An MMD and FDA compliant, intelligent self-care platform

Continuous Estimation of Glycosylated Hemoglobin (HbA1c) based on Self-monitoring Blood Glucose (SMBG) data and Laboratory HbA1c Measurements

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Agenda

- Introduction to established biomarker, HbA1c
- Objectives
- Materials and Methods
- Results
- Discussion & Conclusions

Introduction

- Glycosylated hemoglobin (HbA1c, A1C, ‘long-term sugar level’) is **the biomarker of glycemic control**
- Diabetes related risks are heavily linked to the glycosylation of proteins in all parts of the body

DCCT (1983-1992) findings:
Intensive blood glucose control reduces risk of

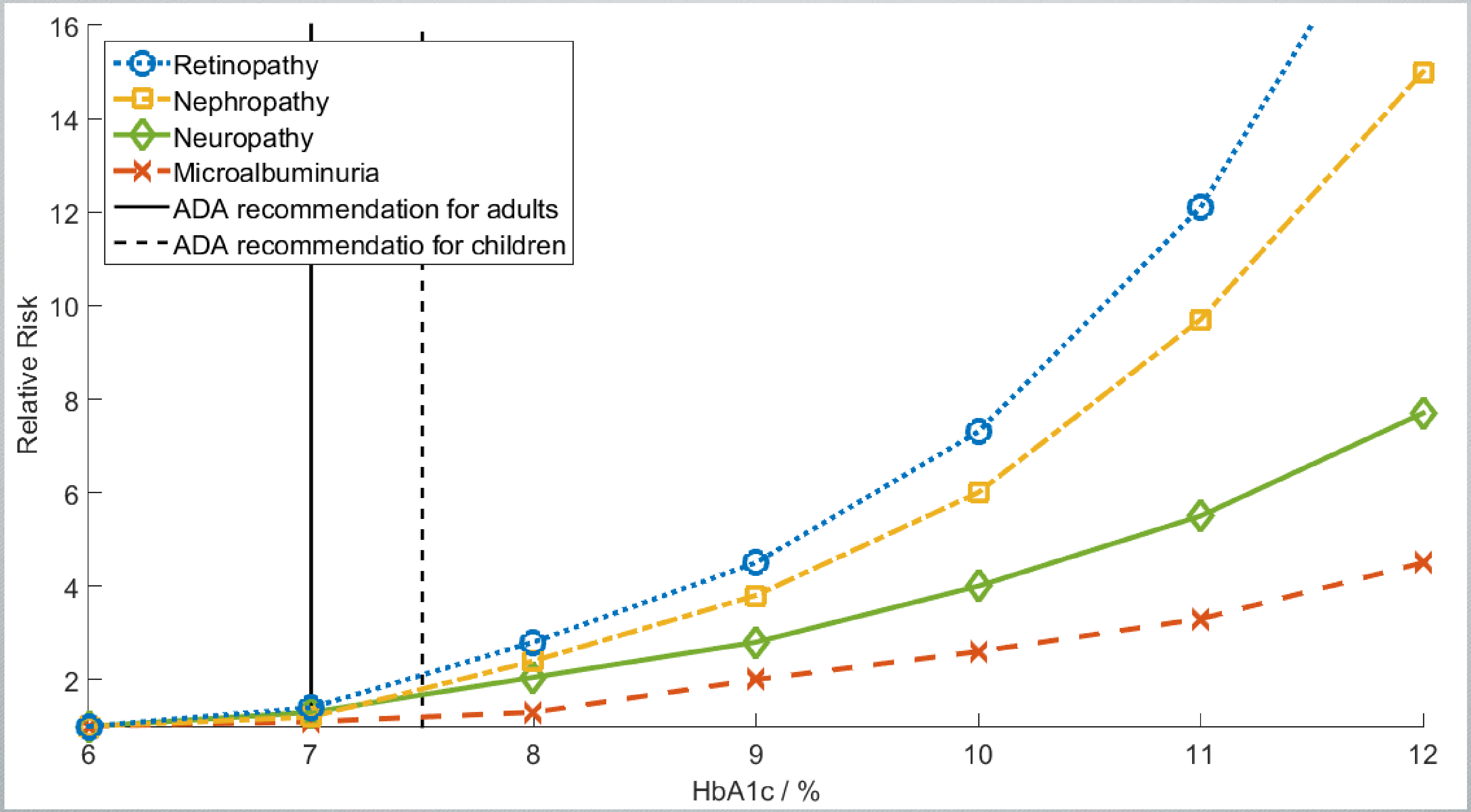
- eye disease by **76%**
- nerve disease by **60%**
- kidney diseas by **50%**

EDIC findings (1993-2005):
Intensive blood glucose control reduces risk of

- any cardiovascular disease by **42%**
- nonfatal heart attack, stroke, or death from cardiovascular causes by **57%**

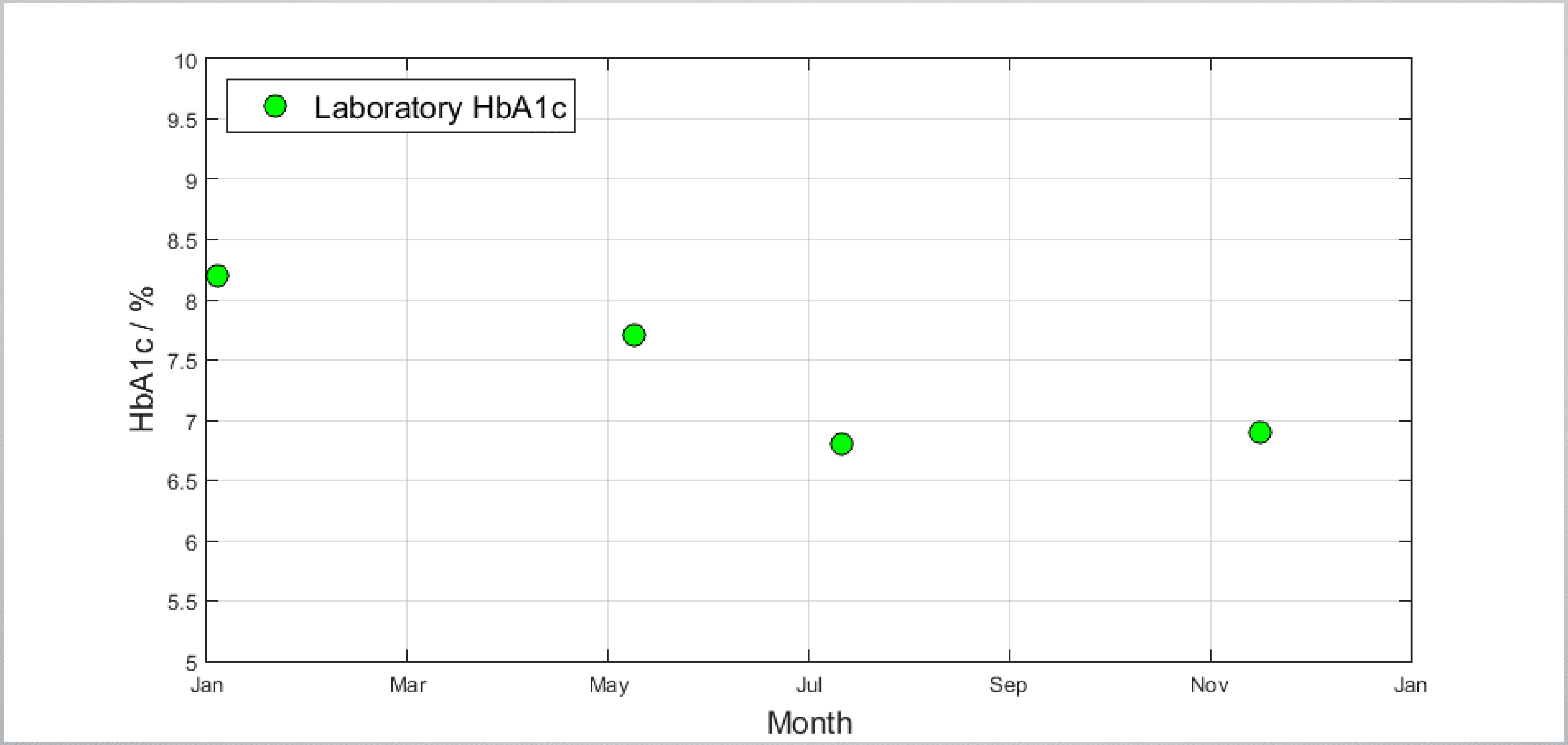
National Institutes of Health; 2008; 08-3874

Relative Risk of Complications versus HbA1c: DCCT

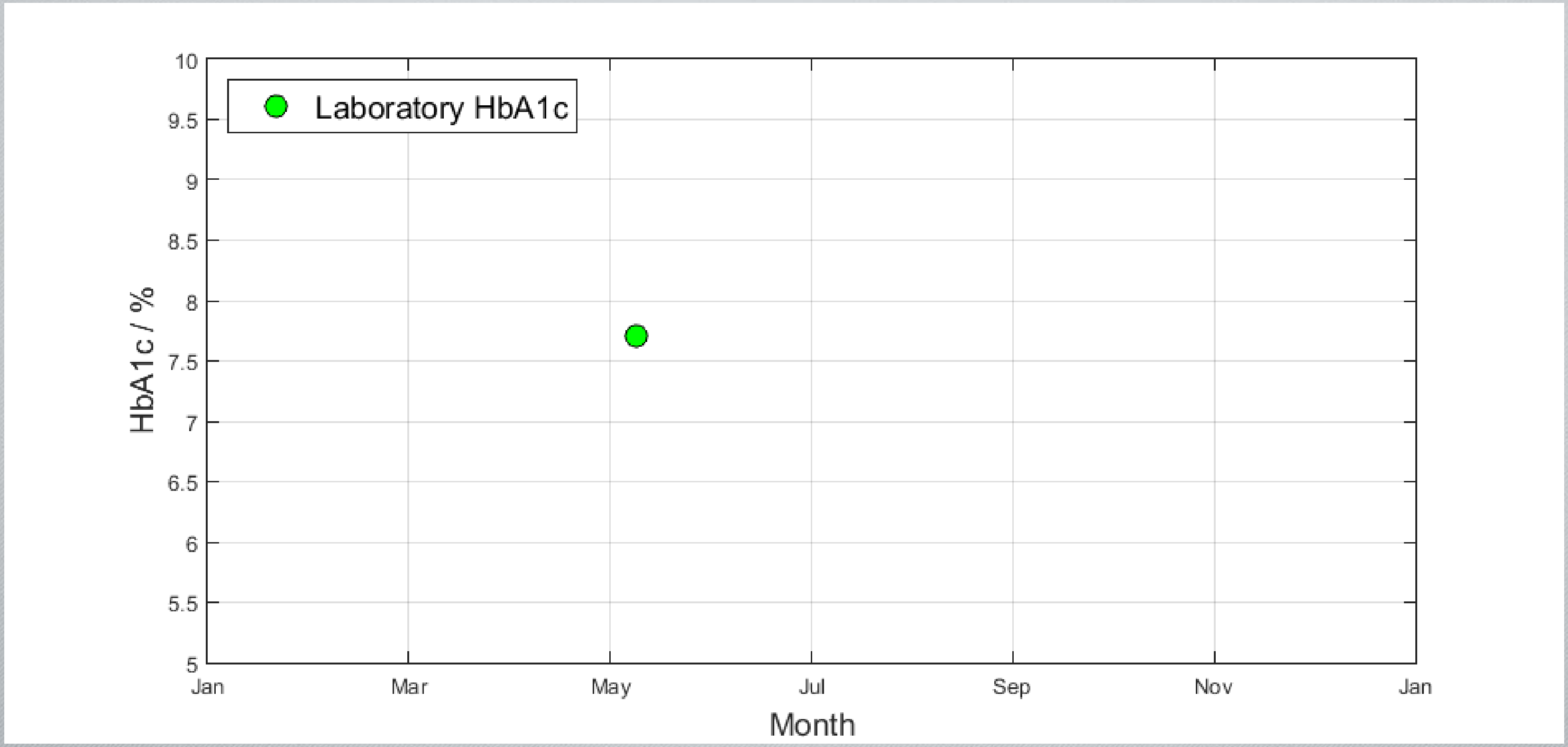


Skyler, J.; 1996; *Endocrinol Metab Clin North Am.*; 25; 243-254

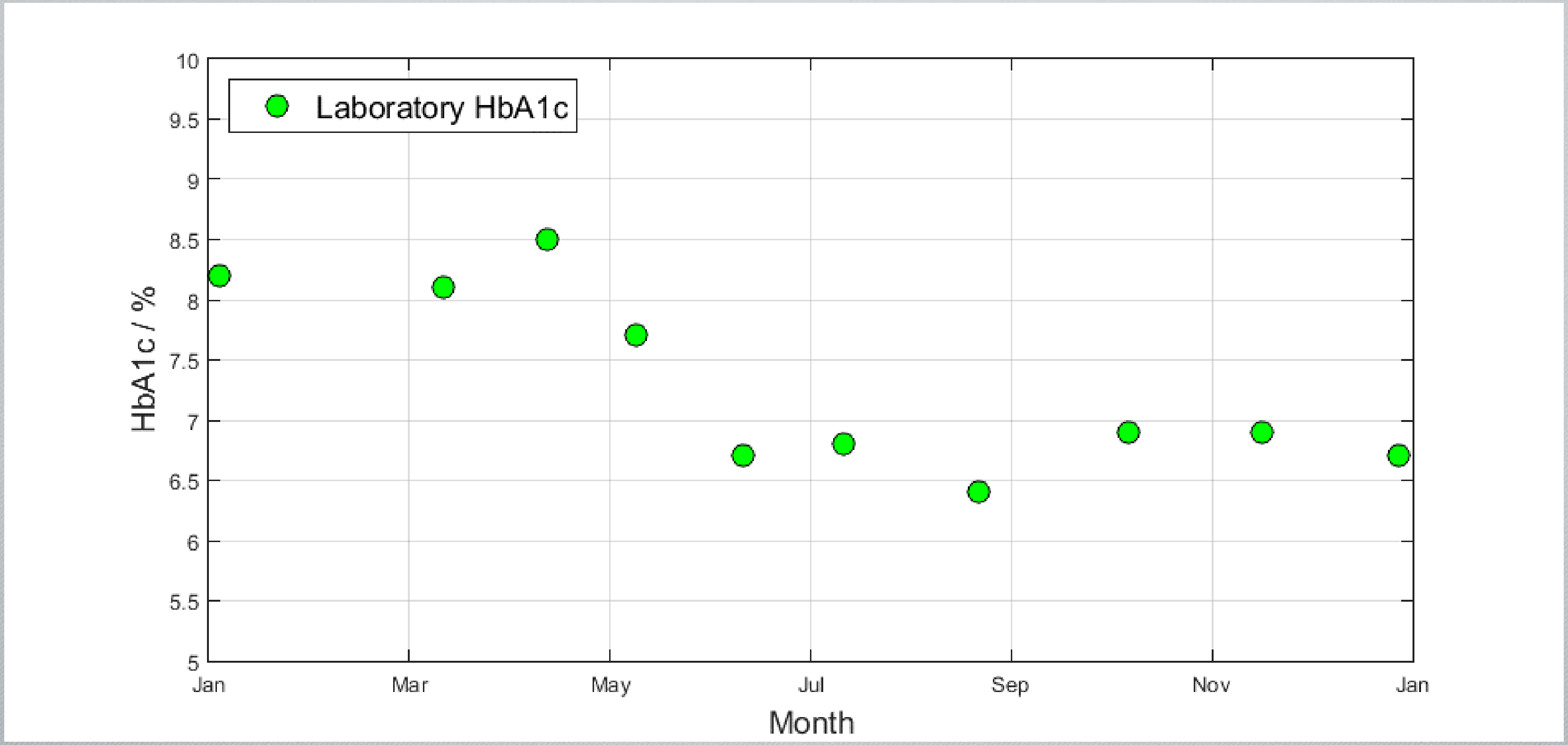
Life time of erythrocytes is about 120 days →HbA1c measured four times in a year?



Common case in Finnish health care: HbA1c measured only once a year!



Reseach case:
HbA1c measured about once a month



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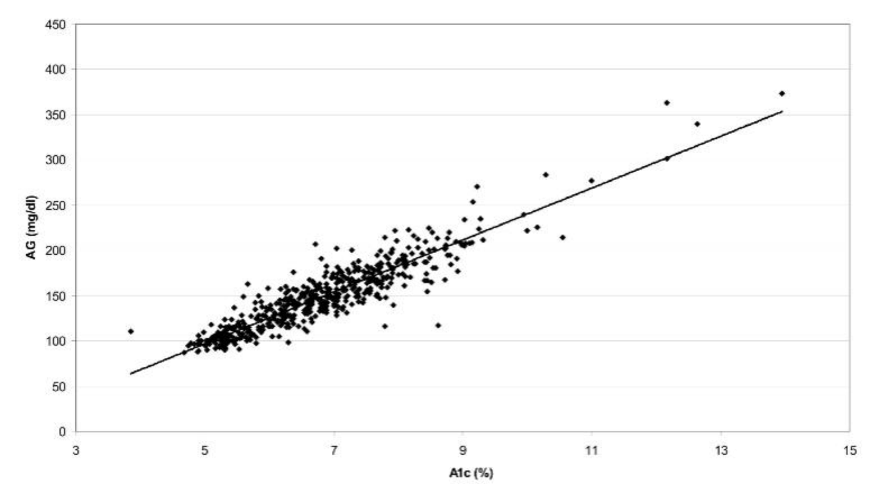
A1c-Derived Average Glucose (ADAG) study 2006-2008

- Multicentered study included 507 subjects with Type 1 and Type 2 diabetes
- Design to determine the mathematical relationship between HbA1c and average blood glucose (AG)
- Subjects had 2 days of continuous glucose monitoring performed four times during the study period and seven-point self-monitoring of capillary glucose performed at least 3 days per week

- Linear regression for estimated HbA1c (eA1c):

eA1c(%) = 0.63*AG(mmol/L)+1.63



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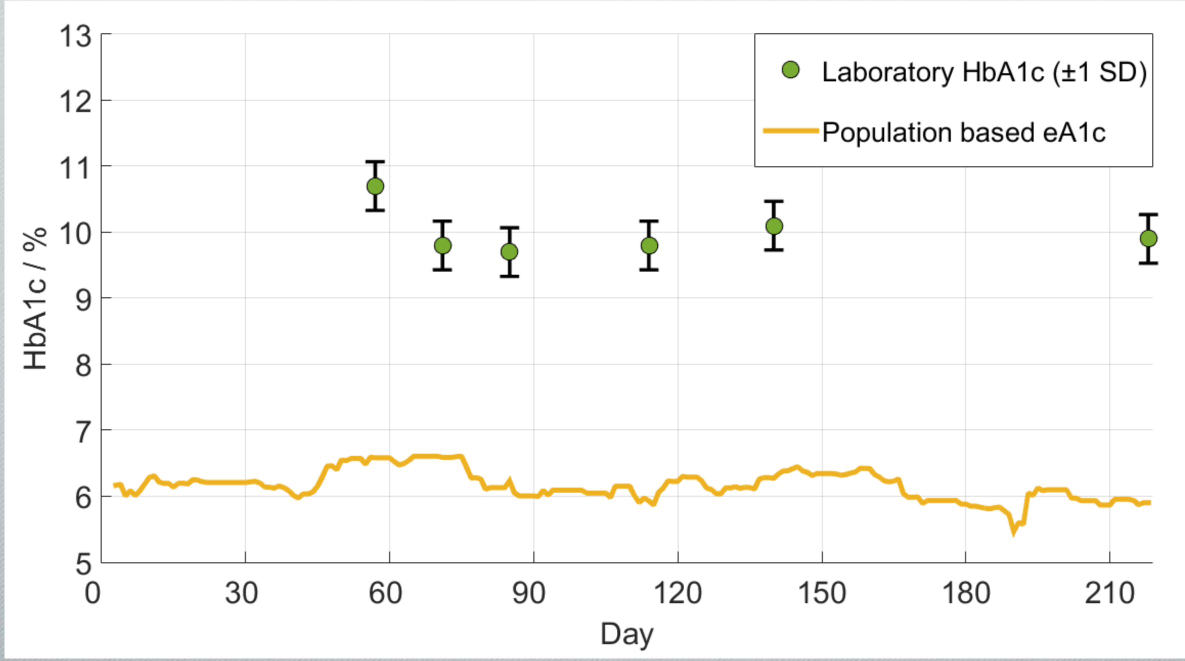
Nathan, DM. et al; 2008; *Diabetes Care;* Aug.; 31:8; 1473-1478

Example from our study

- HbA1c laboratory measurements do not match with average of self-monitored blood glucose (SMBG) values
- Blood glucose measurement habits are biased

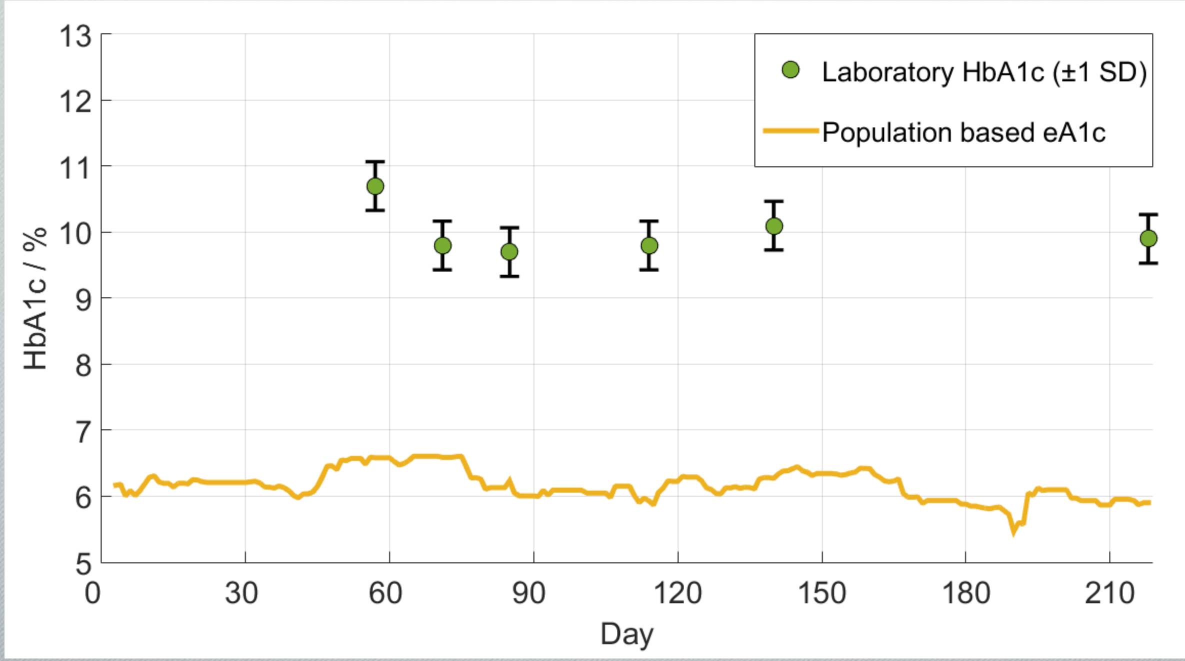


Objectives

- Define individually adaptive Continuous A1c

→ Fills unmonitored gaps

→ Guide in day-to-day diabetes management



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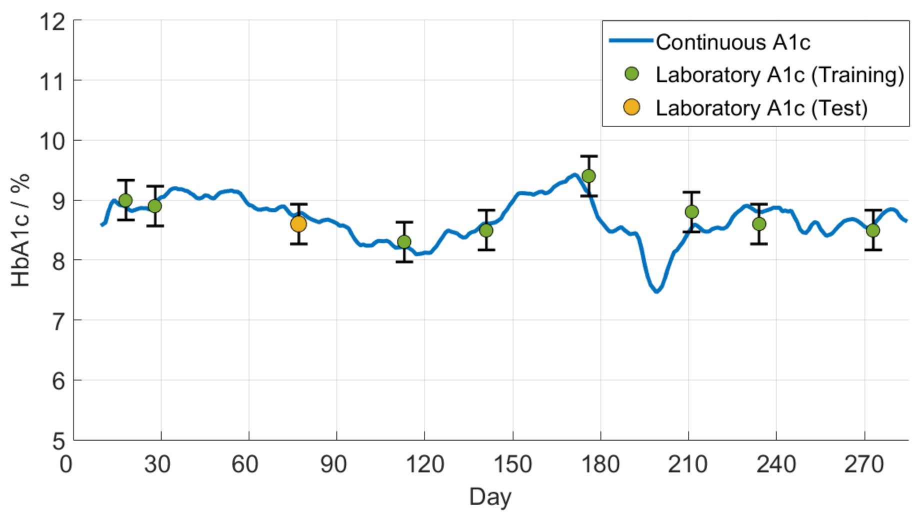
Materials and Methods

- 30 diabetics during 1 year period
- Individual’s had their normal blood glucose measurement habits
  →No predifened measurement schedule
- In average subjects reported
  - 2.51 SMBG values per day
  - 4.17 Laboratory HbA1c measurements per year
- HbA1c change:
  - 2.50 %-units/month
  +0.95 %-units/month
- Estimation algorithm utilizes a linear compination of multible statistical parameters such as mean, skewness, etc. in addition to laboratory HbA1c measurements

Materials and Methods

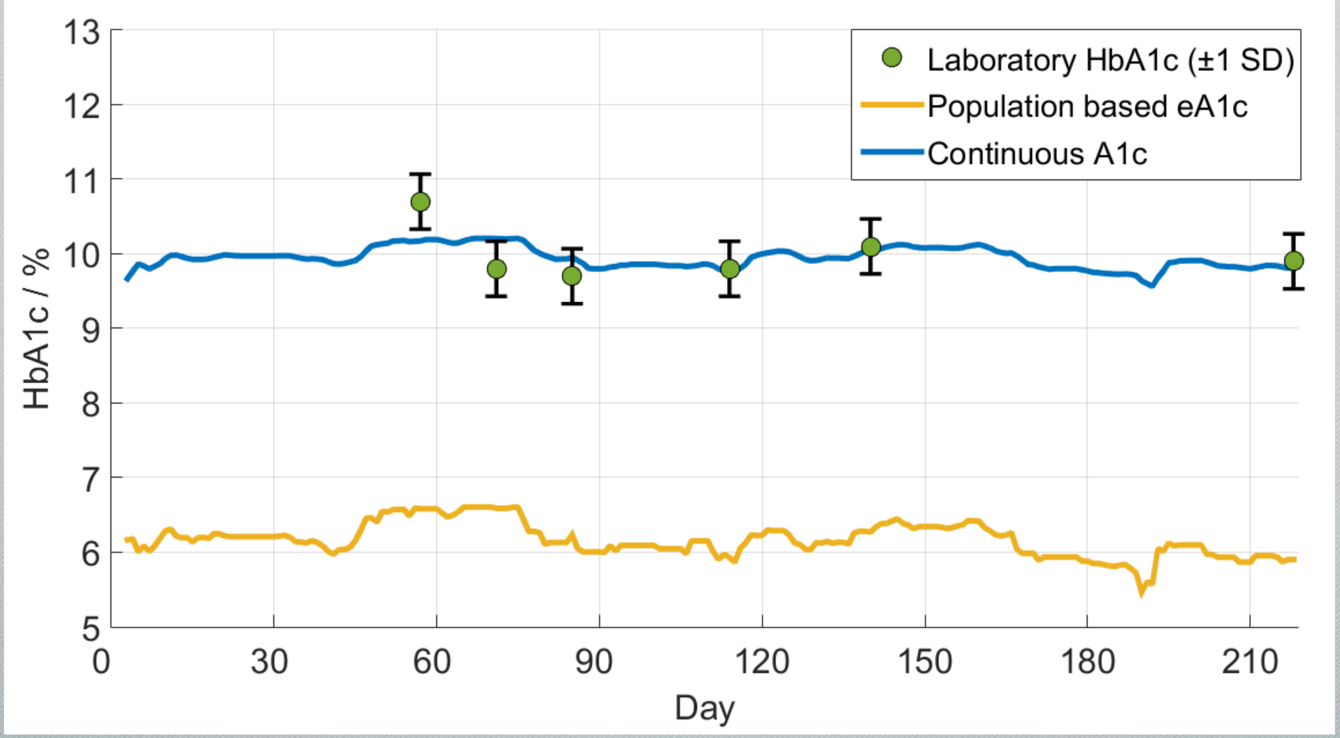
- Leave-one-out cross-validation was used to calculate mean absolute deviation (MAD) and mean absolute relative deviation (MARD)



- Error grid analysis:
  - Percentage of measurements within 10% error margin
  - Percentage of measurements within 20% error margin

Results: Example

- Method can estimate A1c with biased measurement habits



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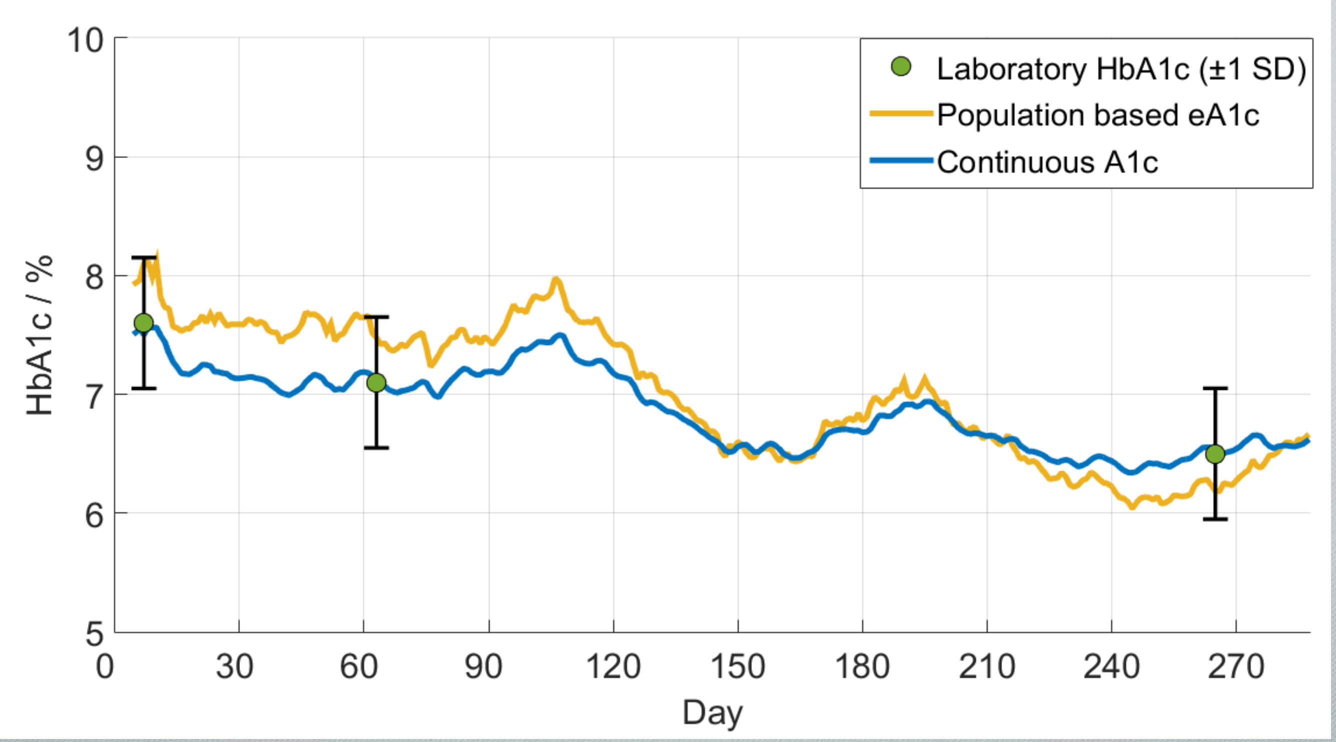
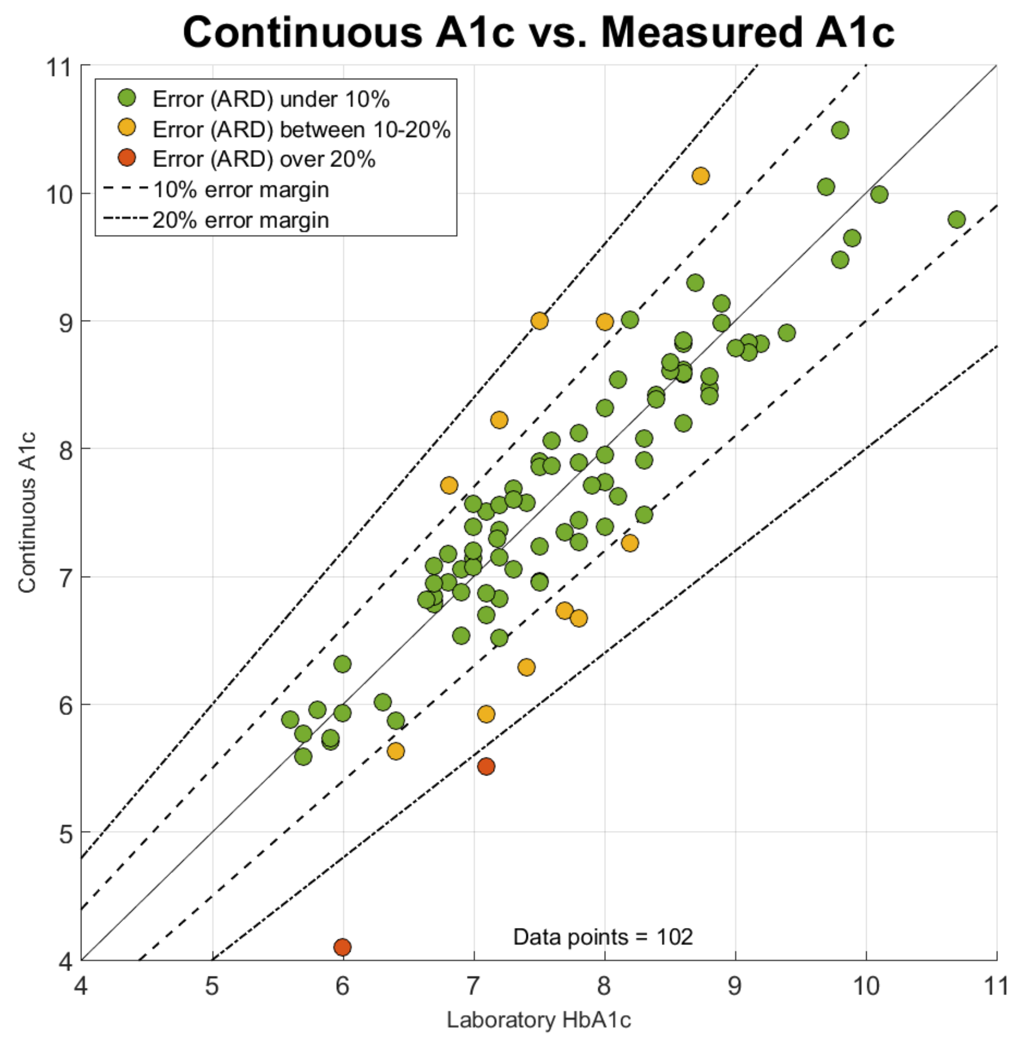
Results: Example 2

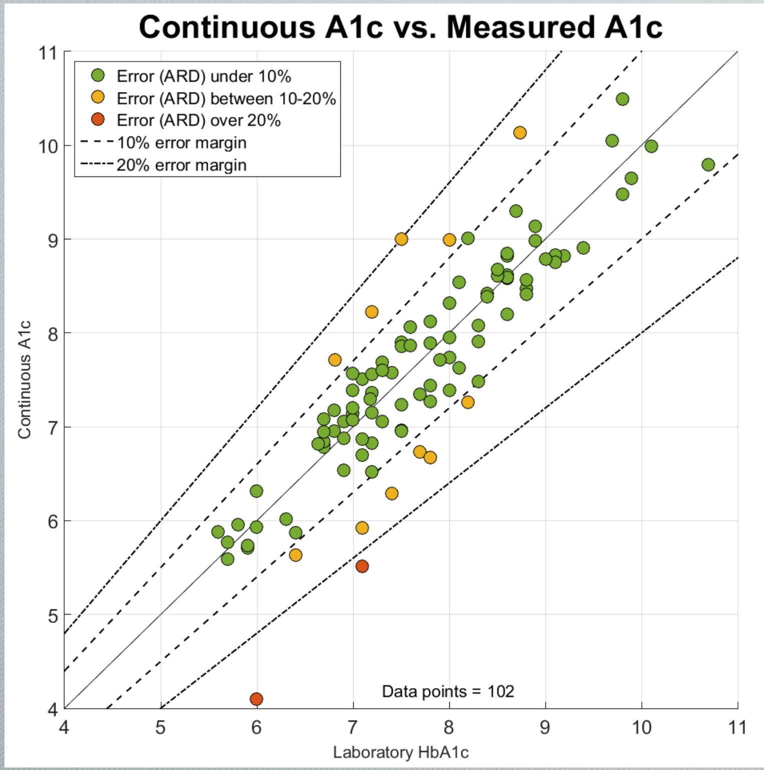
- Method can estimate A1c with good accuracy and utilizes the available data efficiently



Results: Error grid



Results: Error Grid



- MAD and MARD were **0.41** and **5.38 %**, respectively.

	Population based eA1c	**Continuous A1c**	Dynamic eA1c*
Correlation (R)	**0.46**	**0.89**	0.76
Within 10 %	**51.26 %**	**87.25 %**	77.50 %
Within 20 %	**85.71 %**	**98.04 %**	97.90 %

* Different data

Kovatchev, B. et al; 2014; *Diabetes Technology & Therapeutics*; 16:5; 303-309

Discussion & Conclusions

- HbA1c is the biomarker of glycemic control and it is measured 2-4 times in a year
  → Unmonitored gaps
- Here, a mathematical model was developed to estimate individual's HbA1c by using their routine SMBG and laboratory HbA1c measurements
- Algorithm needs reference HbA1c for calibration
- Sample size in the study was only 30 diabetics
- Results show that the method works with biased and irregular measurement patterns

Discussion & Conclusions

Continuous A1c…

- utilizes routine monitoring data
- fills unmonitored gaps
- guides in day-to-day diabetes management
- enables fast feed-back
- increases reliability towards treatment

Thank You!

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