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# Glycemic Control in Older Adults With Diabetes Mellitus

**Elbert S. Huang, MD, MPH** and **Andrew M. Davis, MD, MPH**

Section of General Internal Medicine, University of Chicago, Chicago, Illinois

## Summary of the Clinical Problem

Diabetes in older adults presents a significant public health challenge. The prevalence of the disease increases sharply with age, affecting 12.2%of adults aged 45 to 64 years but 21.8% of adults aged 65 to 74 years.[1] Historically, diabetes treatment goals have included achieving near-normal levels of glucose ($HbA_{1c}$ <7%), blood pressure (<130/80 mm Hg), and low-density lipoprotein cholesterol (<100 mg/dL [<2.59 mmol/L])[2] to reduce the risk of complications. However, clinical trials that inform diabetes recommendations have tended to exclude older patients and those with significant comorbid illnesses. Thus, risk factor target goals are unclear in older patients who have numerous comorbidities and diminished functional status.

## Characteristics of the Guideline Source

This updated guideline[3] (Table) was developed by the AGS, a not-for-profit organization of health care professionals devoted to improving the health, independence, and quality of life of all older people. The AGS guideline expert panel consisted of general internists, family practitioners, geriatricians, clinical pharmacists, health services researchers, and certified diabetes educators. Potential conflicts of interest of panel members were disclosed. A draft of the guideline was posted on the AGS website for public comment and sent for peer review to organizations with special interest and expertise in treatment of diabetes. The guidelines did not have a specific funding source apart from the grant funding of individual panelists.

**Corresponding Author:** Elbert S. Huang, MD, MPH, University of Chicago, Section of General Internal Medicine, 5841 S Maryland Ave, MC 2007, Chicago, IL 60637 (ehuang@medicine.bsd.uchicago.edu).

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**MAJOR RECOMMENDATIONS** These comprehensive guidelines emphasize an individualized approach to diabetes care goals and treatment among adults. The glycemic control recommendations suggest a general goal for glycated hemoglobin ($HbA_{1c}$) in older adults of 7.5% to 8.0% (level IA evidence). A target $HbA_{1c}$ level between 7.0% and 7.5% may be appropriate if it can be safely achieved in healthy older adults with few comorbidities and good functional status (level IA evidence). Higher $HbA_{1c}$ targets (8%–9%) are appropriate for older adults with multiple comorbidities, poor health, and limited life expectancy (level IIA evidence).

**Related guidelines and other resources**

2012 American Diabetes Association consensus panel statement

2015 Update of a position statement from the American Diabetes Association and European Association for the Study of Diabetes

2012 Position statement on behalf of the International Association of Gerontology and Geriatrics, the European Diabetes Working Party for Older People, and the International Task Force of Experts in Diabetes

## Evidence Base

This review was an update of the original AGS guideline published in 2003, which had a similar breadth of topics.[4] Randomized clinical trials, systematic reviews, or meta-analyses from 2002 to 2012 were reviewed for each topic.[5] At the time of the 2003 guidelines, the primary source of data on diabetes care was the UK Prospective Diabetes Study (UKPDS), which excluded adults older than 65 years. In 2008, 3 major clinical trials—ACCORD, ADVANCE, and the Veterans Affairs Diabetes Trial (VADT)—evaluated intensive glycemic control (eg, $HbA_{1c}$ ≤6.5% in ADVANCE), and these informed the new guidelines. All 3 trials included adults aged 65 years or older but had few participants older than 75 years; all excluded older adults with significant functional impairment or comorbid illnesses.

## Benefits and Harms

The UKPDS demonstrated the benefits of tighter glycemic control ($HbA_{1c}$ of about 7.0% vs 7.9%) in reducing microvascular complications in middle-aged patients with newly diagnosed type 2 diabetes. During the posttrial follow-up, as participants became 65 years or older, the reduction in microvascular complications persisted, and benefits of reducing mortality and myocardial infarctions became apparent.

Building on the UKPDS, the ACCORD, ADVANCE, and VADT trials studied glycemic control for preventing cardiovascular disease (CVD) events in high-risk middle-aged and older adults with type 2 diabetes. The ACCORD trial enrolled patients with diabetes aged 40 to 79 years and randomly assigned them to intensive glucose control therapy ($HbA_{1c}$ <6.0%) or standard therapy ($HbA_{1c}$ of 7.0%–7.9%). The trial was ended after a mean follow-up of 3.5 years because the intensive therapy group had a higher mortality rate than the standard therapy group. In contrast to ACCORD, ADVANCE did not show excessive deaths and confirmed some reduction in microvascular disease from intensive glucose control. ADVANCE randomized participants with type 2 diabetes aged 55 years or older and achieved mean $HbA_{1c}$ levels of 6.5% and 7.3%, respectively, at 5 years of follow-up. The intensive therapy group had a 10% relative reduction (18.1% vs 20.0% absolute rates, respectively) in the combined outcome of major macrovascular and microvascular events. However, the microvascular benefits of ACCORD and ADVANCE were not seen in VADT, which randomized 1791 veterans to intensive glucose control (an absolute reduction of 1.5% in $HbA_{1c}$) vs standard control. The intensive and standard therapy groups achieved median $HbA_{1c}$ levels of 6.9% and 8.4%, respectively. The VADT found no significant differences in major CVD events, death, or microvascular events between the 2 groups after a median follow-up of 5.6 years. In post hoc analyses, adults with diabetes for longer than 20 years had an increased risk of CVD events with intensive therapy.

In all 3 trials, the incidence of hypoglycemia requiring medical assistance was 2 to 3 times more frequent in the intensively treated groups. Because the population of older adults with diabetes has been largely excluded from trials, data from epidemiological studies on the relationship between glycemic control and complications are relevant. In adults aged 50 years or older with type 2 diabetes from the UK General Practice Research Database, both lowest (6.1%–6.6%) and highest (10.1%–11.2%) $HbA_{1c}$ values were associated with

increased all-cause mortality and cardiac events.[6] In a retrospective cohort study of 71 092 patients with type 2 diabetes aged 60 years or older, the risk of any nonfatal complication increased linearly for $HbA_{1c}$ greater than 6.0%, but mortality had a U-shaped relationship with $HbA_{1c}$. Mortality risk was lowest among study participants with $HbA_{1c}$ levels between 6.0% and 9.0% (adjusted HR, 0.83). All age groups had this U-shaped relationship.[7]

Overall, intensive glycemic control appears to produce microvascular benefits in the medium term (5–10years) and cardiovascular/mortality benefits in the long term (>10 years). These findings are particularly relevant for younger patients with new-onset diabetes. However, for older patients with longer durations of diabetes, risks of hypoglycemia and potentially increased mortality may mitigate these benefits.

## Discussion

Current guidelines for management of older patients with diabetes from multiple organizations agree on the concept of individualizing the goals of diabetes care but have conflicting recommendations, especially for the lower boundaries of glucose control. The American Diabetes Association (ADA) made specific recommendations for glycemic and blood pressure control targets and provided a framework for stratifying patients by health status into classes labeled “healthy,” “complex,” or “very complex,” with $HbA_{1c}$ goals of less than 7.5%, less than 8.0%, and less than 8.5%, respectively.[8] However, lower $HbA_{1c}$ boundaries were not identified. The updated AGS guidelines also endorsed a 3-tier stratification scheme for glycemic targets but specified lower boundaries for optimal glycemic levels. Thus, a healthy 75-year-old patient treated with met for min who has an $HbA_{1c}$ level of 6.5% would be appropriately treated according to ADA guidelines but would be over-treated according to AGS guidelines.

Decisions about targets and treatments in older patients cannot be made without knowledge of other issues that may affect adherence. Functional limitations, cognitive impairment, social isolation, limited health literacy, and financial constraints can limit a patient’s ability to self-monitor and carry out recommended treatments. Efforts to improve target and treatment selection will likely need to be embedded within programs that cost-effectively address such limitations, such as through enhanced care coordination and management between visits.[9]

## Areas in Need of Future Study or Ongoing Research

More research is needed to better understand the risks and benefits of tighter glycemic control among very old patients (aged >75 years) and those with comorbidities. Increasing observational evidence suggests that clinicians often do not differentiate treatments for older patients who differ widely in health status.[9]The new AGS guidelines highlight the need for practical clinical decision support and communication tools to individualize targets and treatments by health status and patient preference. Such tools also provide an opportunity to study whether highly individualized diabetes goals, combined risk factor approaches, and newer oral agents will lead to better diabetic, cardiovascular, and overall health outcomes in older patients.

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## Table

Guideline Rating

| Rating Standard | Rating |
|---|---|
| 1. Establishing transparency | Good |
| 2. Management of conflict of interest in the guideline development group | Good |
| 3. Guideline development group composition | Good |
| 4. Clinical practice guideline–systematic review intersection | Good |
| 5. Establishing evidence foundations and rating strength for each guideline recommendation | Good |
| 6. Articulation of recommendations | Fair |
| 7. External review | Good |
| 8. Updating | Fair |
| 9. Implementation issues | Fair |