

Genetics and Type 2 diabetes: Why weight loss alone may not be enough for some people

People who develop Type 2 diabetes fall into one of two categories — those whose blood sugar can be controlled with dietary and other lifestyle changes, and those whose blood sugar can only be controlled with medication. Doctors do not know which patients will respond to lifestyle interventions and which patients will not. New research could make the trial and error nature of Type 2 diabetes treatment a thing of the past.

A recent team effort by researchers based in Scotland, Sweden, the US, and Canada has led to the identification of a [genomic signature](#) in patients whose Type 2 diabetes status improved as a result of lifestyle interventions. The genomic signature was responsible for an increase in insulin sensitivity in these patients only, and not in those whose Type 2 diabetes status did not respond to lifestyle interventions.

Since the scientists were able to examine how certain genes associated with insulin resistance respond to treatment, they also “discovered a potential explanation for why not all people eliminate their [Type 2 diabetes risk](#) by following a lifestyle and exercise training program,” said Dr. Iain J. Gallagher, a member of the research team. Their findings will inspire future research and could also lead to changes in the clinical treatment of Type 2 diabetes.

[Type 2 diabetes](#) is a chronic illness that affects the way the body metabolizes glucose — the body’s main source of energy. The illness is caused by a complex combination of [environmental and genetic factors](#), and symptoms can include low energy, increased thirst and urination, headaches, trouble concentrating, vision difficulties, and weight loss. Some individuals will not have any symptoms until the disease has significantly progressed.

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A hallmark of Type 2 diabetes is insulin resistance, when [cells are not able to respond](#) to insulin, a hormone secreted by the pancreas that enables glucose to enter cells (where it is then converted to ATP). The body’s cells can no longer easily take up glucose, which then builds up in the bloodstream — a condition known as high blood sugar or hyperglycemia. The pancreas responds by making more insulin. This can allow for just enough glucose uptake necessary for proper functioning, but eventually the individual [may develop prediabetes](#) — a stage before Type 2 diabetes that affects nearly 1 in 3 adult Americans.

When the pancreas can no longer keep up with insulin production, [Type 2 diabetes develops](#). Some people who are on their way to developing Type 2 diabetes or have already received a formal diagnosis are able to achieve healthy blood sugar levels by making significant lifestyle changes. These lifestyle changes can include calorie restriction, changes to dietary composition, and/or increased physical activity. Others require medications like Metformin or insulin.

If left uncontrolled, Type 2 diabetes can lead to blindness, kidney failure, heart disease, nerve damage, and even the need for [amputation](#) due to tissue damage.

Though many typically presume that anyone with Type 2 diabetes can reverse their diagnosis by simply eating right and exercising — with some calling Type 2 diabetes the “[fat diabetes](#)” — science has shown that this is not always possible.

Dr. Andres Palacio, an endocrinologist with [Tenet Florida Physician Services](#), told Genetic Literacy Project that “lifestyle interventions are the cornerstone for diabetes management, but unfortunately — as we have seen in studies and in our everyday practice — adherence to lifestyle interventions has not been an effective strategy. We continue to see a rise in diabetes and obesity.”

Additionally, Palacio added, “diabetes has a strong genetic component and having a family member with diabetes is a strong risk factor for developing it.”

In a recent clinical trial called DiRECT (the UK’s Diabetes Remission Clinical Trial), participants with Type 2 diabetes were placed on a calorie restricted diet for a year. About 46 percent of the clinical trial participants achieved remission, or [non-diabetic blood sugar levels](#). The researchers stated that while weight loss can reverse the processes underlying Type 2 diabetes, remission of the illness depends on the beta cells’ ability to recover. [Beta cells](#) are pancreatic cells responsible for making and releasing insulin.

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In the 54 percent that did not achieve remission during the clinical trial, the researchers said that some did not lose enough weight, but this explanation did not account for the full 54 percent. Others lost a significant amount of weight, but this had no effect on their Type 2 diabetes status.

Dr. Eric Sodicoff, author of “The Phoenixville Nutrition Guide,” told Healthline that “identifying such patients early is ideal, and [the DiRECT] study clearly established that the longer a patient has lived with Type 2 diabetes, the less likely they are going to respond to a calorie-restriction method.”

What is clear is that Type 2 diabetes cannot be treated with a [one-size-fits-all](#) protocol. Researchers at the Broad Institute of MIT and Harvard and Massachusetts General Hospital recently found that there are “five distinct groups of DNA sites that appear to drive distinct forms of the illness in unique ways.” This means that there appears to be five Type 2 diabetes subtypes, each with its own underlying set of cellular processes, and each with its own unique clinical presentation.

“This study has given us the most comprehensive view to date of the genetic pathways underlying [Type 2 diabetes], which if not adequately treated can lead to devastating complications,” said [Miriam Udler](#), an endocrinologist at Massachusetts General Hospital.

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