



Glycemia risk index (GRI): a metric designed to facilitate the interpretation of continuous glucose monitoring data: a narrative review

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Abstract

The Glycemia Risk Index (GRI) is a novel composite metric that integrates both hypoglycemia and hyperglycemia episodes to provide a comprehensive view of glycemic control in individuals with type 1 or type 2 diabetes. Unlike traditional metrics such as HbA_{1c} or time-in-range (TIR), the GRI highlights extreme glycemic excursions and aligns more closely with clinical perceptions of glycemic risk. It correlates well with other CGM-derived indicators and has demonstrated relevance in various settings, including the management of individuals using hybrid closed-loop systems. In individuals with HbA_{1c} ≤ 7%, the GRI can reveal hidden risks not captured by HbA_{1c} alone, highlighting its added value in routine clinical assessment. Despite these strengths, the GRI has limitations. It was developed using CGM data from healthy adults on intensive insulin therapy, limiting generalization to other populations. Unlike HbA_{1c} or TIR, it is not yet validated against hard clinical outcomes. As CGM technology evolves, the GRI holds promise as a valuable tool, provided its current limitations are addressed through further research and clinical integration.

Keywords Ambulatory glucose profile · Continuous glucose monitoring · Glycemia risk index · GRI · Hyperglycemia · Hypoglycemia · Advanced hybrid closed-loop systems

Introduction

Traditional glycemic metrics such as glycated hemoglobin (HbA_{1c}) and Time in Range (TIR), which is the percentage of time spent with glycemia between 70 and 180 mg/dl, have well-known limitations. HbA_{1c} reflects long-term average glucose levels but fails to capture glycemic variability and acute hypo- or hyperglycemia. TIR, while increasingly used, does not weigh the severity or direction of glucose excursions. The recently proposed Time in Tight Range (TITR) provides a more stringent measure of euglycemia but remains impacted by glycemic variability and does not fully account for extreme variations. In this context, the recently proposed Glycemia Risk Index (GRI) introduces a composite, weighted measure that integrates both hypo- and hyperglycemia risk, more closely reflecting clinical perception of glucose control.

The GRI is a composite metric designed to provide a global assessment of glycemic profile in people with type 1 (T1D) or type 2 (T2D) diabetes. The GRI was first described

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by Klonoff et al. in a 2022 [1], and it aimed to simplify and integrate the interpretation of data from continuous glucose monitoring (CGM). To create this measure, 330 clinicians worldwide collaborated to analyze and classify, on the basis of a common scale, the 14-day CGM tracings of 225 insulin-treated adults with T1D and T2D diabetes. These analyses were used to generate GRI equations, which integrate both hypoglycemia and hyperglycemia events, giving greater weight to extreme glycemic episodes, especially hypoglycemia.

The GRI closely corresponds to clinicians' previous rankings of the overall quality of glycemic profiles ($r = 0.95$). The GRI offers a more detailed and nuanced analysis of glycemic control than traditional measures, such as HbA_{1c} and TIR.

This article explores the benefits and limitations of using the GRI, drawing on several recent and relevant studies in the field.

Materials and methods

A literature search was conducted on PubMed and Google Scholar using the following keywords: “Glycemia Risk Index”, “GRI”, “glucometrics”, “Time In Range”, “Time in Tight Range” and “continuous glucose monitoring.” The search yielded 21 recent articles, published between 2023 and 2025, which examine the clinical applications of the GRI in monitoring diabetic patients. These studies offer a scientific foundation that enhances comprehension of this indicator, clarifying both its clinical indications and limitations, and supporting its integration into routine practice.

GRI: A comprehensive measurement tool

The GRI is based on standardized metrics of the Ambulatory Glucose Profile (AGP) and uses the following inputs: percentages of time spent within the TIR: 70–180 mg/dL; <54 mg/dL (very low glucose hypoglycemia: VLow); 54 to <70 mg/dL (low glucose hypoglycemia: Low); <70 mg/dL (time below range (TBR): VLow + Low); >180 to 250 mg/dL (high glucose hyperglycemia: High); > 250 mg/dL (very high glucose hyperglycemia: VHigh); and > 180 mg/dL (time above range (TAR) > 180 mg/dL: VHigh + High).

The hypoglycemia and hyperglycemia components of the GRI are calculated as follows:

- Hypoglycemic component: $V\text{Low} + (0.8 \times \text{Low})$.
- Hyperglycemic component: $V\text{High} + (0.5 \times \text{High})$.

$\text{GRI} = (3.0 \times \text{Hypoglycemic component}) + (1.6 \times \text{Hyperglycemic component})$.

Equivalent,

- $\text{GRI} = (3.0 \times V\text{Low}) + (2.4 \times \text{Low}) + (1.6 \times V\text{High}) + (0.8 \times \text{High})$.

This formula gives greater weight to episodes of hypoglycemia and extreme hyperglycemia, thus reflecting more accurately the risks associated with these events.

An important question in clinical practice is: what duration of CGM data is required to reliably calculate the GRI? Shah et al. [2] evaluated the correlation between 90-day GRIs and 7-, 14-, and 30-day GRIs; although a retrospective CGM duration of 14 days is optimal, 7 days of CGM data may be sufficient to estimate the 90-day GRI to monitor changes in quality of interstitial glucose control.

GRI visualization and interpretation

The GRI can be graphically represented as a grid (Fig. 1: GRI-Grid), in which hypoglycemia and hyperglycemia components are individualized. This visualization makes it easier for clinicians and patients to interpret the data and track changes in glycemic control.

Each patient is positioned in one of five zones (designated A to E), corresponding to quintiles ranging from the best glycemic control (1st–20th percentiles) to the worst glycemic control (81–100th percentiles) [1]. This graph allows clinicians to track changes over time among same individuals and to compare them with other groups or reference targets.

Comparison of GRI with other glucose metrics

Traditionally, measures such as TIR (70–180 mg/dL) in combination with HbA_{1c} have been used to assess the overall glycemic control of individuals or groups of patients.

However, the GRI offers a more comprehensive overview by providing not only the relative length of time a patient spends in the target range, but also episodes of extreme hypo- or hyperglycemia, often underestimated by isolated TIR measures [3]. A study by Kim et al. [3] showed that even when the TIR remains constant, the GRI can reveal significant variations in episodes of hypo- or hyperglycemia, providing a more detailed view of the extreme glycemic risks encountered by patients. The GRI is positively correlated with HbA_{1c}, mean glucose, coefficient of variation of glucose measurement (CV), and negatively with TIR, demonstrating its ability to reflect both overall glucose exposure as well as glucose variation [4, 5].

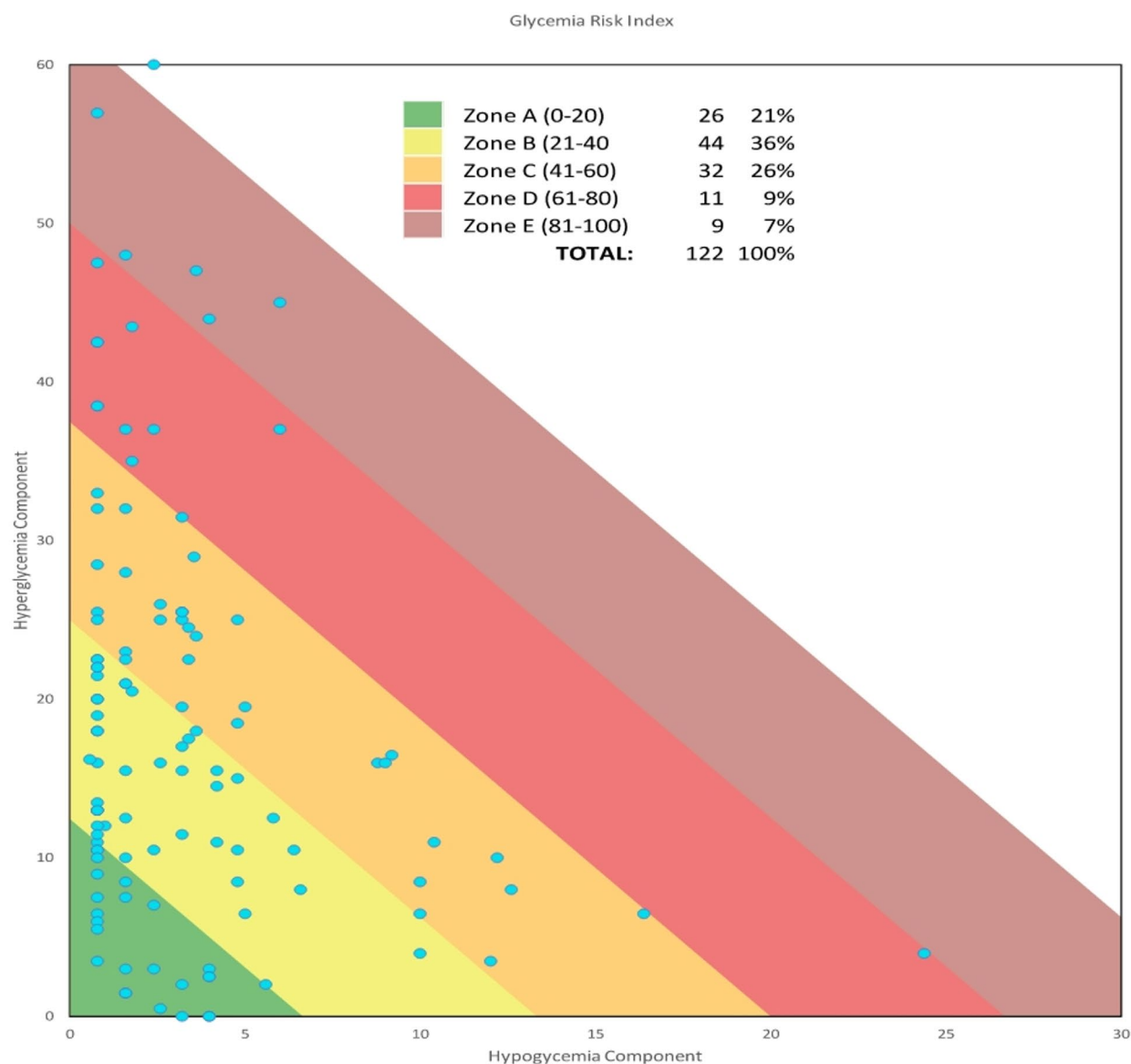


Fig. 1 GRI grid from 122 individuals

Another emerging indicator, Time in Tight Range (TITR), defined as the percentage of daily time spent between 70 and 140 mg/dL, aims to improve assessment of euglycemia. Although correlated with TIR, TITR appears to be more discriminating, particularly in patients who already achieve fair glycemic control. In a recent study conducted in pediatric and adult patients treated with advanced closed-loop systems, TITR showed a significant correlation with GRI ($r=0.647$; $p<0.001$), suggesting complementarity in capturing overall glucose dynamics [6].

Clinical applications of GRI

The clinical utility of the GRI was increasingly acknowledged in various clinical settings. For example, in a study by Rizzi et al., the use of an advanced hybrid closed-loop (AHCL) system significantly improved the GRI from 41.0 to 28.5 ($P=0.008$) in 56 patients over a one-year period, with correlated improvements in TITR (70–140 mg/dL) and in HbA_{1c}. This study illustrates how the GRI can be used to better assess the added value of new technologies in diabetes management [4]. Another study by Resmini et al. [7] involved 198 patients treated with different insulin therapy modalities and assessed the GRI before and after switching to an AHCL system. Switching to AHCL resulted in rapid

and lasting improvement in GRI irrespective of previous insulin therapy modalities. Other studies of similar designs confirmed these observations [8, 9]. A recent work has correlated GRI results with the effectiveness and safety criteria of an AHCL treatment. In this cohort of 136 patients living with T1D, setting a GRI threshold at 26 was helpful with a single number to detect patients who require further support [10]. The GRI has also been studied in clinical trials of patients with T2D, such as in the IDEAL study (iGlar-Lixi (Suliqua®), whose main objective was to compare the effects of de-intensification from a multiple daily injection insulin (MDI) regimen to a fixed combination of basal insulin + GLP-1 receptor agonist. In the iGlarLixi group, the GRI measurements at the end of follow-up were better than those in the MDI group [11].

GRI data have been associated with indicators of quality of life in people living with diabetes. Diaz-Soto et al. demonstrated that high GRI values were correlated with increased diabetes-related psychological stress, lower treatment satisfaction, and reduced quality of life. These correlations highlight the importance of the GRI not only as a clinical measurement tool, but also as an indicator of patient's well-being [12].

There is emerging research focused on the link between the GRI and vascular complications associated with chronic hyperglycemia. Notably, in T2D patients, an elevated GRI was associated with increased risk of diabetic retinopathy, albuminuria and indices of atherosclerosis [13–15].

Zhong et al. [16] examined the usefulness of the GRI in 140 patients with newly-diagnosed T1D to identify those who likely to benefit from transient remission of hyperglycemia, also known as the “honeymoon period”. In this study, the GRI was able to distinguish various patterns of glycemic variability, offering the possibility of designing personalized monitoring and management strategies tailored to patients who are likely or unlikely to progress to remission.

Although the GRI equations were computed from adult CGM data, their use in pediatric settings have also been explored. Bukara-Radujkovic and Miljkovic reported that the GRI may represent a valuable parameter for assessment and management of young patients in routine clinical practice [17].

Thus, Panfil et al. conducted a study among 1182 young T1D patients and showed that the GRI could evaluate diabetes management performance among young people and identify those who require additional support to improve glycemic control. This study shows that the GRI can be a useful tool for clinicians in adjusting therapeutic interventions according to patients' behaviors [18].

A recent study by Oriot et al. [19] examined individual GRI distribution among 216 adults living with T1D whose HbA_{1c} was $\leq 7\%$ (mean $6.6 \pm 0.3\%$), which is often

considered as indicative of good overall metabolic control. The aim was to determine whether CGM could reveal aspects of glycemic control that would not have been reflected by HbA_{1c}. The 90-day CGM data were used to analyze the hypoglycemia and hyperglycemia components and calculate the GRI. Despite achieving an HbA_{1c} $\leq 7\%$, 39% of participants exhibited GRI values in the unfavorable zones C, D, or E (41 st–100 th percentiles), underscoring limitations in glycemic control not captured by HbA_{1c} alone. These patients tended to be younger, had a higher body mass index (BMI), and had significantly higher coefficients of variation of glucose. Thus, their hypo- and hyperglycemic components were greater, reflecting greater glycemic variability and increased exposure to glycemic extremes.

These results highlight that, even in T1D or T2D patients with HbA_{1c} $< 7.0\%$, a more thorough assessment of glycemic control via the GRI may identify risks in glucose management that would otherwise not be apparent.

These observations highlight the importance of complementing standardized assessments of glycemic control, such as HbA_{1c} and TIR, with additional measures such as the GRI for more precise, personalized diabetes management.

Limitations of the GRI in clinical practice

Despite its potential as a standardized metric for assessing glycemic risk, the Glycemia Risk Index (GRI) presents several limitations that must be considered before its widespread adoption in clinical practice.

First, most studies to date have focused on relatively homogeneous cohorts, often with limited sample sizes and based on intermittent or real-time CGM data. These systems, particularly in the case of hypoglycemia, may exhibit lower accuracy, directly affecting the reliability of the hypoglycemic component of the GRI [20].

Second, the GRI was initially developed based on expert consensus using CGM data from clinical trials involving healthy adults treated with multiple daily insulin injections. Although recent studies support its utility in broader contexts [17, 18, 21], its generalizability remains limited. The original development cohort excluded several key populations, including older adults, children, pregnant women, and individuals with complex chronic conditions. Furthermore, in groups where HbA_{1c} is a poor proxy for glycemic control—such as patients with chronic kidney disease or those managed with non-intensive insulin regimens—the applicability of the GRI remains uncertain. Extending its use to these populations may lead to inappropriate or misleading clinical conclusions. For instance, glycemic targets for Time Above Range (TAR) and Time Below Range (TBR)

are more stringent in certain subgroups (e.g., older adults or pregnant women). The current GRI formula may insufficiently weight these deviations, particularly in terms of hypoglycemia. In vulnerable populations, such as frail older adults, recommended targets are <1% for glucose values <70 mg/dL and 0% for <54 mg/dL—considerably stricter than the general targets of <4% and <1%. In such cases, the GRI may underestimate clinically relevant hypoglycemic risk.

Third, while the GRI provides a convenient global assessment, it lacks temporal resolution. It does not account for fluctuations in glucose levels across critical periods, such as nocturnal versus diurnal, or pre- versus postprandial phases, thereby limiting its utility in tailoring treatment strategies. Additionally, the GRI may fail to discriminate between patients with substantially different metabolic profiles. Individuals with divergent TIR, TITR, or glycemic variability may fall within the same GRI risk zone, potentially masking meaningful differences in glycemic control (see Fig. 1).

Fourth, unlike TIR or HbA_{1c}, the GRI has not yet been extensively evaluated for its association with clinical outcomes such as microvascular or macrovascular complications. Current evidence is largely derived from retrospective analyses and remains insufficient to draw firm conclusions [13–15].

Finally, except for its implementation on the platform www.sweetspot.health, the GRI has not yet been widely incorporated into CGM data interpretation platforms, limiting its accessibility and clinical integration.

To fully establish the role of the GRI in diabetes care, prospective, multicenter, and ethnically diverse studies are needed to validate its robustness, interpretability, and predictive value across a variety of clinical settings.

Conclusion

The GRI offers a valuable addition to the assessment of glucose control in people with diabetes. By integrating both hypo- and hyperglycemic risks into a single composite measure, the GRI provides clinicians with complementary insights beyond traditional glucose metrics such as HbA_{1c} and TIR.

It may provide evidence for more treatment personalization and help uncover unappreciated glycemic risks otherwise undetected. While promising, its clinical relevance should be interpreted with caution, considering current limitations related to validation, usability, and integration into care platforms. As continuous glucose monitoring technology continues to advance, the GRI could play a useful role in enhancing the understanding of glycemic patterns and informing patient-centered diabetes management—provided

its usefulness is validated across broader and more diverse diabetic populations.

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Declarations

Conflict of interest The authors declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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