

Should the Target A1C Level Be Less Than 7 Percent?

Yes: This Should Be the Target for Most Patients

KEVIN PETERSON, MD, MPH, FRCS,
FAAFP, *University of Minnesota Medical
School, Minneapolis, Minnesota*

In 1993, the DCCT (Diabetes Control and Complications Trial) demonstrated that better glycemic control reduces microvascular disease in patients with type 1 diabetes mellitus.¹ Ten years later, the EDIC (Epidemiology of Diabetes Interventions and Complications) trial established that macrovascular disease was also reduced by the DCCT.² In 1998, the UKPDS (United Kingdom Prospective Diabetes Study) demonstrated that intensive glycemic control also reduces microvascular disease in patients with type 2 diabetes, but that macrovascular disease reduction is only a statistical trend.³

Although these landmark studies provided the basis for establishing recommended A1C targets, subsequent guidelines often used optimistic interpretations of the evidence.⁴ In 1999, the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial began to evaluate whether a normal A1C level (less than 6 percent) provided better macrovascular protection than was obtained by intensively treated patients in the UKPDS (7.5 percent).⁵ The ACCORD trial identified 10,251 patients with type 2 diabetes and existing cardiovascular disease to ensure high cardiovascular event rates. By 2010, the trial demonstrated in 65-year-old patients with preexisting cardiovascular disease that lowering A1C levels to less than 6 percent resulted in higher mortality rates and no reduction in the primary composite outcome (cardiovascular-related death, nonfatal stroke, nonfatal myocardial infarction).⁶

Although other trials, including ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) and VADT



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(Veterans Affairs Diabetes Trial), did not show increases in mortality from intensive control, they also did not show a reduction in cardiovascular disease outcomes from low A1C levels.^{7,8} Although we all agree that these trials demonstrate that not everyone should target a normal A1C level, we should also recognize that these clinical trial populations are different from the general population. A closer examination of the evidence shows why family physicians should still recommend an A1C target of less than 7 percent in most patients.

Normal blood glucose levels are at least theoretically better than abnormal blood glucose levels. Having a normal blood glucose level causes no known problems, whereas even mildly abnormal A1C levels of 5.5 to 6.4 percent can cause damage to the vascular endothelium.⁹ Although it has not been proven that surrogate endothelial measures reflect patient-oriented outcomes, it is clear that no level of elevated blood glucose is known to be safe over many years of exposure. The ACCORD trial treatment strategy aggressively lowered A1C levels, with a target of less than 6 percent, but as A1C levels went down, serious hypoglycemic events tripled.¹⁰ The study demonstrated the potential danger of aggressive treatment in older populations with heart disease. But what does that mean for most patients?

The optimal A1C level for any individual with type 2 diabetes depends on many factors. The VADT demonstrated the importance of diabetes duration in determining the impact of intensive glycemic control.¹¹

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Combined analysis of the ACCORD trial, VADT, and the ADVANCE trial suggests that intensive therapy has the greatest benefit early in the course of the disease.¹² The most reasonable interpretation of the evidence is that effective prevention of cardiovascular disease includes intensive glycemic control that begins early in the course of diabetes, before cardiovascular disease becomes established. Once the blood vessels are damaged, the opportunity to alter cardiovascular disease progression is limited. The average patient in the ACCORD trial had diabetes for 10 years before entering the study. In primary care, most patients begin treatment at diagnosis, not after 10 years.

Another important consideration is the patient's age. Even small declines in glomerular filtration rate or slow advances in retinopathy have important consequences in patients who will have diabetes for many years.^{13,14} The average patient in the ACCORD trial was 64 years of age. However, primary care patients usually present 10 years earlier, and type 2 diabetes is increasingly being diagnosed at even younger ages. Their potential lifetime exposure often will be many times longer than in patients from the ACCORD trial. The EDIC trial took 10 years to observe protective macrovascular effects resulting from the DCCT intervention. That is less important for a 65-year-old than for a 45-year-old.

Trying to identify a single A1C target for everyone with diabetes has never been a good idea. Certainly, it is not a good idea to treat every patient as if he or she were 64 years old with cardiovascular disease and a 10-year history of diabetes. The best A1C target for an individual should account for length of diagnosis, age, cardiovascular disease, and other comorbidities. Of course, in a practical sense, accommodation needs to be made for mental health, physical limitations, and social challenges. Nevertheless, the best A1C target should be 7 percent for patients in good health, for patients with newly diagnosed diabetes, for younger patients with the potential for long duration of disease, or even for older patients whose disease is easily controlled and who do not have hypoglycemia.

Simply stated, the best treatment depends on the individual. This family medicine–friendly affirmation is both satisfying and the single most important lesson from the ACCORD trial. Be aggressive with patients who are young, healthy, have newly diagnosed diabetes, and do not have heart disease or other comorbidities, and be less aggressive with persons who are older and frail.

Address correspondence to Kevin Peterson, MD, MPH, FRCS, FAAFP, at peter223@umn.edu. Reprints are not available from the author.

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