They lost weight and did everything right, but one group still faces type 2 diabetes years later

April 24 2026, by Birgit Niesing

Credit: Pavel Danilyuk from Pexels

A healthy diet, weight loss, and increased physical activity can effectively prevent type 2 diabetes. However, not all individuals at

elevated diabetes risk benefit equally from lifestyle interventions. People classified in Tübingen's type 2 diabetes risk cluster 5 show rising blood glucose levels, the strongest decline in insulin secretion, and a persistently high risk of diabetes—even after years of stable and substantial weight loss.

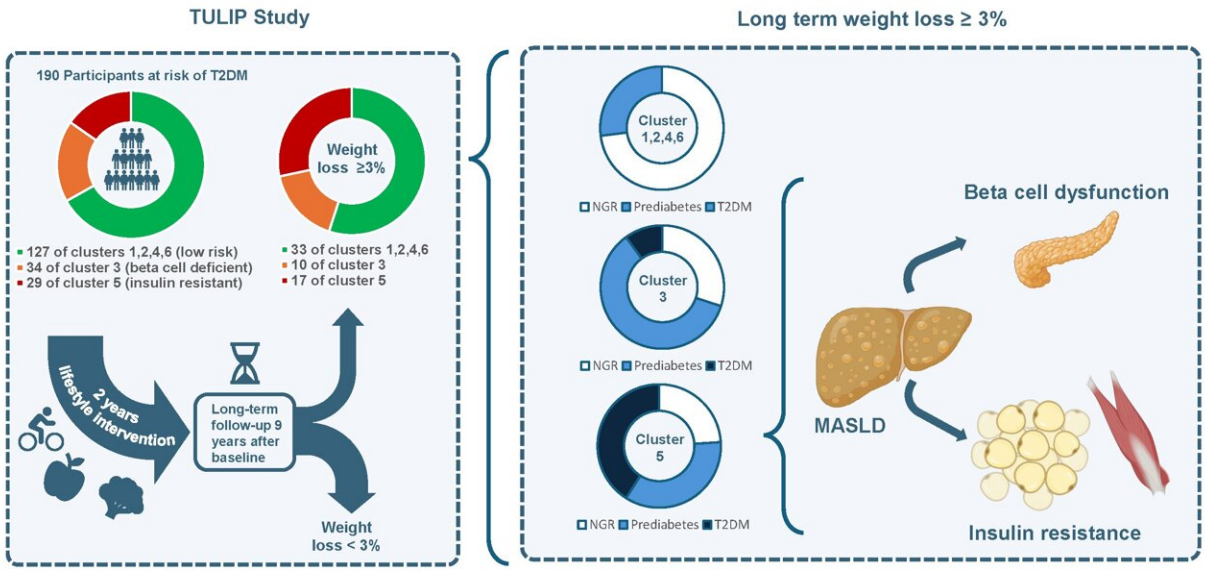
These findings are reported by researchers from the German Center for Diabetes Research (DZD), the University Hospital Tübingen and Helmholtz Munich in the journal *Diabetes*.

In a study published several years ago, DZD researchers were able to classify individuals with a risk of type 2 diabetes into six clearly distinguishable risk clusters that differ significantly in diabetes incidence, and the progression of diabetes-related complications. Among these, clusters 3 and 5 show a particularly high risk of developing type 2 diabetes.

In the current analysis, the research team investigated whether the effectiveness of prevention of diabetes also differs between risk groups in the context of sustained long-term weight loss.

Individuals in cluster 5 remain at high diabetes risk despite lifestyle changes

The study was based on data from the Tübingen Lifestyle Intervention Program (TULIP). Participants with an increased risk of type 2 diabetes completed a two-year lifestyle intervention and were subsequently followed for approximately nine years. The analysis focused on individuals who were able to achieve substantial and sustained long-term weight reduction.



Despite a sustained and large amount of weight loss, people in diabetes risk cluster 5 had deterioration of glycemia, the largest decrease of insulin secretion among the clusters and a high risk of T2D. Credit: Norbert Stefan, Created with BioRender.com

"We were particularly interested in whether individuals in risk clusters 3 and 5 differed from those in other clusters with regard to improvements in blood glucose levels and the prevention of type 2 diabetes," explains Professor Norbert Stefan, the lead author of the study.

"We were very surprised to find that, despite a large and sustained weight loss of 8% and after a very long follow-up period of nine years, individuals in risk cluster 5 showed increasing blood glucose levels, declining insulin secretion, and a persistently high risk of type 2 diabetes."

Fatty liver and insulin resistance may explain the findings

Why does lifestyle intervention protect individuals in risk cluster 5 less effectively against diabetes? The authors examined mechanisms that could explain the unfavorable metabolic trajectory observed in this group. Their data suggest that insulin resistance—most likely caused by pronounced fatty liver disease and fatty liver–related impairment of insulin secretion from pancreatic beta cells—led to rising blood glucose levels in individuals in cluster 5.

These findings are consistent with earlier observations showing that fatty liver disease and insulin resistance are the dominant pathophysiological mechanisms in individuals classified in Tübingen's type 2 diabetes risk cluster 5, making them particularly susceptible to type 2 diabetes and cardiovascular disease.

Precision prevention strategies are needed

The present results indicate that individuals in risk cluster 5 do not benefit to the same extent from lifestyle interventions as those in other clusters, even with significant and sustained weight loss—particularly with respect to glucose metabolism. If these findings are confirmed in a prospective study, a more tailored approach to diabetes prevention will be required, in which high-risk phenotypes such as cluster 5 may need more intensive or targeted interventions.

More information: Caroline Z. Meier et al, Different Metabolic Responses to Long-term Weight Loss After Lifestyle Intervention Among Type 2 Diabetes Risk Clusters: Results From the TULIP Study, *Diabetes* (2026). DOI: 10.2337/db25-0757

Provided by German Center for Diabetes Research