PERSONAL PERSPECTIVE

Keisha: Contributing to Research on Long-Term Outcomes of Medical/ Lifestyle Management Versus Bariatric Surgery in Type 2 Diabetes

For 51-year-old Keisha, who resides in Pittsburgh, Pennsylvania, and works as a customer service representative for a large financial services and insurance company, family has always been important. In 1994, she and her husband welcomed twin girls, and 2 years later, a baby boy. Her first pregnancy resulted in a difficult delivery. "I almost died on the table," she recalled. When she became pregnant with her son, she felt that her doctor was not considering her complete health picture beyond her basic prenatal appointments. Notably, Keisha doesn't recall ever being screened for high blood sugar (glucose) or type 2 diabetes during either pregnancy. (More information on type 2 diabetes is provided at the end of this feature.) Her son weighed more than 9 pounds, and she experienced yet another very difficult delivery. Thankfully, all three babies were born healthy.

However, shortly after the birth of her son, Keisha began experiencing extreme fatigue and an overall loss of energy. Her symptoms were so intense that she lost her job at the time due to falling asleep at work. She sought out a new doctor who, based upon the results of her blood tests, suspected she may have developed gestational diabetes (a form of diabetes that develops during pregnancy and can lead to type 2 diabetes), and it had gone unrecognized and untreated. At age 23, Keisha was diagnosed with full-blown type 2 diabetes.

DEALING WITH DIFFICULT HEALTH ISSUES

The diagnosis of type 2 diabetes came as a surprise to Keisha as she had no family history of the disease, and she tried her best to maintain a healthy diet. However, she had a difficult time losing the weight she had gained after the birth of her son, despite her efforts. To get her blood sugar under control, her doctor prescribed insulin (a hormone treatment commonly used in people with type 2 diabetes), but her blood sugar continued to rise. Keisha's type 2 diabetes was difficult to manage, especially while she was caring for three young children, and she developed other health problems associated with excess weight. She had trouble breathing and could barely climb a flight of stairs. She also developed fibromyalgia, a musculoskeletal condition commonly diagnosed in women and people with type 2 diabetes that causes pain throughout the body, fatigue, and trouble sleeping.

PARTICIPATING IN CLINICAL RESEARCH AND UNDERGOING BARIATRIC SURGERY

After years of health issues, Keisha began seeing a new doctor at the University of Pittsburgh Medical Center (UPMC) who suggested bariatric surgery, also called metabolic surgery, to manage her obesity and

type 2 diabetes. She was told about a randomized clinical trial, being conducted right there at UPMC, that was designed to compare initial outcomes of bariatric surgery versus a structured weight-loss program for people with type 2 diabetes and overweight or obesity. Her doctor explained that the trial, called the Triabetes study, was randomizing participants into one of three interventions—one of two different surgical procedures or an intensive lifestyle weight-loss intervention. Keisha knew this meant there was no guarantee she would be assigned to one of the surgery groups. But she saw this as an opportunity to potentially improve her health and contribute to clinical research. So, in 2010, she enrolled in the study and underwent Roux-en-Y gastric bypass surgery, a type of bariatric surgery that staples the stomach to create a small pouch that holds less food and bypasses the rest. "I felt so lucky about my assignment! I was excited and ready to get back to my old self," she exclaimed. And that she did.

"Without these studies, my health would not be what it is today.... They gave me a lot of life back to raise my family," Keisha said, referring to her participation in clinical research.

Keisha underwent an initial assessment 2 weeks after surgery and then every 3 months for 1 year after her surgery, consistent with standard practice. At the follow-up visits, she was weighed, had her blood pressure checked, and had blood drawn. She was also counseled for lifestyle modifications, which included a diet program and increased physical activity. Keisha changed her diet, adhered to instructions, and noticed results almost immediately. She lost a substantial amount of weight, going from 170 to 125 pounds, and, remarkably, her type 2 diabetes went into remission—she no longer needed any medication to treat the disease.

THE UPS AND DOWNS OF TYPE 2 DIABETES AND OVERWEIGHT/OBESITY

A few years after the Triabetes study concluded, study coordinators approached Keisha and asked her if she would be willing to participate in a follow-up observational study, the Alliance of Randomized Trials of Medicine versus Metabolic Surgery in Type 2 Diabetes, or ARMMS-T2D. This study would combine data from four independent randomized trials conducted across the United States, including the Triabetes study, with a goal of determining long-term blood sugar control and safety and efficacy of surgery compared to lifestyle intervention for people with type 2 diabetes and overweight/obesity. Keisha jumped at the chance. "The study coordinators kept me grounded ... they made sure I kept doing what I needed to do to stay healthy," she said. And so, in 2016, she enrolled in the ARMMS-T2D study.

"The study coordinators kept me grounded ... they made sure I kept doing what I needed to do to stay healthy," Keisha said, referring to her decision to continue in the ARMMS-T2D study.

Everything was going very well for Keisha. For several years after her surgery, she experienced good health. And then the COVID-19 pandemic swept the world, presenting unprecedented challenges. Like many others, Keisha found it difficult to maintain her healthy habits. She began snacking frequently, and the weight she had lost crept back on. Even worse, her blood sugar increased significantly, and her diabetes was no longer in remission. But Keisha persisted. She began working closely with ARMMS-T2D study staff, and she remained diligent about going to follow-up appointments. "My doctor ... she really listens to me. She did what we needed to do to get things right," Keisha remarked. She worked hard to lose weight, and she began taking insulin. Her HbA1c

level (a measurement of blood sugar), which had been very high at 12 percent, dropped to 7 percent—an impressive accomplishment. She hopes to lose another 10 pounds and be medication-free once again.

"Before I joined these studies and had surgery, I had no strength. I was always tired. And now I have so much energy to play with my grandson!" Keisha said about her participation in clinical research.

When asked how she feels today, Keisha replied, "Before I joined these studies and had surgery, I had no strength. I was always tired. And now I have so much energy to play with my grandson!" Keisha is looking forward to a happy, healthy future. She plans to get out more, perhaps take a vacation, since the pandemic kept her isolated for so long. When asked what she would say to others who may be considering participating in a clinical trial, Keisha added, "Without these studies, my health would not be what it is today.... They gave me a lot of life back to raise my family."

More Information on the Alliance of Randomized Trials of Medicine Versus Metabolic Surgery in Type 2 Diabetes: ARMMS-T2D

Type 2 diabetes develops when the body can no longer overcome "insulin resistance" to keep blood sugar (glucose) levels from getting too high. Our bodies extract energy from the foods we eat, converting it into the form of blood sugar that is the main fuel used by our body's cells. The hormone insulin is made by the pancreas and acts in the tissues of the body (*e.g.*, muscle) to promote absorption of sugar from the blood. In some people, their bodies can become resistant to insulin, requiring the pancreas to produce more of the hormone to keep blood sugar at a healthy level. Type 2 diabetes occurs when the pancreas loses its capacity to produce enough insulin to compensate for the body's insulin resistance.

Type 2 diabetes and obesity continue to rise in the United States and worldwide, causing significant comorbidities such as cardiovascular disease and kidney disease, and they are a driving force behind preventable deaths. Together, type 2 diabetes and obesity contribute to substantial individual health burden and societal health care costs.

Despite recent advances in medications that achieve weight loss comparable to bariatric surgery, the drugs are costly and require continued use to maintain weight loss. In addition, their longer-term risks and benefits are still being evaluated. Several small randomized clinical trials (RCTs)—the gold standard for studying causal relationships between interventions and outcomes—and observational studies have suggested that bariatric surgery is superior to medical and lifestyle therapies for treatment of type 2 diabetes. But observational studies do not prove cause and effect, and the RCTs have been limited in number, participants enrolled, type of surgery, and follow-up duration. Therefore, long-term studies comparing bariatric surgery with a newer generation of medications (*e.g.*, GLP-1 agonists) for weight loss are needed. But, for now, despite increasing evidence supporting surgical options, many clinicians do not recommend surgery unless a person has a body mass index (BMI, a measure of weight relative to height) of 35 kg/m^2 or higher.

To evaluate long-term efficacy, durability, and safety of bariatric surgery to treat type 2 diabetes, the NIDDK-supported Alliance of Randomized Trials of Medicine versus Metabolic Surgery in Type 2 Diabetes (ARMMS-T2D) consortium

PERSONAL PERSPECTIVE

combined data from four, independent, single-center, randomized trials conducted in the United States between May 2007 and August 2013. The original studies (including the Triabetes study discussed earlier in this feature) evaluated the effectiveness of bariatric surgery compared to intensive lifestyle and medication therapy involving oral and injectable diabetes medications, including insulin, for adults with type 2 diabetes and overweight/obesity. While some participants in the study were prescribed GLP-1 agonists to help control blood sugar and boost weight loss as part of their medical management of diabetes, these drugs were not specifically examined in the study. Investigators from the four original studies pooled their results to provide a larger and more geographically diverse dataset. Follow-up data were collected through July 2022.

In total, 262 participants from the original studies enrolled in ARMMS-T2D. About 60 percent were randomized to surgery and underwent one of three different surgical procedures. The remaining participants were randomized to a medical/lifestyle management group with an intervention that had previously been shown to be effective for weight loss. Results were measured at 7 years with continued follow-up for 12 years.

At 7 years, participants who underwent surgery had an average 20 percent weight loss compared to 8 percent in the medical/lifestyle group. The surgery group had greater improvements in blood sugar control, measured by HbA1c, with 54 percent achieving an HbA1c of less than 7 percent, compared to only 27 percent of participants in the medical/lifestyle group. More participants who had surgery achieved diabetes remission compared to participants in the medication/lifestyle group, and the percent of participants using medications to treat diabetes in the surgery group decreased from 98 percent to 61 percent yet remained largely unchanged in the medication/lifestyle group. The results and differences between groups remained significant at 12 years.

The ARMMS-T2D findings provide important insights about the benefits of bariatric surgery in people with type 2 diabetes and obesity and exemplify how public investments in research can lead to clinical advances and long-term health improvements for millions of Americans with these diseases.