Diabetes Basics

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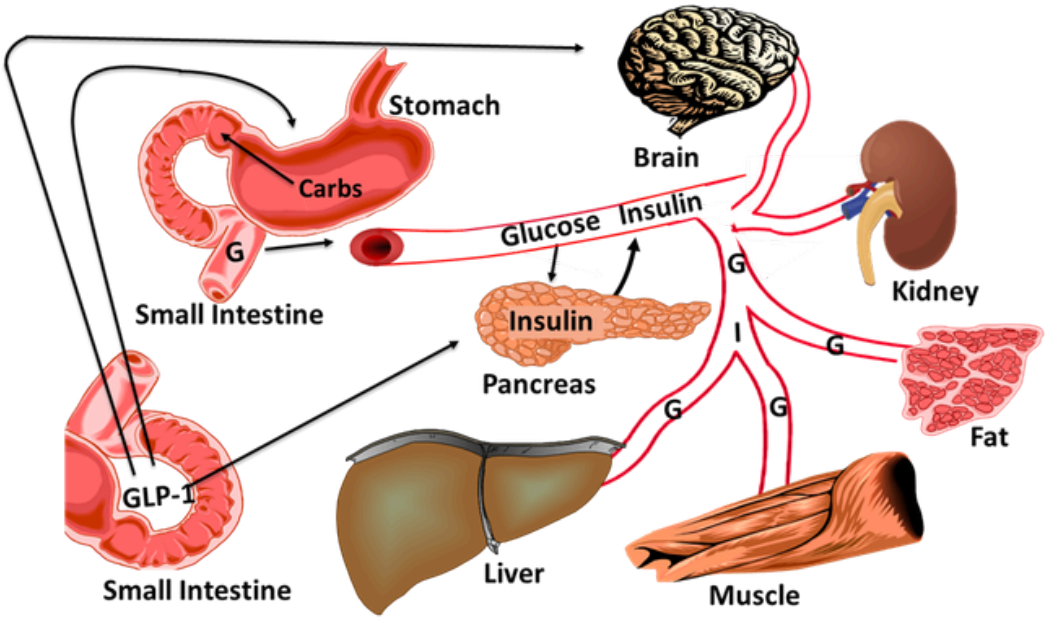
Part 1: What is Glucose?

Glucose is a simple sugar molecule or carbohydrate that is present in many foods. Like other animals, humans use glucose as a form of energy. Glucose molecules circulate through the body and provide the energy that the brain, muscles, fat and other organs need to properly function. Indeed, the brain is the biggest user of glucose in humans. Without sufficient glucose levels through the circulation, the brain and other organs will die within a few minutes. Glucose is therefore a crucial molecule for health. Low levels of glucose in the blood (hypoglycemia) can be immediately fatal; high levels (hyperglycemia) can cause long-term serious health problems. The body has therefore evolved many mechanisms that keep glucose levels within the narrow, normal range of 4 to 8 mmol/L. These are shown in the figure.

Figure: Controls for Glucose Levels

Legend: G – glucose; I – insulin; Carb - carbohydrate



Glucose enters the body with food. After food is broken down by the stomach and small intestine, the glucose molecules are absorbed into the blood stream (shown as blood vessels in the figure). The glucose molecules first go to the liver, which stores some of the glucose as starch, and allows the rest of it to enter the circulation. Once in the circulation, the level of glucose is closely monitored by cells in the pancreas called beta cells. Levels above 4.5 mmol/l stimulate the beta cells to make and secrete insulin into the circulating blood. The insulin then lowers the level by promoting removal of glucose from the bloodstream by muscle, fat, and other organs. It also signals the liver to keep all its stored glucose from entering the blood.

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What is Glucose? - Continued

The main signal that tells the pancreatic beta cells to make insulin is the glucose level. This signal is magnified by another hormone called GLP-1 (which stands for glucagon-like peptide-1). This hormone is made by the intestine when food enters the intestine and signals the beta cells to make more insulin. It also signals the body that food is being eaten by telling the brain to reduce appetite, and the stomach to retain the food until it is digested. This helps reduce overeating and prevent high glucose levels.

Insulin is the key signal that lowers glucose levels. If glucose levels go too low, several hormones signal the liver to secrete some of its stored glucose into the bloodstream. These hormones include glucagon, steroids, and adrenaline. Once glucose rises above 4.5, levels of these hormones fall as levels of insulin rise. Diabetes develops when the beta cells of the pancreas are unable to make enough insulin to keep the glucose from rising, The next blog in the series discusses the definition of diabetes in more detail.

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Part 2: The Definition of Diabetes

The first piece in this blog series describes how someone without diabetes maintains glucose levels within the tight normal range of 4 to 8 mmol/L. Persistently higher glucose levels mean the beta cells of the pancreas can't make enough insulin to keep glucose from rising. A diagnosis of diabetes is made when the glucose level after an 8 hour fast is 7 mmol/L or higher, and when glucose levels at any time are 11.1 mmol/L or higher. Diabetes is also diagnosed when a test called the hemoglobin A1c level or the A1c level - which is an index of typical glucose levels in the last 3 months - is 6.5% or higher. Glucose levels or A1c levels that are higher than normal but lower than the diabetes cut offs indicate that the person has prediabetes meaning that their glucose levels are not high enough to be called diabetes but are still higher than perfectly normal. These criteria are summarized in the table.

Diagnostic Criteria or Thresholds for Diabetes	
Persistent Fasting Glucose Levels after an 8 hour fast	7.0 mmol/L or higher
Persistent Random Glucose Levels	11.1 mmol/L or higher
Persistent Hemoglobin A1c or A1c levels	6.5% or higher

But where did these criteria come from? The observation that people can develop a disease that is linked to high sugar levels goes back to antiquity, well before anybody could measure glucose or any sugar. Indeed, the word diabetes mellitus reflects ancient observations that there were some people who urinated frequently, and whose urine was sweet smelling. Indeed, the word diabetes literally means "the flowing of sweetness". The 19th century saw the development of urine tests for glucose and the recognition that high levels were linked to medical problems like blindness and foot infections. Subsequent studies done over the next 100 years showed that abnormal blood vessels in the back of the eye began to appear once glucose levels rose above the numbers in the table. That was the basis for choosing glucose thresholds that are used today to distinguish people with diabetes from those without diabetes.

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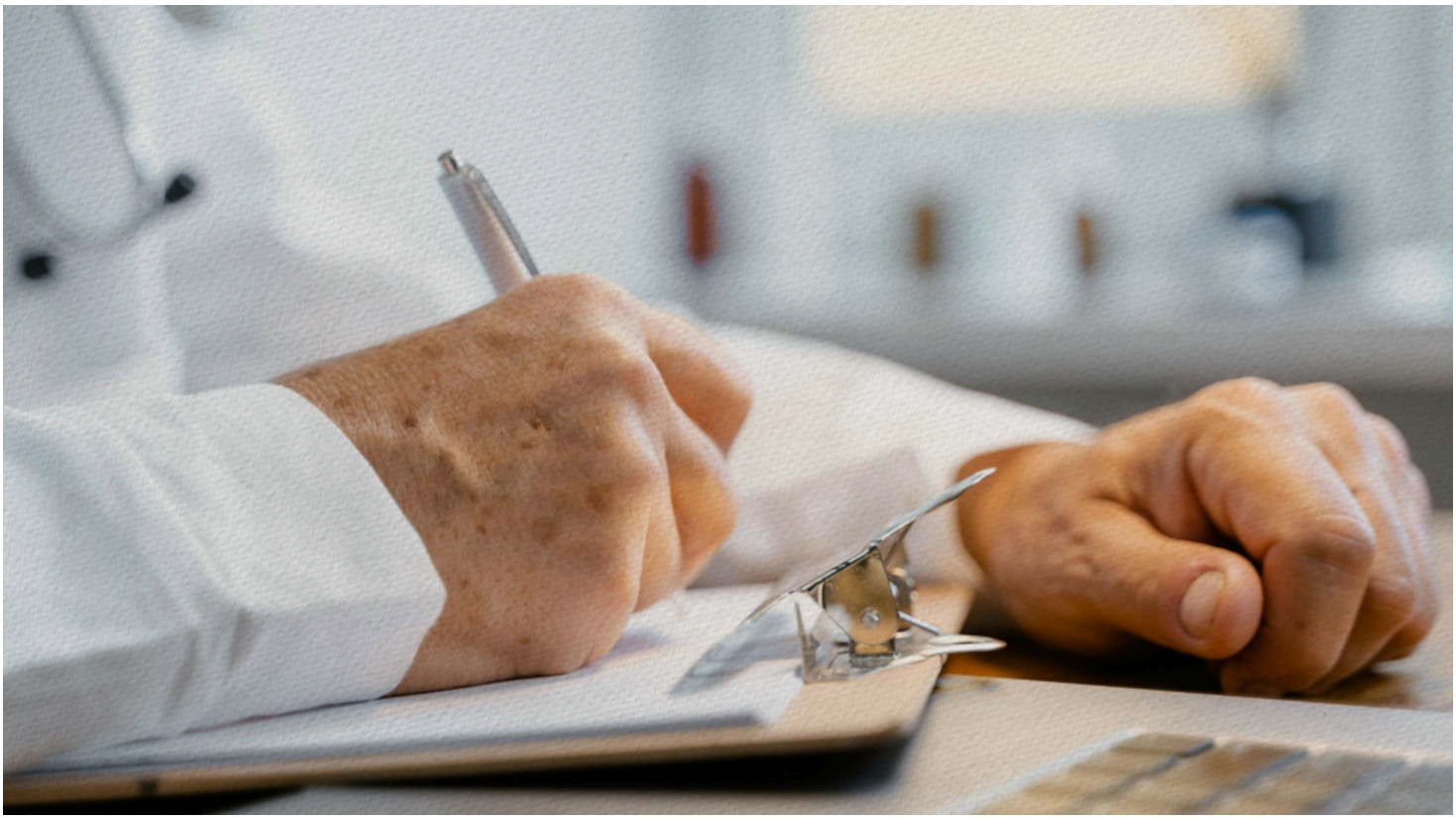
The Definition of Diabetes - Continued

Strictly speaking, therefore, the diagnostic glucose levels for diabetes were chosen because higher levels promote abnormal changes in the back of the eye. However, it turns out that diabetes-range glucose levels put people at much higher risk of a wide range of long-term health problems including blindness, kidney failure, amputations, heart attacks, strokes, dementia, and other problems. In addition, high glucose levels can acutely cause dehydration, low energy level, reduced well being, and a variety of infections.



The good news is that medicine has developed a wide range of diet, activity, and drug related therapies that can very effectively reduce glucose levels into the normal in people with diabetes. These will be discussed in the next piece.

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Part 3 - How is Glucose Measured?

Diabetes is diagnosed when the level in the blood is persistently higher than the thresholds described in the last blog. So how is the glucose level measured?

First, the glucose level at a point in time can be measured in a standard blood sample, in which the amount of glucose is detected by another chemical (the enzyme glucose oxidase) that binds to it. Second, this enzyme can be used to measure the level in a drop of blood from a finger prick.

Third, the glucose oxidase enzyme can be bound to a tiny metal or plastic needle that is inserted just under the skin, and that detects the level of glucose repeatedly throughout the day (instead of just at one point in time). This is what happens with continuous glucose monitoring (CGM) technologies. Every time the enzyme detects glucose it activates an electrical signal that indicates the level – the higher the level, the stronger the signal. Note that CGM detects glucose in the fluid under the skin that comes from the blood, but not in the blood. Therefore, the glucose needs to leave the blood vessel before it can be detected, and this can take time. That is why people who wear a CGM notice that levels take about 15 to 30 minutes to rise after eating or drinking.

Finally, one other way is routinely used. The test is called the hemoglobin A1c level. It does not directly measure glucose. Instead, it measures a type of hemoglobin (which is a protein in red blood cells that transports oxygen from the lungs to the body) called hemoglobin A1c. This protein - also called the A1c - binds to glucose levels and tightly sticks to it. So people with higher average glucose levels in their blood have higher A1c levels. Because A1c levels fluctuate a lot slower than the glucose levels, it is a good test of the average glucose levels over a 2–3-month window. Importantly, the A1c level is not the same thing as the glucose level and should be thought of as an indicator or index that is linked to it, in the same way that body weight is an indicator of the amount of muscle or fat.

In summary, glucose can be measured in a blood tube, a drop of blood, or under the skin with CGM. The A1c can also provide an indicator of the average amount of glucose in the prior 2-3 months. These tests are used to guide and assess glucose management in people with diabetes.

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Part 4 - How Common is Diabetes & Why Does it Develop?

Unfortunately, diabetes is extremely common. Approximately 1 in 10 people aged 20 and over throughout the world have diabetes. This is an average with numbers varying by age, country, ethnic origin or ancestry, weight, weight distribution, socioeconomic status, and medical history. In Canada the number is 1 in 10 adults, and 1 in 5 over 65. Notably, these rates have been rising and have doubled from 1 in 20 adults to 1 in 10 adults over the last 30 years. These statistics apply to type 2 diabetes; type 1 diabetes accounts for about 5-10% of all people with diabetes, affecting between 1 in 100 to 1 in 200 adults in Canada.

So why does diabetes develop? Unfortunately, we do not have a simple answer. The best answer is that diabetes emerges from interactions between an individual's composition or make-up (including their genetics, their parents, their development, and other unknowns) and their environment (including geography, economics, availability of types of food, opportunities for physical activity, daily routines, and other unknowns). There is no one thing that causes diabetes just as there is no one thing that causes a weather system

Regardless of the "why", the information in the first blog in this series illustrates the "how" of diabetes. In people without diabetes, glucose levels are kept from rising by insulin that comes from the pancreas. Diabetes develops when your pancreas is unable to make enough insulin to keep your glucose levels in the normal range.

The next blog discusses the symptoms of a high glucose level and when to suspect and screen for the possibility of diabetes.

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Part 5 - What Are the Symptoms of Diabetes and When Should it Be Suspected?

Diabetes is a disease defined by an elevated glucose level. The symptoms that people experience as a result depend on the degree of elevation – higher levels usually mean more symptoms, but this varies from person to person. Unfortunately, these symptoms are not specific. Thus, they could be due to a wide variety of different conditions instead of diabetes. The good news is that a simple blood test for glucose or A1c can easily rule diabetes in or out.

The most common symptoms of diabetes include:

- Excess urination
- Getting up more than 2 times per night to urinate
- Excess thirst and more frequent episodes of dehydration
- Intermittent blurriness of vision or change in glasses prescription
- Low energy, excess sleepiness, headaches, or tiredness
- Unexplained weight gain or weight loss
- Increased hunger
- Yeast infections in the groin or other areas
- Urinary tract infections
- Numbness or tingling in the hands or feet

Anyone experiencing anything in the list can easily ask their doctor to check for diabetes with a simple blood test. If the glucose and A1c is normal, it means the symptoms are not due to diabetes and other reasons need to be sought.

Finally, because diabetes is so common and because it rises with age and is associated with many serious diseases, most doctors will test for diabetes in middle-aged and older adults every year, or at the time of hospitalization for any reason, or when any new serious disease is diagnosed.

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Part 6 - What Are the Long-Term Health Consequences of Diabetes?

As discussed previously, diabetes is very common and can cause a variety of non-specific symptoms. These may be obvious and interfere with sleep or daily routines. Or they may be so subtle that affected people may ignore them. As a result, about 1 out of 4 Canadians with diabetes do not know that they have it. This is because they've never been tested for it. Unfortunately, not knowing that you have diabetes doesn't protect you from its consequences. And diabetes can indeed lead to a wide variety of serious health problems over time. The good news is that detecting and optimally treating diabetes has been proven to clearly reduce the severity and frequency of many of these problems.

The table below provides a list of serious health outcomes that occur more frequently or at a younger age in people with diabetes than in people without diabetes. Note that the table shows all possible things that might occur over a lifetime. Because these outcomes also occur in people without diabetes as they age, many doctors think of diabetes as a disease that can accelerate or speed up the aging process. Most importantly, evidence that modern therapies can reduce the likelihood of many of these outcomes suggests that they may slow this aging process.

Long-term Health Consequences of Diabetes		
Blindness	Heart attack	Hip Fractures
Cataracts	Heart failure	Imbalance & Frailty
Kidney failure	Stroke	Arthritis
Foot ulcers	Cancers	Erectile Dysfunction
Chronic foot pain	Cognitive Decline	Sexual Dysfunction
Leg/Foot amputation	Depression	Infertility
Liver cirrhosis	Sleep Apnea	Constipation or Diarrhea

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What Are the Long-Term Health Consequences of Diabetes? - Continued

In addition to the problems in the table, one other important problem may not be recognized by people with diabetes and their healthcare provider. This is the emotional, mental, and financial, cost of dealing with diabetes over many years. Many people with diabetes feel guilt or shame about having diabetes or about how they are treating it. Moreover, even with the best drug plans, people with diabetes need more doctor visits and spend more money than unaffected people. **As stated elsewhere on Knowing-Diabetes.com, people are not to blame for having or developing diabetes. And if they are doing their best to manage it, that is good enough.**

The next piece will discuss proven ways to reduce the likelihood of these problems from ever developing.

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Part 7 - What Causes the Long-Term Consequences of Diabetes and How Can They Be Delayed or Prevented?

In the last piece we listed the long-term health consequences of diabetes. Because diabetes is, by definition, a disease that is defined by high glucose levels, exposure of the body to higher-than-normal glucose over long periods of time does cause many of these serious health consequences. But like everything in medical science, it's not that simple. The abnormal regulation of glucose levels by the body leads to many other changes. These contribute to some or all the serious health consequences in poorly understood ways. The good news is that medical science does not need to understand why something occurs before it can identify ways to reduce or delay it from occurring. That is indeed the case for many of the long-term health consequences of diabetes.

Therapeutic approaches that are currently proven to reduce or prevent these consequences are listed in the table. As shown, they can be easily by remembered by the memory code: "ABCDE-S".

The ABCDE-S of Reducing Serious Long-term Health Problems in Diabetes

Code	Meaning	Explanation
A	A1c	Optimal glucose or A1c levels for you
B	BP	Optimal blood pressure control for you
C	Cholesterol	Optimal LDL levels using statins or other drugs for you
D	Drugs	Drugs proven to prevent serious outcomes
E	Everyday	Eating patterns and routine exercise or physical activity
S	Stop Smoking	Smoking magnifies the risk of diabetes
S	Screening	For eye disease, and foot disease by routine exams
S	Self Care	Taking charge of diabetes with the healthcare team

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What Causes the Long-Term Consequences of Diabetes and How Can They Be Delayed or Prevented? - Continued

Everyone is different and the optimal combination of approaches for one person will not be optimal for another. The best way to personalize or tailor the right approach is by working closely with your healthcare team.

The next piece will focus on the drugs that are available in Canada to lower glucose levels and how they work.

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Part 8 - What Tools Can Effectively Lower Glucose Levels?

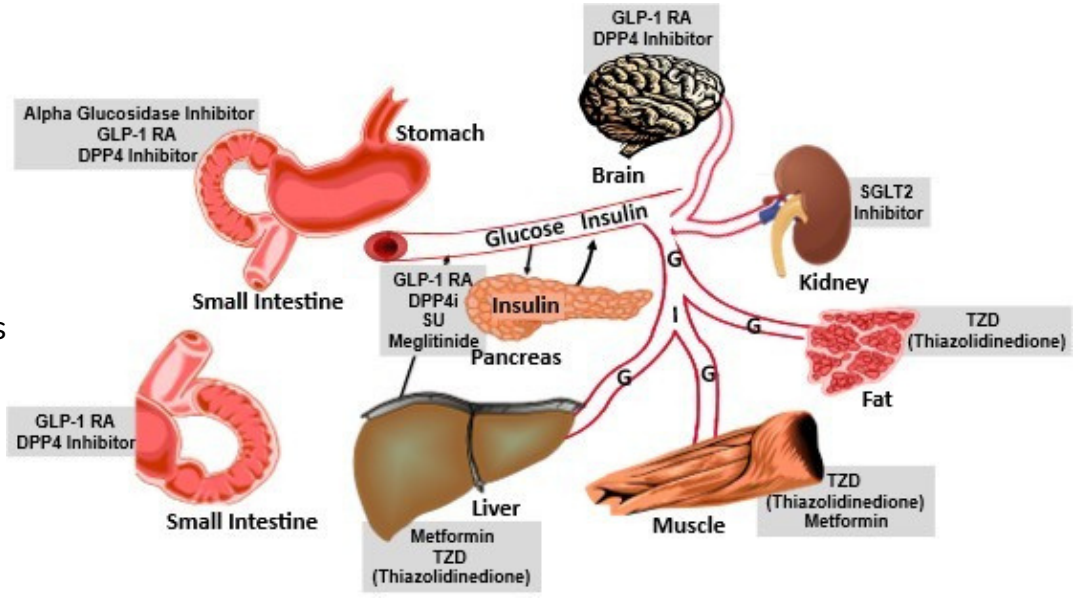
Several blogs on Knowing-Diabetes.com discuss the role of modest changes in diet, physical activity, weight, and the benefit of CGM for achieving good glucose levels. These represent the foundation upon which an optimal regimen can be built, and like any foundation, it needs to be firm. Other blogs discuss specific glucose lowering drugs. This blog provides an overview of all the drugs that are currently approved for glucose lowering in Canada.

Nine classes or categories of drugs are currently approved in Canada for lowering glucose levels in people with type 2 diabetes. Of these, only insulin is approved for type 1 diabetes. The table and figure summarize these drug classes and show the organs that they affect the most. There are clearly many other effects that cannot be captured in a short piece such as this. Nevertheless, thinking about the drugs in this way can help understand the basis for combining different classes of drugs.

Classes of Glucose Lowering Drugs	
Metformin	Thiazolidinedione (TZD)
Sulfonylureas (SU)	DPP4 Inhibitor (DPP4i)
Meglitinides	Glucagon-like Peptide-1 Receptor Agonist (GLP-1RA)
Insulin	SGLT2 Inhibitor (SGLT2i)
Alpha glucosidase Inhibitor (AGI)	

Note that one can mix and match most of these with guidance from the health care team. The main exception is DPP4i and GLP-1 RAs (because they have similar effects on the organs).

Figure:
Main Sites of Action of Glucose Lowering Drugs



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Part 9 - Diabetes Care is Preventative Care

I began this 9-part primer on diabetes by describing how a healthy individual maintains normal glucose levels. I then focused on the basics of diabetes. To review, diabetes is a chronic disease that develops when the body can no longer maintain normal glucose levels. The high glucose levels can make you feel unwell. Over time, glucose plus a wide variety of known, suspected, and unknown factors increase the chance of developing a wide variety of serious health problems throughout life. These can affect almost any organ in the body. They also include several emotional and mental consequences such as shame, guilt, depression, and anxiety in addition to the financial and logistical burdens of dealing with a chronic disease throughout a lifetime. The fact that diabetes is so common and that both type 1 and type 2 diabetes rates are rising means that more than 1 in 10 Canadians are wrestling with these concerns. That's the bad news.

The good news is that there is so much that people with diabetes can do to reduce and even eliminate the burdens of diabetes by working collaboratively with their healthcare team. Even better - this is only going to get easier and more effective with time due to ongoing medical research and innovation. Canadian medical researchers are in fact leading much of this work and Canada's contribution to improving the lives of people with diabetes is recognized around the world.

The bottom line and the most important message is that a diagnosis of diabetes is serious, stressful and upsetting. But it is not the end of the world. It is the beginning of an opportunity to work with the healthcare team to identify the best way to ensure that the next 20, 30, 40, or 80 years of life remain productive and healthy.

Diabetes care is preventive care. The ultimate form of diabetes care is diabetes cure or elimination, and at least complete remission. We are not totally there yet. But we are working hard to get there through ongoing clinical trials and related research being conducted all around the world.

https://knowing-diabetes.com/