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Diabetes Debunked: What You Need To Know

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DEBUNKING DIABETES:
WHAT YOU NEED TO KNOW

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Abstract

The goal of this Honors creative project is to encourage health literacy in populations who are curious about Type 2 Diabetes or have Type 2 Diabetes. From personal experience, I have seen noncompliance in diabetics and wondered why since it is a serious, progressive disease. After researching, I found that some diabetics do not understand the scope of their disease, especially since many of the dangerous complications that arise from Type 2 Diabetes do not present until later in the disease when it is too late. For my senior project, I decided to write an educational paper as a supplement to health education. It is a semi-comprehensive article about what Type 2 Diabetes really is, the physiological foundations, the treatment options, and tips for adherence. The idea is to boil complex terms into more practical language so that people who do not have backgrounds in biology or biochemistry could understand the content. The tone is meant to be more casual, as if one were having a conversation with them. Since Type 2 Diabetes can affect people as early as 30 years, I decided to also convert the paper into a podcast to reach the younger populations. Podcasts are a great, transportable way to access information, and they have risen in popularity over the past few years. I will be submitting both the “magazine” article and podcast mini-series script.

Keywords: Type 2 Diabetes, physiology, diet, exercise, medication

INTRODUCTION

You are not alone. There are more than 30 million people living in the United States that have diabetes, professionally diagnosed or not. Even if you're reading this just for fun or know someone with diabetes, I welcome you. The aim of this paper is to provide a deeper understanding about Type 2 Diabetes, addressing what it actually means and the most common treatment options. Often times, individuals with diabetes get minimal information about their condition. All you hear is something to do with high sugar, having to take all these medications, and then you can't eat cake. Tragic. While this piece is in no way a replacement for real medical treatment, I hope it finds you well.

WHAT IS TYPE 2 DIABETES?

Type 2 Diabetes (T2D) is a metabolic disorder of the pancreas, resulting in the dysfunction and inability of the body to break down and use sugar. This is a classic definition of T2D, and there's a lot to unpack.

First, "metabolic" pertains to the chemical processes of your body that it performs to stay alive. This includes the breakdown of the food you eat, the creation and storage of fat we all hate, and the usage of energy during exercise. The pancreas is one of the organs of your body that directly participates in metabolism. The pancreas is charged with many functions, however the one we will talk about is its ability to create insulin. Insulin is what they call a hormone, or a chemical that can travel all over the body, acting as a messenger. When insulin is released from the pancreas, it tells the rest of the body that there is sugar in the blood stream to be used. And voila! You have the energy to get on with your day. In T2D, two things can happen: not enough insulin is released from the pancreas to effectively inform the rest of the body about the rising

sugar levels, or the receptors that receive the insulin signals do not respond to its message. Either way, the sugar stays unused in your bloodstream.

Let me put this in an analogy: picture your mailman, your mail, and a mailbox. On a normal day, the mailman directly puts your mail into your mailbox, and you walk to your mailbox and pull out your mail. Simple. In T2D, let's say your mailman sprained his ankle on the job and couldn't deliver your mail, so now you have no idea that your grandma sent you $20 for your birthday. Another scenario would be that your mailman delivers your mail as normal, but you're out of town and thus, didn't pick up your mail. The mailman is your pancreas, the mail is insulin, and the mailbox represents the receptors on your cells. And of course, you are your cells.

Type 1 Diabetes is a little different than T2D. It's categorized as an autoimmune disease because your body thinks that the cells of your pancreas don't belong and tries to destroy them. In the mailman analogy, it would be as if the mailman permanently never came to work because he got arrested, and thus your mail never gets delivered. However, since T1D results in an increase of sugar in the blood, the symptoms and complications are similar to T2D. (Fisher et al, 2000)

It is important to note that diabetes is a progressive disease (Brunton, Tenzer-Iglesias & Unger, 2008)). This mean that once you get it, you can't be cured of it, and it only gets worse if it goes untreated. One study showed that function decreases by 4% annually after diagnosis (Lavernia, 2009). It's a scary idea, and one reason as to why it's so important for people to understand what T2D really means.

PHYSIOLOGICAL FOUNDATIONS OF TYPE 2 DIABETES

Since metabolism is so central to the functioning of the body, Type 2 Diabetes has wide ranging effects and complications. These complications include cardiovascular diseases, neuropathy, nephropathy, and retinopathy. Many of these probably sound familiar. In this section, I will briefly go over the important organ systems that T2D affects and hopefully we will be able to see the connections between T2D and its' complications. We will also see how medication works to fight T2D.

Before we get into it, I want to highlight the theme of physiological balance. As we understand the organ systems of the body, we find how tightly regulated the body keeps itself to work. Keep this in mind as we see how T2D can really throw things for a loop.

Endocrine System

The pancreas is one of the central organs to the Endocrine System. The Endocrine system is responsible for carrying chemical messengers, like insulin, throughout the body. These chemical messengers, called hormones, allow for parts of your body to communicate with each other. In the instance of insulin, insulin informs the cells of your body that there is sugar in the blood stream to use. This process is important because sugar, or glucose, is the principle source of energy for your body. In a normal, healthy body, insulin can be released from the pancreas in two ways: basal insulin and bolus or prandial insulin (Levine, 2008). Basal insulin is insulin that is continuously released from the pancreas in small amounts. This keeps your blood sugar levels in check when you're not eating. In order to consistently supply your body with energy during times of fasting, your liver will break down glucose stores and release it into your bloodstream. This process is called glycogenolysis. Basal insulin ensures that your starving body is utilizing

this sugar and not allowing it to build up in your system. When you do finally eat, your digestive system sends an entire load of sugar into your blood. In order to quickly uptake all this sugar, your pancreas releases bolus insulin to keep up. Of course, the pancreas can only release so much insulin, and your cells can only uptake so much sugar. Whatever is left is converted into storage by your liver.

In T2D, either your pancreas is doing a poor job releasing either type of insulin, or the cells of your body just aren't responsive to the signals. Either way, the excess sugar is left in the blood, leading to the condition called hyperglycemia. This can be problematic for many reasons. For one, the cells of your body, including your brain aren't getting the energy they need to function, resulting in feelings of fatigue or listlessness. For two, the physical amount of sugar particles in the blood can be damaging to the cardiovascular system. This can lead to hypertension, reduced ability to heal and reduced immunity, and other cardiovascular diseases. Three, it affects how your body can filter its blood. This damages your kidneys and causes you to have to urinate more and become prone to urinary tract infections. And these are only some of the complications and side effects.

Another important hormone that your pancreas makes is glucagon. Glucagon is released by a different type of cell in the pancreas than insulin. Its job is to signal your body that your blood glucose levels are low. Ergo, it will stimulate your liver to undergo glycogenolysis, promote gluconeogenesis, slow down the use of glucose by your body, and breakdown of fat stores. Gluconeogenesis is the synthesis of glucose from other sources in your body, like proteins.

Renal System

To understand how your kidneys and urinary system work, we need to understand a bit more about a chemistry principle called tonicity. Tonicity relates two concentrations of two different solutions to each other. The most common type of solution is when a solid is mixed and dissolved evenly into a liquid. Your blood is a solution. It has tons of particles floating about other than sugar: there are proteins, salts, hormones, etc. These all contribute to the concentration of your blood. Tonicity can be applied when your blood changes concentration, or when it is compared to the concentration of other solutions in your body. There are three ways to compare two different solutions: hypotonic, isotonic, and hypertonic. When referencing one solution, it can be less concentrated than the other, hypotonic, of equal concentration, isotonic, or of greater concentration, hypertonic, to the other. For example, the sugar concentration of your blood, called the blood glucose level, prior to eating a huge meal is hypotonic to the blood glucose level after you eat a large meal. Remember this concept as we talk about the kidneys and how urine is made.

The principle function of your kidney is to filter your blood so much that it is then called urine. The portion of your kidney that does this filtration and "cleansing" of the blood is called the nephron. Blood enters your kidneys through arteries that progressively get smaller and smaller in diameter. This causes the pressure in these blood vessels to increase a lot. This dramatic increase of pressure actually squeezes the blood out of the blood vessel and into another space of the nephron called the lumen. The proteins, sugars, and salts get filtered out of the blood as best as possible, so that the solution remaining in the lumen of the nephron is mostly water with a few other chemicals and compounds. We will call this liquid pre-urine. It travels through the nephron, alternatively being exposed to hypertonic and isotonic areas so that the cleanest,

least concentrated solution is created by the end. Eventually, it becomes urine and is sent to the urinary bladder for storage until you get rid of it.

In diabetic individuals with hyperglycemia, the blood that enters the kidney is extremely hypertonic relative to the cells of the kidney. As it gets squeezed into the lumen, the amount of sugar that passes through is a great deal more than usual. There are ways for the lumen to transport sugar out and back into the blood stream, but in diabetic patients, there is just too much. In the end, the pre-urine is more hypertonic than normal. When it travels through the segments of the nephron called the Loop of Henle and in the collecting duct, the nephron tries to lower the concentration by adding more water into the pre-urine, increasing the volume of urine excreted. This sort of "return-to-balance" is the reason why diabetics have to urinate a lot and are thirstier. Their kidney is getting rid of a lot of water just to try to lower the concentration of the urine. Moreover, the excessive amount of sugar in the urine can lead to greater instances of urinary tract infections. Urinary tract infections are when bacteria called *Escherichia coli* invade portions of the urinary tract, including your bladder, ureters, and kidney. *E. coli* loves to feed on sugar, so when you have a lot of sugar in your usually-sterile-urine, it creates a great opportunity for them to make a home.

One of the systems that tries to restore balance in the kidney and circulatory system is the renin-angiotensin system. As we have already seen, the cardiovascular and renal systems are closely connected. The renin-angiotensin system tries to ensure that the blood and the pre-urine in the lumen in the kidney are the correct tonicities. Abnormally increased blood sugar, like in T2D, can overwhelm this system and lead to kidney dysfunction. We saw how the nephron responds to increased sugar concentration. The renin-angiotensin system also acts on the cardiovascular system by trying to retain solutes and water for the blood. This results in

hypertension, or increased blood pressure. Remember, that increased blood pressure is one mechanism to how blood is filtered in the nephron. When the blood pressure increases even more, it can damage the kidney. Overtime, sustained hyperglycemia can cause autoregulation to fail, and result in damage called nephropathy (Dobesh, 2006). Nephropathy is a complication developed later in the progression of the T2D, but still quite serious. It is detected by small amounts of blood in the urine at least twice in a six-month period.

Cardiovascular System

Your cardiovascular system is basically a highway system that various chemicals and organs use to communicate with each other, as well as supply organs with nutrients. As we have seen, hormones like insulin use your blood vessels to move through your body, while the kidney uses blood to dispose of waste and create urine. You can think about dividing the cardiovascular system into the heart and the blood vessels. From this division, you get two different circulations that blood passes through, but they are essentially all along one path. Let's first trace how blood travels through the body. First, it must be understood that blood moves in only one direction, and the entire circulation of the body is more like a freaky circle. There is no "beginning" and "end" and there are tons of branching. Now that being said, let's start in the heart. Quick anatomy lesson: there are two atriums, two ventricles, two atrioventricular valves (or doorways) and two semilunar valves (also doorways). Conceptually, you can picture the heart as a square with a T-crossed through it. The two upper boxes are the right and left atriums, and the bottom two boxes are the right and left ventricles. Blood enters the heart via the Vena Cava into the right atrium. It then passes through the tricuspid valve (doorway) into the right ventricle. From the right ventricle, it passes through the pulmonary valve (doorway) and goes into the pulmonary artery

leading into the lungs where it becomes oxygenated. From the lungs, it goes into the left pulmonary veins, into the left atrium. From the left atrium, it passes through the mitral value (another doorway) into the left ventricle. From the left ventricle, it flows into the aorta via the aortic valve and to the rest of the body. Both the aorta and the vena cava divide into smaller blood vessels that flow in different directions, so that blood can reach all parts of the body. When blood moves throughout the heart and lungs, it's called pulmonary circulation. As it leaves the heart via the aorta, it enters systemic circulation. It will then re-enter pulmonary circulation when it flows into the right atrium.

Systemic circulation (and parts of pulmonary as we saw) is divided into veins and arteries. For systemic circulation, veins take de-oxygenated blood from the organs back to the heart and lungs to be oxygenated. Arteries take oxygenated blood from the heart and lungs to the organs to supply them with oxygen. As arteries near a specific destination, they divide, and the diameter of the blood vessels progressively get smaller. These are called arterioles. As they become smaller and further branched, they become capillaries. Capillaries are the blood vessels that make contact with the functional portions of organs and where most of nutrient and chemical (including oxygen) exchange occurs. As capillaries exit organs, they become venules, or small veins. They then become veins and then the vena cava as they near the heart. It is important to note that while blood flow is unidirectional, the branching nature of the cardiovascular system allows for organs to be supplied by different blood vessels at the same time. Ergo, one single blood cell does not trace itself through every single organ of the body, but rather through one passageway where it deposits the nutrients and oxygen in a specific sequence of organs then meets up with the rest of the blood before entering the heart.

As blood passes through the blood vessels, it exerts a force on the walls of said blood vessels. This force is measured as blood pressure and can be an indicator of how hard your heart is working to push blood through the vessels. When measuring blood pressure, there are always two numbers in fraction form, the top one being greater than the bottom one. The top number is your systolic blood pressure, and the bottom number is your diastolic blood pressure. The words "systolic" and "diastolic" refer to the alternating contracting and relaxing of your heart. "Systolic" refers to when either your atriums or ventricles are contracting. "Diastolic" refers to when either your atriums or ventricles are relaxing. Your heart doesn't contract all at once, rather your atriums contract together, pushing blood into the ventricles, which are relaxed. After they stop contracting, the tricuspid and mitral valves slam shut, the aortic and pulmonary valves open, and then your ventricles contract, forcing the blood into the lungs and the rest of circulation. The controlled closing and opening of valves and contracting and relaxing of the chambers ensure that unidirectional flow that we talked about. How fast this happens is often based on the needs of the body. This brings us back to blood pressure.

Blood pressure is dependent on how strongly the heart is pumping blood (cardiac output), the constriction of blood vessels in systemic circulation, the volume of the blood, and how thick the blood is. As blood pressure increases, the heart has to work harder to push all the blood through the body. Diseases like T2D can increase blood pressure, creating more work for the heart. This effect is worsened by the fact that due to poor nutrition; diabetics have plaque build-up in their blood vessels, which increase the constriction of the blood vessels. Overtime, the mechanisms that control blood clotting and blood pressure become destabilized (Addai-Mensah et al, 2019). These reasons are why cardiovascular diseases are major complications to T2D. In fact, cardiovascular disease is the leading cause of death for those with diabetes (Dobesh, 2006).

Cardiovascular complications are split into “microvascular” and “macrovascular”. Both bad. Macrovascular complications include coronary artery diseases, hypertension, congestive heart failure, arrythmias, strokes, and heart attacks. Microvascular complications include neuropathy, retinopathy, and nephropathy (Brunton, Tenzer-Iglesias & Unger, 2008). If you had not guessed it already, macrovascular complications have to do with large arteries and veins, and your heart, while microvascular complications deal with small arterioles, capillaries, and venules. Arrythmias are when your heart doesn’t pump blood correctly. It can include tachycardia, where your heart pumps blood faster than normal, bradycardia, which is slower than normal, or dysrhythmias, where the alternating contracting and relaxing of your heart chambers is all out of order. Strokes and heart attacks are when your brain or heart don’t get the oxygen and nutrients, they require due to blockages in the blood vessels.

Additionally, with the decreased efficiency of circulation in diabetics, they are known to heal more slowly than other individuals. Normally, when one gets injured, the pro-inflammatory molecules, nutrients, and clotting factors that aid in healing arrive at the site via the circulatory system. When diabetics get injured, all the molecules that help with healing are slower to arrive. The same principle applies to diabetics weakened immune systems. The cells and molecules that aid in the immune response are slow to arrive at the site of infections, allowing the bacteria and/or virus to spread.

Nervous System

Like the cardiovascular system, the nervous system treks through your entire body, carrying with its information that allows for long distance communication. The nervous system consists of the brain, spinal cord, and all the neurons that branch from these two structures. The

brain and the spinal cord are considered the “Central Nervous system (CNS)” while everything else is the “Peripheral Nervous System (PNS).” These two divisions are interconnected and work together to control behavior and body processes so that you can respond to your environment and the needs of your body. The brain and spinal cord are where information is integrated, processed, and stored. The PNS contains the neurons that control your muscles, glands, heart, and gut, among other things. They send environmental information to the brain via the spinal cord. Once the brain integrates all this information, it will send commands out to your muscles and glands to respond. The PNS also innervates organs like the heart and lungs that function without your conscious awareness of it.

Like any other organ system, the nervous system is made of cells. The cells of the nervous system are called neurons and neuroglia. Neurons transfer, integrate, and receive information, while neuroglia structurally and nutritionally support the neurons. Neurons are responsible for the five senses; there are specialized neurons in the skin, in your eye and nose, on your tongue, and in your ears that perceive what’s going on around your body, and then they transfer it to the brain. There are also neurons in the body that perceive what’s going in in your body, like the sense of where one is, balance, and relative body positions. Damage to these nerves can result in some major literal and metaphorical blind spots. Often times, one hears about retinopathy and neuropathy as serious complications of T2D. In retinopathy, the sensory cells for sight located in the retina of the eye are seriously damaged. In diabetics, this is caused by increased blood pressure. Neuropathy is characterized by numbness or weakness in the extremities of the body, like hands and feet. Similar to retinopathy, the prolonged, elevated blood pressure damage the sensory neurons in these areas.

Digestive System

The Digestive system is central to the utilization of nutrients obtained from food. Without proper breakdown and absorption of carbohydrates, proteins, fats, cholesterol, and vitamins and minerals, we would die. I will talk a lot about the three of the four macromolecules in the nutrition label section under Treatment. In this section, I will overview how the body breaks down and absorbs carbohydrates, lipids, and proteins.

The carbohydrates that are most relevant to nutrition are sugars. Sugars have three levels of structure: polysaccharides, oligosaccharides/disaccharides, and monosaccharides. Monosaccharides are single sugar molecules, like glucose. Monosaccharides are the best form of sugar for the body to use. Oligosaccharides and disaccharides are when two or more monosaccharides bind together. Polysaccharides are when more than 30 monosaccharides bind together. Usually, we eat sugars in the form of polysaccharides like starch and cellulose in plants. Digestion starts in the mouth, specifically the teeth, saliva, and tongue. The mechanical tearing apart of food and minimal chemical breakdown of sugars by salivary amylase (an enzyme) start off the process. Nothing happens in the stomach. Digestion resumes in the small intestine where the polysaccharides and oligosaccharides meet pancreatic amylase and brush border enzymes. These enzymes break down the poly- and oligosaccharides into disaccharides and monosaccharides. The monosaccharides move from the intestines into the neighboring blood vessels via specialized transporters in the wall of your small intestine.

Proteins are made up of molecules called amino acids. Protein digestion starts in the stomach with the enzyme pepsin. Pepsin breaks down proteins into smaller amino-acid chains. As the short-chain amino acids enter the small intestine, they contact enzymes like trypsin, elastase, and chymotrypsin that breaks them down into even smaller peptide chains. Finally,

peptidases like carboxypeptidase, dipeptidase, and aminopeptidase break down the peptide chains into single amino acid molecules. These amino acids are absorbed from the small intestine into the circulatory system.

Lipids are different than the other two macromolecules because they aren't just long chains of building blocks. The breakdown of lipids is more like separating them out so that they can be absorbed and transported in smaller units. There are triglycerides and cholesterol. Triglycerides (TAGs) are three fatty acids attached to a glycerol molecule. Triglycerides are what we call fat. "Digestion" begins in the mouth with lingual lipase, however very minimally. The majority of digestion occurs in the small intestine where it meets pancreatic lipase and bile acids. The pancreatic lipase takes off fatty acids from the TAGs, making them into monoglycerides and glycerides, while bile acids emulsify large lipid particles, like cholesterol. Emulsification means breaking down large fat globules into smaller droplets. This is not breaking any bonds in TAGs or cholesterol, just separating them out. This allows for pancreatic lipase to act more efficiently, since their target is smaller. The monoglycerides, free fatty acids, and cholesterol are absorbed by the small intestine and packaged into chylomicrons. Chylomicrons are particles made of lipids and proteins. The proteins designate where the chylomicrons move to. They first enter nearby lymphatic vessels, and from there into circulation.

CAUSES AND RISK FACTORS OF TYPE 2 DIABETES

Despite its vast reach, the actual cause of Type 2 Diabetes (T2D) is unknown. Nevertheless, research has compiled a few risk factors that can contribute to the development of the disease. Many of these risk factors are also "comorbidities", which means that they are diseases by themselves, but can occur with T2D. The risk factors include overweightness and obesity, lack of exercise, smoking, poor diet, medications that affect sugar metabolism, family history, race, age, hypertension and other cardiovascular diseases, being male (except women when pregnant), and cultural factors (Brunton, Tenzer-Iglesias, & Unger, 2008; Kraege et al, 2019; Lavernia, 2009; Levine, 2008).

Biological Risk Factors

Overweightness and obesity are in part, symptoms of poor diet and lack of exercise. Your body only really needs a certain number of calories a day to carry out regular functioning, and maybe a little more if you exercise. Of course, there's a huge difference between eating 1500 calories worth of fat and carbohydrates and 1500 calories balanced between proteins, fats, and carbohydrates. With poor eating, many people consume at least their recommended amount and more. Research has shown that as one eats more and more, their body adjusts itself and becomes tolerant to the pleasure that food naturally gives us. It's actually very similar to the mechanism of tolerance in drug addiction. Eating more also makes the body more tolerant to insulin signaling. Ergo, overtime, overweight and obese individuals just eat more and more, but their bodies are not utilizing the excess carbohydrates (Lavernia, 2009). As one consumes more food than the body needs, it converts it to lipid or glycogen and stores it. We commonly see these fat stores in our bellies, arms, and thighs. However, fat can also be stored in and around our organs, which

can be dangerous. Glycogen is found in our liver and muscles. Lack of exercise worsens the effects of poor eating habits. Without physical activity to utilize all that excess fat and sugar, the body stores it.

Hypertension is a common comorbidity of T2D, mostly due to its contributions to other cardiovascular diseases (Dobesh, 2006). Moreover, both hypertension and T2D are partly caused by poor diet and exercise.

Genetics and family history also play a huge role in developing T2D. While there has not been a specific gene found that is associated w/ T2D, twin, family, and community studies like the Framingham study have demonstrated large genetic associations (Meigs, Cupples, & Wilson, 2000). Moreover, it is possible that the risk is additive; this means that your risk of developing T2D is at least twice more if both parents have it than just one (Meigs, Cupples, & Wilson, 2000).

Social Risk Factors

Social risk factors include health literacy, ethnicity and culture (Abdulla et al, 2019; Rivera-Adams, 2003). Health literacy is the ability to understand medical information, and then be able to apply what you know to how you monitor your health (Abdulla et al, 2019). It's extremely important for individuals like yourself to be literate, and unfortunately, health literacy is not where it needs to be globally. Improving health literacy has been shown to improve diabetic outcomes and increase self-care behaviors (Abdulla et al, 2019; Elnaem, Nik Mohamed, & Huri, 2019). This is really important in slowing or stopping the progression of the disease and preventing others from developing it. It seems one of the best way to encourage health literacy is the "teach back" method, where physicians and health practitioners have patients repeat what

they learned as a way to minimize misunderstanding and encourage comprehension (Abdulla et al, 2019).

Culture and Ethnicity are also huge contributing factors to developing T2D. For example, Latinx populations are 2x more likely to develop T2D than non-Latinx. A part of this has to do with lack of access to health care services, poor experiences with health professionals, a community mentality, cuisine, and external locus of control (Rivera Adams, 2003). “Community mentality” is the general concept that Latinx populations think of themselves as a whole, rather than individuals. They are very group-oriented and that mentality bleeds into how they think about their health. Examples would include putting the health of the family over one’s own. Additionally, lack of familial connectedness and organization are associated with lesser disease management (Fisher et al, 2000). Some studies have demonstrated an external locus of control, where Latinx individuals have claimed that the development of their disease was related to God, either as a test of faith, or as a punishment (River Adams, 2003). African Americans also are two times more likely to develop T2D than European Americans. While there is no specific gene, African Americans tended to be more insulin resistant, have higher body mass indices, lower education levels and income, and greater African ancestry (Cheng et al, 2012).

TREATMENT

Treatment of Type 2 diabetes is where it gets really interesting. It is more standard to start off conservatively, with changes in diet and exercise, and then progress towards using medication and insulin. As we have seen, T2D is closely related to diet and exercise, and it makes sense to first try to rebalance the body via diet and exercise in the beginning before using medication.

To start, when can a physician *officially* diagnose T2D? Usually, physicians will first observe trends in fasting glucose levels before further testing. The guideline for this is usually fasting glucose levels after 10-14 hours of fasting to be greater than 100 mg/dL. If one does have this, physicians can either follow-up with hemoglobin A1c level testing, fasting prandial glucose levels, random plasma glucose levels, and 2-hour plasma glucose levels after taking 75 grams of oral glucose (Brunton, Tenzer-Iglesias, & Unger, 2008). Hemoglobin A1c (A1c) levels below 5.7% are considered normal. If an individual has A1c levels between 5.7% and 6.4%, they are considered to be in "prediabetes". A1c levels over 6.5% on two separate occasions are considered to be diabetes. Hemoglobin A1c is red blood cell protein that can become glycated by the sugar floating around in the blood. "Glycated" just means that the sugar attaches to the protein as it moves through the blood. This is normal and happens to everybody.

After diagnosing, it's standard for primary care physicians to regularly check up on their patients every 3 or 6 months, depending on how controlled an individual is. Usually after official diagnosis, A1c levels are routinely used to check this. Tests are conducted every 3 or 6 months because red blood cells live for an average of 3 months. When one is controlled, check-ups can be less often, resulting in 6-month checkups. When one is uncontrolled, check-ups have to be more frequent, resulting in 3-month checkups. "Controlled" diabetes is considered to be A1c

levels below 7%, while “uncontrolled” diabetes is when the A1c is above 7%. These are the standards set by the American Diabetes Association (ADA). Other organizations like the American Association of Clinical Endocrinologists and the European Association for the Study of Diabetes have stricter regulations, setting the bar to 6.5%. Studies have shown these tighter measures may be more realistic for those without comorbidities, and that too strict of measures have resulted in death (Brunton, Tenzer-Iglesias, & Unger, 2008; Largay, 2009).

It is important to regularly test A1c levels, as it has been closely associated with lower risk of microvascular complications, cardiovascular events, and reduced risk for death (Largay, 2009; Selvin et al, 2010).

The Nutrition Label

It is extremely important for everybody, not just diabetics, to eat healthy. However, I fear there is a lot of misconception about what that means and what you “should” and “should not” eat. I do want to preface that exercise is still important for weight loss, weight management, and overall wellbeing. A healthy diet can only do so much. Moreover, the magic word is MODERATION. Even healthy foods can become *unhealthy* if eaten too much.

We have already seen how the digestive system breaks down carbohydrates, lipids, and proteins, but I want to explore a bit more into how the body utilizes these macronutrients.

First concept. Carbohydrates are not bad for you. Carbohydrates include what we call in everyday terms “sugar” and also a group of molecules called glycoconjugates. There are three levels of sugar organization: monosaccharides, disaccharides, and polysaccharides. A monosaccharide is just one sugar molecule floating about. Glucose is the most common and well-known monosaccharide. It’s the body’s primary choice of energy. There are other types of

monosaccharides that you've probably heard before. There are fructose, galactose, ribose and deoxyribose. You've probably heard of fructose from "high fructose corn syrup", which is known to be bad for you. It is because it concentrates an exceptional amount of unneeded carbohydrates in one little tablespoon and is often used to sweeten packaged foods. Galactose is found in milk and sucrose (a more complex sugar). Deoxyribose and ribose are part of your genetic material. When two monosaccharides join, they form disaccharides. Common disaccharides are lactose and sucrose. Lactose is the sugar found in milk made of galactose and glucose, and sucrose can be found in many foods, made of glucose and fructose. As more monosaccharides bind together, either in a single chain or in branching patterns, they form polysaccharides. Polysaccharides exist in the body as storage units for energy when you are not eating. They are called glycogen. You can also eat polysaccharides. A common one is starch found in foods like potatoes. Starch can have an infinite amount of glucose molecules together and can vary from food to food. The reason for why potatoes are often looked down upon for eating is for its compact sugar reserve. A raw, medium sized Russet potato with its skin on gives you 33 grams of starch and can still have you wanting to eat more. Fiber is also a well-known carbohydrate. Fiber actually offers no nutritional value. The bonds in fiber cannot be broken down by the body since it lacks the appropriate enzymes. Instead, fiber helps digestion move smoothly. It bulks up and softens stool so that it is easier to pass.

Like the other macromolecules to be discussed, carbohydrates have an energy equivalent. In the United States, we measure our food in calories. You often hear a standard intake of calories is 2000. This often just accounts for energy required for basic body functioning and a predominantly sedentary lifestyle, this changes per person, of course. One gram of glucose contributes about 4 calories. Ergo, the 33 grams of starch from your medium sized Russet potato

(which can be considered approximately 33 grams of glucose) just contributed 132 calories to your day.

The bottom line, however, is that you should not “cut out carbs”. It is completely unrealistic. Carbohydrates exist abundantly in foods that are not sweet, like beans. Moreover, it’s required by the body to function. What we should focus on is avoiding foods high in carbohydrates that offer no other nutritional value. Foods such as candy derive the majority of their calories from sugar. “Natural” sources of sugar like fruit are still healthy to eat because they also contain micronutrients like calcium, phosphorus, potassium, and vitamin C. Calcium is used by your bones and muscles, phosphorus used to cell membranes, bones, DNA, etc. Vitamin C is used as an antioxidant, which can prevent damage to DNA, joint, lungs, and blood vessels (Halliwell & Gutteridge, 1984). Of course, you shouldn’t eat *only* fruit, because your body also needs protein and fat to function.

Glycoconjugates are when sugars are bound to other macromolecule types like protein and/or lipids. These molecules are really important for cell communication, immunity, and joint health. The receptor that insulin binds to is a type of glycoconjugate; it’s a glycolipid.

Fat is another controversial topic it seems. Like carbohydrates, there are different classes of “fat”. To begin, “fat” is not “cholesterol”, but they are both lipids. Lipids is the umbrella term for a class of macromolecules, just as carbohydrates are for sugars and glycoconjugates. Lipids include triglycerides (this is what “fat” is), phospholipids, and cholesterol. Triglycerides are three fatty acid molecules bound to a glycerol molecule. Fatty acid molecules are abundant in energy and are the secondary source of energy for the body. They come in many forms; two important divisions are saturated and unsaturated. Saturated fatty acids have higher energy content and mainly found in foods that come from animals. Unsaturated fatty acids have

relatively lower energy content and are found in plant-derived products. Unsaturated fatty acids are commonly associated with being slightly more healthy than saturated fatty acids. They are also known to aid in anti-inflammatory responses (Satija et al, 2015). The commonly known omega-3 and omega-6 fatty acids are a type of unsaturated fatty acid. Fats are then classified by their saturated and/or unsaturated fatty acids. Ultimately, TAGs are used as transportable energy units. When there is excess sugar in the bloodstream, the body will convert this sugar into TAGs and then ship them to adipocytes, which then store it. Adipocytes, or fat cells, expand according to amount of TAGs it's storing. Adipocytes are found in the connective tissue of the skin (which contributes to one's cookie pouch) and around organs (which can be dangerous). When one is expending energy without using the immediate source of sugar in the blood stream (e.g. during exercise or during fasting), the body will take TAGs from your fat cells to quickly break down and use for energy. This break down of stored TAGs is ketogenesis. Lipoproteins are the structures that carry TAGs and cholesterol throughout the body. More on this later. One gram of TAGs equates to 9 calories. Thus, as you can see, fats have more energy potential than glucose, however, they are still not the preferred source. This is why it's so hard to lose weight; the process of breaking down fat is a lot more difficult than storing it. Moreover, your body will burn through glycogen stores before even attempting to touch your adipocytes.

Phospholipids are the second type of lipid. It is used in cell membranes, which is pretty important since you replenish your cells all the time, especially after injury, and you need cell membranes for that.

Cholesterol is where it gets complicated again. I want to first stress that cholesterol IS required by your body to function. Like all things, too much cholesterol is bad for you, but we can get into that later. Cholesterol is the structural basis for many hormones and

neurotransmitters in your body, an example being testosterone and estrogen. It is also present in cell membranes. Often times, you hear that there are two types of cholesterol: “healthy” HDL and “unhealthy” LDL. This is a huge misconception. HDL and LDL are NOT types of cholesterol, they are CARRIERS of cholesterol. Similar to how carbohydrates can bind to lipids or proteins, HDL and LDL are lipids and proteins bound together. HDL stands for “high density lipoprotein” and LDL stands for “low density lipoprotein”. The proteins that the TAGs, cholesterol, and phospholipids bind to tell the structure where to go in the body. The connotation “healthy” and “unhealthy” comes from the route they are designed for in your body. When you eat lipids, whether it be fats or cholesterol, it gets packaged into ultra-low-density-lipoproteins, also called chylomicrons. Chylomicrons transport these lipids to your liver for either break down as energy (a process called beta-oxidation) or for storage. During starvation mode, your liver can import TAGs from your muscles and/or adipocytes to undergo beta oxidation. The lipoproteins that transport the TAGs to the liver are your HDL lipoproteins. They’re “healthy” because they’re enabling your body to utilize excess fat. When your liver needs to send lipids to your muscles and adipocytes, they utilize very-low-density-lipoproteins (VLDL) and LDL to carry them. These lipoproteins are “unhealthy” because they are storing lipids, but also the surface of these lipoproteins actually can adhere to the walls of your blood vessels, creating plaques. These plaques contribute to cardiovascular diseases such as atherosclerosis, hypertension, strokes, and heart attacks. The rate at which these plaques grow is mostly based on diet and genetics. Often times, if a diabetic is also diagnosed with hyperlipidemia or hypercholesteremia, there is a point that they get a coronary artery scan to check if their major arteries are blocked in any way. If so, they are often prescribed statins. Statins inhibit cholesterol synthesis (your body will synthesize cholesterol to make hormones and if your dietary needs are not met) and can stabilize plaque

growth. Ultimately, these plaque growths are another reason why microvascular and macrovascular complications for T2D manifest. The ultimate take away message is cholesterol is cholesterol and you should always monitor how much of it you eat.

Protein is also very important to your diet. Proteins are another macromolecule that your body requires to function. Proteins themselves are made of amino acids. There are 20 total amino acids, 11 of them your body can make itself, and 9 of them you have to eat in your diet since they're still used by your body (there is some discrepancy in whether there are 20 or 21 naturally occurring amino acids or if there are 10 essential and 10 nonessential. The main take away is that you have to eat proteins to obtain the amino acids you cannot make) (Aliu, Kanungo, & Arnold, 2018). The ones your body cannot synthesize itself are called the essential amino acids. THEREFORE, if you buy any "health" product that promises to supply you more than 10 amino acids, you are probably wasting your money. Amino acids are integral to body functioning because they make proteins, which have a whole multitude of functions. Proteins are the workers of your body; they carry out the processes of metabolism and intercellular communication, immunity, muscle structure, and very rarely, they can be used as energy sources (Aliu, Kanungo, Arnold, 2018). Your body cannot store amino acids; excess amino acids get broken down by a myriad of processes. The structures that make up the amino acids can be recycled either as energy or used for other structures. Amino acid catabolism results in the formation of ammonia, a substance that is very toxic to your body. The urea cycle takes this ammonia and converts it to urea, which is disposed of in urine and through exhalation. However, an over-excess of amino acid can overwhelm the urea cycle, exposing the body to too much ammonia. It is important to note that the body can actually handle a great deal amount of ammonia toxicity before serious health problems arise (Ryer-Powder, 1990).

One gram of protein offers 4 calories. The source of protein is heavily debated between vegans, vegetarians, and rest of the population. In the next section, I will weigh the pros and cons of specific diets and you can decide for yourself which one you want.

Dieting

Nutrition therapy is using changes in diet to treat disease (Evert et al, 2019). I do want to note that while we really only discussed the three macromolecules (nucleic acids don't really contribute to diet, however genes are a risk factor for developing T2D), there are a plethora of micronutrients like vitamins and minerals that are important to your diet. However, we will mostly be focusing on carbohydrates, proteins, and lipids. Additionally, diet recommendations should be adapted to each individual person. While I provide a general framework of diet recommendations, one should always consult their physicians and nutritionists for more information.

The general formatting of this section will first be overall recommendations for carbohydrate, lipid, and protein intake, followed by information and studies performed about common diets.

<u>Recommendations</u>

According to the Nutrition Consensus published by the ADA in 2019, the recommended amount of carbohydrates for an adult (aged 19 and above) without diabetes is 130 grams/day. They calculated this number from the amount of energy your brain and body need to function daily. Diabetics are recommended to make fiber at least 14 grams of those carbohydrates. This fiber should come from healthful sources like nonstarchy vegetables, fruits, and grains. Studies have shown that this increase to 14 grams has moderately reduced A1c levels (Evert et al, 2019)

Lipid recommendations for those in prediabetes include increasing the amount of polyunsaturated fat and fatty acids, including omega-3-faty acids (Evert et al, 2019). Consuming these types of fats, besides saturated and trans fats, have indicated lowered risk of developing T2D and lowered triglyceride levels in the blood. In one study, increasing eicosapentaenoic acid (EPA) to 1800 mg/day resulted in improved postprandial (which means right after consuming food) TAGs, blood glucose levels, and endothelial functioning (type of tissue that supports a variety of organs in your body). EPA is an omega-3-fatty acid derived from many types of fish. Often times, people consume fish oil supplements to increase their unsaturated fatty acid levels without realizing that they are also consuming saturated fatty acids, which have more negative effects (Bajpai & Bajpai, 1993. In another study, adding 4 g of icosapent ethyl with statin therapy resulted in lower CVD complications, but slightly higher rates of hospitalization for atrial fibrillation and bleeding (Evert et al, 2019) In other words, be careful in choosing which foods to obtain "healthy" fats.

For proteins, the ADA recommends protein to contain 30% of your total energy intake. This resulted in greater weight loss and better A1c, with varied results in fasting glucose, lipids, and blood pressure (Evert et al, 2019).

I want to note, diabetic or not, dieting can be dangerous if done incorrectly. Always consult a physician or dietitian before pursuing one. Additionally, I will not go into the types of fasting.

Diets

The USDA promotes a general diet for Americans that emphasizes vegetables, whole fruits and grains, minimal dairy and protein from multiple sources. Other common diets in the US are vegetarianism and veganism, low fat diet, very low-fat diet, low carbohydrate diet, very low carbohydrate diet, Mediterranean diet, DASH diet, and the Paleo diet.

Vegetarianism and veganism emphasize eating only plant-derived foods, excluding "flesh" foods. Veganism goes a little further and excludes all animal-derived products like eggs. Studies have shown that these types of diets reduce the risk of diabetes by 20% and A1c (Evert et al, 2019; Satija et al, 2015). They are also related to weight loss and lowering LDL (Evert et al, 2019). Often times, people try vegetarianism and veganism to lose weight, but somehow can't seem to reach their goal weight. This is where cognizant dieting is important. There are basically two types of plant-based dieting: those w/ healthful foods and those without it. Healthful plant-based diets include whole grains, fruit, vegetables and nuts; they're rich in dietary fiber, antioxidants, unsaturated fats, and vitamins and minerals. Unhealthy plant-based diets include fruit juices, sugar-sweetened beverages, refined grains, desserts, and potatoes (Satija et al, 2015). See the difference? Healthful plant-based diet will actually reduce the risk the developing T2D by 34%, while unhealthful plant-based diet will increase the diabetes risk by 15% (Satija et al, 2015).

A low-fat diet is one where total fat comprises less than 30% of total calories, 10% being saturated fat. There's a huge emphasis on vegetables, fruits, starches and lean proteins, with very little dairy, since all of these types of food do not contain a lot of fat. It has been shown to reduce the risk of diabetes and weight loss, only.

The very low-fat diet is where only 10% of your calories are from fat, 70-77% are from carbohydrates, and 13-20% are from protein. This type of diet emphasizes fiber, beans, fruits,

whole grains, fish and egg whites. It is linked to weight loss and lowered blood pressure (Evert et al, 2019).

The low-carbohydrate diet is where 25-45% of one's total calorie intake from carbohydrates. To achieve this, it emphasizes vegetables low in carbohydrates like salad greens, broccoli, cucumbers, and cabbage, fruit, fat from animal foods, oils, butter, and avocado, and fish and shellfish (Evert et al, 2019). The very low carbohydrate diet has been successful in reducing A1c, weight, blood pressure, and triglycerides, as well as increasing HDL.

The very low-carbohydrate diet is where carbs are less than 26% of one's total calorie intake. The point is the induce ketogenesis. To achieve this goal, more than 50% of total calories are from fat. The results are the same as the low carbohydrate diet (Evert et al, 2019).

The Mediterranean Diet is basically being pescatarian and consuming a lot of olive oil. There is a huge emphasis on vegetables and fish, with diary and red meat in lower frequency. It has been shown to reduce the risk of T2D, A1c, triglycerides, and cardiovascular disease (Evert et al, 2019; Satija et al, 2015).

The Paleo diet, named after the Paleolithic era, is centered around what is assumed hunters and gathers ate during the Paleolithic era. This means that you eat lean meat, fish, vegetables, eggs, nuts, berries. Foods like grains, dairy, and refined fats are avoided since hunters and gathers did not have stable enough societies to cultivate the land. Studies or more or less inconclusive, though some studies show greater lowering of A1c and increased insulin sensitivity in short durations (Masharani et al, 2015). However, skepticism still holds regarding the benefits of Paleo over a longer period of time (Andrikopoulos, 2016; Masharani et al, 2015).

The Dash Diet is short for "Dietary Approaches to Stop Hypertension". As assumed, it lowers blood pressure, but also weight and risk of developing diabetes. These types of diets

reduce sodium, saturated fats, red meat, sweets, and sugary beverages (Evert et al, 2019). There is some support out there that it can help with insulin sensitivity (Shirani, Salehi-Abargouei, & Azadbakht, 2013),

Exercise

Exercise is tricky since everybody's body is different. If you don't exercise at all, ANY exercise will probably do you good. Generally speaking, combined aerobic and resistance exercise is the best way to exercise and has been shown to reduce A1c (Johannsen et al, 2013). Individually, aerobic exercise is great for reducing A1c and increasing insulin sensitivity. Resistance training has been shown to offer a myriad of benefits, from fat degradation and weight loss, to increased insulin sensitivity (Zanuso et al, 2010).

It is important to know that the intensity of the aerobic and resistance training is more important than how long you do it (Zanuso et al, 2010). Therefore, jogging for 30 minutes is going to be less beneficial than if you spent 30 minutes alternating between 15 minutes springs and one-minute rests.

Medication

As I have said earlier, it's usually customary to start treating T2D with dieting and exercise before breaking out the medications. Let's say we are at that point. You've tried your darndest to eat right and exercise, but that A1c is still above 7%. To begin, there is not necessarily a hard and fast rule to prescribing medication. Every physician and endocrinologist have their preferred medications, and every person has their own formulary, tolerability, etc. (Lew & Wick, 2015). Of course, that being said, Metformin is often times the first medication

prescribed. It's an old medication, with minimal side effects, is quite effective in decreasing A1c and presents cholesterol benefits (Brunton, Tenzer-Iglesias, & Unger, 2008; Largay, 2009; Lew & Wick, 2015). Metformin is a glucophage; it lowers the blood glucose level by decreasing the absorption of glucose in the intestines, decreasing liver gluconeogenesis, and increases insulin sensitivity in organs so that they can uptake and use the sugar. Due to how Metformin is absorbed and excreted by the body, it can be hard on the kidneys. This is why those with renal failure are cautioned against using it. Nevertheless, everybody who takes Metformin are required to monitor renal functioning in the form of blood tests during their diabetes follow-ups. While the side effects of Metformin are minimal, those that can occur are hypoglycemia and weight changes (although extremely rare), lactic acidosis, and gastrointestinal discomfort (Brunton, Tenzer-Iglesias, & Unger, 2008; Lew & Wick, 2015).

If Metformin fails to control A1c levels, a second medication is added. These come in the form of insulin, sulfonylureas, thiazolidinediones (Brunton, Tenzer-Iglesias, & Unger, 2008; Drucker et al, 2010), meglitinide, alpha-glucosidase inhibitors, and SGLT2 inhibitors (Lew & Wick, 2015). You will see that all of these medications have different ways of enacting on the body. Since we don't know exactly what causes T2D, medication prescription is sometimes like a guess-and-check to see which suits an individual the most. We'll talk about insulin in a little bit.

Sulfonylureas encourage the pancreas to release more insulin by binding to surface-cell receptors on the pancreas (Ashcroft, 1996). Due to the increased insulin levels in the blood, sulfonylureas can lead to hypoglycemia and weight gain (Lew &Wick, 2015). Hypoglycemia is a condition where one has too low of blood sugar. Weight gain can be due to the increased absorption of glucose by organs that may not be equipped to utilize it efficiently. Therefore, they

store it instead. Examples of common sulfonylureas that you may have heard of are Amaryl (glimepiride), Glucotrol (glipizide), and Diabeta (glyburide).

Meglitinides also increase pancreatic insulin secretion. In fact, they have very similar mechanisms of action, they just use different receptor types than sulfonylureas. Meglitinides act on your body and exit your body a lot faster than sulfonylureas, making them ideal for postprandial glycemic loads. They very rarely cause hypoglycemia and can be associated with a little bit of weight gain (Guardado-Mendoza et al, 2013; Lew & Wick, 2015). Common meglitinides are Prandin (repaglinide) and Starlix (natelginide).

Thiazolidinediones bind onto a receptor in the nucleus called the peroxisome proliferator receptor-gamma (PPR-gamma), altering the transcription of your genes. Due to this mechanism of action, thiazolidinediones have a variety of effects. Ultimately, these medications increase insulin sensitivity in your adipose tissue, muscles, and liver (Hauner, 2002). Due to the increased uptake of glucose, weight gain is common. In those with pre-existing cardiovascular diseases, it can potentially increase the risk of congestive heart failure and heart attack, however for those without a CVD comorbidity, it can lower the risk of developing one, strokes, and improve lipid levels (Brunton, Tenzer-Iglesias, & Unger, 2008; Hauner, 2002; Largay, 2009; Lew & Wick, 2015). Common thiazolidinediones are Avandia (rosiglitazone) and Actos (pioglitazone).

A (alpha)-glucosidase inhibitors are unique in their mechanism. A-glucosidase break the α -glucose bond between glucose molecules in oligosaccharides, a key part of carbohydrate digestion. Thus, α-glucosidase inhibitors block this breakdown, lowering how many monosaccharides are absorbed into the body. With this lowered postprandial blood glucose level, there is a low risk of hypoglycemia and weight gain. However, gastrointestinal discomfort is a

possibility (Lew & Wick, 2015). Common α-glucosidase inhibitors are Glyset (miglitol) and Precose (acarbose).

SGLT-2 inhibitors stand for sodium glucose co-transporter-2 inhibitors. Sodium glucose co-transporter-2 are found in the kidney. They aid in the reabsorption of glucose and secretion of sodium in the nephron. SGLT-2 inhibitors block the reabsorption of glucose and just let it be excreted in the urine. Beneficial side effects include weight loss, however, can be bad for renal function and increased occurrence of urinary tract infections (Kalra, 2014; Lew & Wick, 2015). Common SGLT-2 inhibitors include Farxiga (dapagliflozin), Invokana (canagliflozin), and Jardiance (empagliflozin).

If a second medication does not work, insulin is often increased, or another oral medication utilized if A1c is really close to being under control.

Insulin is often an attractive diabetes-fighting medication because there is no maximum dose, it can be associated with less weight gain than other medication, and it is easily adjustable. The two broad categories of insulin therapies are basal insulin therapies and postprandial insulin therapies (Levine, 2008). Basal insulin therapies support basal insulin levels. These include human analogs like glargine, protamine Hagedorn, and detemir. These insulins supply the body with a continuous insulin supply, just like basal insulin does. Therefore, they are intermediate-acting to long-acting medications. Common basal insulin therapies are Novolin (protamine Hagedorn), Levemir (determir), Toujeo, Lantus, and Basaglar (glargine), and Tresiba. Postprandial or bolus insulin therapies supply the body with insulin right after a meal; they are fast acting and short lasting. Bolus insulin therapies include regular human insulin, rapid-acting insulin analogs, or inhaled insulins (Levine, 2008).

As we saw in the risk section, there are a lot of comorbidities and complications associated with T2D. Many times, physicians and endocrinologists will prescribe medication that are either compatible with these types of comorbidities, or fight both diseases. A common category is antihypertensives. These work to lower blood pressure, which can slow the progression of diabetic complications like nephropathy (Dobesh, 2006). Two of the most common antihypertensives are angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs). ACE inhibitors interfere with the renin-angiotensin-aldosterone system, but ultimately lower blood pressure via nonhemodynamic mechanisms. ARBs prevent angiotensin II from binding, causing blood vessel dilation. Other medications that treat hypertension are thiazide diuretics, beta blockers, or calcium channel blockers (Dobesh, 2006).

The last type of medication that I will talk about is still very new and not used often due to the little amount of research done (Largay, 2009). It's called incretin-based therapy. Incretin is made in the intestines and has glucose-lowering properties (Drucker et al, 2010; Lavernia, 2009). Advantages of incretin-based therapies range from improved glycemic control to improvements in TAG, HDL, LDL, and total cholesterol levels. A major disadvantage is that they are expensive, but that is because they are so new (Brunton, Tenzer-Iglesias, & Unger, 2008). Additionally, they have been found to do little for those with advanced diabetes (Lavernia, 2009). Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) are types of incretins that help regulate glucose absorption during digestion and insulin synthesis. Dipeptidyl peptidase-4 (DPP-4) are enzymes that break down these incretins. The medications derived from incretin research are GLP-1 receptor agonists and DPP-4 inhibitors. This makes sense; they increase the molecules that lower glucose and decrease the molecules that prevent the lowering of glucose. GLP-1 receptor agonists essentially increase insulin secretion, decrease

glucagon release, and increase the feeling of being full after eating (Lew & Wick, 2015). Side effects of GLP-1 receptor agonists are pancreatitis and medullary thyroid cancer in animal studies. However, it has minimal weight loss and nausea, and low risk of hypoglycemia. Known GLP-1 receptor agonists include Trulicity (dulaglutide), Victoza (liraglutide), and Ozempic (semaglutide). DPP-4 inhibitors promote postprandial insulin secretion. It also has low risk of hypoglycemia and has been shown to be weight neutral (Lew & Wick, 2015). Unfortunately, it has been associated with nasopharyngitis, UTIs, headaches, and heart failure. Common medications out on the market include Januvia (sitagliptin) and Tradjenta (linagliptin).

Other diabetes medications that I will not discuss, but are still out there are amylin-mimetics, bile acid sequestrants, and bromocriptine (Drucker et al, 2010; Lew & Wick, 2015).

Adherence

Motivation and sticking to a regimen can be extremely hard. One of the first steps you can take is to get a health care provider that you can trust, who is aware of your own values and attitudes, and is willing to educate you about your health (Bussell et al, 2017).

Other important factors that contribute to treatment adherence is your own self-efficacy, rationality, and responsibility (Swarna Nantha, Hasque, & Paul Chelliah, 2019). Self-efficacy is the belief in oneself about if they can accomplish their goals. Without self-efficacy, there is no chance for you to improve your habits. Improving self-efficacy can be about accomplishing small goals first, having a social support system, and being more knowledgeable about your disease (Heiss & Petosa, 2015). What one should not do is adjust their medications themselves or be belittle the seriousness of the disease (Swarna Nantha, Hasque, & Paul Cehlliah, 2019). These detract form self-efficacy and can be harmful to your health. Rationality is thinking logically

about your disease, while responsibility is internally understanding that you are the one responsible for your own health.

CLOSING REMARKS

And there it is! A semi-comprehensive guide to Type 2 Diabetes. I hope you learned a lot and that you feel empowered to better your own health!

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Episode 1: What is Type 2 Diabetes

Intro:
Hi! My name is Maggie Hutson and welcomed to Diabetes Debunked: What You Need to Know. What this podcast is really all about is debunking some misconceptions about Type 2 Diabetes and provide some deeper information about the condition. Whether you, yourself have it, a friend has it, or you just want to learn more, I welcome you. This is in no way supposed to replace real medical care, it's just a supplemental tool anyone can use.

Topic #1: what is type 1 diabetes

This is episode 1 of Diabetes Debunked. We're going to talk about what Type 2 diabetes really is and what it means to have it. We'll even dive a litter deeper into the physiological foundations of it all.

So, let's get started. At its core, Type 2 Diabetes is when your body cannot properly utilize the sugar you eat. There are two reasons for this: (1) your pancreas is not sending enough insulin throughout the body. Or (2) your body is not responding to the insulin the pancreas is sending out. For those who don't know, insulin is a compound created by the pancreas that lets the organs and muscles of your body know that there is sugar in the blood to be used. So, when your pancreas doesn't send enough insulin out, your organs have no idea that there is sugar just floating about in the blood. Or if your organs don't recognize the insulin, they still do not use the sugar.

If this doesn't make sense yet, let me use an analogy. I'm a huge fan of analogies, and they'll pop up frequently. We all get paper mail still, so hopefully this is still relatable to you. Imagine your mailman, a letter, and a mailbox. On a typical day, your mailman will take that letter and stick it in your mailbox, and then at some point you go get your mail. Great. Now let's say your mailman is super into ultimate frisbee and sprained his ankle. He can't deliver mail anymore, and you don't get your letter. Sad. Or another situation where you're out of town and even though your mailman did his job, you didn't receive the $20 that your g-ma sent you for your birthday. In either situation, you didn't get your mail. This is what Type 2 Diabetes is. The scenario where your mailman sprained his ankle is synonymous to your pancreas failing to send out insulin. Both did not do their jobs, and you did not get your mail/insulin and thus did not get your $20. The scenario where you are out of town is synonymous to the organs of your body not recognizing the insulin. It's basically as if nobody is there to receive the message.

The consequences of your body not utilizing the sugar in your blood are numerous. Complications like diabetic foot, kidney damage, and cardiovascular disease all stem from this malfunction. I want to stress at this point that Type 2 Diabetes is a progressive disease. This means that it gets worse and worse as time goes by. When you first get diabetes, the complications of it don't immediately hit you. This is why many diabetics go uncontrolled because they don't feel the immediate bad effects of it. Nevertheless, this is why it's important to know NOW and try to manage it as best as possible.

Now, I'm sure some of you are wondering, how is this different than Type 1 Diabetes? Let me tell ya. In Type 1 Diabetes, your pancreas is making less insulin because your body is actually destroying the cells that make it. In Type 2 diabetes, we have no solid idea as to why your pancreas slows down insulin production. But in Type 1, which is classified as an autoimmune disease, your body is attacking your pancreas. Since the outcome is more or less the same, Type 1 Diabetes can have the same symptoms and complications.

Topic #2: physiological foundations

Okay so this next part is deensseee so bear with me. I'll be going into the physiological foundations of Type 2 Diabetes. What that means is I'll show you how your body normally functions, and then demonstrate how Type 2 diabetes messes it all up. Going into this next part, a key concept to understand is this thing called "physiological balance." Your body is amazing at maintaining a status quo. When one gets type 2 diabetes, your body adapts to the changes, and it obviously isn't for the best. The five systems we will go over are Endocrine, Kidney, Cardiovascular, Nervous, and Digestive.

Endocrine

Your endocrine systems is essentially a messaging system via chemical messengers called hormones. Another big messaging system in your body is the nervous system, which we will talk about later. The pancreas is part of the endocrine system. This makes insulin a hormone. We will center on insulin and glucagon, another hormone, however your endocrine system makes tons of hormones that are responsible for vast amount of functioning.

In a normal body, your pancreas releases hormones in two ways: basal and bolus. Bolus is also called prandial or post prandial, depending on the context. I will be switching off between these terms. Basal insulin is when your pancreas releases small amounts of insulin all the time. This regulates sugar levels in the blood, and makes sure your organs are continuously absorbing said sugar. Makes sense since you're doing stuff all day all the time. Bolus insulin is released during huge sugar influxes, usually after one eats. The huge amount of insulin released keeps up with the large amounts of sugar. As we know, in Type 2 diabetes, your pancreas either does NOT do this, or your body just doesn't respond to it. Therefore, your body is not getting the energy source it needs, and the elevated blood glucose levels can be very damaging to your cardiovascular and nervous systems. The lack of energy use results in listlessness and fatigue, common symptoms of Type 2 Diabetes.

Glucagon is another important hormone of the endocrine system. Glucagon hops in when blood glucose levels are super low and there is no readily available sugar for your body to use. This is usually when you first wake up or you just haven't eaten all day. Glucagon tells your liver to either break down energy stores, or to make sugar. Yes. You heard me. Make sugar. This process is called gluconeogenesis and it only happens when absolutely necessary since it's a very complicated pathway. Glycogenolysis is the breakdown of energy stores. Glucagon also slows down sugar use and encourages fat breakdown.

Bottom line, with T2D, you have a lot of sugar in your blood. This is called hyperglycemia. This immediately causes problems with your kidneys and your cardiovascular system. Let's talk about your kidney system first.

Renal

Your kidneys are part of your urinary system. They are primarily responsible for filtering your blood and making urine. To do this requires a very important principle called Tonicity. Ergo, here's a super quick chemistry lesson. Tonicity is a term to describe the relative concentrations of one solution to another. Solutions are when solids are mixed in liquids, or gases mixed in liquids, or liquids in liquids. Your blood is technically a solution. The plasma, which is predominantly water, is filled with blood cells, platelets, ions, hormones, proteins, etc. There are three ways to describe solutions: hypotonic, isotonic, and hypertonic. When a solution is hypotonic, it is less concentrated than another solution, in terms of the same particle. Isotonic is when two solutions are the same in concentration of the same particle. Hypertonic is when a solution is more concentrated than another in terms of the same particle. Here's an analogy. Picture lemonade. Lemonade is water, sugar, and lemon juice. I've never actually made lemonade, so these recipes will probably be horrible if you actually drank them. If you make one lemonade with one liter of water, 6 cups of sugar, and 4 cups of lemon juice, and another with one liter of water, 5 cups of sugar, and 5 cups of lemon juice, the lemonades themselves are isotonic if you add all of the particles together. Lemonade #1 has a total of 10 cups of flavorings, and Lemonade #2 also has a total of 10 cups. However, lemonade #1 would be considered hypertonic in sugar than lemonade #2, and hypotonic in lemon juice. When two solutions are put beside each other, with a separation that allows for particles to move across it, they want to equal out. Therefore, if Lemonade #1 and Lemonade #2 were put beside each other with a magical barrier that only allowed sugar to cross, sugar will spontaneously move from Lemonade #1 (which is 6 cups of sugar) to Lemonade #2 (which is 5 cups of sugar) until they both have 5 ½ cups of sugar.

Okay so keep this in mind when we take a trip through the kidney. To begin, there is this area of the kidney called the nephron. The nephron is where urine is actually made. The rest of the kidney is just a huge collection place for urine until it travels to the bladder. There are millions of nephrons in your kidney, and they all drain to the same place called the renal pelvis in the kidney. As blood vessels enter the kidney and travel to the nephron, it encounters this thing called the glomerulus. Here, blood is squeezed out of the blood vessel into this space called the lumen of the nephron. This squeezing is filtering the blood of large proteins, sugars, and salts. Of course, some sugar still gets in, and there are transporters that take this sugar and put it back into the blood. The liquid that successfully makes it through is called pre-urine. It travels along in the tubes of the nephron. It is alternatively exposed to areas that are hyper and hypotonic to it. This allows for further filtration as water is added to the preurine and more ions are filtered out. The end destination in the nephron is called the collection duct, and there, it is officially called urine.

In diabetic individuals, the blood that enters the kidney is extremely hypertonic relative to the cells of the kidney. The amount of sugar that gets across is too much for the nephron to handle, so it just stays in the pre-urine. This causes the preurine to be hypertonic to the rest of the nephron. This means that when it enters the Loop of Henle in the medulla of the kidney, which is

usually more hypertonic than the preurine, water is retained. This means that your urine has a lot more volume, and this is why diabetics tend to urinate more than normal and are thirstier. The excess sugar in their urine is also why diabetics have higher risk of developing urinary tract infections. If you don't know what a urinary tract infection is, it's when E. coli grows where it shouldn't and causes inflammation. E. coli looovvesss sugar. So when an individual has a lot of sugar in their urine, E. coli will be living their best lives in your bladder, ureters, or kidneys, depending on how long you've had it. The elevated blood sugar content also increases overall blood pressure. While this has major cardiovascular complication, it can also damage the small blood vessels in the kidney. This damages the kidney, resulting in nephropathy.

Cardiovascular

Let's move onto the cardiovascular system. The cardiovascular system is comprised of the blood vessels that trek throughout your body, and your heart. Many hormones and proteins ride your cardiovascular system to get to where they need to be. To understand how type 2 diabetes affects your cardiovascular system, we need a quick anatomy lesson. Let's start with your heart. There are four chambers of the heart: two atriums and two ventricles. Conceptually, you can picture the heart as a square with a T crossed in it. The two upper boxes are the right and left atriums, and the two lower boxes are the right and left ventricles. Separating the atriums form the ventricles are the atrio-ventricular valves, which are like little doorways that rhythmically open and shut to either allow blood to pass through. There are also two semilunar valves, one per each ventricle. The pulmonary semilunar valve allows blood to flow form the right ventricle into the lungs, while the aortic semilunar valve allows blood to flow from the left ventricle into the aorta, which leads to the rest of the body. Blood travels from the vena cava into the right atrium, through the first atro-ventricular valve into the right ventricle. It exits the heart via the pulmonary valve into the lungs and then returns to the heart via the left atrium. From the left atrium, it flows through the second atrio-ventricular valve into the left ventricle, and then exits the heart via the aortic valve. Blood then traverses your body, depositing oxygen and nutrients along the way, until it returns to the heart via the vena cava. Arteries take blood from the heart to the rest of the body, carrying with it oxygen and nutrients from the lungs. Veins take deoxygenated and nutrient-depleted blood from the rest of the body back to the heart. As arteries near organs, they get smaller in diameter until we call them arterioles. These get even smaller and more branched and become capillaries. Capillaries are the primary site of exchange between the circulatory system and an organ. As blood leaves the organs, they exist via venules. Venules get bigger and become veins. As blood circulates the body, it's unidirectional. However, when blood moves through the body, it's more like a freaky circle. A single blood cell does not hit every single organ in your body, rather it has it's own route, and then meets up with the rest of the blood at specific points like the aorta or vena cava.

As blood moves through your blood vessels, it exerts a force. This is called blood pressure. The force of blood pressure is dependent on how strong the heart is pumping (cardiac output), the constriction of blood vessels in systemic circulation, the volume of blood, and how thick the blood is. It's measured in fraction form. The top number is systolic blood pressure, and the bottom is diastolic blood pressure. These allude to the contracting and relaxing of your heart atriums and ventricles. Type 2 diabetes increases blood pressure because it increases the volume of blood, how thick the blood is, and (indirectly through eating), the constriction of blood

vessels. As elevated blood pressure progresses, the mechanisms that try to regulate it become destabilized, leading to cardiovascular diseases. There are two types of cardiovascular complications for diabetics: macrovascular and microvascular. Macrovascular complications pertain to large blood vessels and your heart, while microvascular complications pertain to the small arterioles, capillaries, and venules. Macrovascular complications include coronary artery disease, hypertension, congestive heart failure, arrythmias, strokes, and heart attacks. Microvascular complications include neuropathy, retinopathy, and nephropathy.

With the decreased efficiency of circulation in diabetics, they are also slow to heal and have weakened immune systems. Like I said earlier, many things travel through the body using your cardiovascular systems. These include healing agents and immunologic agents. When you cut yourself, the clotting factors, proinflammatory factors, and nutrients are slower to get to the site of injury, and thus you take longer to heal. You are also more prone to infection since the cells and molecules related to immunity are also slow to get to the site of injury.

Nervous

As I've stated, neuropathy is also a complication of Type 2 diabetes. This is about damage to the nervous system. The nervous system consists of your brain, spinal cord, and all the neurons that branch from these two structures. The brain and spinal cord are considered your "Central Nervous system", while everything else is your "peripheral nervous system". The central nervous system is more to do with integration, processing, and storing of information, while the peripheral nervous system has more to do with collecting information and carrying out the orders of the central nervous system. If your nervous system was a spy agency, the CNS would be headquarters, and the PNS would be all the agents. The cells of your nervous system are called neurons. In the PNS, there are specialized neurons called sensory cells. They're responsible for the five senses, therefore you can find them in your nose, eyes, skin, ears, and tongue. Like all cells, they need blood to supply them nutrients. As we have seen, diabetic individuals usually have elevated blood pressure due to the hyperglycemia. These can damage your sensory nerves and the nerves that transmit the sensory information to your brain. This is what retinopathy and neuropathy are. It's altered vision and inability to sense your surroundings.

Ok last organ system: your digestive system. There are actually a lot of organs of your digestive system, and then there are accessory organs that just secrete stuff into the organs of the digestive system. Your pancreas is an accessory organ, and you'll see how shortly.

Digestive

Digestion is central to obtaining the nutrients from the food you eat. Without proper breakdown and absorption of carbohydrates, proteins, fats, cholesterol, vitamins, and minerals, you would probably die. I'll only discuss the three nutrients that you obtain from food: carbohydrates, proteins, and lipids. This section is more to understand how these nutrients get into the bloodstream. Their effects and how Type 2 diabetes will be discussed in episode 3, when I talk about the nutrition label.

Sugars are the most relevant carbohydrate when it comes to digestion. Sugar comes in many forms: as long branching chains called polysaccharides, as medium length chains called oligosaccharides, or as singular sugar molecules called monosaccharides. Monosaccharides are the best form of sugar for the body to use. So the role of digestion is to break down the polysaccharides that you eat into monosaccharides. Common polysaccharides that we eat are starch and cellulose. It begins in the mouth. Let's say it's a cheat day and you're eating a super, greasy cheeseburger. You're chewing it up, everything is mixing with the saliva in your mouth, and you swallow. Sugar breakdown doesn't actually really start until the small intestine. Here, the pancreas injects the small intestine with pancreatic amylase. This is an enzyme that breaks the bonds in polysaccharides, creating oligosaccharides and disaccharides. Along the walls of the intestine are brush border enzymes. These take the oligosaccharides and disaccharides and break them into monosaccharides. The monosaccharides then move from the intestine into the neighboring blood vessels via specialized transporters.

Like carbohydrates, proteins are best absorbed in their most simple state. These would be amino acids. Amino acids bond together in chains called polypeptide chains. These chains are what make proteins. Protein digestion begins in the stomach. All the protein in the juicy burger are broken down by pepsin into their peptide chains. Pepsin is an enzyme in the stomach. As the broken down food enter the small intestine, they meet more enzymes that break them into shorter peptide chains. And then there are peptidases that break these peptide chains into single amino acid molecules. Amino acids enter the circulatory system via their own special transporters, too.

Lipids are a little different than proteins and carbohydrates because they aren't made of monomers that just link together. Instead, digestion is more like pulling apart lipids molecules, or making globs of fat smaller. It begins in the mouth. The fat from your burger begins to break down via lingual lipase, an enzyme in your saliva. Like the other nutrients, the majority of digestion is in the small intestine. Here, the pancreas injects pancreatic lipase into the small intestine, and the gall bladder injects bile. The pancreatic lipase rips apart fat, making it into free fatty acids and monoglycerides. The bile acids emulsify the lipid globules, making them into small droplets. The emulsification lets the pancreatic lipase work more efficiently. Finally, the monoglycerides, free fatty acids, and cholesterol are absorbed and packaged up. They eventually enter circulation.

Closing Remarks:
In this episode of Diabetes Debunked: What You Need to Know, we discussed what Type 2 Diabetes really is and how it affects the normal functioning of your body. In the next episode, we will discuss the risk factors of Type 2 Diabetes and start talking about treatment options.

Episode 2: Risks, Exercise, and Diet

Intro:
Hi! My name is Maggie Hutson and welcomed to Diabetes Debunked: What You Need to Know. What this podcast is really all about is debunking some misconceptions about Type 2 Diabetes and provide some deeper information about the condition. Whether you, yourself have it, a friend has it, or you just want to learn more, I welcome you. This is in no way supposed to replace real medical care, it's just a supplemental tool anyone can use.

Topic #1: Risks

This is episode 2 of Diabetes Debunked. We're going to talk about the risk factors of Type 2 Diabetes and how dieting and exercise can help prevent or treat Type 2 Diabetes. In the next and last episode of this miniseries, we will go into more of the medication side of treatment. If you are new here, I suggest you first listen to Episode 1: What Is Type 2 Diabetes to get more of the foundational knowledge.

So lets get started. When I was first researching the risks of Type 2 Diabetes, I also had a goal in mind to uncover the motivational and psychological factors that underlie Type 2 Diabetes. I found that it was easier to divide risk factors into "Biological" risk factors and "Social" risk factors. I'll go over each individually.

For biological risk factors, it's probably no surprise that most of them are considered "comorbidities." Comorbidities are medical conditions that an individual can have, independent of another disease. All the risk factors of Type 2 Diabetes include overweightness and obesity, lack of exercise, smoking, poor diet, medications that affect sugar metabolism, family history, race, age, hypertension and other cardiovascular diseases, and being male. What a risk factor means is that if you have these conditions, then you are more likely to develop Type 2 Diabetes. The major comorbidities are obesity and other cardiovascular diseases. Overweightness and obesity are in part symptoms of a poor diet and lack of exercise. Your body only needs a certain amount of calories a day to function, and when one consumes more than that allotted amount, your body will take the excess sugar and fats and store it. Your body is amazing at storing excess energy; if anything, it's too good. Historically, human beings have lived in times where they didn't know when their next meal was, and our current bodies are still living like that. Research has shown as one eats more and more, our bodies become more tolerant to the food we eat, both in our brains and in our endocrine system. When we eat, we usually get pleasure from it. The dopamine pathway in our brains are extremely active, giving us a sense of pleasure. Overtime, as we eat too much, this area becomes less active. It's similar to the tolerance mechanism for drug addiction. Moreover, insulin signaling deteriorates and satiety decreases. Therefore, those who are overweight can quickly become obese. It's actually some pretty fascinating research. Ok so although we don't know exactly how obesity and overweightness directly contribute/cause Type 2 Diabetes, there is a strong relationship between those who are obese and those who have Type 2 Diabetes.

Hypertension and other cardiovascular diseases are another big risk factor of Type 2 Diabetes. Once again, we are not sure exactly how they contribute, but we have already seen how they can relate to neuropathy, a major complication of Type 2 Diabetes.

Genetics and family history play a huge role in Type 2 Diabetes. Researchers have yet to find a specific gene or set of genes that is/are associated with the condition, but family studies, twin studies, and community studies have shown a strong genetic role. Some research has shown that the contribution from your parents is more or less additive. This means that if both parents have Type 2 Diabetes, then you are at least twice as likely to develop it than if one parent had it.

Social risk factors are a little bit trickier and honestly require a whole different podcast series since they are so numerous and interconnected. I will only go over two large factors: health literacy and ethnicity and culture.

Health literacy is the ability to understand medical information, and then use that information to guide your health behavior is positive ways. This can be in the form of understanding what your doctor is saying to you during appointments, being able to understand your medicine bottles, or even just knowing what Type 2 Diabetes is. It is extremely important for all individuals to be health literate, not just those with Type 2 Diabetes, because it can greatly improve health outcomes. One of the best ways to promote health literacy that you can do with your doctor is the "teach back" method. This is when you try to organize and repeat back to what your physician tells you during appointments. This makes sure that you understand what is going on, and that you and your physician are seeing eye-to-eye.

Culture and Ethnicity as risk factors encompass a vast amount of behaviors, relationships, etc. If you didn't know, Latinx populations and African American populations are twice more likely to develop Type 2 Diabetes than non-Latinx white communities and European Americans. The underlying social factors for this can include lack to health care, poor experience with health care professionals, and cuisine. For Latinx communities, there's a huge emphasis on community, where one looks after the group before they look after themselves. Moreover, in interviewing Latinx men and women about their Type 2 Diabetes, a common theme researchers discovered was an external locus of control, centralized on religion. Many Latinx individuals believed their condition was like a test of faith or punishment handed down by God. When an individual has this type of mentality, they have less belief in themselves that they can fix it.

Topic #2: Diagnosing Diabetes

Okay so now that we've sort of covered what Type 2 Diabetes is and some risk factors of it, let's get to the good stuff. Treatment. I want to note that there is technically no "cure" for type 2 diabetes. Even if you are the best patient ever, you exercise, eat a healthy diet, and adhere to your medications, Type 2 diabetes doesn't just "go away." Rather, all that treatment does is help manage the symptoms of Type 2 Diabetes and hold off the development of complications. This is still super important, so please don't be disheartened. I've seen patients who have been able to get their A1c levels back to a normal person, but that doesn't mean their pancreas is pumping out more insulin, or their body suddenly recognizing the signaling. It just means they have adapted to their condition and managing it.

To start off, let's talk about how one diagnoses Type 2 Diabetes. Usually, physicians track fasting glucose levels first. This means, how many sugar molecules are in your blood when you haven't eaten in 10-14 hours. This indicates how well your body can balance itself. A normal range is anything below 100 mg/dL, anything above warrants further testing. This makes sense, because remember, when you are in starvation mode, your body does it's best to maintain blood glucose. When you're diabetic, your body isn't taking in the sugar just floating about in the blood, leading to elevated levels. Okay so an elevated fasting glucose level, a hemoglobin A1c test is administered. Hemoglobin A1c is a protein that floats around in your blood, picking up sugar molecules as it does. They often hitch a ride onto red blood cells. So, if your A1c is below 5.7%, then you're good, and your elevated fasting glucose was just a hiccup. However, if your A1c is above 6.5% on two separate occasions, then you can officially be diagnosed with Type 2 Diabetes. If your A1c falls between 5.7% and 6.5%, then you are in "prediabetes", which means you should probably start exercising more or eating better. After diagnosing Type 2 Diabetes, it's standard to see your primary care doctor or endocrinologists routinely after. You usually go at 3- or 6-month intervals, depending on how "controlled" you are. Remember that hemoglobin A1c attaches itself to red blood cells? Well, red blood cells live for about 3 months in your body. When you are an uncontrolled diabetic, physicians need to monitor you at every life cycle of your red blood cells. When you are controlled, physicians can relax a little and check you ever two life cycles. "Uncontrolled" diabetes is when your A1c is above 7%, when "controlled" diabetes is when it's under 7%. These are the standards set by the American Diabetes Association. Other organizations like the American Association of Clinical Endocrinologists and the European Association for the Study of Diabetes have set this bar to 6.5%, with varying success. It seems that if you don't have any pre-existing conditions, like those comorbidities we talked about, then you could probably benefit from this stricter A1c. However, if you do have a comorbidity, this measure can be harmful to you. Monitoring A1c is really important, because it is closely associated with lowering the risk of microvascular complications, cardiovascular events, and reduced risk of death.

Topic #3: The Nutrition Label

At this point, I'm sure you're thinking, okay so how do I become "controlled". Well, the best way to start is eating a healthy diet and exercising. It's actually customary to first try lifestyle changes before prescribing any sort of medication. I'll first go overeating, and then exercise.

The key word to dieting is MODERATION. Even healthy foods can be harmful if eaten too much. I'm going to quickly go over the three macromolecules most often monitored during eating, and then the types of diets people use to manage Type 2 Diabetes.

First, carbohydrates. The word "carbohydrates" or "carbs" I believe is quite misunderstood by the general populace. The word "carbohydrate" is a biochemical term used to describe what we call in everyday life "sugar." However, there are actually two general categories of carbohydrates: sugar and glycoconjugates. Sugars have three levels of organization, monosaccharides, disaccharides, and polysaccharides. Monosaccharides are single sugar molecules by themselves. Common monosaccharides include glucose, fructose, galactose, ribose, and deoxyribose. Glucose is the body's primary source of energy, it's the preferred, the creme de la crème. The others are commonly eaten, however your body has a weird way of either using

them for things than energy, like how ribose and deoxyribose is used for your genetic material, or converting them into glucose to then be used for energy. When two monosaccharides bind together, they form disaccharides. Common disaccharides are lactose and sucrose. Lactose is the sugar found in milk, which is weird becomes when we first think of milk, we think of diary and fat. I'm here to tell you that your glass of milk actually has a lot of sugar in it, but it is a good source of calcium for growing bones. As three or more monosaccharides bind together, they from oligosaccharides and polysaccharides. Oligosaccharides are a weird term for "shorter" polysaccharides, but the community thought it smart to give them their own name since a special set of them have important functions (breastmilk). Common polysaccharides that we eat are starch and fiber. When we store excess energy, we actually create glycogen, a storage polysaccharide, and put it in our liver and muscles. Starchy foods get a bad rep for the amount of sugar they contain. But like I said, it's all about moderation. It's also important to balance your plate. Foods that are high in fructose, like candy, are bad because they offer no other nutritional value. However, your body uses fructose every day. The bottom line is that carbohydrates aren't bad for you, and you should not strive to cut them out of your diet. They are essential to diet, and you need enough of it for your body to properly function. Moreover, foods that offer a lot of "natural" sugar like fruit, is considered healthy because they offer so much more as well, like vitamin C, calcium, phosphorus, etc.

Now many people count calories to help them with weight loss. This can be good and bad. If one is so overweight that just counting down the sheer volume of calories will help them, then that's great, However, when you start getting to your normal weight range, it becomes more important to monitor where those calories come from than just the amount. This is why in every macromolecule I'll discuss the energy equivalents to each. For carbohydrates, the energy equivalent is 4 calories per one gram of glucose. That means that one medium sized Russet potato that has 33 grams of glucose (in the form of starch), contributes roughly 132 calories to your day. Be mindful that it is an energy conversion to glucose. Other forms of sugars have different energy conversions.

I didn't really discuss glycoconjugates because you don't use them for energy. Rather, they are most used by signaling in your body, communication, immunity, and joint health. Glycoconjugates are when sugar molecules are bound to proteins or lipids. When insulin tells your muscles to import glucose form the blood, it actually binds to a receptor on the surface of the muscle cell. That receptor is a glycoconjugate; it's a sugar bound to a lipid.

Fat is another controversial topic it seems. Like carbohydrates, it's often misunderstood. To begin, fat is not cholesterol, but they are both lipids. Lipids is the overarching term to describe a class of macromolecules. The three categories are triglycerides, which is what fats are, phospholipids, and cholesterol. Triglycerides are three fatty acids attached to a glycerol molecules. Remember back in digestion, when pancreatic lipase tears apart triglycerides? It removes two of the fatty acid chains, making them monoglycerides. Triglycerides, or TAGS, are abundant in energy. They are the second preferred choice of energy for the body. However, they're usually used as storage units. When your body has excess sugar, it will convert that glucose into fat and store it in adipocytes found in your skin and around your organs. There are two types: saturated and unsaturated fats, but they're really talking about the fatty acid chains of the fats. Therefore, there are saturated fatty acids and unsaturated fatty acids. Saturated fatty

acids have higher energy content and come from animal products. Unsaturated fatty acids are less energy dense and are found in plant-derived products. Saturated fatty acids are considered to be less healthy because they tend to be more solid, giving them a greater chance to block your arteries, than unsaturated fatty acids. The commonly known omega 3 and 6 fatty acids in fish are unsaturated fatty acids.

One gram of triglyceride will give your 9 calories. As you can see, fats have higher energy content than glucose, but glucose is still the primary choice. This is why it's so hard to lose weight. The process of breaking down fat for energy is slower than just storing it. Moreover, your body will burn through its glycogen stores before it even touches your fat.

Phospholipids are the second category of lipids. They are essential to cell membranes, and cell life.

Cholesterol is a doooooozzzyy. Like all the macromolecules, cholesterol is essential to body functioning and it just simply cannot be avoided. Cholesterol is the structural foundation for many of the hormones of your body, including testosterone and estrogen, and it's present in cell membranes. You often hear the two types of cholesterol: healthy HDL and unhealthy LDL. Let me clear this up real quick. Cholesterol is cholesterol. When you eat it, there is no good and bad, not in the same sense of saturated and unsaturated fats, where there are structural differences. HDL and LDL cholesterol are the two of the many ways cholesterol is transported through the body. As we had discussed in digestion, after cholesterol is absorbed into the body from the small intestine, it gets packaged away and sent into the blood stream. Well, it's first packaged in chylomicrons, which is just lipids plus proteins. The proteins tell the lipids where to go in the body, usually to the liver. This is where HDL and LDL comes in. HDL and LDL stand for "high-density lipoprotein" and "low density lipoprotein". They are essentially carriers of cholesterol, just as chylomicrons are. HDL is considered healthy because they take lipids from your muscles and adipocytes and transport them back to your liver for use. They enable your body to use its excess fats. LDL is considered unhealthy because they take lipids from your liver and ship it to your muscles and adipocytes for storage. Additionally, the proteins on LDL can actually accidentally deposit these lipids in your blood vessels instead of their original destination. This can create plaques, leading to blood vessel constriction. As we saw in the cardiovascular section, this can lead to hypertension. It can also contribute to atherosclerosis, stroke, and heart attack. Elevated lipid in the blood can be means of prescribing statins. Statins stabilize plaque growth and try to shrink plaques. Cholesterol has to energy equivalent because it's not used by your body for energy.

Proteins are also very important for your body. Proteins are made of amino acids. There are 20 naturally occurring amino acids, 11 your body can make itself, and 9 you have to eat from your diet because your body cannot make them (there is some discrepancy on the number. Some scientists say 21 amino acids, and some say there are 10 essential and 10 nonessential. The main take away is that you need to eat protein to get whatever amino acid you lack). Proteins are the workers of your body. They carry out metabolism, intercellular communication, immunity, muscle structure, and very rarely, can be used for energy. VERY RARELY. It is a complete last resort effort. You will lose fat before you lose muscle mass. It is important to know that amino acids cannot be stored in the body like carbohydrates and lipids. Therefore, they are broken

down, their parts recycled for other functions. The resulting ammonia is then converted into urea and then gotten rid of in your urine.

One gram of protein offers 4 calories. The source of protein is heavily debated among carnivores and omnivores and vegans and vegetarians. In this next part, I will describe specific diets and you can decide for yourself which one you want.

Topic #4: Diets

Dieting is really just how you eat. I can only cover a small amount of the diets possible for you, and even so ,you should still do your own research and consult your doctor or nutritionist before starting any dietary changes. I will be focusing most on carbohydrates, proteins, and lipids.

According to the ADA in their national consensus in 2019, the recommended amount of carbohydrates one should eat without diabetes is 130 grams/day. This is calculated from the base amount of energy one requires for a mostly sedentary lifestyle. They say that those with diabetes should make at least 14 grams of those 130 grams come from fiber. This fiber can be from nonstarchy vegetables, fruits, whole grains, or supplements. Lipid recommendations include polyunsaturated fats, like omega-3 fatty acids. Many people supplement their diet with fish oils to obtain more unsaturated fats like eicosapentaenoic acid and icosapent ethyl. I just want to warn these people that they are also consuming saturated fats in those supplements, so be very careful. For protein, the ADA recommends proteins to be 30% of your total energy. This has been associated with greater weight loss, lower A1c, and better fasting glucose, lipids, and blood pressure.

The USDA promotes a general diet that emphasizes vegetables, fruits, whole grains, and protein from various sources, with minimal diary and fat. The diets I will be briefly discussing are vegetarianism and veganism, the low fat diet, the very low fat diet, low carbohydrate diet, very low carbohydrate diet, the Mediterranean diet, the DASH diet, and the Paleo diet.

If you are unaware, vegetarianism and veganism cut out “flesh foods”, while veganism completely cuts out any animal-derived product. These diets have been shown to reduce the risk of diabetes by 20%, and lower A1c levels, weight, and LDL. However, plant-based dieting can be done wrong. There are two types of plant-based dieting: those filled with healthful foods and those without them. Since the only requirement to be a vegetarian and/or vegan is the lack of animal products, it leaves a lot of open room for interpretation. Healthful plant-based diets are those that include whole grains, fruit, vegetables, and nuts. These are rich in fiber, antioxidants, unsaturated fats, vitamins, and minerals. Unhealthy plant-based diets are filled with fruit juices, sugar sweetened beverages, refined grains, and sadly, potatoes. Healthful plant based diets reduce the risk of developing Type 2 diabetes by 34%, while unhealthy plant-based diets actually increase the risk of developing diabetes by 15%. Be mindful of this lesson in all types of eating.

A low fat diet is one where the total fat comprises less than 30% of total calories, and less than 10% of that is saturated fat. This allows for mostly vegetables, fruits, starches, and lean proteins. It has been shown to reduce the risk of diabetes and lead to weight loss. Very low fat diets are when only 10% of your calories are from fat, while 70-77% are from carbohydrates, and 13-20%

are from protein. This diet emphasizes fiber, beans, fruits, whole grains, fish, and egg whites. While it does not reduce the risk of developing Type 2 diabetes or A1c, it is good for weight loss and lowering blood pressure.

The low carbohydrate diet is where 25-45% of your diet is from carbohydrates. To achieve this, one must eat salad greens, broccoli, cucumbers, cabbage, fruit, shell fish and fish, and overall more fat. It has been successful in reducing A1c, weight, blood pressure, TAGs, and increase HDL. The very low carbohydrate diet is where carbs are less than 26% of ones total caloric intake. The idea is to induce ketogenesis in your body, which is the break down of stored fat. More than 50% of total calories must come from fat.

The Mediterranean diet is basically being pescatarian and eating a lot of olive oil. There's a huge emphasis on vegetables and fish, with minimal diary and red meat. It has been shown to reduce the risk of Type 2 Diabetes, A1c, TAGs, and cardiovascular disease.

The Paleo diet is named after the Paleolithic era, where humans were just hunters and gatherers. This calls for a diet of lean meat, fish, vegetables, eggs, nuts, and berries. Anything else is more or less prohibited because humans were not developed enough to eat those kinds of foods. The research is more or less inconclusive. While some have shown a lowering of A1c and increased insulin response in short duration, the general tone is cautionary as we don't really know how well the Paleo diet works in the long term.

And lastly, the DASH diet. The DASH diet stands for "Dietary Approaches to Stop Hypertension", This means reducing sodium, saturated fats, red meat, sweets, and sugar beverages. There is support out there that it can help with insulin sensitivity.

The last point I want to stress before we move on to exercise is when you eat. I did not discuss fasting strategies, which many also use to treat diabetes. I chose to leave this out for the sake of time, however, you should do your own research and consult a physician and/or nutritionist if it interests you. The only thing I have to say is that your body is extremely good at adapting. As we have seen, in both starvation mode and when there is a huge influx of food, your body has ways of adjusting. Just keep that in mind.

Topic #5: Exercise

The last topic of this podcast is exercise. Exercise is tricky since everybody's body is different. If you don't exercise at all, really ANY exercise will do you good. For those who are just starting, the best kind of exercise is where you combine both aerobic and resistance exercise. Aerobic is one that gets your heart pumping. You're burning through glucose and glycogen stores. Resistance exercise, or weight training, is where you are using your muscles. It doesn't burn as much calories as aerobic training, but it is still important for health. Additionally, the intensity of these exercising is more important than how long you do it. This means that 30 minutes of just walking at a leisurely pace will be less beneficial than you doing 30 minutes of 15 second sprints with one minute rests.

Closing remarks:

In this episode of Diabetes Debunked: What You Need to Know, we discussed the risk factors of Type 2 Diabetes and talked about the dieting and exercise one could do to help avoid developing type 2 diabetes or managing it. In the next episode, we will discuss medication options and adherence.

Episode 3: Medication and Motivation

Intro:
Hi! My name is Maggie Hutson and welcomed to Diabetes Debunked: What You Need to Know. What this podcast is really all about is debunking some misconceptions about Type 2 Diabetes and provide some deeper information about the condition. Whether you, yourself have it, a friend has it, or you just want to learn more, I welcome you. This is in no way supposed to replace real medical care, it's just a supplemental tool anyone can use.

Topic #1: Medication

This is episode 3 of Diabetes Debunked, and the last episode of this miniseries. We're going to talk about the medication options for managing Type 2 Diabetes and briefly go into the motivational factors behind adhering to treatment. If you are new here, I suggest you first listen to Episode 1: What Is Type 2 Diabetes and Episode 2: Risks, Diet, and Exercise.

As I've said before, it's usually customary to treat Type 2 Diabetes with dieting and exercise before diving into medication. So lets say we are at that point. You've done your best to eat right and exercise, but you still can't seem to get that A1c below 7%. To start, there is no hard and fast rule to prescribing medication. Every physician have their favorites, and every person has their own formulary, tolerability, etc.

That being said, many physicians like to prescribe Metformin first. Metformin is a super old medication, therefore we know that it has minimal side effects and is quite effective at lowering A1c. Metformin is considered a Glucophage. It lowers blood glucose levels by decreasing the absorption of glucose in the small intestines, decreases liver gluconeogenesis, which is the synthesis of glucose by the liver, and increase insulin sensitivity in your organs. Metformin can be hard on your kidneys, which is why if you're prescribed it, you have to do blood work to check up on your renal function. Those with preexisting renal failure are cautioned against using it. Otherwise, Metformin rarely produced hypoglycemia, which is too low of blood sugar, and is considered to be weight neutral. This means that it causes neither weight loss nor weight gain. The negative side effects, though more or less rare, are lactic acidosis and gastrointestinal discomfort. Lactic acidosis is when your blood is too acidic due to the lactic acid, a byproduct of glucose metabolism. If Metformin fails, a second medication is added. These include insulin, sulfonylureas, thiazolidinediones, meglitinide, alpha-glucosidase inhibitors, and SGLT2 inhibitors. This is where it gets a bit more technical, so try to bear with me. You'll see that all these medications have different effects on the body, called mechanism of action. Since we don't know the real cause of Type 2 Diabetes, and there are two ways it displays, prescribing medication can almost be like a guess and check method that balancing A1c reduction and side effects. We'll talk about insulin in a bit.

Common sulfonylureas are Amaryl, Glucotrol, and Diabeta. They stimulate the pancreas to release more insulin by binding to the cells of the pancreas. Due to the increased insulin levels in the blood, sulfonylureas can lead to hypoglycemia and weight gain. The weight gain may be due to the increased uptake of glucose by organs that have not yet adjusted to it; so instead of uses the glucose, they store it.

Common meglitinides are Prandin and Starlix. Meglitinides also increase insulin production, but they use a separate receptor than sulfonylureas. Meglitinides act on your body and exit your body a lot faster than sulfonylureas, making them ideal for prandial glucose loads. They rarely cause hypoglycemia, though they can be associated with a little bit of weight gain.

Common Thiazolidinediones include Avandia, and Actos. Thiazolidinediones actually enter your cells and alter gene transcription. This encourages insulin sensitivity in your adipose tissue, muscles, and liver. Due to the increase glucose uptake, weight gain is common. It can accentuate any preexisting cardiovascular diseases, do it should probably be avoided if you have them. If not, thiazolidinediones have been shown to reduce cardiovascular disease risk.

Alpha-glucosidase inhibitors include Glyset and Precose. They're unique because they prevent the breakdown of oligosaccharides into monosaccharides during digestion. Therefore, less sugar is absorbed in the small intestine. With the lowered postprandial glucose level, there is a low risk of hypoglycemia and weight gain, however GI discomfort is a possibility.

SGLT-2 inhibitors stand for sodium glucose co-transporter-2 inhibitors. They include Farxiga, Invokana, and Jardiance. They act upon the kidney, blocking reabsorption of glucose in the nephron. This just lets the excess glucose be excreted in the urine. Weight loss is common, however renal function can be impaired, and it make you more susceptible to urinary tract infections.

When the addition of second medications don't work, insulin is often increased or another medication is added, depending on how close you are to the target A1c.

And now for insulin. Not every diabetic is prescribed insulin because it does nothing for them or it's too expensive, etc. However, insulin is an attractive treatment because there is no maximum dose, its associated with less weight gain, and it's easily adjustable. Insulin medication can come in basal insulin therapy or bolus insulin therapy. These types aid in either the basal insulin secretion or bolus insulin secretion that we had discussed in episode 1. Basal insulin therapies range from intermediate-acting or long-acting; they include Novolin, Levemir, Toujeo, Lantus, Basaglar, and Tresiba. Bolus insulin therapies include regular human insulin, rapid acting insulin analogs, or inhaled insulins.

As we saw in the risk section, there are a lot of comorbidities and complications associated with Type 2 Diabetes. Therefore, medication that treat diabetes must be compatible with these comorbidities. Sometimes, they even aid in treating them. A common one is antihypertensive treatment. Antihypertensives lower blood pressure. These include angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs). Both of these interfere with your body's natural mechanism for controlling blood pressure. In this case, they help your body control it better. Other medications that treat hypertension are thiazide diuretics, beta blockers, or calcium channel blockers.

The last medication I want to discuss is incretin-based therapy. Incretin-based therapies are not commonly prescribed because they are so new to the market. Studies have shown them to be

good at lowering blood glucose, TAGs, and cholesterol, however they can be really expensive and are not that effective for those with advanced diabetes. There are three types of incretin-based therapies: GLP-1 receptor agonists and DPP-4 inhibitors. GLP-1 receptor agonists increase glucose absorption during digestion and insulin production. DPP-4 inhibitors prevent the breakdown of the enzymes that aid in glucose absorption and insulin production. Known side effects of incretin-based therapies include pancreatitis and medullary thyroid cancer in animal studies, nasopharyngitis, UTIs, headaches, and heart failure. However, there is minimal weight loss or gain, nausea, and low risk of hypoglycemia. GLP-1 receptor agonists include Trulicity, Victoza, and Ozempic, while common DPP-4 inhibitors include Januvia and Tradjenta.

Other diabetic medications that I will not discuss, but still out there, include amylin0mimetics, bile acid sequestrants, and bromocriptine.

And that concludes the treatment of Type 2 Diabetes. If you want more information about treatment options and physiological foundation, there are specifics that I did not include in this podcast in the paper that I wrote along side this podcast.

Topic #2: Adherence

Alright so last topic of this miniseries: Adherence. Adherence is probably the hardest thing to do when diagnosed with any disease. However, do not be discouraged! You're bettering your chances by listening to me drone on and one about Type 2 diabetes than if you had not! Otherwise, one of the first steps you can take is to get a health care provider than you trust, who is aware of your own values and attitudes, and is willing to talk to you about your health. As I had described earlier, health literacy can have a huge impact on how well you maintain your good health behaviors. Having a provider that makes understanding easier, is the best way to start off.

Another important factor: self-efficacy. Self-efficacy is the belief in oneself that they can accomplish their goals and change their environment. Without self-efficacy, there is simply no chance to improve ones' habits. You have to believe in yourself. Improving self-efficacy can be done by accomplishing small goals first, having an amazing social support system, and just being more knowledgeable about your situation. What you should NOT do is adjust your medications yourself or belittle the seriousness on your disease. This detract from self-efficacy, and can be really harmful to your health.

Closing remarks:
And there you have it folks! The end of this miniseries. I hope you learned a lot, that some things were cleared up for you, and that you are empowered to better your own health!