

## The ADVANCE Study

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### **INTENSIVE BLOOD GLUCOSE CONTROL AND VASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES.**

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**BACKGROUND:** In patients with type 2 diabetes, the effects of intensive glucose control on vascular outcomes remain uncertain. **METHODS:** We randomly assigned 11,140 patients with type 2 diabetes to undergo either standard glucose control or intensive glucose control, defined as the use of gliclazide (modified release) plus other drugs as required to achieve a glycated hemoglobin value of 6.5% or less. Primary end points were composites of major macrovascular events (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) and major microvascular events (new or worsening nephropathy or retinopathy), assessed both jointly and separately. **RESULTS:** After a median of 5 years of follow-up, the mean glycated hemoglobin level was lower in the intensive-control group (6.5%) than in the standard-control group (7.3%). Intensive control reduced the incidence of combined major macrovascular and microvascular events (18.1%, vs. 20.0% with standard control; hazard ratio, 0.90; 95% confidence interval [CI], 0.82 to 0.98;  $P=0.01$ ), as well as that of major microvascular events (9.4% vs. 10.9%; hazard ratio, 0.86; 95% CI, 0.77 to 0.97;  $P=0.01$ ), primarily because of a reduction in the incidence of nephropathy (4.1% vs. 5.2%; hazard ratio, 0.79; 95% CI, 0.66 to 0.93;  $P=0.006$ ), with no significant effect on retinopathy ( $P=0.50$ ). There were no significant effects of the type of glucose control on major macrovascular events (hazard ratio with intensive control, 0.94; 95% CI, 0.84 to 1.06;  $P=0.32$ ), death from cardiovascular causes (hazard ratio with intensive control, 0.88; 95% CI, 0.74 to 1.04;  $P=0.12$ ), or death from any cause (hazard ratio with intensive control, 0.93; 95% CI, 0.83 to 1.06;  $P=0.28$ ). Severe hypoglycemia, although uncommon, was more common in the intensive-control group (2.7%, vs. 1.5% in the standard-control group; hazard ratio, 1.86; 95% CI, 1.42 to 2.40;  $P<0.001$ ). **CONCLUSIONS:** A strategy of intensive glucose control, involving gliclazide (modified release) and other drugs as required, that lowered the glycated hemoglobin value to 6.5% yielded a 10% relative reduction in the combined outcome of major macrovascular and microvascular events, primarily as a consequence of a 21% relative reduction in nephropathy. (ClinicalTrials.gov number, NCT00145925.) 2008

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