Personalized adjustment to improve the accuracy of HbA1c at reflecting hyperglycemic exposure in different racial groups: a prospective clinical study

Pratik Choudhary, Tim Dunn, Yongjin Xu, Ramzi Ajjan

Disclosures

PC has received personal fees from Abbott, Dexcom, Medtronic, Insulet, Vertex, Novo Nordisk, Sanofi, Lilly and Embecta

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Aims

- Evaluate and address the variability in A1C-Average Glucose conversion, especially in different racial groups
- Improve A1C accuracy at reflecting average glucose levels using personalized A1c (pA1c), by individual adjustment across different individuals and racial groups

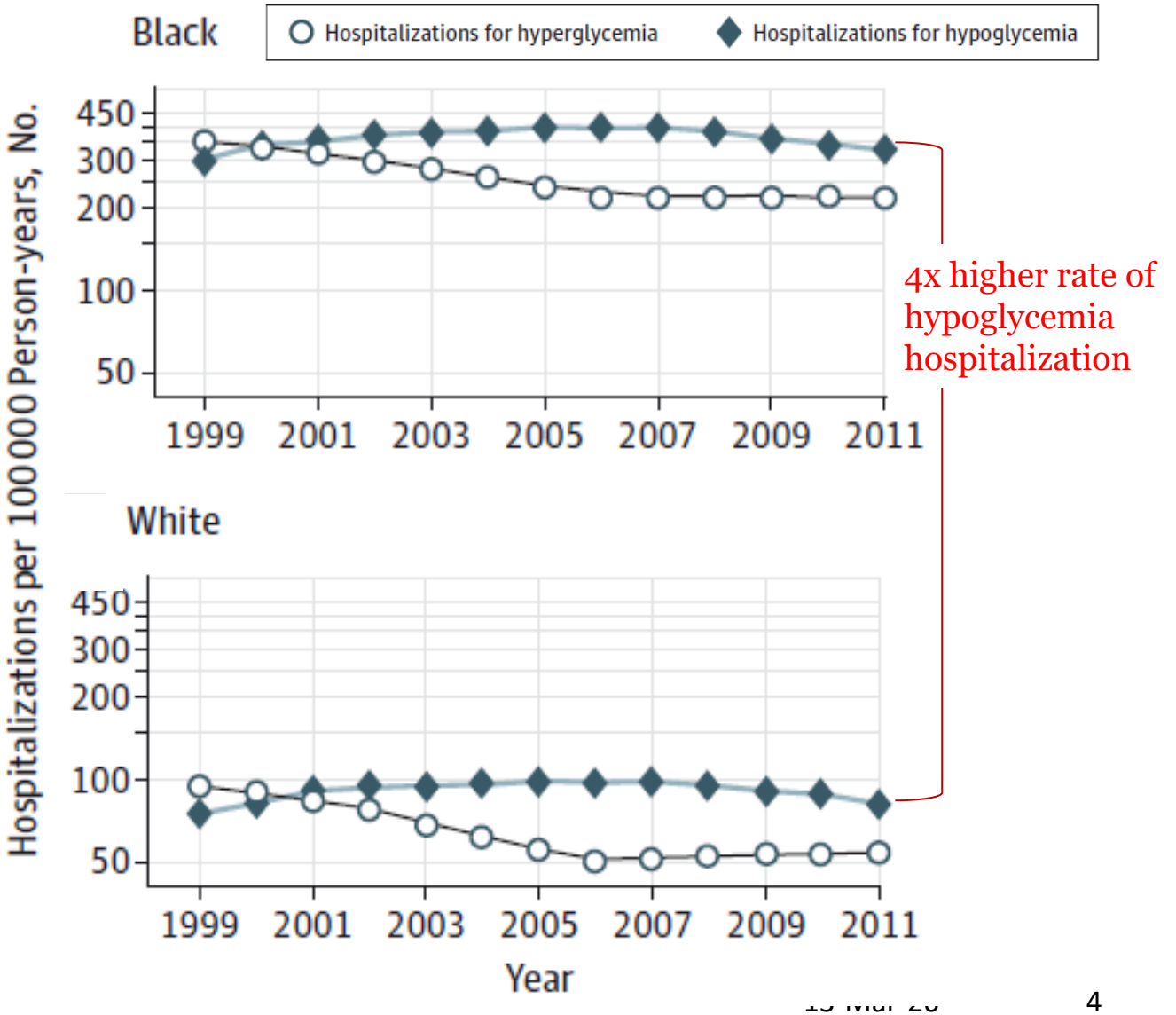
Table 6.1—Equivalent A1C levels and estimated average glucose (eAG)

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).

HbA1c and average glucose in different populations

- The 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, potentially associated with:
  - Risk of diabetes overdiagnosis[1]
  - Greater hypoglycemic hospitalizations[2], perhaps due to overtreatment of elevated laboratory A1C

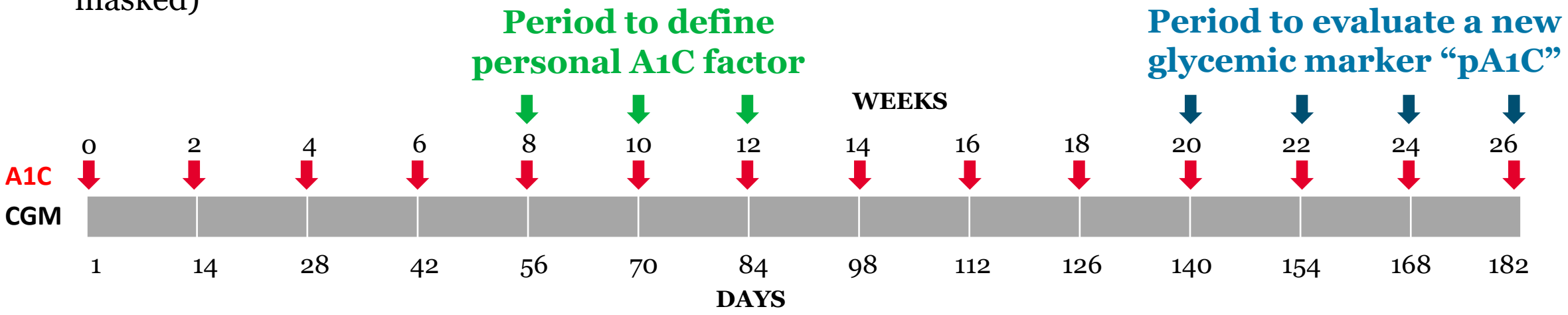


[1]Ram et al, BMJ Open Diabetes Res Care. 2024; 12(2):e003470
[2]Lipska et al. JAMA Intern Med. 2014; 174(7):1116-24.

GDAC Study[1]

[1]"Glucose-Derived A1C": NCT05189938

- 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)



Personalized A1c (pA1c)

Estimation of personal glycation ratio (PGR)

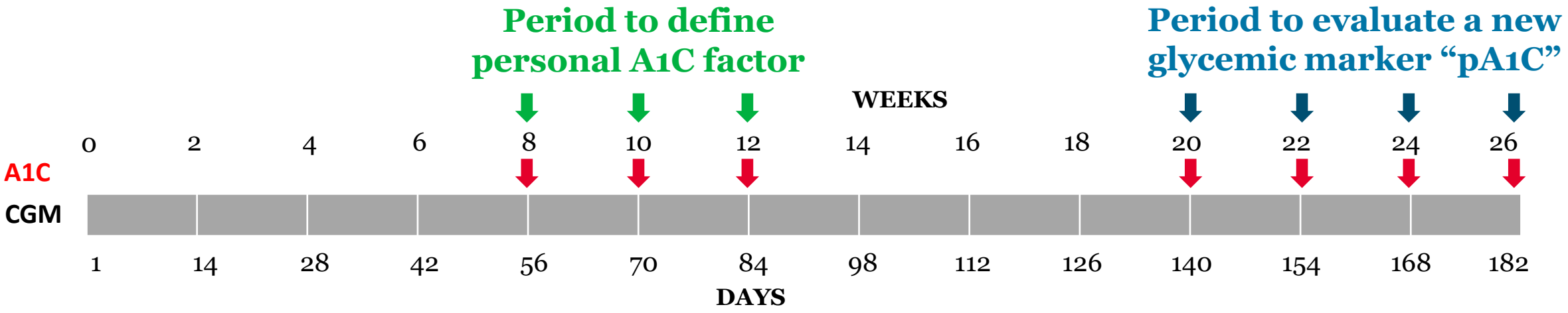
$$PGR = \left(AG^{-1} + K_M^{-1}\right) * \left(100 * A1C^{-1} - 1\right)^{-1} * 10^5$$

$$K_M = 473$$

Application of PGR

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

$$PGR_{ref} = 65.1$$



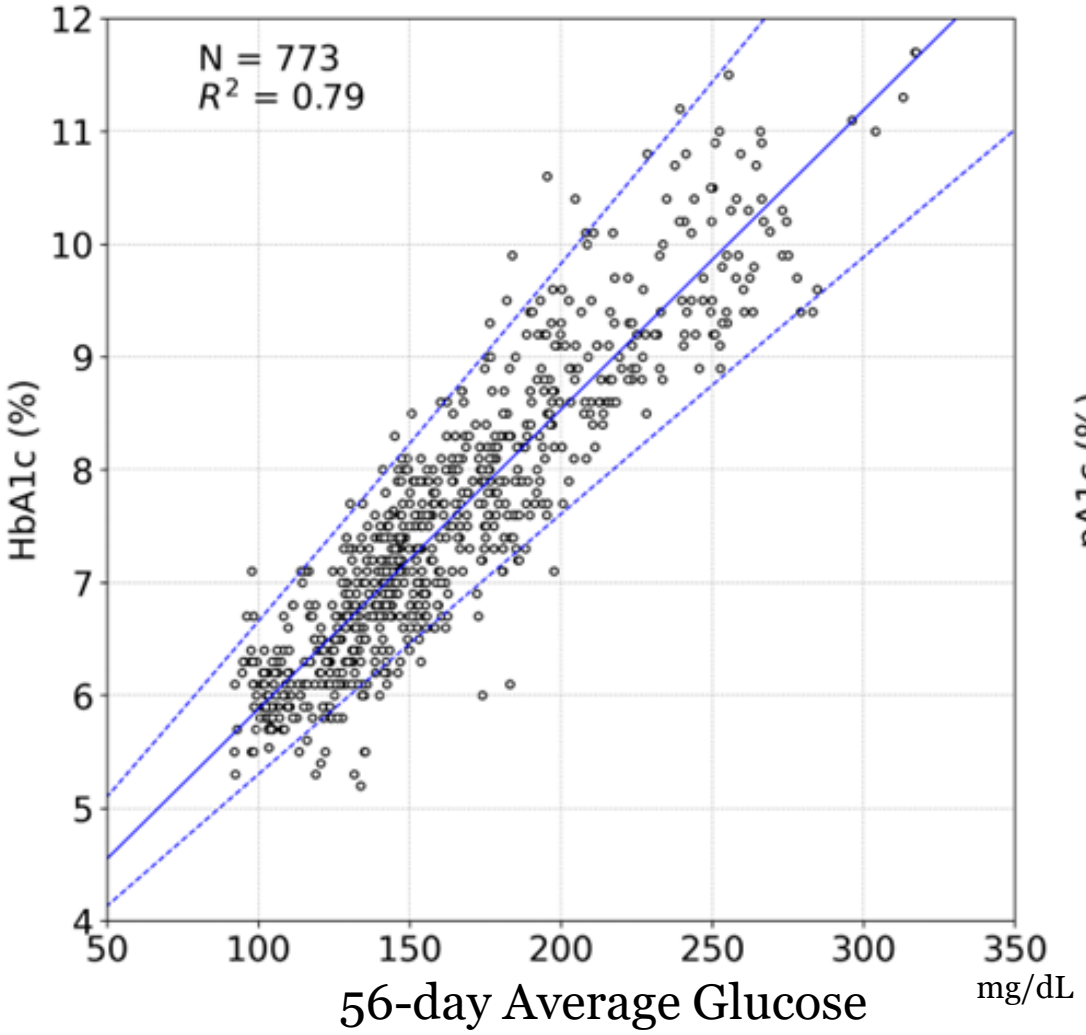
Results: Participant characteristics

	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)

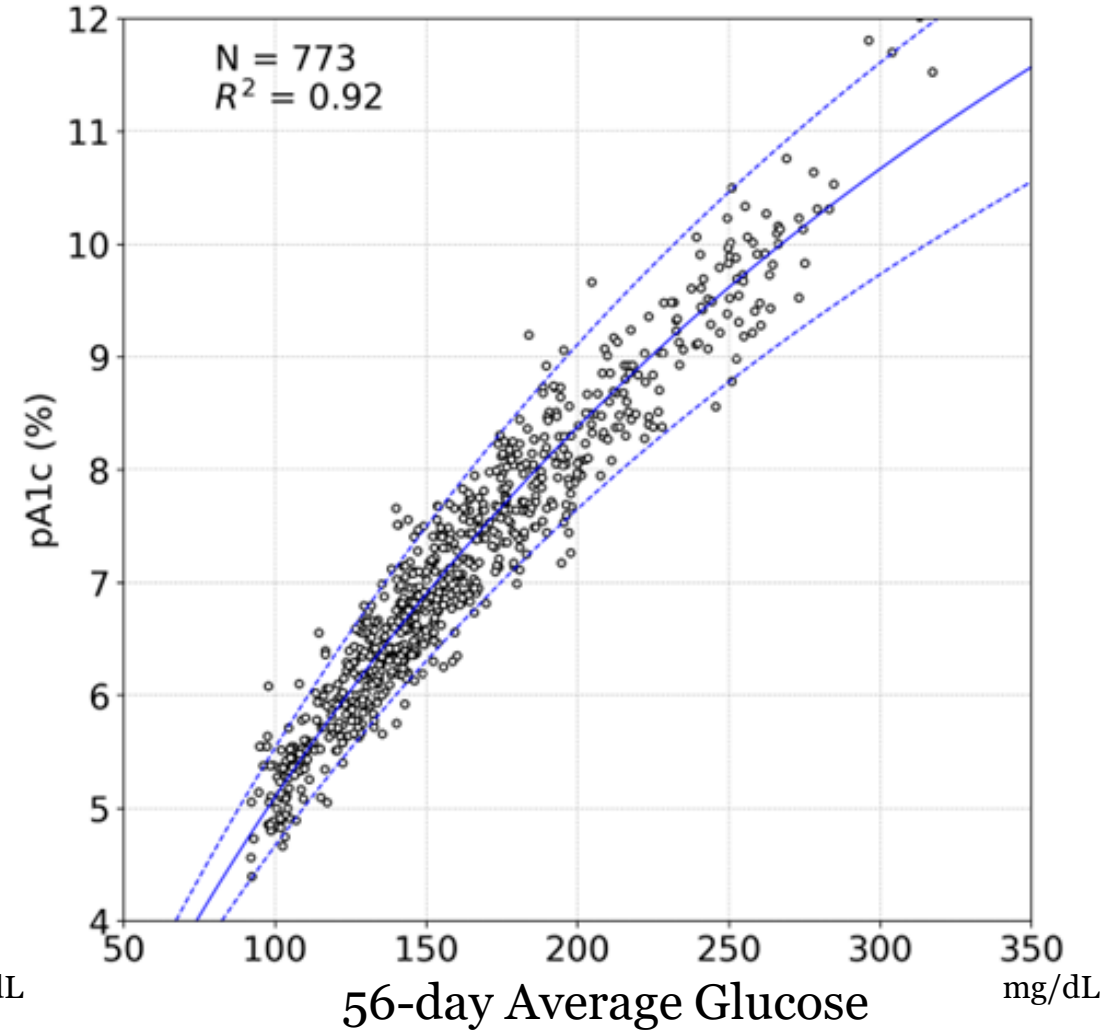
Data are presented as Mean (SD) unless otherwise indicated.

Results: better correlation between AG and pA1c

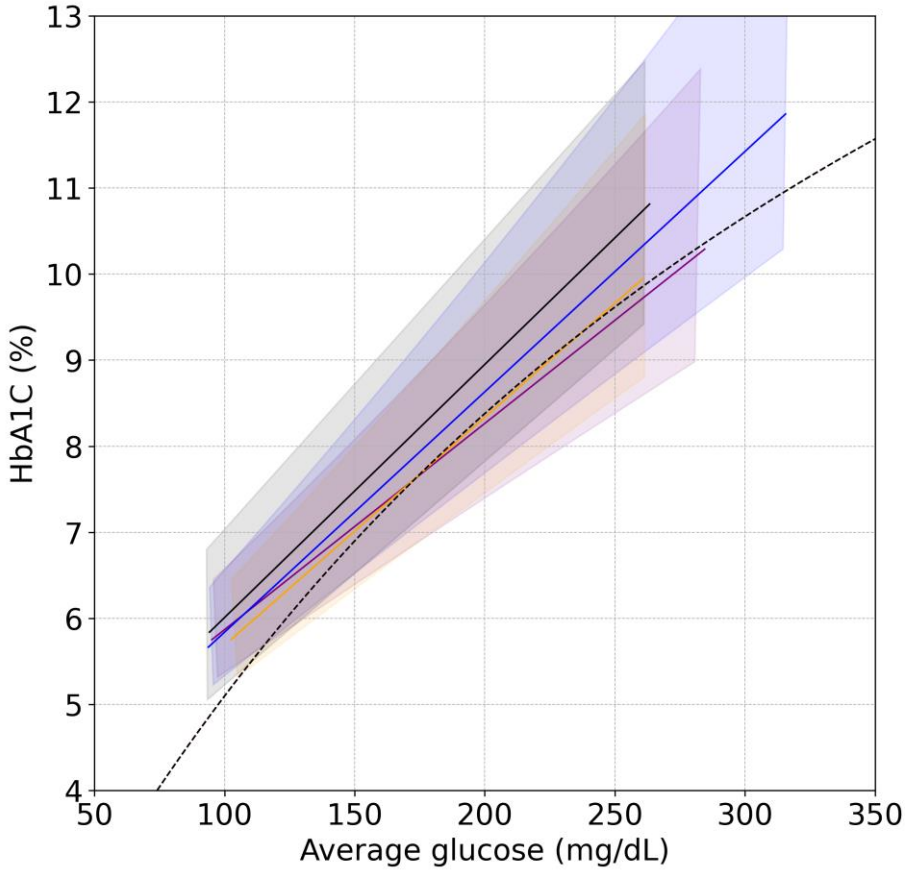
Lab A1c



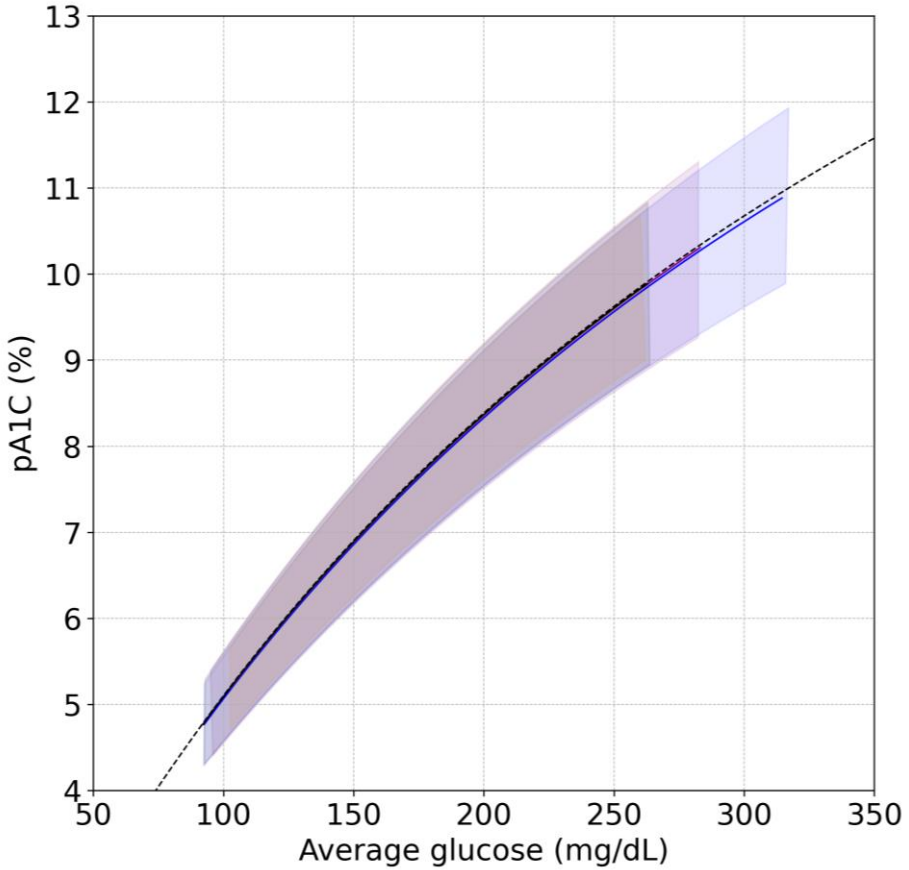
Personalized A1C



pA1c removes the racial differences between AG and HbA1c



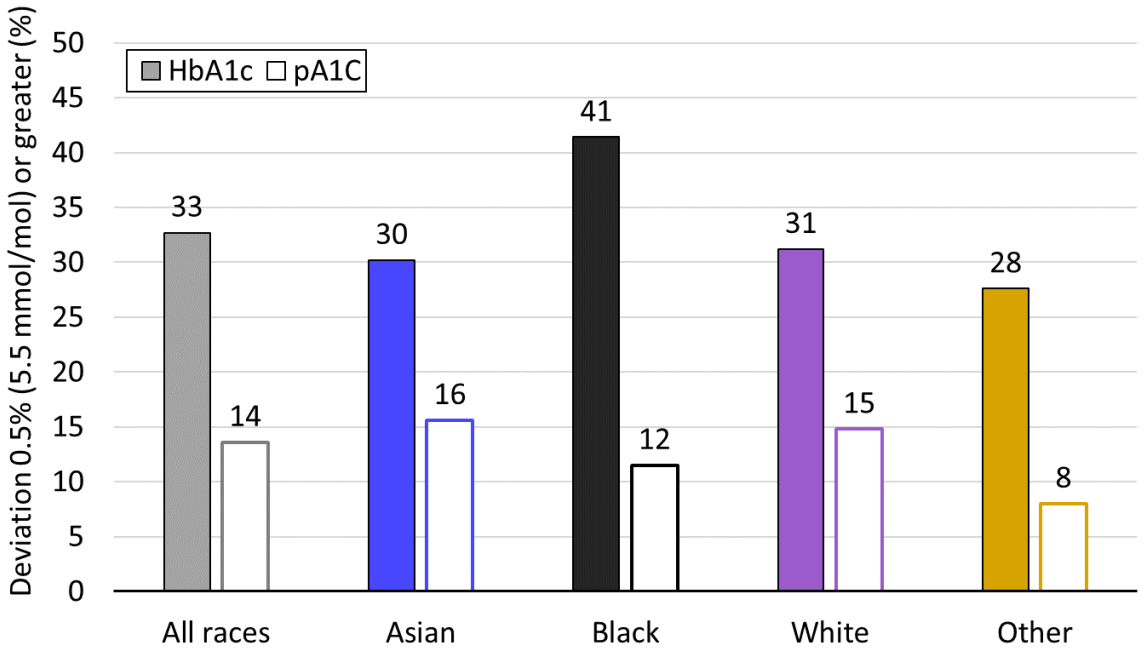
Black
Asian
Other
White



HbA1C	Average Glucose (mg/dL)			
%	Black	Asian	White	Other
5	66 (40-91)	70 (54-86)	64 (45-82)	74 (57-91)
6	100 (69-130)	106 (84-128)	105 (80-131)	112 (89-135)
7	134 (99-168)	142 (113-170)	147 (114-180)	150 (120-179)
8	168 (129-207)	177 (141-213)	189 (147-231)	187 (150-225)
9	202 (158-245)	213 (169-257)	231 (180-282)	225 (180-270)
10	236 (188-283)	249 (196-302)	272 (211-334)	263 (209-317)

pA1C	Average Glucose (mg/dL)			
%	Black	Asian	White	Other
5	98 (87-112)	98 (87-112)	98 (87-112)	98 (87-112)
6	124 (110-143)	124 (110-143)	124 (110-143)	124 (110-143)
7	154 (135-179)	154 (135-179)	154 (135-179)	154 (135-179)
8	187 (164-219)	187 (164-219)	187 (164-219)	187 (164-219)
9	225 (195-266)	225 (195-266)	225 (195-266)	225 (195-266)
10	269 (231-322)	269 (231-322)	269 (231-322)	269 (231-322)

pA1c provides clinically meaningful accuracy improvements



	All	Asian	Black	White	Other
N	773	262	174	250	87
HbA_{1c}	33%	30%	41%	31%	28%
pA1C	14%	16%	12%	15%	8%
Relative improvement	58%	48%	72%	53%	71%
HbA_{1c} 7.0% (53 mmol/mol) or less					
N	321	107	68	95	51
HbA_{1c}	25%	17%	24%	34%	29%
pA1C	9%	10%	10%	11%	2%
Relative improvement	64%	39%	56%	69%	93%
HbA_{1c} greater than 7.0% (53 mmol/mol)					
N	452	155	106	155	36
HbA_{1c}	38%	39%	53%	30%	25%
pA1C	17%	19%	12%	17%	17%
Relative improvement	56%	51%	77%	41%	33%

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.