

## Weight Loss

### WHAT IS THE EXTENT OF THE PROBLEM?

As the prevalence of overweight and obesity continues to rise, the resultant complications and associated morbidities take an ever increasing toll on those affected, as well as on total health-care costs. Analysis from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 revealed that 17.1% of US children and adolescents were overweight, and 66.3% of adults were either overweight or obese.<sup>1</sup>

Furthermore, obesity has been found to be underdiagnosed in outpatient settings according to a recent analysis. Only 29% of visits by adult patients who were obese—according to their body mass index (BMI)—had a documented diagnosis of obesity,<sup>2</sup> while only 63% of adolescents have both their height and weight measured annually; very few receive diet or exercise counseling.<sup>3</sup>

Even more concerning are the predictions for future rates of overweight and obesity based on current trends. Using NHANES data, researchers from the Johns Hopkins Bloomberg School of Public Health predict that by 2030, 86.3% of all US adults will be overweight or obese, with more than half obese. They predict that by 2048 all adults will be overweight or obese if the trends in weight gain continue. Additionally, a doubling in total healthcare costs attributable to obesity/overweight every decade to \$860.7-\$956.9 billion US dollars is expected by 2030, accounting for 16-18% of total US healthcare costs.<sup>4</sup>

### HOW ARE OBESITY AND OVERWEIGHT DEFINED?

In adults, overweight is defined as a BMI of 25.0 to 29.9 kg/m<sup>2</sup>, and obesity is defined as a BMI ≥ 30 kg/m<sup>2</sup>. The definition in children and adolescents (age 2-18) has not been as clearly defined, but in 2005 the Institute of Medicine defined obesity in this age group as a BMI of > 30 kg/m<sup>2</sup>, or 95<sup>th</sup> percentile for age and gender (whichever is smaller). Prior to this definition, children in these categories of weight were termed overweight, but not obese; the definition change reflects a growing concern for the magnitude of the problem in children, as well as in adults.<sup>5</sup>

Although BMI is perhaps the easiest to assess and the most frequently used measure of weight, it is also the least useful anthropometric index. As discussed below, other markers such as waist circumference or the waist-to-hip ratio appear to be better predictors of risk.

### WHAT ARE SOME OF THE CAUSES OF WEIGHT GAIN?

#### Food choices and inactivity

Certainly, a sedentary lifestyle combined with a nutrient-poor, but calorie-rich diet contributes greatly to the obesity epidemic

in the US. For example, consumption of sugar-sweetened beverages (SSBs) have been linked to the obesity epidemic, and from 1977 to 2001, energy intake from soft drinks and fruit drinks increased by 135%. Analysis of NHANES data also shows that the number of individuals that consume SSBs daily has increased to 63%, combined with an increase in portion size. They also found SSB consumption to be highest in those groups most at risk for obesity and Type 2 diabetes.<sup>6</sup> This increase has affected children too—NHANES 1999-2004 data shows that children and adolescents now derive 10% to 15% of their total calories from sugar-sweetened beverages and 100% fruit juice, with increasing consumption in all age groups.<sup>7</sup>

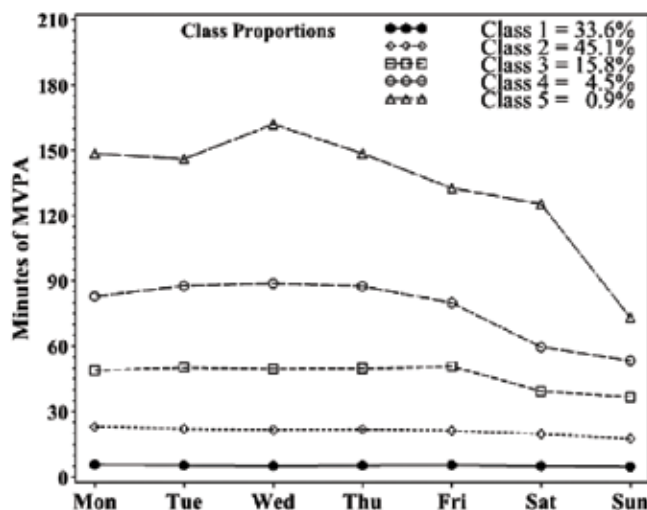


Figure 1\* Five latent classes: MVPA. Class proportions have been weighted to account for the complex sample design.

Along with the increased consumption of empty calories has come a decrease in physical activity. Epidemiological data from the NHANES 2003-2004 study found that 34% of the entire US population averages 5.3 minutes of moderate to vigorous physical activity (MVPA) per day, while another 45% had a mean of 21 minutes per day. This means that 79% of the US population is falling short of minimum recommendations for physical activity (See Figure 1).<sup>8</sup>

When an increase in calories is combined with a decrease in physical activity, the energy gap between calories consumed and calories burned widens. A recent study clearly demonstrated the relationship between physical activity, SSB intake, and not only anthropomorphic indices such as BMI, but also with that of insulin resistance (IR). In a study of nearly 7,000 ado-

lescents, increased consumption of SSBs was independently associated with increased HOMA-IR (an index of insulin resistance), systolic blood pressure, waist circumference, and BMI percentile for age and sex, as well as decreased HDL cholesterol concentrations. Higher levels of physical activity were also independently associated with decreased HOMA-IR, LDL cholesterol concentrations, triglyceride concentrations, and increased HDL cholesterol concentrations. Furthermore, low SSB intake and high physical activity levels appear to modify each other's effects of decreasing HOMA-IR and triglyceride concentrations and increasing HDL cholesterol concentrations.<sup>9</sup>

### INSULIN RESISTANCE AND INFLAMMATION

The majority of overweight and obese individuals have some degree of IR, and inflammation is now thought to be a corollary of obesity.<sup>10, 11</sup> Adipocytes have only recently been recognized as a functional endocrine organ, because they release a number of biologically-active signals, or adipokines, which influence insulin sensitivity and initiate the induction of inflammatory cytokines. Obesity leads to an increase in the number and size of adipocytes, which activates this network of inflammatory signaling pathways. While it is still unclear which precedes which, obesity and insulin resistance certainly fuel each other, making weight loss much more challenging once obesity is established.

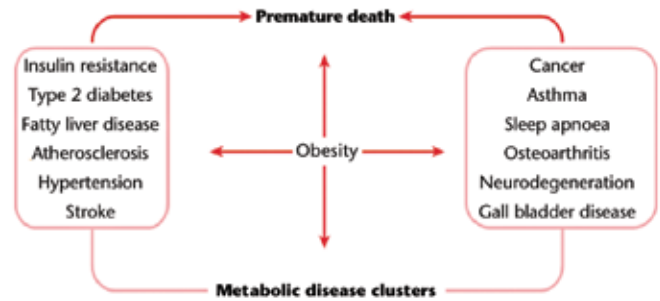
Abnormal glucose homeostasis was also found to be predictive of the amount of weight regained after weight loss, as demonstrated recently in a prospective trial. Following an oral glucose tolerance test (OGTT), subjects who had the lowest glucose concentrations were found to have the greatest risk for weight gain over time. The authors speculate that insulin resistance is responsible for this effect, given its association with weight gain, weight regain after loss, and lower blood glucose concentrations during an OGTT. This effect is likely due to the fluctuations in blood glucose levels after a meal; with poor glucose homeostasis, glucose concentrations have more significant highs and lows. It is very likely that these lows in glucose levels stimulate hunger, leading to greater appetite and calorie intake, and ultimately to weight regain.<sup>12</sup>

### WHAT ARE THE CONSEQUENCES OF EXCESS WEIGHT?

The metabolic diseases associated with overweight and obesity are many, including Type 2 diabetes, atherosclerosis, allergic disease (including food allergy), hypertension, sleep apnea, and urinary incontinence.<sup>13, 14, 15, 16</sup> While not all of the mechanisms are clearly understood, the underlying increase in systemic inflammation and insulin resistance are thought to mediate many of these consequences, which are often clustered together (See Figure 2).

### HOW IS BODY WEIGHT BEST ASSESSED?

Although BMI is the most commonly used assessment tool, other anthropometric indices appear to be better predictors of risk. This is in large part because the distribution of excess adiposity may be more important than total adiposity, a distinction which is not captured by BMI alone. Both waist circumference (WC) and waist-to-hip ratios (WHR) are better predictors of risk, because they assess abdominal/central adiposity, which is more closely associated with cardiovascular



**Figure 2 Clustering of metabolic diseases.** Obesity is considered to be a central feature that increases the risk for a vast array of diseases, with significant morbidity and mortality. In general, the mechanistic basis of the link between obesity and the diseases listed on the right are poorly understood compared with that of those listed on the left.

incident risk.<sup>17</sup> It has been suggested that WHR is a superior predictor of cardiovascular disease (CVD) risk because it includes a measurement of hip circumference, which is inversely associated with dysglycemia, dyslipidemia, diabetes, hypertension, CVD, and death. A recent study found that WHR is also a stronger predictor of subclinical atherosclerosis than either WC or BMI; the association with atherosclerotic burden was strongest for WHR, intermediate for waist circumference, and weakest for BMI, using carotid intimal medial thickness (IMT) as a marker (See Figure 3).<sup>18</sup>

Given the close connection between insulin resistance and other metabolic abnormalities, the assessment of insulin resistance, glucose, systemic inflammation, and other lipid markers should be done as part of a comprehensive evaluation.

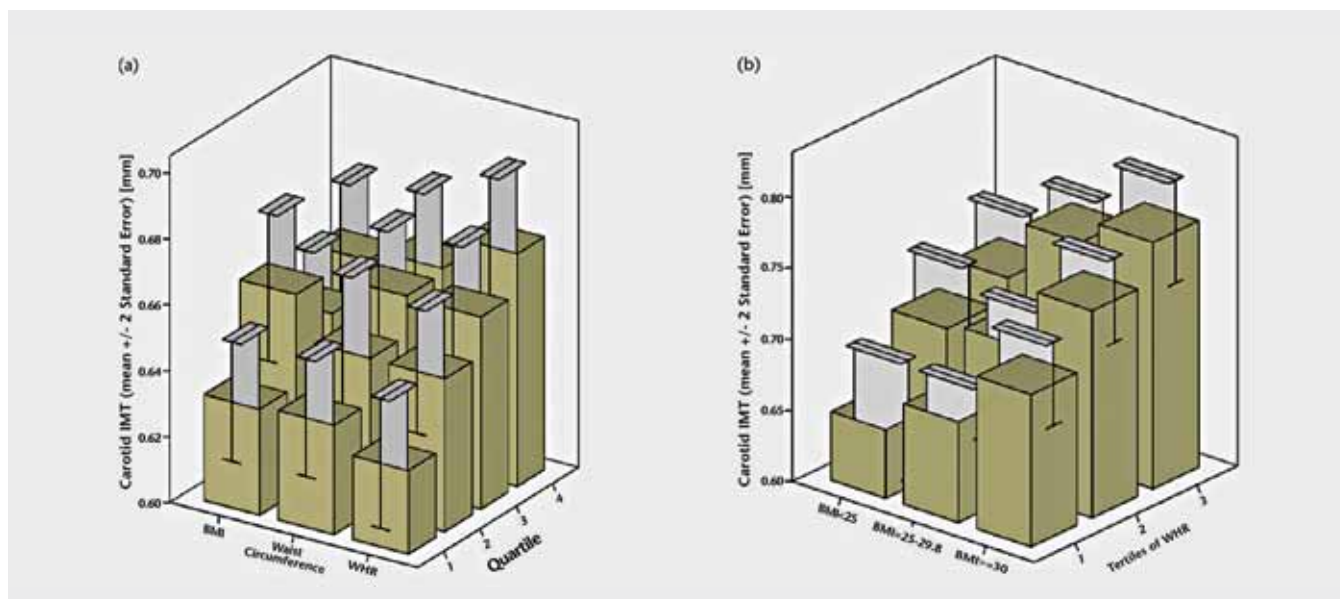
### HOW IS WEIGHT LOSS ACHIEVED?

Considering the high recidivism rate for weight regain, there may be no single program that is effective for everyone. However, a combination of dietary changes, increasing physical activity, targeting insulin resistance and inflammation, and addressing personal motivation are all powerful tools for weight loss.

#### *Diet & Exercise*

Consistently, reduced calorie diets are associated with meaningful weight loss, often regardless of the type of macronutrients emphasized.<sup>19</sup> Calorie restricted diets also improve endothelial function in peripheral arteries within 12 weeks in overweight and obese adults.<sup>20</sup> However, it has recently been demonstrated that in response to a reduction in caloric intake, metabolic adaptations take place, which lower sedentary energy expenditure, and, in free-living adults, lead to a reduction in physical activity—two changes that may be responsible for the inability to lose weight the longer a calorie restricted diet is in place.<sup>21</sup> Certainly, calorie restriction alone is not enough to lose weight.

Although it is unclear what macronutrient composition is most associated with weight loss, a recent trial found that less favourable effects on flow-mediated vasodilatation and lipid risk factors were found with an Atkins diet compared to Ornish and South Beach diets. Specifically, saturated fat content was inversely correlated to brachial artery dilatation, and this effect



**Figure 3** Carotid intimal-medial thickness across tertiles of waist circumference by traditional body mass index categories. **a)** For BMI < 25 kg/m<sup>2</sup>: P = 0.049 for trend across waist circumference tertiles. For BMI = 25-29.9 kg/m<sup>2</sup>: P = 0.001 for trend across waist circumference tertiles. For BMI ≥ 30 kg/m<sup>2</sup>: P = 0.01 for trend across waist circumference tertiles. **b)** Carotid intimal-medial thickness across tertiles of waist-to-hip ratio by traditional body mass index categories. For BMI < 25 kg/m<sup>2</sup>: P = 0.002 for trend across WHR tertiles. For BMI = 25-29.9 kg/m<sup>2</sup>: P = 0.001 for trend across WHR tertiles. For BMI ≥ 30 kg/m<sup>2</sup>: P = 0.997 for trend across WHR tertiles.

was also seen when comparing a low-carbohydrate diet to a low-fat diet.<sup>22, 23</sup>

The Mediterranean diet has also been associated with better glycemic control in obese individuals, and, given its high compliance rate, may be more suited to addressing underlying insulin resistance.<sup>24</sup> Certainly, a low glycemic index diet rich in fruits, vegetables, and fiber that is low in saturated fat has been found to be effective not only for weight loss, but for controlling hunger. By reducing energy density with high fiber intake, satiety is reached before caloric intake is excessive.<sup>25, 26, 27</sup>

Appetite control is also improved by increasing physical activity, an effect that may be mediated by a number of gastrointestinal peptides.<sup>28, 29</sup> While the weight loss and improvements in glucose tolerance may not be different in groups that either restrict calories or increase their physical activity, there does seem to be a preservation of lean mass in those who combine moderate to vigorous exercise with caloric restriction.<sup>30, 31</sup>

While aerobic exercise is an important part of a weight loss program, resistance training appears to have unique benefits as well. Regular resistance training has been shown to improve insulin sensitivity and fasting glycemia, while reducing abdominal fat in a trial that enrolled older men with Type 2 diabetes.<sup>32</sup> And in a trial with overweight women, weight loss resulting from resistance training was found to maintain both strength and resting energy expenditure compared to women who lost weight with no exercise or with aerobic exercise.<sup>33</sup> Clearly, strength training plays an important role in preventing the drop in metabolism that is normally seen with longer term weight loss and calorie restriction. Lastly, one study

suggests that the benefits to glucose homeostasis from resistance training may in part be determined by ethnicity, as African American men with Type 2 diabetes lost more weight and had greater improvements in insulin sensitivity with resistance training than did white men.<sup>34</sup>

One small study suggests that subclinical hypothyroidism may interfere with the benefits of exercise on metabolism and insulin sensitivity; this warrants thyroid function evaluation if weight loss is not occurring as expected with regular physical activity and dietary changes.<sup>35</sup>

### Supplementation

In combination with diet and exercise changes, nutritional supplementation has been shown to improve appetite control and insulin sensitivity, to reduce inflammation, and to assist with overall weight loss.

### PGX

Given the importance of dietary fiber in regulating glucose homeostasis, reducing energy density (which improves appetite control), and for minimizing glucose highs and lows that occur postprandially, the use of PolyGlycopleX (PGX) has considerable therapeutic potential for weight loss. PGX typically lowers after-meal blood glucose levels by approximately 35 to 70% and also lowers insulin secretion by approximately 40%, producing a whole body insulin sensitivity index improvement of nearly 60%. Because PGX minimizes glucose fluctuations that occur postprandially, this has the effect of reducing appetite. The glucose lows associated with poor glucose homeostasis are prevented, and hunger is reduced. In a recent trial comparing PGX, a highly-viscous fiber, to low and medium viscosity fibers,

PGX was found to have the greatest reduction in caloric and gram intake, an effect likely to lead to significant weight loss.

### Other supportive therapies include:

- **PGX® Weight Loss Meal Replacement** – contains a full spectrum of vitamins and minerals, 20 g of high quality undenatured whey protein and 5 g PGX—the dose found to control appetite and reduce cravings for several hours. It also contains medium chain triglycerides (MCTs) derived from coconuts, which have been shown to lead to greater total loss of trunk adiposity, and intraabdominal adipose tissue when compared to olive oil, likely through an increase in fat oxidation. (Available in *Double Chocolate*, *Very Strawberry* and *French Vanilla*).
- **Calm-Pro™** – contains Suntheanine L-Theanine, a natural amino acid found in green tea. Extensive research on L-Theanine shows that in higher doses (100-300 mg), it can reduce emotionally-driven food cravings and stabilize mood.<sup>36</sup>
- **Omega-3 Fatty Acids** – in addition to the reduction in inflammation and improvements in insulin sensitivity seen with n-3 fatty acids, they may also modulate satiety.

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### FIGURES

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