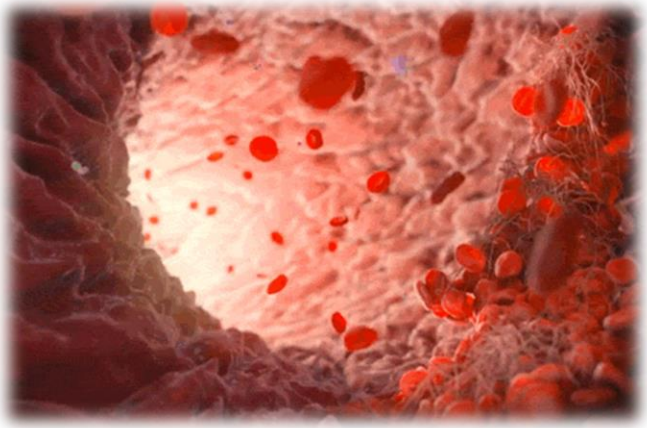
Diagnosis Diabetes in Estonia

What will provide Hb A1c capillary technology ?

Sébastien SAMMUT, PhD
Sebia, France

29/08/2019

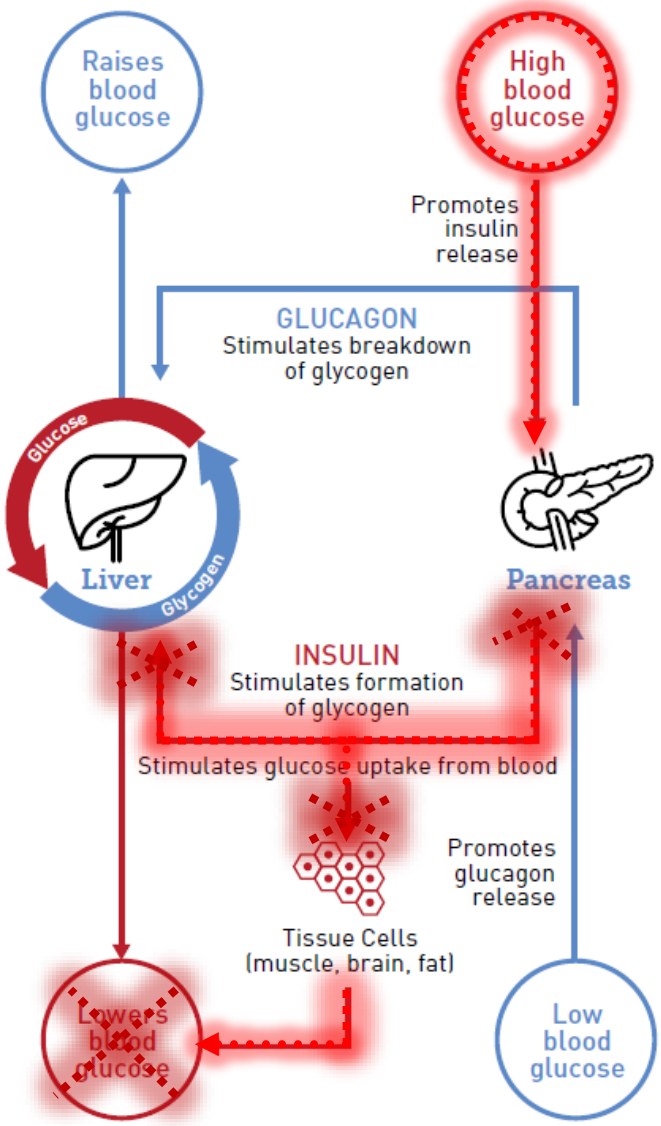


Diabetes
a global health problem

12% of global health expenditure is spent on diabetes
($673 billion)

https://diabetesatlas.org/key-messages.html

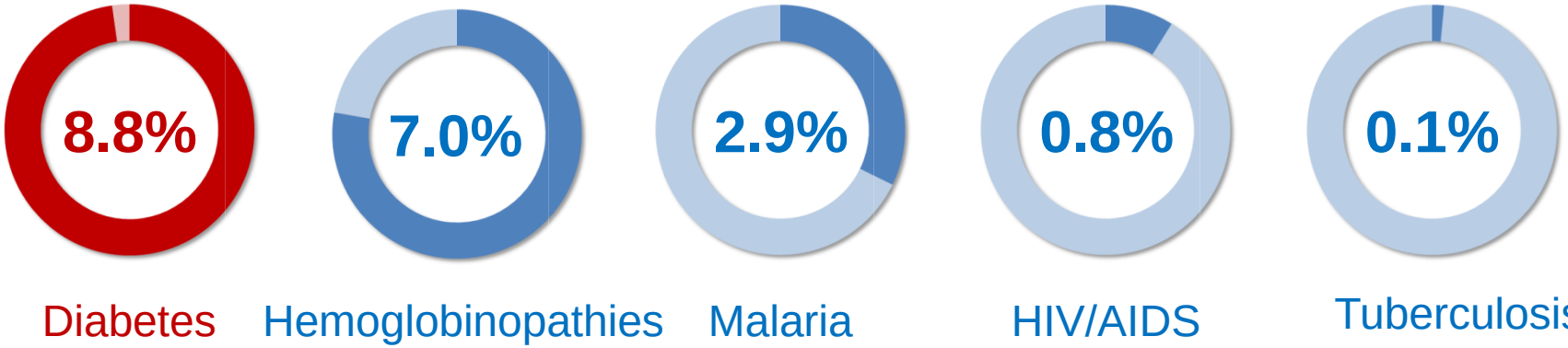
What is diabetes?



- **Diabetes is a chronic condition that occurs when the body cannot produce enough insulin or cannot use insulin**

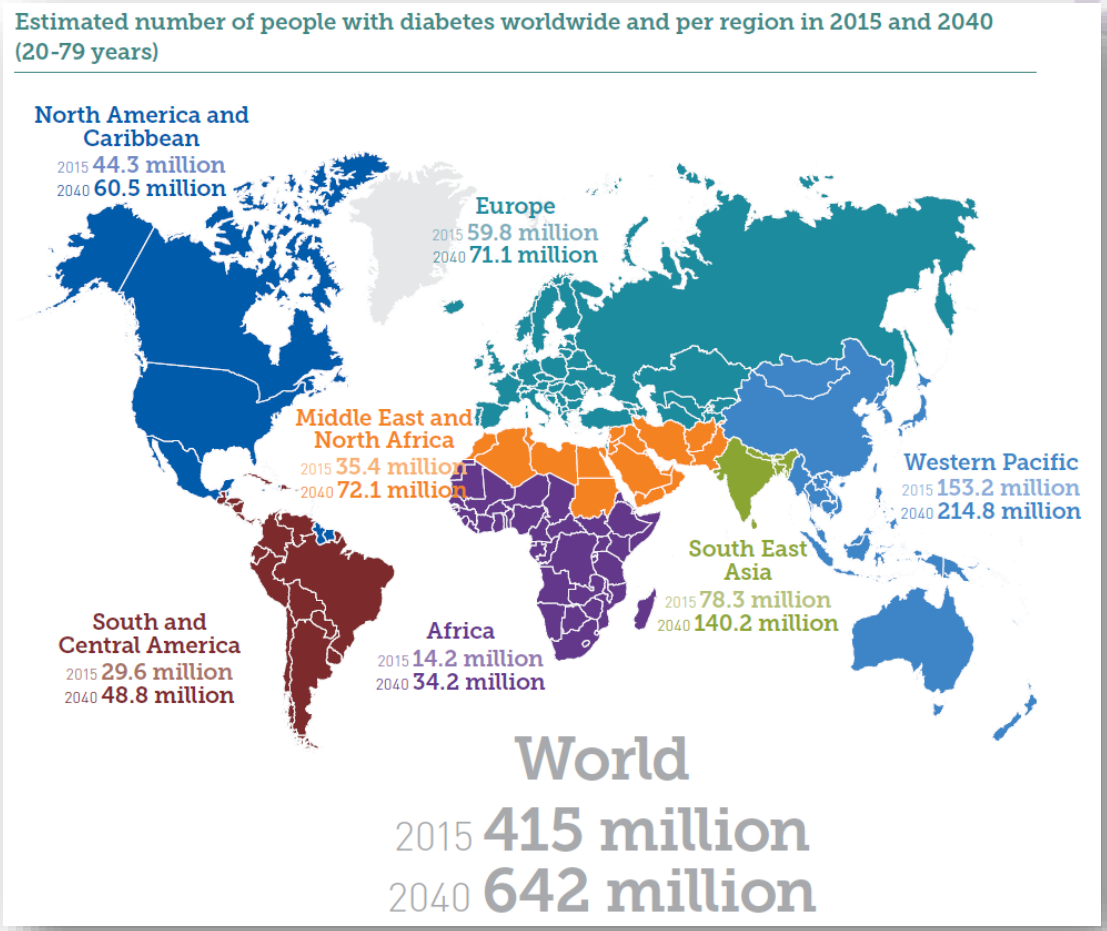
Adapted from IDF DIABETES ATLAS Eighth edition 2017

Some figures...
Diabetes vs other major diseases



Major diseases prevalence in the world (WHO)

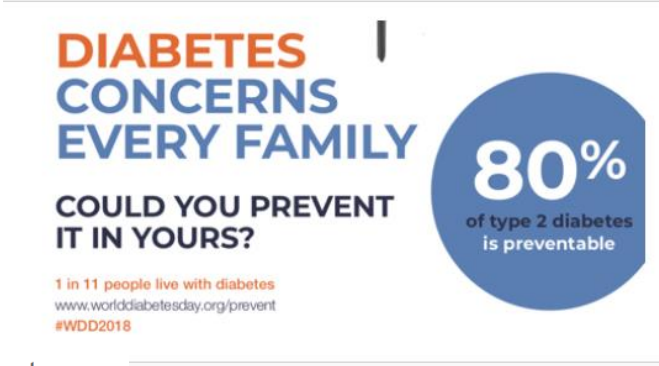
Some figures...
People with diabetes per country



Adapted from International Diabetes Federation Atlas (2015)

Some figures
Diabetes in Estonia

EESTI DIABEEDILIIT
Estonian Diabetes Association



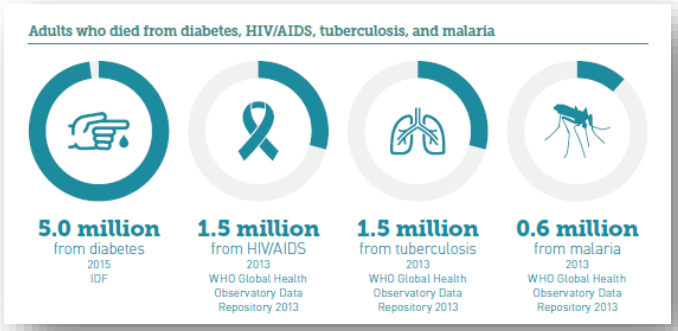
Eestis on diabeet diagnoositud umbes 70 000 inimesel, maailmas põeb diabeeti ca 415 miljonit inimest.

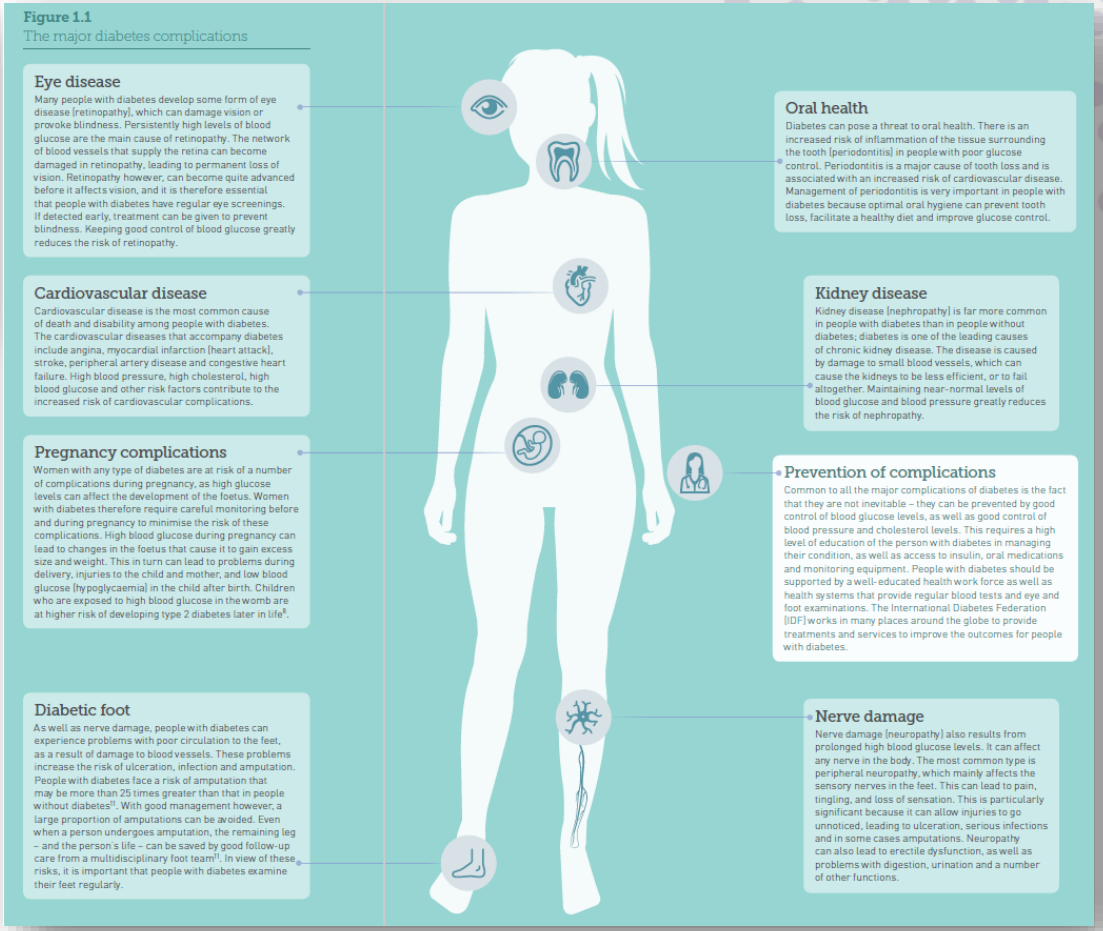
- Diabeet (vana nimega suhkruhaigus) on krooniline ainevahetushaigus, mis vajab igapäevast ja pidevat eneseravi.
- Diabeedi puhul ei tooda kõhunääre insuliini piisavalt või üldse mitte või insuliini mõju organismis on puudulik.
- Eestis on ligikaudu 7000 1 tüübi diabeeti põdevat inimest.
- II tüübi diabeeti põeb teadaolevalt ligikaudu 60-65 000 inimest. Lisaks sellele arvatakse, et umbes sama palju inimesi põeb II astme diabeeti enese teadmata.

- About 70 000 people are diagnosed with diabetes in Estonia
- In addition, it is believed that about the same number of people suffer from stage II diabetes **unknowingly**

Adapted from http://diabetes.ee/

Diabetes: a global health problem





From IDF Diabetes Atlas, Seventh edition, 2015

Diabetes in Estonia

High probability of premature death (30 - 70 yo) from NCDs in Estonia among European countries

EUROPEAN JOURNAL OF GENERAL PRACTICE, 2018
VOL. 24, NO. 1, 112–117
https://doi.org/10.1080/13814788.2018.1429594

BACKGROUND PAPER

OPEN ACCESS Check for updates

Challenges for clinical practice and research in family medicine in reducing the risk of chronic diseases. Notes on the EGPRN Spring Conference 2017 in Riga

Vija Silina[a] and Ruth Kalda[b]

amily Medicine and Public Health, University of

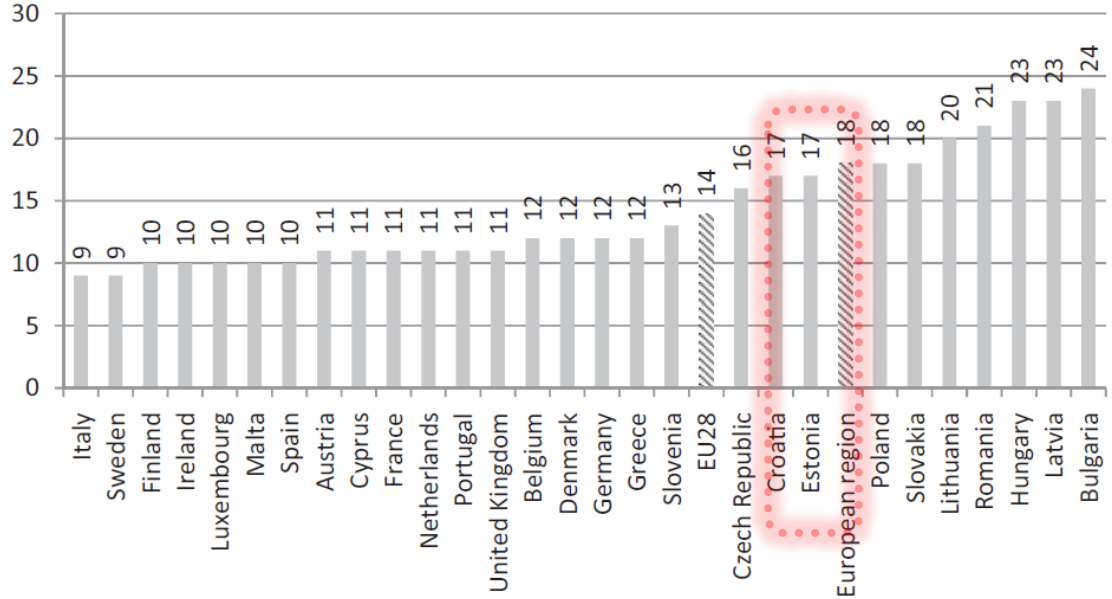
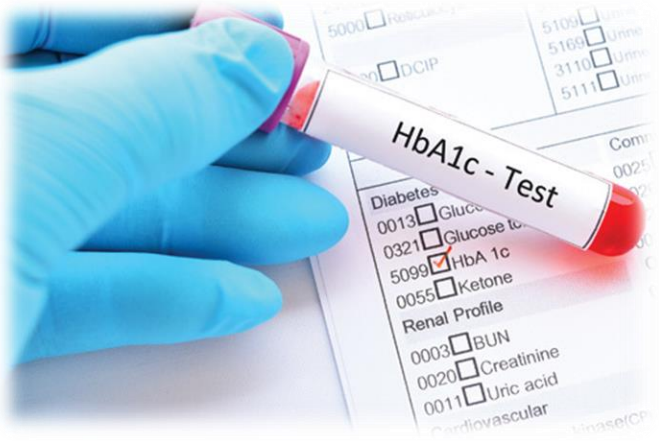


Figure 1. Probability (%) of premature death (dying between age 30 and 70 years) from four main NCDs (cardiovascular diseases, cancer, diabetes, chronic lung disease) in EU countries and in the WHO European region, data from 2015 [5].



How to diagnose diabetes?

The guidelines

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*
OR
A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

Adapted from the American Diabetes Association (ADA) guidelines (2018)

Diabetes Management

European Journal of General Practice, 2010; 16: 85–91

informa
healthcare

ORIGINAL ARTICLE

Meeting targets in type 2 diabetes care contributing to good glycaemic control. A cross-sectional study from a primary care setting in Estonia

ANNELI RÄTSEP[1], RUTH KALDA[1] & MARGUS LEMBER[2]

[1]*Department of Family Medicine, University of Tartu, Estonia, and* [2]*Department of Internal Medicine, University Estonia*

In Estonia 39% of the patients reached the recommended target of HbA1c <6.5% only

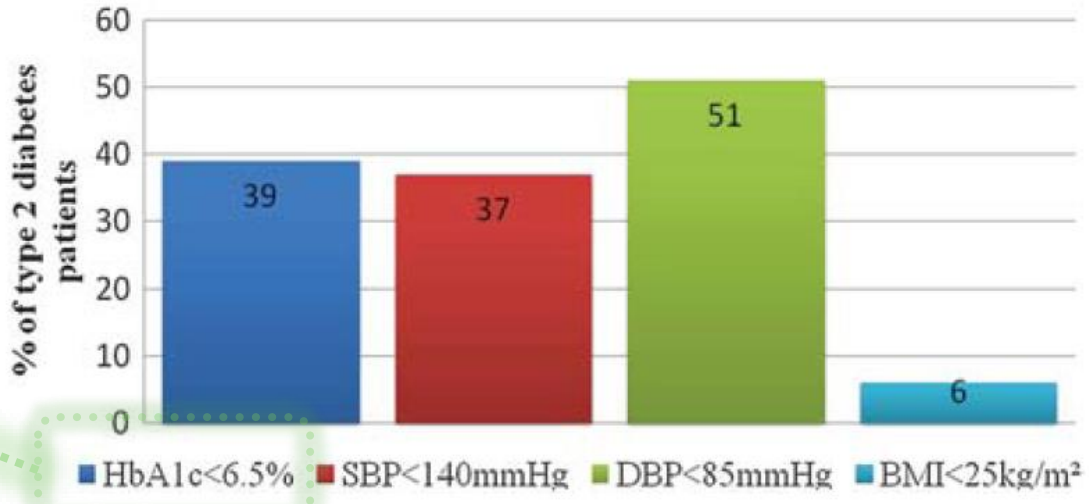


Figure 1. Distribution of type 2 diabetes patients meeting the clinical targets recommended in the guidelines.

The guidelines

A1C GOALS

For glycemic goals in children, please refer to Section 12 "Children and Adolescents." For glycemic goals in pregnant women, please refer to Section 13 "Management of Diabetes in Pregnancy."

Recommendations

- A reasonable A1C goal for many nonpregnant adults is <7% (53 mmol/mol). **A**
- Providers might reasonably suggest more stringent A1C goals (such as <6.5% [48 mmol/mol]) for selected individual patients if this can be achieved without significant hypoglycemia or other adverse effects of treatment (i.e., polypharmacy). Appropriate patients might include those with short duration of diabetes, type 2 diabetes treated with lifestyle or metformin only, long life expectancy, or no significant cardiovascular disease. **C**
- Less stringent A1C goals (such as <8% [64 mmol/mol]) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the goal is difficult to achieve despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin. **B**

Individualized A1c target

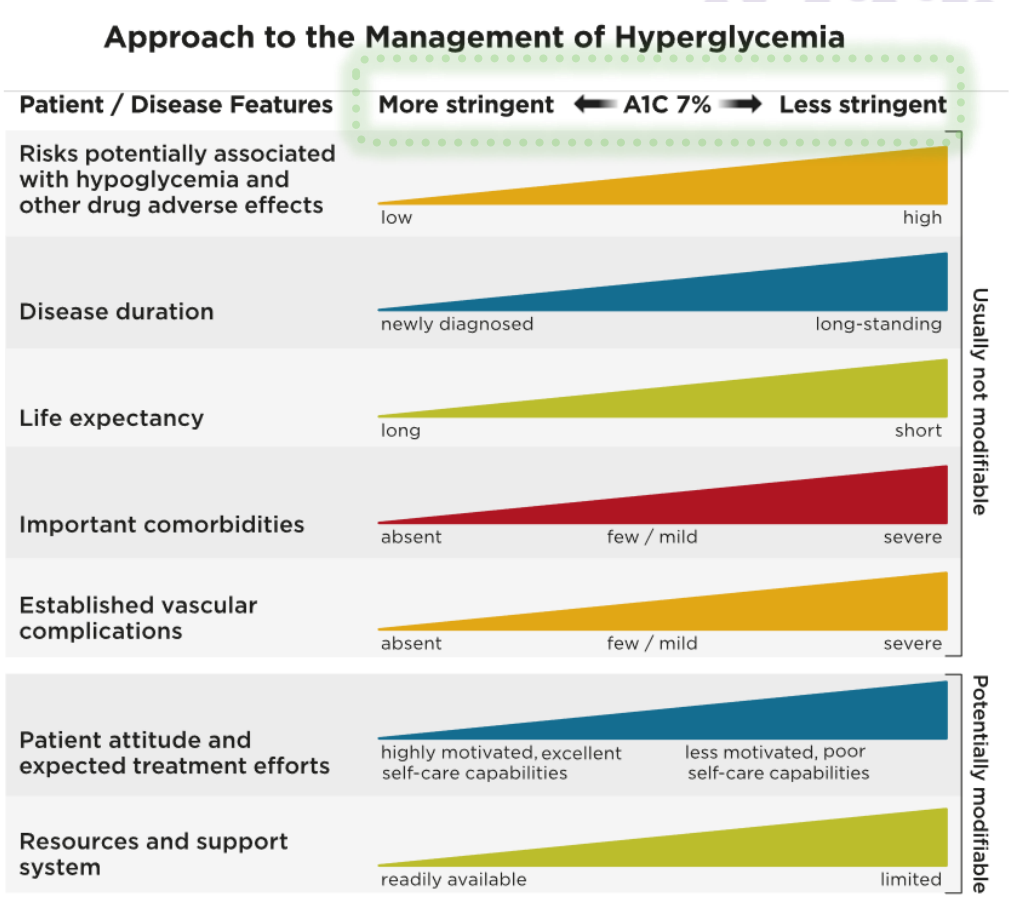


Figure 6.1—Depicted are patient and disease factors used to determine optimal A1C targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. Adapted with permission from Inzucchi et al. (72).

Adapted from the American Diabetes Association (ADA) guidelines (2018)

Diabetes Management

MAYO CLINIC

ORIGINAL ARTICLE

Severe Hypoglycemia Attributable to Intensive Glucose-Lowering Therapy Among US Adults With Diabetes: Population-Based Modeling Study, 2011-2014

Grace K. Mahoney, MS; Henry J. Henk, PhD; and Rozalina G. McCoy, MD, MS

Abstract

Objective: To estimate the contemporary prevalence of intensive glucose-lowering therapy among US adults with diabetes and model the number of hypoglycemia-related emergency department (ED) visits and hospitalizations that are attributable to such intensive treatment.

Patients and Methods: US adults with diabetes and glycated hemoglobin (HbA_{1c}) levels less than 7.0% who were included in the National Health and Nutrition Examination Survey (NHANES) between 2011 and 2014. Participants were categorized as clinically complex if 75 years or older or with 2 or more activities of daily living limitations, end-stage renal disease, or 3 or more chronic conditions. Intensive treatment was defined as any glucose-lowering medications with HbA_{1c} levels of 5.6% or less or 2 or more with HbA_{1c} levels of 5.7% to 6.4%. First, we quantified the proportion of clinically complex and intensively treated individuals in the NHANES population. Then, we modeled the attributable hypoglycemia-related ED visits/hospitalizations over a 2-year period based on published data for event risk.

Results: Almost half (48.8% [10,719,057 of 21,980,034]) of US adults with diabetes (representing 10.7 million US adults) had HbA_{1c} levels less than 7.0%. Among them, 32.3% (3,466,713 of 10,719,057) were clinically complex, and 21.6% (2,309,556 of 10,719,057) were intensively treated, with no difference by clinical complexity. Over a 2-year period, we estimated 31,511 hospitalizations and 30,954 ED visits for hypoglycemia in this population; of these, 4774 (95% CI, 954-9714) hospitalizations and 4804 (95% CI, 862-9851) ED visits were attributable to intensive treatment.

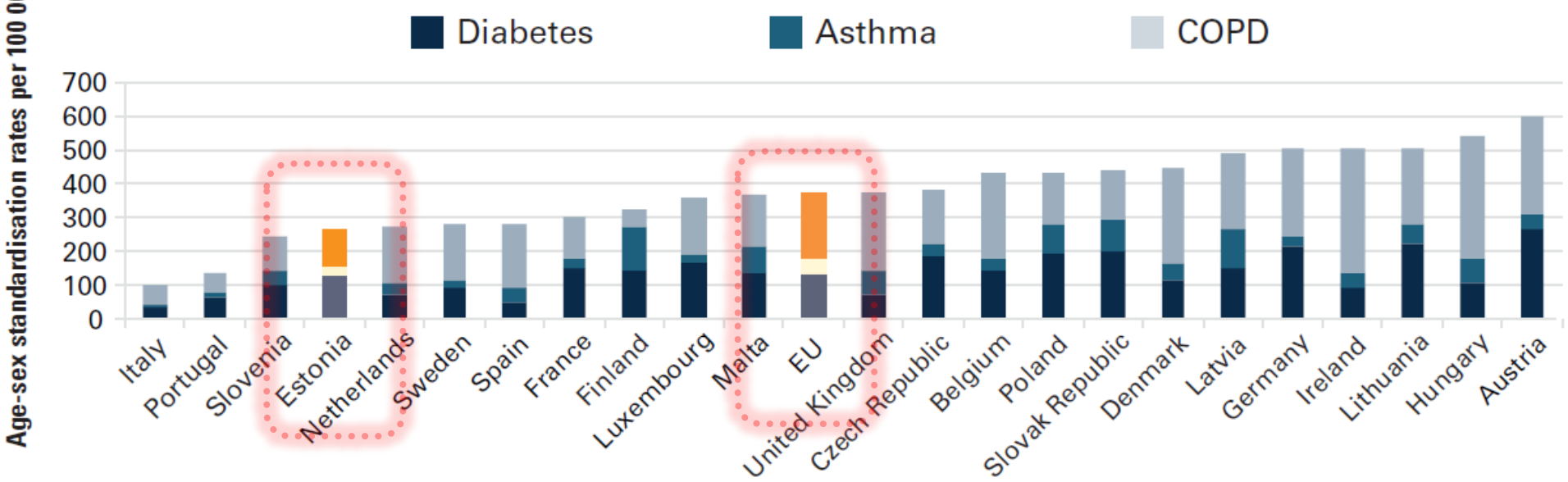
Conclusion: Intensive glucose-lowering therapy, particularly among vulnerable clinically complex adults, is strongly discouraged because it may lead to hypoglycemia. However, intensive treatment was equally prevalent among US adults, irrespective of clinical complexity. Over a 2-year period, an estimated 9578 hospitalizations and ED visits for hypoglycemia could be attributed to intensive diabetes treatment, particularly among clinically complex patients. Patients at risk for hypoglycemia may benefit from treatment deintensification to reduce hypoglycemia risk and treatment burden.

Individualized
A1c target will avoid hospitalizations because of hypoglycemia (9578 hospitalizations attibuted to intensive treatment)

Diabetes in Estonia

Avoidable hospital admissions for diabetes can be improved

FIG. 7.10 Avoidable hospital admissions for diabetes, asthma and chronic obstructive pulmonary disease (COPD) in selected European countries and Estonia, 2015



Source: OECD Health Statistics, 2017.

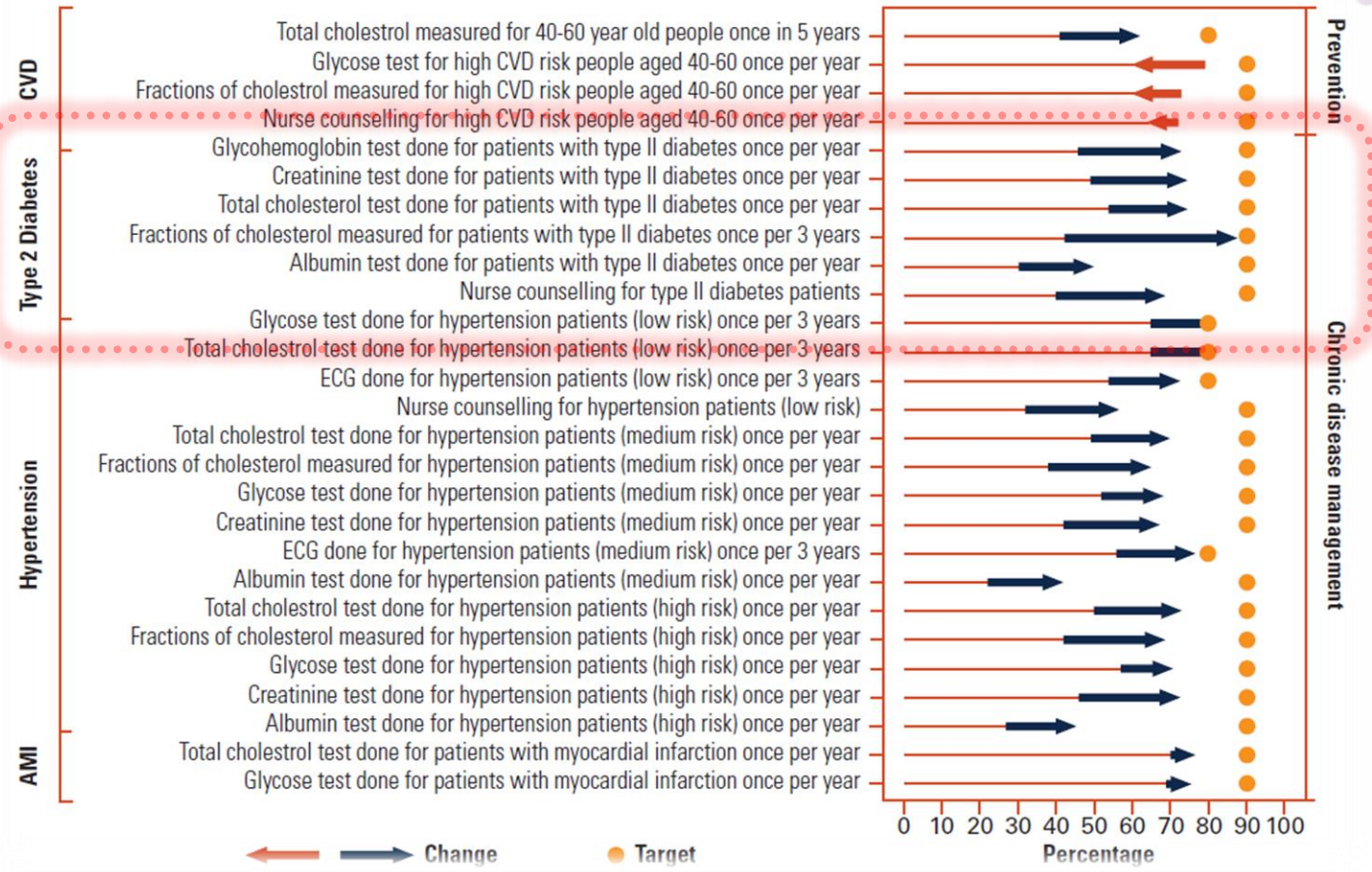
Note: Rates are not adjusted by health care needs and health risk factors.

Diabetes in Estonia

Goal of a quality bonus system (2006) :

- increase the quality and effectiveness of preventive services
- improve monitoring of chronic diseases

FIG. 3.8 Goal achievements for quality bonus system indicators (between 2006–2014)



Adapted from Health Systems in Transition Vol.20 No.1 2018 Estonia Health system review

The guidelines

- **According to the ADA:**
  - Hb A1c testing must be done on a certified method (NGSP, DCCT, IFCC)
  - POC are not recommended for diagnosis
  - Interpretation of the Hb A1c value must be done according to factors impacting glycemia, such as hemoglobinopathies!

What is Hb A1c?

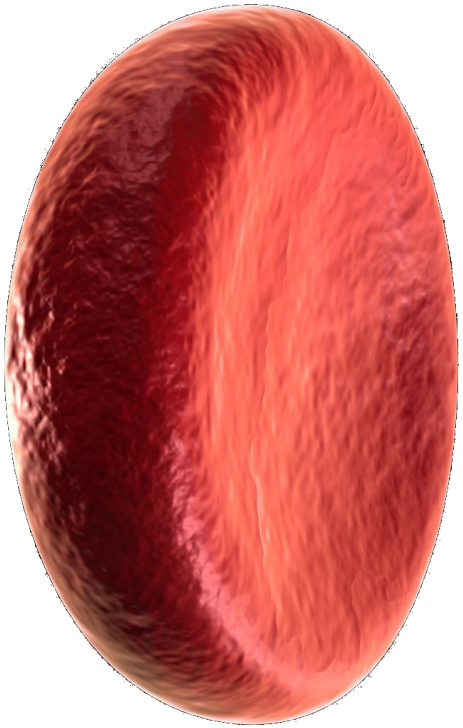
What is Hb A1c?

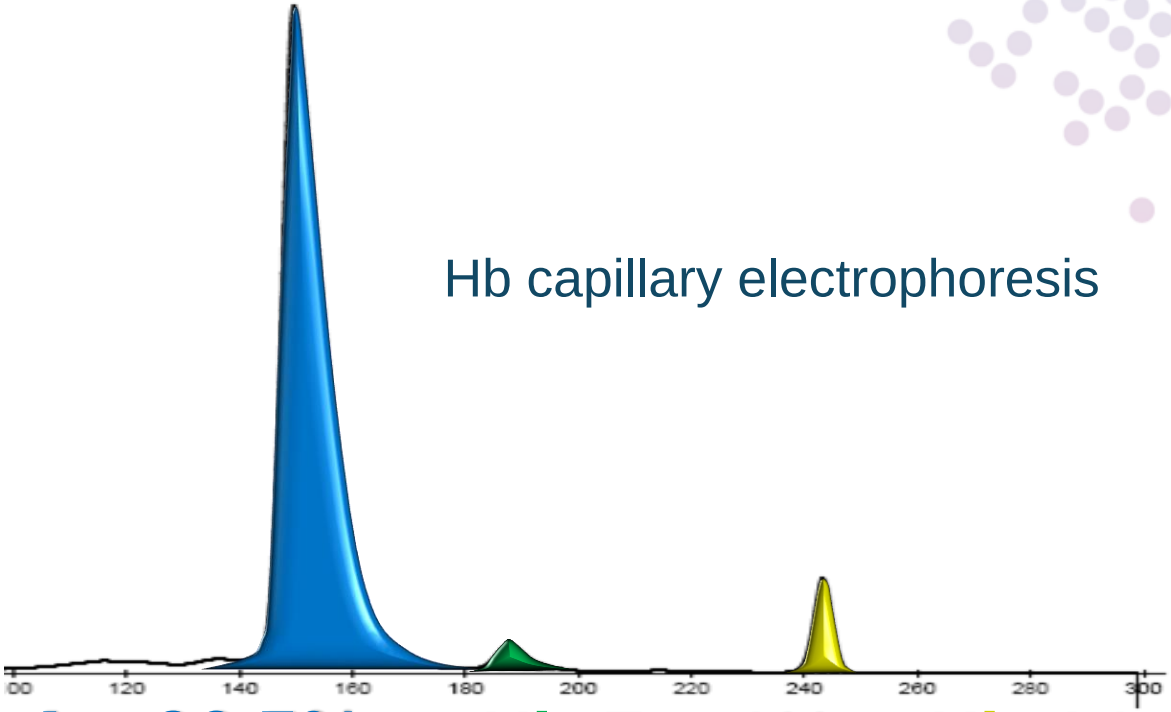
	What it is:	What it is not:
Hb	Hemoglobin...	Not bilirubin, Not albumin, ...
A	... more precisely the A fraction ...	Not all the Hb fractions, not Hb S or Hb C, ...
1	... which is glycated...	Not glycosylated (labile), not carbamylated, ...
c	... with glucose on the N-terminal valine(s) of the Beta chain(s)	Not with fructose, not on the Alpha chain, not elsewhere on the Beta chain, ...

What is Hb A1c?

- **Definition (IFCC) :**
  - **Hemoglobin (Hb A)** that is **irreversibly glycated** at one or both **N-terminal valines** of the **beta chains**
- **Interests:**
  - Hb A1c is a mesure of the hemoglobin glycation
  - Because the RBC have a lifespan of 120 days, Hb A1c reflects mean glycemia of the last 3 months
  - Hb A1c gives info on the long-term glycemic control and allows to monitor the risk of developing complications

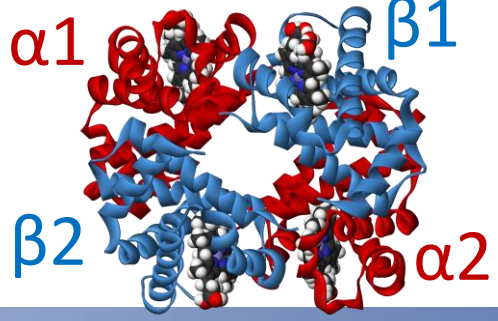
What is Hb A1c?



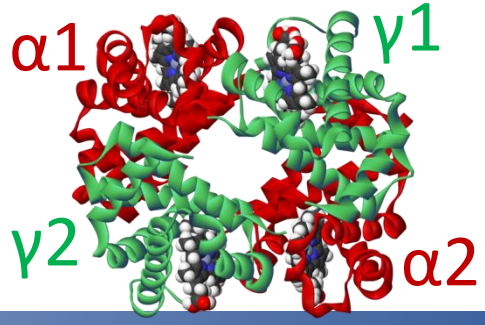


Hb capillary electrophoresis

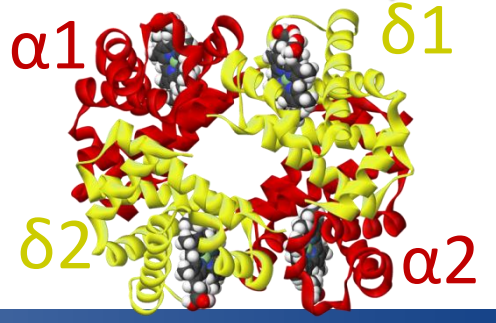
Hb A > 96,5%



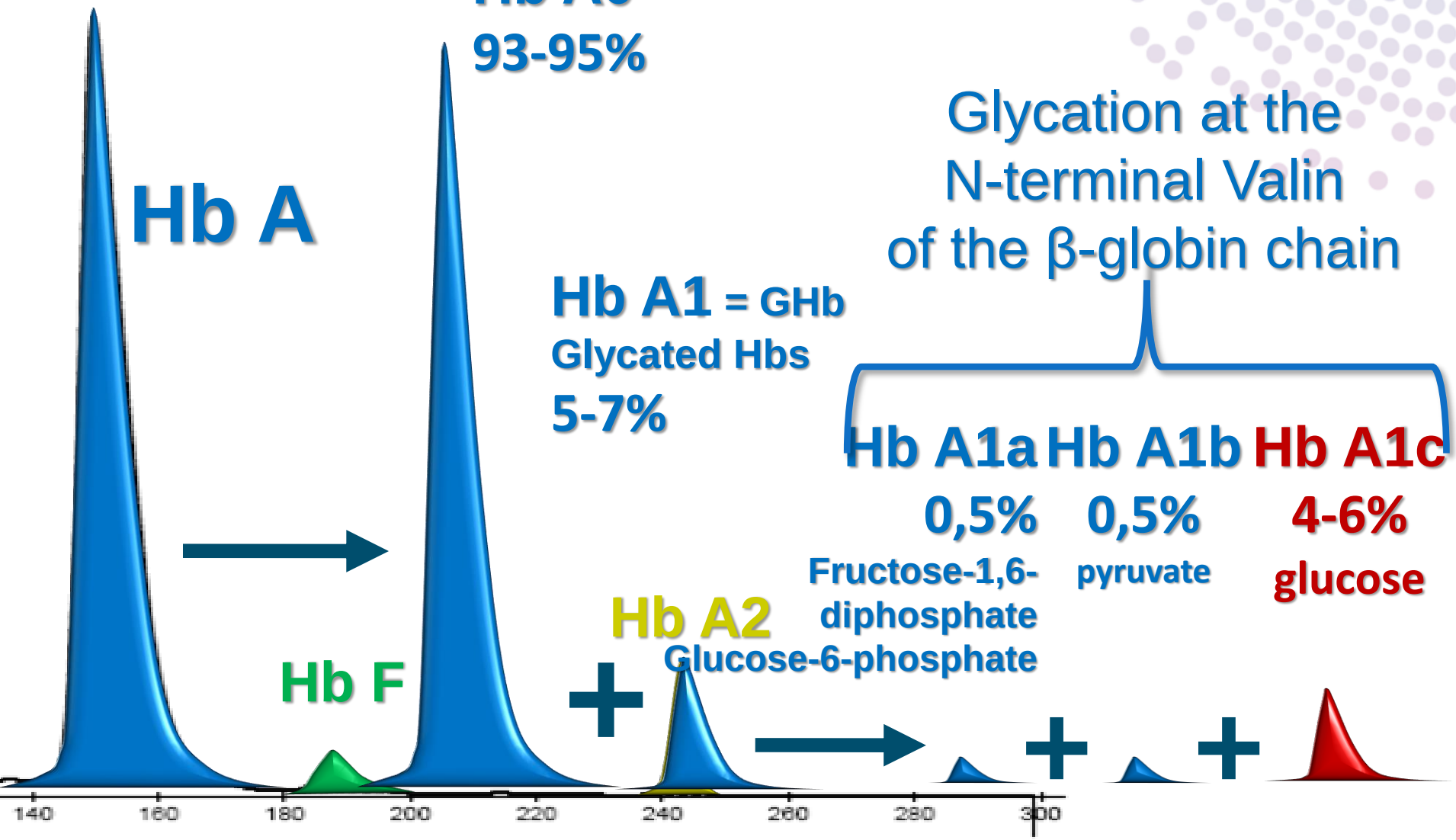
Hb F < 1%



Hb A2 < 3,5%



What is Hb A1c?



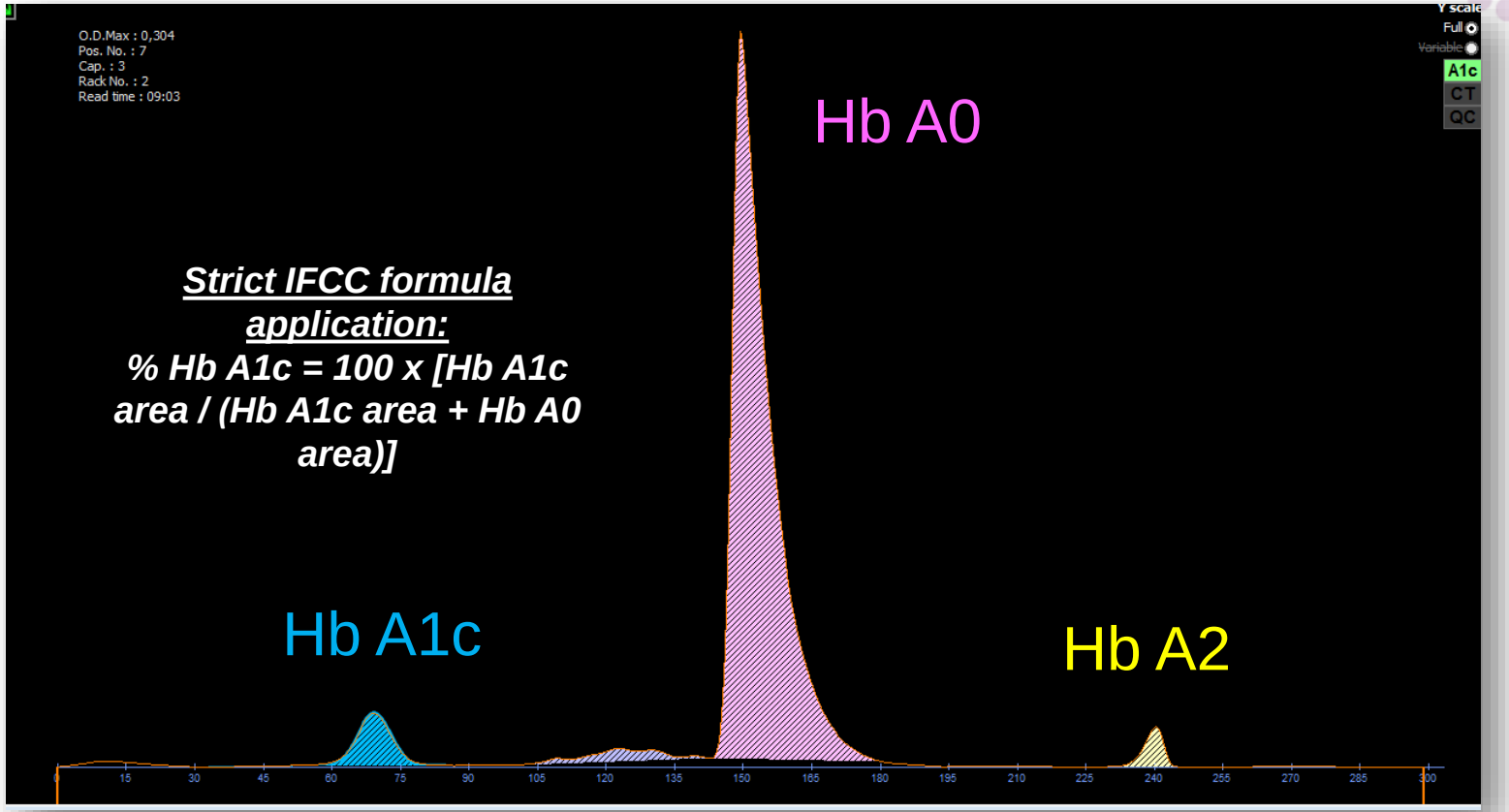
How to measure Hb A1c?

- **Strict IFCC formula:**

$$\%\ \text{Hb A1c} = \frac{\text{Hb A1c}}{(\text{Hb A1c} + \text{Hb A0})}$$

How to measure Hb A1c?

- **Hb A1c on capillary electrophoresis:**

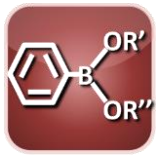


How to measure Hb A1c?

- **Most common laboratory methods:**

[Hb A1c] + [Hb A2c] / [Total Hb]

Immunoassay



Total glycated Hb / Total Hb

Boronate Affinity

[Hb A1c] + [Hb A2c] / [Total Hb]

Enzymatic

Hb A1c Area / ∑ Hb A Area

HPLC

Hb A1c Area /
(Hb A1c Area + Hb A0 Area)

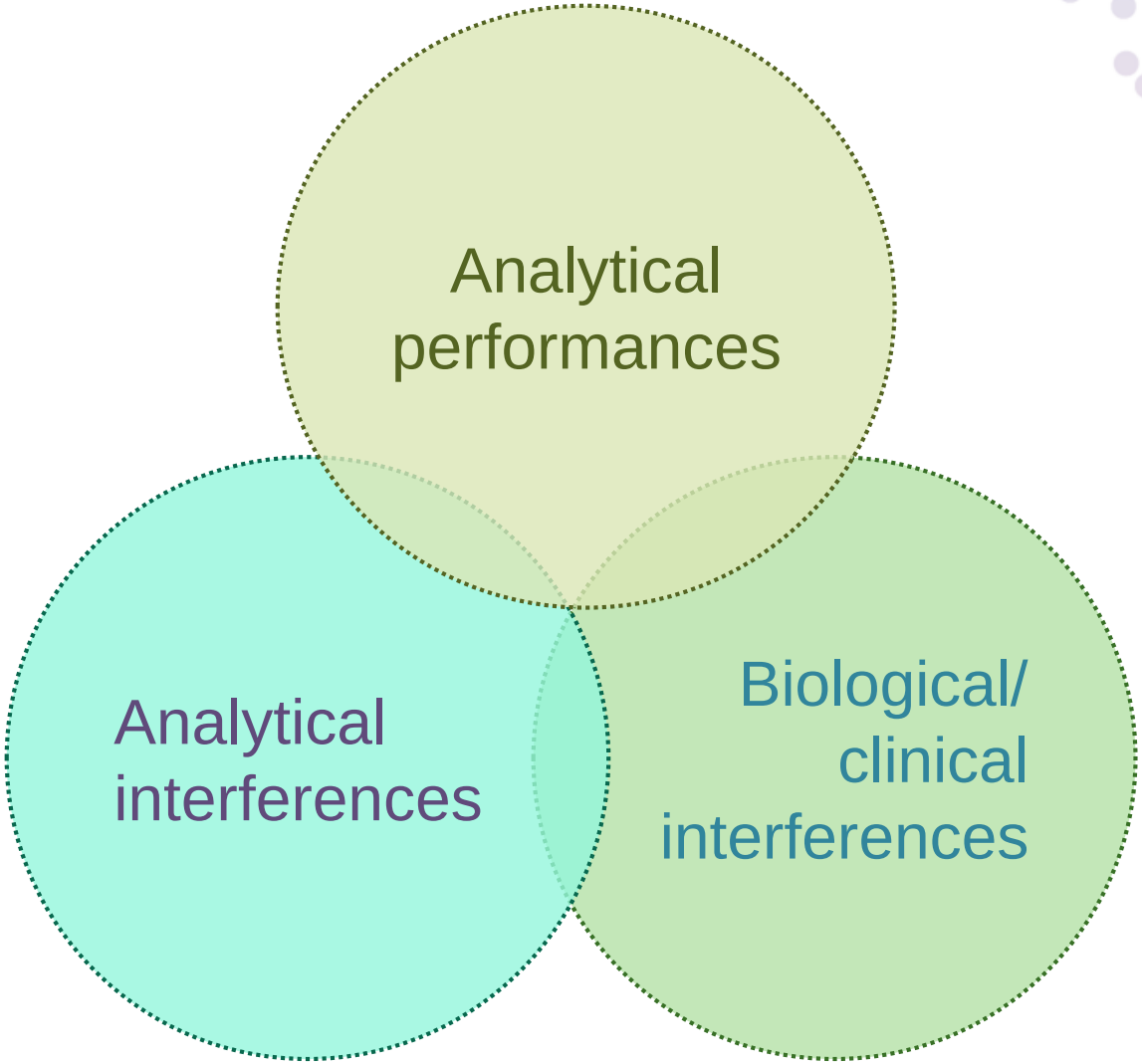
Capillary Electrophoresis

"Blind" methods:
only a Hb A1c value

Separative methods:
Hb A1c value + Hb profile

When choosing/using Hb A1c method,
What should we pay attention to?

What should we pay attention to?



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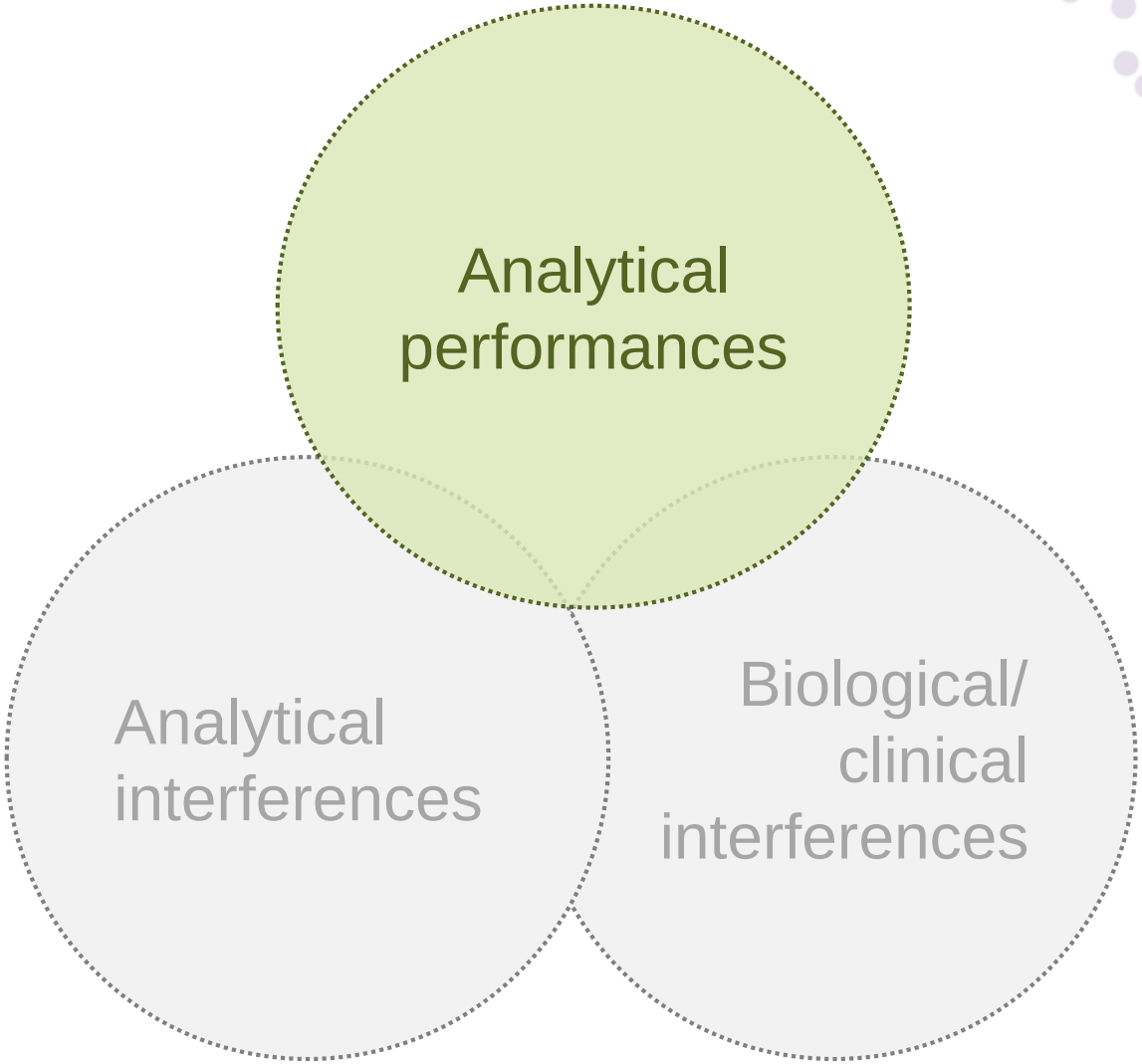
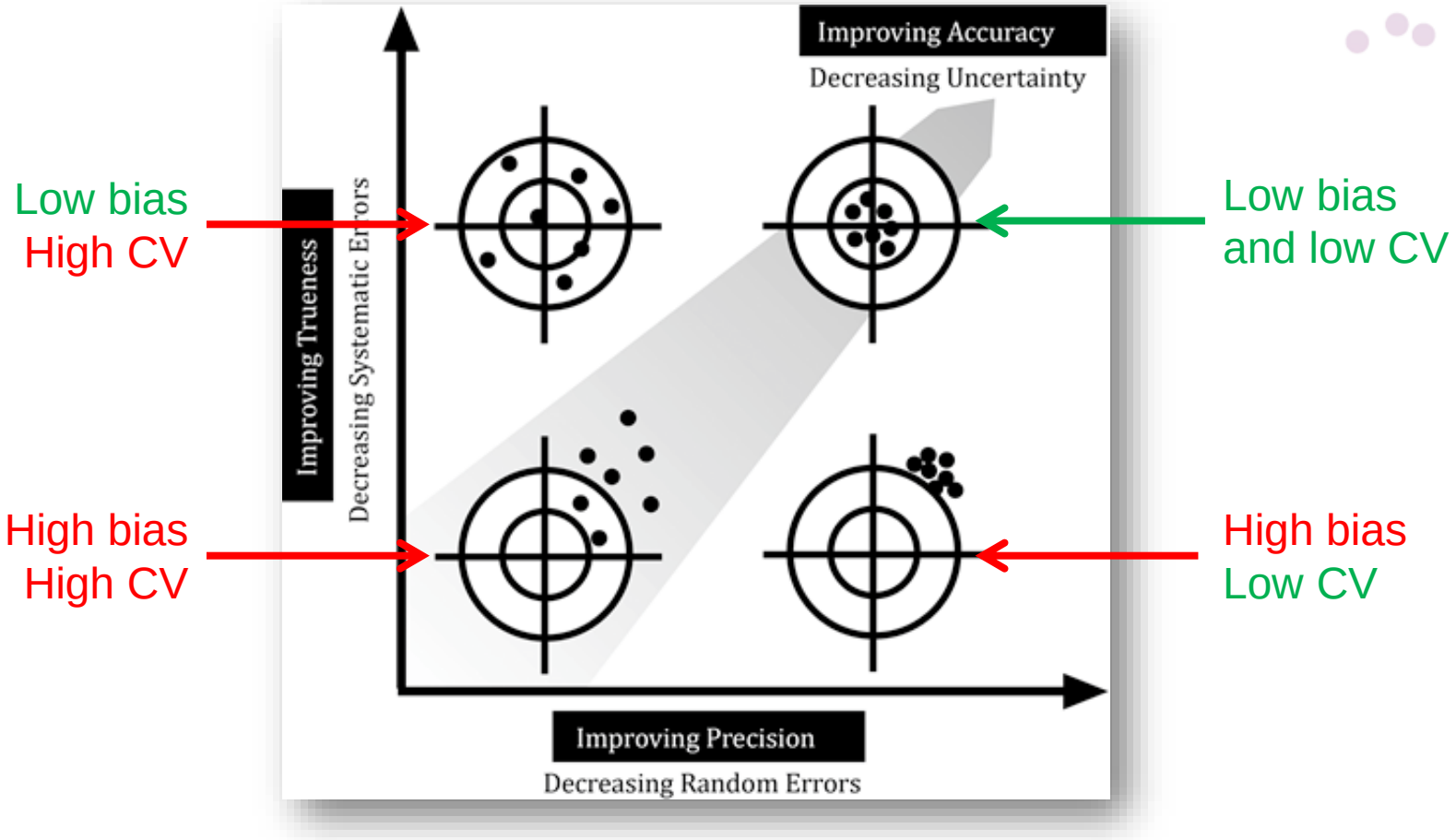


What should we pay attention to? *Analytical performances*

- **Accuracy = Only Imprecision (*CV*)?**

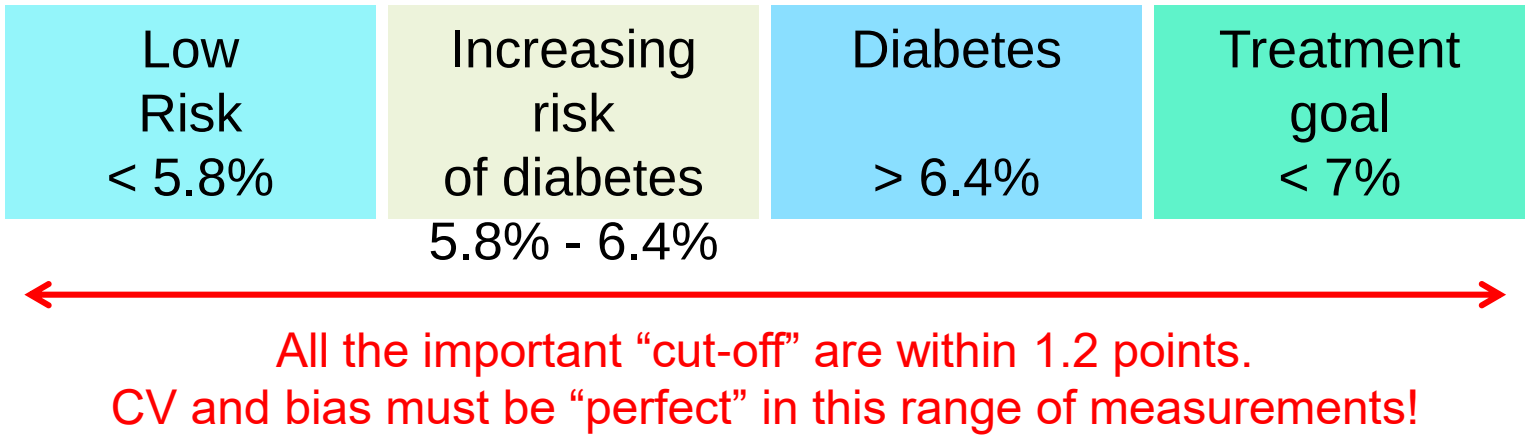
What should we pay attention to? *Analytical performances*

- **Accuracy = Imprecision (*CV*) and Trueness (*bias*)**



What should we pay attention to?
Analytical performances

- **Accuracy = Imprecision (*CV*) and Trueness (*bias*)**



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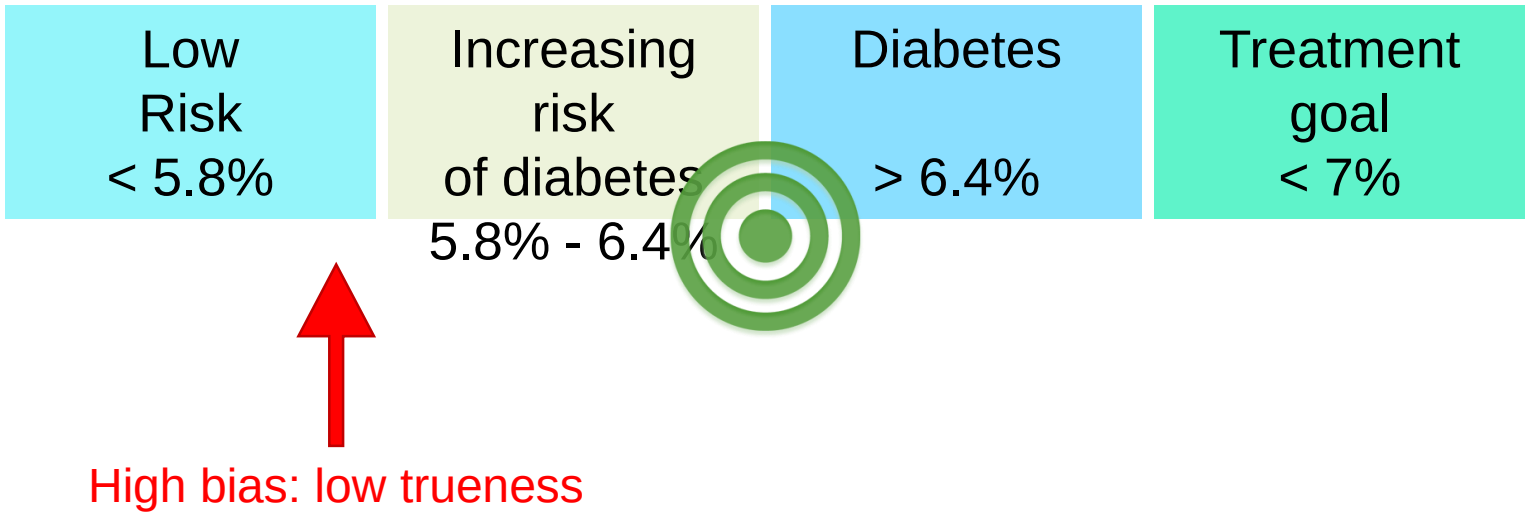
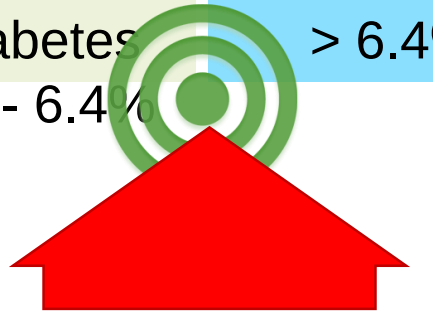


What should we pay attention to? *Analytical performances*

- **Accuracy = Imprecision (*CV*) and Trueness (*bias*)**

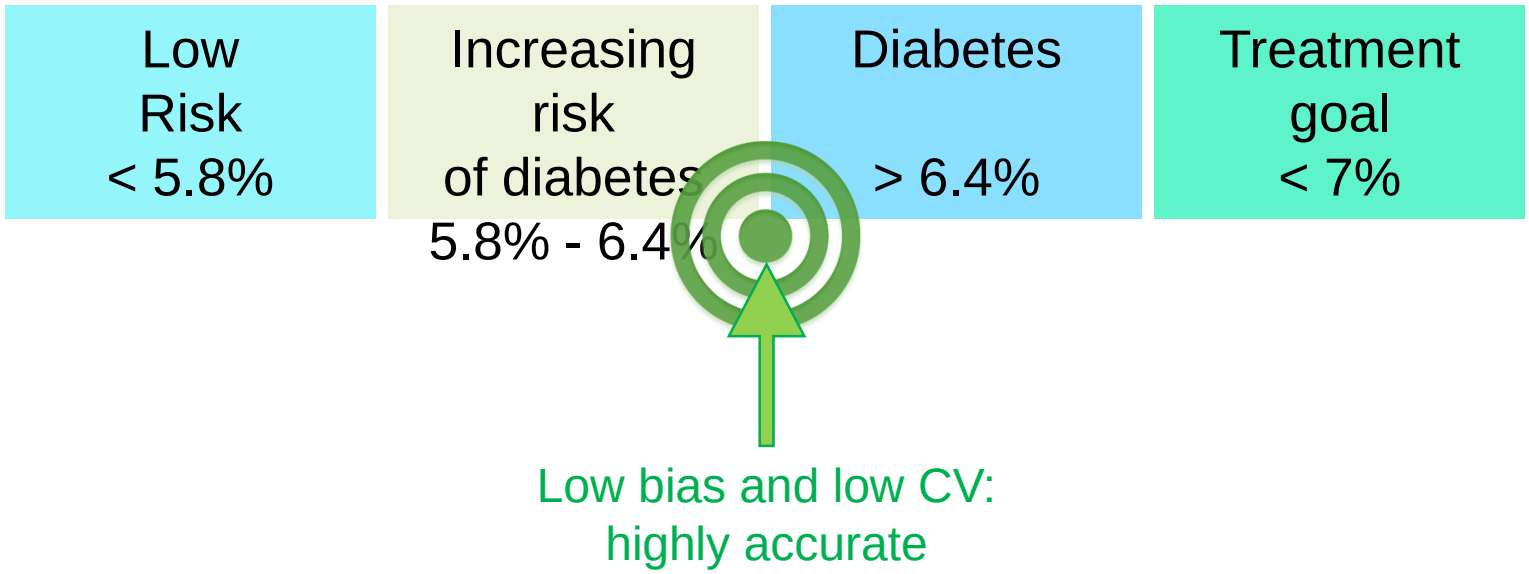
Low Risk < 5.8%	Increasing risk of diabetes 5.8% - 6.4%	Diabetes > 6.4%	Treatment goal < 7%



High CV: low precision

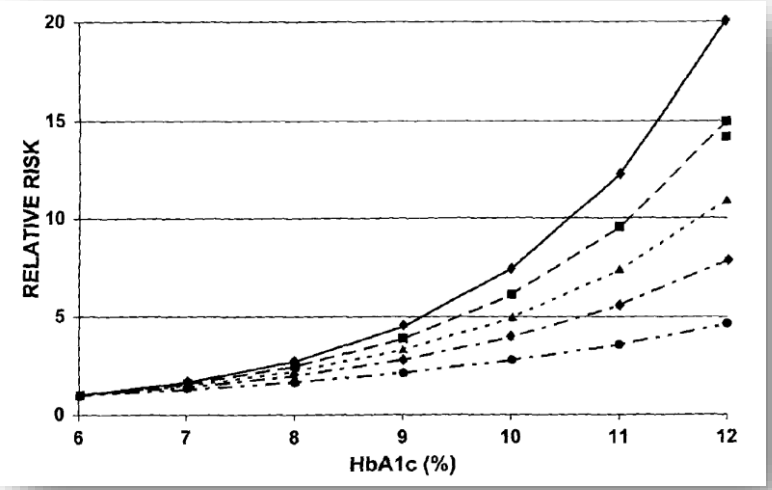
What should we pay attention to? *Analytical performances*

- **Accuracy = Imprecision (*CV*) and Trueness (*bias*)**

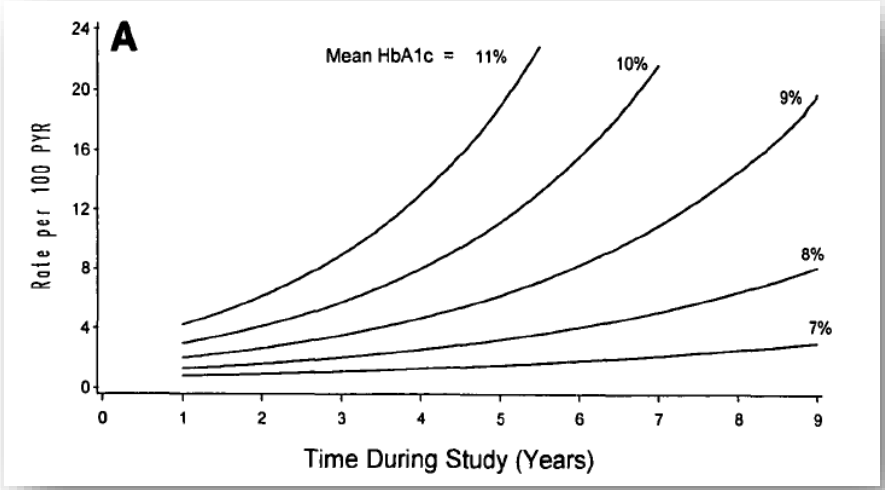


What should we pay attention to?
Analytical performances

- **Accurate Hb A1c method = better patient management**



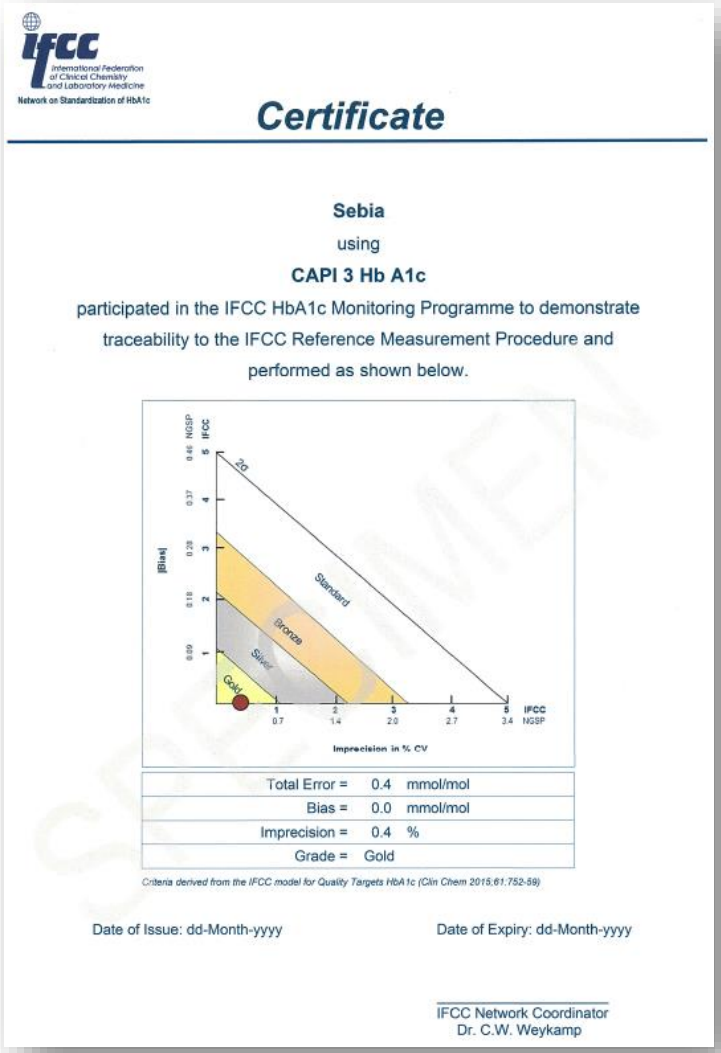
Risk of retinopathy progression (DCCT, diabetes 1995)



Risks for development of various complications (Skyler JS, Endocrinol Metab Clin North Am, 1996)

For example, increase by 1 point the Hb A1c (from 7% to 8%) means multiply by 2 the risk to develop complications after 7 years

What should we pay attention to?
How to assess analytical performances?



ifcc
International Federation of Clinical Chemistry and Laboratory Medicine
Network on Standardization of HbA1c

Certificate

Sebia

using

CAPI 3 Hb A1c

participated in the IFCC HbA1c Monitoring Programme to demonstrate traceability to the IFCC Reference Measurement Procedure and performed as shown below.

Total Error =	0.4	mmol/mol
Bias =	0.0	mmol/mol
Imprecision =	0.4	%
Grade =	Gold	

Criteria derived from the IFCC model for Quality Targets HbA1c (Clin Chem 2015;61:752-59)

Date of Issue: dd-Month-yyyy

Date of Expiry: dd-Month-yyyy

IFCC Network Coordinator
Dr. C.W. Weykamp

- **IFCC certificates given to manufacturers**
- **Example with capillary electrophoresis instrument:**
  - Bias = 0.0 mmol/mol and CV = 0.4 %
  - Ranks “Gold” (Biological Variation model)
  - σ = 25 (Sigma-metrics model)

Goals: CV < 2% NGSP or 3% IFCC, Bronze « Rank » (BV model), σ > 2 (Sigma-metrics)

What should we pay attention to?
How to assess analytical performances?

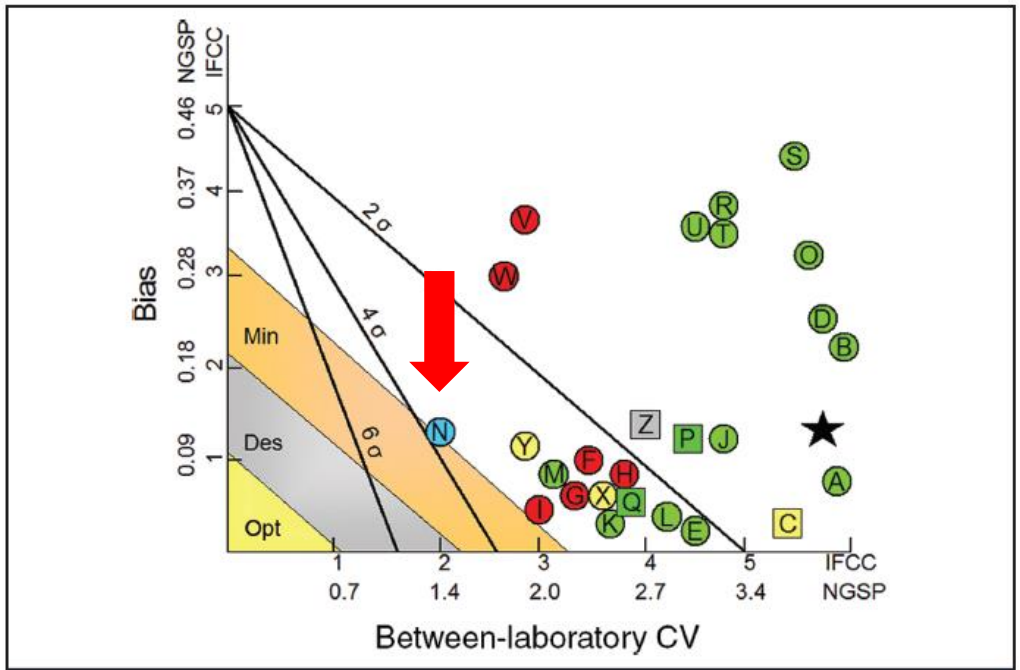


Fig. 2. Models applied to 26 manufacturer/instrument means in CAP 2014 GH2-A survey.

Mean within-manufacturer interlaboratory CV on the *x* axis; mean manufacturer absolute bias on the *y* axis. The black star represents the overall mean of all laboratories. The dots (laboratory instruments) and squares (POCT instruments) represent specific manufacturers with colors for analytical principles: green, immunoassays; red, ion-exchange HPLC; yellow, affinity HPLC; blue, capillary electrophoresis; gray, dry chemistry. Abbott Architect c System (A), Abbott Architect I System (B), Axis-Shield Afinion (C), Beckman AU systems (D), Beckman UniCel DxC Synchron (E), Bio-Rad D10 (F), Bio-Rad Variant II (G), Bio-Rad Variant II Turbo (H), Bio-Rad Variant Turbo 2.0 (I), Roche Cobas c311 (J), Roche Cobas c500 series (K), Roche Cobas Integra 400 (L), Roche Cobas Integra 800 (M), Sebia Capillarys 2 Flex Piercing (N), Siemens Advia Chemistry Systems (O), Siemens DCA 2000/2000+ (P), Siemens DCA Vantage (Q), Siemens Dimension ExL (R), Siemens Dimension RxL (S), Siemens Dimension Vista (T), Siemens Dimension Xpand (U), Tosoh G7 Auto HPLC (V), Tosoh G8 Auto HPLC (W), Trinity Biotech HPLC (X), Trinity Biotech Premier Hb9210 (Y), Ortho Clin Diag Vitros 5,1 FS, 4600, 5600 Chem System (Z). For more details, see online Supplemental Table 1. opt, Optimum; des, desirable; min, minimum.

Analysis of the CAP GH2-A survey

- Chemistry (IA)
- Boronate Affinity
- HPLC
- Capillary electrophoresis

What should we pay attention to?
How to assess analytical performances?

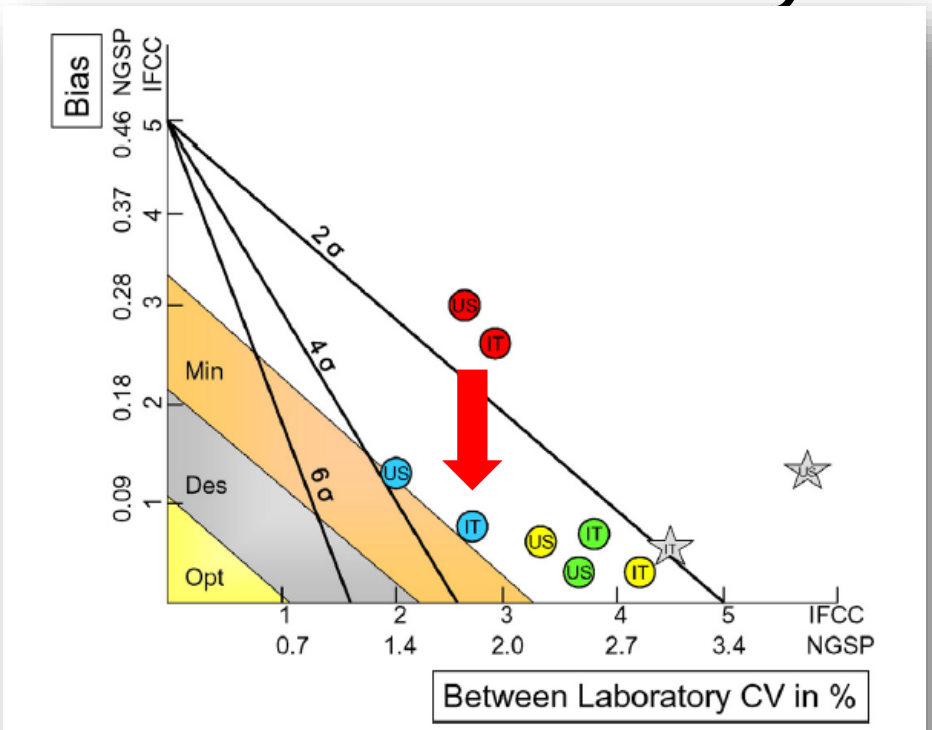
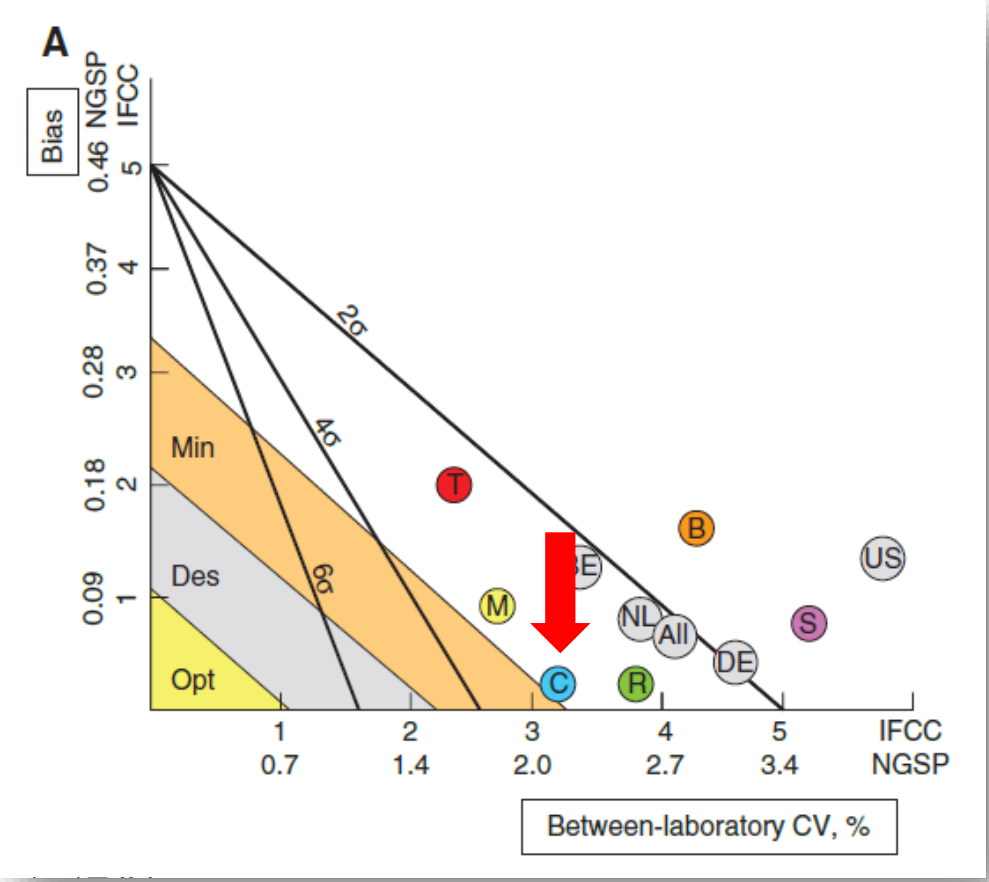


Fig. 3. Quality target models applied to 4 manufacturer/instruments means in the present study and in the CAP 2014 GH2-A survey. Mean within-manufacturer interlaboratory CV on the *x* axis; mean manufacturer absolute bias on the *y* axis. The gray stars represent the overall mean of all laboratories in Italy (star inscribed IT) and United States (US). The dots represent the means of analytical devices of manufacturers in both countries: Tosoh (red), Roche (green), Sebia (blue), and Bio-Rad (yellow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Analysis of the Italian Hb A1c EQA scheme

- Roche (IA)
- Bio-Rad (HPLC)
- Tosoh (HPLC)
- Sebia (capillary electro.)

What should we pay attention to?
How to assess analytical performances?



Analysis of a new European EQA scheme

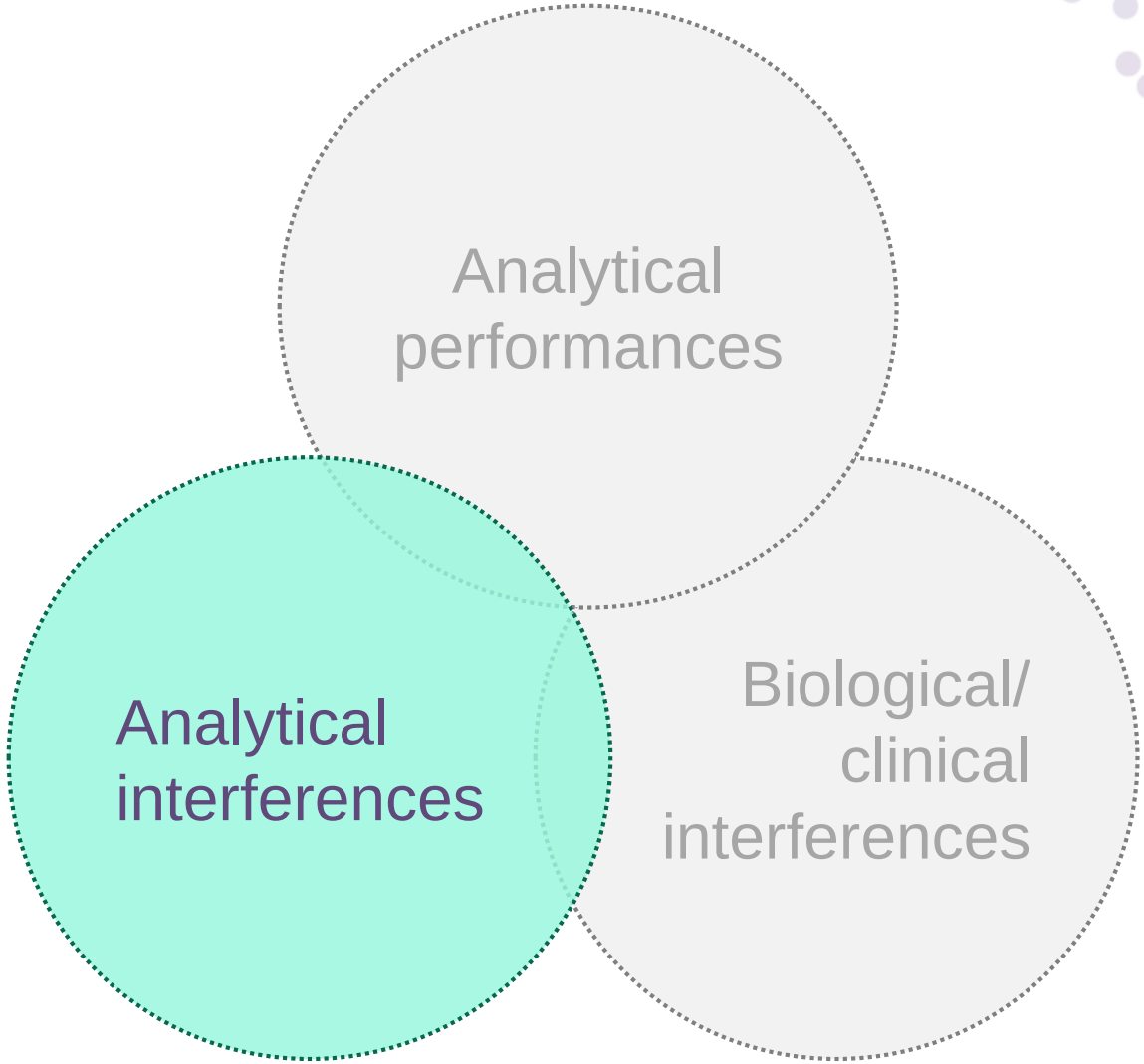
- Roche (IA)
- Menarini/Arkray (HPLC)
- Tosoh (HPLC)
- Sebia (capillary electro.)
- Bio-Rad (HPLC)
- Siemens (IA)

What should we pay attention to?
Analytical interferences

- Each instrument is IFCC and NGSP certified

A solution fitted to your needs !

What should we pay attention to?



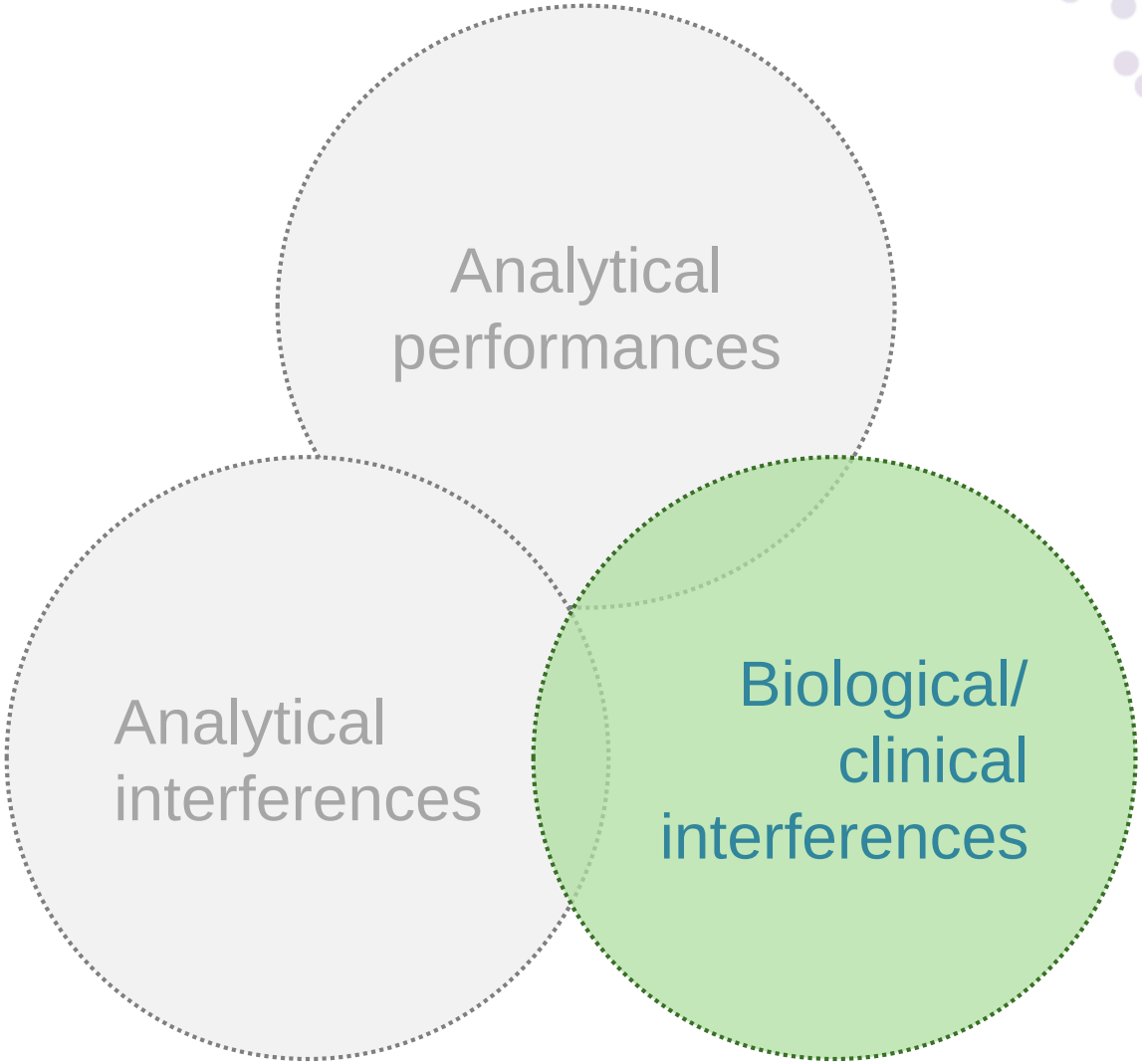
What should we pay attention to?
Analytical interferences

- Triglycerides, total hemoglobin, aspirin, etc

- List of interferences on the NGSP website:
  - http://www.ngsp.org/interf.asp and http://www.ngsp.org/factors.asp

Method (listed in alphabetical order by manufacturer)	**Interference (Yes/No)**					
	Hb C trait	***Hb S trait***	***Hb E trait***	***Hb D trait***	***Elevated HbF***	***Carb Hb***
Sebia Capillarys 2 Flex Piercing	No 13,59	No 13,59	No 13, 54,59	No 13,59	No ≤15% 48	No 48,49, 50
Sebia Capillarys 3 Tera	No 13,59	No 13,59	No 13, 54,59	No 13,59	-	-

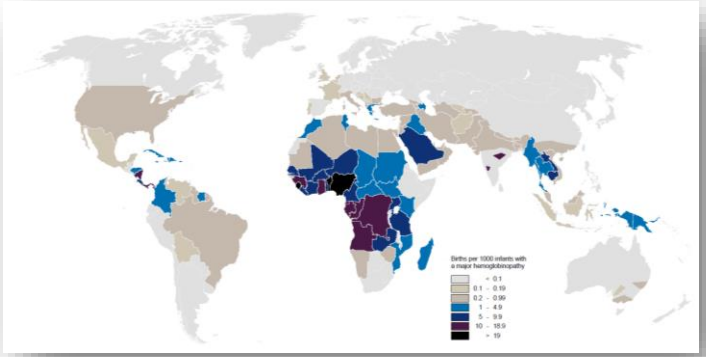
What should we pay attention to?

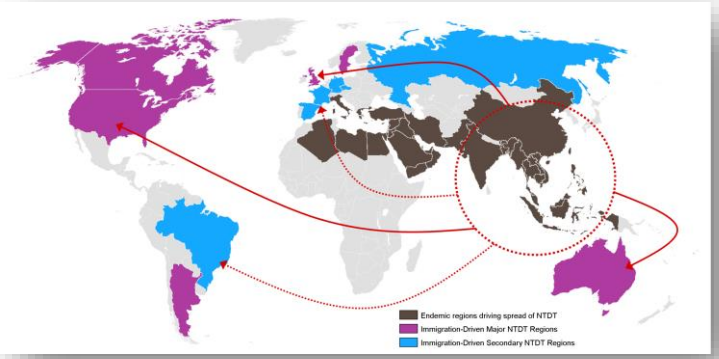


What should we pay attention to?
Biological/clinical interferences

- **Presence of any pathological condition that could impact RBC lifespan and thus the Hb A1c production:**
  - Hemoglobin variants (e.g. Hb S)
  - Thalassemias

- **Around 7% of the worldwide population is carrier for an hemoglobinopathies (WHO)**

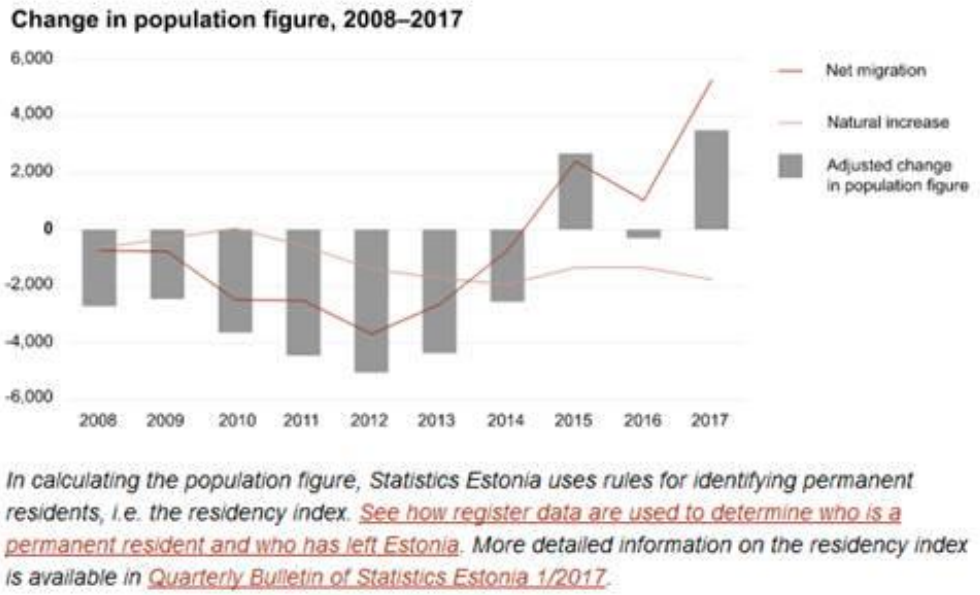




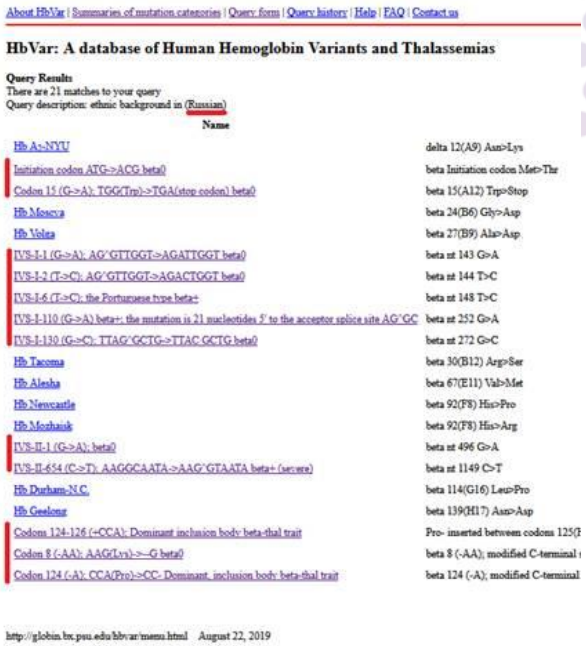
What should we pay attention to? *Biological/clinical interferences*

- **In Estonia, according to the genetic background (Finnish, Russian…), β-thalassemia, and Beta Hb Variant are found (HbS, Hb E, HbD, HbC)**

Beta Thalassemia



In calculating the population figure, Statistics Estonia uses rules for identifying permanent residents, i.e. the residency index. See how register data are used to determine who is a permanent resident and who has left Estonia. More detailed information on the residency index is available in Quarterly Bulletin of Statistics Estonia 1/2017.



http://globin.bx.psu.edu/cgi-bin/hbvar/query_vars3

- **In Estonia, there is a change in population with a positive net migration**

What should we pay attention to?
Biological/clinical interferences

Blind methods (IA, BA, ENZ)	Separative methods (CE, HPLC)
5.1% 32 mmol/mol	5.1% 32 mmol/mol

What should we pay attention to?
Biological/clinical interferences

Blind methods
(IA, BA, ENZ)

5.1%
32 mmol/mol

Just a number. No added value.

Separative methods
(CE, HPLC)

5.1%
32 mmol/mol

What should we pay attention to?
Biological/clinical interferences

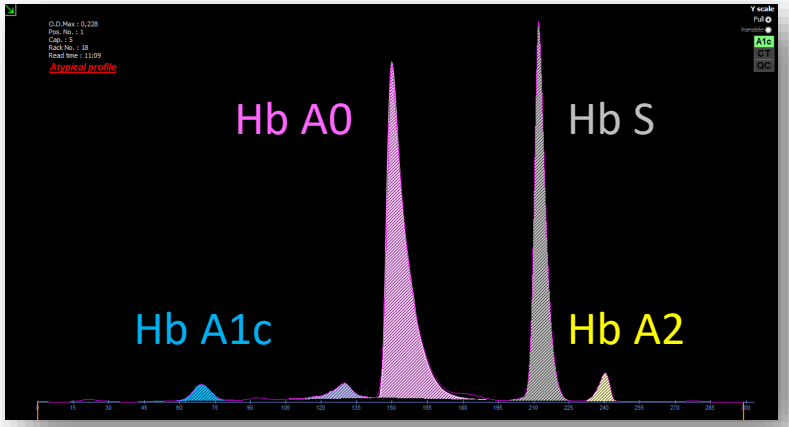
Blind methods
(IA, BA, ENZ)

5.1%
32 mmol/mol

Just a number. No added value.

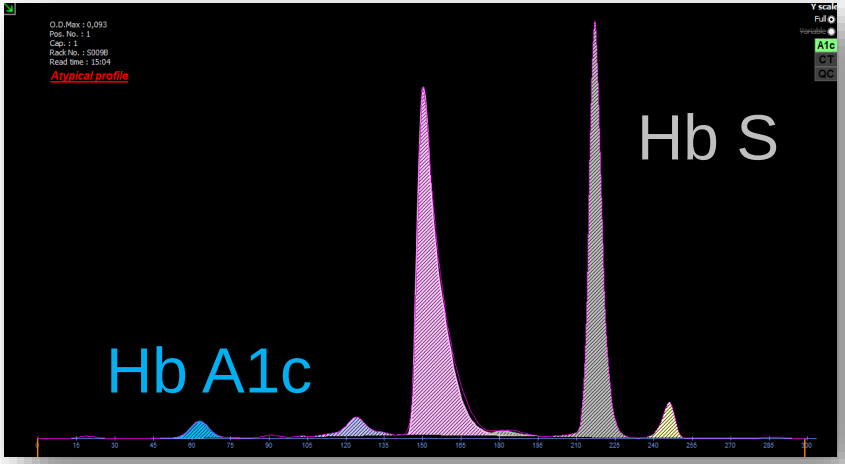
Separative methods
(CE, HPLC)

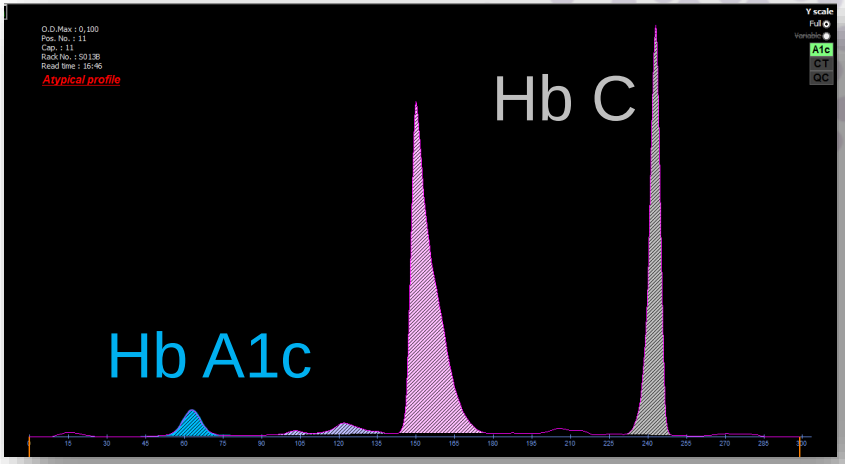
5.1%
32 mmol/mol

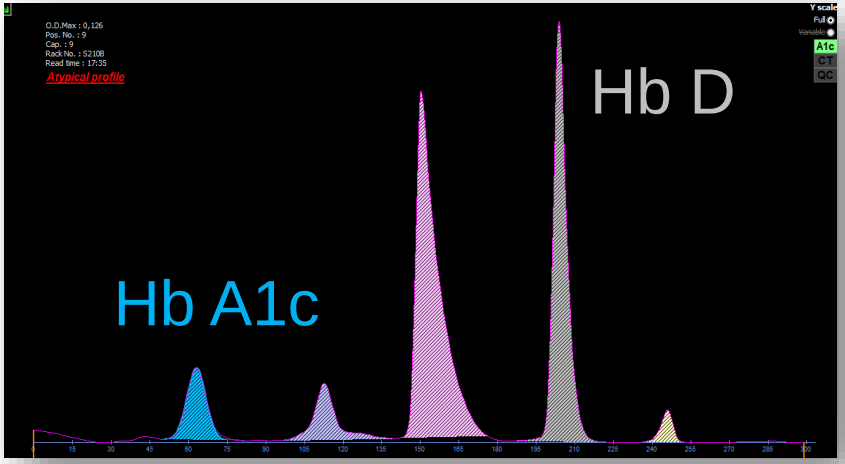


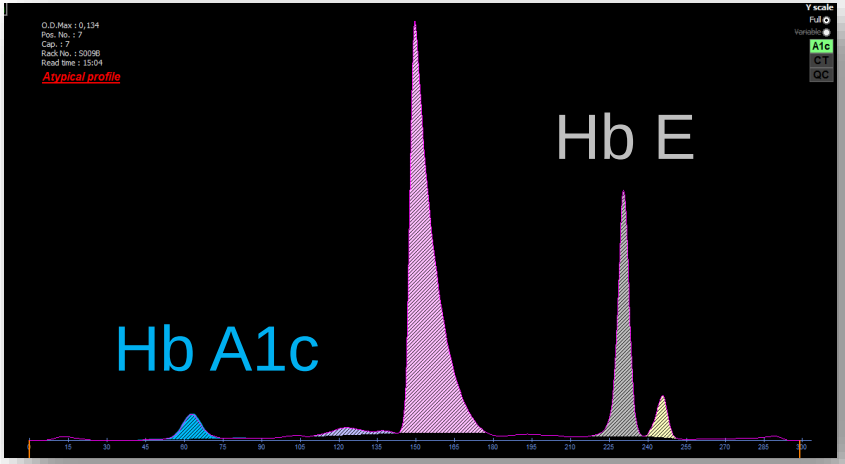
Appropriate comment for the clinician

What should we pay attention to?
Biological/clinical interferences









What should we pay attention to?
Biological/clinical interferences

Effect of RBC Lifespan on HbA1c

1. Difficult to accurately measure rbc lifespan
2. rbc lifespan ranges 100 - 140 days (average 120 d)
3. Assume rbc lifespan is 120 ± 10 d
4. If HbA1c is 7.0% with lifespan of 120 days

   110 days = 6.4%

   130 days = 7.6%

Adapted from Sacks D, AACC Webinar 2012

What should we pay attention to?
Biological/clinical interferences

Tabela Análise descritiva de dados de HbA1c, área de Hb, % de área de Hb e glicemia de jejum associados ao perfil cromatográfico por HPLC dos clientes com genótipos de Hb AA, AS e AC obtidas das amostras de sangue total periférico dos 150 clientes participantes do estudo

Variáveis	(n)	Média	Mediana	Desvio padrão	EPM
A1c HbAA	78	8,05	7,85	1,92	0,21
Área HbAA	–	1768592,37	1729388	396034	44842
GJ HbAA	–	159	147	65,20	7,383
A1c HbAS	40	7,96	7,30	2,18	
Área HbAS	–	2049242,17	2028470	4829	
GJ HbAS	–	155	132	80,1	
% Área S	–	34,51	35,05	2,73	0,43
A1c HbAC	32	7,65	7,15	2,26	0,40
Área HbAC	–	2088948,25	1962029	772525	136564
GJ HbAC	–	153	133	81,46	15,97
% Área C	–	30,36	30,45	3,54	0,62

Hb: hemoglobina; HPLC: high-performance liquid chromatography; EPM: erro padrão da média; GJ: glicemia de jejum.

Patients with Hb A/S or Hb A/C have a lower Hb A1c

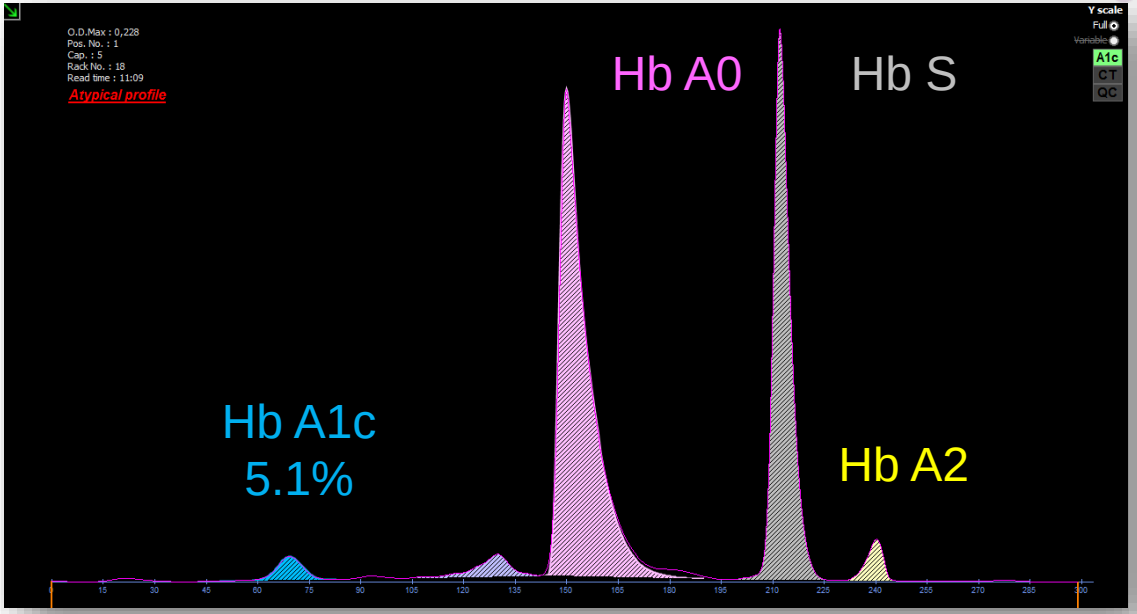
Adapted from Menezes MGS et al., J Bras Patol Med Lab. 2012

What should we pay attention to?
Biological/clinical interferences

Male, 72y

Presence of abnormal Hb peak = Hb S

Sickle Cell Trait, possibly leading to spuriously low Hb A1c value



Detection of Hb S
while Hb A1c is measured

What should we pay attention to?
Biological/clinical interferences

Table 1. Hemoglobin (Hb) A_{1c} ($Hb A_{1c}$) Values Obtained by 4 Different Methods in the Presence of Homozygous and Compound Heterozygous Hb Variants

	Hb A_{1c} %			
Hb Variant	Variant II Turbo 1.0[a,b]	Synchron System[c]	Primus[d]	Integra[e]
SC	24.7	4.7	4.9	6.3
SC	22.0	4.3	4.7	6.1
SC	24.2	4.3	4.1	5.6
SC	26.9	4.6	4.5	6.0
SC	25.9	4.6	4.3	5.5
SS	14.4	4.6	3.3	4.0
SS	13.8	4.4	3.1	3.9
SS	15.8	5.1	4.0	4.5
SS	17.7	4.4	3.1	4.0
SS	23.2	4.2	3.9	4.7
S–β-thalassemia	13.3	4.6	4.9	4.2
S–β-thalassemia	33.0	5.3	5.3	5.8
S–β-thalassemia	10.8	5.4	6.7	7.3
S–β-thalassemia	8.9	5.1	5.4	6.3
S–β-thalassemia	36.3	4.5	4.7	5.4

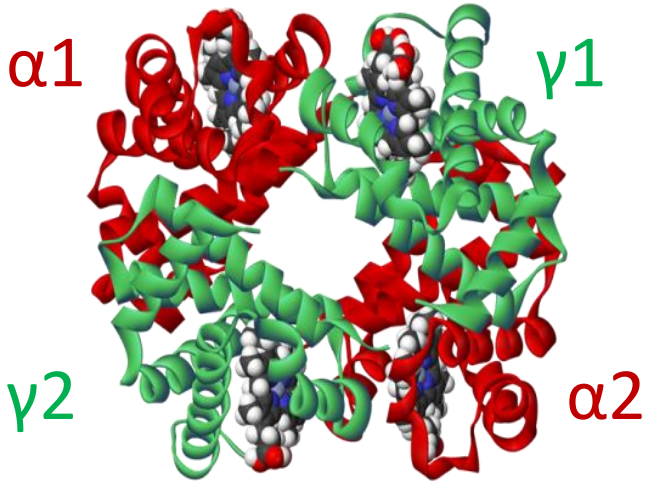
Adapted from Rhea JM et al., Arch Pathol Lab Med. 2013

Patients with Sickle Cell Disease have no Hb A and thus, no Hb A1c. But some HPLC, IA and BA methods give a Hb A1c results, without any warning!

What should we pay attention to?
Biological/clinical interferences

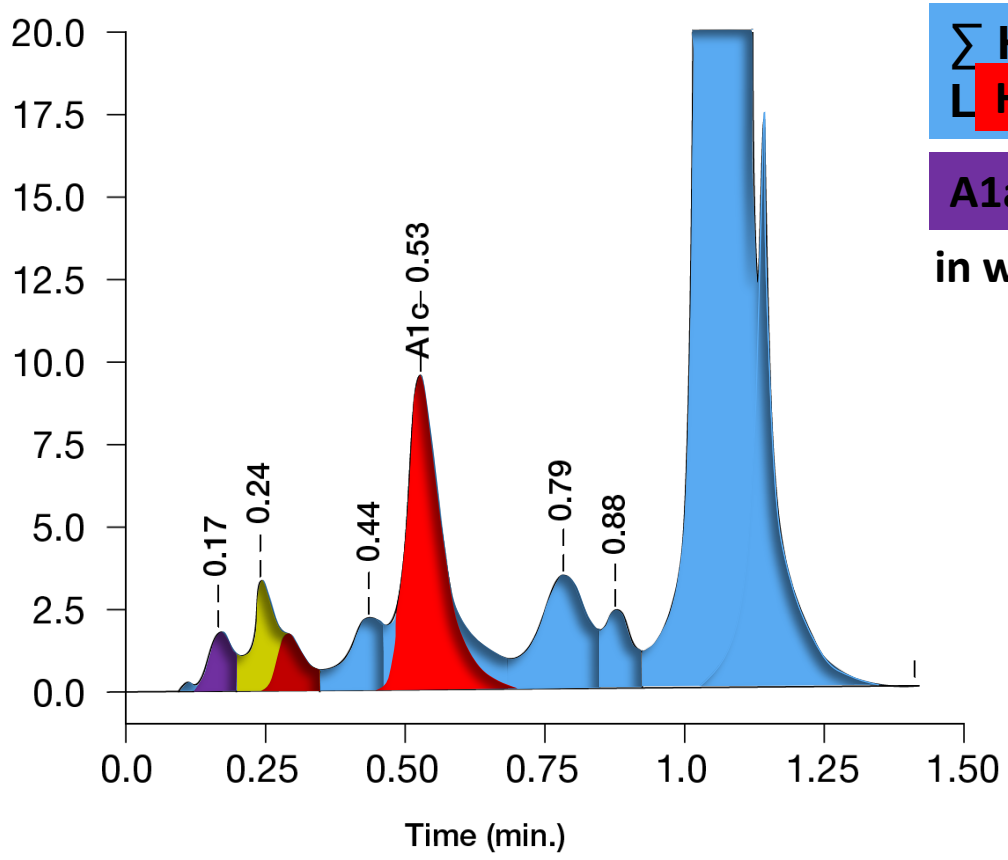
Fœtal Hb

- **Increased level of HbF in case of**
  - Hereditary persistence of HbF
  - β-thalassemia
  - Sickle cell disease
  - Pregnancy
  - Anemia
  - Leukemias
  - Diabetes (Insulin treatment)



Analytical interference on HPLC

Peak Name	Calibr	%	Retention Time (min)	Peak Area
A1a	—	[illegible]	0.170	24718
A1b	—	2.5	0.245	64268
LA1c	—	1.7	0.440	42265
A1c	9.6*	—	0.529	190731
P3	—	3.8	0.786	96362
P4	—	1.5	0.882	37068
Ao	—	82.0	1.044	2069482



%HbA1c =

[100 x (HbA1c area / ∑ HbA area)]

∑ HbA area = ($HbA1a_1/a_2$ /a HbA1b A1b + L HbA1c HbA1c + P3 + HbA0)

$A1a_1$ +$A1a_2$ & A1b are minor glycated HbA

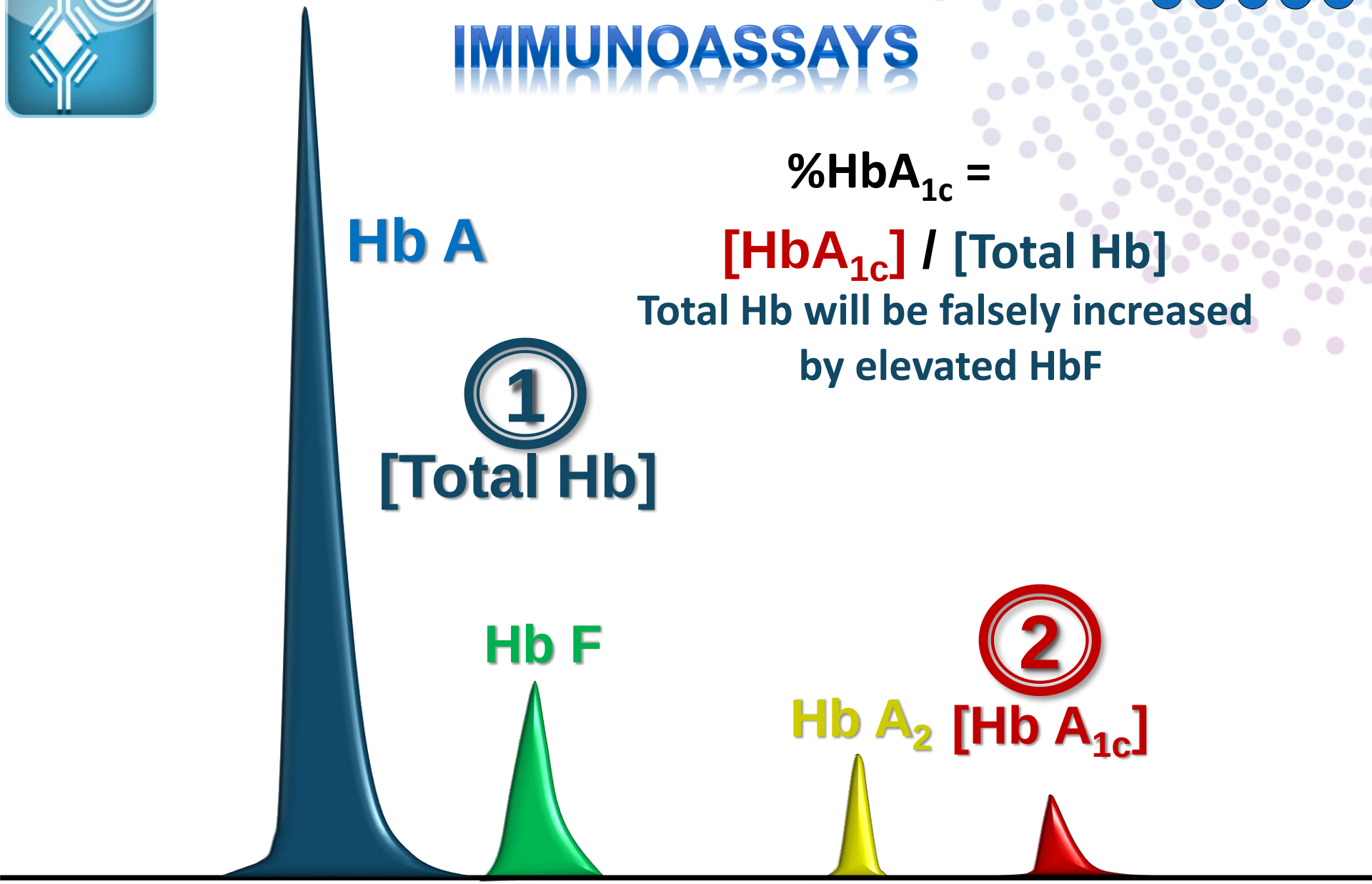
in which the HbF co-elutes

IMMUNOASSAYS

$\%HbA_{1c}$ =

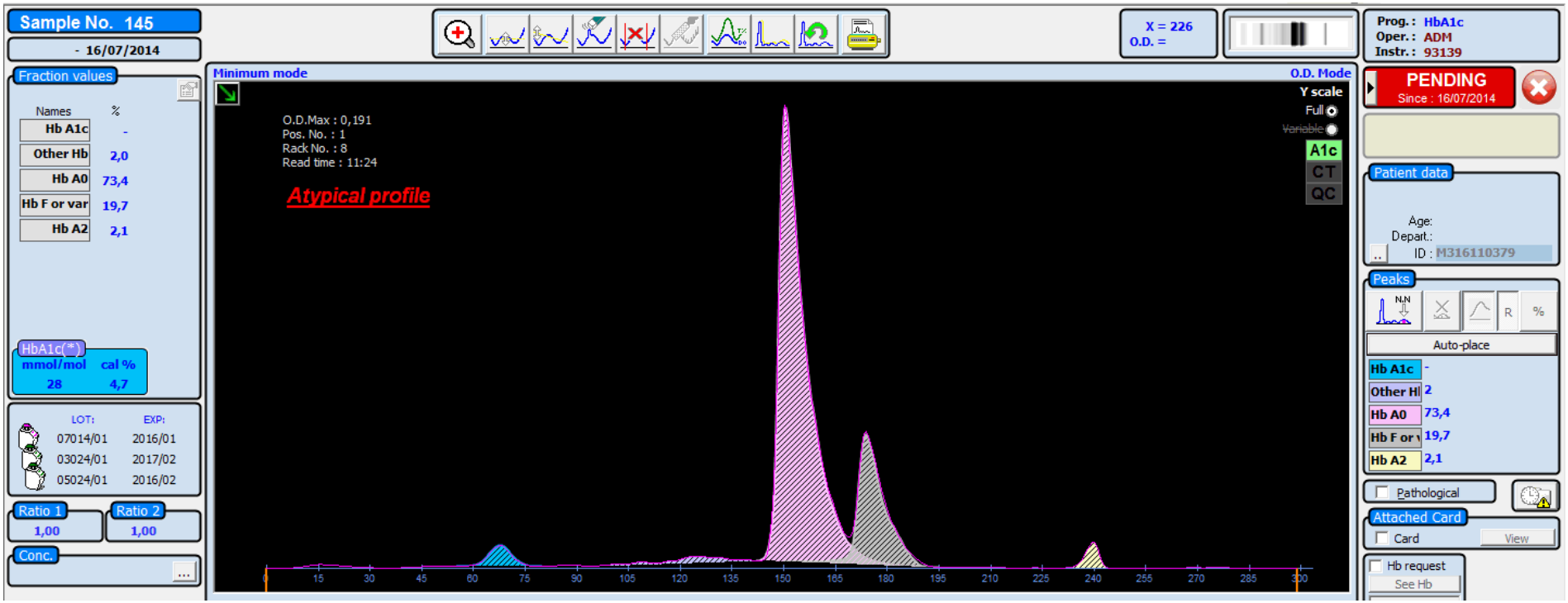
$[HbA_{1c}]$ / [Total Hb]

Total Hb will be falsely increased by elevated HbF



CAPILLARY ELECTROPHORESIS

Profile with HbF ≤23%, Hb A1c can be reported with a comment after evaluating the clinical context



What should we pay attention to? *Biological/clinical interferences*

- **Presence of any pathological condition that could impact Hb A1c production (clinical and/or analytical interferences):**
  - Iron Deficiency Anemia
  - Vitamine B12 deficiency
  - Antiretroviral treatment
  - Hyperthyroidism
  - Etc

Factor influencing A_{1c}	Increased A_{1c}	Decreased A_{1c}	Variable change in A_{1c}
1. Erythropoiesis	Iron deficiency, vitamin B_{12} deficiency, decreased erythropoiesis	Administration of erythropoietin, iron or vitamin B_{12}; reticulocytosis, chronic liver disease	
2. Altered hemoglobin			Fetal hemoglobin, hemoglobinopathies, methemoglobin
3. Glycation	Alcoholism, chronic renal failure, decreased erythrocyte pH	Ingestion of aspirin, vitamin C, vitamin E; certain hemoglobinopathies, increased erythrocyte pH	Genetic determinants
4. Erythrocyte destruction	Increased erythrocyte lifespan: splenectomy	Decreased erythrocyte lifespan: hemoglobinopathies, splenomegaly, rheumatoid arthritis, drugs such as antiretrovirals, ribavirin, and dapsone	
5. Assays	Hyperbilirubinemia, carbamylated hemoglobin, alcoholism, large doses of aspirin, chronic opiate use	Hypertriglyceridemia	Hemoglobinopathies

Figure 1 Factors influencing A_{1c}.

Adapted from Gallagher EJ et al, Journal of Diabetes 2009

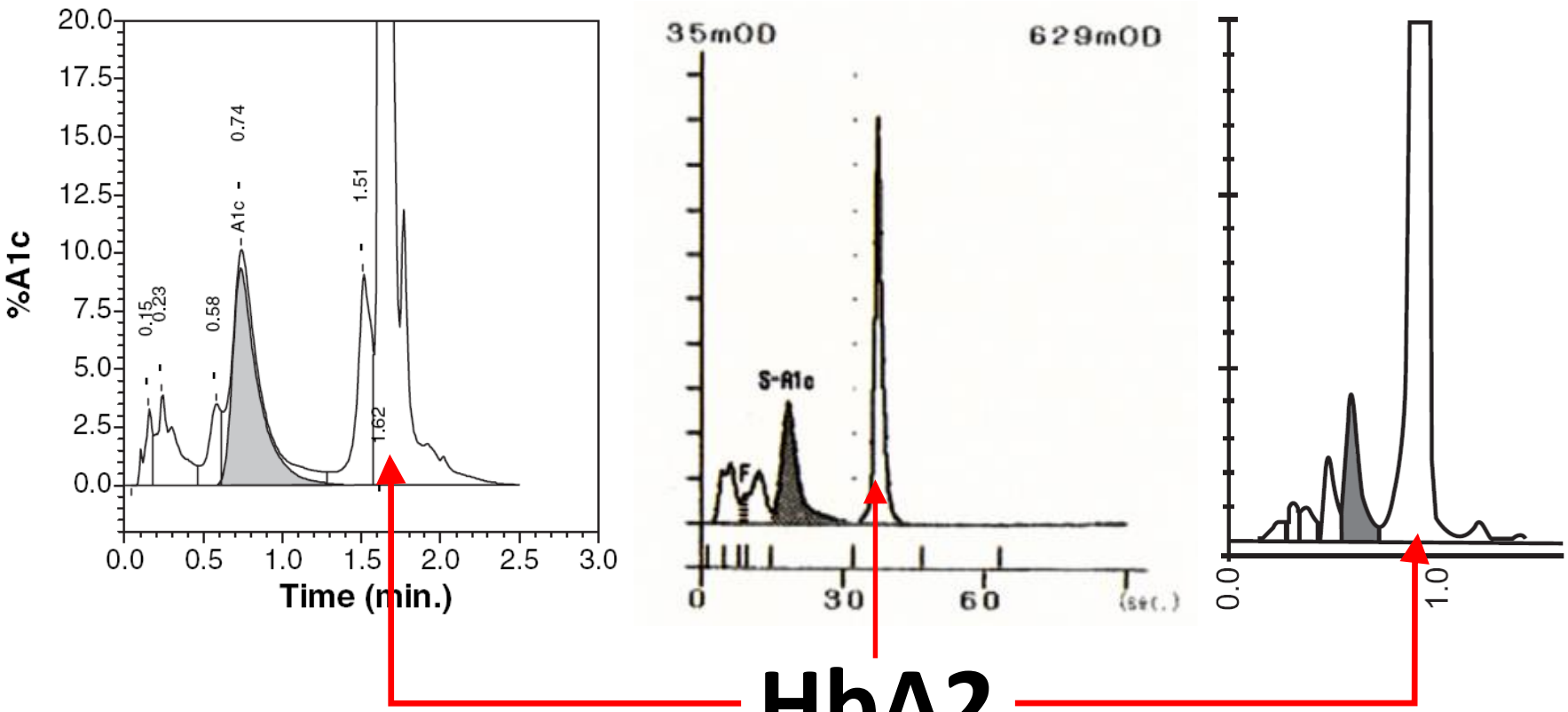
What should we pay attention to?
Biological/clinical interferences

Pathology	Effect on Hb A1c	Effect on Hb
Iron Deficiency Anemia	Spuriously high Hb A1c values	Lowered Hb A2
Vitamine B12 deficiency	Spuriously high Hb A1c values	Elevated Hb A2
Antiretroviral treatment	Spuriously low Hb A1c values	Elevated Hb A2
Hyperthyroidism	Spuriously high Hb A1c values	Elevated Hb A2

Hb A2 can be seen and quantified by CE and few HPLCs

What should we pay attention to?
Biological/clinical interferences

HPLC using short elution program (HbA1c mode)

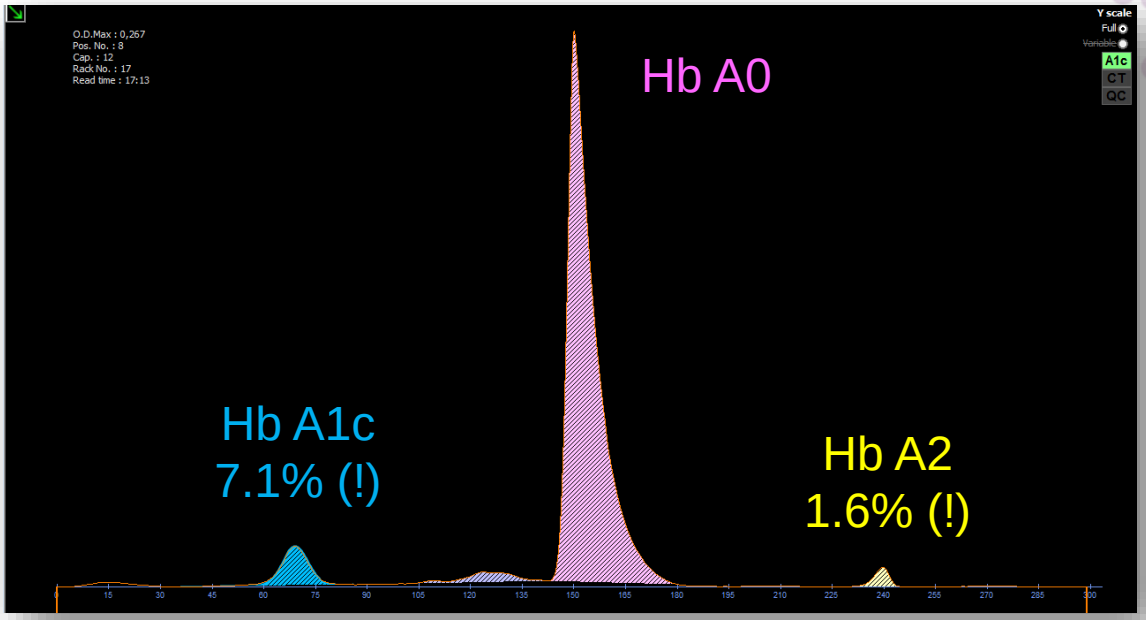


What should we pay attention to?
Biological/clinical interferences

Female, 57y

MCV = 77.6 fl (!)
Iron = 6.06 µmol/l (!)
Ferritine = 13.3 µg/l (!)
Transferrine = 3.38 g/l (!)

IDA, possibly leading to spuriously high Hb A1c value



Detection and quantification of the Hb A2 while Hb A1c is measured

Presence of SEBIA Hb A1c capillary technology in the Nordic countries

(Dark-Green) Estonia. **(Light-Green)** The rest of the European Union (EU). **(Dark-grey)** The rest of Europe. **(Light-grey)** The surrounding region.

SEBIA Hb A1c capillary technology experience worldwide

- Allows autonomous overnight running for big laboratories
- Faster TAT compared to track solution
- Cost saving solution compared to total laboratory automation
- Many possibilities of workflow due to multiple techniques on board and the system flexibility

St Giovanni hospital in Florence, Italy
Two MC3 configurations for HbA1c/Hb and P6/IT

Sebia support
Scientific Activities

We value and support good scientific practices

Main activities

- Technology evaluations
- Laboratory accreditation
- Clinicians' education programs
- User's assistance for interpretation
- Scientific Advisory Board
- KOL collaboration

The Sebia support

Customer support – STC and Sebia Academy

- Fully dedicated to total customer satisfaction offering daily assistance for technical and scientific matters

- Second Level support composed by 6 PhDs, highly qualified to answer to the customers needs

SCIENTIFIC AND TECHNICAL SUPPORT

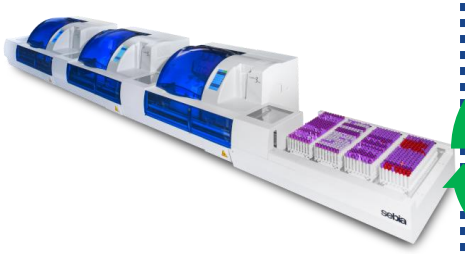
The Scientific Support Department based in our local Headquarters and at the Sebia affiliates level is dedicated to ensure customer support – 6 Highly qualified PhD

Sebia Academy

In the last 3 years, the Scientific & Technical Support Department at the Headquarters in France, delivered training to about 5600 people (customers and distributors), both on site and during local events.

Unique Sebia Hb A1c Separative Solution: We do it right, better, and faster!

Direct customers
Laboratories



Productivity
Walk-away
Accuracy

Indirect customers
Clinicians

Accuracy
Medical expertise

Indirect customers
Patients

Comprehensive results
Reliable treatment

Accurate and Fast Diagnostic → Optimal treatment → Less complication

Conclusions

sebia

Conclusion

- **Hb A1c is an important diabetes marker**
  - Long-term glycemia
- **Hb A1c responds to a strict IFCC definition and calculation**
  - Hb A1c is not glycated hemoglobin
- **Hb A1c production is sensible to pathologies affecting RBC lifespan**

Conclusion

- **When choosing/using Hb A1c method, we should pay attention to:**
  - The analytical performances (CV and bias)
  - The analytical interferences (all conditions that interfere with the measure)
  - The biological/clinical interferences (all condition that can lead to misinterpretation of the Hb A1c value)

- **Only separative technique (such as capillary electrophoresis) bring medical added values**
  - Allow simultaneous detection of several pathological conditions
  - Permit a correct Hb A1c interpretation

Any questions?

Tänan tähelepanu eest!