Prospective use of Personal Glycation Ratio Improves Racial Differences in Glycated Hemoglobin Assessment of Average Glucose

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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, Medtronic, NCQA, Novo Nordisk, Onduo, Roche Diabetes Care, Sanofi and United Healthcare, Vertex Pharmaceuticals and Zealand Pharma

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AIMS

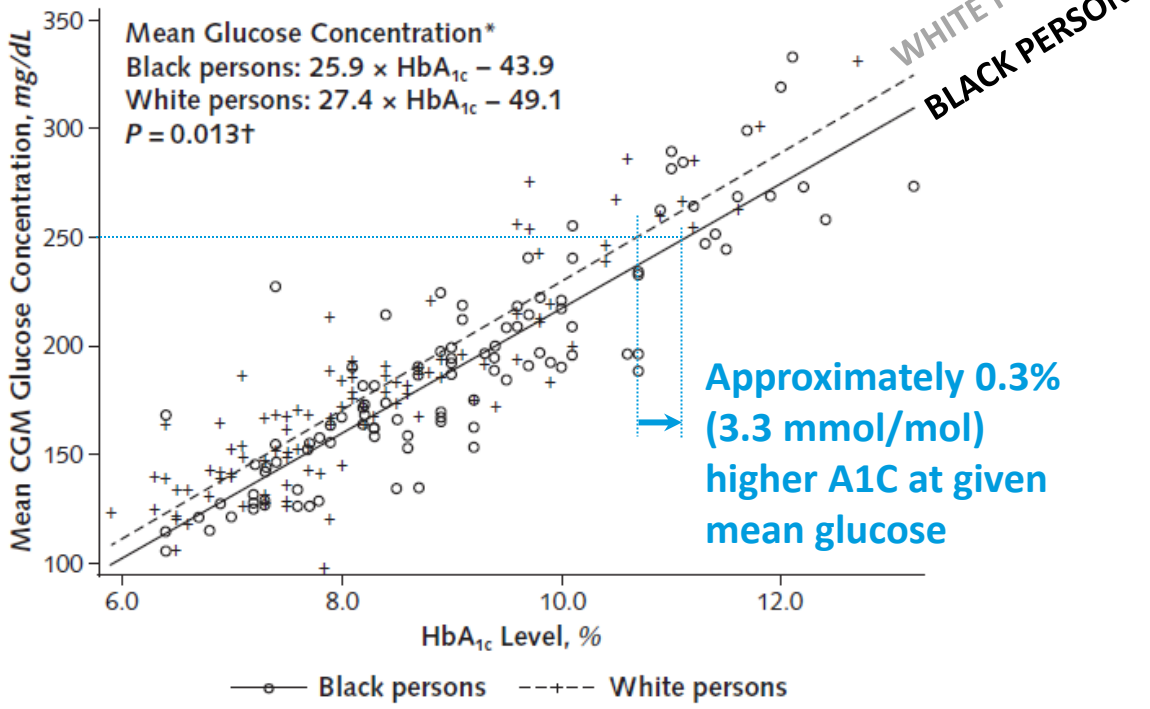
- Glycated hemoglobin (A1C) and average glucose (AG) are important glycemic markers and ideally should agree well.
- However, the CGM-derived Glucose Management Indicator (GMI) is frequently discordant with laboratory A1C.
- We evaluated a personalized approach for assessment of average glycemia by A1C, and further investigated the effects of racial background.

Component Ref Range & Units	1 mo ago (1/4/24)	4 mo ago (9/25/23)	6 mo ago (7/24/23)	1 yr ago (10/24/2
Hemoglobin A1C <=5.6 %	7.8 ^	7.1 ^	7.1 ^	7.1 ^
Estimated Average Glucose (Calc) < 117 mg/dL	177	157 CM	157 CM	

Comment: Estimated average glucose (eAG) converts A1c into glucose units (mg/dL) and estimates average glucose over the past approximately 3 months

Racial differences in A1C reported in type 1 diabetes

Figure 1. Mean glucose concentration as measured by CGM versus HbA_{1c} level, by race.



CONCLUSION:

On average, HbA1c levels overestimate the mean glucose concentration in Black persons compared with White persons, possibly owing to racial differences in the glycation of hemoglobin.

"Our results provide the strongest evidence to date that **nonglycemic factors** partially account for the higher HbA1c levels observed in Black persons with diabetes."

"...these results indicate that interpretation for a given patient **requires knowledge of that patient's mean glucose–HbA1c relationship**."

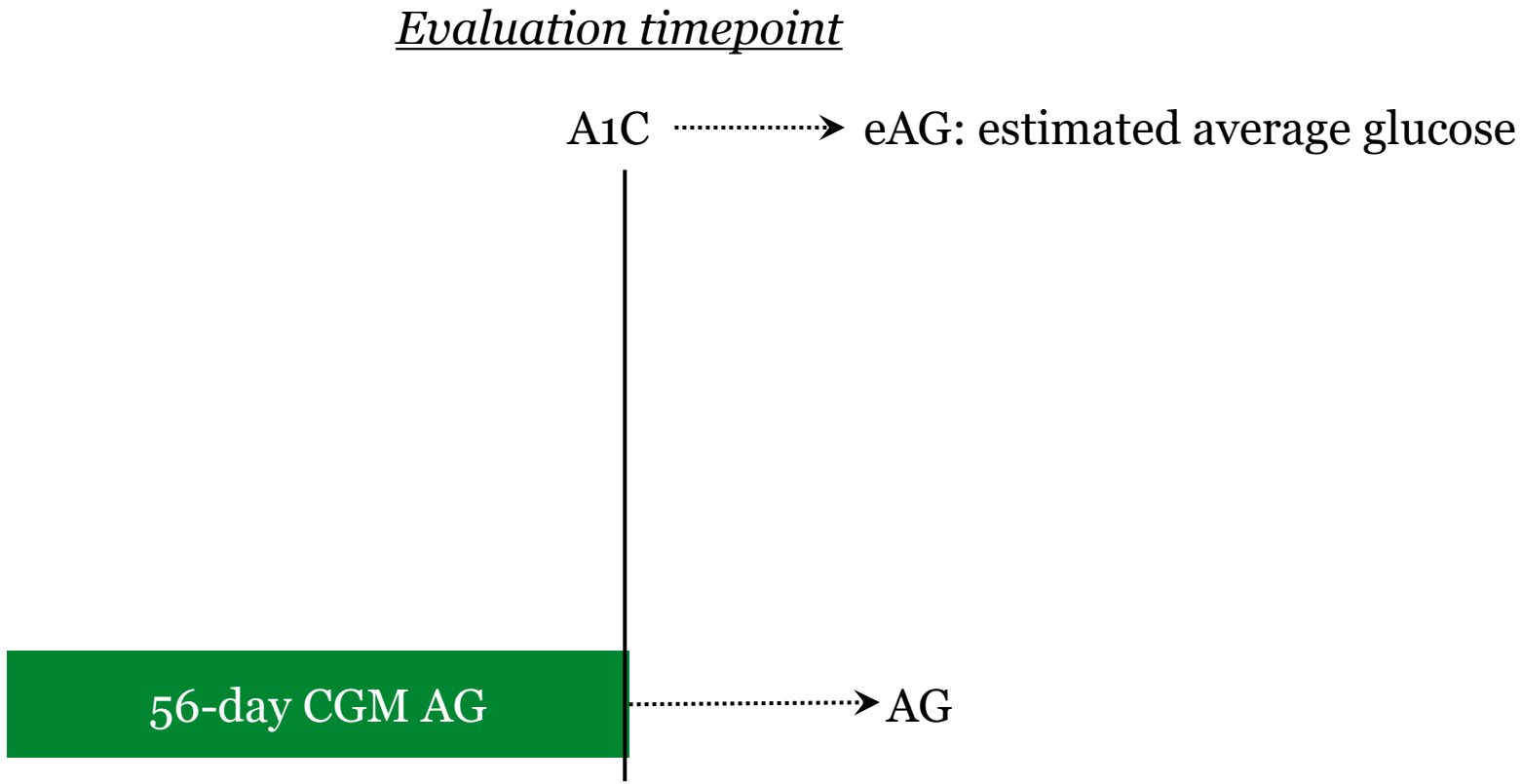
Bergenstal, et al., Racial Differences in the Relationship of Glucose Concentrations and Hemoglobin A1c Levels. Ann Intern Med, 2017, https://doi.org/10.7326/M16-2596

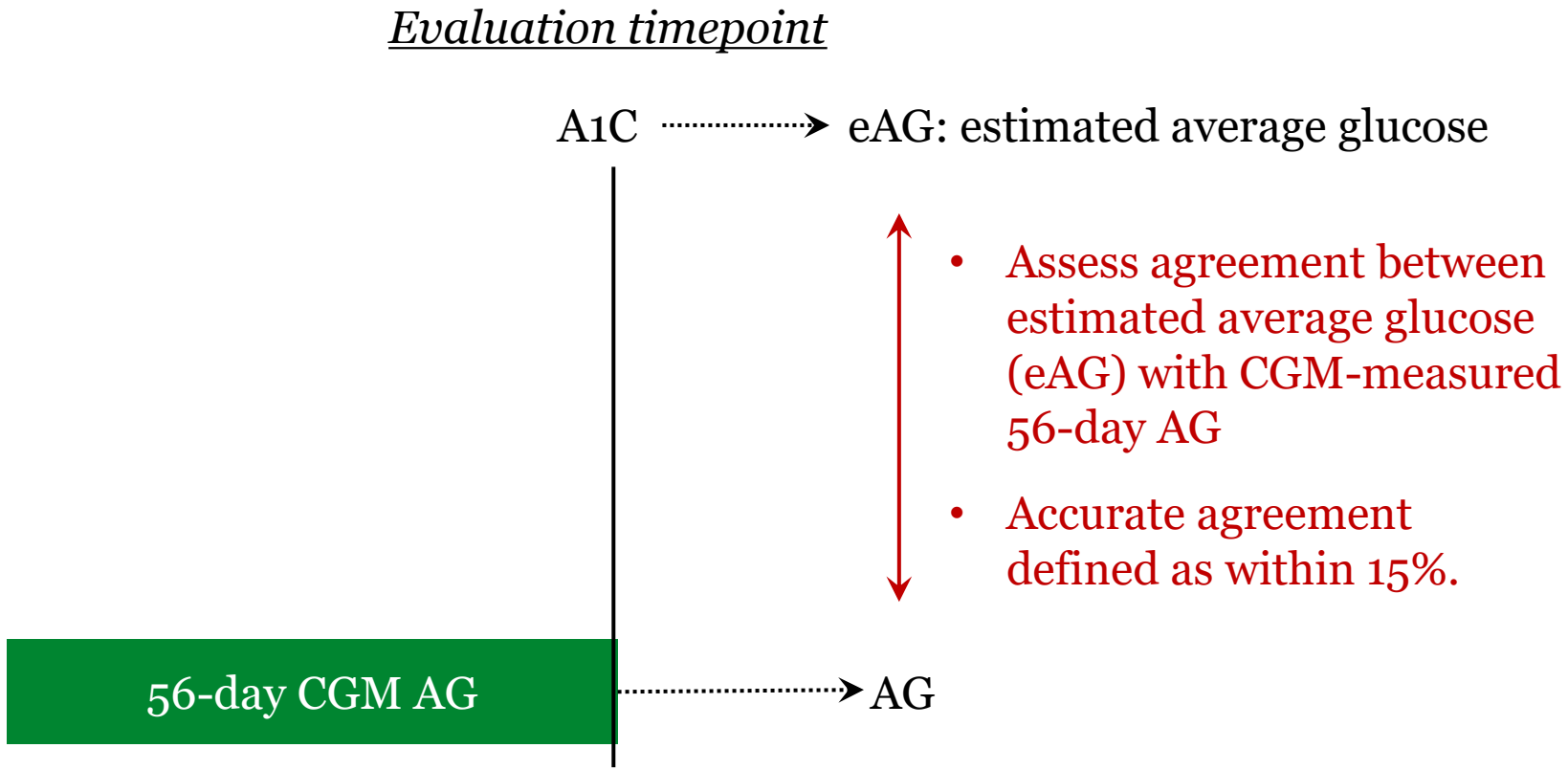
METHODS

Participant characteristics, HbA1c and CGM data

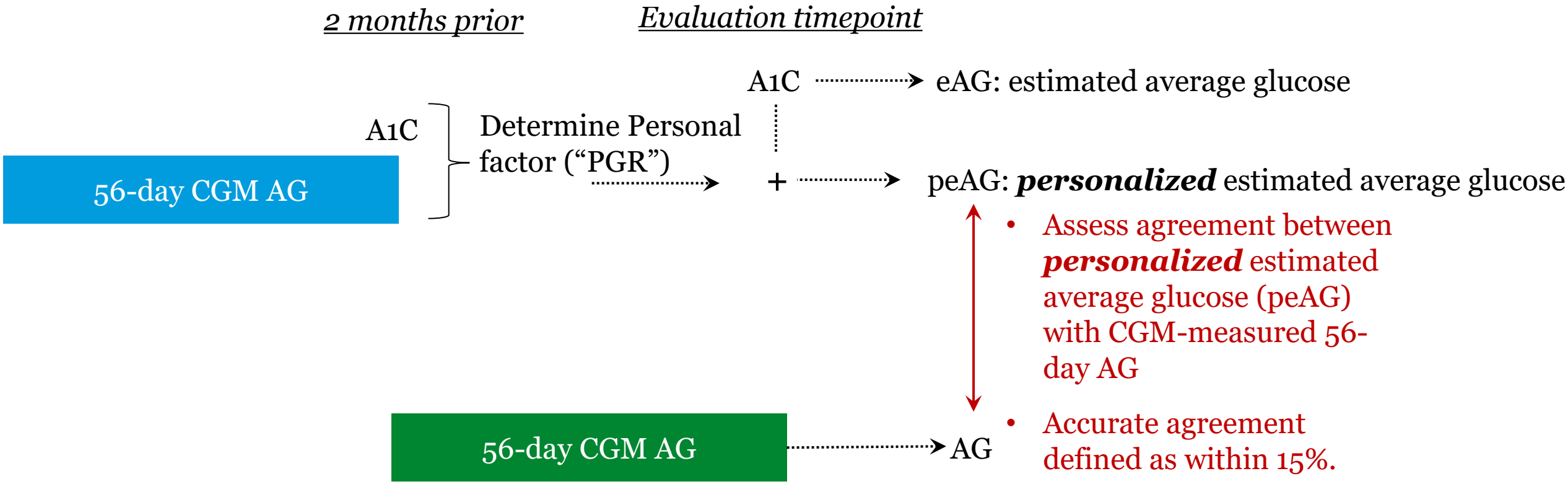
	All	Non-Hispanic Black persons	Non-Hispanic White persons
N	87	35	52
Type 1 diabetes	100%	100%	100%
Age [range], years	38 [10-72]	36 [10-71]	39 [10-72]
Female [%]	54 [62%]	21 [60%]	33 [63%]
T1D Duration [range], years	19 [1-61]	16 [1-46]	22 [3-61]
HbA1c, %	8.3	8.8	7.9
HbA1c, mmol/mol	67	73	63
Average Glucose* (mg/dL)	173	182	167
Average Glucose* (mmol/L)	9.6	10.1	9.3

Mean values unless indicated otherwise
* 56-day average CGM glucose preceding HbA1c


Evaluation timepoint
A1C
eAG: estimated average glucose
56-day CGM AG
AG


Evaluation timepoint
A1C
eAG: estimated average glucose
56-day CGM AG
AG
• Assess agreement between estimated average glucose (eAG) with CGM-measured 56-day AG
• Accurate agreement defined as within 15%.

METHODS


2 months prior
Evaluation timepoint
A1C
eAG: estimated average glucose
A1C
Determine Personal factor ("PGR")
56-day CGM AG
+
peAG: personalized estimated average glucose
Assess agreement between personalized estimated average glucose (peAG) with CGM-measured 56-day AG
56-day CGM AG
AG
Accurate agreement defined as within 15%.

METHODS

2 months prior *Evaluation timepoint*

A1C ⋯→ eAG: estimated average glucose[1]

A1C → Determine Personal factor ("PGR") ⋯→ + ⋯→ peAG: ***personalized*** estimated average glucose[2]

eAG = 28.7 * A1C – 46.7

56-day CGM AG

$$PGR = \frac{\frac{1}{\text{Average Glucose}} + \frac{1}{K_M}}{\frac{1}{A1C} - 0.01} * 10^3$$

where:

$K_M = 473$ mg/dL [3]

$$peAG = \frac{1}{\frac{PGR * 10^{-3}}{A1C} - \left(PGR * 10^{-5} + \frac{1}{K_M}\right)}$$

56-day CGM AG ⋯→ AG

[1] ADA Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2024. *Diabetes Care*. 2024 Jan 1;47(Suppl 1):S111-S125

[2] Dunn, et al. *Diabetes Technol Ther*. 2023 Jun;25(S3):S65-S74

[3] Nishimura, et al. *J Biol Chem*. 1993;268(12):8514-8520.

RESULTS

A1C —ADAG→ eAG: estimated average glucose

Overall (n=87)

62% of eAG values accurate v. AG

AG

A1C —PGR→ peAG: ***personalized*** estimated average glucose

Overall (n=87)

93% of eAG values accurate v. AG

AG

accurate = within 15% of the paired AG.

RESULTS

A1C ADAG eAG: estimated average glucose

Overall (n=87)

non-Hispanic Black persons (n=35)

non-Hispanic White persons (n=52)

62% of eAG values accurate v. AG

- 46% of eAG values accurate v. AG
- 73% of eAG values accurate v. AG

AG

A1C PGR peAG: ***personalized*** estimated average glucose

Overall (n=87)

non-Hispanic Black persons (n=35)

non-Hispanic White persons (n=52)

93% of eAG values accurate v. AG

- 89% of eAG values accurate v. AG
- 96% of eAG values accurate v. AG

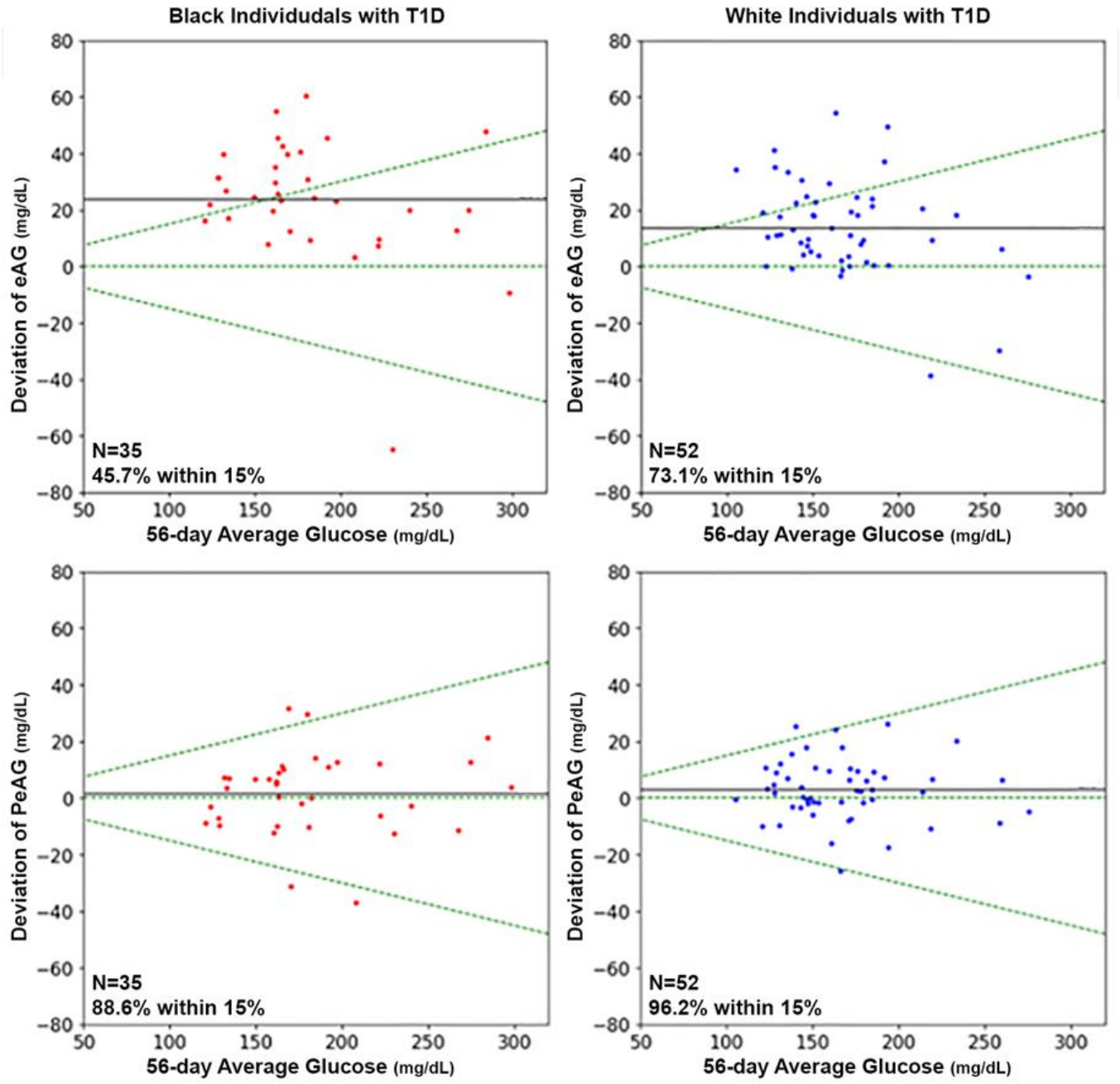
AG

accurate = within 15% of the paired AG.

RESULTS

- Overall:
  - 93% of peAG values accurate
  - 62% of eAG values accurate

  accurate = within 15% of the paired AG.
- The new peAG provided a more accurate assessment of average glucose than eAG for **non-Hispanic Black persons** (n=35)
  - 89% of peAG values accurate
  - 46% of eAG values accurate
- peAG more accurate for **non-Hispanic White persons** (n=52)
  - 96% of peAG values accurate
  - 73% of eAG values accurate



- Further research is needed to evaluate the method
- Personal – rather than categorical – adjustment is supported due to the wide variance of the glucose-A1C relationship with-in any racial or ethnic group[1].

[1] Karter AJ, et al. *Diabetes Technol Ther*. 2023 Oct;25(10):697-704.

- A practical, unbiased, and more accurate estimate of average glycemia derived from A1C can be achieved by use of the personal glycation ratio.
- The exact role of this glycaemic marker at predicting diabetes complications requires further evaluation.

Thank you