Hemoglobin A1c Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: ACP Update

THE AMERICAN COLLEGE OF PHYSICIANS ISSUES 4 RECOMMENDATIONS, 2 OF WHICH ARE CHALLENGED BY THE OTHER ORGANIZATIONS. REVIEW ALL OF OUR DIABETES GUIDELINE SUMMARIES WHEN CONSIDERING HOW TO PROCEED.

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Summary of Recommendation

Type 2 diabetes (T2DM) is a chronic disease that has been increasing in the United States over the past decade. Currently, 9% of the U.S. population has been diagnosed with T2DM. Uncontrolled diabetes is associated with vision loss, neuropathy, foot ulcers, amputations, myocardial infarctions, and end-stage renal disease. T2DM is also a financial burden for patients and the government — in 2012, the total direct and indirect costs of diabetes was $245 billion. The purpose of these guidelines was to review the available evidence and other current guidelines to determine an optimal target HbA1c for patients with T2DM (see below for details of what the American College of Physicians [ACP] included in its review).

Four Recommendations

Based on the its review, the ACP produced 4 guidance statements for determining an ideal HbA1c target:

1. Personalize goals for glycemic control in patients with T2DM based on a discussion of benefits and harms of pharmacotherapy, patients' preferences, patients' general health and life expectancy, treatment burden, and costs of care.
2. Aim to achieve an HbA1c level between 7% and 8% in most patients with T2DM.
3. Consider deintensifying pharmacologic therapy in patients with T2DM who achieve HbA1c levels <6.5%.
4. Treat patients with T2DM to minimize symptoms related to hyperglycemia and avoid targeting an HbA1c level in patients with a life expectancy <10 years due to advanced age (age ≥80 years), residence in a nursing home, or chronic conditions (such as dementia, cancer, end-stage kidney disease, severe chronic obstructive pulmonary disease, or congestive heart failure) because the harms outweigh the benefits in this population.

ACP concluded that an HbA1c target between 7% and 8% is reasonable for most patients. Older patients with a short life expectancy should have no HbA1c goal but, rather, they should have a focus on decreasing symptoms of diabetes and diabetes-related treatment. If patients have an HbA1c <6.5%, treatment should be reduced or stopped.

What ACP Reviewed

Six guidelines were included for critical review — each included a specific recommendation for glycosylated hemoglobin (HbA1c). The National Institute for Health Care and Excellence and the American Association of Clinical Endocrinologists and American College of Endocrinology had the most stringent HbA1c recommendations; both recommended an HbA1c goal of 6.5% to 7%, depending on the treatment regimen and if it could be achieved safely. The American Diabetes Association and Scottish Intercollegiate
Guidelines Network recommended a goal of 7% for the general population. The Institute for Clinical Systems Improvement suggested a goal of <7% or 8%, depending on patient factors. The U.S. Department of Veterans Affairs’ had varying goals depending on life expectancy, extent of microvascular disease, and presence of other comorbid conditions. For example, patients with no microvascular disease and a life expectancy of >10 years have a suggested target HbA\textsubscript{1c} of 6% to 7%. Patients with a shorter life expectancy and several comorbid conditions may do better with an HbA\textsubscript{1c} target of 8% to 9%.

The guidelines also reviewed several landmark trials related to intensive versus standard treatment of T2DM. The ACCORD trial found that targeting an HbA\textsubscript{1c} of <6% increased risk for all-cause mortality and severe hypoglycemic events. The ADVANCE trial used a goal of <6.5% and saw no difference in cardiovascular events or all-cause mortality between intensive treatment versus standard of care treatment. Patients in the intensive treatment group had more severe hypoglycemic events compared with the standard of care group.

The next pair of trials, UKPDS 33 and 34, demonstrated some improvement with more intensive goals. In the UKPDS 33 trial, the goal was a fasting glucose of <108 mg/dL. Patients had fewer diabetes-related events, but there were no differences in diabetes-related death, all-cause death, or amputations. The UKPDS 34 trial demonstrated less diabetes-related death and all-cause mortality in the intensive treatment group (median HbA\textsubscript{1c}, 7.4%); however, hypoglycemia was more common and adding metformin early in treatment to sulfonylurea increased the risk of diabetes-related death.

Lastly, the VADT trial (median HbA\textsubscript{1c} was 6.9% in the intensive treatment group) demonstrated that intensive treatment did not reduce the risk of major cardiovascular events or death, but severe hypoglycemia events were more common.

Our Clinical Advisor’s Take:

While basically agreeing with statements 1 and 4, a joint commentary by the American Association of Clinical Endocrinologists, American Diabetes Association, American Association of Diabetes Educators, and the Endocrine Society disagrees with statements 2 and 3 above. Instead, they countered with:

1. ACP’s interpretation of the findings in the evaluated trials (ACCORD, ADVANCE, VADT, and UKPDS) did not account for the differences in patient populations in these trials.
2. The positive “legacy effect” (long-term benefits of early aggressive control of the of HbA\textsubscript{1c}, even if the level rises after the first 5 to 10 years) in patients with recently diagnosed T2DM.
3. The improvement in morbidity, mortality, weight, and cardiovascular disease outcome seen with the newer SGLT2 and GLP-1 receptor agonist drug classes was not taken into account in the ACP review because these drug classes were not studied in the trials reviewed.
Consult our other diabetes-related guideline summaries, which will help you arrive at the best decisions for individual patients (you can search for them by title in the Practical Reviews: Chronic Diseases database):

- 2018 Standards of Medical Care in Diabetes: American Diabetes Association
- Obesity Management for the Treatment of Type 2 Diabetes: American Diabetes Association
- Oral Pharmacologic Treatment of Type 2 Diabetes Mellitus: A Clinical Practice Guideline Update from the American College of Physicians
- Pharmacologic Approaches to Glycemic Treatment: American Diabetes Association

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CITATION