

Study of type 2 diabetes medications show differences in medication acceptance, quality-of-life, insulin secretion

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DIABETES



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Diabetes affects more than 1 in 10—or more than 38 million—Americans. People with diabetes who keep their blood sugar levels in the near-normal range generally have a much lower risk of developing diabetes complications such as heart, kidney, and eye

diseases. The challenge is that most people with diabetes require more than one medication to control blood sugar levels over time.

The Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness, or [GRADE](#), study was designed to compare four major medications approved by the FDA to treat diabetes in combination with metformin, the usual first-line drug.

Major results focusing on the relative differences in [blood glucose](#) (sugar) levels and the occurrence of cardiovascular outcomes, like heart attacks and stroke, were published in two papers in *The New England Journal of Medicine* in September 2022. Subsequently, 10 scientific papers published in the April issue of *Diabetes Care* report further important differences between the four medications commonly used to treat type 2 diabetes.

The GRADE study was conducted at 36 U.S. centers and nine subsites between 2013 and 2021, including the Pennington Biomedical Research Center in Baton Rouge, and included more than 5,000 volunteer participants with type 2 diabetes from diverse racial and ethnic groups.

They participated over five years during which [insulin glargine](#), liraglutide, glimepiride and sitagliptin were compared.

Beyond the differences in blood sugar control between the four diabetes medications shown in the previous publications, the current findings examined individual characteristics that were associated with the achievement of lower and higher average blood sugar levels over time.

For example, the inability to maintain good blood sugar control was largely driven by younger age and higher blood sugar levels at baseline. Understanding these factors can help to identify people who would benefit from more aggressive diabetes management.

Another set of analyses revealed that adding liraglutide to metformin improved quality of life after the first year of treatment, but this benefit was subsequently lost. The improvement with liraglutide was related to the degree of weight loss, particularly in those who had the highest weight at baseline.

Of note, assignment to [insulin therapy](#) was well-accepted by the participants, with even better compliance than for the other medications, and there were no adverse effects of [insulin](#) therapy on the participants' distress related to diabetes. In fact, treatment with insulin and the other injectable medication, liraglutide, lowered distress related to diabetes. These findings largely debunk the myth that patients are intolerant of insulin therapy or that once started it diminishes quality of life.

The sensitivity to insulin action and insulin secretion from the pancreas' beta-cells are known to be important contributors to type 2 diabetes. Their respective roles were reported in separate papers. The loss of insulin secretion was critically related to the progressive worsening of [blood sugar control](#) with all four medications, with reduced insulin sensitivity contributing to the outcomes of treatment.

The two most common causes of death during the study were cardiovascular disease and cancer, with no differences among the four treatment groups.

"GRADE has previously shown which medications worked best at achieving and maintaining blood glucose targets over time. The current findings provide additional information regarding the relative benefits and risks of the medications which should help patients and their health care providers choose the best medication to treat their diabetes," said GRADE Study Chair Dr. David M. Nathan, director of the Massachusetts General Hospital Diabetes Center.

Drs. William Cefalu and Daniel Hsia served as Principal Investigators of GRADE, along with Dr. Frank Greenway and Celeste Waguespack as co-investigators. The entire Clinical Trials Unit at Pennington Biomedical was also instrumental in successfully completing the study.

"Diabetes and obesity are two major diseases that we study every day at Pennington Biomedical. Learning more about the medications currently being used to treat these diseases is an important step toward eliminating them completely," said Pennington Biomedical Executive Director John Kirwan.

"We thank everyone who volunteered to participate in the GRADE study and all the people at Pennington Biomedical and the other research sites across this country who worked in this important study."

More information: [GRADE study overview](#)

Provided by Louisiana State University

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