
ACP publishes controversial guidance on type 2 diabetes: Sets A1c goal between 7%-8%; Recommends relaxed pharmacotherapy at A1c <6.5% and for patients 80+ years-old - March 6, 2018

Executive Highlights

- **In a shocking piece published in the [Annals of Internal Medicine](#) today, the American College of Physicians (ACP) recommends A1c goal between 7%-8% for the majority of type 2s.** This is one piece of a four-part guidance on type 2 diabetes care, which also suggests personalizing A1c targets, de-intensifying pharmacotherapy once patients reach A1c <6.5%, and avoiding A1c goal-setting for elderly patients (≥80 years-old).
- **In our view, the guidance is off-base and potentially harmful.** More than 30% of type 2s in the US have an A1c above 9%, so we're surprised and dismayed that ACP would spend time advocating for the relaxation of A1c targets. There is no mention of CGM, which is perhaps the best way to individualize a diabetes treatment plan. While urging for individualization, the ACP article gives few concrete recommendations on how to do this, and actually makes it easier not to individualize in some respects (e.g. a blanket statement to avoid targeting A1c in older patients, no push for CGM). In general, the ACP expresses concern over hypoglycemia and weight gain associated with insulin and SUs (which is valid), but fails to mention advanced drug classes like SGLT-2s, GLP-1s, combination therapy of any kind, or even DPP-4s. Notably, [research from Dr. Medha Munshi](#) has found that higher A1c does not necessarily protect against hypoglycemia.
- **The ACP's guidance statements are incongruous with what most thought leaders today consider best practice in diabetes care.** Dr. Irl Hirsch underscored the importance of outcomes beyond A1c, and argued that this document over-emphasizes A1c. Dr. Satish Garg said simply, "it makes no sense. Today, every organization should value CGM information, especially when so many diabetes associations have published guidelines in that area in the past five years" (we couldn't agree more). Dr. John Buse shared particular concern over guidance statement #4, pertaining to patients over the age of 80, which sets up a slippery slope of suboptimal diabetes care. "I do not think the guidelines will be widely embraced as dogma, but as a cover for not dealing with tough cases among the elderly," Dr. Buse told us.

The American College of Physicians (ACP) published [new guidance](#) on type 2 diabetes care in the [Annals of Internal Medicine](#) today, and our initial reaction was simply "WHAT?". ACP lists four guidance statements, including an egregious suggestion that providers aim for an A1c target between 7%-8% in the majority of type 2 patients. This stands in stark contrast to ADA's recommendation of ≤7%, while AACE considers ≤6.5% optimal, whenever it can be achieved in a safe and affordable manner. ADA's Chief Scientific, Medical, and Mission Officer Dr. William Cefalu and past President of AACE Dr. George Grunberger defended lower targets in this [NPR piece](#).

In subsequent guidance statements, ACP encourages providers to relax pharmacotherapy for patients with A1c <6.5% and for older patients with shorter life expectancy. We take serious issue with both of these recommendations as well.

At a high level, ACP seems very cautious about increase in hypoglycemia and weight gain at lower A1c, but the guidance relies far too much on insulin and SUs as grounds for these concerns. The authors specify at the beginning that they don't review newer therapies, and as such, there is not a single mention of advanced classes (SGLT-2s, GLP-1s) that reduce A1c without additional hypo risk, also promoting weight loss and offering cardio/renal protection. No combination therapy of any kind gets a mention. There's nothing on

DPP-4 inhibitors, either, which are somewhat more affordable than SGLT-2s and GLP-1s at the moment, and will be the first to go generic. DPP-4s are also glycemic-dependent (minimizing hypo risk), and are at least weight neutral. It's embarrassing for ACP not to realize how far behind it is on this front.

Moreover, there's no mention of CGM, whether intermittent or real-time. CGM is perhaps the best way to individualize a diabetes treatment plan (which ACP does advocate for - we give the college credit for this), to monitor hypoglycemia, and to make sure therapy is making a difference on beyond-A1c outcomes that really matter to patients, namely [time-in-range](#). While urging individualization, the ACP article gives few recommendations on how to do this, and actually makes it easier not to individualize in some respects (e.g. a blanket statement to avoid targeting A1c in older patients, which we're pretty tired of hearing).

Cost cannot be ignored, and we understand that SGLT-2 inhibitors, GLP-1 agonists, fixed-ratio combinations, and CGM are out of reach for many. We appreciate that ACP emphasizes cost considerations upfront (in guidance statement #1), but we think it's an oversight to write nothing at all on these advanced drugs or devices, especially since they would address the organization's concerns related to hypo and weight. The new guidance seems like a missed opportunity to push for better reimbursement of more effective/safer products; instead, ACP shies away entirely from what most thought leaders would prescribe in best practice diabetes care. Certainly, patient advocates are calling for more access/affordability around CGM and cardioprotective drugs, and we wonder if any advocacy groups were consulted in drafting this document.

Notably, more than 30% of type 2s in the US have an A1c >9%. For this reason, in particular, we're surprised and dismayed that ACP would spend time and effort advocating for the relaxation of A1c targets.

In checking with experts overnight (see below for quotes), we sensed a perspective of "oh, bless ACP's heart ... they are *trying!*". We absolutely acknowledge the challenges of internal medicine on the diabetes front, and we applaud the attempt at improving diabetes management from the clinician view, though we think this document needs a bit of an overhaul (that's probably an understatement). Ultimately, while the new ACP guidance means well, we direct the college and these authors to [this article](#) by the Joslin's highly-regarded Drs. Katie Weinger and Medha Munshi. Also see our Close Concerns [coverage of the paper](#) from last year.

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Select Quotes from Diabetes Thought Leaders

On the Importance of Glycemic Outcomes Beyond A1c

- **Dr. Irl Hirsch:** "First, I am a very proud member of the ACP. They do great work, and here in Washington State their recommendations are almost Talmudic for the general internists. **But there are a lot of problems with this latest recommendation, and there is a more important point, the 'beyond A1c' point.** Looking at the ADAG data, the range of A1c from 7%-8% would be mean glucose on CGM of 123-217 mg/dl! So what is it? Because that is what that range of A1c means (and recall that ADAG had no one with CKD, liver disease, or anemia, so this is better than it would be for a typical internist). **I think what this does is it further pushes doctors to treat the A1c and not the glucose."**

- **Dr. Satish Garg:** "It makes no sense. Today, every organization should value CGM information, especially when so many diabetes associations have published guidelines in that area in the past five years."

On ACP's Methods, Exclusion of Newer Therapies

- **Dr. John Buse:** "I do not think it is a particularly robust process that they used - largely a review of guidelines. They specifically state that they ignored the recent trials, as they were not treat-to-target studies. That seems unfortunate, as more data has been generated since the VADT (the last trial they report) than before it. My review of the same studies suggests that the A1c achieved had no negative effect on outcomes, and that it was the intensity of effort to achieve the target and the methods used that may be problematic."
- **Dr. John Buse:** "No study in the history of mankind has targeted 8%. We have no idea the impact of their recommendation. It is possible that the governors of ACP and a Stakeholder Group had more insight and better judgment than someone who has devoted >35 years specifically to the study of diabetes care working with an individual patient - the ultimate Stakeholder - but I have my doubts."

On Relaxing Targets for Older Patients

- **Dr. Satish Garg:** How easy is it to predict when someone will die in 10 years? "It is more or less impossible to predict when someone will die unless one has eternal knowledge. It is also important to keep in mind that despite guidelines we are nowhere close to 7% for the general population, and recommending higher A1c around 8% will only make glucose control worse. The thing I agree with is their recommendation to individual goals."
- **Dr. John Buse:** "Their heart is in the right place. I do think some of what they recommend is reasonable, while other bits throw the baby out with the bath water. For example, they call out people at age 80 for higher targets because the average life expectancy is less than 10 years. The average 85-year-old will live six years, and a quarter will live 10 years. Doctors can't predict when someone is going to die in six months to get them into hospice."
- **Dr. John Buse:** "I do not think the guidelines will be widely embraced as dogma, but as a cover for not dealing with tough cases among the elderly."

Four Guidance Statements

- **Guidance statement #1:** Clinicians should personalize goals for glycemic control in patients with type 2 diabetes on the basis of a discussion of benefits and harms of pharmacotherapy, patient's preferences, patients' general health and life expectancy, treatment burden, and costs of care.
 - **On the surface, we love this emphasis on personalization.** We appreciate that ACP alludes to shared decision-making between patient/provider, and we agree that each of the factors listed here is important: cost is a major determinant of care, patient preferences should be taken into account, and efficacy must be balanced with side-effects for any drug. That said, the guidance doesn't contain many concrete suggestions as to *how* providers should be individualizing care. CGM would help toward this goal, but it's left out of the document. An over-reliance on life expectancy as a factor in treatment decisions is a slippery slope, and is actually quite the opposite of individualization - it hastily buckets all elderly patients together, without due consideration of unique lifestyle, personal priorities, access, etc.
- **Guidance statement #2:** Clinicians should aim to achieve an A1c level between 7% and 8% in most patients with type 2 diabetes.

- **We disagree strongly, vehemently.** We believe this new guidance has the potential to be quite negative for patients and for those treating diabetes. We would have far rather seen advice for relaxing A1c goals in certain people who really *need* it, i.e. those required to take sulfonylureas or regular mealtime insulin due to cost constraints. A higher A1c target should not be set for the vast majority of Americans with diabetes.
- **Guidance statement #3:** Clinicians should consider de-intensifying pharmacologic therapy in patients with type 2 diabetes who achieve A1c levels less than 6.5%.
 - **Once again, we firmly disagree. In fact, we're disappointed by this conclusion from ACP.** Since the document only mentions insulin and sulfonylureas, both associated with hypoglycemia and weight gain (SUs even associated with beta cell burnout and potential CV harm), our best interpretation of this recommendation is that it's narrow-minded and outdated. It does make sense to lower insulin dose for many patients who surpass a <6.5% A1c target, since this is a complicated drug to titrate/dose, and since it can lead to hypoglycemia and fear of hypoglycemia. Sulfonylureas should be stopped whenever possible, but that's because this class would never be approved today. Withdrawing therapy may not be an option for type 2s taking bolus insulin with meals. The document does not acknowledge newer, next-gen insulins that come with less hypoglycemia risk, such as Novo Nordisk's Tresiba (insulin degludec) or Sanofi's Toujeo (insulin glargine U300); basal insulin/GLP-1 combos can even stimulate some weight loss (as seen in clinical trials of Novo Nordisk's Xultophy). There's good reason to continue GLP-1 agonists and SGLT-2 inhibitors for CV/renal benefit, and indeed, we anticipate that these advanced agents will prove their cost-effectiveness over time.
 - **Dr. Hirsch provided additional clarity on why this third guidance statement is problematic:** "This is problematic for those *not* receiving drugs that cause weight gain or hypoglycemia. Furthermore, even with the older drugs, the UKPDS clearly showed a gradient with A1c and complications risk, and **why if I have someone with an A1c below 6.5% on metformin, an SGLT-2 inhibitor, and a GLP-1 agonist (especially with known CV disease) would I want to de-intensify therapy? I think a greater emphasis on glucose with individualized targets are needed, not a global statement that all patients with type 2 diabetes who are successful with pharmacotherapy need to be de-intensified.**"
- **Guidance statement #4:** Clinicians should treat patients with type 2 diabetes to minimize symptoms related to hyperglycemia and avoid targeting an A1c level in patients with a life expectancy less than 10 years due to advanced age (80 years or older), residence in a nursing home, or chronic conditions (such as dementia, cancer, end-stage kidney disease, or severe chronic obstructive pulmonary disease or congestive heart failure) because the harms outweigh the benefits in this population.
 - **This statement is especially tragic because of Dr. Buse's suggestion of how the new ACP guidance will be digested publically - "as a cover for not dealing with tough cases among the elderly."** It seems criminal to categorize all 80+ year-olds together and to suggest they receive restricted therapeutic choice: There's no consideration of how CGM or advanced drugs might be prescribed to these patients in order to minimize hypo risk while still allowing individuals to set and pursue their personal goals for diabetes management. Notably, [research from Dr. Medha Munshi](#) has found that higher A1c does not protect against hypoglycemia in older patients with diabetes on insulin. We're disappointed by the recommendation to raise A1c goal in those with shorter life expectancy, because as Dr. Jay Skyler so eloquently argued at [Keystone 2017](#), what does that *mean*? He described 80-year-old patients that ski or mountain climb regularly, and indeed, this guidance seems like the antithesis of personalized diabetes care.

ACP Methods

- **Dr. Buse noted that the methods behind this [paper](#) were "not particularly robust," and he highlighted a conspicuous absence of recent trials.** The authors reviewed treatment guidelines from ADA, AACE/ACE, NICE, ICSI, SIGN (the Scottish Intercollegiate Guidelines Network), and the US Department of Veterans Affairs and Department of Defense. In the article, they scrutinize certain studies that form the basis of these professional guidelines, including ACCORD, ADVANCE, UKPDS, and VADT - all the studies called out were completed more than a decade ago. In discussing ACCORD, the authors predictably emphasize the increase in mortality that led to early termination, but what they fail to recognize is the possible link between severe hypoglycemia in the study and heightened risk of death (Prof. Simon Heller just spoke to this at CODHy). We found this ironic, given that hypoglycemia is a primary concern driving ACP's recommendation of higher-than-usual A1c targets. Dr. Hirsch pointed to Dr. Matthew Riddle's analysis ([Diabetes Care, 2010](#)) showing a reduction of mortality with lower A1c levels - he called this "quite compelling" and argued that "internists need to appreciate the complexity of the data." Yes.

-- by Payal Marathe and Kelly Close