CONTENT KNOWLEDGE | Diabetes

INTRODUCTION

Diabetes is a disease that occurs when blood glucose, blood sugar, is elevated above normal. In essence, diabetes describes the symptoms of a disease, not the underlying disease process itself. This is easily understood when one considers that there are two types of diabetes (type 1 and type 2) that share a disease description, but substantially different causal mechanisms (pathologies). The reason they share the same name is not due to their underlying causes, but due to a common presenting symptom: elevated blood sugar.

The name diabetes mellitus is derived from two Greek words: diabetes and mellitus. Diabetes translates to mean, “siphon”, while mellitus translates to mean, “like honey”. The condition was given this name because it was usually diagnosed by the sweet smell or taste of a person’s urine. The urine was sweet due to the fact that levels of sugar in the blood were so high that it was being filtered out into the urine.

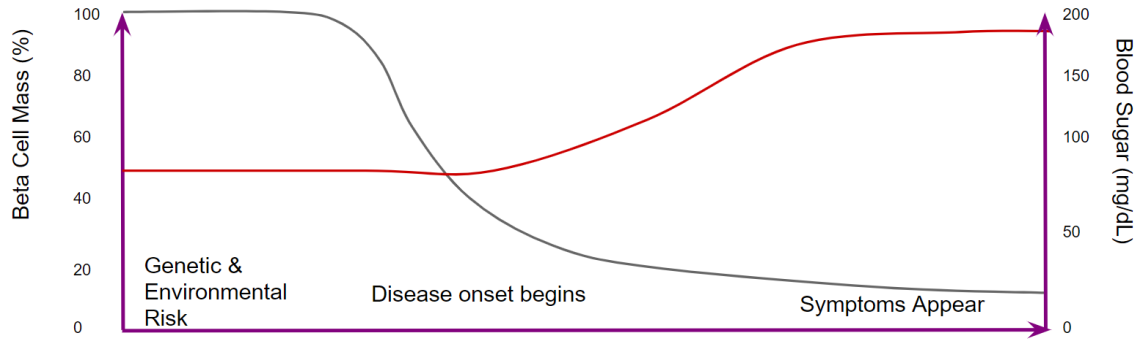
This is largely where the similarities of type 1 and type 2 diabetes end, as they are fundamentally different diseases, with different root causes, trajectories, and treatment strategies. This module will focus primarily on type 2 diabetes, but will discuss type 1 diabetes to highlight the marked differences between them.

Type 1 Diabetes

Type 1 diabetes is a disease of insulin insufficiency and/or a complete lack of insulin; it is primarily an autoimmune disease that is the result of the destruction of the insulin producing cells, beta islet cells, in your pancreas. It typically, but not always, presents early in life (before the age of 30). We shall briefly cover the natural history of this disease and how treatment may differ from type 2 diabetes, but we will not cover it in great detail as the focus will be on type 2 diabetes.

The natural history of Type 1 diabetes typically presents as follows. An individual is born with some genetic risk of the disease and there is some environmental risk. Their life progresses as normal until something sets the autoimmune process of the body slowly destroying the beta islet cells. This process begins a bit slowly at first and there are no real symptoms as there are more than enough cells to produce the required insulin and blood sugar levels remain stable.

Eventually, the beta-cell destruction reaches a point where there are not enough cells to meet the body's demand for insulin and blood sugar levels begin to rise and a variety of symptoms set in: glucose in the urine, increased urination, thirst, mood swings, and malaise. The disease is diagnosed through a combination of tests, usually some form of a blood glucose measurement test (e.g. fasting glucose draw, HbA1c, oral-glucose tolerance test) and/or a test for antibodies associated with type 1 diabetes.



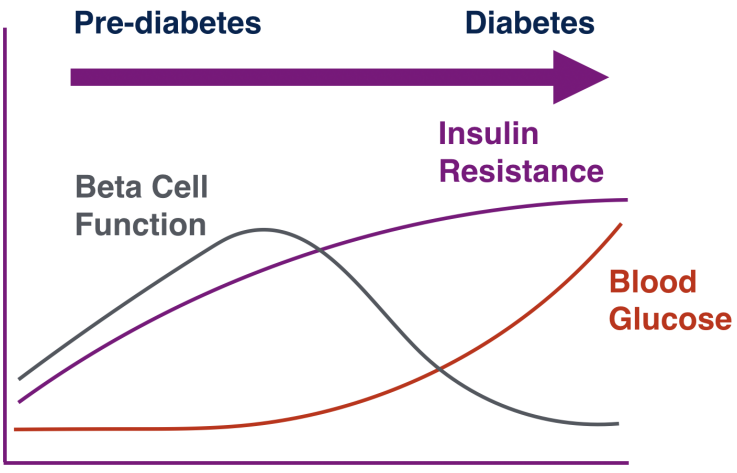
The lack of insulin makes type 1 diabetes, in essence, a disease of catabolism. This can be seen among people who have type 1 diabetes and do not manage the disease well with insulin medication.

What Causes Type 1 Diabetes

The exact cause of type 1 diabetes is still not precisely well understood, but it appears to be a combination of a genetic predisposition and an environmental trigger (like most other auto-immune disorders). Many of the environmental triggers are: environmental exposure, viral or bacterial infection, stress, other auto-immune diseases. Type 1 diabetes often manifests itself early in life but can happen at any stage in life with infancy (<5 years of age), teenage years (13-18), and young adulthood (20-25), being the most common periods of disease onset.

Type 2 Diabetes

Whereas type 1 diabetes is a disease of insulin insufficiency, type 2 diabetes is primarily a disease of insulin resistance in early stage disease followed by insulin sufficiency in later stages due to



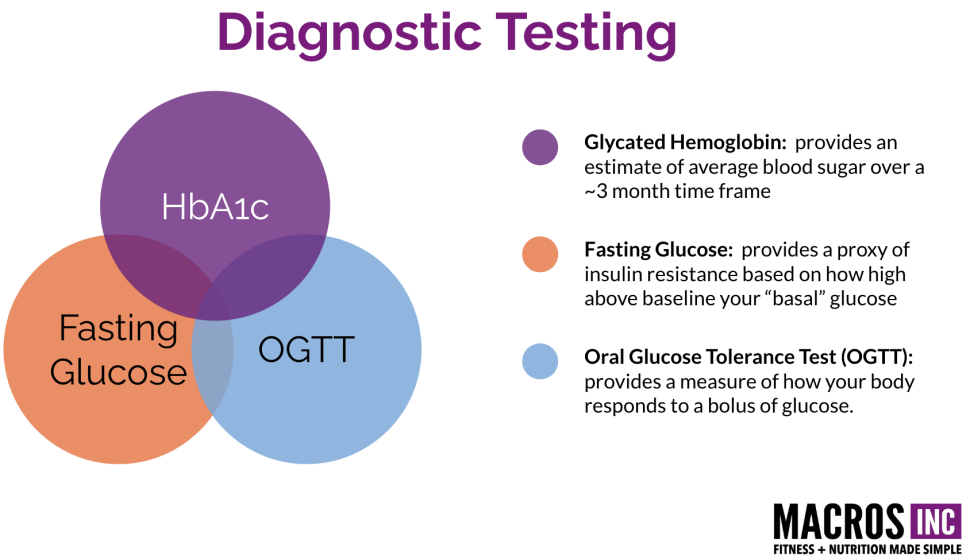
beta islet cell death. The cell death does not initiate the disease like it does in type 1, but is the result of the disease processes that occur during the progression of diabetes and leads to more advanced disease. Traditionally, type 2 diabetes was considered adult-onset diabetes as it typically presented in adulthood; however, it is now presenting in childhood at higher and higher prevalence.

The natural history of type 2 diabetes differs quite substantially from type 1 diabetes. In type 2 diabetes, the underlying disease process begins with an increase in insulin resistance. The cause of which is usually the result of obesity (more on this later), this rise in insulin resistance is met with a compensatory increase in beta-cell function. Beta cells release above normal levels of insulin to help maintain normal levels of blood sugar. This process proceeds and the beta-cell function eventually begins to decline and the increased insulin secretion is not enough to keep up with the demand. At this point blood glucose begins to rise above normal and elevated levels of glucose are found in the body. This disease process is important to understand. By the time elevated blood glucose is discovered, the disease process is well underway. By the time a clinical diagnosis is made, the underlying disease process has been occurring for years.

How Type 2 Diabetes is Diagnosed

Type 2 diabetes is primarily diagnosed by the main symptom (not the root cause) of the disease, by blood glucose or markers of blood glucose (*i.e.* HbA1c). There are currently three primary ways in which type 2 diabetes is diagnosed:

- Fasting Glucose
- Oral Glucose Tolerance Test
- HbA1c



Each test measures something very different and it is important to understand what each one means and how to interpret the test.

A **Fasting Glucose** provides a proxy of insulin resistance. Essentially it measures what your basal level of glucose is and then estimates what your level of insulin resistance is by making a determination of how far above normal your blood sugar is. The problem with this test is that it does not accurate account for things like stress, illness, infection, exercise status, or the natural variation we have as individuals for what "normal" basal glucose levels should be.

A **Glycated Hemoglobin** test (HbA1c) provides an estimate of the average blood sugar over a ~3 month time frame. This measure is generally more accurate for disease status than fasting glucose or an oral glucose tolerance test. However, in people with relatively high red blood cell turnover (*e.g.* endurance athletes), these tests can also be inaccurate.

An **Oral Glucose Tolerance Test** provides a measure of how your body responds to a bolus of glucose, which in theory is a measure of how insulin resistant you are at that time. It has similar issues as a **Fasting Glucose** test, but is also more dynamic than fasting glucose and can often result in false positives.

There is an additional important aspect of these tests to understand. Diagnoses are made based on cutoff criteria. Meaning that diagnosis is rather binary, when the disease itself occurs along a spectrum as it is a disease process and not a binary situation. For example, utilizing a fasting blood glucose level, someone with a 199 mg/dL reading would be considered to not have diabetes, while someone with a reading of 201 mg/dL would be considered to have diabetes. However, the individual with a 199 mg/dL has roughly the same level of insulin resistance and a similar disease state (may different in the progression of other complications, but the insulin resistance levels would be similar). Additionally, it is important to remember that at the time of diagnosis, the disease process is in swing and has been occurring for months, if not years or even decades.

"While the disease process begins much earlier than elevated blood glucose appears, clinically it is diagnosed based on measures of glycemia.

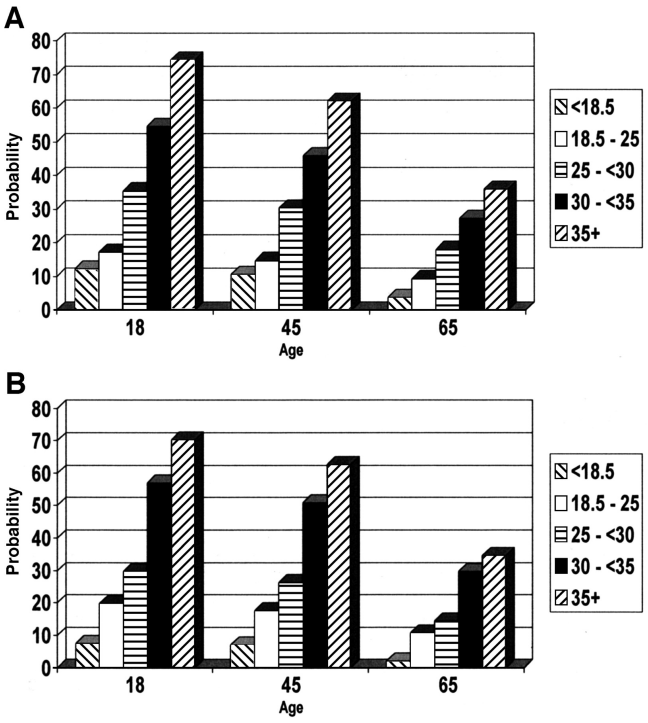
This means that by the time an individual receives a diagnosis, the disease process is in full swing."

What Causes Type 2 Diabetes

This brings us to the very natural question of, "what causes type 2 diabetes". ***Based on the last century of research, there appears to be no singular cause of type two diabetes from the standpoint of exposure variables. Rather it appears to arise out of an accumulation of different risk factors, with each factor contributing differently for each person.*** The primary risk factors that are involved in the development of type 2 diabetes are: obesity, physical activity, age, race/ethnicity, genetics, and environmental insults.

Obesity subsumes much of the risk for developing diabetes, with the lifetime risk of developing diabetes increasing as BMI increases. For example, the lifetime risk of developing diabetes for an individual with a BMI of ~ 8.5-25 is ~10-15% while an individual with a BMI of 35+ is between 30-75%, depending on age.

Why does obesity increase the risk of developing diabetes? Well the answer here is both incredibly complex and at the same time very simple. It comes down to the principle of energy overload. Essentially, when skeletal muscle cells and fat cells contain more energy than they normally can, several processes occur that result in the cells becoming insulin resistant. This insulin resistance can, at least to some degree, slow down the amount of energy that enters the cells to try and help address the present energy overload.



Additionally, along with intracellular energy overload, obesity can result in our adipose tissue (fat cells) that is located not only in our fat stores (*e.g.* the fat under our skin) but also the fat that is within our skeletal muscle, to produce inflammatory molecules. These inflammatory molecules also contribute to insulin resistance.

Physical activity, independent of weight loss, appears to activate some molecular machinery within our muscle tissue that helps improve insulin resistance. This is primarily related to utilizing some of the stored energy within the cells, but also lowers inflammation and oxidative stress that contributes to insulin resistance.

Age is directly correlated with insulin resistance and it is believed that as cells age they become less capable of defending against the contributors to insulin resistance.

Race/ethnicity goes hand-in-hand with **genetics** such that there are some genetic predispositions that appear to affect the threshold at which individuals can tolerate "energy overload" before insulin resistance begins to manifest.

Interesting Fact: In sepsis, which is a systemic infection and inflammatory response, there is such substantial inflammation that virtually the whole body becomes insulin resistant. This causes both hyperglycemia (high blood sugar) as well as increased fatty acids in the blood and increased amino acids in the blood.

What Does Having Type 2 Diabetes Mean for Our Metabolism?

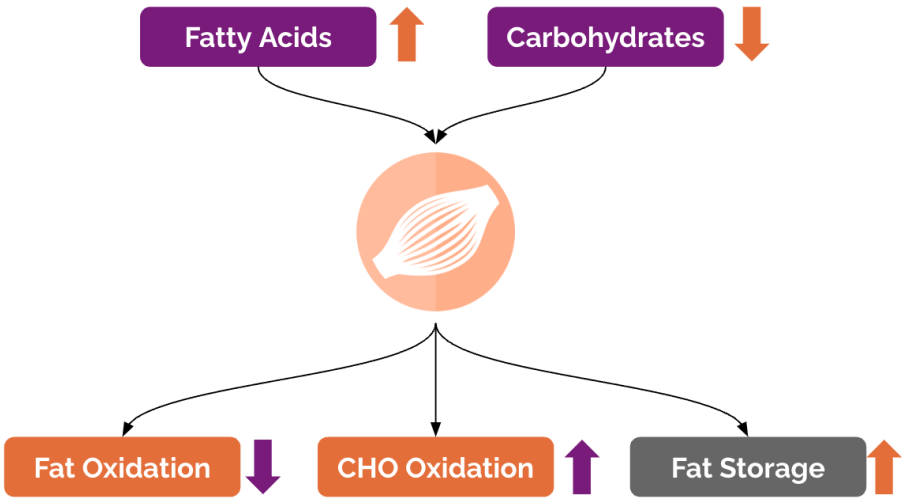
One of the most important concepts for people to understand is that diabetes is not simply a disorder of elevated blood sugar, but of disordered metabolism, affecting virtually every organ system. This will change how you respond to exercise and what you should prioritize for your diet. However, the actual effect on metabolism is often not what people expect. In fact, contrary to what most people think, fat metabolism is what is primarily impaired among people with type 2 diabetes.

"We often confuse the symptom of diabetes, elevated blood glucose, with what is actually going on under the metabolic hood."

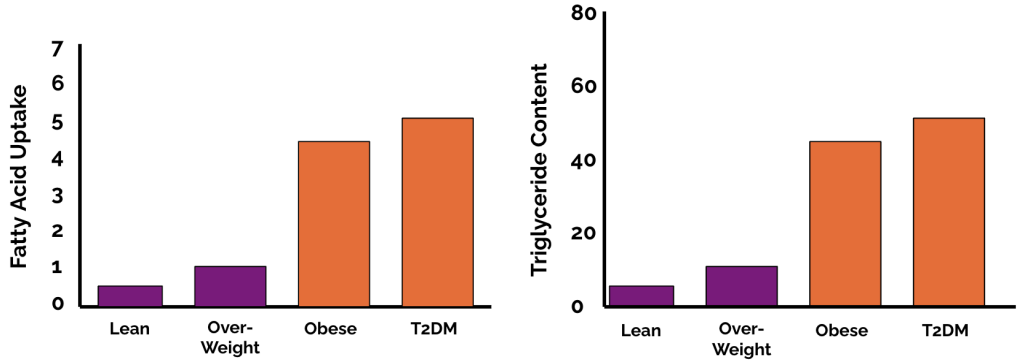
In fact, one of the most interesting aspects of type 2 diabetes is that fat metabolism is impaired, while glucose metabolism is relied upon more heavily. This has been confirmed by hundreds of studies. Here is a summary of the major metabolic changes that occur among people with type 2 diabetes compared to people without type 2 diabetes:

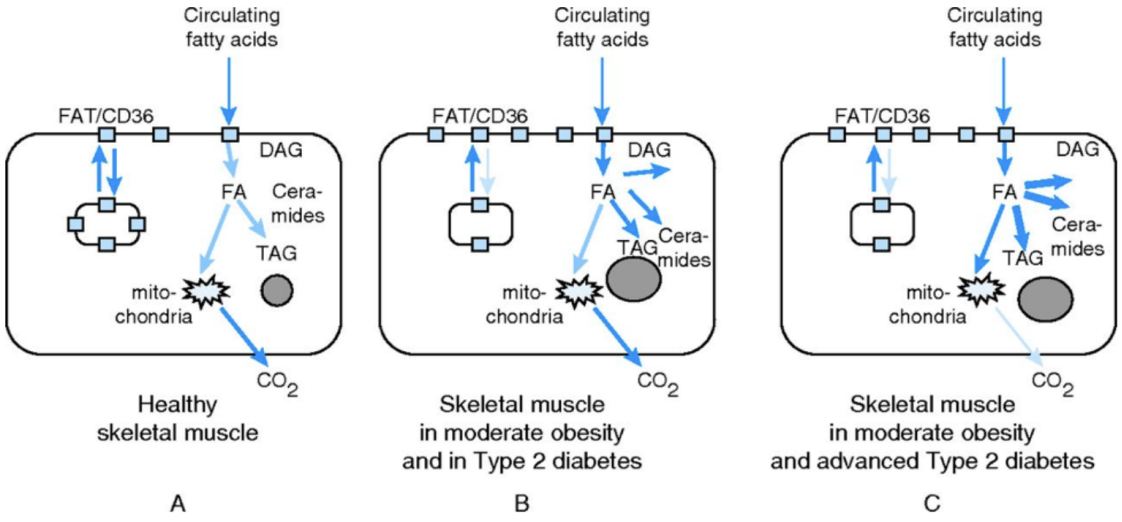
- **Increased** uptake of fatty acids into muscle tissue

- **Decreased** uptake of glucose into muscle tissue
- **Decreased** fatty acid oxidation in muscle tissue
- **Increased** carbohydrate oxidation in muscle tissue
- **Increased** fatty acid storage in muscle tissue.



Essentially, what this means is that when people have type 2 diabetes their body is in a state of producing more glucose than their muscle cells can take up, but their muscle cells are taking up higher amounts of fatty acids. Additionally, their muscle cells are utilizing high rates of glucose because of their reduced capacity to metabolize fatty acids, which leads to an increase in fat storage, making the insulin resistance problem even worse.





What Does This Mean For Me?

To summarize, diabetes results in a disordered metabolism that effectively changes how your body metabolizes carbohydrates and fatty acids and puts it in a state favoring fat storage and not fat oxidation. This shift does have some effects on how the body functions, especially during exercise. Specifically, individuals with diabetes actually utilize MORE carbohydrates for energy at lower levels of activity and LESS fatty acids for energy at lower levels of activity. For example, at ~40% of maximal effort, a lean person without diabetes gets ~60% of their energy from fatty acids and 40% from carbohydrates. Conversely, at the same intensity, a person with diabetes gets almost 100% of their energy from carbohydrates and almost no energy from fatty acids.

"Individuals with diabetes show different metabolic responses to exercise

Understanding how their body responds differently is critical for appropriate exercise programming."

What exactly does this mean for you as an individual if you have diabetes and still exercise (which you definitely should)? Well, essentially it means that your body's ability to perform high-intensity exercise for sustained periods is going to be less than someone without diabetes, and this is not due to lack of effort, but metabolically you will have slightly less capacity. This often means that higher intensity exercise will require shorter spurts of exercise and longer recovery periods between sets.

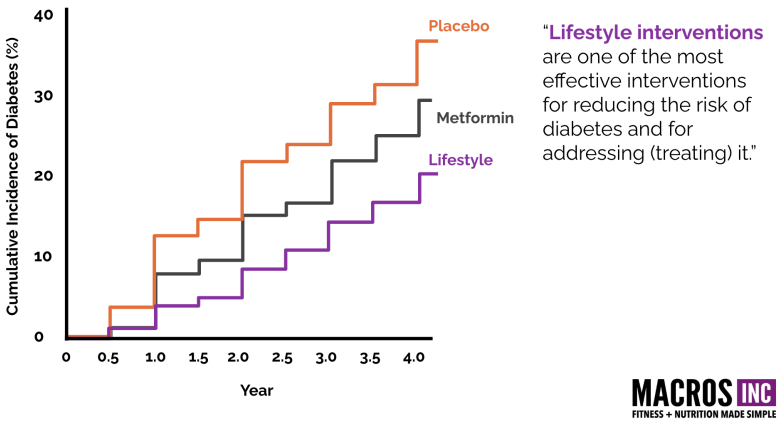
What Can We Do About Diabetes?

When we think about what actions we can take to help address, improve, or treat diabetes, there are three routes available:

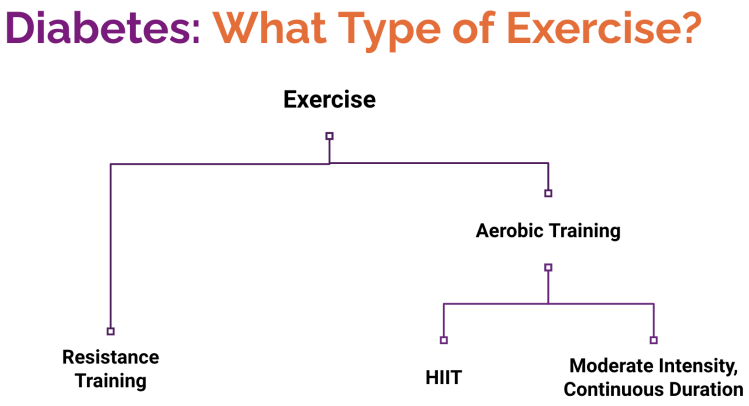
- Dietary modification
- Exercise and/or physical activity
- Medical interventions (often pharmaceutical or surgical).

This module will focus primarily on the two main lifestyle interventions (diet and exercise) and leave the medical interventions for a later date.

Lifestyle interventions, such as diet and exercise, is one of the most effective tools for preventing type 2 diabetes as well as improving symptoms and putting it into remission. In fact, the Diabetes Prevention Program, which was a very large study examining the effect of lifestyle intervention compared to standard frontline medical therapy (metformin), found that lifestyle interventions were actually far more effective than medication for preventing individuals with prediabetes from developing diabetes. Furthermore, recent studies have shown that among people with recently diagnosed type 2 diabetes, weight loss interventions that utilize diet and exercise can result in at least partial remission of type 2 diabetes in ~80% of individuals.

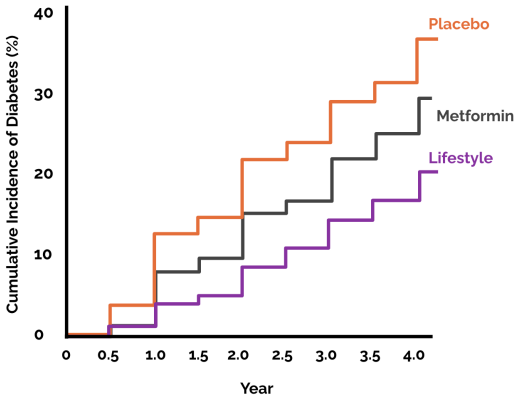


The next question would be, what type of exercise and how much is needed to help prevent and improve diabetes? First, let's discuss the two major categories of exercise: resistance training and aerobic training (aka cardio). Aerobic training can be broken down further into **h**igh **i**ntensity **i**nterval **t**raining (HIIT) and moderate intensity, continuous



duration training (what we often think of as cardio).

The most correct way to think about exercise among people with type 2 diabetes is that any form of exercise is beneficial and each type has slightly better effects on some outcomes than others. One is not necessarily better than the other, they just provide slightly different benefits. Each type of exercise should be considered based on their ability to improve different aspects of the symptomology and root cause of diabetes as well as what the client enjoys and is able to do consistently. Below are two tables that sum up the effects of each type of exercise.



"**Lifestyle interventions** are one of the most effective interventions for reducing the risk of diabetes and for addressing (treating) it."

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	Resistance Training	HIIT	MICD	Conclusion
Body Weight	Lowest Effect	Biggest Effect	Biggest Effect	HIIT or MICD Most Effective for Weight Loss
Glucose Control	Moderate Effect	Moderate Effect	Moderate Effect	Similar Results Across Exercise Type
Lean Body Mass	Largest Effect	Minimal Effect	Minimal Effect	Resistance Training is Most Effective for Lean Body Mass
Cardiovascular Risk	Moderate Effect	Moderate Effect	Moderate Effect	Similar Effects, Slight Edge to Both Aerobic Forms
VO2 Max	Minimal Effect	Moderate-to-High Effect	Moderate-to-High Effect	HIIT or MICD Most Effective for Improve Aerobic Capacity

	Aerobic Training	Resistance Training	Combined Exercise
Body Weight	Reduction in Body Weight	Minimal Reduction in Body Weight	Reduction in Body Weight
Glucose Control	Improves Glucose Control	Improves Glucose Control	Largest Improvement in Glucose Control
Fat Mass Reductions	Reductions in Visceral Fat	Reductions in Visceral Fat	Reductions in Visceral Fat
Strength Increases	Minimal Strength Increases	Modest to Robust Strength Increases	Modest to Robust Strength Increases

The differential effects of both cardiovascular based exercise and resistance exercise suggest that individuals should ideally engage in both, and that HIIT or moderate, steady state cardio are both very good, viable options for aerobic training. The exact exercise prescription should be based on the individual's total capacity, experience, and programmed around any specific limitations they may have.