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How Much Evidence Do We Need to Change Practices in Which We Firmly Believe?

Enough already! Randomized trials show that tight glucose control in patients with long-standing type 2 diabetes isn't beneficial.

Should the glycosylated hemoglobin (HbA_{1c}) level goal in patients with long-standing type 2 diabetes be 7%? 6.5%? Lower? Although many clinicians believe in tight control for patients with type 2 diabetes, recent studies suggest that this practice is not beneficial. Several recently published commentaries cite evidence that challenges current beliefs and practices.

In the first major trial (done in the 1960s) of tight glucose control in patients with type 2 diabetes, oral glucose-lowering agents were associated with higher cardiovascular mortality and no differences in microvascular complications compared with placebo.¹ Insulin also was not associated with clinical benefit.

In three recent large randomized trials (ACCORD,² ADVANCE,³ and VADT⁴), tight control in patients with long-standing type 2 diabetes did not lower overall mortality, cardiovascular-related mortality, stroke, amputations, or even clinical (as opposed to surrogate) microvascular endpoints. Differences in specific outcomes in these trials might be related to different treatments or to duration of diabetes in participants. In some studies, fewer intensively treated patients reached composite outcomes (such as "any diabetes complications"), but the bulk of improvement was in nonclinical outcomes (e.g., incident albuminuria). Tight control was associated with severe hypoglycemia and weight gain. In the UKPDS study,⁵ published a decade ago, nonobese intensively treated participants with newly diagnosed type 2 diabetes were less likely to reach microvascular endpoints (including "need for photocoagulation," but not visual loss) but showed no difference in mortality (cardiovascular, diabetes-related, or all-cause) compared with nonobese control patients. Among obese participants, metformin alone lowered long-term mortality and myocardial infarction rate, but sulfonylureas and insulin did not; tight control did not lessen risk for microvascular complications. Metformin and sulfonylureas in combination were associated with excess diabetes-related deaths and all-cause mortality.

Because trials do not support tight control and because of the cost, burden, and harms associated with tight control, we should be emphasizing cardiovascular risk reduction (particularly control of blood pressure and cholesterol levels) and healthy lifestyles for patients with type 2 diabetes.⁶ Several groups of editorialists suggest aiming for HbA_{1c} levels of 7.0% or 7.5% in patients in whom this goal is achievable with one medication and adjusting this target for others based on symptoms, side effects, treatment burden, and patient values and preferences.^{6,7,8} Commentary authors suggest that the HbA_{1c} goals for practice guidelines should not be <7% and that, to encourage individualized treatment, performance measures should set an upper limit (e.g., 9%) rather than a lower limit (e.g., <7%).⁷

Randomized trial results often are not available to answer important clinical questions. In this case, they are. We shouldn't ignore them. Many clinical trials are completed that show benefits, and much time passes, before new treatments are adopted; similarly, many trials that show lack of benefit, or even harm, might be required before clinicians abandon ineffective practices that have become routine. Haynes and Haynes ask, "What does it take to put an ugly fact through the heart of a beautiful hypothesis?" and they quote poetry: "The chains of habit are too weak to be felt until they are too strong to be broken."⁹ Social psychology literature suggests that people cling to belief even in the face of mountains of evidence to the contrary. But, as physicians and scientists, we should embrace change when new evidence consistently contradicts our prior beliefs and clinical practice.

— [Richard Saitz, MD, MPH, FACP, FASAM](#)

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Citation(s):

1. Meinert CL et al. A study of the effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes: II. Mortality results. *Diabetes* 1970; 19:Suppl:789.