

# Glycemic Control and Type 2 Diabetes Mellitus: The Optimal Hemoglobin A<sub>1c</sub> Targets. A Guidance Statement from the American College of Physicians

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This guidance statement is derived from other organizations' guidelines and is based on an evaluation of the strengths and weaknesses of the available guidelines. We used the Appraisal of Guidelines, Research and Evaluation in Europe (AGREE) appraisal instrument to evaluate the guidelines from various organizations. On the basis of the review of the available guidelines, we recommend:

**Statement 1:** To prevent microvascular complications of diabetes, the goal for glycemic control should be as low as is feasible without undue risk for adverse events or an unacceptable burden on patients. Treatment goals should be based on a discussion of the benefits and harms of specific levels of glycemic control with the

patient. A hemoglobin A<sub>1c</sub> level less than 7% based on individualized assessment is a reasonable goal for many but not all patients.

**Statement 2:** The goal for hemoglobin A<sub>1c</sub> level should be based on individualized assessment of risk for complications from diabetes, comorbidity, life expectancy, and patient preferences.

**Statement 3:** We recommend further research to assess the optimal level of glycemic control, particularly in the presence of comorbid conditions.

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**D**iabetes mellitus is a leading cause of morbidity and mortality in the United States. Approximately 20.8 million people in the United States (7% of the population) have diabetes, and approximately 90% to 95% of people with diabetes have type 2 diabetes. The incidence rate of diabetes in the United States for 2005 is 1.5 million cases in people age 20 years or older. Various trials have validated the need for tight glycemic control (1–3). Various important indices used to measure blood glucose levels include fasting or preprandial glucose, 2-hour postprandial glucose, bedtime glucose, and hemoglobin A<sub>1c</sub> levels. The terms *glycosylated hemoglobin* or *glycated hemoglobin* are also used in the literature in lieu of *hemoglobin A<sub>1c</sub>*.

The purpose of this paper is to present the available guidelines from various organizations to help internists and other primary care physicians with effective management for glycemic control in type 2 diabetes mellitus and target level for hemoglobin A<sub>1c</sub>. The target population for this guideline is all patients with type 2 diabetes. This evidence is based on the review of the guidelines presented in this paper. This guidance statement is derived from other organizations' guidelines and is based on an evaluation of strengths and weaknesses of the available guidelines.

## METHODS

The American College of Physicians (ACP) Clinical Efficacy Assessment Subcommittee (CEAS) made a policy decision to address the clinical topic areas designated by

the Institute of Medicine (IOM) as priorities for improvement in their quality chasm report (4) and their priorities report (5). In the case of an IOM priority area where multiple guidelines are available from many reputable organizations, the CEAS decided to use a different methodological approach rather than develop another guideline on the topic. The CEAS felt that it would be more useful to provide clinicians with a rigorous review of the currently available guidelines so that they could make evidence-based care decisions. Glycemic control in diabetes mellitus was a priority area cited in the IOM report, and it is currently also a high-priority target of many pay-for-performance and pay-for-reporting programs throughout the United States. Thus, the CEAS developed this guidance statement for our members to address the evidence base for needed improvements of glycemic control in diabetes mellitus and how implementation of evidence-based guidelines can help improve the care they deliver.

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**Table 1. Guideline Evaluation Criteria\*****Primary criterion**

There is an explicit link between the recommendations and the supporting evidence (AGREE instrument Q12).

**Secondary criteria**

Systematic methods were used to search for evidence (AGREE instrument Q8).

The criteria for selecting the evidence are clearly described (AGREE instrument Q9).

The methods used for formulating the recommendations are clearly described (AGREE instrument Q10).

The recommendations are specific and unambiguous (AGREE instrument Q15).

The guideline has been externally reviewed by experts prior to its publication (AGREE instrument Q13).

There are explicit quality criteria used to grade the evidence and recommendations (CEAS criteria).

The quality criteria used by the authors to grade the evidence and recommendations are satisfactory (CEAS criteria).

There is no identifiable bias that might have influenced the selection of evidence (CEAS criteria).

Are the recommendations based on evidence only from randomized, controlled trials? (CEAS criteria).

Is another form of evidence used in the recommendations (e.g., consensus statements, cohort studies, case-control studies?) (CEAS criteria).

The methods used to combine the results from the relevant literature are clearly described and reported (CEAS criteria).

The authors used satisfactory meta-analytic techniques in the evidence review (CEAS criteria).

**Tertiary criterion**

It meets all criteria, in particular good methods and good evidence (CEAS criteria).

\* AGREE = Appraisal of Guidelines, Research and Evaluation in Europe; CEAS = Clinical Efficacy Assessment Subcommittee of the American College of Physicians; Q = question.

We followed the Appraisal of Guidelines, Research and Evaluation in Europe (AGREE) collaboration method to produce this report (6). The AGREE appraisal instrument asks 23 questions in 6 domains: scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, applicability, and editorial independence. The AGREE criteria do not consider information about the guideline development process that lies outside of the guideline document and is not specifically mentioned in the guideline document. Each guideline is scored by using a simple additive metric. Before conducting the evaluation, members of the guiding team from the ACP and the authors agreed on a method of stratifying the ratings into 3 main categories; these criteria are outlined in **Table 1**. We did not weigh scores according to these 3 categories but note our findings in our overall qualitative assessment of the guidelines as discussed here. Specifically, we viewed a lack of an explicit link between evidence and recommendations as a major flaw. A second tier of criteria included whether the authors performed a systematic search, used explicit criteria for selecting evidence, and described methods for formulating recommendations. The remaining AGREE criteria were considered as part of the overall score.

We began by searching MEDLINE in February 2005 using the keyword *diabetes*, limited to *guideline*. This produced 416 articles. We then supplemented this by searching the National Guideline Clearinghouse for guidelines on diabetes. We reviewed the titles and abstracts of each document. Most of these articles did not address glycemic control (many were on such topics as screening, diagnosis of diabetes, or management of hypertension). We also excluded primary research studies, duplicate references, and outdated references (for example, the American Diabetes Association's standards of care are updated annually, so we used only the most recent guideline). We excluded articles that were not in English because of the extensive resources needed for the translation (another 8 to 12 references; the number varied because there were duplicate publications of some guidelines). We also excluded the University of Michigan guidelines because an author of our manuscript was the team leader for those guidelines. Finally, several guidelines (typically those produced by individual U.S. states) were excluded because they were explicit adoptions of other guidelines, most often those of the American Diabetes Association. We updated the search in May 2006, discovering 12 new citations, but other than an update to 1 guideline, we did not identify any new relevant guidelines.

We then obtained copies of the identified guidelines if they were available to the general public, either electronically or through publication in medical journals. These guidelines were reviewed independently by 2 reviewers using the AGREE method, with a focus on the 3 major categories that were viewed as important by the CEAS. Each guideline was scored; scores were tabulated across the domains of interest and were compared (**Table 2**). Although total quantitative scores varied somewhat, the qualitative assessment of guideline quality was highly consistent between the 2 reviewers; indeed, the overall rankings of the quality of the guidelines were nearly identical.

Guidelines were then parsed for specific recommendations relating to glycemic control (most of the guidelines encompassed a broad range of diabetes management recommendations, rather than focusing on glycemic control alone). Specific comments relating to decisions about glycemic management goals were recorded to generate an assessment of how these goals varied across guidelines. Recommendations were based on the level of evidence supporting the recommendations along with the overall quality of the guideline.

## GUIDELINES FROM OTHER ORGANIZATIONS

### American Association of Clinical Endocrinologists (2002)

The guideline states that normalization of blood glucose levels should be the goal. The suggested target hemoglobin A<sub>1c</sub> level is 6.5% or less (8).

**Comments:** This guideline is based on consensus review with no systematic literature review.

**Table 2. Mean Guideline Scores across Domains of the Appraisal of Guidelines, Research and Evaluation in Europe Instrument\***

AGREE Domains	Guidelines								
	AACE	AAFP	ADA	AGS	CDA	ICSI	NICE	SIGN	VHA
<b>Scope and purpose</b>									
1. The overall objective(s) of the guideline is (are) specifically described.	4	4	3.5	4	4	3.5	4	3.5	4
2. The clinical question(s) covered by the guideline is (are) specifically described.	2	4	3	3.5	4	3	4	4	4
3. The patients to whom the guideline is meant to apply are specifically described.	3	3.5	3	3.5	4	2.5	4	4	3.5
Subtotal	9	11.5	9.5	11	12	9	12	11.5	11.5
<b>Stakeholder involvement</b>									
4. The guideline development group includes individuals from all the relevant professional groups.	1.5	4	2	2	4	2.5	3.5	3.5	3
5. The patients' views and preferences have been sought.	1.5	2	1.5	2.5	1.5	2	3	3	2.5
6. The target users of the guideline are clearly defined.	2	4	3.5	3.5	4	3	4	3	3.5
7. The guideline has been piloted among target users.	1	2	1.5	1.5	1.5	1.5	4	1.5	1.5
Subtotal	6	12	8.5	9.5	11	9	14.5	11	10.5
<b>Rigor of development</b>									
8. Systematic methods were used to search for evidence.	1	4	1	4	4	3.5	4	4	3
9. The criteria for selecting the evidence are clearly described.	1	4	2	3.5	2	3.5	4	3.5	3.5
10. The methods used for formulating the recommendations are clearly described.	1	3.5	2	4	4	3.5	4	4	4
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	2.5	4	2	3.5	2.5	3.5	3.5	3	4
12. There is an explicit link between the recommendations and the supporting evidence.	2	4	3	3.5	3	4	3	4	4
13. The guideline has been externally reviewed by experts prior to its publication.	4	4	2	4	3	2	4	4	4
14. A procedure for updating the guideline is provided.	2	2	2.5	1.5	2.5	1.5	3.5	4	4
Subtotal	13.5	25.5	14.5	24	21	21.5	26	26.5	26.5
<b>Clarity and presentation</b>									
15. The recommendations are specific and unambiguous.	3.5	2	3	3	4	3.5	3	3.5	3
16. The different options for management of the condition are clearly presented.	3.5	3	3	3	2	3	2.5	2.5	3.5
17. Key recommendations are easily identifiable.	1.5	2	4	4	4	2.5	4	3.5	3.5
18. The guideline is supported with tools for application.	3.5	2	2	2	4	3	2	2.5	2
Subtotal	12	9	12	12	14	12	11.5	12	12

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Table 2—Continued

AGREE Domains	Guidelines								
	AACE	AAFP	ADA	AGS	CDA	ICSI	NICE	SIGN	VHA
<b>Applicability</b>									
19. The potential organizational barriers in applying the recommendations have been discussed.	2.5	3	1	2	3.5	2	2	2	2
20. The potential cost implications of applying the recommendations have been considered.	2	2.5	1	1.5	2	2	2	2	2.5
21. The guideline presents key review criteria for monitoring or audit purposes.	3.5	2	4	4	4	3.5	4	4	3
Subtotal	8	7.5	6	7.5	9.5	7.5	8	8	7.5
<b>Editorial independence</b>									
22. The guideline is editorially independent from the funding body.	1	4	1.5	2	3	3	4	3.5	3
23. Conflicts of interest of guideline development members have been recorded.	1	1.5	1	4	1	2.5	1	1.5	1
Subtotal	2	5.5	2.5	6	4	5.5	5	5	4
<b>Total score</b>	<b>50.5</b>	<b>71</b>	<b>53</b>	<b>70</b>	<b>71.5</b>	<b>64.5</b>	<b>77</b>	<b>74</b>	<b>72</b>

\* AACE = American Association of Clinical Endocrinologists; AAFP = American Academy of Family Physicians; ADA = American Diabetes Association; AGREE = Appraisal of Guidelines, Research and Evaluation in Europe; AGS = American Geriatrics Society; CDA = Canadian Diabetes Association; ICSI = Institute for Clinical Systems Improvement; NICE = National Institute for Health and Clinical Excellence; SIGN = Scottish Intercollegiate Guidelines Network; VHA = Veterans Health Administration.

**American Academy of Family Physicians (1999–2005)**

The guideline states that because of differences in patients’ life expectancies and comorbid conditions, it is inappropriate to set a uniform target hemoglobin A<sub>1c</sub> level for all patients with type 2 diabetes (7).

**Comments:** This guideline is very comprehensive. It clearly discusses the literature search, and the recommendations follow the evidence. This guideline has not been updated since 1999. Because the guideline does not state a specific target hemoglobin A<sub>1c</sub> level, assessing guideline-concordant care will be difficult.

**American Diabetes Association (2006)**

The guideline states that lowering hemoglobin A<sub>1c</sub> values has been associated with a reduction of microvascular and neuropathic complications of diabetes (9). The hemoglobin A<sub>1c</sub> goal for patients in general is less than 7%. The American Diabetes Association also recommends that more stringent goals, such as a normal hemoglobin A<sub>1c</sub> value of less than 6%, be considered in individual patients if they are achievable without significant hypoglycemia. Less stringent goals may be appropriate for patients with limited life expectancies, very young or older adults, and individuals with comorbid conditions. Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness, perioperatively, after myocardial infarction, and in pregnancy.

**Comments:** These are the most commonly cited and

adopted guidelines. However, there is no reference to a systematic review used as the basis for these recommendations.

**American Geriatrics Society (2003)**

The guideline states that, for older persons, target hemoglobin A<sub>1c</sub> levels should be individualized. A reasonable goal for hemoglobin A<sub>1c</sub> in relatively healthy adults with good functional status is 7% or lower. For frail older adults, persons with a life expectancy of less than 5 years, and others in whom the risks of intensive glycemic control outweigh the benefits, a less stringent target, such as 8%, is appropriate (10).

**Comments:** These recommendations are based on a comprehensive literature review but are limited to geriatric populations and such conditions as depression, urinary incontinence, falls, and cognitive impairment.

**Canadian Diabetes Association (2003)**

The guideline states that glycemic targets must be individualized; however, therapy in most patients with type 1 or type 2 diabetes should be targeted to achieve a hemoglobin A<sub>1c</sub> level of 7.0% or lower in order to reduce the risk for microvascular and macrovascular complications (11). If it can be safely achieved, lowering postprandial plasma glucose targets toward the normal range (hemoglobin A<sub>1c</sub> value ≤6.0%) should be considered.

**Comments:** These recommendations may place a higher weight on evidence from observational studies than

do other guidelines. In addition, the recommendation to achieve the target level of 6% or lower is based on consensus.

#### **Institute for Clinical Systems Improvement (2004)**

The guideline states that the goal for glycemic control is a hemoglobin A<sub>1c</sub> level less than 7.0% (12). The hemoglobin A<sub>1c</sub> target should be individualized; higher levels may be appropriate in patients with advanced age, at high risk for hypoglycemia, and with limited life expectancy (12).

**Comments:** There was no information about stakeholders involved in the development of this guideline. Recommendations were based on comprehensive review, but description of the process was limited.

#### **National Institute for Health and Clinical Excellence (2002)**

The guideline states that for each individual, a target hemoglobin A<sub>1c</sub> (aligned with the Diabetes Control and Complications Trial) between 6.5% and 7.5% should be set on the basis of the risk for macrovascular and microvascular complications (13).

**Comments:** This guideline is based on a very comprehensive evidence review. However, the guideline is long because of the breadth of topics covered.

#### **Scottish Intercollegiate Guidelines Network (2001)**

This guideline suggests that good glycemic control should be maintained to reduce risk, noting that the target should be “around 7.0%” (14).

**Comments:** This guideline is based on a very comprehensive evidence review and focused on prevention and management of complications of diabetes. However, it does not have a section focusing just on glycemic control.

#### **Veterans Health Administration (2003)**

The guideline states that for patients with very mild or no microvascular complications of diabetes, and those without major concurrent illnesses and with a reasonable life expectancy, the hemoglobin A<sub>1c</sub> target should be 7% (15).

**Comments:** This guideline has a comprehensive discussion of risks and benefits of glycemic control.

### **SUMMARY**

Guidelines differed in whether they recommended a specific hemoglobin A<sub>1c</sub> target, and for those that did, the choice of target hemoglobin A<sub>1c</sub> varied. All guidelines except those from the American Academy of Family Physicians set hemoglobin A<sub>1c</sub> targets. Most guidelines used a target hemoglobin A<sub>1c</sub> level of approximately 7%, but several recommended tailoring the target hemoglobin A<sub>1c</sub> according to such factors as risk for microvascular and macrovascular complications, patient life expectancy, and comorbid conditions. All guidelines agree on setting individualized target hemoglobin A<sub>1c</sub> levels.

### **CONCLUSIONS**

On the basis of the review of the available guidelines, we recommend the following:

*Statement 1: To prevent microvascular complications of diabetes, the goal for glycemic control should be as low as is feasible without undue risk for adverse events or an unacceptable burden on patients. Treatment goals should be based on a discussion of the benefits and harms of specific levels of glycemic control with the patient. A hemoglobin A<sub>1c</sub> level less than 7% based on individualized assessment is a reasonable goal for many but not all patients.*

The goals for glycemic control should be as low as is feasible without undue risk for adverse events, such as hypoglycemia. Clinicians should counsel patients and emphasize the importance of good glycemic control. Clinicians should discuss treatment goals with each patient and agree jointly on goals that are feasible, given the patient's comorbid conditions, preferences, and ability to manage the treatment regimen. Therapy in many patients should be targeted to achieve a hemoglobin A<sub>1c</sub> value less than 7% to reduce the risk for complications from diabetes. However, this goal will not be appropriate for all patients. In patients who are older or frail, at increased risk for adverse complications from tight control, or have substantially reduced life expectancy from comorbid conditions, hemoglobin A<sub>1c</sub> goals higher than 7% may be appropriate. In patients who are at increased risk for microvascular complications, stringent targets may be appropriate.

*Statement 2: The goal for hemoglobin A<sub>1c</sub> level should be based on individualized assessment of risk for complications from diabetes, comorbidity, life expectancy, and patient preferences.*

With consideration of the importance of glycemic control, the goals for glycemic control should be individualized on the basis of the life expectancy of the patient, presence or absence of microvascular and macrovascular complications, risk for adverse events related to glucose control, and patient preferences. Less stringent targets may be appropriate in patients who have short life expectancy or are at higher risk for adverse complications of therapy.

*Statement 3: We recommend further research to assess the optimal level of glycemic control, particularly in the presence of comorbid conditions.*

Understanding the benefits and harms of various levels of glycemic control remains challenging, particularly in complex patients with other comorbid conditions. In addition to the importance of glycemic control, management of blood pressure and lipid levels is also essential to prevent complications of diabetes. Further research that elucidates optimal level of glycemic control in patients of different ages, in patients with comorbid conditions, and in patient populations representative of those seen in practice would provide important additional guidance for management of diabetes.

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**Note:** Guidance statements are guides only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All ACP guidance statements are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.

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