

Summary for patients:

Hemkens LG, Grouven U, Bender R, Günster C, Gutschmidt S, Selke GW, Sawicki PT. Risk of malignancies in patients with diabetes treated with human insulin or insulin analogues: a cohort study. *Diabetologia* (2009).

Insulin analogues and cancer: the possibility of a link needs further investigation

Everyone who has type 1 diabetes and some people who have type 2 diabetes are dependent on using insulin medication. Insulin is a hormone. Insulin is absolutely essential for the body to be able to convert food into energy.

Human insulin has been in wide use for decades and its safety is well-established. Modified forms of human insulin have also become available since the 1990s. They are called insulin analogues. Some newer insulin analogues have only been used for a few years.

The slight modifications in the chemical structure of insulin analogues mean that they act a little differently. However, they do not control diabetes better than human insulin.

A study from Germany has raised questions about a particular insulin analogue, and whether it could accelerate the development of cancer. These questions need to be investigated in long-term rigorous trials that compare what happens to patients using different types of insulin analogues.

What did the researchers study and what were their conclusions?

The researchers did not do a trial or scientific experiment. They studied the data from Germany's largest statutory (public) health insurer which had been collected between 1998 and the middle of 2005. This gave them information on nearly 130,000 people from all around Germany who had started using insulins, and who had not had a cancer diagnosed before 2001.

The research identified a statistically significant link between the people who had a cancer diagnosed and the people who had used the insulin analogue glargine (brand name Lantus). Glargine came into use in Germany in 2000. There were not as many people using any of the other insulin analogues on their own, so that the researchers could only draw more definitive conclusions about glargine.

How many additional cases of cancer could have occurred? Compared with people using similar doses of human insulin, out of every 100 people who used glargine alone over an average of about one and half years, one additional person was diagnosed with cancer. This increase was not explained by any of the other drugs they were known to be taking, or by any other factor that the researchers found in the database.

Some studies by other researchers have found an increased cancer risk with insulin analogues, and other studies have not. The researchers of this much larger new German study therefore concluded that definitive research that can provide answers about the long-term impact of all insulin analogues is urgently needed.

Why do the researchers think it is possible that the insulin analogue glargine affects people's risk of cancer?

There are two main reasons the researchers think this link needs investigation:

- The increase in cancer was “dose-dependent”. That means when people used higher doses of that analogue, the rate of people who got cancer increased as well. If a drug does harm, and a higher dose does even more harm, then that is a sign that the problem could be linked to that drug.
- Insulin analogues act differently than human insulin. The analogues have been shown in laboratory studies to be more “mitogenic”. That means they could encourage cells to split into two identical cells and so make tumours grow more quickly.

The researchers stress that they have not proven that any one particular type or brand of insulin leads to a large increase in cancer.

What are the implications of these results for patients currently using insulin analogues?

The researchers do not recommend that people with diabetes stop using insulin. They also stress that there is no cause for alarm: there are several alternative insulin preparations patients can use. The researchers suggest that these alternatives could be considered until there is more convincing data on the safety of analogues.

Glargine (Lantus) is a long-acting insulin analogue that is injected once a day. People with diabetes have a number of other options:

- In type 1 and type 2 diabetes: Using long acting human insulin or a mixture of long- and short-acting human insulin twice a day instead of the once-daily analogue.
- In type 2 diabetes: Managing their diabetes with short-acting human insulin before meals only.
- In type 2 diabetes: Losing weight so that they might need less insulin medication (or even none at all).

The researchers stress that no one should stop using insulin without speaking with their doctor first.

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The authors of this research come from Germany's national Institute for Quality and Efficiency in Health Care (IQWiG), and the research Institute of the country's largest statutory health insurer (WIdO). You can read more about IQWiG and insulin at IQWiG's

website for patients: www.informedhealthonline.org in English or www.gesundheitsinformation.de in German.

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