventory, body adiposity and prevalence of diseases in a quota sample of czech adults. *International Journal of Obesity (2005)*, 30(5), 830-836.
- Halaas, J. L., Gajiwala, K. S., Maffei, M., Cohen, S. L., Chait, B. T., Rabinowitz, D., et al. (1995). Weight-reducing effects of the plasma protein encoded by the obese gene. *Science (New York, N.Y.)*, 269(5223), 543-546.
- Hall, W. L., Millward, D. J., Long, S. J., & Morgan, L. M. (2003). Casein and whey exert different effects on plasma amino acid profiles, gastrointestinal hormone secretion and appetite. *The British Journal of Nutrition*, 89(2), 239-248.
- Hamdy, O., & Zwiefelhofer, D. (2010). Weight management using a meal replacement strategy in type 2 diabetes. *Current Diabetes Reports*, 10(2), 159-164.
- Haslam, D., & James, W. (2005). Obesity. *Lancet*, 366(9492), 1197-1209.
- Hays, N. P., Bathalon, G. P., McCrory, M. A., Roubenoff, R., Lipman, R., & Roberts, S. B. (2002). Eating behavior correlates of adult weight gain and obesity in healthy women aged 55-65 y. *The American Journal of Clinical Nutrition*, 75(3), 476-483.
- Hays, N. P., & Roberts, S. B. (2008). Aspects of eating behaviors "disinhibition" and "restraint" are related to weight gain and BMI in women. *Obesity (Silver Spring, Md.)*, 16(1), 52-58.

- Hetherington, M. M., Foster, R., Newman, T., Anderson, A. S., & Norton, G. (2006). Understanding variety: Tasting different foods delays satiation. *Physiology & Behavior*, 87(2), 263-271.
- Hertzler, S. R. & Kim, Y. (2003). Glycemic and insulinemic responses to energy bars of differing macronutrient composition in healthy adults. *Medical Science Monitor*, 9(2), CR84-90.
- Heymsfield, S. B. (2010). Meal replacements and energy balance. *Physiology & Behavior*, 100(1), 90-94.
- Heymsfield, S. B., van Mierlo, C. A., van der Knaap, H. C., Heo, M., & Frier, H. I. (2003). Weight management using a meal replacement strategy: Meta and pooling analysis from six studies. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 27(5), 537-549.
- Hill, A. M., Buckley, J. D., Murphy, K. J., & Howe, P. R. (2007). Combining fish-oil supplements with regular aerobic exercise improves body composition and cardiovascular disease risk factors. *The American Journal of Clinical Nutrition*, 85(5), 1267-1274.
- Hochstenbach-Waelen, A., Westerterp-Plantenga, M. S., Veldhorst, M. A., & Westerterp, K. R. (2009). Single-protein casein and gelatin diets affect energy expenditure similarly but substrate balance and appetite differently in adults. *The Journal of Nutrition*, 139(12), 2285-2292.
- Hochstenbach-Waelen, A., Soenen, S., Westerterp, K. R., & Westerterp-Plantenga, M. S. (2011). Effects of a supra-sustained gelatin-milk protein diet compared with (supra-)sustained milk protein diets on body-weight loss. *British Journal of Nutrition*, 105(9), 1388-1398.
- Holbrook, E. A., Barreira, T. V., & Kang, M. (2009). Validity and reliability of omron pedometers for prescribed and self-paced walking. *Medicine and Science in Sports and Exercise*, 41(3), 670-674.
- Howarth, N. C., Huang, T. T., Roberts, S. B., & McCrory, M. A. (2005). Dietary fiber and fat are associated with excess weight in young and middle-aged US adults. *Journal of the American Dietetic Association*, 105(9), 1365-1372.
- Howarth, N. C., Saltzman, E., McCrory, M. A., Greenberg, A. S., Dwyer, J., Ausman, L., et al. (2003). Fermentable and nonfermentable fiber supplements did not alter hunger, satiety or body weight in a pilot study of men and women consuming self-selected diets. *The Journal of Nutrition*, 133(10), 3141-3144.
- Howarth, N.C., Saltzman, E., Roberts, S.B., (2001). Dietary Fiber and Weight Regulation. *Nutrition Reviews*, 59(5), 129-139.

- Howlett, J., & Ashwell, M. (2008). Glycemic response and health: Summary of a workshop. *The American Journal of Clinical Nutrition*, 87(1), 212S-216S.
- Hun, C. S., Hasegawa, K., Kawabata, T., Kato, M., Shimokawa, T., & Kagawa, Y. (1999). Increased uncoupling protein2 mRNA in white adipose tissue, and decrease in leptin, visceral fat, blood glucose, and cholesterol in KK-ay mice fed with eicosapentaenoic and docosahexaenoic acids in addition to linolenic acid. *Biochemical and Biophysical Research Communications*, 259(1), 85-90.
- Jenkins, D. J., Wolever, T. M., Taylor, R. H., Barker, H., Fielden, H., Baldwin, J. M., et al. (1981). Glycemic index of foods: A physiological basis for carbohydrate exchange. *The American Journal of Clinical Nutrition*, 34(3), 362-366.
- Johnson, F., Pratt, M., & Wardle, J. (2012). Dietary restraint and self-regulation in eating behavior. *International Journal of Obesity (2005)*, 36(5), 665-674.
- Johnston, C. S., Tjonn, S. L., & Swan, P. D. (2004). High-protein, low-fat diets are effective for weight loss and favorably alter biomarkers in healthy adults. *The Journal of Nutrition*, 134(3), 586-591.
- Jonnalagadda, S. S., Harnack, L., Liu, R. H., McKeown, N., Seal, C., Liu, S., et al. (2011). Putting the whole grain puzzle together: Health benefits associated with whole grains--summary of american society for nutrition 2010 satellite symposium. *The Journal of Nutrition*, 141(5), 1011S-22S.
- Kabir, M., Skurnik, G., Naour, N., Pechtner, V., Meugnier, E., Rome, S., et al. (2007). Treatment for 2 mo with n 3 polyunsaturated fatty acids reduces adiposity and some atherogenic factors but does not improve insulin sensitivity in women with type 2 diabetes: A randomized controlled study. *The American Journal of Clinical Nutrition*, 86(6), 1670-1679.
- Kajioka, T., Tsuzuku, S., Shimokata, H., & Sato, Y. (2002). Effects of intentional weight cycling on non-obese young women. *Metabolism: Clinical and Experimental*, 51(2), 149-154.
- Kalergis, M. & Macdonald, A. (2009). Discretionary food fortification: implications of consumer attitudes. *Canadian Journal of Dietary Practices and Research*, 70(4), e26-31.
- Keesey, R. E. (1993). Physiological regulation of body energy: Implications for obesity. In A. J. Stunkard, & T. A. Wadden (Eds.), *Obesity: Theory and therapy* (2nd ed., pp. 77). New York: Raven Press.
- Keim, N. L., Canty, D. J., Barbieri, T. F., & Wu, M. M. (1996). Effect of exercise and dietary restraint on energy intake of reduced-obese women. *Appetite*, 26(1), 55-70.

- Kimball, S., & Jefferson, L. (2001). Regulation of protein synthesis by branched-chain amino acids. *Current Opinion in Clinical Nutrition and Metabolic Care*, 4(1), 39-43.
- King NA, Hopkins M, Caudwell P, Stubbs RJ, Blundell JE. (2009). Beneficial effects of exercise: Shifting the focus from body weight to other markers of health. *Br J Sports Med*, 43, 924-927.
- King, N. A., Caudwell, P., Hopkins, M., Byrne, N. M., Colley, R., Hills, A. P., et al. (2007). Metabolic and behavioral compensatory responses to exercise interventions: Barriers to weight loss. *Obesity (Silver Spring, Md.)*, 15(6), 1373-1383.
- King, N. A., Caudwell, P. P., Hopkins, M., Stubbs, J. R., Naslund, E., & Blundell, J. E. (2009). Dual-process action of exercise on appetite control: Increase in orexigenic drive but improvement in meal-induced satiety. *The American Journal of Clinical Nutrition*, 90(4), 921-927.
- King, N. A., Craig, S. A., Pepper, T., & Blundell, J. E. (2005). Evaluation of the independent and combined effects of xylitol and polydextrose consumed as a snack on hunger and energy intake over 10 d. *The British Journal of Nutrition*, 93(6), 911-915.
- King, N. A., Hopkins, M., Caudwell, P., Stubbs, R. J., & Blundell, J. E. (2008). Individual variability following 12 weeks of supervised exercise: Identification and characterization of compensation for exercise-induced weight loss. *International Journal of Obesity (2005)*, 32(1), 177-184.
- Klem, M. L., Wing, R. R., McGuire, M. T., Seagle, H. M., & Hill, J. O. (1997). A descriptive study of individuals successful at long-term maintenance of substantial weight loss. *The American Journal of Clinical Nutrition*, 66(2), 239-246.
- Kochanek, K., Jiaquan, X., Murphy, S., Minino, A. & Hsiang-Ching, K. (2011). *National vital statistics reports, deaths: Preliminary data for 2009*. Retrieved 6/10, 2011, from http://www.cdc.gov/nchs/data/nvsr/nvsr59/nvsr59_04.pdf
- Kojima, M., Hosoda, H., Date, Y., Nakazato, M., Matsuo, H., & Kangawa, K. (1999). Ghrelin is a growth-hormone-releasing acylated peptide from stomach. *Nature*, 402(6762), 656-660.
- Kratz, M., Callahan, H. S., Yang, P. Y., Matthys, C. C., & Weigle, D. S. (2009). Dietary n-3-polyunsaturated fatty acids and energy balance in overweight or moderately obese men and women: A randomized controlled trial. *Nutrition & Metabolism*, 6, 24.
- Krebs, J. D., Browning, L. M., McLean, N. K., Rothwell, J. L., Mishra, G. D., Moore, C. S., et al. (2006). Additive benefits of long-chain n-3 polyunsaturated fatty acids and weight-loss in the management of cardiovascular disease risk in overweight hyperinsulinaemic women. *International Journal of Obesity (2005)*, 30(10), 1535-1544.

- Krieger, J. W., Sitren, H. S., Daniels, M. J., & Langkamp-Henken, B. (2006). Effects of variation in protein and carbohydrate intake on body mass and composition during energy restriction: A meta-regression 1. *The American Journal of Clinical Nutrition*, 83(2), 260-274.
- Kristensen, M., Jensen, M. G., Riboldi, G., Petronio, M., Bugel, S., Toubro, S., et al. (2010). Wholegrain vs. refined wheat bread and pasta. effect on postprandial glycemia, appetite, and subsequent ad libitum energy intake in young healthy adults. *Appetite*, 54(1), 163-169.
- Kunesova, M., Braunerova, R., Hlavaty, P., Tvrzicka, E., Stankova, B., Skrha, J., et al. (2006). The influence of n-3 polyunsaturated fatty acids and very low calorie diet during a short-term weight reducing regimen on weight loss and serum fatty acid composition in severely obese women. *Physiological Research / Academia Scientiarum Bohemoslovaca*, 55(1), 63-72.
- Lambert, P. D., Couceyro, P. R., McGirr, K. M., Dall Vechia, S. E., Smith, Y., & Kuhar, M. J. (1998). CART peptides in the central control of feeding and interactions with neuropeptide Y. *Synapse (New York, N.Y.)*, 29(4), 293-298.
- Layman, D. K. (2009). Dietary guidelines should reflect new understandings about adult protein needs. *Nutrition & Metabolism*, 6, 12.
- Layman, D. K., Evans, E. M., Erickson, D., Seyler, J., Weber, J., Bagshaw, D., et al. (2009). A moderate-protein diet produces sustained weight loss and long-term changes in body composition and blood lipids in obese adults. *The Journal of Nutrition*, 139(3), 514-521.
- Ledikwe, J. H., Rolls, B. J., Smiciklas-Wright, H., Mitchell, D. C., Ard, J. D., Champagne, C., et al. (2007). Reductions in dietary energy density are associated with weight loss in overweight and obese participants in the PREMIER trial. *The American Journal of Clinical Nutrition*, 85(5), 1212-1221.
- Lee, K. W., Song, K. E., Lee, H. S., Kim, Y. K., Lee, S. W., Kim, D. J., et al. (2006). The effects of goami no. 2 rice, a natural fiber-rich rice, on body weight and lipid metabolism. *Obesity (Silver Spring, Md.)*, 14(3), 423-430.
- Leibel, R. L., Rosenbaum, M., & Hirsch, J. (1995). Changes in energy expenditure resulting from altered body weight. *The New England Journal of Medicine*, 332(10), 621-628.
- Lejeune, M., Westerterp, K., Adam, T., Luscombe-Marsh, N., & Westerterp-Plantenga, M. (2006). Ghrelin and glucagon-like peptide 1 concentrations, 24-h satiety, and energy and substrate metabolism during a high-protein diet and measured in a respiration chamber RID A-5371-2010. *American Journal of Clinical Nutrition*, 83(1), 89-94.
- Levine, J. A., Eberhardt, N. L., & Jensen, M. D. (1999). Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science (New York, N.Y.)*, 283(5399), 212-214.

- Levine, J. A., Lanningham-Foster, L. M., McCrady, S. K., Krizan, A. C., Olson, L. R., Kane, P. H., et al. (2005). Interindividual variation in posture allocation: Possible role in human obesity. *Science (New York, N.Y.)*, *307*(5709), 584-586.
- Li, J., Zhang, N., Hu, L., Li, Z., Li, R., Li, C., et al. (2011). Improvement in chewing activity reduces energy intake in one meal and modulates plasma gut hormone concentrations in obese and lean young chinese men. *The American Journal of Clinical Nutrition*, *94*(3), 709-716.
- Lichtman, S. W., Pisarska, K., Berman, E. R., Pestone, M., Dowling, H., Offenbacher, E., et al. (1992). Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *The New England Journal of Medicine*, *327*(27), 1893-1898.
- Ludwig, D. S. (2000). Dietary glycemic index and obesity. *The Journal of Nutrition*, *130*(2S Suppl), 280S-283S.
- Luke, A., Dugas, L. R., Ebersole, K., Durazo-Arvizu, R. A., Cao, G., Schoeller, D. A., et al. (2009). Energy expenditure does not predict weight change in either nigerian or african american women. *American Journal of Clinical Nutrition*, *89*(1), 169-176.
- Luo, J., Margolis, K. L., Adami, H. O., Lopez, A. M., Lessin, L., Ye, W., et al. (2007). Body size, weight cycling, and risk of renal cell carcinoma among postmenopausal women: The women's health initiative (united states). *American Journal of Epidemiology*, *166*(7), 752-759.
- Macfarlane, D. J., & Thomas, G. N. (2010). Exercise and diet in weight management: Updating what works. *British Journal of Sports Medicine*, *44*(16), 1197-1201.
- Marmonier, C., Chapelot, D., & Louis-Sylvestre, J. (2000). Effects of macronutrient content and energy density of snacks consumed in a satiety state on the onset of the next meal. *Appetite*, *34*(2), 161-168.
- Mayer, J. (1953). Glucostatic mechanism of regulation of food intake. *The New England Journal of Medicine*, *249*(1), 13-16.
- McAuley, P. A., & Blair, S. N. (2011). Obesity paradoxes. *Journal of Sports Sciences*, *29*(8), 773-782.
- McKiernan, F., Hollis, J.H. & Mattes, R.D. (2008). Short-term dietary compensation in free-living adults. *Physiology and Behavior*, *93*(4-5), 975-983.

- McMillan-Price, J., Petocz, P., Atkinson, F., O'Neill, K., Samman, S., Steinbeck, K., et al. (2006). Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: A randomized controlled trial. *Archives of Internal Medicine*, 166(14), 1466-1475.
- Mellinkoff, S. M., Frankland, M., Boyle, D., & Greipel, M. (1956). Relationship between serum amino acid concentration and fluctuations in appetite. *Journal of Applied Physiology*, 8(5), 535-538.
- Mena, M. P., Sacanella, E., Vazquez-Agell, M., Morales, M., Fito, M., Escoda, R., et al. (2009). Inhibition of circulating immune cell activation: A molecular antiinflammatory effect of the mediterranean diet. *The American Journal of Clinical Nutrition*, 89(1), 248-256.
- Merrill, E. P., Kramer, F. M., Cardello, A., & Schutz, H. (2002). A comparison of satiety measures. *Appetite*, 39(2), 181-183.
- Mestek, M. L., Westby, C. M., Van Guilder, G. P., Greiner, J. J., Stauffer, B. L., & DeSouza, C. A. (2010). Regular aerobic exercise, without weight loss, improves endothelium-dependent vasodilation in overweight and obese adults. *Obesity (Silver Spring, Md.)*, 18(8), 1667-1669.
- Miller, C. K., Gabbay, R. A., Dillon, J., Apgar, J. & Miller, D. (2006). The effect of three snack bars on glycemic response in healthy adults. *Journal of the American Dietetic Association*, 106(5), 745-748.
- Miller, W. C., Koceja, D. M., & Hamilton, E. J. (1997). A meta-analysis of the past 25 years of weight loss research using diet, exercise or diet plus exercise intervention. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 21(10), 941-947.
- Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gotzsche, P. C., Devereaux, P. J., et al. (2010). CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *Journal of Clinical Epidemiology*, 63(8), e1-37.
- Mokdad, A. H., Marks, J. S., Stroup, D. F., & Gerberding, J. L. (2004). Actual causes of death in the united states, 2000. *JAMA : The Journal of the American Medical Association*, 291(10), 1238-1245.
- Monsivais, P., Carter, B. E., Christiansen, M., Perrigue, M. M., & Drewnowski, A. (2011). Soluble fiber dextrin enhances the satiating power of beverages. *Appetite*, 56(1), 9-14.
- Montani, J. P., Viicelli, A. K., Prevot, A., & Dulloo, A. G. (2006). Weight cycling during growth and beyond as a risk factor for later cardiovascular diseases: The 'repeated overshoot' theory. *International Journal of Obesity (2005)*, 30 Suppl 4, S58-66.

- Mori, M., Kawada, T., Ono, T., & Torii, K. (1991). Taste preference and protein nutrition and L-amino acid homeostasis in male sprague-dawley rats. *Physiology & Behavior*, 49(5), 987-995.
- Morrison, C. D., Xi, X., White, C. L., Ye, J., & Martin, R. J. (2007). Amino acids inhibit agrp gene expression via an mTOR-dependent mechanism. *American Journal of Physiology. Endocrinology and Metabolism*, 293(1), E165-71.
- Nakazato, M., Murakami, N., Date, Y., Kojima, M., Matsuo, H., Kangawa, K., et al. (2001). A role for ghrelin in the central regulation of feeding. *Nature*, 409(6817), 194-198.
- Neel, J. V. (1962). Diabetes mellitus: A "thrifty" genotype rendered detrimental by "progress"? *American Journal of Human Genetics*, 14, 353-362.
- Niwano, Y., Adachi, T., Kashimura, J., Sakata, T., Sasaki, H., Sekine, K., et al. (2009). Is glycemic index of food a feasible predictor of appetite, hunger, and satiety? *Journal of Nutritional Science and Vitaminology*, 55(3), 201-207.
- Noakes, M., Foster, P. R., Keogh, J. B., & Clifton, P. M. (2004). Meal replacements are as effective as structured weight-loss diets for treating obesity in adults with features of metabolic syndrome. *The Journal of Nutrition*, 134(8), 1894-1899.
- Noreen, E. E., Sass, M. J., Crowe, M. L., Pabon, V. A., Brandauer, J., & Averill, L. K. (2010). Effects of supplemental fish oil on resting metabolic rate, body composition, and salivary cortisol in healthy adults. *Journal of the International Society of Sports Nutrition*, 7, 31.
- Olson, M. B., Kelsey, S. F., Bittner, V., Reis, S. E., Reichek, N., Handberg, E. M., et al. (2000). Weight cycling and high-density lipoprotein cholesterol in women: Evidence of an adverse effect: A report from the NHLBI-sponsored WISE study. women's ischemia syndrome evaluation study group. *Journal of the American College of Cardiology*, 36(5), 1565-1571.
- O'Neil, C. E., Zanovec, M., Cho, S. S., & Nicklas, T. A. (2010). Whole grain and fiber consumption are associated with lower body weight measures in US adults: National health and nutrition examination survey 1999-2004. *Nutrition Research (New York, N.Y.)*, 30(12), 815-822.
- Pan, A., & Hu, F. B. (2011). Effects of carbohydrates on satiety: Differences between liquid and solid food. *Current Opinion in Clinical Nutrition and Metabolic Care*, 14(4), 385-390.
- Perrigue, M. M., Monsivais, P., & Drewnowski, A. (2009). Added soluble fiber enhances the satiating power of low-energy-density liquid yogurts. *Journal of the American Dietetic Association*, 109(11), 1862-1868.

- Pischon, T., Nothlings, U., & Boeing, H. (2008). Obesity and cancer. *The Proceedings of the Nutrition Society*, 67(2), 128-145.
- Poppitt, S. D., McCormack, D., & Buffenstein, R. (1998). Short-term effects of macronutrient preloads on appetite and energy intake in lean women. *Physiology & Behavior*, 64(3), 279-285.
- Poppitt, S. D., Proctor, J., McGill, A. T., Wiessing, K. R., Falk, S., Xin, L., et al. (2011). Low-dose whey protein-enriched water beverages alter satiety in a study of overweight women. *Appetite*, 56(2), 456-464.
- Potier, M., Fromentin, G., Calvez, J., Benamouzig, R., Martin-Rouas, C., Pichon, L., Tomé, D. & Marsset-Baglieri, A. (2009). A high-protein, moderate-energy, regular cheesy snack is energetically compensated in human subjects. *British Journal of Nutrition*, 102(4), 625-631.
- Potier, M., Fromentin, G., Lesdema, A., Benamouzig, R., Tome, D., & Marsset-Baglieri, A. (2010). The satiety effect of disguised liquid preloads administered acutely and differing only in their nutrient content tended to be weaker for lipids but did not differ between proteins and carbohydrates in human subjects. *The British Journal of Nutrition*, 104(9), 1406-1414.
- Qi, L., & Cho, Y. A. (2008). Gene-environment interaction and obesity. *Nutrition Reviews*, 66(12), 684-694.
- Queenan, K. M., Stewart, M. L., Smith, K. N., Thomas, W., Fulcher, R. G., & Slavin, J. L. (2007). Concentrated oat beta-glucan, a fermentable fiber, lowers serum cholesterol in hypercholesterolemic adults in a randomized controlled trial. *Nutrition Journal*, 6, 6.
- Raben, A., Agerholm-Larsen, L., Flint, A., Holst, J. J., & Astrup, A. (2003). Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. *The American Journal of Clinical Nutrition*, 77(1), 91-100.
- Rampersaud, E., Mitchell, B. D., Pollin, T. I., Fu, M., Shen, H., O'Connell, J. R., et al. (2008). Physical activity and the association of common FTO gene variants with body mass index and obesity. *Archives of Internal Medicine*, 168(16), 1791-1797.
- Reda, T. K., Geliebter, A., & Pi-Sunyer, F. X. (2002). Amylin, food intake, and obesity. *Obesity Research*, 10(10), 1087-1091.
- Renehan, A. G., Tyson, M., Egger, M., Heller, R. F., & Zwahlen, M. (2008). Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. *Lancet*, 371(9612), 569-578.

- Rigik, E. (2011). Forecasting snack bar sales. *Convenience Store Decisions*.
<http://www.csdecisions.com/2011/05/27/forecasting-snack-bar-sales/>.
Accessed June 13.
- Roberts, S. B. (2000). High-glycemic index foods, hunger, and obesity: Is there a connection? *Nutrition Reviews*, 58(6), 163-169.
- Rolls, B. J. (2009). The relationship between dietary energy density and energy intake. *Physiology & Behavior*, 97(5), 609-615.
- Rolls, B. J., & Bell, E. A. (2000). Dietary approaches to the treatment of obesity. *The Medical Clinics of North America*, 84(2), 401-18, vi.
- Rolls, B. J., Bell, E. A., & Thorwart, M. L. (1999). Water incorporated into a food but not served with a food decreases energy intake in lean women. *The American Journal of Clinical Nutrition*, 70(4), 448-455.
- Rolls, B. J., Castellanos, V. H., Halford, J. C., Kilara, A., Panyam, D., Pelkman, C. L., et al. (1998). Volume of food consumed affects satiety in men. *The American Journal of Clinical Nutrition*, 67(6), 1170-1177.
- Rolls, B. J., & Hammer, V. A. (1995). Fat, carbohydrate, and the regulation of energy intake. *The American Journal of Clinical Nutrition*, 62(5 Suppl), 1086S-1095S.
- Roseberry, A. G., Liu, H., Jackson, A. C., Cai, X., & Friedman, J. M. (2004). Neuropeptide Y-mediated inhibition of proopiomelanocortin neurons in the arcuate nucleus shows enhanced desensitization in ob/ob mice. *Neuron*, 41(5), 711-722.
- Rosenbaum, M., Hirsch, J., Gallagher, D. A., & Leibel, R. L. (2008). Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. *The American Journal of Clinical Nutrition*, 88(4), 906-912.
- Ross R, J. P. (2008). Is weight loss the optimal target for obesity-related cardiovascular disease risk reduction? *Can J Cardiol*, 24((Suppl D)), 25D-31D.
- Roumen, C., Corpeleijn, E., Feskens, E. J., Mensink, M., Saris, W. H., & Blaak, E. E. (2008). Impact of 3-year lifestyle intervention on postprandial glucose metabolism: The SLIM study. *Diabetic Medicine : A Journal of the British Diabetic Association*, 25(5), 597-605.
- Ruzickova, J., Rossmeisl, M., Prazak, T., Flachs, P., Sponarova, J., Veck, M., et al. (2004). Omega-3 PUFA of marine origin limit diet-induced obesity in mice by reducing cellularity of adipose tissue. *Lipids*, 39(12), 1177-1185.

- Sacks, F. M., Bray, G. A., Carey, V. J., Smith, S. R., Ryan, D. H., Anton, S. D., et al. (2009). Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. *The New England Journal of Medicine*, 360(9), 859-873.
- Salas-Salvado, J., Bullo, M., Babio, N., Martinez-Gonzalez, M. A., Ibarrola-Jurado, N., Basora, J., et al. (2011). Reduction in the incidence of type 2 diabetes with the mediterranean diet: Results of the PREDIMED-reus nutrition intervention randomized trial. *Diabetes Care*, 34(1), 14-19.
- Sanchez, D., Miguel, M., & Aleixandre, A. (2012). Dietary fiber, gut peptides, and adipocytokines. *Journal of Medicinal Food*, 15(3), 223-230.
- Savage, J. S., Marini, M., & Birch, L. L. (2008). Dietary energy density predicts women's weight change over 6 y. *The American Journal of Clinical Nutrition*, 88(3), 677-684.
- Schoeller, D. A., Cella, L. K., Sinha, M. K., & Caro, J. F. (1997). Entrainment of the diurnal rhythm of plasma leptin to meal timing. *The Journal of Clinical Investigation*, 100(7), 1882-1887.
- Schwartz, M. W., Sipols, A. J., Marks, J. L., Sanacora, G., White, J. D., Scheurink, A., et al. (1992). Inhibition of hypothalamic neuropeptide Y gene expression by insulin. *Endocrinology*, 130(6), 3608-3616.
- Seagle, H. M., Strain, G. W., Makris, A., Reeves, R. S., & American Dietetic Association. (2009). Position of the american dietetic association: Weight management. *Journal of the American Dietetic Association*, 109(2), 330-346.
- Sigal, R. J., Kenny, G. P., Boule, N. G., Wells, G. A., Prud'homme, D., Fortier, M., et al. (2007). Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: A randomized trial. *Annals of Internal Medicine*, 147(6), 357-369.
- Skov, A. R., Toubro, S., Ronn, B., Holm, L., & Astrup, A. (1999). Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *International Journal of Obesity and Related Metabolic Disorders : Journal of the International Association for the Study of Obesity*, 23(5), 528-536.
- Slabber, M., Barnard, H. C., Kuyl, J. M., Dannhauser, A., & Schall, R. (1994). Effects of a low-insulin-response, energy-restricted diet on weight loss and plasma insulin concentrations in hyperinsulinemic obese females. *The American Journal of Clinical Nutrition*, 60(1), 48-53.
- Sloth, B., Krog-Mikkelsen, I., Flint, A., Tetens, I., Bjorck, I., Vinoy, S., et al. (2004). No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet. *The American Journal of Clinical Nutrition*, 80(2), 337-347.

- Smeets, A. J., Soenen, S., Luscombe-Marsh, N. D., Ueland, O., & Westerterp-Plantenga, M. S. (2008). Energy expenditure, satiety, and plasma ghrelin, glucagon-like peptide 1, and peptide tyrosine-tyrosine concentrations following a single high-protein lunch. *Journal of Nutrition*, *138*(4), 698-702.
- Smith, C. E., & Tucker, K. L. (2011). Health benefits of cereal fibre: A review of clinical trials. *Nutrition Research Reviews*, , 1-14.
- Smith, T. J., Sigrist, L. D., Bathalon, G. P., McGraw, S., Karl, J. P., & Young, A. J. (2010). Efficacy of a meal-replacement program for promoting blood lipid changes and weight and body fat loss in US army soldiers. *Journal of the American Dietetic Association*, *110*(2), 268-273.
- Snowling, N. J., & Hopkins, W. G. (2006). Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: A meta-analysis. *Diabetes Care*, *29*(11), 2518-2527.
- Soenen, S., & Westerterp-Plantenga, M. S. (2007). No differences in satiety or energy intake after high-fructose corn syrup, sucrose, or milk preloads. *The American Journal of Clinical Nutrition*, *86*(6), 1586-1594.
- Solah, V. A., Kerr, D. A., Adikara, C. D., Meng, X., Binns, C. W., Zhu, K., et al. (2010). Differences in satiety effects of alginate- and whey protein-based foods. *Appetite*, *54*(3), 485-491.
- Somogyi, V., Gyorffy, A., Scalise, T. J., Kiss, D. S., Goszleth, G., Bartha, T., et al. (2011). Endocrine factors in the hypothalamic regulation of food intake in females: A review of the physiological roles and interactions of ghrelin, leptin, thyroid hormones, oestrogen and insulin. *Nutrition Research Reviews*, 1-23.
- Stengel, A., & Tache, Y. (2011). Interaction between gastric and upper small intestinal hormones in the regulation of hunger and satiety: Ghrelin and cholecystokinin take the central stage. *Current Protein & Peptide Science*, *12*(4), 293-304.
- Stiegler, P., & Cunliffe, A. (2006). The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports Medicine (Auckland, N.Z.)*, *36*(3), 239-262.
- Streppel, M. T., Arends, L. R., van 't Veer, P., Grobbee, D. E., & Geleijnse, J. M. (2005). Dietary fiber and blood pressure: A meta-analysis of randomized placebo-controlled trials. *Archives of Internal Medicine*, *165*(2), 150-156.
- Stubbs, R. J., Sepp, A., Hughes, D. A., Johnstone, A. M., Horgan, G. W., King, N., & Blundell, J. (2002). The effect of graded levels of exercise on energy intake and balance in free-living men, consuming their normal diet. *European Journal of Clinical Nutrition*, *56*(2), 129-140.

- Stubbs, R., & Whybrow, S. (2004). Energy density, diet composition and palatability: Influences on overall food energy intake in humans. *Physiology & Behavior*, 81(5), 755-764.
- Stunkard, A. J., & Messick, S. (1985). The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of Psychosomatic Research*, 29(1), 71-83.
- Suzuki, K., Simpson, K. A., Minnion, J. S., Shillito, J. C., & Bloom, S. R. (2010). The role of gut hormones and the hypothalamus in appetite regulation. *Endocrine Journal*, 57(5), 359-372.
- Svetkey, L. P., Stevens, V. J., Brantley, P. J., Appel, L. J., Hollis, J. F., Loria, C. M., et al. (2008). Comparison of strategies for sustaining weight loss: The weight loss maintenance randomized controlled trial. *JAMA : The Journal of the American Medical Association*, 299(10), 1139-1148.
- Tao, Y. X. (2005). Molecular mechanisms of the neural melanocortin receptor dysfunction in severe early onset obesity. *Molecular and Cellular Endocrinology*, 239(1-2), 1-14.
- Thomas, D. E., Elliott, E. J., & Baur, L. (2007). Low glycaemic index or low glycaemic load diets for overweight and obesity. *Cochrane Database of Systematic Reviews (Online)*, (3)(3), CD005105.
- Thorsdottir, I., Tomasson, H., Gunnarsdottir, I., Gisladdottir, E., Kiely, M., Parra, M. D., et al. (2007). Randomized trial of weight-loss-diets for young adults varying in fish and fish oil content. *International Journal of Obesity (2005)*, 31(10), 1560-1566.
- Trabulsi, J., & Schoeller, D. A. (2001). Evaluation of dietary assessment instruments against doubly labeled water, a biomarker of habitual energy intake. *American Journal of Physiology. Endocrinology and Metabolism*, 281(5), E891-9.
- Tremblay, A., & Chaput, J. P. (2009). Adaptive reduction in thermogenesis and resistance to lose fat in obese men. *The British Journal of Nutrition*, 102(4), 488-492.
- Trier, C. M., & Johnston, C. S. (2012). Ingestion of nutrition bars high in protein or carbohydrate does not impact 24-h energy intakes in healthy young adults. *Appetite*, 59(3), 778-781.
- Trogdon, J. G., Finkelstein, E. A., Hylands, T., Dellea, P. S., & Kamal-Bahl, S. J. (2008). Indirect costs of obesity: A review of the current literature. *Obesity Reviews*, 9(5), 489-500.
- Tudor-Locke, C., & Bassett, D. R., Jr. (2004). How many steps/day are enough? preliminary pedometer indices for public health. *Sports Medicine (Auckland, N.Z.)*, 34(1), 1-8.

- U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2011). *Dietary guidelines for americans 2010*. Retrieved May 15, from <http://www.cnpp.usda.gov/Publications/DietaryGuidelines/2010/PolicyDoc/PolicyDoc.pdf>
- van Raalte, D. H., Li, M., Pritchard, P. H., & Wasan, K. M. (2004). Peroxisome proliferator-activated receptor (PPAR)-alpha: A pharmacological target with a promising future. *Pharmaceutical Research*, *21*(9), 1531-1538.
- van Rossum, C. T., Pijl, H., Adan, R. A., Hoebee, B., & Seidell, J. C. (2006). Polymorphisms in the NPY and AGRP genes and body fatness in dutch adults. *International Journal of Obesity (2005)*, *30*(10), 1522-1528.
- Vazquez, C., Montagna, C., Alcaraz, F., Balsa, J. A., Zamarron, I., Arrieta, F., et al. (2009). Meal replacement with a low-calorie diet formula in weight loss maintenance after weight loss induction with diet alone. *European Journal of Clinical Nutrition*, *63*(10), 1226-1232.
- Veldhorst, M., Smeets, A., Soenen, S., Hochstenbach-Waelen, A., Hursel, R., Diepvens, K., et al. (2008). Protein-induced satiety: Effects and mechanisms of different proteins. *Physiology & Behavior*, *94*(2), 300-307.
- Veldhorst, M. A., Nieuwenhuizen, A. G., Hochstenbach-Waelen, A., van Vught, A. J., Westerterp, K. R., Engelen, M. P., et al. (2009a). Dose-dependent satiating effect of whey relative to casein or soy. *Physiology & Behavior*, *96*(4-5), 675-682.
- Veldhorst, M. A. B., Nieuwenhuizen, A. G., Hochstenbach-Waelen, A., Westerterp, K. R., Engelen, M. P. K. J., Brummer, R. M., et al. (2009b). A breakfast with alpha-lactalbumin, gelatin, or gelatin plus TRP lowers energy intake at lunch compared with a breakfast with casein, soy, whey, or whey-GMP. *Clinical Nutrition*, *28*(2), 147-155.
- Viskaal-van Dongen, M., Kok, F. J. & de Graaf, C. (2010). Effects of snack consumption for 8 weeks on energy intake and body weight. *International Journal of Obesity*, *34*(2), 319-326.
- Visona, C., & George, V. A. (2002). Impact of dieting status and dietary restraint on postexercise energy intake in overweight women. *Obesity Research*, *10*(12), 1251-1258.
- Wadden, T. A., West, D. S., Neiberg, R. H., Wing, R. R., Ryan, D. H., Johnson, K. C., et al. (2009). One-year weight losses in the look AHEAD study: Factors associated with success. *Obesity (Silver Spring, Md.)*, *17*(4), 713-722.

- Wanders, A. J., van den Borne, J. J., de Graaf, C., Hulshof, T., Jonathan, M. C., Kristensen, M., et al. (2011). Effects of dietary fibre on subjective appetite, energy intake and body weight: A systematic review of randomized controlled trials. *Obesity Reviews : An Official Journal of the International Association for the Study of Obesity*, 12(9), 724-739.
- Weigle, D., Breen, P., Matthys, C., Callahan, H., Meeuws, K., Burden, V., et al. (2005). A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. *American Journal of Clinical Nutrition*, 82(1), 41-48.
- Werle, C. O., Wansink, B. & Payne, C. R. (2011). Just thinking about exercise makes me serve more food. Physical activity and calorie compensation. *Appetite*, 56(2), 332-335.
- Wernette, C. M., White, B. D., & Zizza, C. A. (2011). Signaling proteins that influence energy intake may affect unintentional weight loss in elderly persons. *Journal of the American Dietetic Association*, 111(6), 864-873.
- Westerterp, K. R. (2010). Physical activity, food intake, and body weight regulation: insights from doubly labeled water studies. *Nutrition Reviews*, 68(3), 148-154.
- Whybrow, S., Hughes, D. A., Ritz, P., Johnstone, A. M., Horgan, G. W., King, N., Blundell, J. E. & Stubbs R. J. (2008). The effect of an incremental increase in exercise on appetite, eating behavior and energy balance in lean men and women feeding ad libitum. *British Journal of Nutrition*, 100(5), 1109-1115.
- Whybrow, S., Mayer, C., Kirk, T.R., Mazlan, N. & Stubbs R.J. (2007). Effects of two weeks' mandatory snack consumption on energy intake and energy balance. *Obesity*, 15(3), 673-685.
- Wildman, R. P., Muntner, P., Reynolds, K., McGinn, A. P., Rajpathak, S., Wylie-Rosett, J., et al. (2008). The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: Prevalence and correlates of 2 phenotypes among the US population (NHANES 1999-2004). *Archives of Internal Medicine*, 168(15), 1617-1624.
- Williams, G., Noakes, M., Keogh, J., Foster, P. & Clifton, P. (2006). High protein high fibre snack bars reduce food intake and improve short term glucose and insulin profiles compared with high fat snack bars. *Asia Pacific Journal of Clinical Nutrition*, 15(4), 443-450.
- Williams, P. G., Grafenauer, S. J., & O'Shea, J. E. (2008). Cereal grains, legumes, and weight management: A comprehensive review of the scientific evidence. *Nutrition Reviews*, 66(4), 171-182.

- Williamson, D. A., Lawson, O. J., Brooks, E. R., Wozniak, P. J., Ryan, D. H., Bray, G. A., et al. (1995). Association of body mass with dietary restraint and disinhibition. *Appetite*, 25(1), 31-41.
- Wing, R. R., & Phelan, S. (2005). Long-term weight loss maintenance. *The American Journal of Clinical Nutrition*, 82(1 Suppl), 222S-225S.
- Woo, R. & Pi-Sunyer, F. X. (1985). Effect of increased physical activity on voluntary intake in lean women. *Metabolism*, 34(9), 836-841.
- Wyatt, S.L. (2011). State of the snack industry 2010. SymphonyIRI Group. <http://www.symphonyiri.com/Portals/0/SNAXPO-2011.pdf> . Accessed June 23.
- Wynne, K., Stanley, S., McGowan, B., & Bloom, S. (2005). Appetite control. *The Journal of Endocrinology*, 184(2), 291-318.
- Yu, Y., Deng, C., & Huang, X. F. (2009). Obese reversal by a chronic energy restricted diet leaves an increased arc NPY/AgRP, but no alteration in POMC/CART, mRNA expression in diet-induced obese mice. *Behavioural Brain Research*, 205(1), 50-56.
- Zaveri, S., & Drummond, S. (2009). The effect of including a conventional snack (cereal bar) and a nonconventional snack (almonds) on hunger, eating frequency, dietary intake and body weight. *Journal of Human Nutrition and Dietetics : The Official Journal of the British Dietetic Association*, 22(5), 461-468.
- Zhang, L., Bijker, M. S., & Herzog, H. (2011). The neuropeptide Y system: Pathophysiological and therapeutic implications in obesity and cancer. *Pharmacology & Therapeutics*, 131(1), 91-113.
- Zhang, Y., Proenca, R., Maffei, M., Barone, M., Leopold, L., & Friedman, J. M. (1994). Positional cloning of the mouse obese gene and its human homologue. *Nature*, 372(6505), 425-432.
- Zhang, Y., von Deneen, K. M., Tian, J., Gold, M. S., & Liu, Y. (2011). Food addiction and neuroimaging. *Current Pharmaceutical Design*, 17(12), 1149-1157.
- Zinn, A. R. (2010). Unconventional wisdom about the obesity epidemic. *The American Journal of the Medical Sciences*, 340(6), 481-491.

APPENDIX A
GELATIN TRIAL IRB APPROVAL LETTER



To: Carol Johnston
HSC

RC **From:** Carol Johnston, Chair *JD*
Biosci IRB

Date: 10/28/2011

Committee Action: Expedited Approval

Approval Date: 10/28/2011

Review Type: Expedited F2 F4 F7

IRB Protocol #: 1110006995

Study Title: Gelatin Ingestion and Calorie Compensation with Exercise

Expiration Date: 10/27/2012

The above-referenced protocol was approved following expedited review by the Institutional Review Board.

It is the Principal Investigator's responsibility to obtain review and continued approval before the expiration date. You may not continue any research activity beyond the expiration date without approval by the Institutional Review Board.


Adverse Reactions: If any untoward incidents or severe reactions should develop as a result of this study, you are required to notify the Biosci IRB immediately. If necessary a member of the IRB will be assigned to look into the matter. If the problem is serious, approval may be withdrawn pending IRB review.

Amendments: If you wish to change any aspect of this study, such as the procedures, the consent forms, or the investigators, please communicate your requested changes to the Biosci IRB. The new procedure is not to be initiated until the IRB approval has been given.

Please retain a copy of this letter with your approved protocol.


APPENDIX B

PROTEIN BAR TRIAL IRB APPROVAL LETTER



Office of Research Integrity and Assurance

To: Carol Johnston
HSC

From:  Carol Johnston, Chair
Biosci IRB

Date: 11/04/2009

Committee Action: **Exemption Granted**

IRB Action Date: 11/04/2009

IRB Protocol #: 0911004514

Study Title: Eating Matrix Study

The above-referenced protocol is considered exempt after review by the Institutional Review Board pursuant to Federal regulations, 45 CFR Part 46.101(b)(6).

This part of the federal regulations requires that the information be recorded by investigators in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. It is necessary that the information obtained not be such that if disclosed outside the research, it could reasonably place the subjects at risk of criminal or civil liability, or be damaging to the subjects' financial standing, employability, or reputation.

You should retain a copy of this letter for your records.

APPENDIX C

GELATIN TRIAL SUBJECT TRACKING CALANDER

Refrigerator Powder and Pedometer Calendar

NOVEMBER / DECEMBER

SUN	MON	TUE	WED	THUR	FRI	SAT
NOV 27 Step# _____ Powder _____	NOV 28 Step# _____ Powder _____	NOV 29 Step# _____ Powder _____	NOV 30 Step# _____ Powder _____	1 Step# _____ Powder _____	2 Step# _____ Powder _____	3 Step# _____ Powder _____
4 Step# _____ Powder _____	5 Step# _____ Powder _____	6 Step# _____ Powder _____	7 Step# _____ Powder _____	8 Step# _____ Powder _____	9 Step# _____ Powder _____	10 Step# _____ Powder _____
11 Step# _____ Powder _____	12 Step# _____ Powder _____	13 Step# _____ Powder _____	14 Step# _____ Powder _____	15 Step# _____ Powder _____	16 Step# _____ Powder _____	17 Step# _____ Powder _____
18 Step# _____ Powder _____	19 Step# _____ Powder _____	20 Step# _____ Powder _____	21 Step# _____ Powder _____	22 Step# _____ Powder _____	23 Step# _____ Powder _____	24 Step# _____ Powder _____
25 Step# _____ Powder _____	26 Step# _____ Powder _____	27 Step# _____ Powder _____	28 Step# _____ Powder _____	29 Step# _____ Powder _____	30 Step# _____ Powder _____	31 Step# _____ Powder _____

JANUARY

SUN	MON	TUE	WED	THUR	FRI	SAT
1 Step# _____ Powder _____	2 Step# _____ Powder _____	3 Step# _____ Powder _____	4 Step# _____ Powder _____	5 Step# _____ Powder _____	6 Step# _____ Powder _____	7 Step# _____ Powder _____
8 Step# _____ Powder _____	9 Step# _____ Powder _____	10 Step# _____ Powder _____	11 Step# _____ Powder _____	12 Step# _____ Powder _____	13 Step# _____ Powder _____	14 Step# _____ Powder _____
15 Step# _____ Powder _____	16 Step# _____ Powder _____	17 Step# _____ Powder _____	18 Step# _____ Powder _____	19 Step# _____ Powder _____	20 Step# _____ Powder _____	21 Step# _____ Powder _____
22 Step# _____ Powder _____	23 Step# _____ Powder _____	24 Step# _____ Powder _____	25 Step# _____ Powder _____	26 Step# _____ Powder _____	27 Step# _____ Powder _____	28 Step# _____ Powder _____
29 Step# _____ Powder _____	30 Step# _____ Powder _____	31 Step# _____ Powder _____	30 Step# _____ Powder _____	31 Step# _____ Powder _____	Step# _____ Powder _____	Step# _____ Powder _____

FEBRUARY

SUN	MON	TUE	WED	THUR	FRI	SAT
Step# _____ Powder _____	Step# _____ Powder _____	Step# _____ Powder _____	Step# _____ Powder _____	Step# _____ Powder _____	1 Step# _____ Powder _____	2 Step# _____ Powder _____

My 2nd Visit is _____ My 3rd Visit is _____ My 4th Visit is _____ My 5th Visit is _____

Instructions

Pedometer: Place your pedometer on either hip or mid-back each morning. When you take it off at night, mark on the calendar the number of steps you took that day.

Powder: Within one hour of awakening each morning, measure out the test product using the measuring scoop provided and stir into 1 cup of ice-cold water or other beverage. Consume the chilled drink prior to ingestion of any food or beverages. Place a check mark on the calendar for each day you drank the product. If you forget to drink the product, do not check the calendar.

APPENDIX D
GELATIN TRIAL SUBJECT TRACKING FORM

Subject #					
Pre-screen Date:			Week 0 (Baseline) Date:		
Consent			Weight:		
Weight:			Pedometer Download		
Height:			3-day record hand-in		
BMI:			Next visit reminder		
% FAT:			Notes:		
Waist:					
Stride length measurement:					
Calendar hand-out					
3-day records (3) handout					
Test Product Hand out					
TFEQ					
Next visit reminder					
Notes:					
Week 2 Date:			Week 4 Date:		
Weight:			Weight:		
Pedometer Download			Pedometer download		
3 day record hand in			Gift Card		
Next Visit Reminder			Next Visit Reminder		
Notes:			Notes:		

Week 6 Date:			
Weight			
Waist Circumference			
Pedometer Download and hand-in			
3 day record hand-in			
Calendar hand-in			
Gift Card			
Exit Survey			
Notes:			

APPENDIX E

GELATIN TRIAL WEIGHT AND BODYFAT GRAPHS

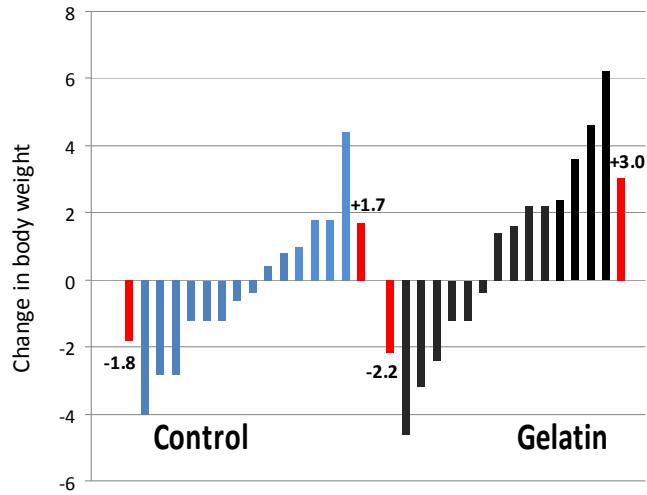


Figure 5. Individual variation in weight change among the study participants.

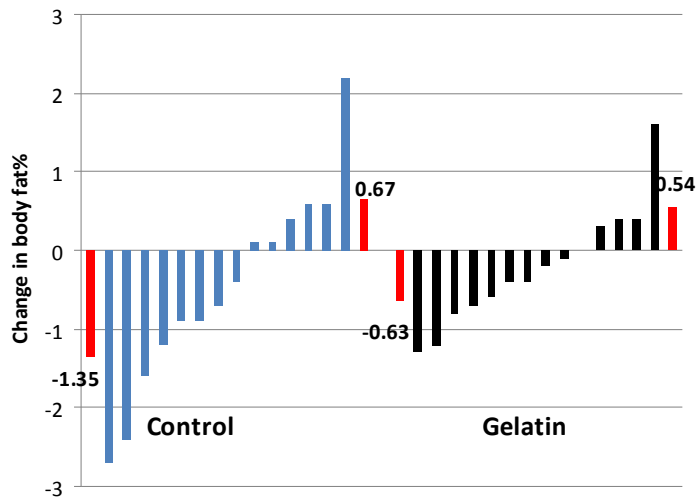


Figure 6. Individual variation in % body fat change among the study participants.

APPENDIX F
GELATIN TRIAL STATISTICS BY WEIGHT GAIN OR LOSS

Table 7.Comparison of outcome measures by weight gain or loss¹

	Weight Gainers	Weight Losers	<i>P</i> value Time Effect	<i>P</i> value Interaction
Activity ²				
Baseline	7043±1684	5550±2031	0.001	0.961
Trial avg.	8430±1825	6973±1861		
Energy Intake ³ (kcal, 3 d avg.)				
Baseline	1846±491	1580±542	0.392	0.320
Week 6	1830±445	1794±457		

¹ Means ± SD. *P* values for repeated measures ANOVA.² Sample size: n = 14 and n = 13 for the weight gainers and weight losers, respectively.³ Sample size: n = 12 and n = 11 for the weight gainers and weight losers, respectively.