HbA1c and average glucose discordance: Personalized A1C improves the discrepancy, particularly in Black individuals

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Disclosures

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HbA1c and average glucose

In clinical practice, the relationship between average glucose and HbA1c can differ across individuals

The important ADAG Study[1] established A1C-to-Average Glucose conversion that is adopted in ADA Standards of Care[2]. However, the study had limitations[3]:

- **Retrospective regression not evaluated prospectively**
- **Limited CGM data** (median of 13 days with 39 days of SMBG over 90-day study period)
- **Predominately White (83%) study participants**
- **Excluded common conditions**:
  liver, kidney or other conditions that affect A1C by altered RBC lifespan

Table 6.1—Equivalent A1C levels and estimated average glucose (eAG)

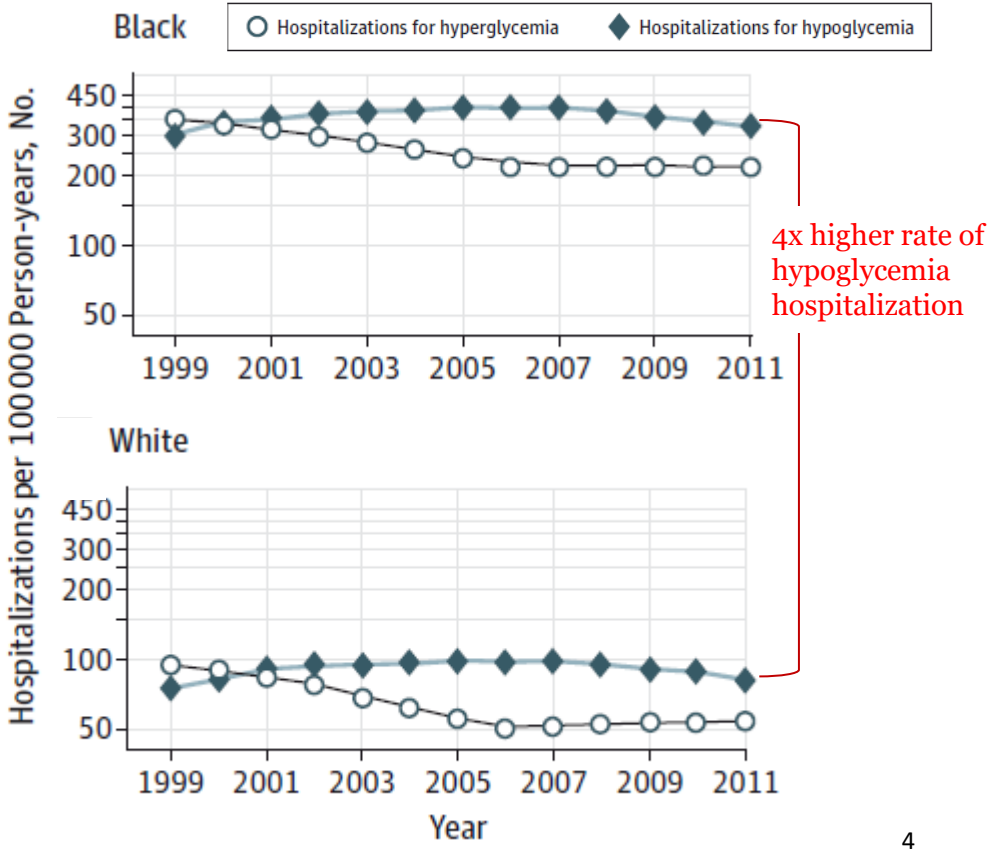
A1C (%)	mg/dL*	mmol/L
5	97 (76–120)	5.4 (4.2–6.7)
6	126 (100–152)	7.0 (5.5–8.5)
7	154 (123–185)	8.6 (6.8–10.3)
8	183 (147–217)	10.2 (8.1–12.1)
9	212 (170–249)	11.8 (9.4–13.9)
10	240 (193–282)	13.4 (10.7–15.7)
11	269 (217–314)	14.9 (12.0–17.5)
12	298 (240–347)	16.5 (13.3–19.3)

Data in parentheses are 95% CI. A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG. *These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes. The correlation between A1C and average glucose was 0.92 (19,20). Adapted from Nathan et al. (19).

[1]Nathan et al, Diabetes Care 2008; 31:1473–1478
[2]Diabetes Care 2024;47(Suppl. 1):S111–S125
[3]Kahn & Fonseca. Diabetes Care. 2008; 31(8):1704-7.

HbA1c and average glucose in different populations

- HbA1c-average glucose relationship also varies between different populations
- Black individuals tend to have higher HbA1c for a given average glucose, related to altered red blood cell biology, leading to:
  - Risk of diabetes overdiagnosis[1]
  - Greater hypoglycemic hospitalizations[2], perhaps due to overtreatment of elevated laboratory A1C



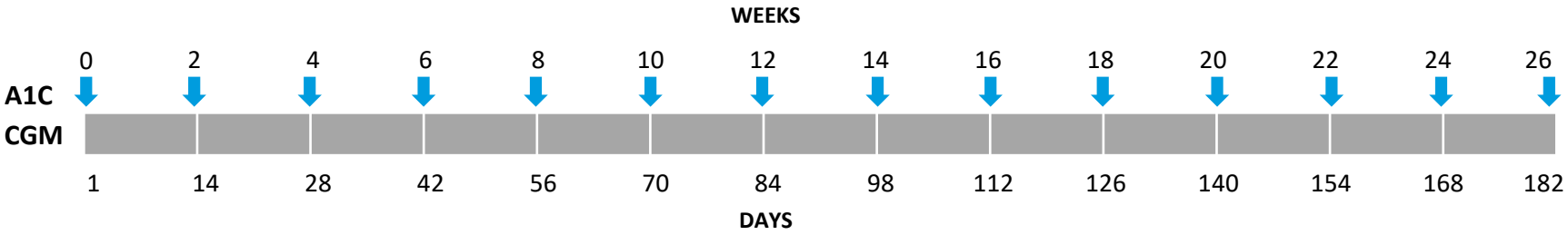
[1]Ram et al, BMJ Open Diabetes Res Care. 2024; 12(2):e003470
[2]Lipska et al. JAMA Intern Med. 2014; 174(7):1116-24.

Aims

- **Evaluate the size of the problem by analysing different racial groups and adopting a prospective study design**
- **Improve A1C accuracy at reflecting average glucose levels, across different individuals and racial groups**

GDAC Study[1]

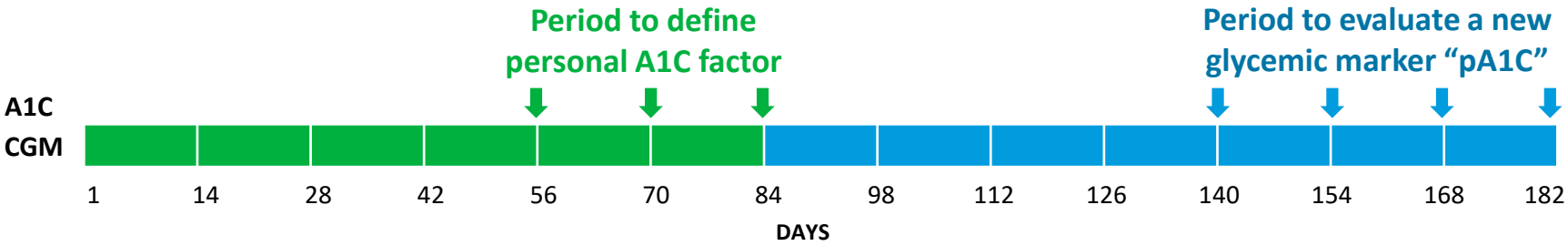
- A prospective 6-month US-UK study (18 centers) in individuals aged 4 years or older with T1D or T2D and including different racial groups
  - For those aged 18 years and over: venous blood samples were measured for HbA1c
  - For those 4-17 years old had venous blood HbA1c at days 0, 56, 126, and 182 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 and HbA1c≥15.5%
- Participants wore two CGM sensors simultaneously (choice of 1 unmasked & 1 masked or 2 masked)



[1]"Glucose-Derived A1C": NCT05189938

Personalized HbA1c (pA1C)

- HbA1c and CGM data were evaluated for up to week 12 to determine a personal glycation ratio (PGR)
- Individual PGR was applied to calculate personally adjusted HbA1c (pA1C)[1] at weeks 20-26.
- HbA1c and pA1C were then assessed for agreement with average glucose in the prior 56 days.



[1]Dunn TC, Xu Y, Bergenstal RM, Ogawa W, Ajjan RA. Diabetes Technol Ther. 2023 Jun;25(S3):S65-S74.

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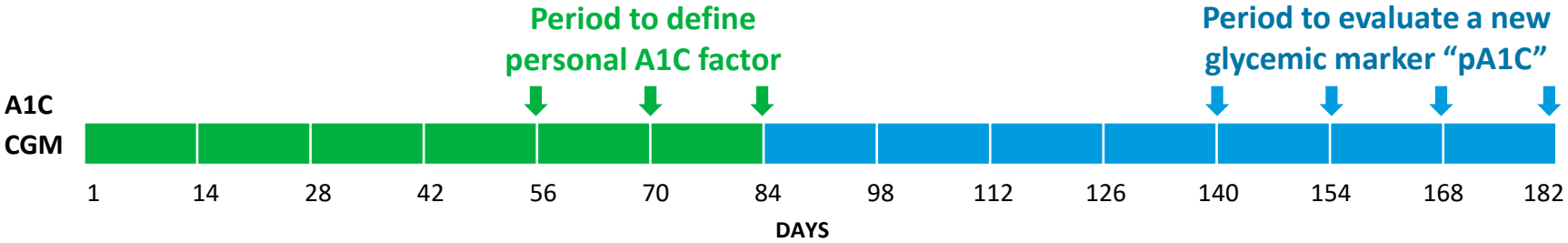
$$PGR = \left(AG^{-1} + K_M^{-1}\right) * (100 * A1C^{-1} - 1)^{-1} * 10^5$$

$$K_M = 472$$

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

$$PGR_{ref} = 65.1$$



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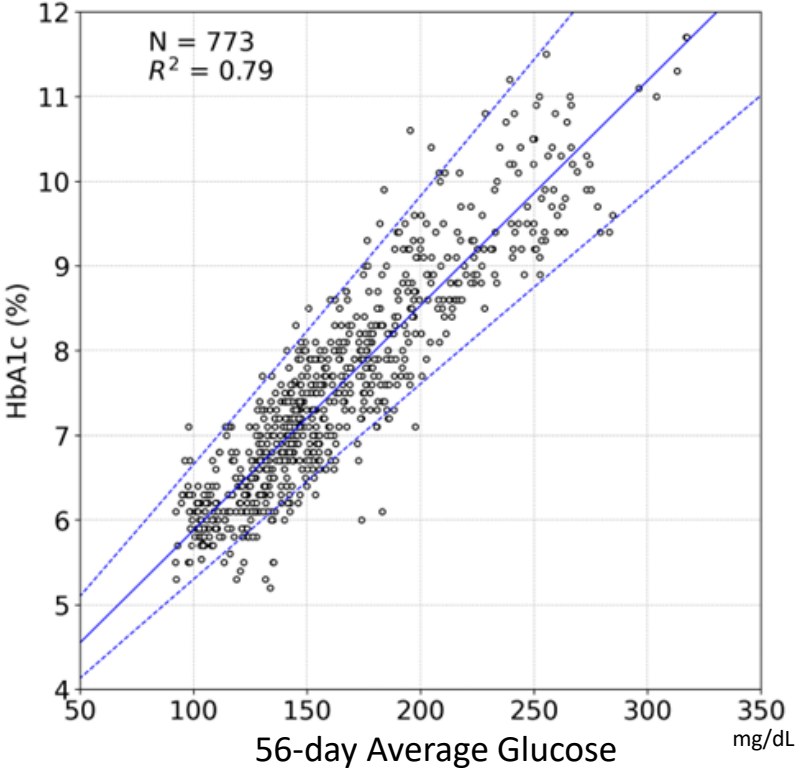
Results: Participant characteristics

	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)

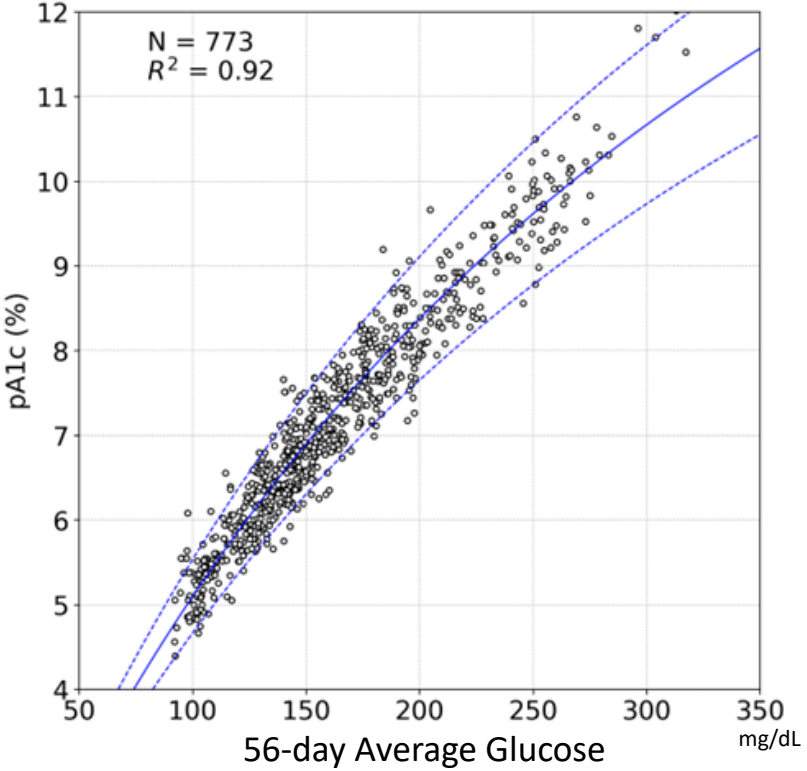
Data are presented as Mean (SD) unless otherwise indicated.

Results (1)

Lab HbA1c



Personalized A1C



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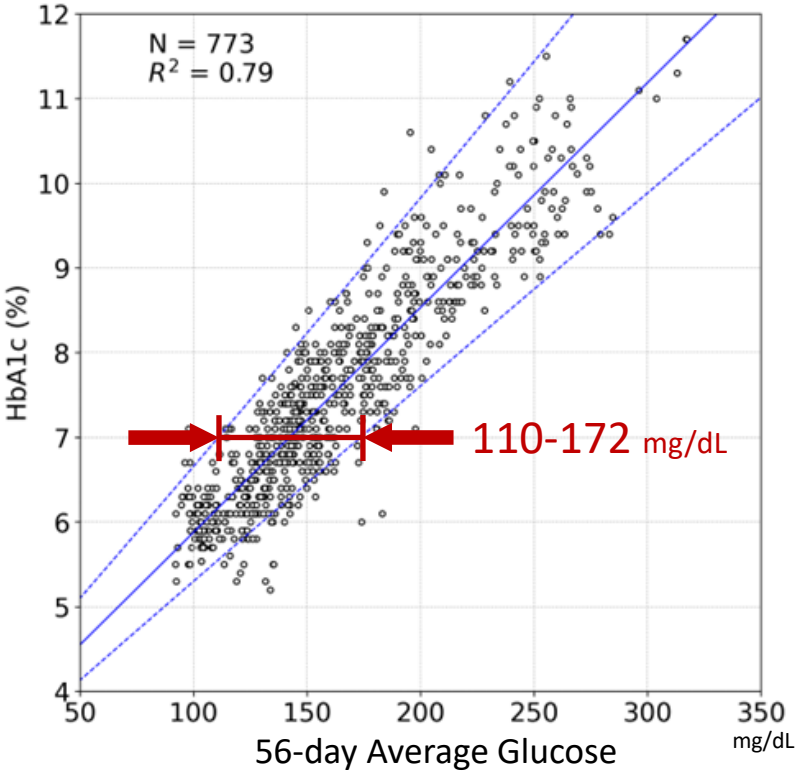
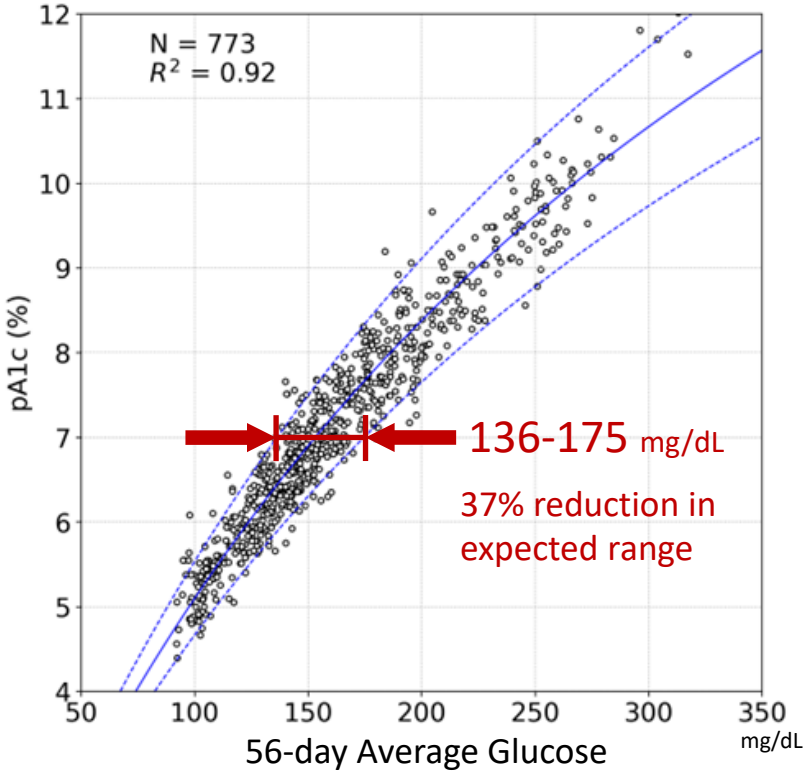
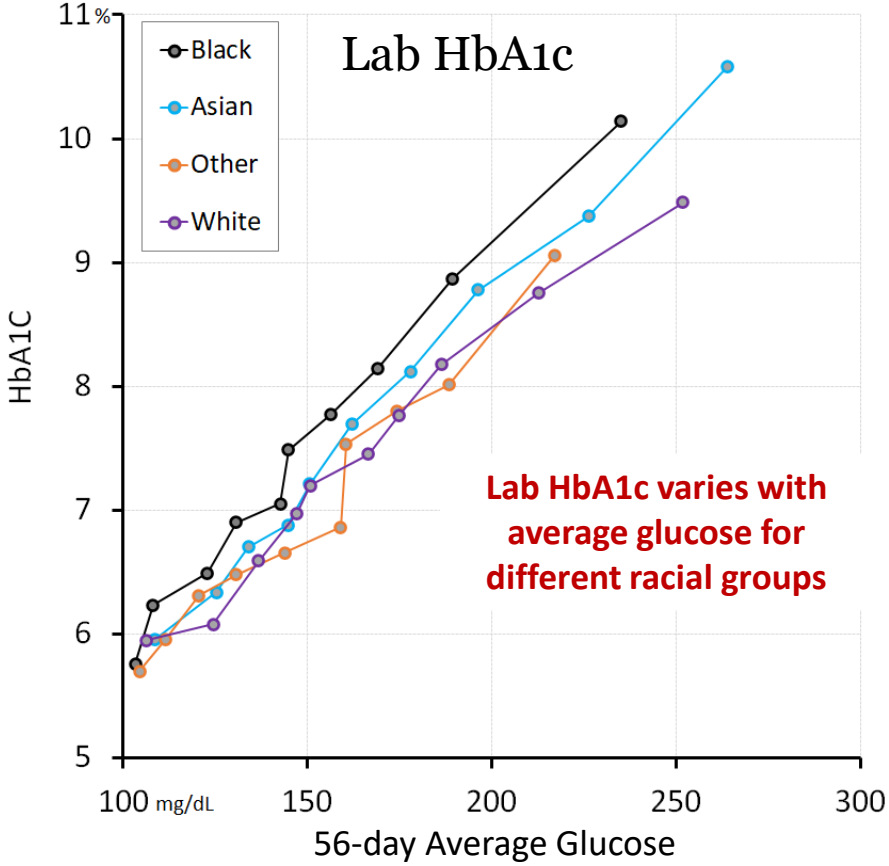


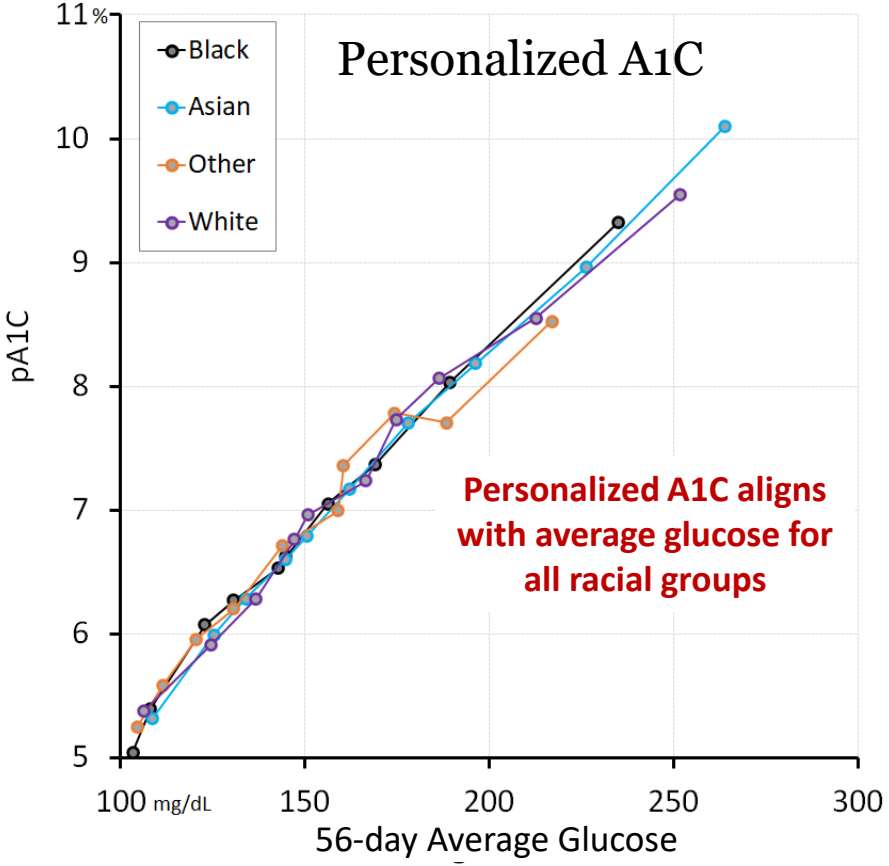
Personalized A1C



For comparison: ADAG at 7% (123-185 mg/dL)

Results (2)


Lab HbA1c
Black
Asian
Other
White
11 %
10
9
8
7
6
5
HbA1C
100 mg/dL
150
200
250
300
56-day Average Glucose
Lab HbA1c varies with average glucose for different racial groups


Personalized A1C
Black
Asian
Other
White
11 %
10
9
8
7
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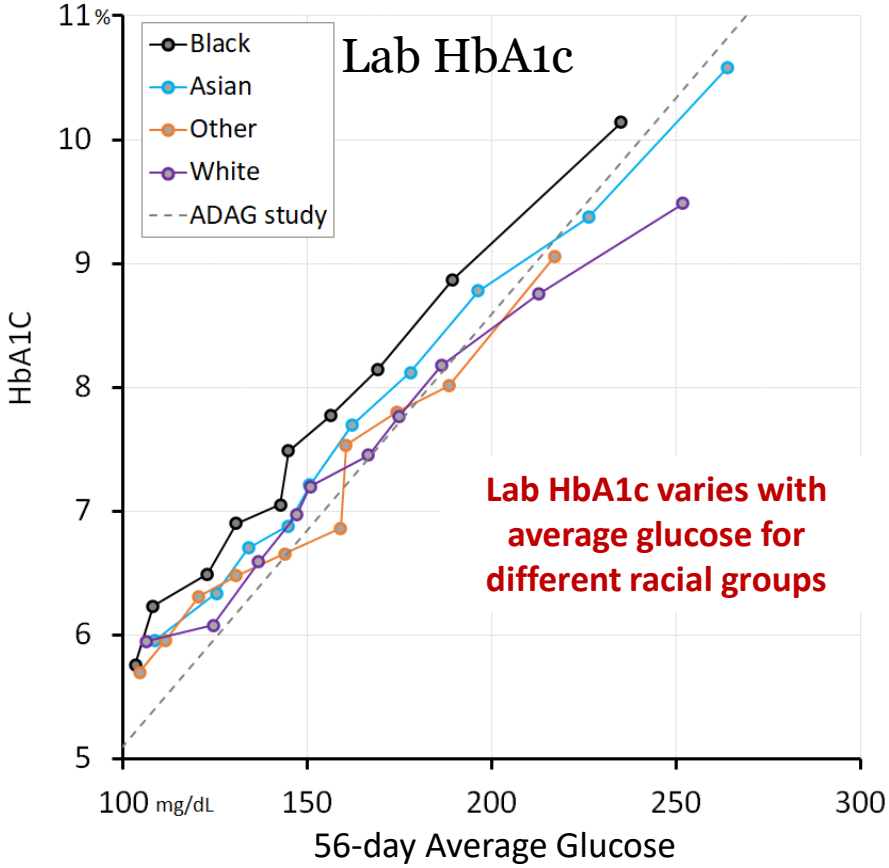
pA1C
100 mg/dL
150
200
250
300
56-day Average Glucose
Personalized A1C aligns with average glucose for all racial groups

Results (2)


Lab HbA1c
Black
Asian
Other
White
ADAG study
HbA1C
11%
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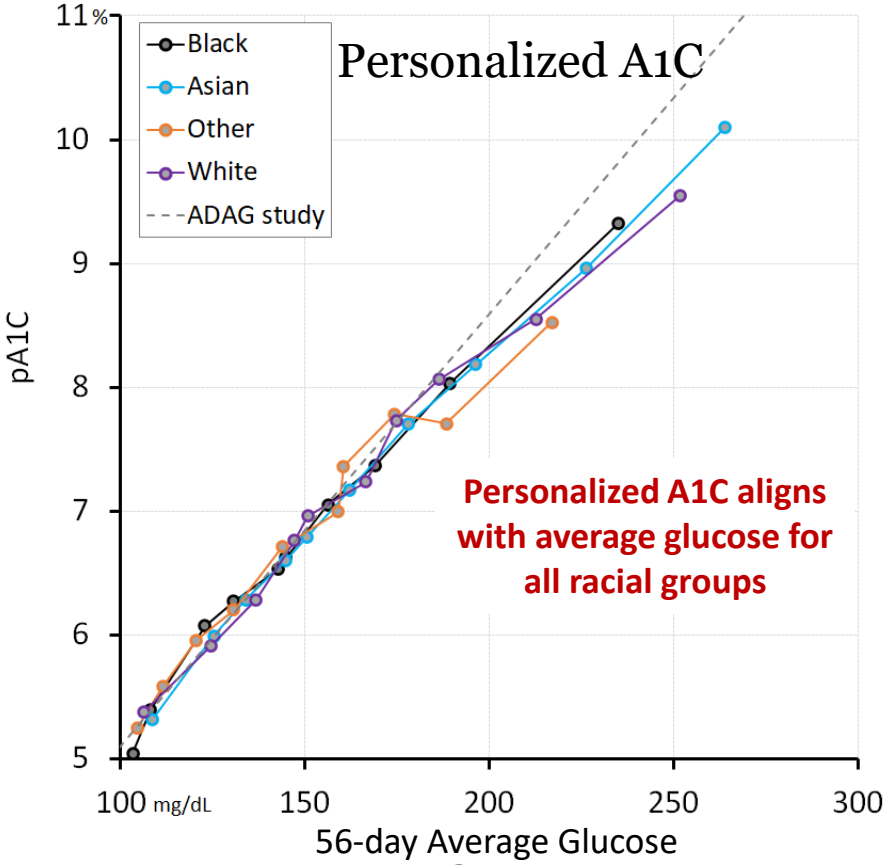
Lab HbA1c varies with average glucose for different racial groups


Personalized A1C
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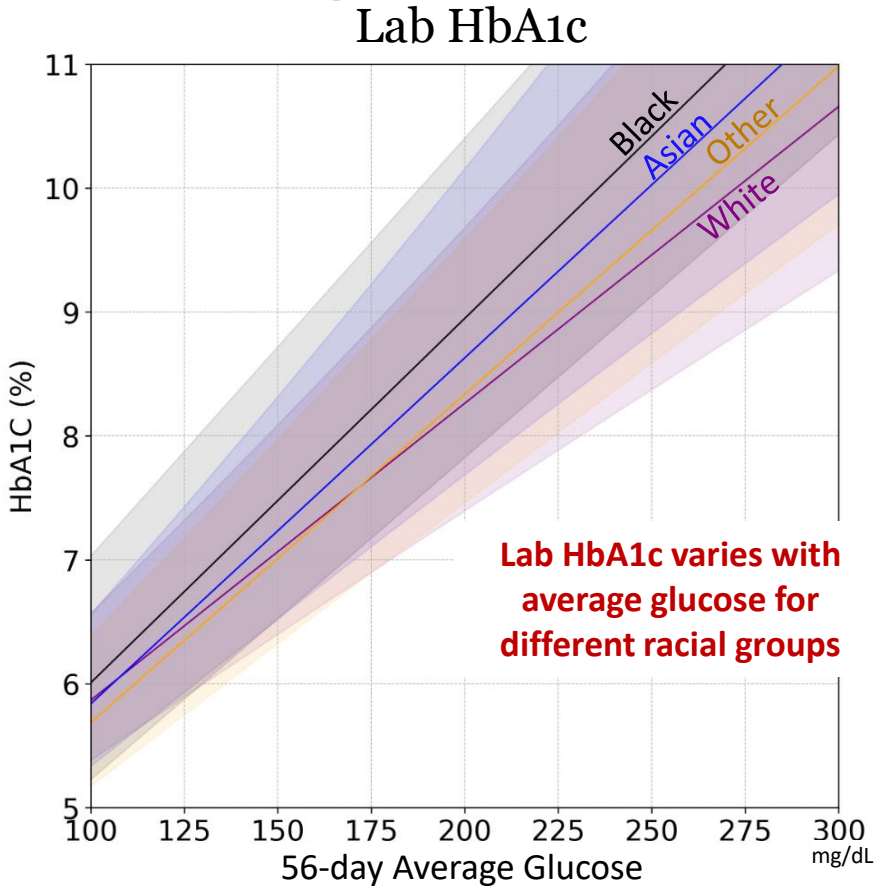
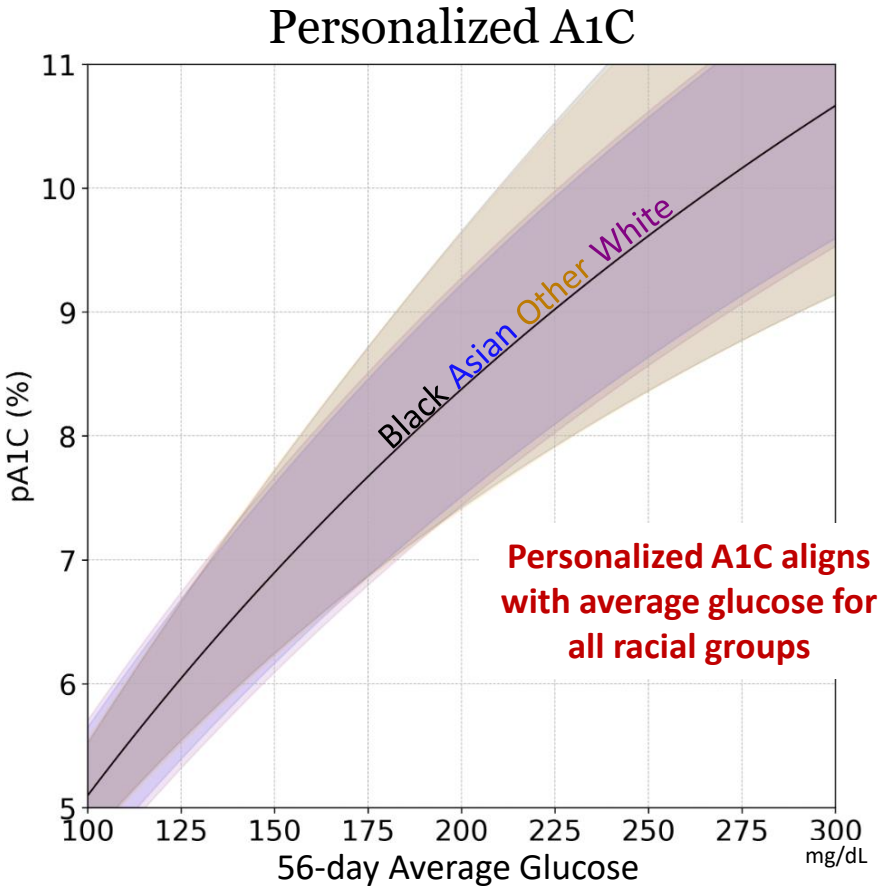
56-day Average Glucose
Personalized A1C aligns with average glucose for all racial groups

Results (3)


Lab HbA1c
HbA1C (%)
11
10
9
8
7
6
5
Black
Asian
Other
White
100
125
150
175
200
225
250
275
300
mg/dL
56-day Average Glucose
Lab HbA1c varies with average glucose for different racial groups


Personalized A1C
pA1C (%)
11
10
9
8
7
6
5
Black Asian Other White
100
125
150
175
200
225
250
275
300
mg/dL
56-day Average Glucose
Personalized A1C aligns with average glucose for all racial groups

Conclusions

- Clinically significant discordance between laboratory A1C and average glucose discordance is not uncommon, particularly in Black individuals.
- Personalized A1C is superior to laboratory HbA1c at reflecting individualized average glycemia across all racial groups, potentially improving clinical management in diabetes and reducing health disparities.
- Routine clinical use of Personalized A1C has the potential to improve glycemic management.