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Glycemic Control in Nonpregnant Adults With Type 2 Diabetes

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Summary of the Clinical Problem

In the United States, type 2 diabetes affects 30 million people and is a major cause of morbidity and mortality.[1] Glycemic control has been shown to reduce diabetes complications, particularly for mi-crovascular disease.[2,3] However, increasing recognition of adverse events due to intensive diabetes treatments has prompted major disagreements about optimal glycemic targets.

Characteristics of the Guideline Source

The updated guidance statement (Table) was funded by the ACP and developed by the ACP Clinical Guidelines Committee, composed of 12 clinicians and 2 nonclinician representatives with expertise in primary care, health care administration, and health services research.[4,5] Potential conflicts of interest were disclosed and resolved prior to each meeting. The final guideline was revised based on peer review and online comments.

Evidence Base

The committee searched the National Guideline Clearinghouse and the Guidelines International Network library to identify English-language guidelines on HbA_{1c} targets for the treatment of type 2 diabetes. Two guidelines were identified from the Health and Care Excellence (NICE) and the Institute for Clinical Systems Improvement. Committee members included 4 additional guidelines from the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE), the American Diabetes Association (ADA), the Scottish Intercollegiate Guidelines Network (SIGN), and the Department of Veterans Affairs/US Department of Defense. Guidelines were rated on scope and purpose, stakeholder involvement, rigor of development, clarity, applicability, and editorial independence.[6]

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The committee also reviewed major studies that examined “treat-to-target” glycemic control strategies, including ACCORD,[7] ADVANCE, [8] UKPDS,[2] and VADT.[3] Recommendations were not graded on their strength or by level of supporting evidence.

Benefits and Harms

The ACP guidance statement recommends that clinicians personalize HbA_{1c}goals by weighingthe long-term benefits of more intensive HbA_{1c} control (eg, fewer microvascular complications) against potential harms (eg, hypoglycemia, medication burden, and cost), patient preferences, life expectancy, comorbidities, and functional status.[5]

For most patients with type 2 diabetes, the ACP recommends an HbA_{1c} target range between 7% and 8%.[5] Although the major trials found that more intensive glycemic control led to reductions in microvascular events, the ACP emphasizes that these reductions were in surrogate microvascular outcomes (eg, albuminuria) and that evidence of reductions in clinically significant microvascular outcomes (eg, end-stage renal disease) remains unclear.[3,7,8]

The ACP also recommends deintensifying pharmacologic therapy in patients with type 2 diabetes who have HbA_{1c} levels less than 6.5%, based on increased mortality among patients randomized to intensive treatments in ACCORD[7] and a greater risk of severe hypoglycemia without mortality benefit among patients randomized to intensive treatments in ADVANCE.[8]

For older patients with limited life expectancy, the ACP recommends that care be guided by symptoms rather than HbA_{1c} goals.[5] The committeejustified this recommendation by notingthat intensive glycemic control in clinical trials did not demonstrate cardiovascular or mortality benefits until at least 10 years of follow-up.[2,3]

Discussion

The 2018 ACPguidance statement is oriented to the potential harms and uncertain benefits of intensive HbA_{1c} control.[5] These recommendations, with the exception of personalizingglycemicgoals, are a substantial departure from existing clinical guidelines.

One major distinction is the recommendationtoaimfor HbA_{1c}tar-gets between 7% and 8% for most patients with type 2 diabetes. In contrast, 4ofthe 6 evaluated guidelines recommend a general HbA_{1c} goal of less than 6.5% or less than 7%. This disagreement potentially reflects differing perspectives ofthe guideline writers. Nationally representative data suggest that up to 70% of US adults have characteristics (eg, high comorbidity, preexisting diabetes complications, longer duration of diabetes) that limit the benefits of achieving HbA_{1c} levels less than 7%.[9] Thus, the ACP guideline appears to take a population-based approach attuned to potential harm in the general US population with diabetes. In contrast, theADA,AACE/ACE, SIGN, and NICE take more of an individual patient perspective and seek to minimize diabetes-related complications if possible (eg, the AACE/ACE guidelines advise that an HbA_{1c} level less than 6.5% is considered optimal “if it can be achieved safely”).

The ACP guidance statement adds to an important conversation about balancingthe benefitsand harms of intensive therapy. However, these recommendations could have unintended consequences. In the United States, younger adults with diabetes have the highest HbA_{1c} levels and have the most to gain from intensive HbA_{1c} control because of their long remaining life expectancy and the longterm benefits ("legacy effects") of lower HbA_{1c} values.[2,3,7] A serious concern is that clinicians may apply ACP recommendations to this group, which could lead tosystematic undertreatment and worse outcomes foryounger adults. Moreover, clinicians have little current guidance on maintaining HbA_{1c} levels within a narrow range or safely deintensifying diabetes medications as patients age and develop comorbidities. It is likely that effectively communicating such medication changes to patients will be difficult because patients may be accustomed to tracking HbA_{1c} levels and may prefer a proactive approach to diabetes management. More relaxed targets may also reduce the impetus to identify and treat adults with currently undiagnosed type 2 diabetes that is relatively early in its course.

In this era of individualized care, the ACP guidance statement reorients the tradition of glycemic goal setting by establishing higher HbA_{1c} target ranges and explicitly recommending deintensification. It recognizes the importance of reducing adverse events in populations for whom there is unclear benefit and potential harm from intensive glycemic control; however, its recommendations may have unintended consequences for patients who are newly diagnosed, relatively young, and less likely to have major adverse effects from medications.

Areas in Need of Future Study or Ongoing Research

High-quality, long-term randomized trials have improved knowledge of glycemic control in type 2 diabetes, but important gaps remain. Despite consensus that personalizing goals for glycemic control is important, little evidence exists for how to personalize goals consistently. Similarly, while protocols for deintensification are being developed, the long-term safety and benefits of deintensification are largely unknown. The intensity of glycemic and blood pressure control may be too narrow a focus for diabetes care, given the newer medications (ie, sodium-glucose cotransporter 2 inhibitors, glucagon-like peptide 1 agonists) that may have independent cardioprotective effects. A broader risk-benefit calculation based on clinical factors (glycemic control, blood pressure, dyslipidemia, tobacco use, renal function, duration of diabetes, medications) as well patient preferences regarding various risks and therapies may better determine personalized goals in the future.

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REFERENCES

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and its Burden in the United States. 2017 http://www.diabetes.org/assets/pdfs/basics/cdc-statistics-report-2017.pdf. Accessed May 17,2018.
2. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N EnglJ Med. 2008;359(15):1577–1589. doi:10.1056/NEJMoa0806470 [PubMed: 18784090]
3. Hayward RA, Reaven PD, Wiitala WL, et al. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2015; 372(23):2197–2206. doi:10.1056/NEJMoa1414266 [PubMed: 26039600]
4. Qaseem A, Wilt TJ, Kansagara D, et al. Hemoglobin A_{1c} targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: a guidance statement update from the American College of Physicians. Ann Intern Med. 2018;168(8):569–576. doi: 10.7326/M17-0939 [PubMed: 29507945]
5. American College of Physicians Clinical Guidelines Committee. https://www.acponline.org/about-acp/who-we-are/leadership/committees-boards-councils/clinical-guidelines-committee. Accessed May 16,2018.
6. Brouwers MC, Kho ME, Browman GP, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. CMAJ. 2010;182(18):E839–E842.doi:10.1503/cmaj.090449 [PubMed: 20603348]
7. Gerstein HC, Miller ME, Genuth S, et al. Long-term effects of intensive glucose lowering on cardiovascular outcomes. N Engl J Med. 2011;364 (9):818–828.doi:10.1056/NEJMoa1006524 [PubMed: 21366473]
8. Patel A, MacMahon S, Chalmers J, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008; 358(24):2560–2572. doi:10.1056/NEJMoa0802987 [PubMed: 18539916]
9. Laiteerapong N, John PM, Nathan AG, Huang ES. Public health implications of recommendations to individualize glycemic targets in adults with diabetes. Diabetes Care. 2013;36(1):84–89. doi: 10.2337/dc11-2344 [PubMed: 22961575]

MAJOR RECOMMENDATIONS

- Personalize hemoglobin A_{1c} (HbA_{1c}) goals for patients with type 2 diabetes based on discussions of benefits and harms of pharmacotherapy; patient preferences, health, and life expectancy; treatment burden; and costs of care.
- Aim for an HbA_{1c} level between 7% and 8% in most patients with type 2 diabetes.
- Consider deintensifying pharmacologic therapy in patients with type 2 diabetes and HbA_{1c} levels less than 6.5%.
- Treat patients with type 2 diabetes to minimize hyperglycemia symptoms and avoid targeting an HbA_{1c} level in patients with a life expectancy of less than 10 years due to advanced age, nursing home residence, or end-stage chronic conditions.

Table.

Guideline Rating

Rating Standard	Rating
Establishing transparency	Good
Management of conflict of interest in the guideline development group	Good
Guideline development group composition	Good
Clinical practice guideline-systematic review intersection	Fair
Establishing evidence foundations and rating strength for each guideline recommendation	Poor
Articulation of recommendations	Good
Externalreview	Fair
Updating	Poor
Implementation issues	Fair