COMMENTARY

Risks of Tight Glucose Control in Older Adults: Time to Focus Beyond Mortality

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The therapeutic management of older adults living with type 2 diabetes presents important clinical challenges. Age-related physiological and pathophysiological changes—such as altered pharmacokinetics, impaired glucose homeostasis, and declining renal function—make older patients more susceptible to adverse drug effects, particularly from glucose-lowering therapies (1,2). In this context, intensive glycemic control strategies must be approached with caution, as they may confer greater risks than benefits (3). This is especially relevant for individuals with limited life expectancy, in whom the potential long-term benefits of tight glycemic control are unlikely to be realized and may be outweighed by immediate harms.

Over the past 15 years, clinical guidelines have increasingly acknowledged the heterogeneity of the older population with diabetes and have endorsed individualized treatment goals. Rather than applying uniform ("one-size-fits-all") glycemic targets, current recommendations emphasize the need to tailor glucose control based on the patient's overall health status, functional ability, comorbidities, and life expectancy. More relaxed HbA_{1c} targets are generally advised for patients with frailty, cognitive impairment, or multiple chronic conditions (3,4). This paradigm shift toward personalized care was largely influenced by the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial: a potential association was reported between intensive glucose lowering and increased all-cause mortality in high-risk patients (5). Since then, much of the literature in this field has focused on the relationships between glycemic control and either mortality or hypoglycemia in older adults (6–9). However, critical knowledge gaps persist regarding the association between glucose control and other clinically relevant outcomes in this population (10). In this issue of *Diabetes Care*, Shabnam et al. (11) address a timely and underexplored question by examining the relationship between sustained tight glycemic control and the risk of serious fall-related events in older adults with type 2 diabetes.

In this large observational cohort study, using U.K. primary care data linked to hospital and mortality records, Shabnam et al. (11) examined whether sustained tight glycemic control—defined according to three consecutive HbA_{1c} values <7% while on insulin and/or sulfonylurea therapy—was associated with increased risk of hospitalization for falls and fractures in older adults with type 2 diabetes. The study included 21,365 individuals aged ≥70 years (mean age 77.5 years, 45% women, average diabetes duration 5 years). Most participants had multiple chronic conditions, including cardiovascular disease, chronic kidney disease, and dementia, and nearly all in the exposed group were treated with sulfonylureas (90%) and/or insulin (9%). Median HbA_{1c} for the exposed group was 6.4% (46 mmol/mol), compared with 6.8% (51 mmol/mol) for the nonexposed. In comparison with matched nonexposed individuals, there is no evidence of increased risk of falls, fractures, or combined outcomes in the exposed group (e.g., hazard for falls 1.04 [95% CI 0.96–1.11]). Over a 10-year period, absolute risks of hospitalization for falls increased with age for both groups, ranging from 15.6% to 36.8% among exposed individuals vs. 15.1% to 36.0% among nonexposed, with no evidence of a difference between groups in absolute risk across age strata. While a separate association was observed between severe hypoglycemia and fall risk, the study did not identify a meaningful increase in serious fall or fracture events specifically linked to sustained HbA_{1c} <7% during treatment with insulin or sulfonylureas.

Inherent to observational studies with use of real-world data from electronic health records (EHRs), the potential for unmeasured confounding remains an important limitation (12,13). Although the study accounted for many clinical and demographic characteristics, residual confounding by factors such as frailty, cognitive status, or psychosocial conditions cannot be fully excluded. In addition to these concerns, the use of EHRs to define outcomes such as falls presents further challenges. Falls are often undercoded or misclassified—sometimes recorded as their resulting injuries rather than the fall itself—particularly in primary care settings, where awareness of glycemic control

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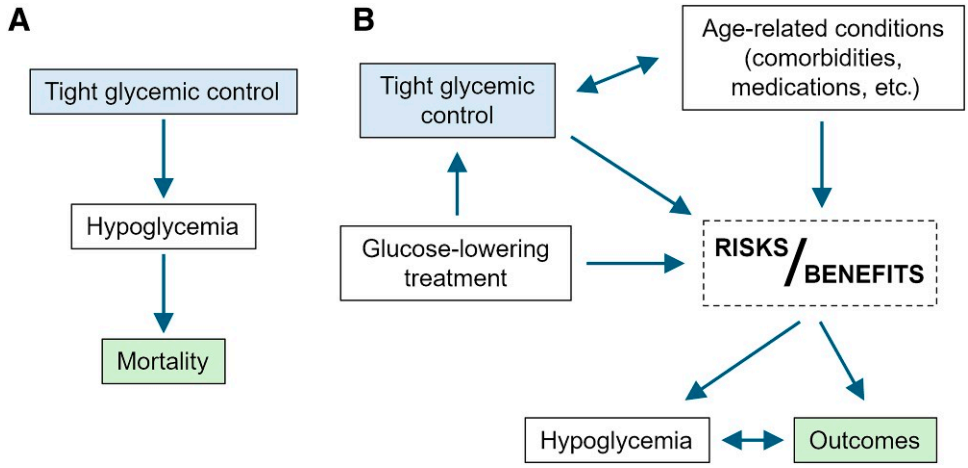

Figure 1—*A* and *B*: Illustration of the necessary shift from the traditional, assumption-driven model of research (*A*) to a more comprehensive and patient-centered framework (*B*). The new model emphasizes the importance of balancing the potential risks and benefits of glucose-lowering treatments in studying their use in older adults living with type 2 diabetes.

targets may influence the likelihood of documentation. Recent work by Wang et al. (14) demonstrated substantial discrepancies in outcome ascertainment across EHR sources, reinforcing the need for caution in relying on routine data to identify complex clinical events. These limitations may contribute to outcome misclassification and attenuate observed associations and should be considered in interpreting the study's findings. However, this constraint is largely offset by the high methodological rigor of the study—particularly the careful matching on key clinical characteristics and the extensive multivariable adjustment for other important confounding variables. The strengths of the approach taken enable the investigation of clinically relevant questions that would be challenging—or ethically problematic—to address through prospective experimental designs (15).

Several aspects of the work of Shabnam et al. are worth highlighting, particularly for the implications for future research in this field. First, the authors' careful decision to describe the exposure as "sustained HbA_{1c} <7%" (or tight glycemic control) rather than labeling it as "diabetes overtreatment" reflects a nuanced and appropriate approach. For >15 years, this situation has often been considered in the literature as a potential marker of overtreatment (6,7,9,16). However, sustained HbA_{1c} <7% while on insulin or sulfonylureas can only be considered overtreatment if it leads to net harm, which was not demonstrated in this study (17). This supports the authors' cautious and precise terminology. In recent years, particularly with the development of continuous glucose monitoring and new evidence published in *Diabetes Care* (8,18), the previously assumed link between sustained glycemic control and elevated hypoglycemia risk in older adults has been increasingly challenged (Fig. 1*A*). This study by Shabnam et al. therefore illustrates a more reasoned and evidence-informed use of the concepts of low HbA_{1c} and overtreatment.

Second, the study focuses on a clinically meaningful yet underexplored outcome: serious fall-related events leading to hospitalization. This outcome is highly relevant to the day-to-day well-being of older patients and underscores the importance of investigating a broader range of outcomes in assessing the risks and benefits of glucose-lowering therapies in this population (Fig. 1*B*). Similarly, accounting for the clinical complexity of older patients—including age-related conditions and broader health context—is essential to understanding how the benefit-risk balance may be altered (3). Moving beyond a narrow explanation centered only on treatment, hypoglycemia, and mortality is not sufficient (Fig. 1*A*). Expanding our view of treatment-related risks and benefits by broadening the scope of outcomes considered in this field is essential to better inform clinical decision-making.

Finally, future studies would benefit from incorporating the perspectives of older adults themselves. Understanding patient preferences and what matters most to them is critical to identifying and prioritizing outcomes that have previously been overlooked but may be highly valued by this population.

The work by Shabnam et al. represents an important step toward improving our understanding of the benefit-risk balance of glucose-lowering treatments in older adults with type 2 diabetes (Fig. 1). The study provides valuable insights that can help refine treatment strategies and support a more individualized and patient-centered approach to care.

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References

1. Gates BJ, Walker KM. Physiological changes in older adults and their effect on diabetes treatment. Diabetes Spectr 2014;27:20–28
2. Kirkman MS, Jones Briscoe V, Clark N, et al. Diabetes in older adults. Diabetes Care 2012;35:2650–2664
3. American Diabetes Association Professional Practice Committee. 13. Older adults: Standards of Care in Diabetes—2025. Diabetes Care 2025;48(Suppl. 1):S266–S282
4. Christiaens A, Henrard S, Zerah L, Dalleur O, Bourdel-Marchasson I, Boland B. Individualisation of glycaemic management in older people with

type 2 diabetes: a systematic review of clinical practice guidelines recommendations. Age Ageing 2021;50:1935–1942
5. Bonds DE, Miller ME, Bergenstal RM, et al. The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. BMJ 2010;340:b4909
6. Lipska KJ, Ross JS, Miao Y, Shah ND, Lee SJ, Steinman MA. Potential overtreatment of diabetes mellitus in older adults with tight glycemic control. JAMA Intern Med 2015;175:356–362
7. Baretella O, Alwan H, Feller M, et al. Overtreatment and associated risk factors among multimorbid older patients with diabetes. J Am Geriatr Soc 2023;71:2893–2901
8. Christiaens A, Boureau A-S, Guyomarch B, et al.; HYPOAGE Study Group. Diabetes overtreatment and hypoglycemia in older patients with type 2 diabetes on insulin therapy: insights from the HYPOAGE cohort study. Diabetes Care 2025;48:61–66
9. Lega IC, Campitelli MA, Austin PC, et al. Potential diabetes overtreatment and risk of adverse events among older adults in Ontario: a population-based study. Diabetologia 2021;64:1093–1102
10. Munshi MN, Meneilly GS, Rodríguez-Mañas L, et al. Diabetes in ageing: pathways for developing the evidence base for clinical guidance. Lancet Diabetes Endocrinol 2020;8:855–867
11. Shabnam S, Ling S, Gillies C, et al. Glucose control, sulfonylureas, and insulin treatment in older adults with type 2 diabetes and risk of falls and fractures: an observational study. Diabetes Care 2025;48:1744–1751
12. Moriarty F, Thompson W, Boland F. Methods for evaluating the benefit and harms of deprescribing in observational research using routinely collected data. Res Social Adm Pharm 2022;18:2269–2275
13. Hernán MA, Robins JM. Estimating causal effects from epidemiological data. J Epidemiol Community Health 2006;60:578–586
14. Wang A, Seeley AE, Sydes MR, et al. Agreement and utility of coded primary and secondary care data for long-term follow-up of clinical trial outcomes. BMC Med Res Methodol 2025;25:156
15. Blonde L, Khunti K, Harris SB, Meizinger C, Skolnik NS. Interpretation and impact of real-world clinical data for the practicing clinician. Adv Ther 2018;35:1763–1774
16. Christiaens A, Henrard S, Boland B, Sinclair AJ. Overtreatment of older people with type 2 diabetes-a high impact frequent occurrence in need of a new definition. Diabet Med 2023;40:e14994
17. Katz MH, Grady D, Redberg RF. Undertreatment improves, but overtreatment does not. JAMA Intern Med 2013;173:93
18. Bilal A. Understanding diabetes overtreatment in older adults: are we at an intersection? Diabetes Care 2025;48:47–49