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Optimizing HbA1c Targets and Continuous Glucose Monitoring to Mitigate Dementia Risk in Type 1 Diabetes: A Narrative Review

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Abstract

This review seeks to answer a practical question: what HbA1c range minimises the risk of dementia in people with type 1 diabetes and how continuous glucose monitoring (CGM), may influence glycaemic patterns that are linked to cognitive outcomes? Methods: Narrative review (2013 - 2025) of PubMed and Google Scholar articles on adults and adolescents with type 1 diabetes linking glycaemic control to cognitive outcomes and continuous glucose monitoring. Type 2 diabetes data were cited only when T1D evidence was lacking. Results: In five randomised trials, the use of continuous glucose monitoring (CGM) systems lowered HbA1c by up to 0.6 percentage points, shortened time spent <70 mg/dL by 20-100 min/day, and reduced the incidence of severe hypoglycaemia by 65 - 72% in adolescents, adults, and adults aged ⩾60 years. Registry data in individuals aged ⩾50 years showed a 66% higher risk of dementia after a single hospital-treated episode of severe hypoglycaemia and a sixfold increase when severe hypoglycaemia and hyperglycaemia co-occurred. Maintaining HbA1c between 6.0 and 7.9% for ⩾ 50% of follow-up lowered dementia incidence by ~ 45%, whereas a predominance of values ⩾8% increased it by 65 - 80%. Conclusions: These findings indicate that CGM-driven glycaemic stabilisation is a promising strategy for reducing neurodegenerative risk in people with type 1 diabetes. Stable mid-range glycaemia (HbA1c ≈7%), while avoiding both chronic hyperglycaemia and severe hypoglycaemia, appears the most defensible therapeutic target. Continuous glucose monitoring should be prioritised for adults with impaired awareness, recurrent severe events or advanced age, yet its direct cognitive benefit remains unproven.

Keywords **type 1 diabetes; HbA1c thresholds; continuous glucose monitoring; dementia risk; cognitive decline**

INTRODUCTION

Life expectancy of people diagnosed with type 1 diabetes has improved. In children diagnosed with type 1 diabetes after 1965, the gap in life expectancy compared with non - diabetic peers had narrowed to just 4 - 6 years, compared to more than 17 - year deficit seen in earlier cohorts [1]. Dementia is one of a clinically relevant complications of type 1 diabetes, particularly when the disease is sub - optimally managed. Large prospective cohorts show that adults with diabetes are more likely to develop dementia than people without [2], especially when poorly controlled [3]. These two factors combined are likely to increase the number of people living with type 1 diabetes - related dementia in the future, burdening healthcare services and diminishing the quality of life for patients and their families. In 2019, the World Health Organization estimated that dementia imposed a global societal cost of about US$ 1.3 trillion, roughly 1.5 % of the world's GDP [4]. To better understand how to prevent those complications it is required to determine factors that underlie the development of dementia in people with type 1 diabetes. Through a narrative review, we seek to present current evidence-base regarding this subject matter.

MATERIALS AND METHODS

Data collection and analysis

We performed a narrative review of studies published between 2013 and 2025, using PubMed and Google Scholar, that examined the relationship between glycaemic control and cognitive outcomes in adults and adolescents with type 1 diabetes and the possible role of continuous glucose monitoring (CGM). Searches incorporated keywords such as "type 1 diabetes AND dementia", "glycaemic control AND risk of dementia", "CGM AND hypoglycaemia", and "life expectancy AND type 1 diabetes".

We focused primarily on research in type 1 diabetes and supplemented the discussion with findings from type 2 diabetes when T1D - specific data were unavailable. Two independent reviewers screened titles and abstracts (last search - April 2025); disagreements were resolved by consensus.

Inclusion and exclusion criteria

For this narrative review we included only full-text articles accessible via PubMed or Google Scholar, published between 2013 and 2025 in English or Polish. Eligible study designs comprised randomised controlled trials (including long-term or open-label extensions), prospective or retrospective cohort studies and population-based registry analyses, provided they enrolled $\geqslant$30 participants per intervention arm in RCTs or $\geqslant$50 individuals in observational studies.

Studies had to involve individuals aged $\geqslant$12 years with type 1 diabetes of at least one year's duration. Evidence from studies analysing type 2 diabetes was accepted only when no type 1 diabetes data were available for a given question.

At least one of the following outcomes was required: clinically confirmed dementia or mild cognitive impairment, validated neuropsychological test performance, long-term glycaemic indices, or the incidence of the American Diabetes Association, ADA, level 3 severe hypoglycaemia.

We excluded papers published before 2013, case reports and uncontrolled series with <50 patients, conference abstracts, letters to the editor, commentaries, preclinical studies and purely economic models lacking clinical outcomes. Articles written in languages other than English or Polish were deemed ineligible, as were studies that did not allow extraction of type 1 diabetes data despite such data being

available elsewhere. Research confined to children under 12 years, acute hypoglycaemia clamp experiments, or complications unrelated to cognition were also excluded.

AI assistance

In preparing this work, we used ChatGPT for the purpose of translation and editing only. We then reviewed and edited the manuscript for its intellectual content and academic rigour.

RESULTS

Chronic Hyperglycaemia

Long-term hyperglycaemia underlies many diabetes complications, among them vascular complications, especially microvascular such as nephropathy and retinopathy. It is well established, that lowering HbA1c levels can prevent those complications [5], [6]. A meta-analysis of 28 prospective cohorts comprising more than 2.3 million individuals, provided by Gudala et al. [7], showed that diabetes confers a 73% increase in the overall risk of dementia. Although Alzheimer's disease remains the most frequently recorded subtype among people with diabetes, this predominance mirrors its ubiquity in the general population; within the diabetic population the relative excess is greatest for vascular dementia (RR 2.27 versus 1.56 for Alzheimer's disease). These findings suggest that diabetes-related microangiopathy and macroangiopathy is a main pathological pathway linking chronic hyperglycaemia with cognitive decline [7]. Likewise, in a Swedish population-based cohort with rigorously adjudicated dementia diagnoses, clinical type 2 diabetes raised the risk of vascular dementia by 84% (aHR 1.84) and each 1-SD increase in a genome-wide polygenic risk score for diabetes added another 28%, with neither exposure affecting "pure" Alzheimer's disease [8]. Prospective data from adults with type 1 diabetes indicate that maintaining HbA1c between 6.0 and 7.9% for at least half of the observation period is associated with an ≈ 45% lower incidence of dementia. When the majority of HbA1c values rise to 8.0 - 8.9 %, the hazard of dementia increases by 65%, and at ≥9% it rises by 79%. Concentrations below 6% confer no additional benefit and may even entail a modest, nonsignificant increase in risk, although numbers were small [3]. These findings suggest that keeping HbA1c consistently below 8%, rather than pursuing near-normoglycaemia, is the most pragmatic target for limiting the microvascular and macrovascular injury that underlies vascular dementia in diabetes.

The Satuli-Autere et al. study shows that adults with type 1 diabetes have a roughly two- to threefold higher risk of dementia, with the greatest excess for vascular dementia. This risk is already present in people who have no clinical signs of microvascular or macrovascular disease, suggesting that long disease duration and cumulative hyperglycaemia can start neurodegeneration before vascular damage becomes clinically visible [9]. When these results are considered alongside studies that link dementia to current HbA1c ≥8% and to severe glycaemic swings, the implication is clear – stable glycaemic control and regular screening for complications should begin soon after diagnosis and continue throughout life.

Severe hypoglycaemia

One of the short - term complications of intensive insulin therapy, which is a gold standard in treating type 1 diabetes, is hypoglycaemia. The current ADA Standards of Care (2024) divide hypoglycaemia into three tiers:

- Level 1: plasma glucose <70 mg/dL (3.9 mmol/L) but ≥54 mg/dL (3.0 mmol/L). This is an alert stage – the patient should take fast-acting carbohydrates, although neuro - glycogenic symptoms are usually absent.

- Level 2: plasma glucose <54 mg/dL (3.0 mmol/L). This threshold marks clinically significant hypoglycaemia – cognitive or autonomic impairment can develop quickly, so immediate treatment is required.

- Level 3: any episode requiring external assistance, regardless of the measured glucose. Here consciousness or motor function is impaired to the extent that the person cannot self-treat.

To date, only grade 3 hypoglycaemia has been proven to be a causative factor for dementia in scientific studies. Severe hypoglycaemia continues to pose a clinically significant hazard for individuals who depend on insulin therapy. Evidence from the 30-year DCCT/EDIC follow-up illustrates the magnitude of this risk. At trial entry, intensive therapy, multiple daily injections or continuous subcutaneous insulin infusion, ≥4 - 6 capillary glucose tests per day and a near-normoglycaemic HbA1c target, generated ≈ 61 severe episodes per 100 patient-years, a threefold excess over conventional therapy (one - two injections, infrequent self - monitoring, no explicit target). Three decades later the incidence curves converged – both former treatment groups now sustain ≈38 - 41 episodes per 100 patient-years. Over the entire observation window, ≈53% of participants experienced at least one episode of severe hypoglycaemia, whereas ≈47% remained event-free. Notably, 7% of the cohort accounted for nearly one third of all events, indicating a persistently high-risk minority. A prior episode remains the most powerful predictor of recurrence. Younger age at diagnosis magnifies risk, whereas contemporary pump therapy is protective. Although rigorous glycaemic control still confers a proportional hazard, each 10% reduction in HbA1c increases subsequent risk by roughly 13-15%, advances in technology have mitigated the absolute burden relative to the 1980s baseline [10].

Severe hypoglycaemia (type 3) has emerged as a modifiable risk factor for cognitive decline in type 1 diabetes. In a large U.S. registry of adults aged ≥50 years, a single hospital-treated episode increased the incidence of clinically diagnosed dementia by 66%, and concomitant exposure to both severe hypoglycaemia and hyperglycaemia amplified the risk sixfold [11]. Comparable results were observed in a Japanese geriatric outpatient sample, where any severe episode within the previous five years correlated with lower MMSE and HDS-R scores in a clear dose-response fashion [12]. By contrast, participants in the intensively monitored DCCT/EDIC cohort, recruited as young adults with minimal vascular disease, displayed only a modest acceleration in psychomotor slowing after 32 years, without overt dementia [13].

Differences between these studies can be explained by variations in cohort age, diabetes duration, and the methods used to capture both hypoglycaemic exposure and cognitive outcomes. Older, long-standing patients already bear a substantial microvascular and macrovascular burden. Hospital databases record only the most extreme episodes and administrative data capture frank dementia, whereas DCCT/EDIC relied on self-reported events of mixed severity and tracked subtler neuropsychological endpoints. Taken

together, current evidence suggests that severe hypoglycaemia is a potent, though age - dependent, threat to brain health in type 1 diabetes, with its most pronounced effects manifesting after decades of disease.

Optimal glycaemic control for dementia prevention

Sustained glycaemic exposure constitutes a key determinant of neurocognitive prognosis in diabetes. In older adults with type 1 diabetes, maintenance of at least 50% of longitudinal HbA1c measurements within the range 6.0 - 7.9% (42 - 63 mmol mol^{-1}) is associated with an almost 45% reduction in incident dementia, whereas chronic exposure to values ≥8.0% confers a 65 - 80% excess risk [3]. Large-scale investigations conducted in predominantly type 2 diabetic populations indicate a higher inflection point: dementia incidence increases appreciably only when HbA1c persistently exceeds 9% [14]. Beyond the arithmetic mean, glycaemic stability itself is salient. Among individuals aged ≥ 65 years, spending <6 % of follow-up within the 6 - 9% interval, or exhibiting high within-person variability, results in a further 15 - 30% risk elevation [15], [16]. Several cohorts describe a nonlinear, U-shaped association. In the Hong Kong RAMP-DM programme, the nadir of risk was observed at HbA1c 6.5 - 7.5%; both stringent control < 6%, presumably through a higher burden of hypoglycaemia, and sustained hyperglycaemia >8.5% proved deleterious [17]. By contrast, community-based samples, in which severe hypoglycaemia is uncommon, demonstrate a near-linear relation – each single percent increment in HbA1c accelerated memory decline by ≈0.05 SD per annum [3].

Taken together, these findings support an HbA1c target in the order of 6.5 - 7.5% for most adults with longstanding diabetes, conditional on minimising both chronic hyperglycaemia and glycaemic excursions. Persistent values of ≥ 8 - 9% emerge as a modifiable, dose-dependent contributor to dementia, whereas overly intensive regimens yielding HbA1c <6% may negate benefit in older, insulin treated patients through heightened hypoglycaemic exposure. Variation in apparent thresholds across studies reflects heterogeneity in diabetes phenotype, age distribution, hypoglycaemia prevalence and the metrics employed to characterise glycaemic burden (mean level, time in range, variability). Optimising cognitive outcomes therefore requires not merely the attainment of an appropriate HbA1c average, but also its maintenance with minimal oscillation and without provoking severe hypoglycaemia.

To contextualise the heterogeneity described above, Table 1 isolates the principal methodological features that are likely to drive inter-study divergence in HbA1c thresholds. By comparing each cohort's clinical composition, glycaemic metric, and mode of dementia ascertainment with its headline result, the table highlights how differences in diabetes phenotype, age structure, hypoglycaemia burden, exposure definition, and outcome adjudication can shift the apparent "safe" range of HbA1c.

TABLE 1. FACTORS THAT PROBABLY CAUSE DIFFERENT STUDIES TO REPORT VARYING HBA1C CUT - OFF VALUES

Study	Clinical group under investigation	Principal finding on HbA1c and dementia risk	Methodological attributes that may explain the divergence
Lacy & Whitmer 2018	Older adults (≥ 50 years) with long-standing type 1 diabetes treated within the Kaiser Permanente system.	When ≥ 50 % of HbA1c readings lay between 6.0 % and 7.9 %, dementia incidence fell by ~ 45 %; chronic exposure to ≥ 8 % raised risk by 65 - 80 %, and a non -significant trend towards harm was noted below 6 %.	A pure T1DM cohort experiences frequent insulin - related hypoglycaemia, so the harmful threshold is lower than in T2DM. Dementia was identified only through ICD codes, capturing clinically overt cases.
Moran 2023	Predominantly male U.S. veterans with type 2 diabetes followed in routine care.	Dementia risk rose sharply only when HbA1c persistently exceeded 9 %. Values from 7 % to 8.9 % were risk -	Insulin resistance and infrequent hypoglycaemia in this T2DM group shift the critical threshold upward. Outcome ascertainment relied on

		neutral.	electronic health -record coding.
Underwood 2024	Individuals aged ≥ 65 years with mixed diabetes types, assessed for "time-in-range" (TIR).	Spending < 60 % of follow-up time with HbA1c between 6 % and 9 % increased the hazard of Alzheimer's disease and related dementias by ~ 27 %.	The metric emphasised glycaemic stability rather than mean level - advanced age amplifies the impact of instability on neurodegeneration.
Wang 2024	55 618 adults with type 2 diabetes enrolled in a structured, multidisciplinary primary - care programme.	A U-shaped curve emerged: the lowest dementia risk occurred at HbA1c 6.5 - 7.5 %, whereas both < 6 % and ≥ 9 % were deleterious.	Programme participation limits hypoglycaemia, so very low HbA1c indicates unusually aggressive treatment outside the programme, explaining the left limb of the U - curve.
ELSA 2018	Community - dwelling adults aged ≥ 50 years, most without diagnosed diabetes.	Each 1 % increment in HbA1c accelerated annual memory decline by ~ 0.05 SD. No lower threshold of harm was detected.	Severe hypoglycaemia is rare in this setting, so the relation is driven almost exclusively by chronic glucotoxicity. Cognitive outcomes were measured with detailed neuropsychological tests, capturing subclinical decline.

Continuous Glucose Monitoring (CGM) as an element of strategy for Dementia Prevention in Diabetes

By providing a near-continuous stream of readings, typically >250 measurements per day, CGM captures nocturnal hypoglycaemia, rapid post-prandial excursions, and prolonged periods of hyperglycaemia that conventional capillary self-monitoring often misses, thereby enabling data-driven titration of insulin, dietary adjustments, and early intervention in response to impending lows or highs. Although randomised trials designed to test CGM as a dementia prevention strategy are still lacking, a substantial body of evidence demonstrates that CGM use reliably reduces both severe hypoglycaemic episodes and periods of extreme hyperglycaemia [5].

Both chronic hyperglycaemia and extreme glucose excursions (severe hypoglycaemia or marked variability) have been repeatedly implicated in structural brain injury and accelerated cognitive decline [10]. Conventional self-monitoring of blood glucose (SMBG) captures only isolated time - points and therefore misses nocturnal lows, post-prandial spikes and prolonged periods above target. CGM provides dense, continuous data and actionable real-time alarms, positioning the technology as a plausible neuroprotective tool. In this chapter we will analyse how continuous glucose monitoring affects the severe hypoglycaemia episodes and glycated haemoglobin (HbA1c).

Impact on HbA1c

In the DIAMOND trial, 158 adults with type 1 diabetes (disease duration ≥1 year; mean age ≈48 years; baseline HbA1c ≈8.6 %) who managed their diabetes with multiple daily insulin injections were assigned either to real-time CGM or to conventional finger-stick monitoring for 24 weeks. Participants in the CGM arm achieved a 0.6 percentage – point greater fall in HbA1c, spent roughly half as much time each day below 70 mg/dL, and were twice as likely to reach an HbA1c target below 7.5% compared with those using SMBG alone [18].

In individuals with type 1 diabetes, the most challenging phase for maintaining glycaemic stability occurs during adolescence and early adulthood. Poor metabolic control in this critical window can initiate pathological processes that lead to microvascular and macrovascular complications, which may persist, even when good glycaemic targets are achieved later in adult life. In a randomised trial involving 153 adolescents and young adults (14 - 24 years) with type 1 diabetes treated by multiple daily injections, six months of real-time CGM (Dexcom G6) produced a mean HbA1c decrease of 0.40 percentage points

relative to SMBG, increased time in range by about 1.6 hours per day, and reduced time spent below 70 mg/dL by 20 minutes per day, without raising the incidence of severe hypoglycaemia [19].

As outlined in a preceding chapter, the preventive value of maintaining target HbA1c levels rises with advancing age, such that strict and stable glycaemic control becomes increasingly critical for mitigating dementia risk in older patients. The WISDM trial, which followed 203 individuals aged 60 years or older with established type 1 diabetes managed by multiple daily insulin injections, found that six months of real - time CGM (Dexcom G5) led to an additional 0.3 percentage - point reduction in HbA1c compared with conventional finger - stick monitoring. CGM use also shortened daily exposure to glucose levels below 70 mg/dL by roughly an hour and lowered the rate of clinically significant (< 54 mg/dL) hypoglycaemia by about 65 %, all without increasing time spent above the target range [20].

The closer HbA1c approaches its therapeutic target, the harder it becomes to achieve additional reductions without simultaneously increasing the risk of hypoglycaemic episodes. In the group of adults with well-controlled type 1 diabetes on multiple daily injection therapy, flash CGM reduced daily hypoglycaemia exposure by 46%, from 3.4h per day to 1.9 h per day, while maintaining HbA1c and increasing time in range, underscoring the device's ability to curb low-glucose burden even when average glycaemia is already near target [21].

Impact of CGM use on severe hypoglycaemia

Among people with type 1 diabetes, those who have impaired awareness of hypoglycaemia, an acquired inability to perceive the usual adrenergic and neuro-glycopenic warning symptoms as glucose falls, form one of the groups at greatest risk for severe low glucose events.

The HypoDE study focused precisely on this population: 149 adults with long-standing type 1 diabetes who either lacked hypoglycaemia warning signs or had suffered at least one assistance - requiring event in the previous year. Participants, all on multiple daily injections, were randomised to real-time CGM (Dexcom G5) or conventional fingerstick testing for six months. CGM produced a striking safety benefit: the incidence of severe hypoglycaemia fell by about 72 %, from roughly 11 to 3 - 4 events per 100 patient years, whereas no meaningful change occurred in the control arm. Sensor uses also cut time spent below 54 mg/dL (3.0 mmol/L) by ~40 minutes per day, yet average HbA1c remained virtually unchanged in both groups. Thus, for injection treated adults who cannot reliably sense falling glucose, real - time CGM markedly lowers the frequency and duration of dangerous lows without sacrificing overall glycaemic control [22].

Older adults with type 1 diabetes carry the heaviest burden of dementia risk, owing to their long cumulative exposure to dysglycaemia and the additive impact of age - related neurovascular vulnerability. Within this high - risk group, the WISDM randomised trial demonstrated that real - time CGM can deliver a decisive safety advantage. Over 26 weeks, sensor use cut time spent below 70 mg/dL by about 32 minutes per day and reduced level 2 hypoglycaemia (<54 mg/dL) by roughly 14 minutes, while severe episodes fell from four in the control arm to a single event in the CGM arm. Time in the 70-180 mg/dL range rose by approximately two hours daily, and mean HbA1c improved modestly by 0.3 percentage points without any increase in hyperglycaemia. These data indicate that, in the very population most susceptible to hypoglycaemia related cognitive decline, real-time CGM can substantially lighten the hypoglycaemic load yet preserve, or even enhance, overall glycaemic control [18].

The protective effect of CGM is not limited to people with poor glycaemic control or those already at high risk for dementia. Evidence from the IMPACT trial shows that adults with type 1 diabetes who were

already near target HbA1c (~6.8 %) and retained normal hypoglycaemia awareness also gained a clear safety benefit. Over six months, flash CGM users (FreeStyle Libre) recorded only one assistance - requiring episode, whereas their standard SMBG counterparts experienced four, amounting to an ≈75% relative reduction. Although absolute counts were small, the result indicates that flash CGM can further cut the danger of severe lows even in low risk, well regulated patients, adding to its known ability to halve biochemical hypoglycaemia and prolong time in range [19].

DISCUSSION

Data obtained so far consistently show that the benefits of continuous glucose monitoring (CGM) span all age groups, translating into both improved metabolic control and a marked reduction in hypoglycaemia. In five randomised trials, DIAMOND (adults), GOLD (adults) and Laffel et al. (adolescents and young adults), WISDM (≥60 years), HypoDE (individuals with impaired hypoglycaemia awareness) and IMPACT (well-controlled adults using flash CGM), CGM systems lowered HbA1c by 0.0 - 0.6 percentage points, shortened time spent <70 mg/dL by 20 - 100 min. per day (with the largest absolute reduction of -1.65 h/day in IMPACT), and reduced the incidence of severe, assistance requiring hypoglycaemia by roughly 65 - 72%. The effect was greatest in adults with a baseline HbA1c of about 8.6%, nonetheless remained significant in adolescents (-0.4 pp) and persisted in older adults (-0.3 pp), underscoring the utility of CGM throughout the patient's life course.

In a study of individuals aged ≥50 years, a single hospital treated severe hypoglycaemic episode increased the risk of being diagnosed with dementia by 66%, while the co-occurrence of severe hypoglycaemia and hyperglycaemia multiplied this risk six-fold. Moreover, although about 53% of patients experience at least one such episode, just 7% account for nearly one third of all events, identifying a particularly vulnerable subgroup whose targeted protection could yield disproportionately large benefits [10,11].

Keeping HbA1c within 6.0 - 7.9% for at least half of the observation period was associated with an ≈45% reduction in dementia incidence, whereas predominance of values ≥8% raised the risk by 65 - 80%. Maintaining HbA1c below 6% offered no additional benefit and may even increase risk, probably due to more frequent hypoglycaemic episodes [3].

Taken together, these data indicate that effective neurodegenerative prophylaxis in people with type 1 diabetes requires not only aiming for relatively low but, above all, stable HbA1c levels, minimising large glycaemic fluctuations, and identifying patients with recurrent hypoglycaemia – a group for whom CGM appears particularly promising in the context of dementia prevention.

Limitations in studies exploring the CGM-dementia relationship

The included studies the following limitations:

- *Lack of randomized interventional trials:* Current evidence is drawn mainly from observational cohort studies. Consequently, it remains unclear whether improving glycaemic control truly prevents cognitive decline or merely is associated with it.
- *Data-source constraints:* Registry-based studies relying on ICD-10 codes provide large sample sizes but fail to capture subtle cognitive deficits detectable only through comprehensive neuropsychological testing.

Proposed directions for future research

Our review revealed several evidence gaps, which could be addressed as follows:

- *Prospective studies with neuroimaging:* Correlating CGM metrics (TIR, CV, TBR) with MRI/PET markers would help clarify the impact of glycaemic variability on brain structure and metabolism.
- *Validation of continuous CGM metrics as predictors:* It should be examined whether, for example, CV >36% or TBR >1% accelerates cognitive deterioration in long-term analyses.
- *Interventional studies using closed-loop insulin delivery pumps and continuous glucose monitoring:* It is worth assessing whether reducing hypoglycaemia through advanced CGM plus insulin pump systems translates into a lower risk of developing dementia.

CONCLUSIONS

The evidence presented supports a therapeutic strategy centred on stable mid-range glycaemia, keeping HbA1c close to 7%, while simultaneously limiting both chronic hyperglycaemia and acute hypoglycaemic episodes. Implementation of this approach should give priority to continuous glucose monitoring (CGM) systems in individuals with impaired hypoglycaemia awareness, recurrent severe events or advanced age. The review also exposes critical research gaps: prospective studies evaluating the cognitive benefits of CGM are still lacking, as are randomised trials with neuroimaging or hard cognitive endpoints and mechanistic investigations that link glycaemic fluctuations to brain injury. Filling these gaps will be essential to delineate and realise the full potential of CGM-based personalised therapy for preserving cognitive function.

REFERENCES

1. Lind, M., Svensson, A. M., Kosiborod, M., & Gudbjörnsdottir, S. (2014). Mortality in diabetes diagnosed in childhood: A population-based study. *Diabetologia, 57*(4), 620–626. https://doi.org/10.1007/s00125-013-3142-z
2. Li, L., Wong, D., Fisher, C. A., Conn, J. J., Wraight, P. R., Davies, A., *et al.* (2025). Increased risk of dementia in type 1 diabetes: A systematic review with meta-analysis. *Diabetes Research and Clinical Practice, 222*, 112043. https://doi.org/10.1016/j.diabres.2024.112043
3. Lacy, M. E., Gilsanz, P., Karter, A. J., Quesenberry, C. P., Pletcher, M. J., & Whitmer, R. A. (2018). Long-term glycemic control and dementia risk in type 1 diabetes. Diabetes Care, 41(11), 2339–2345. https://doi.org/10.2337/dc18-0073
4. World Health Organization. (2021). Global status report on the public health response to dementia (1st ed.). https://www.who.int/publications/i/item/9789240033245
5. Kunutsor, S. K., Balasubramanian, V. G., Zaccardi, F., Gillies, C. L., Aroda, V. R., Seidu, S., & Davies, M. J. (2024). Glycaemic control and macrovascular and microvascular outcomes: A systematic review and meta-analysis of intensive glucose-lowering trials in people with type 2 diabetes. *Diabetes, Obesity and Metabolism, 26*(6), 2069–2081. https://doi.org/10.1111/dom.15330

6. Sinha, B., & Ghosal, S. (2021). A target HbA1c between 7 and 7.7% reduces microvascular and macrovascular events in type 2 diabetes regardless of duration of diabetes: A meta-analysis of randomized controlled trials. *Diabetes Therapy, 12*(6), 1661–1676. https://doi.org/10.1007/s13300-021-01038-7

7. Gudala, K., Bansal, D., Schifano, F., & Bhansali, A. (2013). Diabetes mellitus and risk of dementia: A meta-analysis of prospective observational studies. *Journal of Diabetes Investigation, 4*(6), 640–650. https://doi.org/10.1111/jdi.12075

8. Dybjer, E., Kumar, A., Nägga, K., Engström, G., Mattsson-Carlgren, N., Nilsson, P. M., *et al.* (2023). Polygenic risk of type 2 diabetes is associated with incident vascular dementia: A prospective cohort study. *Brain Communications, 5*(2), fcad054. https://doi.org/10.1093/braincomms/fcad054

9. Satuli-Autere, S., Harjutsalo, V., Eriksson, M. I., Hägg-Holmberg, S., Öhman, H., Claesson, T. B., et al. (2024). Increased incidence of neurodegenerative diseases in Finnish individuals with type 1 diabetes. BMJ Open Diabetes Research & Care, 12(4), e004024. https://doi.org/10.1136/bmjdrc-2024-004024

10. Gubitosi-Klug, R. A., Braffett, B. H., White, N. H., Sherwin, R. S., Service, F. J., Lachin, J. M., *et al.* (2017). Risk of severe hypoglycaemia in type 1 diabetes over 30 years of follow-up in the DCCT/EDIC study. *Diabetes Care, 40*(8), 1010–1016. https://doi.org/10.2337/dc17-0262

11. Whitmer, R. A., Gilsanz, P., Quesenberry, C. P., Karter, A. J., & Lacy, M. E. (2021). Association of type 1 diabetes and hypoglycaemic and hyperglycaemic events with risk of dementia. *Neurology, 97*(3), e275–e283. https://doi.org/10.1212/WNL.0000000000012062

12. Shigemoto, S., Imbe, H., Fujisawa, R., Sasagawa, A., Watanabe, D., Tachibana, M., *et al.* (2022). Decreased cognitive function is associated with preceding severe hypoglycaemia and impaired blood glucose control in elderly individuals with type 1 diabetes. *Diabetology International, 13*(4), 679–686. https://doi.org/10.1007/s13340-022-00607-9

13. Jacobson, A. M., Ryan, C. M., Braffett, B. H., Gubitosi-Klug, R. A., Lorenzi, G. M., Luchsinger, J. A., *et al.* (2021). Cognitive performance declines in older adults with type 1 diabetes: Results from 32 years of follow-up in the DCCT/EDIC study. *The Lancet Diabetes & Endocrinology, 9*(7), 436–445. https://doi.org/10.1016/S2213-8587(21)00109-4

14. Moran, C., Lacy, M. E., Whitmer, R. A., Tsai, A. L., Quesenberry, C. P., & Karter, A. J. (2023). Glycaemic control over multiple decades and dementia risk in people with type 2 diabetes. *JAMA Neurology, 80*(6), 597–604. https://doi.org/10.1001/jamaneurol.2023.0820

15. Moran, C., Whitmer, R. A., Dove, Z., Lacy, M. E., Soh, Y., Tsai, A., *et al.* (2024). HbA1c variability and dementia risk in people with type 2 diabetes. *Alzheimer's & Dementia, 20*(8), 5561–5569. https://doi.org/10.1002/alz.13527

16. Underwood, P. C., Zhang, L., Mohr, D. C., Prentice, J. C., Nelson, R. E., Budson, A. E., *et al.* (2024). Glycated haemoglobin A1c time-in-range and dementia in older adults with diabetes. *JAMA Network Open, 7*(8), e2425354. https://doi.org/10.1001/jamanetworkopen.2024.25354

17. Wang, K., Zhao, S., Lee, E. K.-P., Yau, S. Z.-M., Wu, Y., Hung, C.-T., et al. (2024). Risk of dementia among patients with diabetes in a multidisciplinary, primary care management program. JAMA Network Open, 7(2), e2355733. https://doi.org/10.1001/jamanetworkopen.2023.55733

18. Beck, R. W., Riddlesworth, T., Ruedy, K., Ahmann, A., Bergenstal, R., Haller, S., *et al.* (2017). Effect of continuous glucose monitoring on glycaemic control in adults with type 1 diabetes using insulin injections: The DIAMOND randomised clinical trial. *JAMA, 317*(4), 371–378. https://doi.org/10.1001/jama.2016.19975

19. Laffel, L. M., Kanapka, L. G., Beck, R. W., Bergamo, K., Clements, M. A., Criego, A., *et al.* (2020). Effect of continuous glucose monitoring on glycaemic control in adolescents and young adults with type 1 diabetes. *JAMA, 323*(23), 2388–2396. https://doi.org/10.1001/jama.2020.6940

20. Pratley, R. E., Kanapka, L. G., Rickels, M. R., Ahmann, A., Aleppo, G., Beck, R., *et al.* (2020). Effect of continuous glucose monitoring on hypoglycaemia in older adults with type 1 diabetes. *JAMA, 323*(23), 2397–2406. https://doi.org/10.1001/jama.2020.6776

21. Oskarsson, P., Antuna, R., Geelhoed-Duijvestijn, P., Kröger, J., Weitgasser, R., & Bolinder, J. (2018). Impact of flash glucose monitoring on hypoglycaemia in adults with type 1 diabetes managed with multiple daily injection therapy: A pre-specified subgroup analysis of the IMPACT randomised controlled trial. *Diabetologia, 61*(3), 539–550. https://doi.org/10.1007/s00125-017-4504-1

22. Heinemann, L., Freckmann, G., Ehrmann, D., Faber-Heinemann, G., Guerra, S., Waldenmaier, D., *et al.* (2018). Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): A multicentre, randomised controlled trial. *The Lancet, 391*(10128), 1367–1377. https://doi.org/10.1016/S0140-6736(18)30297-6