Unmet Need in the Treatment of Mild-to-Moderate Hypoglycemia in Patients with Type 1 Diabetes

Summary

Hypoglycemia is a frequent, feared, and disruptive complication of diabetes treatment - people with type 1 diabetes may experience 100-200 epiosdes per year. Current recommended therapeutic interventions using glucose-only treatments frequently result in suboptimal outcomes.

This includes rapid glucose fluctuations alongside persistent cognitive and functional symptoms ("*hypo hangover*") following treatment. Over time, recurrent hypoglycemia contributes to reduced quality of life, fear of hypoglycemia, poor treatment adherence, and potential long-term cognitive consequences.

There is a clear unmet need for options in hypoglycemia self-care that go beyond glucose correction to support rapid functional recovery, minimize rebound hyperglycemia, and reduce downstream burden in everyday life.

Limitations of glucose-only options

For decades, the **therapeutic goal** in hypoglycemia management has been focused on **restoration of blood glucose** above 4mmol/L using fast-acting carbohydrate (7).

Current self-care options - glucose tablets, gels, liquids and similar formulations - are optimized to deliver rapid rises in blood glucose, in line with clinical guidelines.

However, clinical and patient-reported experience highlights a lag between peripheral glucose restoration and complete functional recovery *(Figure 1)* (8–11).

Many individuals describe **persistent neuroglycopenic symptoms** - slowed thinking, 'brain fog', confusion - even after glucose readings return to target range.

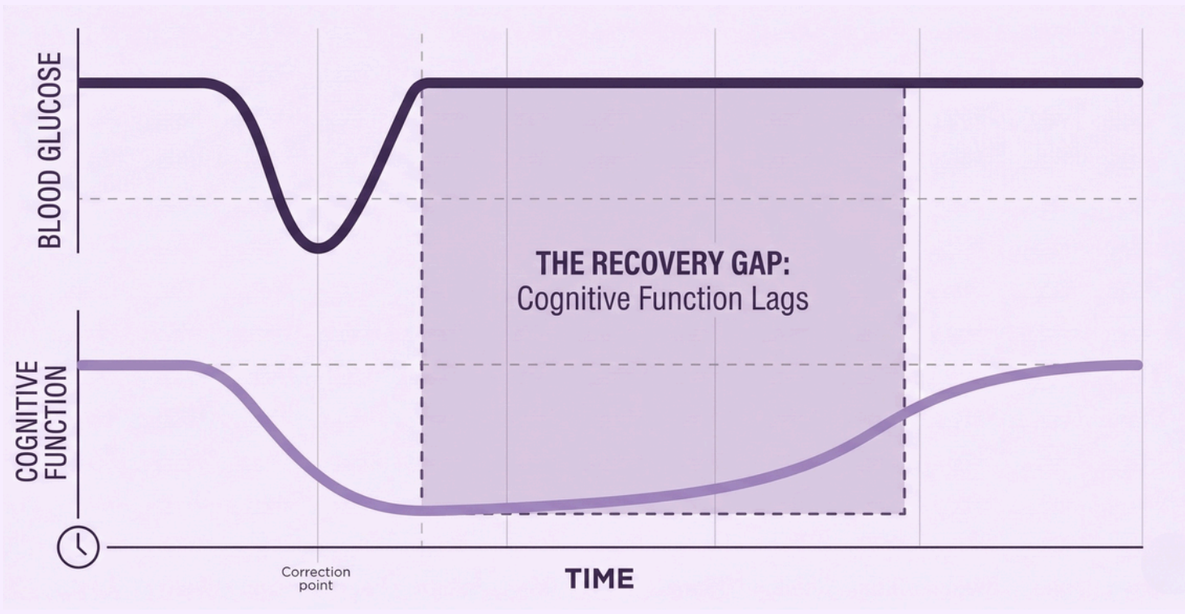


Figure 1. *Schematic of the 'recovery gap': cognitive function remains impaired for a period after blood glucose levels have returned to target range. Note: Data points and time intervals are illustrative approximations only.*

Unmet needs in hypoglycemia self-care

1. Persistent symptoms despite glucose normalisation

Many patients report lingering symptoms for hours or even days following hypoglycemia treatment, even after blood glucose has returned to target range. Commonly reported issues include tiredness, “brain fog,” slowed thinking, impaired concentration, and a general sense of not being “back to normal,” also known as a “hypo hangover” *(Figure 2)* (7–10).

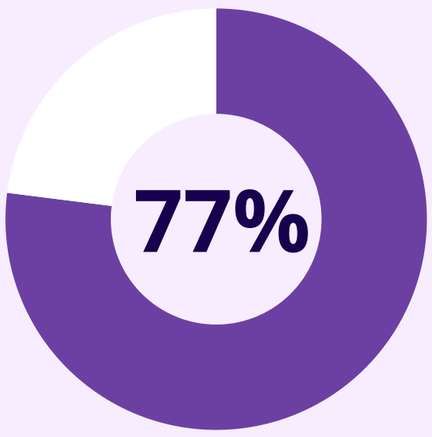
2. Rapid glucose fluctuations

Post-treatment hyperglycemia is common and frustrating for patients. It reflects the combined effects of ingested carbohydrate and residual counter-regulatory hormone activity, which increases hepatic glucose output and induces transient insulin resistance (12). This is amplified by behavioural factors: cognitive impairment during hypoglycemia, fear of recurrent lows, and poor product design often lead to overtreatment. The resulting glucose ‘overshoot’ triggers insulin re-corrections, increasing glycemic variability and increasing risk of secondary, recurrent hypoglycemia once counter-regulatory hormone effects subside (13). Many patients describe this cycle as a “rollercoaster” that can last all day.

3. Product user experience

Many standard self-care options (glucose gels, tablets, shots) have a suboptimal user experience. Products may be unpleasant in taste or texture, difficult to consume quickly, or associated with an unpleasant mouthfeel, which can delay treatment or reduce the likelihood of carrying products consistently (13). Packaging and formulation limitations can also reduce dosing accuracy during real-world scenarios such as driving, working, exercising, or managing nocturnal episodes (13,15).

Hypo self-care experience



Report problems with conventional hypoglycemia self-care products

Figure 2. *Survey of people with T1D (n=40) evaluating experiences with conventional glucose-only products. 77% reported ongoing problems following treatment, including fatigue, weakness, cognitive difficulty or “brain fog” (14).*

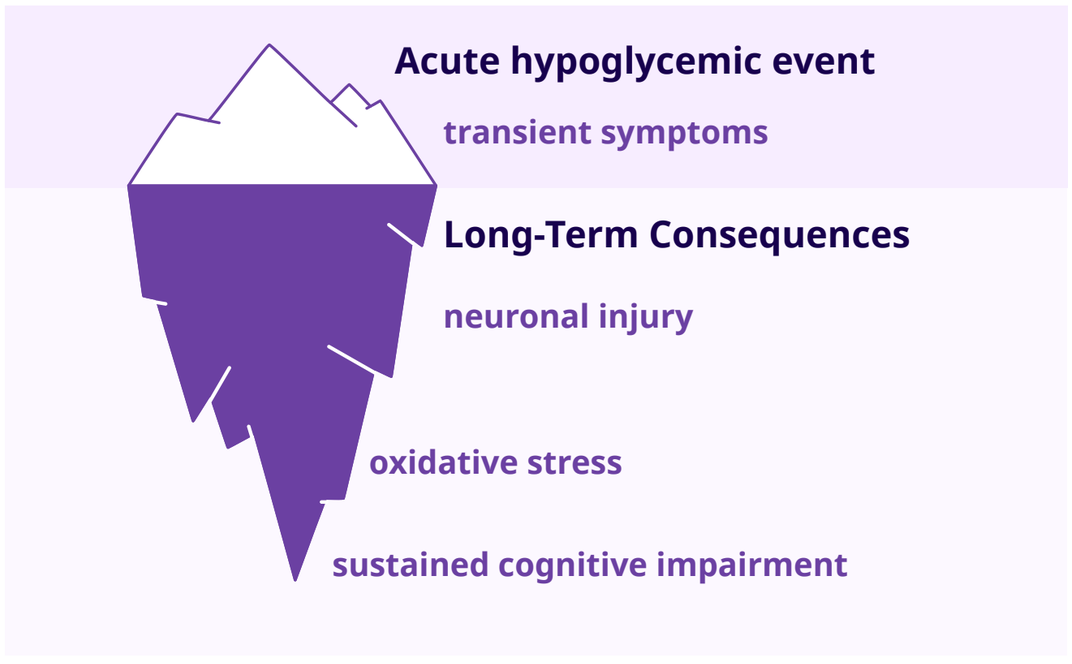
> *If a hypo happens when I am at work, I have to stay and persevere but I am written off for the whole day.*
>
> – Thomas, T1D

4. Emotional burden, adherence

Nearly half (49%) of people with T1D report a significant emotional burden associated with daily management (14). Fear of hypoglycemia, closely linked to prior event frequency and symptom severity (16), can lead to compensatory behaviours such as maintaining higher glucose levels or reducing insulin doses, with implications for long-term glycemic control (17). Many patients also describe the emotional toll of hypoglycemia management, including anxiety, embarrassment, and worries about dependence on others.

3. Long-term impact

The cumulative impact of recurrent hypoglycemia is increasingly recognized. Meta-analyses link recurrent episodes with measurable deficits in processing speed, memory, and executive function (10,11). A dose–response relationship exists: the risk of cognitive decline increases with episode frequency and severity (18,19). This highlights the long-term impact of repeated exposure, even in the absence of severe events. Glucose-only treatments effectively raise blood glucose, but the longer-term neurological consequences—neuronal injury, oxidative stress, and sustained cognitive impairment—are largely unaddressed (Figure 3) (8–11, 20).



Repeated episodes also blunt counter-regulatory responses, impairing awareness and increasing vulnerability to severe events. Beyond the clinical risk, the "recovery gap" results in significant lost productivity and reduced professional/social participation. This creates a cumulative emotional burden for patients and families (21,22). Ultimately, there is a clear need for self-care options that safeguard neurological health and restore full functional capacity.

Figure 3. *Current treatments reliably correct blood glucose levels, but fail to address the cumulative neurological burden accumulating below the surface.*

Patient priorities for treatment

Patient preference research shows that people with T1D prioritize treatments that return them “back to normal” quickly, valuing rapid functional recovery and resolution of cognitive and physical symptoms over glucose correction alone or non-core features such as flavour or “natural” ingredients (Figure 4).

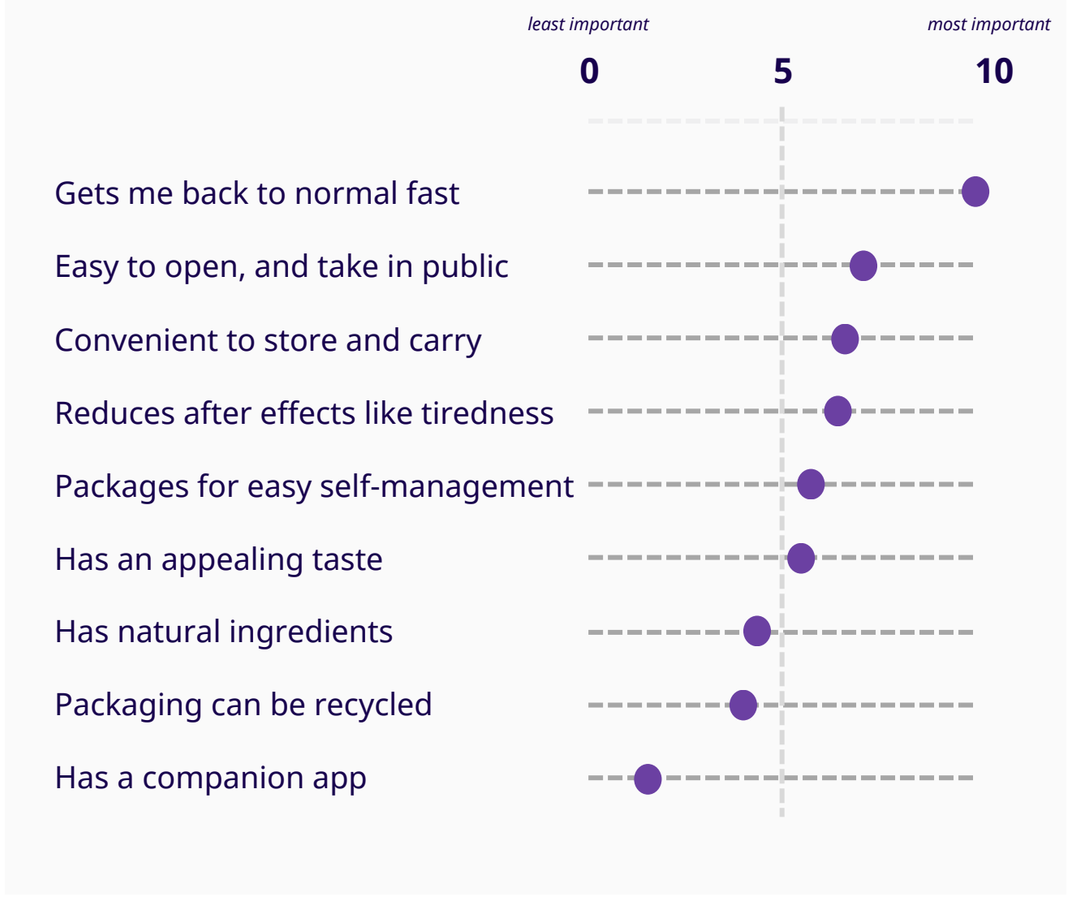


Figure 4. *In a survey of people with T1D (n=26), participants ranked features of an improved hypoglycemia treatment by importance (10 = highest; 1 = lowest) (23). Rapid return to feeling “back to normal” was ranked as the highest priority.*

Conclusions

Glucose-only treatments reliably restore blood glucose levels, but often fall short of achieving complete recovery for patients. Many experience persistent symptoms, glucose ‘overshoot’, emotional burden, and fear-driven behaviours that may compromize glycemic control.

Hypoglycemia represents a cumulative burden that extends beyond acute glucose correction. People with diabetes seek solutions that get them “back to normal” quickly, with stable levels, and are easy to use in everyday life.

These insights highlight a need for innovative options in hypoglycemia self-care that pair glucose correction with rapid cognitive recovery, improved glycemic stability, and real-world usability.

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