HHS Public Access

Author manuscript

JAMA. Author manuscript; available in PMC 2019 July 03.

Published in final edited form as:

JAMA. 2018 November 13; 320(18): 1937–1938. doi:10.1001/jama.2018.13421.

Guidelines on Glycemic Targets for Persons With Type 2 Diabetes

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In Reply We agree that the ACP guidance statement has ignited critical dialogue and attention to an important issue. Our rating for "establishing evidence foundations" was largely based on the lack of justification for including only the 5 long-term randomized trials referenced in existing guidelines.[1] Prioritization of trial data over other data are part of a larger debate about the quality of evidence required to make clinical decisions. Although we agree that trial data, when available, should be considered more heavily, it is impossible for trial data to exist for every important clinical question. Thus, other sources of evidence can be informative for making clinical recommendations.

The major disagreement raised by Dr Kansagara and colleagues is regarding our concerns about potential unintended consequences of the ACP's recommendations for younger, healthier patients with newly diagnosed diabetes. They raise valid points that legacy effects were identified for these patients treated to an HbA_{1c} of 7% to 7.4% and that the magnitude of benefits was small. However, current understanding of the legacy effect is still emerging because to date these relationships have been examined in largely posttrial follow-up studies over decades-long periods. Epidemiological and related evidence does suggest that the relationship between HbA_{1c} and microvascular complications is curvilinear.[2,3] For example, the absolute incidence rate for any complication in the UK Prospective Diabetes Study increased from 2.5% to 6.6% across HbA_{1c} categories ranging from less than 6.0% (median, 5.6%) to 10.0% or greater (median, 10.6%), mostly because of increases in microvascular complications.[3] Therefore, it is likely that very intensive glycemic control (HbA_{1c} <6.5%) would confer a legacy effect of greater magnitude than current estimates. Another major argument against lower HbA_{1c} targets is the risk of higher rates of adverse events. However, severe hypoglycemia in major trials was most prominent among those who were older and had serious chronic conditions, such as baseline kidney disease[4]; the relative risk of adverse events among younger, healthier patients with newly diagnosed diabetes remains unclear.

Kansagara and colleagues find no evidence that higher HbA_{1c} targets may affect decisions to treat or intensify therapy. However, a national survey of 886 physicians found that more than 90% strongly considered the extent of HbA_{1c} elevation when choosing to initiate insulin,[5] suggesting that higher HbA_{1c} targets may lead to less intensive treatment. Moreover, human

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

ecological theory argues that human behavior tends to follow the principle of least effort[6]; for instance, forgoing medications when glycemic targets become easier to achieve. However, we agree that treatment inertia can move in either direction.

In regard to newer medication classes, we acknowledge that evidence is still emerging about their benefits. Because cardiovascular benefits were an unexpected finding during testing for cardiovascular safety, it is still too early to judge their long-term implications for diabetes management. However, because these medications have demonstrated modest reductions in blood pressure, weight, and heart failure risk in addition to their glycemic effects, it is likely that overall treatment complexity will be reduced rather than increased on average for patients receiving these medications.

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