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## IN BRIEF

### Intensive Glucose Lowering in Type 2 Diabetes

The goal for drug therapy of type 2 diabetes is achieving and maintaining a near-normal glycated hemoglobin ($HbA_{1C}$) concentration without inducing hypoglycemia; the target has generally been an $HbA_{1C}$ of 6.5-7.0% or lower. Whether treating to this level prevents macrovascular (cardiovascular) events has been unclear. Now, 2 large randomized, double-blind trials in patients with long-standing diabetes and at high risk for cardiovascular disease have found no decrease in macrovascular events with intensive glucose control.

The ACCORD trial in about 10,000 patients found that patients intensively treated with anti-hyperglycemic drugs, including frequent use of thiazolidinediones, mostly rosiglitazone *(Avandia)*, and insulin, with an $HbA_{1C}$ target of 6.0% (actual median $HbA_{1C}$ 6.4%) did not obtain a significant reduction in major cardiovascular events (the primary endpoint) over a period of 3.5 years. The trial was stopped early because of an unexpected increase in all-cause mortality (257 deaths vs. 203) in intensively treated patients compared to patients with an $HbA_{1C}$ target of 7.0-7.9% (actual median $HbA_{1C}$ 7.5%). The etiology of the higher mortality is unclear.[1]

The ADVANCE trial in about 11,000 similar patients treated to an $HbA_{1C}$ target of 6.5% with a sulfonylurea-based regimen, and infrequent use of thiazolidinediones, also found no decrease in macrovascular events, but no increase in all-cause mortality.[2]

Whether intensive glycemic control would reduce macrovascular events in patients at lower risk has not been established.

1. The ACCORD Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008; 358:2545.
2. The ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008; 358:2560.



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