

Improving alignment between HbA1c and continuous glucose monitoring average glucose: The updated Glucose Management Indicator

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Disclosures: Richard M. Bergenstal, MD

- I have no personal financial disclosures
- My employer, the non-profit HealthPartners Institute, contracts for my services, and I receive no personal income from the following activities:
 - I have participated in clinical research, been a member of a scientific advisory board, and served as a consultant for:
 - Abbott Diabetes Care, Ascensia, Bigfoot Biomedical, Inc., CeQur, Dexcom, Eli Lilly, Embecta, Hygieia, Insulet, Mannkind, Medscape, Medtronic, NCQA, Novo Nordisk, Onduo, Roche Diabetes Care, Sanofi, Tandem, United Healthcare, Vertex Pharmaceuticals and Zealand Pharma
 - HealthPartners Institute holds a patent for glucose data display
 - HealthPartners Institute receives NIH/NIDDK and PCORI funding
- Study work supported by Abbott Diabetes Care

Glucose management indicator (GMI)

- GMI was developed as a CGM metric to reflect mean glucose in HbA1c unit
 - Established using linear regression between AG and HbA1c from clinical trial data
- Recently added as a glycemic management quality metric in the Healthcare Effectiveness Data and Information Set (HEDIS), a quality performance tool in the United States

Table 1—GMI calculated for various CGM-derived mean glucose concentrations

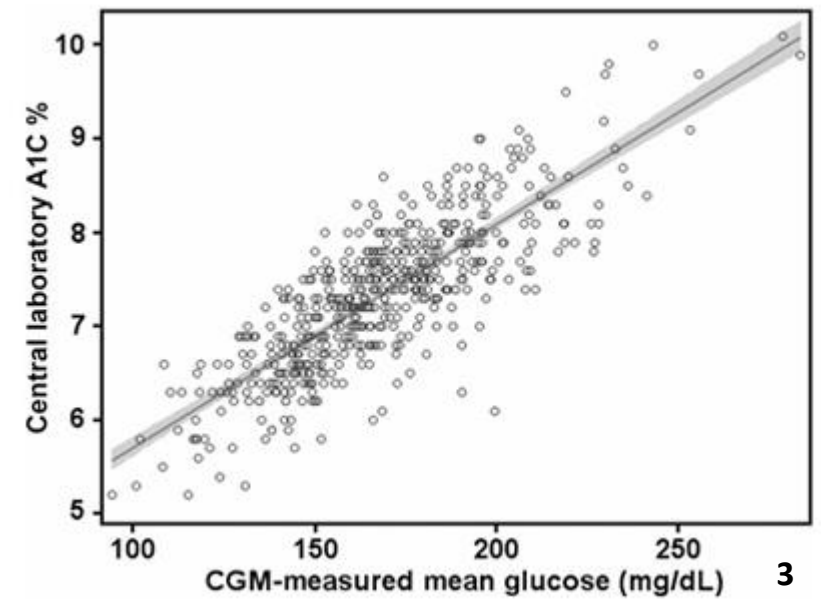
CGM-derived mean glucose (mg/dL)	GMI (%)*
100	5.7
125	6.3
150	6.9
175	7.5
200	8.1
225	8.7
250	9.3
275	9.9
300	10.5
350	11.7

$$GMI = 0.02392 * AG + 3.31$$



Glucose Management Indicator (GMI): A New Term for Estimating A1C From Continuous Glucose Monitoring

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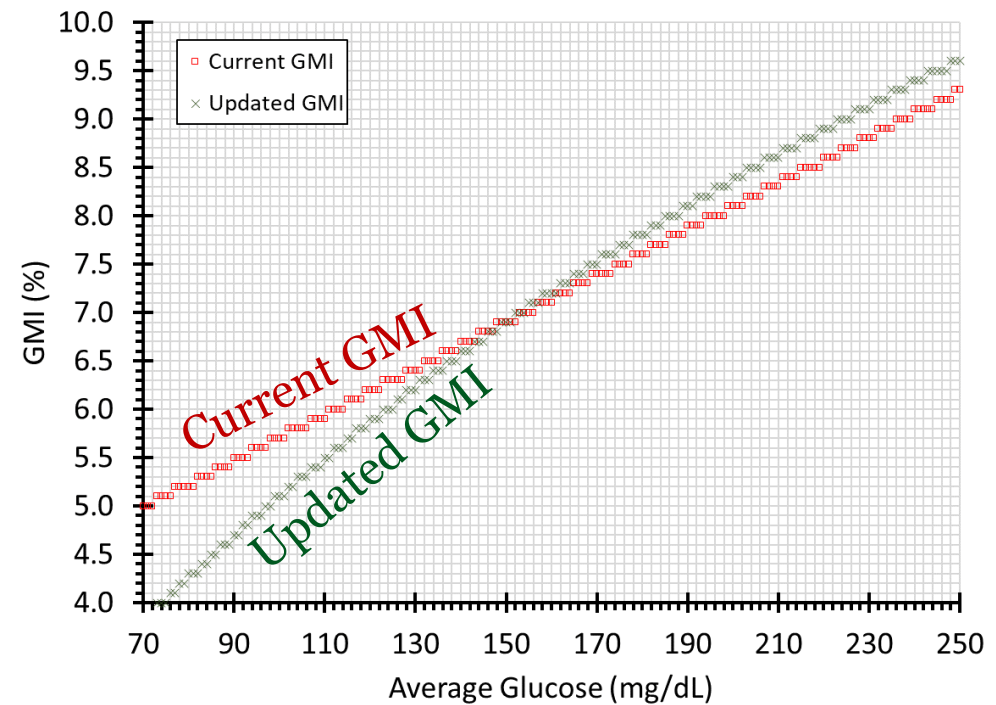
Updated GMI

- GMI was reported to deviate from HbA1c, in upper and especially in the lower A1c range (<6%) [1-3]
- An updated version of GMI was proposed, which was theoretically derived [4]

$$\text{updated GMI} = (15.36 * AG^{-1} + 0.0425)^{-1}$$

parameterized with experimental measurements of apparent hemoglobin glycation rate, K_M of glucose with GLUT1, and RBC life span

1. Shah VN, DuBose SN, Li Z, et. al. Continuous Glucose Monitoring Profiles in Healthy Nondiabetic Participants: A Multicenter Prospective Study. *J Clin Endocrinol Metab.* 2019 Oct 1;104(10):4356-4364.
2. Shah VN, Vigers T, Pyle L, Calhoun P, Bergenstal RM. Discordance Between Glucose Management Indicator and Glycated Hemoglobin in People Without Diabetes. *Diabetes Technol Ther.* 2023 May;25(5):324-328.
3. Selvin E; The Glucose Management Indicator: Time to Change Course? *Diabetes Care* 20 May 2024; 47 (6): 906–914
4. Xu Y, Dunn TC, Ajjan RA. A Kinetic Model for Glucose Levels and Hemoglobin A1c Provides a Novel Tool for Individualized Diabetes Management. *J Diabetes Sci Technol.* 2021 Mar;15(2):294-302.



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

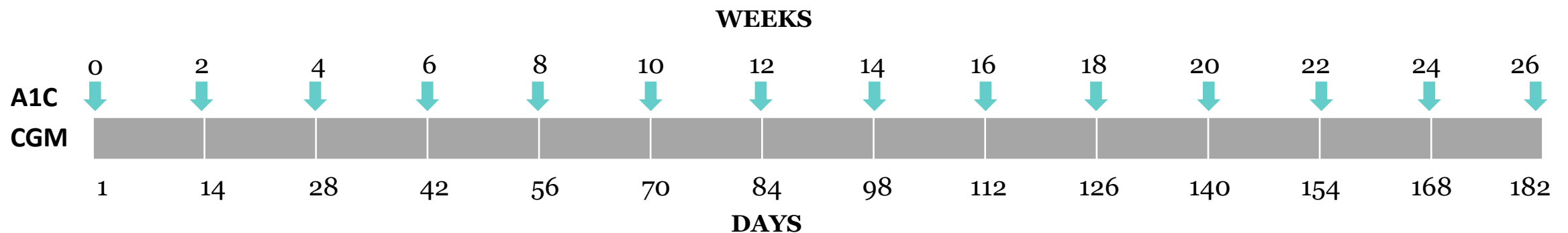
Aims

Evaluate clinical study and real-world data to **assess the ability of an updated GMI metric to:**

- Improve the agreement of uGMI and the HbA1c
- Potentially improve clinical glycemic assessment **and management**

GDAC Study¹

- A prospective 6-month US-UK study (18 centers) in individuals aged 4 years or older with T1D or T2D and including different racial groups
 - For those aged 18 years and over: venous blood samples were measured for HbA1c
 - For those 4-17 years old had venous blood HbA1c at days 0, 56, 126, and 182 and duplicate capillary point-of-care HbA1c measurement for the other timepoints.
- Key exclusion criteria included conditions known to acutely alter red blood cell lifespan
- Participants wore two CGM sensors simultaneously (choice of 1 unmasked & 1 masked or 2 masked)



¹“Glucose-Derived A1C”: NCT05189938

GDAC: Participant characteristics

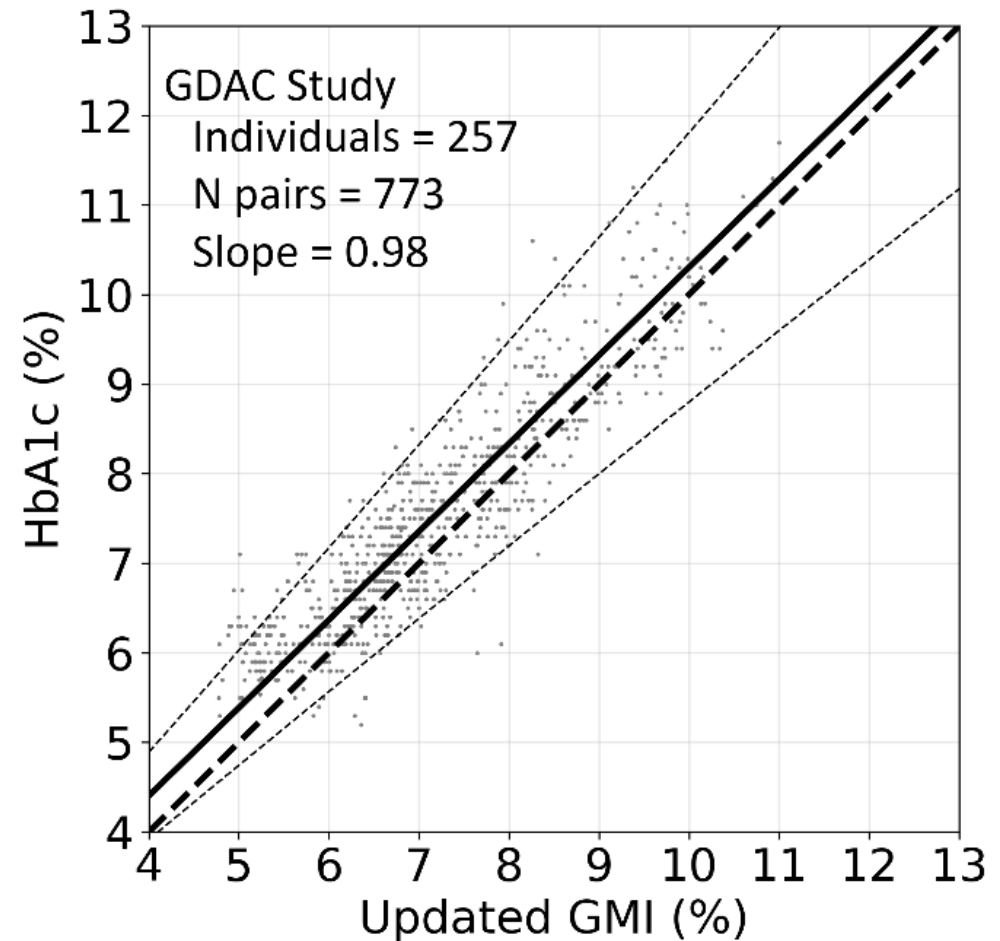
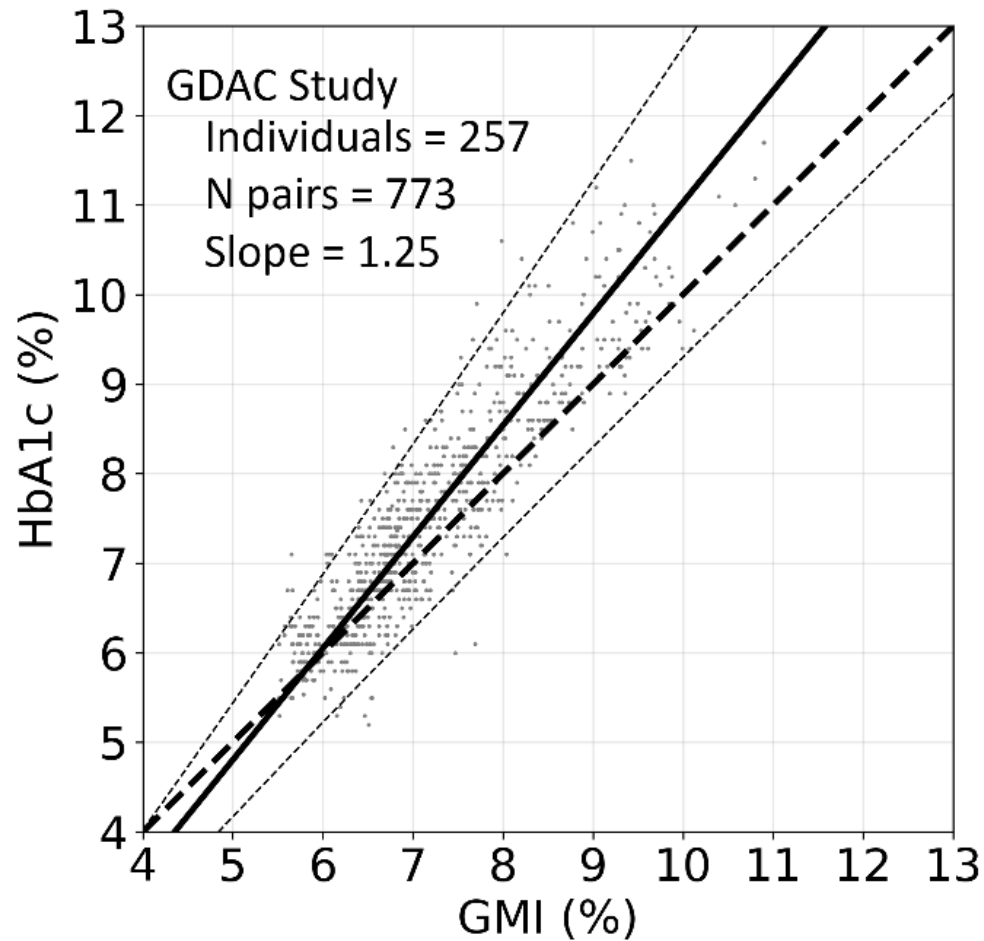
	Black	White	Asian	Other	Overall
Number	59	76	91	31	257
Adult/Pediatric	58/1	73/3	88/3	30/1	249/8
T2D/T1D	52/7	49/27	77/14	25/6	203/54
Female	36 (61%)	31 (41%)	33 (36%)	15 (48%)	115 (45%)
Age (years)	54 (14)	51 (18)	51 (16)	52 (13)	52 (16)
A1C %	7.7 (1.3)	7.5 (1.0)	7.8 (1.4)	7.1 (1.0)	7.6 (1.2)
Average 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)

Data are presented as Mean (SD) unless otherwise indicated.

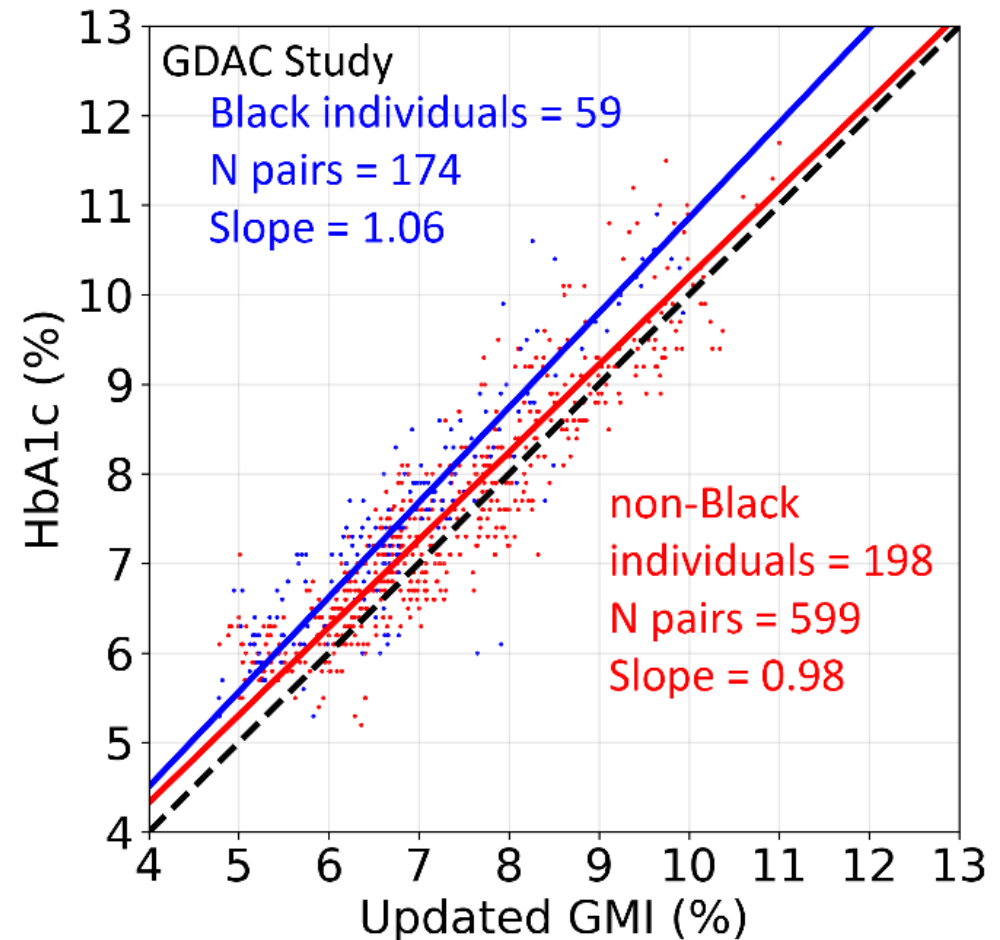
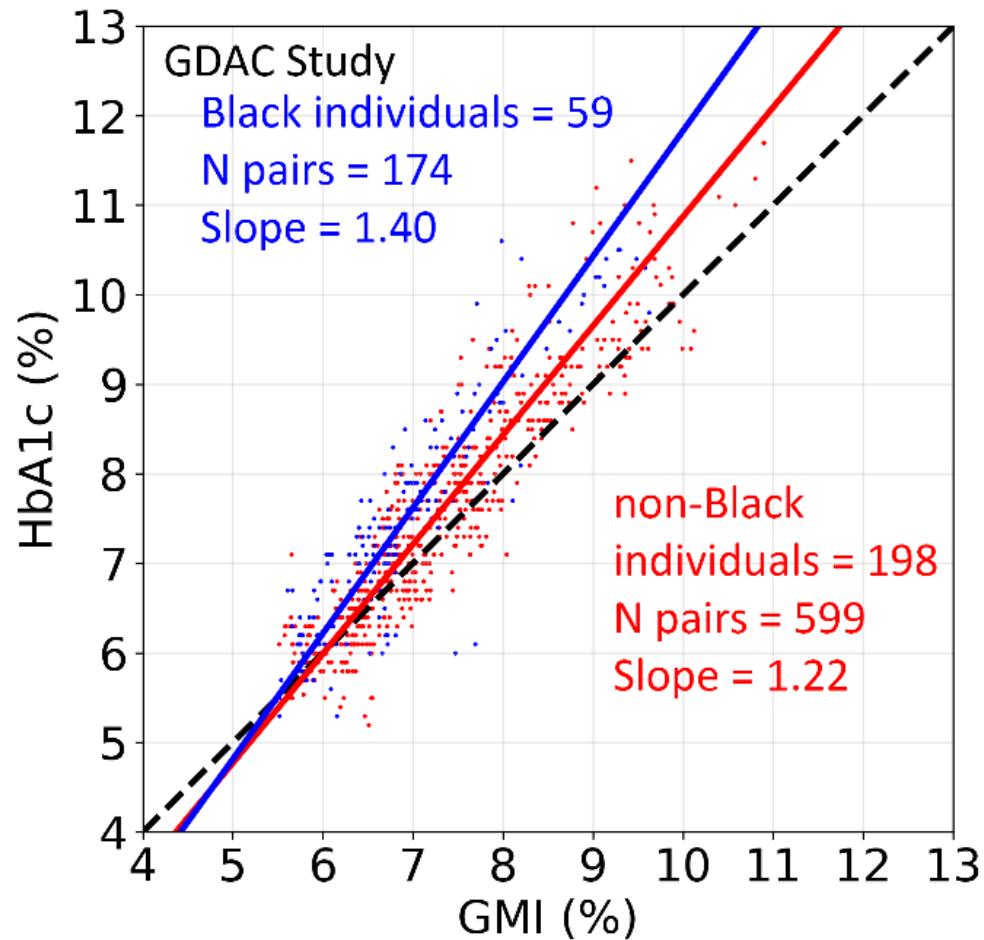
Real-world observations

- Linked real-world deidentified data from
 - LibreView data management platform (Abbott Diabetes Care, Alameda, CA, USA)
 - medical and pharmacy claims data
 - a large reference laboratory A1C dataset
- **18,186 individuals with diabetes**
 - 55% T1D, 37% T2D, 8% gestational or other
 - Mean age 60 years (± 14 years, 6-89)
 - 58% female

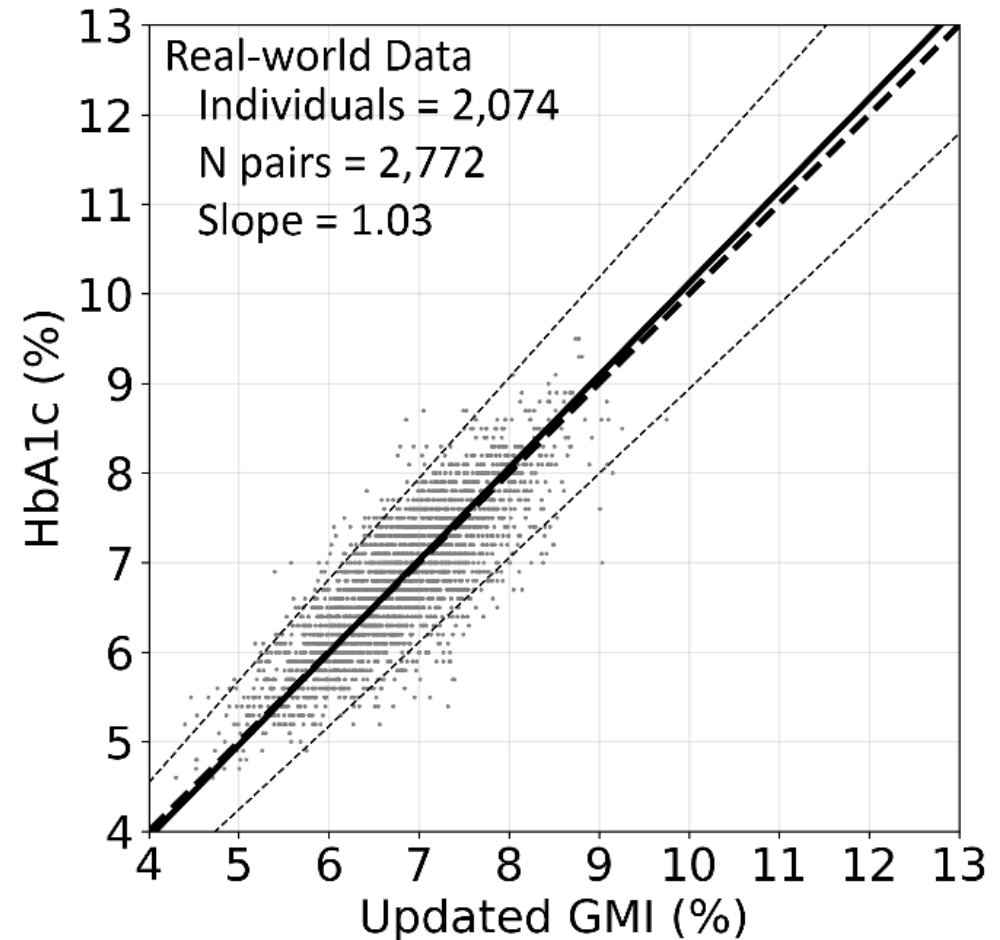
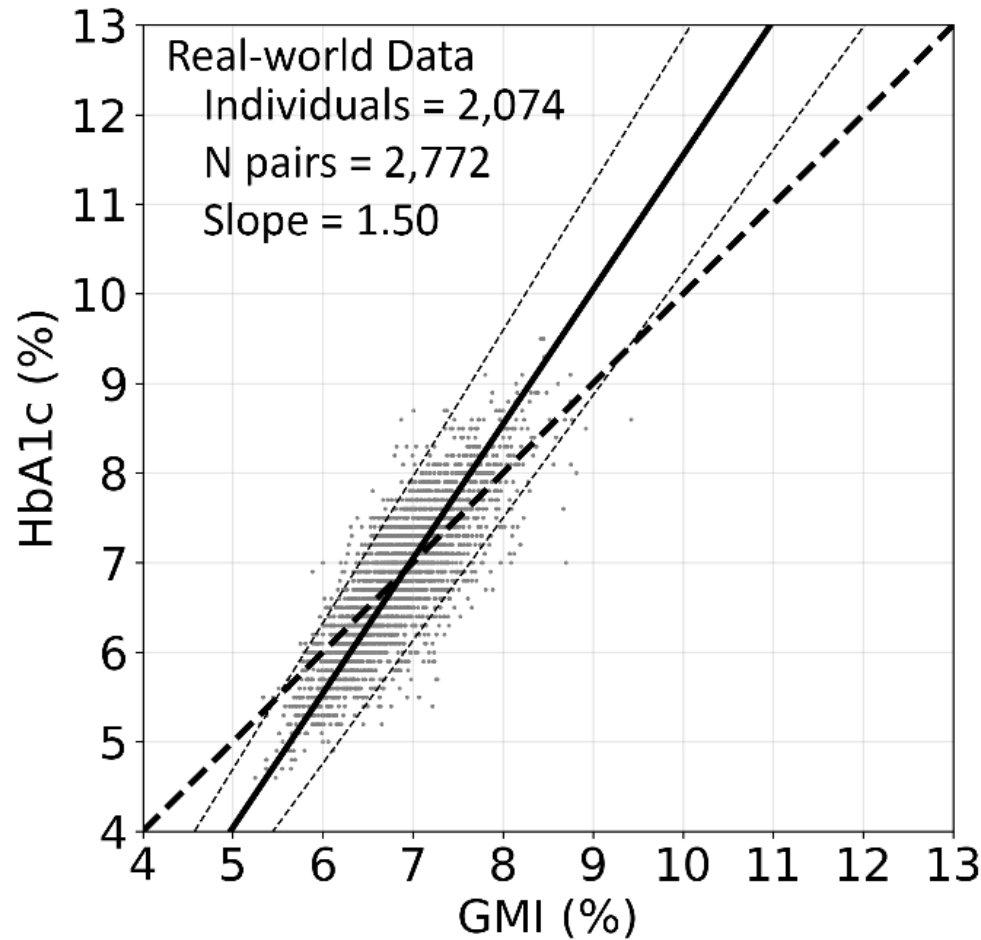
Correlation of HbA1c with GMI and Updated GMI in the GDAC Study



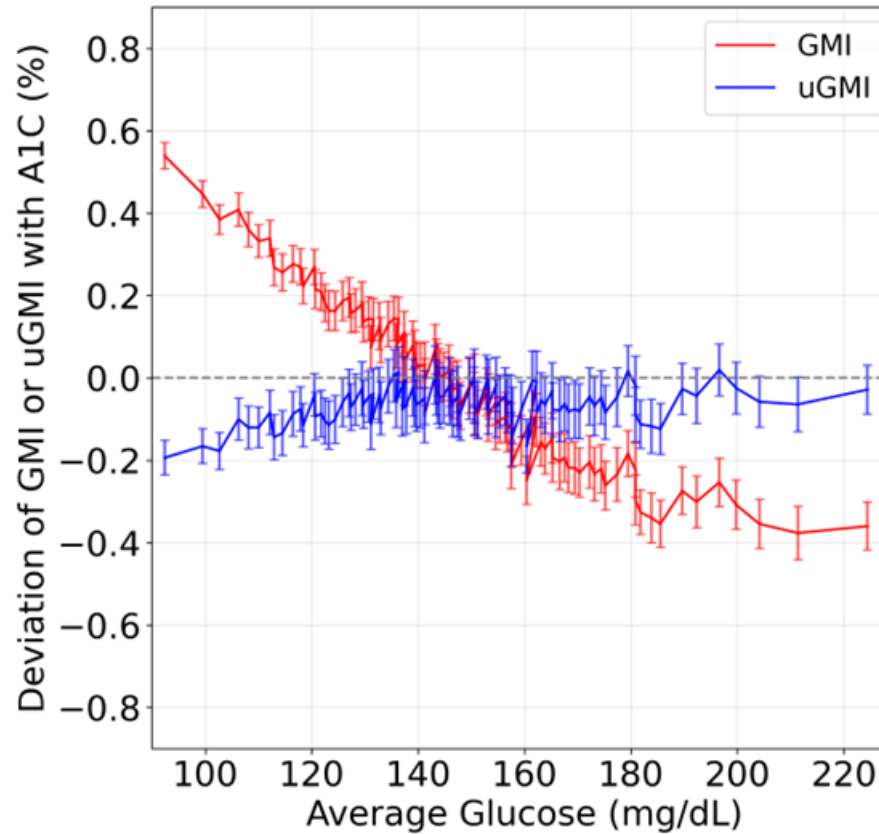
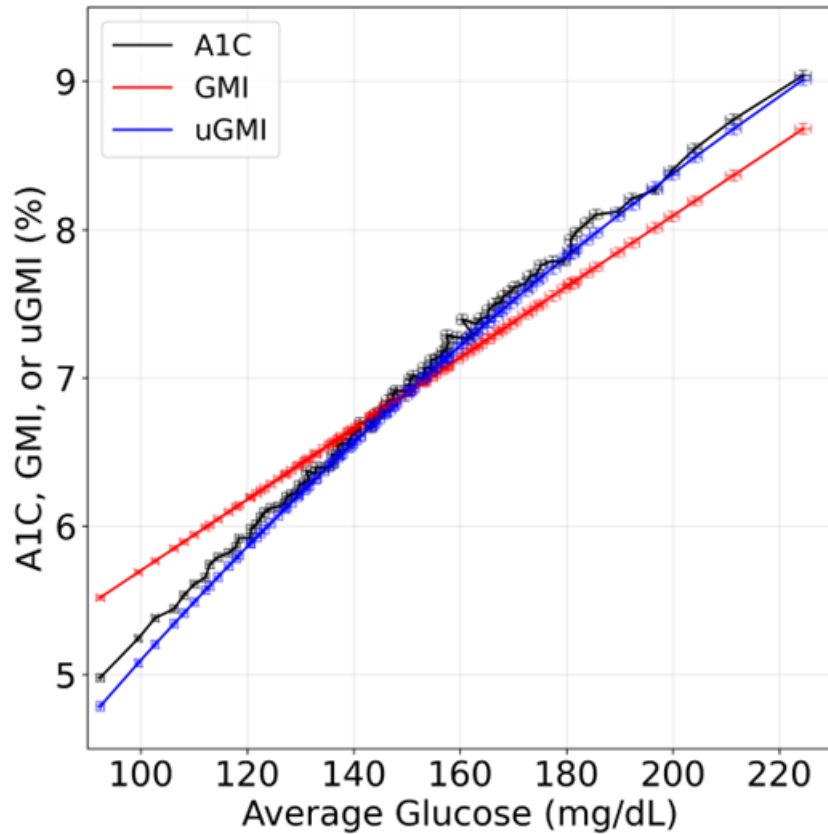
Correlation of HbA1c with GMI and Updated GMI in the GDAC Study – racial difference



Correlation of HbA1c with GMI and Updated GMI in the real-world observation set

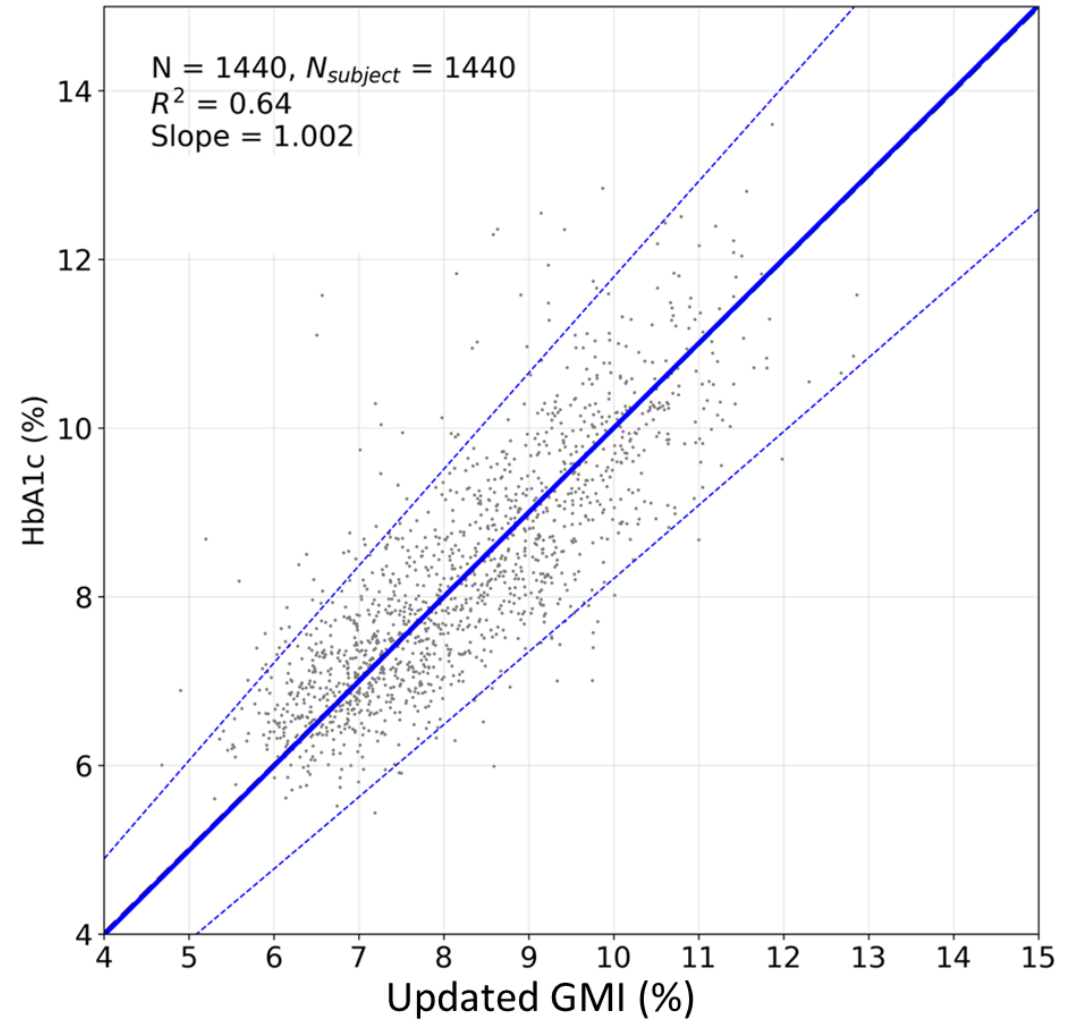
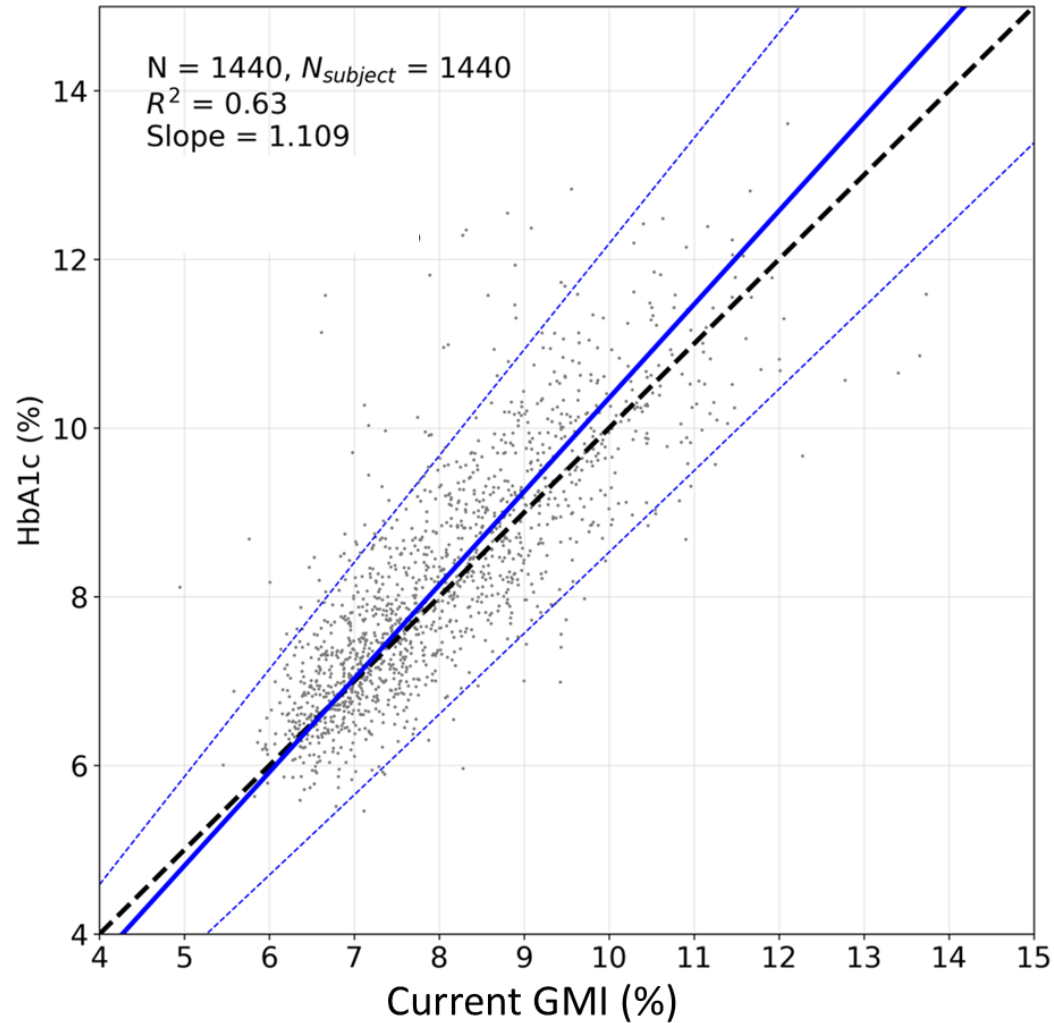


Comparison of average deviations of GMI and Updated GMI with HbA1c in 100 equal-size bins from real-world set



NGSP (mg/dL, %)			
AG	A1C	GMI	uGMI
93	5	5.5	4.8
101	5.3	5.7	5.1
112	5.7	6	5.6
116	5.8	6.1	5.7
121	6	6.2	5.9
133	6.4	6.5	6.3
136	6.5	6.6	6.4
139	6.6	6.6	6.5
150	7	6.9	6.9
167	7.5	7.3	7.4
182	8	7.7	7.9
186	8.1	7.8	8
197	8.3	8	8.3
222	9	8.6	9
238	9.4	9	9.3

DCCT 7-point capillary BG data confirms updated GMI



Conclusions

- The current GMI shows some inaccuracies at both the lower and higher A1C levels, as the regression between these two glycemic markers is not close to unity
- The updated GMI (uGMI) corrects this issue on a population level, aligning regression slopes close to 1 in both real-world and GDAC study sets.
- Large real-world data demonstrates a strong alignment between uGMI and HbA1c population averages
- The uGMI metric better reflects A1C than the original GMI, enhancing CGM data interpretation and potentially improving clinical decision-making.