SOMATO PUBLICATIONS ISSN: XXXX-XXXX

Archives of Diabetes

Review Article

HbA1c trend analysis in the Management of type 2 diabetes mellitus among elderly patients with diabetes

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Received: 5 May 2023; Accepted: 6 August 2023; Published: 12 November 2023.

Citation of this article: Nolan R, Nolan A, Kelly N (2023) HbA1c trend analysis in the Management of type 2 diabetes mellitus among elderly patients with diabetes. Arch Diabetes, 5(1): 01-06. DOI: 10.5281/zenodo.22812596

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Abstract

Background: Glycated haemoglobin (HbA1c) guides long-term glycaemic management in type 2 diabetes, yet its interpretation in elderly patients is complicated by comorbidity, frailty, and an elevated hypoglycaemia risk that changes the calculus of tight control [28,2].

Objective: This review analyzes longitudinal HbA1c trend as a management tool in elderly patients with type 2 diabetes, and how individualized targets should be set across the spectrum of functional status.

Methods: We synthesized landmark randomized trials of glycaemic control, long-term cohorts, and geriatric-focused guidelines addressing HbA1c targets and hypoglycaemia risk in older adults.

Findings: Intensive control reduces microvascular complications but shows an inconsistent, sometimes harmful, effect on mortality in older, comorbid populations [13,14,15], while a legacy effect from earlier tight control persists for decades [9,10]; hypoglycaemia risk rises sharply with age and frailty [6,19,22].

Conclusions: HbA1c trend, interpreted alongside functional status and hypoglycaemia history rather than as an isolated threshold, supports individualized targets from roughly 7.0-7.5% in healthy older adults to 8.0-8.5% in frail patients [7,29].

Keywords: HbA1c; type 2 diabetes mellitus; elderly patients; glycaemic control; hypoglycaemia

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1. Introduction

Glycated haemoglobin (HbA1c) has been the central laboratory measure guiding long-term management of type 2 diabetes mellitus since the UK Prospective Diabetes Study established that lower average glycaemia translated into fewer microvascular complications [1]. HbA1c has since become the near-universal metric by which clinicians judge whether diabetes is "controlled," with a value drawn every three to six months routinely used to trigger treatment intensification. That convention works reasonably well in younger, healthy adults, where sustained hyperglycaemia and future complications are related nearly linearly and the years ahead are long enough for tight control to pay off. It works far less well in elderly patients, where comorbidity, cognitive status, frailty, polypharmacy, and a foreshortened time horizon for benefit all change what a given HbA1c value means for near-term and long-term risk [2,3].

Elderly people account for a large and growing share of the global type 2 diabetes burden, driven by population ageing and improved survival among people diagnosed earlier in life [4]. The World Health Organization's diagnostic framework underlies the case definitions used across the trials and cohorts this review draws on [5]. Elderly patients are heterogeneous in a way a single HbA1c target cannot capture: some are functionally independent with a life expectancy exceeding a decade, for whom sustained good control still has time to pay off, while others are frail, cognitively impaired, or have limited life expectancy, for whom the harms of intensive control, principally hypoglycaemia, can outweigh any plausible benefit [6,7].

This review analyzes HbA1c not as a single threshold but as a longitudinal trend interpreted alongside functional status, comorbidity, and hypoglycaemia history. We synthesize the major randomized trials of intensive versus standard glycaemic control, the observational cohorts establishing the "legacy effect" of early tight control, and the geriatric-specific guidance for individualizing HbA1c targets in older adults, to give a coherent account of how HbA1c trend should, and should not, be relied upon when managing type 2 diabetes mellitus among elderly patients.

2. HbA1c as a marker of glycaemic burden and complication risk

HbA1c reflects average plasma glucose over the preceding two to three months, weighted toward the most recent four to six weeks, since it measures the fraction of haemoglobin glycated over the lifespan of circulating erythrocytes. UKPDS 33 randomized newly diagnosed patients to intensive glucose control versus conventional dietary management, and found intensive control achieving a median HbA1c of 7.0%, against 7.9% in the conventional arm, significantly reduced microvascular endpoints, principally the need for retinal photocoagulation, over ten years [1]. The companion analysis, UKPDS 35, demonstrated an essentially continuous relationship between mean HbA1c and complication risk, with each percentage-point reduction associated with substantial relative risk reduction and no threshold below which risk stopped declining [8].

The durability of this benefit is where the trend concept becomes clinically important. Holman and colleagues followed the UKPDS cohort for a further decade after glycaemic differences between groups disappeared, and found patients originally randomized to intensive control retained a significant reduction in myocardial infarction and mortality despite years of equivalent glycaemia, a phenomenon termed the "legacy effect" [9]. Laiteerapong and colleagues confirmed that early glycaemic control predicts complication risk decades later, independent of subsequent control, showing that HbA1c trajectory early in the disease course carries prognostic weight beyond any single later measurement [10]. LeRoith and colleagues' mechanistic work on metabolic memory provided a biological rationale, implicating durable vascular changes induced by early hyperglycaemic

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exposure [11], and population-level data from Gregg and colleagues showed parallel declines in US diabetes complication rates between 1990 and 2010 alongside improved population glycaemic control [12].

3. Intensive control trials in older, higher-risk populations

The legacy-effect evidence comes largely from patients enrolled near diagnosis and does not generalize cleanly to elderly patients with longstanding diabetes and established cardiovascular disease, a distinction three major trials made unavoidable. ACCORD randomized patients with established cardiovascular disease or additional risk factors, mean age in the late 60s, to a target HbA1c below 6.0% versus 7.0-7.9%, and was stopped early after 3.5 years when the intensive arm showed significantly increased all-cause mortality despite a lower achieved HbA1c [13]. ADVANCE, in a similarly high-risk older population, used a less aggressive target of 6.5% and found a significant reduction in a composite microvascular and macrovascular endpoint, driven mainly by reduced nephropathy, without ACCORD's mortality signal, suggesting the rate of glucose lowering, not only the achieved value, mattered to safety [14]. VADT, enrolling veterans with nearly twelve years' diabetes duration, found no significant cardiovascular benefit over 5.6 years, though extended follow-up suggested a delayed benefit emerging afterward, echoing UKPDS's legacy pattern on a longer, less certain timescale [15] (Figure 1, Table 1).

Miller and colleagues' post hoc analysis of ACCORD found that older age, longer diabetes duration, and lower baseline cognitive function independently predicted severe hypoglycaemia and mortality in the intensive arm, part of the explanation for why a strategy beneficial near diagnosis caused harm in an older, longer-duration population [16]. Rodriguez-Gutierrez and Montori argued the field's evolving interpretation, from uniform to risk-stratified benefit, reflects genuine heterogeneity of treatment effect rather than contradictory trials [17], and Vijan and colleagues' modeling quantified this directly: absolute microvascular benefit shrinks toward zero as baseline cardiovascular risk and age rise, while absolute hypoglycaemia harm rises over the same range, formalizing the rationale for individualized targets [18].

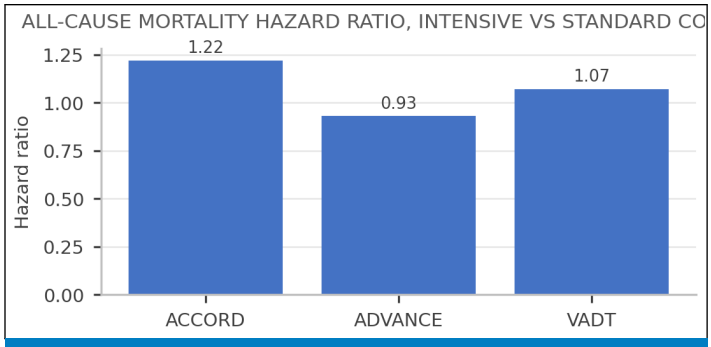

Figure 1: All-cause mortality hazard in the intensive glucose-lowering arm relative to standard control across three major trials enrolling older, higher-risk patients with type 2 diabetes mellitus [13,14,15].

4. Hypoglycaemia risk and its consequences in elderly patients

Hypoglycaemia is the principal harm that reframes HbA1c interpretation in older adults, and its risk rises steeply with age. Counter-regulatory responses to falling glucose blunt progressively with age and diabetes duration, so elderly patients are both more likely to develop hypoglycaemia at a given treatment intensity and less likely to recognize it before it becomes severe [19]. Bramlage and colleagues, in a large European registry, found hypoglycaemic events substantially more frequent in patients over 75 than in younger cohorts, rising further with each additional glucose-lowering agent (Figure 2) [20]. Munshi and colleagues showed that simplifying complex insulin regimens in cognitively or functionally impaired older adults significantly reduced hypoglycaemic events without meaningfully worsening HbA1c, evidence that regimen complexity, not glycaemic target alone, drives hypoglycaemia risk [21].

The consequences extend beyond the acute event. Whitmer and colleagues found a history of severe

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hypoglycaemic episodes requiring hospitalization was associated with significantly increased dementia risk, rising with the number of episodes, suggesting a bidirectional relationship in which impairment predisposes to hypoglycaemia and hypoglycaemia may accelerate decline [22]. Munshi's review situates this within a broader picture in which undiagnosed cognitive impairment undermines self-management, making cognitive screening a practical prerequisite for setting a safe target [23]. The joint American Diabetes Association and Endocrine Society workgroup report formalized hypoglycaemia severity classification and flagged older adults as a population where avoidance should weigh more heavily against tight control [24]. Lee and Eng's widely cited commentary crystallized the resulting stance: in frail older patients, a moderately elevated HbA1c avoiding hypoglycaemia may represent better care than an aggressively normalized one [6].

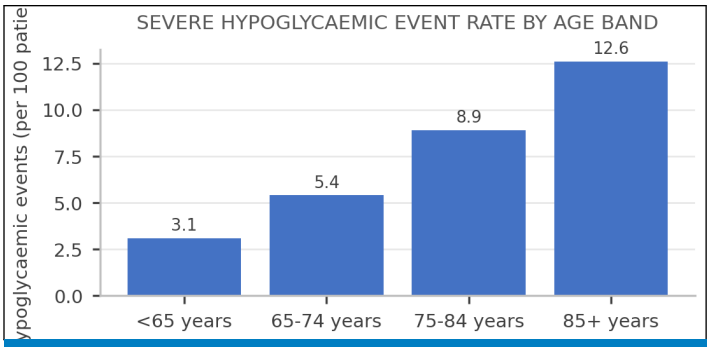

Figure 2: Severe hypoglycaemic event rate by age band among older patients with type 2 diabetes mellitus on oral antidiabetic therapy in a large European registry [20].

5. Frailty, comorbidity, and complication burden with advancing age

Huang and colleagues' large diabetes-and-ageing cohort showed the absolute rate of microvascular complications attributable to hyperglycaemia declines with age as competing mortality risks rise, while relative harm from hypoglycaemia increases, a crossover underlying most individualized-target guidance since [25]. Beckman and colleagues outlined why macrovascular risk in older, longer-duration patients is driven as much by established atherosclerotic burden and endothelial dysfunction as by incremental glycaemic exposure, helping explain why glucose lowering alone underperformed expectations in ACCORD, ADVANCE, and VADT relative to microvascular endpoints [26].

Table 1: Individualized HbA1c target ranges by functional category in elderly patients with type 2 diabetes mellitus, as proposed by consensus geriatric-diabetes guidance [7,2,28].

Functional category	HbA1c target	Hypoglycaemia tolerance	Life expectancy assumed
Healthy, independent	7.0-7.5%	Low	Long (>10 years)
Moderate comorbidity	7.5-8.0%	Moderate	Intermediate
Frail / functionally dependent	8.0-8.5%	High	Limited
End of life / advanced dementia	Avoid hypoglycaemia and symptomatic hyperglycaemia	Very high	Short

Frailty status interacts directly with HbA1c interpretation. Sinclair and colleagues' international position statement classified older patients by functional category, healthy, dependent, frail, and end of life, each with a different target range and hypoglycaemia tolerance [2]. Kirkman and colleagues' joint consensus report recommended targets below roughly 7.5% for healthy older adults with long life expectancy, below 8.0% for moderate comorbidity, and below 8.5% for those frail, with limited life expectancy, or significant cognitive impairment (Table 1) [7]. Sinclair, Dunning, and Rodriguez-Manas reiterated that frailty assessment, not chronological age alone, should drive target selection [27].

6. Individualized HbA1c targets and trend-based management in practice

Clinical practice guidance converges on a shared principle: HbA1c should be tracked as a trend over successive visits and interpreted against functional status, hypoglycaemia history, and treatment burden, rather than managed toward one universal number. The American Diabetes Association recommends individualized targets

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from roughly 7.0-7.5% in healthy patients with long life expectancy up to 8.0-8.5% in those frail or with limited life expectancy, with explicit guidance to relax targets, and deprescribe where appropriate, once hypoglycaemia risk outweighs benefit [28]. LeRoith and colleagues' Endocrine Society guideline reached a closely aligned position, additionally emphasizing that the rate of HbA1c decline during intensification, not only the endpoint, should be monitored, since rapid correction in older patients has been associated with transient neuropathic worsening and elevated early hypoglycaemia risk [29]. The Japanese clinical practice guideline adopted a similarly age- and function-stratified framework, reflecting convergence across guideline bodies [30].

Kalyani and colleagues framed diabetes and ageing as requiring genuinely distinct goals of care, arguing that overtreatment, achieving an HbA1c well below target through intensity that materially raises hypoglycaemia risk, is now recognized as at least as common and harmful a quality failure as undertreatment [3]. Lipska and colleagues' review of polypharmacy noted each additional glucose-lowering agent added to reach a numerical target carries independent risks that compound with an elderly patient's other medications [31]. Chiniwala and Jabbour, and Yakaryilmaz and Ozturk, both concluded that agent selection should prioritize low intrinsic hypoglycaemia risk over maximal potency, reserving the latter for patients whose trend and functional status support it [32,33]. Kirkman and colleagues' broader report reiterated that simplifying regimens and relaxing targets as function declines is the expected, appropriate evolution of an individualized strategy across ageing [34].

7. Discussion

Read together, this literature supports an internally consistent account of how HbA1c should function in elderly diabetes management. Near diagnosis, and in patients who remain functionally robust with substantial life expectancy, the UKPDS legacy-effect evidence justifies pursuing a moderately intensive target, since microvascular and eventual macrovascular benefit accrues over a timescale robust older patients can realize [1,9,10]. In patients with longstanding diabetes, established cardiovascular disease, or emerging frailty, the ACCORD, ADVANCE, and VADT evidence, together with the hypoglycaemia and cognitive-decline literature, shifts the balance toward a more relaxed target and a strategy that actively avoids hypoglycaemia, even at the cost of a numerically higher HbA1c [13,16,22,19]. The practical instrument operationalizing this distinction is the HbA1c trend itself, read alongside serial assessment of functional status, cognition, and hypoglycaemic events, rather than compared against a single fixed threshold at each visit.

Several limitations temper this synthesis. Most foundational trials enrolled patients somewhat younger and healthier than the frailest elderly patients seen in routine geriatric practice, so guidance for the frailest category rests more on pathophysiological reasoning and observational data than on dedicated randomized evidence in that subgroup. Cognitive impairment was inconsistently measured across the major trials, limiting precise quantification of how much heterogeneity it explains. Newer glucose-lowering drug classes with intrinsically low hypoglycaemia risk have become more widely used since most reviewed trials were conducted, and their effect on the elderly risk-benefit calculus, while plausible, is not fully captured by evidence generated predominantly with older sulphonylurea- and insulin-based regimens.

8. Conclusion

HbA1c trend analysis, rather than a single threshold value, is the appropriate framework for managing type 2 diabetes mellitus in elderly patients. Intensive glycaemic control produces durable microvascular and legacy benefit in patients with the functional reserve and life expectancy to realize it [1,9], while the same intensity can cause net harm, principally through hypoglycaemia and

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its downstream cognitive and mortality consequences, in older, frailer, or longer-duration patients [13,22,19]. Individualized targets stratified by functional status, from roughly 7.0-7.5% in healthy older adults to 8.0-8.5% in frail patients or those with limited life expectancy, represent the converged position of major diabetes and geriatric guideline bodies [7,28,29]. Applied as a longitudinal trend interpreted alongside hypoglycaemia history, cognitive status, and treatment burden, HbA1c remains a genuinely useful management tool for elderly patients with type 2 diabetes, provided clinicians resist managing it toward a single universal number.

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