

New study reveals serious long-term complications in youth-onset type 2 diabetes

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Phil Zeitler, MD, Ph.D., has been treating youth with type 2 diabetes for more than 20 years. He and a team of researchers published a paper today on the TODAY2 study in the *New England Journal of Medicine* on

the long-term complications of type 2 diabetes. (TODAY stands for Treatment Options for type 2 Diabetes in Adolescents and Youth. The first phase of the study took place from 2004—2011; phase two from 2011—2020. Both studies involved more than 550 participants from across the country.)

Zeitler is the chair of the TODAY study group and is a professor of pediatrics, endocrinology at the University of Colorado School of Medicine and medical director of the pediatric Clinical and Translational Research Center at Children's Hospital Colorado, both located on the University of Colorado Anschutz Medical Campus.

The TODAY2 study focused on complications of youth-onset type 2 diabetes. Overall, researchers saw a steady decline in blood glucose control over 15 years. In addition,

- 67% of participants had high blood pressure
- nearly 52% had dyslipidemia, or high fat levels in the blood
- nearly 55% had kidney disease
- 32% had evidence of nerve disease
- 51% had eye disease.

Rates did not differ based on the original TODAY study treatment group assignment.

In addition, certain participants had a higher likelihood to develop multiple complications over time, with 28% developing two or more over the follow-up period. Participants who belonged to a minority racial or ethnic group, or who had high blood glucose, high blood pressure, and dyslipidemia were at higher risk for developing a complication.

The study shows that not only is the disease having an impact on youth and young adults at a young age, but it also shows a clustering of

complications. Eighty percent of participants had some complication. The majority had two, three or more complications.

"It is really critical for governments, policymakers, and healthcare systems to be prepared for what this means in terms of healthcare usage; loss of productivity years; loss of life; impact on families; unemployment; as well direct costs—a lot of money will be spent on these kids through dialysis, medications, cardiac bypass and more," Zeitler says.

When asked what he wants people to know about the disease, Zeitler says, "This is not grandma's type 2 diabetes."

He explains, "Youth-onset of type 2 diabetes is associated with an accumulation of diabetes-related complications such as eye disease, kidney disease, nerve disease and other co-morbidities like strokes, heart disease, amputations—and this is occurring at least as rapidly as in adults. Potentially more rapidly."

And as unimaginable as it may seem, teens diagnosed with the [disease](#), and who have lived with it for 10-12 years, have suffered strokes, kidney failure, heart attacks, toe and foot amputations—all while in their 20s.

The initial TODAY study was designed to look at the best treatment approaches: 1) metformin or 2) metformin plus rosiglitazone or 3) metformin plus a lifestyle intervention. Researchers followed the youth to determine the time to loss of glycemic control in participants who had onset of type 2 diabetes in youth. Glycemic control is a medical term referring to the optimal levels of blood sugar (glucose) in a person with diabetes mellitus.

At the time the study began in 2004, type 2 diabetes was a relatively newly recognized problem in adolescents.

"Even at that time, it was recognized that it [type 2 diabetes] seemed to be more aggressive in kids," Zeitler says. "Since they are going to live with it longer, we want good [glycemic] control as early as possible."

Researchers found that therapy with metformin alone was associated with durable glycemic control in only half of children and adolescents with type 2 diabetes. The addition of second pharmacologic agent, but not an intensive lifestyle intervention, was superior to metformin alone. Researchers found that it was very difficult for participants to change their lifestyles; many lived in very challenging home environments.

In 2012, the *New England Journal of Medicine* published the results of this initial study, which is considered a landmark in youth-onset type 2 diabetes. The guidelines that currently exist for the management of type 2 in youth are based on the results.

"The study was so foundational that it immediately translated into treatment recommendations," says Ronald Sokol, MD, director of the Colorado Clinical and Translational Science Institute (CCTSI). The CCTSI's pediatric Clinical Translational Research Center at Children's Hospital Colorado was crucial to the operation of these two studies that lasted 15 years.

The next step is to put together a new cohort of younger children to understand who gets type 2 [diabetes](#) to develop targeted interventions. Zeitler says, "If we want to do any kind of prevention, we need to have a better idea of who is at risk."

More information: , Long-Term Complications in Youth-Onset Type 2 Diabetes, *New England Journal of Medicine* (2021). [DOI: 10.1056/NEJMoa2100165](https://doi.org/10.1056/NEJMoa2100165)

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