

# The Weight Loss-Genetics Program

## What is Considered Obese?

Obesity is objectively assessed by calculating your Body Mass Index or BMI. There is an on-line tool for calculating your BMI from the Center for Disease Control (search “CDC- Adult BMI calculator”). Unless you are an athlete or have an unusual amount of muscle mass, the BMI is a good tool for estimating obesity. A BMI between 25-29.9 is considered over weight, a BMI of greater than 30 is considered obese. Most clinical studies have used BMI as a way of categorizing a person’s risk for developing disease(s) associated with excess weight.

## What are the health consequences of obesity for adults?

People who have obesity are at increased risk for many diseases and health conditions, including the following: <sup>10, 17, 18</sup>

- All-causes of death (mortality)
- High blood pressure (hypertension)
- High LDL cholesterol, low HDL cholesterol, or high levels of triglycerides (dyslipidemia)
- Type 2 diabetes
- Coronary heart disease
- Stroke
- Gallbladder disease
- Osteoarthritis (a breakdown of cartilage and bone within a joint)
- Sleep apnea and breathing problems
- Chronic inflammation and increased oxidative stress<sup>19,20</sup>
- Some cancers (endometrial, breast, colon, kidney, gallbladder, and liver)
- Low quality of life
- Mental illness such as clinical depression, anxiety, and other mental disorders<sup>21,22</sup>
- Body pain and difficulty with physical functioning<sup>23</sup>

## Introduction to Weight-Gain Factors

Obesity is often studied in mice because their food intake (diets) can be closely regulated, their physical activity levels can be increased or decreased, and genetic engineering can be done to produce mutant mice with specific gene variants or even complete gene “Knock-outs”. Studies of normal and genetically altered mice have so far identified about 244 genes that play a role in the development of obesity. We share about 97% of our protein-coding genes with mice however, the genes of similar function are often only partially identical in their DNA sequences. Unfortunately, genetic studies in mice do not always correlate well with human studies however, recent advances in whole genome sequencing for humans have provided us with useful tools for assessing the DNA-coding similarities “of mice and men”. When there is high

similarity between the two genetic-codes, the mouse gene study is more likely to be relevant to understanding how the similar human gene functions. Because controlling for environmental factors that influence obesity is much more difficult in humans, as of 2023, only 74 genes have been identified that are believed to affect the risk for developing obesity. As genetically similar as we are to mice, it is very likely that future research will identify 100 or more additional genes that are risk factors for human weight gain, some of which may turn out to be good therapeutic targets for drugs. Multiple scientific studies have reported that 40-70% of BMI differences between people can be attributed to genetic factors however, there has also been studies that reported that groups of people with similar genetics, but who have different levels of physical activity and different access to calories in their diets, can have very different rates of obesity. Over all, there is little doubt that more physically active lifestyles can lead to lower BMIs and that sedentary behavior is a consequence of higher BMIs.

On average, most over-weight individuals slowly gained about 2 pounds per year and this often occurred without a significant impact on their health. At some point, most individual will choose to attempt weight loss because of its negative impact on their quality of life or because of displeasure with the physical changes they have developed. Some others are coerced into attempting weight loss by their Physicians to help improve a medical problem that is related to excessive weight gain, such as: Type-2 Diabetes, Sleep apnea or Arthritis. It is easy for a doctor to tell a patient that they should "lose some weight", but it is irresponsible of them to not help you achieve that goal (or at least refer you to someone who can). We were guilty of this same indifference to the needs of our over-weight Allergy and Immunology clinic patients, so we created this program initially to help them optimize their chances for sustained weight loss. We are offering it to others because we believe in its fundamental design and have seen first-hand its effectiveness however, without your motivation to make some changes in your life-style choices, no intervention will work for you. No matter what drives you to lose weight, Physician administered programs have a better success rate than self-directed diet plans and access to medications proven to help manage obesity (GLP-1RAs) are not available without a prescription.

### **Why Should I be Evaluated for Genetic Obesity Risk Factors Before Starting a Weight-loss Program?**

A recent study found that there is a wide range of genetic variants in the 5 genes most frequently associated with obesity (ADIPOQ, FTO, GLP-1R, GHRL and INS). Identifying your specific genetic risk-factors for developing obesity can be used to help design a weight loss plan that is directed specifically at curbing over-eating behaviors, addressing satiety (fullness) problems, and selecting appropriate behavior modifications. Also, for some specific genetic variants, a dietary supplement may be beneficial for ameliorating or managing a weight-gain factors. There is no doubt that some thin people are unhealthy and some over-weight people are healthy. We believe that optimizing your health before undertaking a weight loss program and understanding how your genes have affected your weight gain, is an important first step.