# Addressing the shortfalls of Glucose Management Indicator (GMI) and Glycated Hemoglobin (HbA1c): Validation of updated GMI and personalized A1c

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## Introduction

The glucose management indicator (GMI) was developed as a continuous glucose monitoring (CGM) metric that reflects mean glucose in HbA1c units. GMI, established using linear regression between average glucose (AG) and HbA1c, is used as a glycemic management quality metric. However, GMI can deviate from HbA1c, particularly at high and low glucose levels [1-3]. In addition, dissociation in GMI-HbA1c relationship can be due to individual differences in red blood cell (RBC) characteristics.

An updated GMI (uGMI) was proposed to account for populational level biases at high and low glucose levels, while personalized A1c (pA1c) was introduced to cover individual variations in RBC lifespan and glucose utilization [4]. However, uGMI and pA1c were derived from theoretical models and are yet to be tested in real world samples.

## Aims

Validate the clinical utility of uGMI and pA1c through a dedicated study.

## Methods

A prospective 6-month US-UK study (18 centers) was conducted in individuals aged 4 years or older with type 1 or type 2 diabetes (T1D or T2D), including different racial groups. Participants wore CGM sensors for 182 days with blood sampling for HbA1c every two weeks as shown in Figure 1.

[1] Shah VN, DuBose SN, Li Z, et. al. J Clin Endocrinol Metab. 2019 Oct 1;104(10):4356-4364.
[2] Shah VN, Vigers T, Pyle L, Diabetes Technol Ther. 2023 May;25(5):324-328.
[3] Selvin E; Diabetes Care 20 May 2024; 47 (6): 906–914
[4] Xu Y, Dunn TC, Ajjan RA. J Diabetes Sci Technol. 2021 Mar;15(2):294-302.

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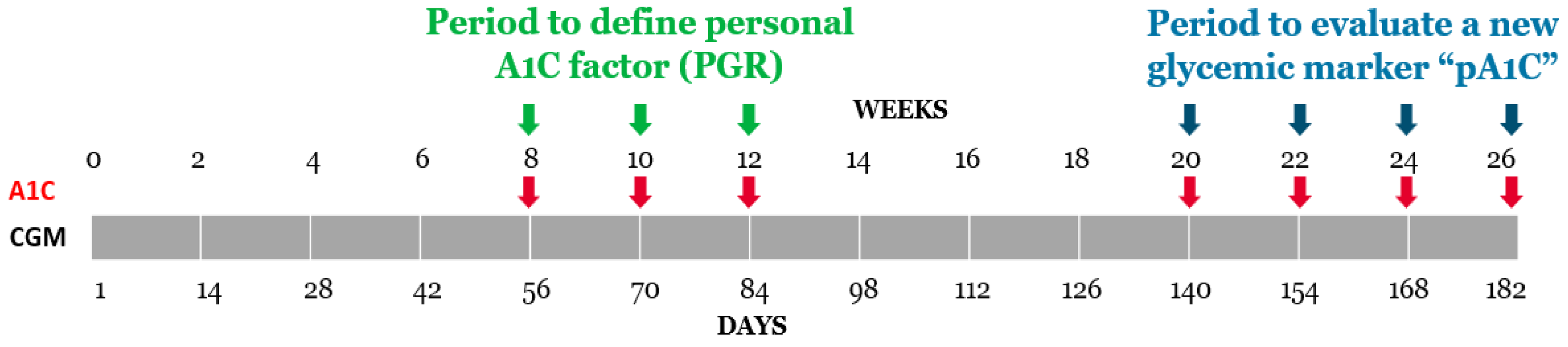


**Figure 1. Study design.** The first 12 weeks were used for calculation of personal glycation factor (PGR) and personalised A1c (pA1c) with the second half of the study dedicated to evaluating pA1c.

### Calculation of GMI, uGMI and pA1c

$$GMI = 0.02392 * AG + 3.31$$

$$uGMI = (15.36 * AG^{-1} + 0.0425)^{-1}$$

For pA1c calculation, Personal glycation factor (PGR) was calculated first followed by pA1c

$$\text{PGR} = \left(\text{AG}^{-1} + \text{K}_\text{M}^{-1}\right) * \left(100 * \text{A1C}^{-1} - 1\right)^{-1} * 10^5$$

$$\text{pA1C} = 100 * \left(1 + \frac{\text{PGR}}{\text{PGR}_{ref}}\left(\frac{100}{\text{A1C}} - 1\right)\right)^{-1}$$

$K_M = 473$
$PGR_{ref} = 65.1$

## Results and conclusions

Main characteristics of study population are summarized in Table 1. Current GMI shows discrepancies at lower and higher A1C levels and uGMI removes the discordance at the population level (Figure 2). The use of pA1c reduces data spread and improves the correlation with uGMI at the individual level (Figure 2)

| | Black | White | Asian | Other | Overall |
|---|---|---|---|---|---|
| **Number** | 59 | 76 | 91 | 31 | 257 |
| **Adult/Pediatric** | 58/1 | 73/3 | 88/3 | 30/1 | 249/8 |
| **T2D/T1D** | 52/7 | 49/27 | 77/14 | 25/6 | 203/54 |
| **Female** | 36 (61%) | 31 (41%) | 33 (36%) | 15 (48%) | 115 (45%) |
| **Age (years)** | 54 (14) | 51 (18) | 51 (16) | 52 (13) | 52 (16) |
| **A1C %** | 7.7 (1.3) | 7.5 (1.0) | 7.8 (1.4) | 7.1 (1.0) | 7.6 (1.2) |
| **Average Glucose mg/dL** | 153 (41) | 164 (38) | 168 (47) | 153 (36) | 161 (42) |
| **Diabetes duration** | 13 (9) | 16 (13) | 15 (10) | 13 (9) | 15 (11) |

**Table 1. Main characteristics of study population.**

| AG (mg/dL) | GMI (%) | Updated GMI (%) |
|---|---|---|
| 90 | 5.5 | 4.7 |
| 100 | 5.7 | 5.1 |
| 120 | 6.2 | 5.9 |
| 140 | 6.7 | 6.6 |
| 150 | 6.9 | 6.9 |
| 160 | 7.1 | 7.2 |
| 180 | 7.6 | 7.8 |
| 200 | 8.1 | 8.4 |
| 240 | 9.1 | 9.4 |
| 250 | 9.3 | 9.6 |

**Table 2. Average glucose (AG) and GMI/uGMI relationships.**

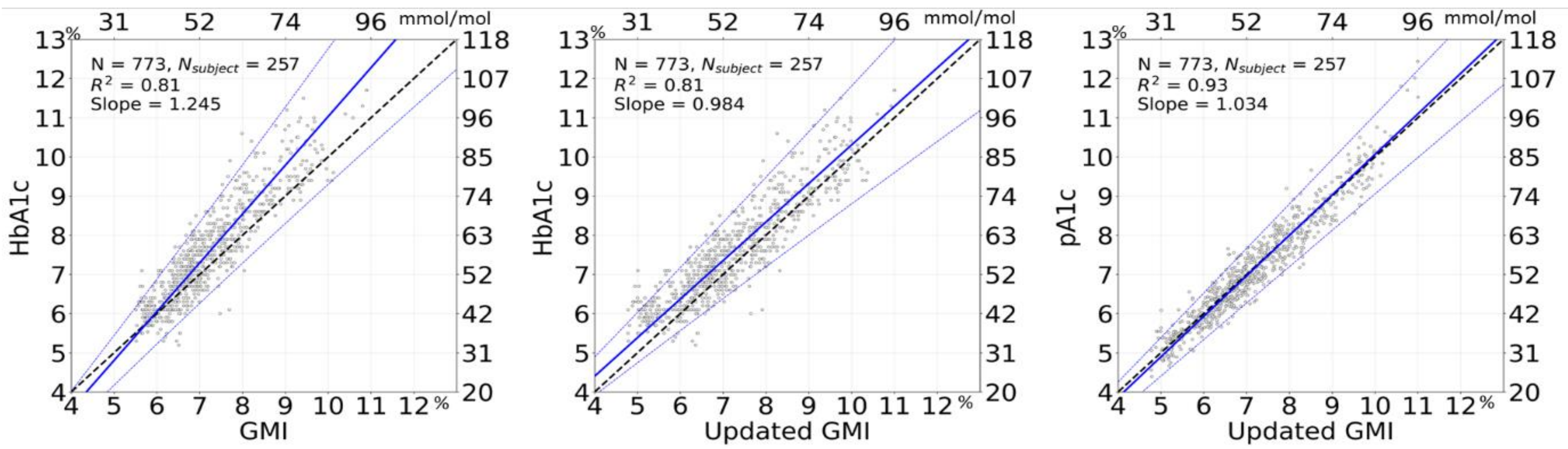


**Figure 2. Use of GMI, uGMI and pA1c.** HbA1c and GMI show discordance at low and high glucose levels that is eliminated by uGMI, while pA1c reduces the spread of data and improves the correlation.