Blood glucose derived GMI and HbA1c have similar associations with retinopathy progression: further analysis of the Diabetes Control and Complications Trial (DCCT)

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DISCLOSURES

- Research: Dexcom, Mannkind
- Consulting: Abbott Diabetes Care, embecta, Lifescan, Hagar
- Funding for the development of this research was provided by Abbott Diabetes Care.

BACKGROUND AND AIMS

- The Diabetes Control and Complications Trial (DCCT) established the clinical utility of HbA1c for diabetes management.
- In addition to HbA1c, the DCCT also captured a 7-point capillary blood glucose profile one day per quarter.

- Our aim was to compare the association of HbA1c and blood glucose derived glucose management indicator (GMI-BG) sensitivity/specificity at predicting retinopathy progression in the DCCT.

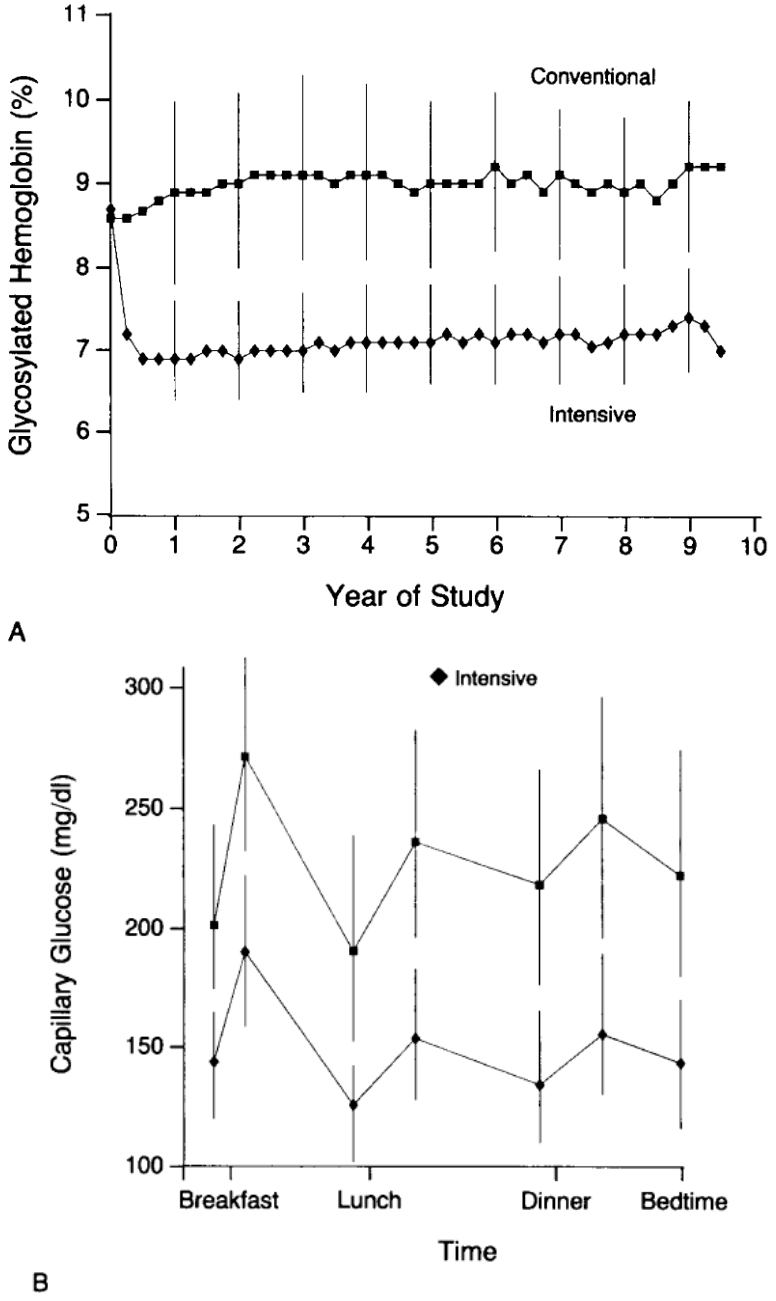

Figure 1. Measurements of Glycosylated Hemoglobin and Blood Glucose in Patients with IDDM Receiving Intensive or Conventional Therapy.

DCCT Research Group; Nathan DM, Genuth S, Lachin J, et al. *N Engl J Med* 1993;329:977–986

METHODS

Ethical Oversight and Data Access

- Received determination of exemption from IRB oversight for the research project
- Executed data transfer agreement for access with National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) repository

METHODS

Data Analysis

- Calculated mean capillary blood glucose for each participant for each 3-month period of study converted to “GMI-BG” using established GMI equation[1]
- The average GMI-BG and HbA1c were calculated separately for each participant before the occurrence of any retinopathy progression
- Retinopathy progression indicated by at least **3 steps** on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale sustained for at least 6 months
- Receiver Operating Characteristic (ROC) curve for sustained retinopathy progression evaluated for HbA1c and GMI-BG
- Evaluation of the accuracy (combined true positive and true negative rates) of the two glycaemic markers at predicting eye complications at all levels of GMI-BG and HbA1c as well as at the routine clinical targets of 6.5% and 7.0% (48 and 53 mmol/mol)

[1]Bergenstal RM, Beck RW, Close KL, et al. *Diabetes Care*. 2018 Nov;41(11):2275-2280.

BASELINE CHARACTERISTICS

	Primary Prevention (no retinopathy at baseline)		**Secondary Intervention** (mild retinopathy at baseline)	
	Conventional Therapy (N = 378)	Intensive Therapy (N = 348)	Conventional Therapy (N = 352)	Intensive Therapy (N = 363)
Age (yr)	26±8	27±7	27±7	27±7
Adolescents, 13-18 yr (%)	19	16	9	10
Male sex (%)	54	49	54	53
White race (%)	96	96	97	97
Duration of type 1 DM (yr)	2.6±1.4	2.6±1.4	8.6±3.7	8.9±3.8
Insulin dose (U/kg of body weight/day)	0.62±0.26	0.62±0.25	0.71±0.24	0.72±0.23
Glycated hemoglobin (%)	8.8±1.7	8.8±1.6	8.9±1.5	9.0±1.5
Mean blood glucose (mg/dl)	229±80	234±86	232±78	234±81
Blood pressure (mmHg)				
Systolic	114±12	112±11	116±12	114±12
Diastolic	72±9	72±9	73±9	73±9
Body weight (% of ideal)	103±14	103±13	105±13	104±12
Current smokers (%)	17	19	19	18

BASELINE CHARACTERISTICS

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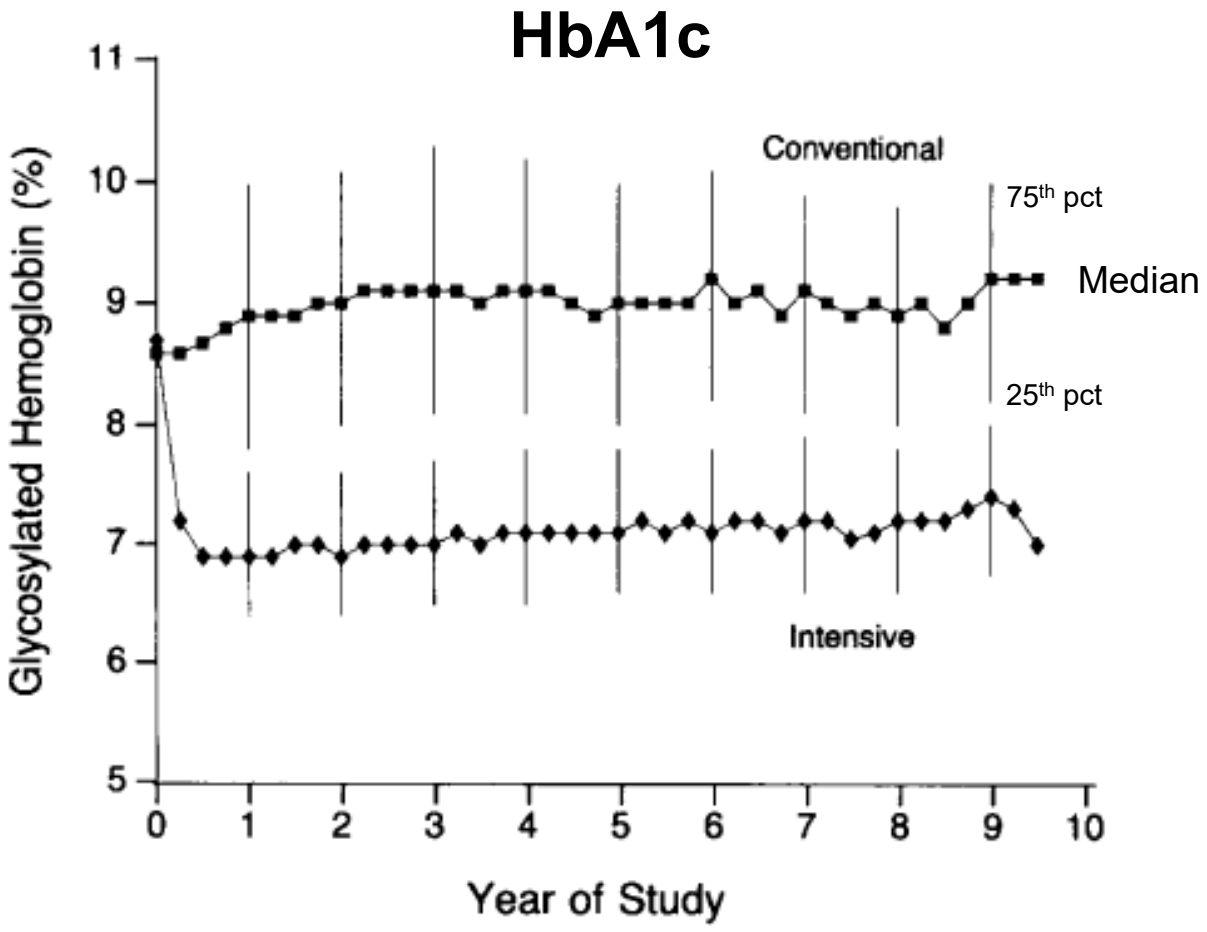
	Conventional Therapy (N = 378)	Intensive Therapy (N = 348)	Conventional Therapy (N = 352)	Intensive Therapy (N = 363)
Serum cholesterol (mg/dl)	173±35	176±33	179±32	178±33
Serum triglycerides (mg/dl)	77±57	75±41	87±44	87±45
Serum HDL cholesterol (mg/dl)	51±13	52±13	49±11	49±12
Serum LDL cholesterol (mg/dl)	106±30	109±29	112±28	112±29
Absence of retinopathy (%)	100	100	0	0
Microaneurysms only (%)	0	0	58	67
Non-proliferative diabetic retinopathy (%)				
Mild	0	0	23	18
Moderate	0	0	19	15
Urinary albumin excretion (mg/24 hr)	12±8	12±9	19±24	21±25
Creatinine clearance (ml/min)	127±28	128±30	130±30	128±31
Clinical neuropathy (%)	2.1	4.9	9.4	9.4

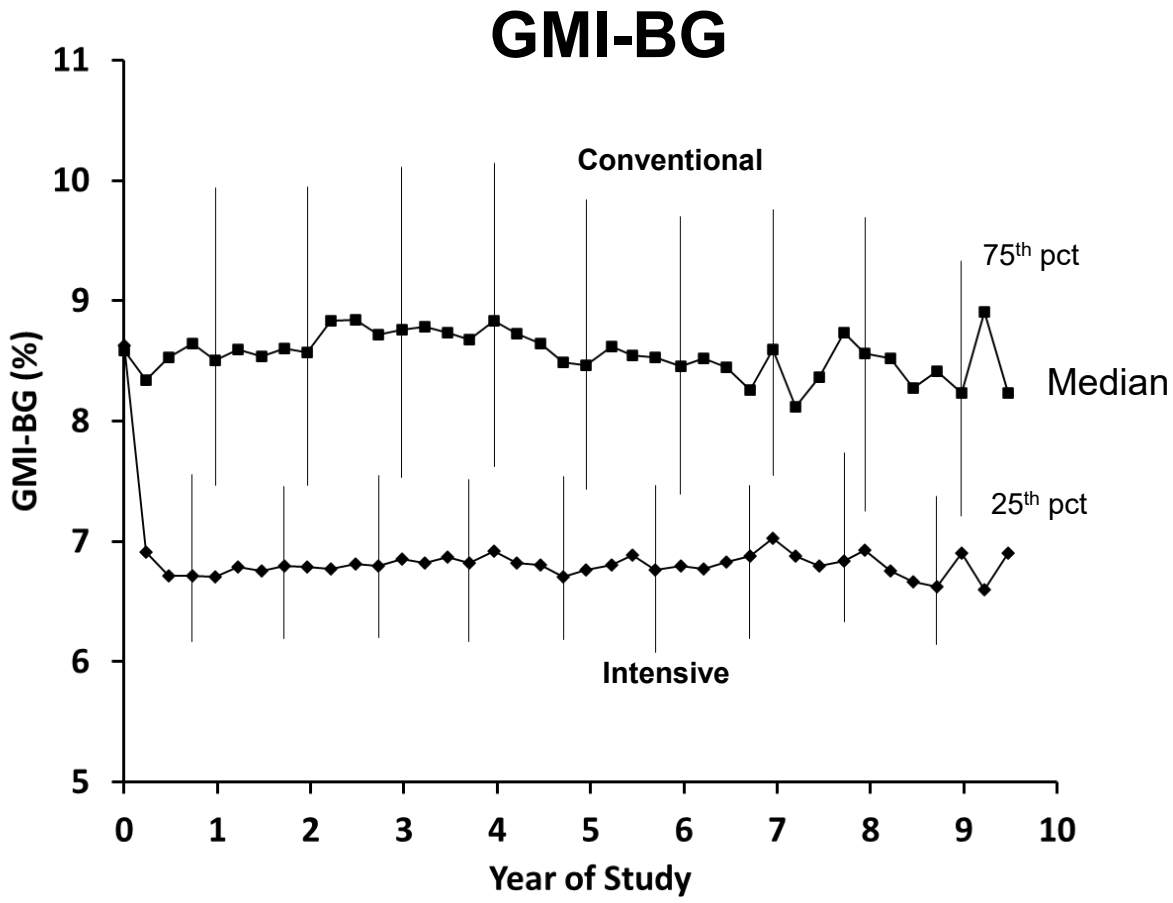
RESULTS

- 24,656 HbA1c and GMI-BG pairs available for analysis

  (n=1440 participants, typically every 3 months, therefore mean follow up of 4.3 years)

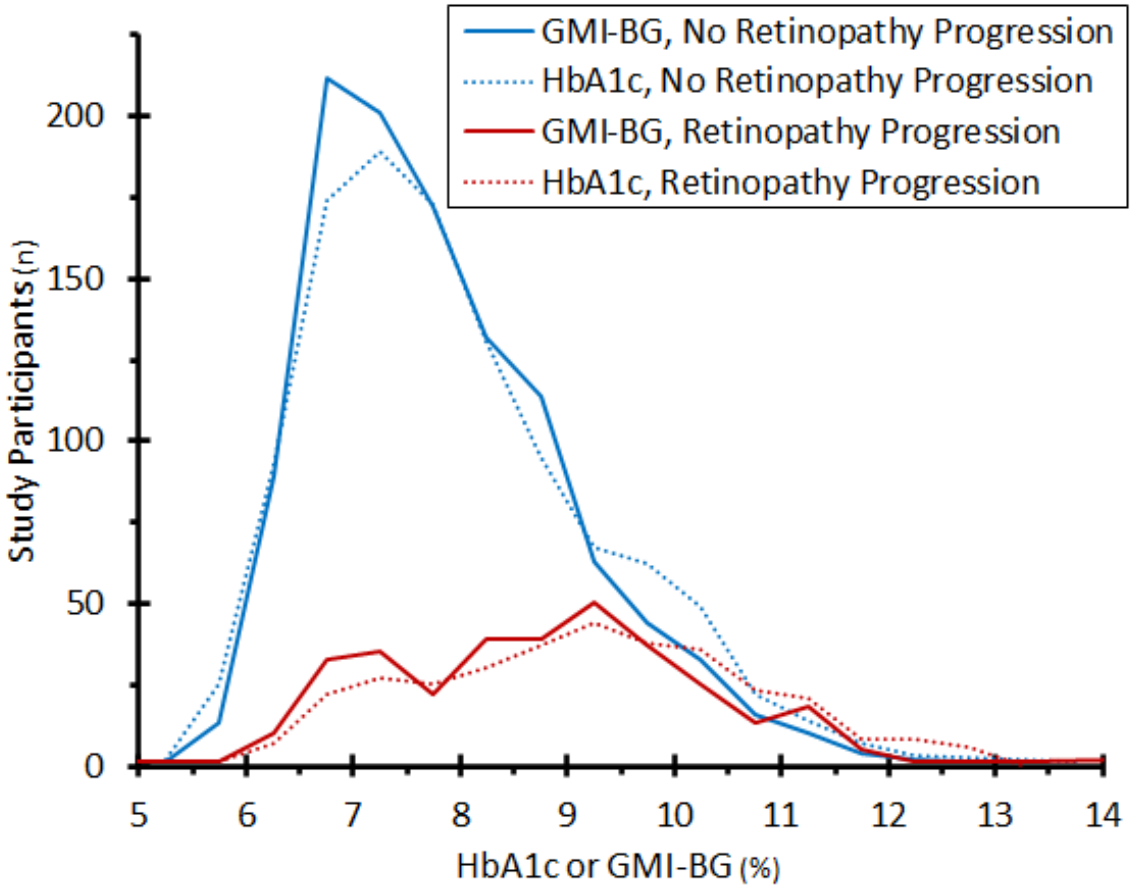
- 333 participants had progression of retinopathy indicated during the trial





RESULTS

- HbA1c and GMI-BG had ***highly similar distributions*** for associations with the sustained progression of retinopathy

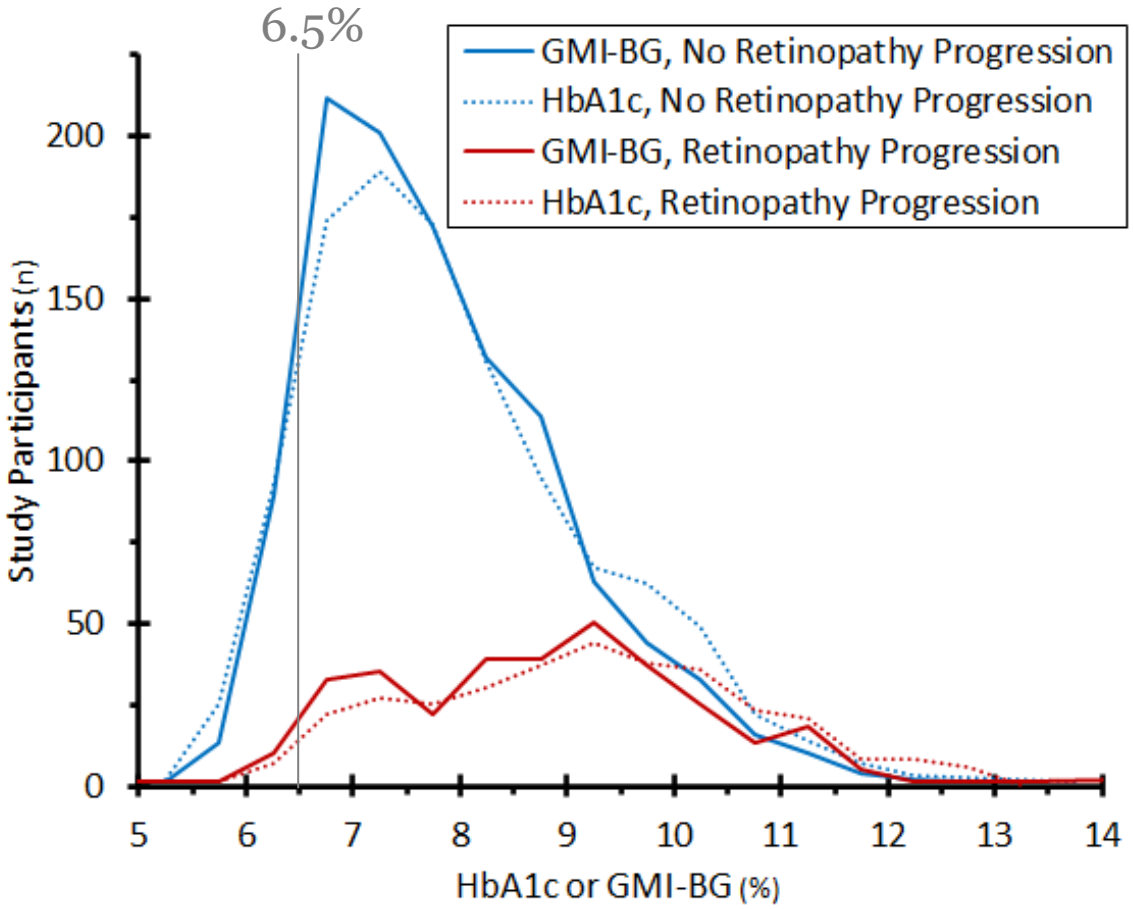


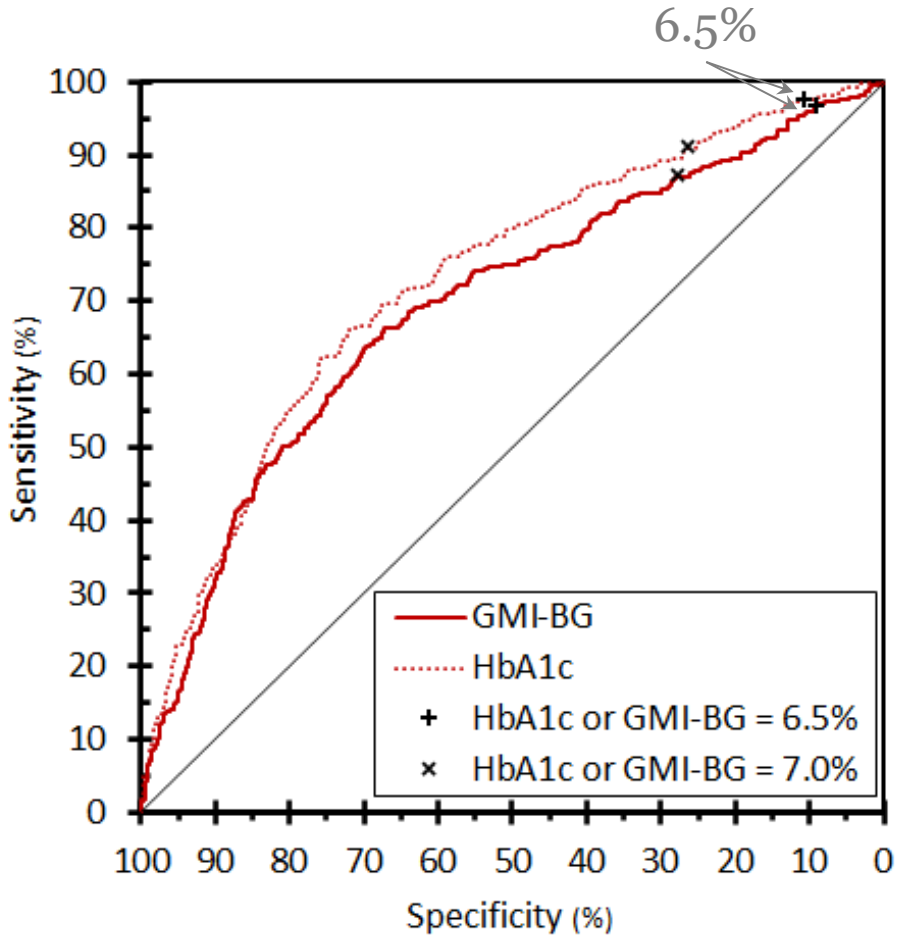
RESULTS

- HbA1c and GMI-BG had statistically indistinguishable accuracy for presence or absence of sustained progress of retinopathy

At 6.5%:

	Sensitivity	Specificity	Accuracy
HbA1c	97.5%	10.8%	30.9%
GMI-BG	96.7%	9.1%	29.3%



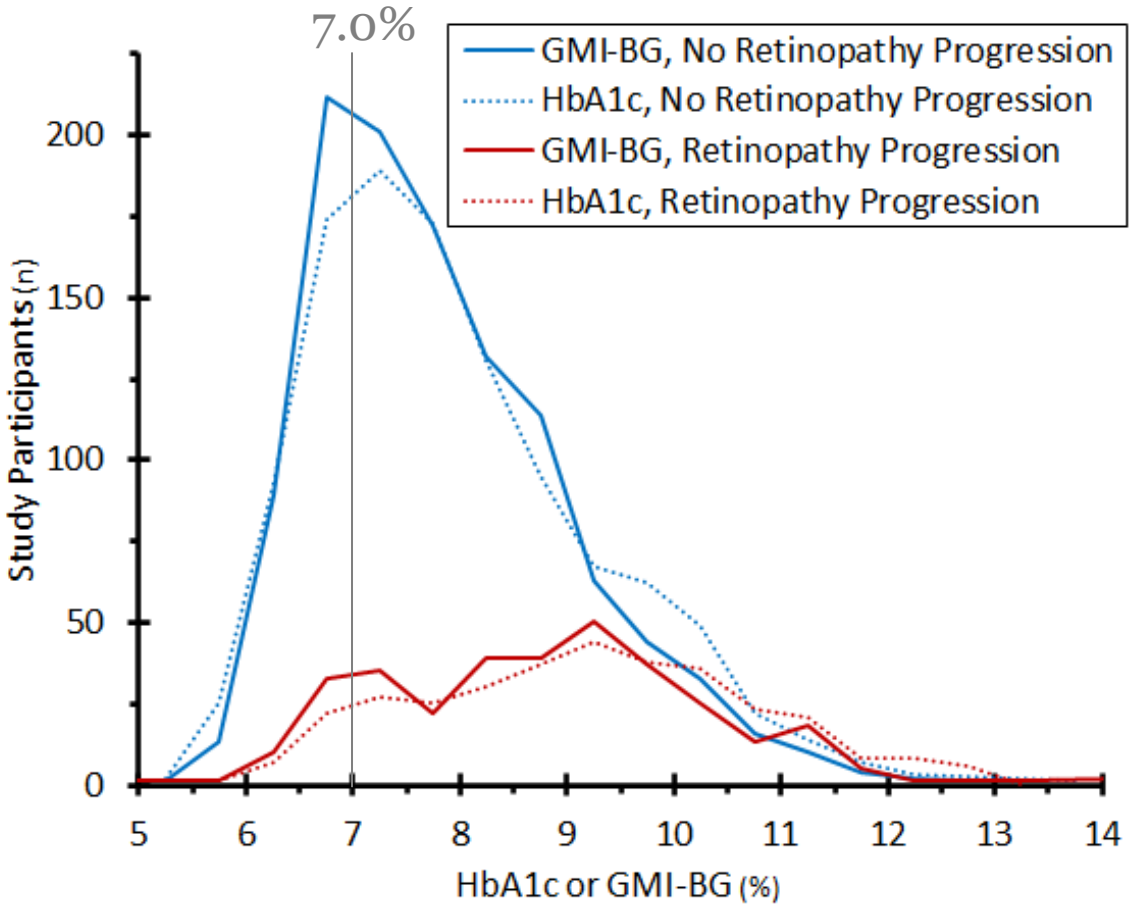


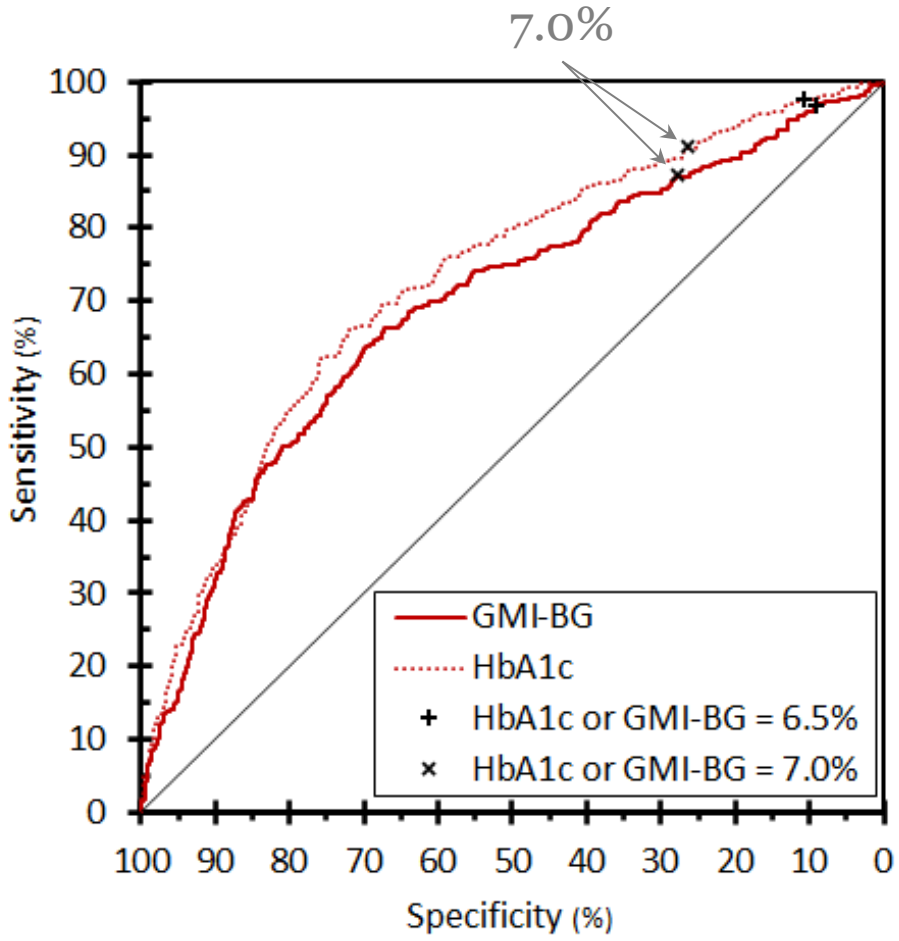
RESULTS

- HbA1c and GMI-BG had statistically indistinguishable accuracy for presence or absence of sustained progress of retinopathy

At 7.0%:

	Sensitivity	Specificity	Accuracy
HbA1c	91.0%	26.5%	42%
GMI-BG	87.1%	27.8%	42%





LIMITATIONS

- Limited, sparse blood glucose may result in more variable GMI-BG compared to GMI using CGM
- Less frequent BG testing in real world settings (2-4/day) also limits available glucose data and may not provide similar results
- Highly homogeneous study group (T1DM, >95% White, <30 years old at baseline) supports future research in more diverse groups

CONCLUSIONS

- High similarity between HbA1c and GMI-BG in the DCCT for indication of sustained progression of retinopathy, despite the intermittent but structured 7-point BG measurement
- Low specificity of HbA1c and GMI-BG at predicting retinopathy complications calls for future work to identify a more accurate glycemic marker that improves the balance between sensitivity and specificity