

The Association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: Retrospective epidemiological analysis of the ACCORD study.

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The **Action to Control Cardiovascular Disease** study is a prospective trial to study the effect of intense control of diabetes. There were three arms in the study. One arm received intensive blood pressure control, another intensive cholesterol control and another intensive glucose control. All of the arms had random placebo groups.

In February 2008 the intensive glucose control intervention was stopped early. There was a higher overall death rate in that intensive glucose control group. The cause was unclear, but one of the assumed causes was low blood glucose (BG). These study researchers went back to the original data to analyze the relationship of death and low BG.

Methods

Participants were able to join the study if they had

- Type 2 diabetes,
- An A_{1c} of 7.5 or more during screening
- Were aged 40-79 with cardiovascular (heart) disease

Or they had

- Type 2 diabetes
- Evidence of subclinical cardiovascular disease or two or more risk factors
- Were aged between 55-79 years

People were excluded if they had a

- History of frequent or recent serious low blood sugar reactions (hypoglycemic coma, seizure in last 12 months or hypoglycemic event that required third party intervention in the last three months).

The primary outcome for the ACCORD study is the first episode of MI, stroke or cardiovascular death. A total of 10251 individuals were enrolled, 460 of whom had died during the course of the study. The study was stopped in January 2008 because it was suspected that patients in the intensive glucose control group were at greater risk of dying. The crude death rate in the intensive control group was 1.41% and in the regular group 1.14%. What was not considered in the conclusion was that there were people included with long standing cardiovascular diseases or other high risk factors. The re-analysis showed that the risk of death among people with at least one hypoglycemic episode was lower in the intensive glucose control group than in the standard glucose control group. It is suspected that the adverse events may have been related to the adverse effect of the drugs chosen. The average weight gain in the intensive glucose

control group was 22 lbs and the theory is that fluid retention, heart failure and congestive heart failure may have contributed to the increased death rate. All of those are potential side effects of the drug rosiglitazone which was used.

Study Results:

Group	Intensive Glucose Control	Regular Glucose Control
Number	5128	5123
Low blood glucose death	2.8%	3.7%
No low blood glucose death	1.2%	1%
Hazard Ratio	1.22	2.3
Glucose Self Monitoring	2-8 times daily	1-3 times daily
Visits for diabetes management	Every 2 months	Every 4 months