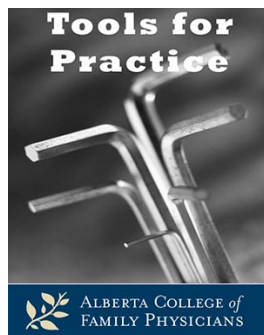


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Evidence Updated: No new evidence
Bottom Line: No change
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Type 2 Diabetes and A1c targets: Pragmatic dogma

Clinical Question: What are reasonable Hemoglobin A1c (A1c) targets for our patients with Type 2 Diabetes Mellitus?

Bottom Line: While many patients can safely attain an A1c at or just below 7%, older patients, those with long-standing diabetes, multiple co-morbidities, and/or high risk of hypoglycemia, reasonable targets are perhaps 7-8% or even higher.

Evidence: Intense management of blood glucose in Type 2 Diabetes examined in \geq ten meta-analyses.¹⁻¹⁰

- Studies varied in ages, co-morbidities, medications, etc., making evidence interpretation and application more difficult.

Five reasonably sized trials fall into two groups:

- Newly diagnosed diabetics, age ~50's, few co-morbidities, receiving single glucose-lowering therapy (to start) versus diet.
 - UKPDS 33: 3,867 patients, sulfonylurea or insulin (median ten year A1c 7.0% versus 7.9%).¹¹
 - Over ten years, significant reduction in death Number Needed to Treat (NNT)=29 and myocardial infarction (MI) NNT=36.¹²
 - UKPDS 34: 753 patients, metformin (median ten year A1c 7.4% versus 8.0%).¹³
 - Over ten years, significant reduction in death NNT=14 and MI NNT=16.¹²
- Older, established diabetics, age ~60's, more co-morbidities, receiving multiple glucose-lowering therapies (to start) for intense versus conventional.
 - ACCORD:¹⁴ 10,251 patients, x3.5 years, A1C 6.4% versus 7.5%.
 - ADVANCE:¹⁵ 11,140 patients, x5 years, A1C 6.5% versus 7.3%.
 - Veterans:¹⁶ 1,791 patients, x5.6 years, A1C 6.9% versus 8.4%.
 - Intense management led to:

- Microvascular improvement:¹⁷ Prevented visual deterioration (three lines worse on Snellen chart) NNT=60 and loss of light touch sensation NNT=49.
- No benefit in cardiovascular outcomes¹⁴⁻¹⁶ except one study found reduced non-fatal MI NNT=100.¹⁵
- Inconsistently worse: mortality in one study¹⁴ Number Needed to Harm (NNH)=96 and hospitalization in another¹⁵ NNH=48.
- Consistently worse:¹⁴⁻¹⁶ Weight gain (gain $\geq 10\text{kg}$ ¹⁴ NNH=8), and hypoglycemia (severe requiring medical assistance NNH=15).

Context:

- New US-European Guidelines¹⁸ recommend less stringent targets in patients with longer disease duration, shorter life expectancy, increased co-morbidities, and high risk of hypoglycemia or other adverse events.
- Cohort data indicates that in established diabetics, A1c of 7.5% may have the lowest mortality.¹⁹
- Macrovascular complications such as cardiovascular events are much more common than end-stage microvascular endpoints such as progression to dialysis or blindness.^{11,20}

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