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# New glucometric parameters:

## glycemic Risk Index (GRI) and Time in Tight Range (TITR)

Interstitial glucose monitoring (IGM) has become an essential tool for assessing glycemic control, providing a large volume of data. To interpret these data, we must evaluate the seven metrics endorsed by the international Time in Range (TIR) consensus and the Ambulatory Glucose Profile (AGP). Parameters such as TIR, time above or below range (TAR and TBR), coefficient

of variation (CV), and the glucose management indicator (GMI), among others, have moved from research protocols into everyday diabetes practice. However, although it is clear that IGM offers an alternative to HbA1c by allowing continuous, comprehensive assessment of interstitial glucose levels, its interpretation is not without challenges.

The 7 glucometric parameters defined in the CGM consensus are highly interdependent, and attempts to improve one may worsen others, complicating interpretation and treatment optimization to achieve good glycemic control. In addition, the simultaneous evaluation of the different AGP report parameters and the daily CGM log requires experience, time, and an inevitable learning curve for the care team—adding workload for professionals caring for people with diabetes. TIR has recently been consolidated as an essential variable of metabolic control and has been linked to chronic microand macrovascular complications, equating TIR > 70% with good metabolic control and an HbA1c of 7% in T1DM and T2DM. Still, using TIR alone lacks sufficient sensitivity for assessing hypoglycemia and extreme glucose values, and therefore glycemic variability (GV). Thus, CGM analysis cannot be simplified to TIR alone. It seems logical to seek new parameters that synthesize existing data and guide clinicians in T1DM management, especially those with less experience.

## GLYCEMIC RISK INDEX

The Glycemic Risk Index (GRI) was first described in 2022 and aims to summarize, in a single parameter, the overall quality of a given patient's glycemic control (1). Its calculation arose from analyzing scores assigned by 330 international T1DM experts to CGM data from 225 insulin-treated people with diabetes (1). The experts' scores depended on 2 components: a hypo(hypo\_C) and a hyperglycemia component (hyper\_C). The sum of these 2 components, weighted by coefficients, yields the GRI, with greater weight placed on hypoglycemia (TBR) and extreme values (1).

$$**GRI = 3.0 \times [TBR < 54 + (0.8 \times TBR 54-70)] + 1.6 \times [TAR > 250 + (0.5 \times TAR 180-250)]**$$

The GRI evaluates a patient's overall glycemic control on a 0 to 100 scale, where 0 is the best and 100 the worst possible control. It can also be categorized and plotted by percentiles (Pc) into 5 zones, from best (Pc 0–20) to worst (Pc 80–100) control, facilitating visualization of results and identification of key leverage points to improve glycemic quality. As inferred from its formula, the GRI allows simultaneous, weighted assessment of 2 essential components of metabolic control—TBR and TAR (and

therefore indirectly TIR)—assigning greater weight to TBR and, specifically, to extreme glucose values (1). Early adopters who incorporated GRI into routine clinical practice demonstrated GRI improvement after initiating automated insulin delivery (AID/AHCL) systems. In our group, in a sample of 137 patients (65 pediatric), we observed better control in the pediatric population expressed via GRI, but with a larger hypoglycemia component (2). It remains to be determined whether GRI relates to diabetes complications. A higher GRI has been associated with increased risk of diabetic retinopathy, with a 20% increase in risk per each GRI percentile rise (3). A strong association has also been shown between GRI and indicators of diabetic nephropathy (3). Regarding GRI's relationship with other glucometric parameters, our group showed that GRI correlates significantly with all analyzed metrics, especially with TIR (strong negative correlation,  $r = -0.917$ ), and that GV affects GRI's correlation with other parameters (2). HbA1c and GRI display a strong positive correlation, which is modified by GV (2).

Advantages: GRI is easy to calculate and automate; it encapsulates metabolic control in a single 0–100 parameter, with a simple, intuitive graphical representation. It is straightforward for prioritizing or tracking the course of the same or different patients and provides a clinically meaningful—not merely mathematical—assessment that can capture changes over time. Limitations: Evidence in day-to-day practice remains limited; there is no established normal/desired value; current CGM platforms do not calculate it automatically; and validated data are lacking in pediatric and pregnancy populations—factors that slow widespread adoption. GRI may be especially useful for care teams with less CGM experience or when a single, simple parameter is needed to prioritize patients who might benefit from specific interventions, enabling rapid comparisons across patients or over time within the same patient.

## TIME IN TIGHT RANGE

Time in Tight Range (TITR) is defined as the time glucose remains between 70 mg/dL and 140 mg/dL. The need for TITR arose from CGM data in healthy individuals. In one study, 85% of healthy participants had < 5% of values > 140 mg/dL, spent most of the »

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» time between 70–140 mg/dL, and rarely reached 140–180 mg/dL, and if they did, it was only briefly after meals. Both hypoand hyperglycemia are harmful to brain development and function; an increasing number of studies describe the

effects of dysglycemia on the blood–brain barrier, the risk of dementia, and the impact of hypoand hyperglycemia on cognition and brain development in young children with T1DM. It therefore seems important to maintain normogly-

cemia to preserve brain function at all ages. T1DR has also emerged alongside new treatments that have not only improved metabolic control but brought glucose values closer to normal. Since the 2019 international T1DR consensus, »



» debate has continued over whether glucose ranges need to be adjusted. The ranges were defined by consensus to align with pre-CGM definitions and were not based on clinical outcomes at that time; a therapeutic target of HbA1c < 7% was equated to TIR 70–180 mg/dL of 70%. Some authors propose that TITR better reflects CGM metrics of normoglycemia and normal glucose values, representing a narrower, physiological time window.

### 1) Usefulness of TITR.

TITR better reflects normal glucose values, and new terms are already being used such as TING (time in normoglycemia) and TINR (time in normoglycemic range). Real-world studies (4,5) show that implementing AHCL systems in T1DM improves metabolic control in both pediatric and adult populations, specifically by improving TITR—that is, time in normoglycemia (70–140 mg/dL)—without changing the time between 140–180 mg/dL.

In T2DM, TITR may help early identification of pre-diabetic stages: when normoglycemic, TIR and TITR are very similar with HbA1c 5%, but with HbA1c 5.5–6.5%, TITR—clearly lower than TIR—marks the difference (6).

### 2) TITR Targets.

A TITR > 50% appears to be a reasonable and safe treatment goal in T1DM. As early as 2019, Peterson established that TITR 50%  $\approx$  HbA1c 6.5%, later corroborated by Castañeda, who proposed that TITR 45%  $\approx$  HbA1c < 7% (5). There is debate over TITR targets and even whether to set different targets by time of day (e.g., a higher nocturnal goal). Higher TITR is easier to achieve in earlier disease (recent diagnosis, remission/honeymoon) and in T2DM due to lower GV and lower TBR. Treatment type also influences TITR, with AHCL users achieving better TITR. In a CGM/metrics international consensus for clinical trials, Battelino et al. (7) suggested TITR > 70% for people with T1DM on AHCL and T2DM on glucose-lowering therapy—very similar to TIR recommendations. This strict target is not met in real-world studies; in some, only ~1.9% achieve TITR > 70%. Thus, TITR targets are still under discussion. ISPAD proposes TITR  $\geq$  50%, and this has been reported as achievable in preschoolers with expe-



TITR BETTER REFLECTS NORMAL GLUCOSE VALUES, AND NEW TERMS ARE EMERGING SUCH AS TING (TIME IN NORMOGLYCEMIA) AND TINR (TIME IN NORMOGLYCEMIC RANGE)

| GMI (%) | Average Glucose (mg/dL) | TITR (%) | TIR (%) |
|---------|-------------------------|----------|---------|
| 6       | 112                     | 69       | 91      |
| 6.5     | 133                     | 54       | 78      |
| 7       | 154                     | 42       | 66      |
| 7.5     | 175                     | 31       | 54      |
| 8       | 196                     | 23       | 44      |
| 8.5     | 217                     | 16       | 34      |
| 9       | 238                     | 11       | 26      |
| 9.5     | 259                     | 8        | 18      |
| 10      | 280                     | 7        | 11      |

TABLE 1. TITR and TIR according to the Glucose Management Indicator (GMI). (Adapted from Beck, Diabetes Technology & Therapeutics, 2024) (9).

» rience teams and technology access. Conversely, in patients without advanced technologies that prevent hypoglycemia, some authors recommend a TITR goal of 40% for T1DM (8).

3) Correlation with Other Parameters.

A strong, non-linear positive correlation between TIR and TITR has been reported (4). The TIR/TITR relationship is influenced by GV: the higher the GV expressed by the coefficient of variation (CV), the higher the TITR that corresponds to a given TIR (4,9). TITR also correlates positively with HbA1c. On average, TITR is 20–25% lower than TIR

when GMI is 6–8% across different cohorts and treatments. The TITR–TIR gap narrows at higher HbA1c values (9). (Table 1)

4) Who Benefits Most from TITR?

Although TIR and TITR are complementary, TITR is preferable when the clinical goal is normoglycemia (HbA1c <5.7–6%), because at those levels TIR becomes insensitive to changes in mean glucose and CV. In such cases, TITR helps patients recognize and visualize additional excursions above target compared with TIR. Tight control is the goal in pregnancy and children (long life expectancy, metabolic memory) and in early diabetes »

» stages (stage 1 and 2). In these patients, TITR should be used.

### 5) How Using TITR Affects Patients.

Potential drawbacks of using TITR include:

- Higher risk of hypoglycemia.
- Higher level of anxiety. Are we introducing a new level of anxiety related to the need for constant monitoring to achieve a tighter target? In a survey conducted among 19 parents and 11 adolescents with T1D, participants acknowledged that implementing TITR resulted in a greater burden and higher stress levels, along with increased effort to stay within target (tight range).
- Using TITR as a goal may lead to a greater number of alarms, which could be mitigated through robust configuration of the alarm settings.

6) Relationship with Complications. TIR is strongly associated with macroand microvascular complications. Given the non-linear TIR–TITR correlation, higher TITR is presumed to be associated with lower long-term complication rates. Recent studies link lower TITR with higher probabilities of complications in T1DM (retinopathy, nephropathy, stroke), even quantifying risk percentages (10). Emerging data also relate TITR to diabetic retinopathy in adults with T2DM, and some authors report that lower TITR is associated with increased all-cause and cardiovascular mortality in T2DM. **D**

## CONCLUSIONS

- Although GRI and TITR are relatively new parameters with potential clinical applicability, longer-term studies are needed to define their utility and target values across different populations.
- While TIR remains the main follow-up parameter—along with HbA1c—to assess potential risk of chronic complications, TITR can be an additional metric to evaluate glycemic control, especially when normoglycemia is the clinical objective.
- GRI, as a single and easy-to-calculate parameter, can be particularly useful for professionals with less CGM interpretation experience, and when prioritizing care for patients with poorer glycemic control.

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