APFCB/ Siemens/ AACB Educational Webinar 24/6/2011

1. IFCC Standardisation of HbA1c
2. Global Units for HbA1c

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Member – IFCC Working Group on Standardisation of HbA1c 1994-2010

Diabetes

Global Epidemic

1985	30 Million
2000	180 Million
2025	320 Million

Long Term Complications

Juvenile Diabetes

15-20% dead in 20 years

40-50% dead in 30 years

Responsible for:

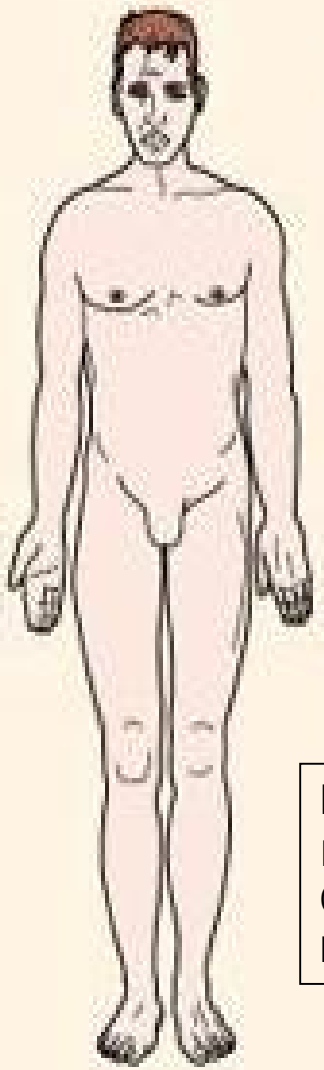
12% of all cases of blindness

25% of all cases of renal failure

40% of all non-traumatic foot and leg amputations

Major long-term complications of Diabetes

Type I Mortality
5.4 -11.5 X ND
Average life expectancy
70% of ND



Retinopathy:
visual impairment
and blindness

25X ND

CVA	2-4X ND
AMI	2-4X ND
PVD	4X ND

Autonomic neuropathy:
diarrhea, impotence

Macroangiopathy:
coronary heart disease
peripheral vascular disease

Gangrene or amputations
15-40X ND
Loss of sensation in feet
60-70% loss

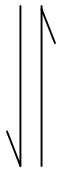
Nephropathy: 15X ND
renal failure

Diabetic foot:
peripheral neuropathy
and ischemia, foot ulcers,
amputations

Reproduction
Impotence 40% versus 5% ND
Congenital malformations in
Pregnancy 2-3X ND

HbA1c FORMATION

Glucose + β N terminal valines HbA



Non Enzymatic
Reversible

Aldimine HbA1c

Non Enzymatic
Irreversible

KETOAMINE HbA1c

60% Glucose binding β N valines
40% Glucose Binding is on the α N Terminal valines and the α and β side chain Lysine groups
(11 on each of 2 α and 2 β chains)

HbA1c GLYCAEMIC CONTROL PARAMETER

50% determined by MBG in past month

25% determined by MBG in prior 1 – 2 months

25% determined by MBG in prior 3 – 4 months

Reference:

Diabetes Care 1993; 16: 1313-4. Tahara, Shima

AIM

The IFCC WG was formed in 1994 with its aim to establish a Global Reference System for HbA1c.

Specific aims were:

(a) To define the heterogenous HbA1c
(b) To prepare pure HbAO and HbA1c
(c) To develop a Reference Method
(d) To establish a Reference Laboratory Network
(e) To prepare secondary reference calibrators and controls
(f) Uniform calibration of commercial methods
(g) Method comparisions vs DCM (USA, Sweden and Japan)

Note: No mention of Global Units

IFCC HbA1c Working Group Members

1994	(8)
Netherlands	3
USA	2
Australia	1
Japan	1
Sweden	1

2009	(13)
Netherlands	2
USA	3
Australia	1
Japan	2
Sweden	1
Germany	2
Italy	1
UK	1

IFCC Working group for standardisation of HbA1c

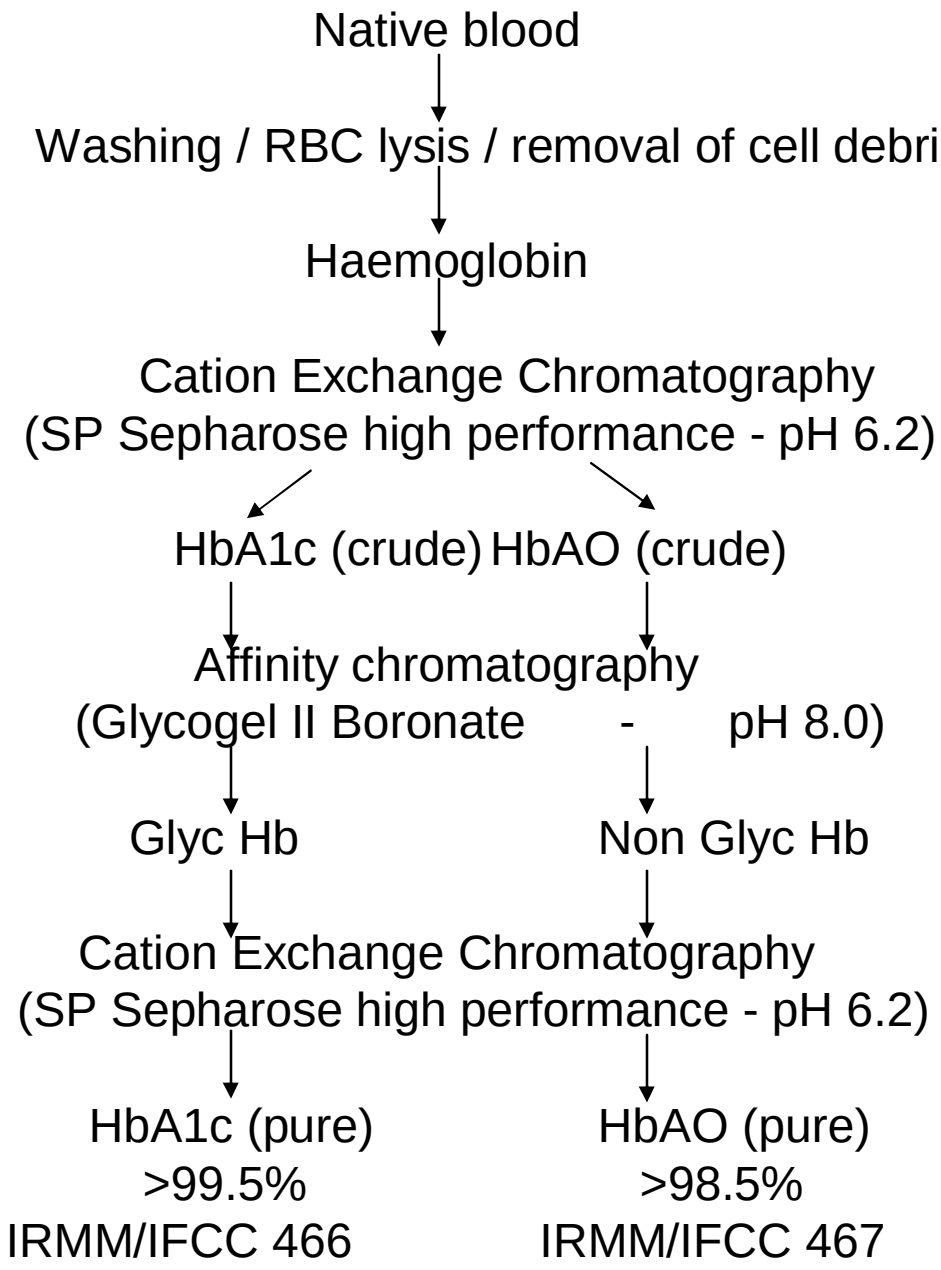
DEFINITION OF HbA1c

HbA1c consists of 2 alpha and 2 beta subunits. 60% of glucose binding occurs on the N terminal valines of the β chains. 40% occurs at lysine side chains on both α + β chains. Glycation is therefore heterogenous.

The IFCC WG has defined HbA1c as βN valine glycated Hb.

(β-N-(1-deoxy)- fructosyl Hb), a hexapeptide, representing the major glycation site of the HbA1c molecule.

PURIFICATION SCHEME FOR THE ISOLATION OF HbA1c AND HbAO

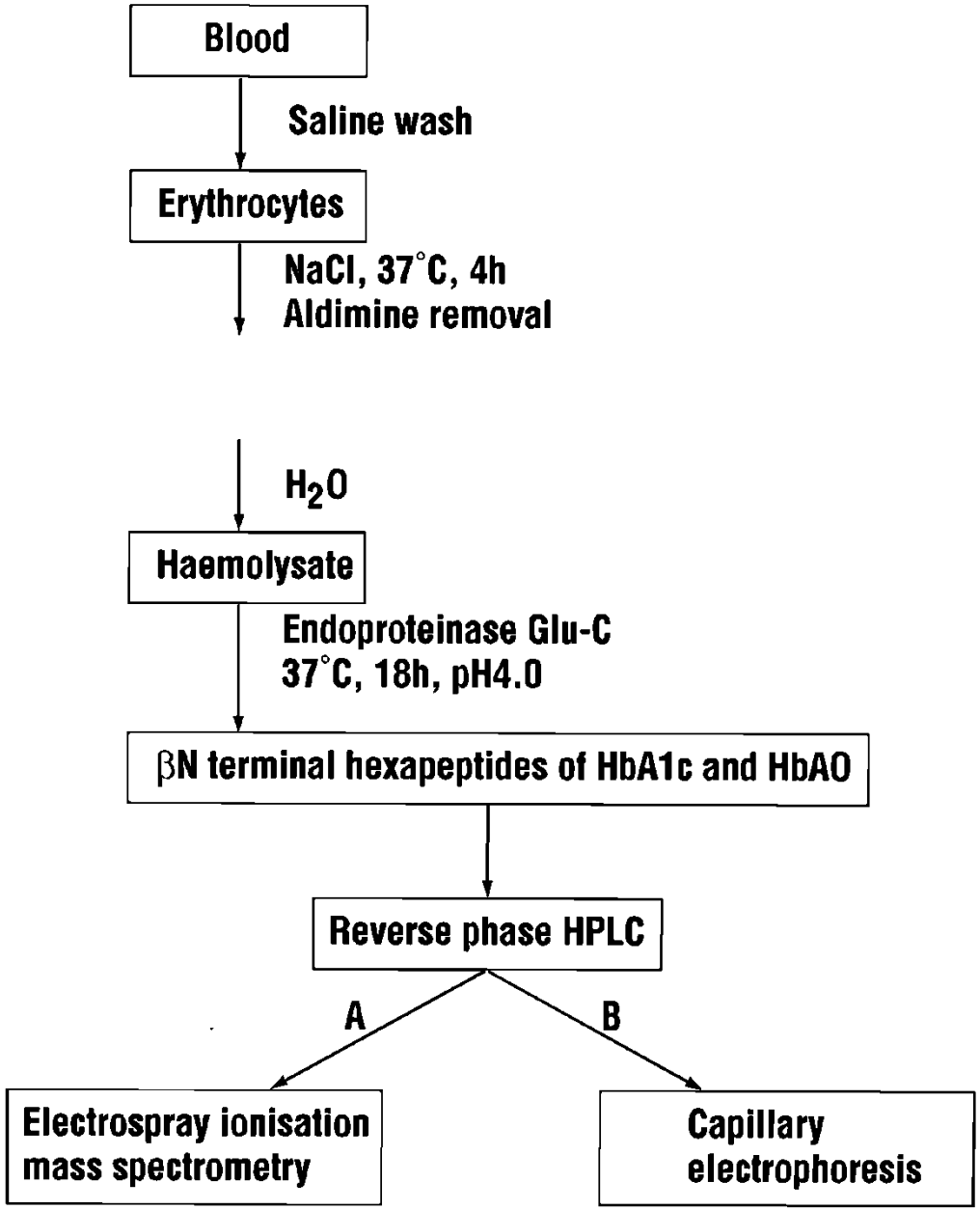


CALIBRATORS FOR THE REFERENCE METHOD

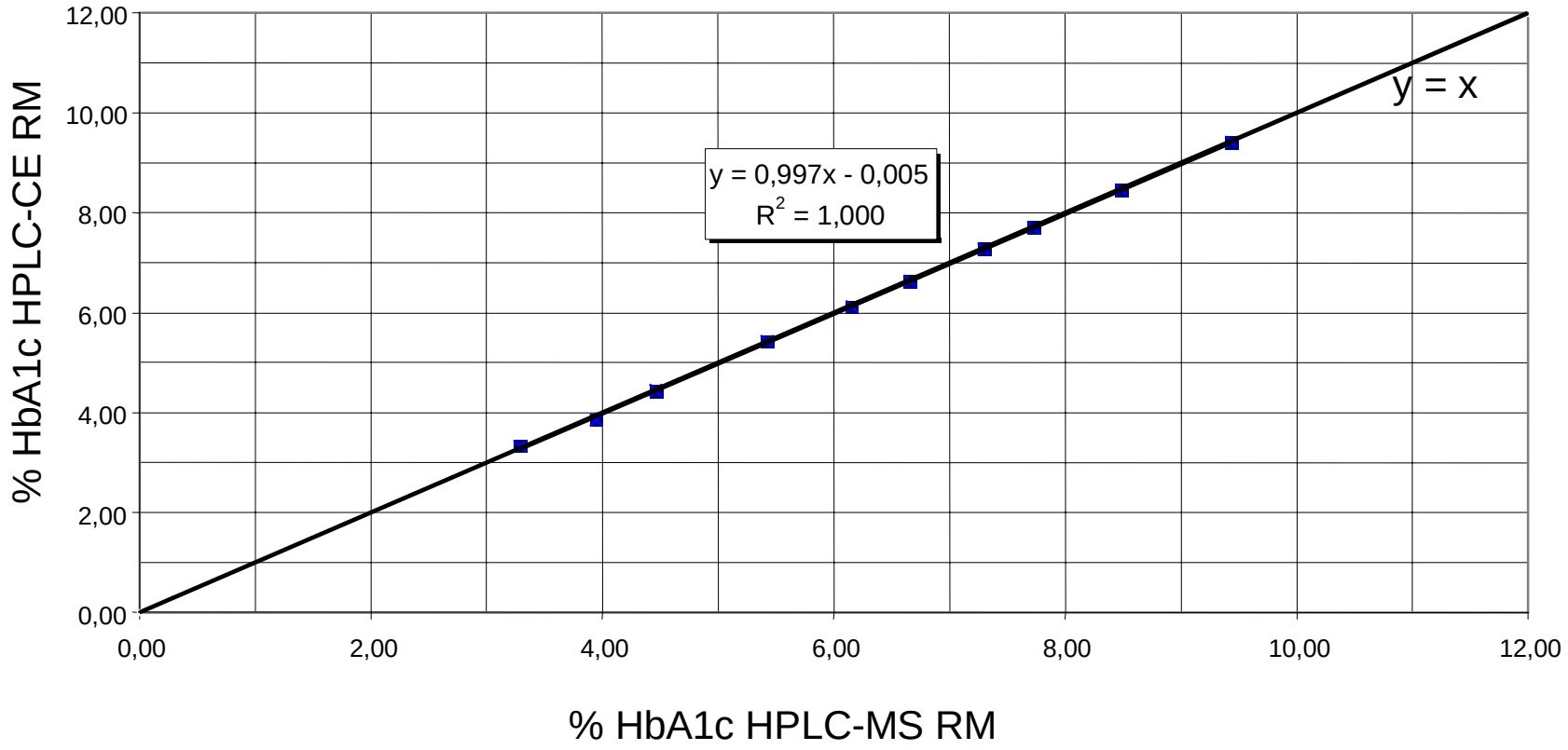
- The calibrators are mixtures of pure HbAO and HbA1c
- A calibrator set consists of six calibrators with different HbA1c concentrations covering the clinically relevant concentration range (0, 3, 6, 9, 12, 15 % HbA1c)
- The preparation is done according to a detailed SOP
- The calibrators are stable at -70°C for at least 5 years
- A New lot is manufactured each year

  Year 1 Checking / confirmation
  Year 2 Used as calibrators
  Year 3 Checking / spare calibrators

IFCC REFERENCE METHODS



COMPARISON HPLC-MS VERSUS HPLC-CE
(4 MS reference labs and 6 CE reference labs)



IFCC NETWORK OF HbA1c PRIMARY REFERENCE LABS

The main task of the IFCC Network is the reliable assignment of HbA1c target values to reference materials, reference panels of blood samples and control materials which are necessary for the implementation and maintenance of the system.

Each Network Laboratory has established one or both (GCMS / Cap EPG) IFCC Methods

Between lab CV% <2.5%

IFCC NETWORK OF PRIMARY REFERENCE LABORATORIES

Atlanta - CDC	USA	MS CE
Colombia – University Hospital (NGSP)	USA	CE
Dusseldorf - Diabetes Institute	Germany	MS
Dusseldorf - Instand	Germany	MS CE
Kanagawa - Biopathological Medicine	Japan	CE
Kawasaki - Standard Reference Centre	Japan	CE
Malmoe - University Hospital	Sweden	CE
Milano - Technological Biomedicine	Italy	MS
Norwood – Bayer Healthcare	USA	MS
Penzberg - Roche Diagnostics	Germany	MS
Tokyo - Keio University Clinical Laboratory	Japan	CE
Winterswijk - Clinical Laboratory	Netherlands	CE
Zwolle - Clinical Laboratory	Netherlands	CE

Total 15 6 x MS 9 x CE

IFCC NETWORK OF HbA1c REFERENCE LABS - ANALYTICAL PERFORMANCE

- The Network runs two intercomparison studies per year
  (6 - 10 samples, range 4 - 12 % HbA1c)

- The labs have to meet performance criteria for precision and trueness in order to be confirmed as approved IFCC reference lab.

- Excellent performance of the Network has been achieved in 20 intercomparison studies

- The Network is able to assign IFCC HbA1c values to reference materials, calibrators and control materials with a very low uncertainty

METHOD COMPARISON STUDIES - PARTICIPANTS

IFCC Network

11 Approved Labs	7 Europe	Kobold, Mosca (2x), Jeppsson Miedema, Weykamp, Susanto
	3 Japan	Hoshino, Umemoto, Takei
	1 USA	Vesper (CDC)
4 Candidates *	2 Europe	Siekmann, Reinauer
	2 USA	Gleeson, Little

DCM's

8 NGSP Network	4 USA	Little, Patel, Nowicki, Cole
	4 Europe	Miedema (2x), Weykamp (2x)
3 JDS	3 Japan	Hoshino, Umemoto, Takei
1 Mono-S	1 Europe	Jeppsson
1 Australia	1 Australia	Goodall
Manufacturers	8 Europe	Bio-Rad, Roche, Menarini, Provalis, Axis Shield, Drew, Olympus, Thermo Electron
	2 Japan	Tosoh, Arkray (Menarini)
	7 USA	Abbott, Bayer, Bio-Rad, BioMerieux Beckman, Primus, Dade-Behring

* All approved as of 2005

IFCC Laboratory Network

IFCC Approved HbA1c Network Laboratories (2011)

- Germany 2
- Italy 1
- Japan 3
- Netherlands 2
- USA 3

IFCC Candidate Reference Laboratories (2011)

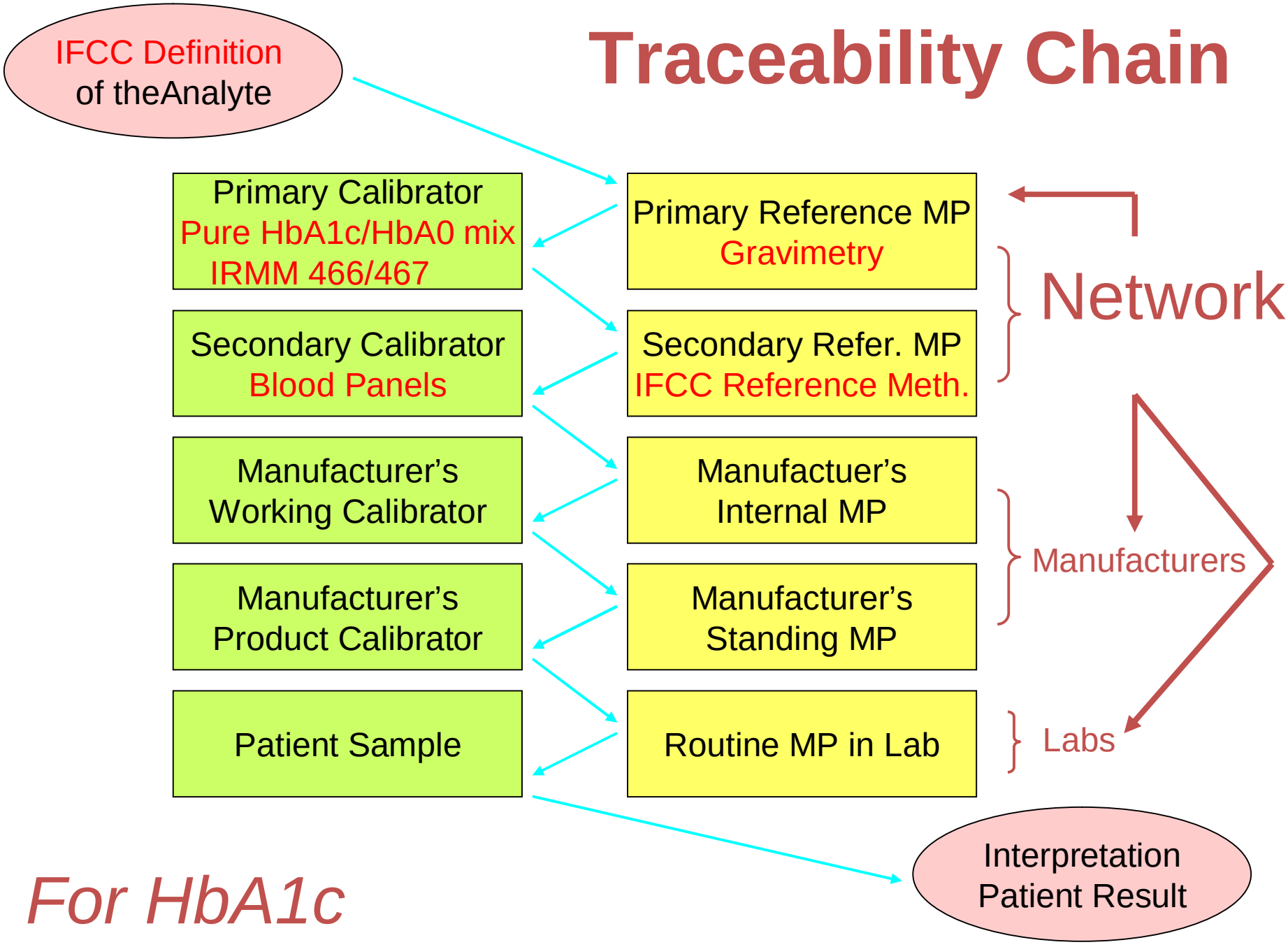
- China (Shanghai)
- France (Reims)
- India (Calcutta)
- South Korea (Seoul)

IFCC laboratory network website: www.ifcchba1c.net

CURRENT DESIGNATED COMPARISON METHODS (JAPAN, SWEDEN, USA)

- All arbitrarily based on different HPLC ion-exchange methods.
- HbA1c is a % peak in a chromatogram.
- Due to interferences, all these methods define their own 'HbA1c' and in %HbA1c values are different for each DCM.
- All DCM's are non specific; possible contamination of the HbA_{1c} peak, while not all HbA1c elutes under the one peak, some under HbAO peak.
- HbA1c numbers are only relative (not true HbA1c values).

Traceability Chain



For HbA1c

CURRENT NATIONAL STANDARDISATION SCHEMES

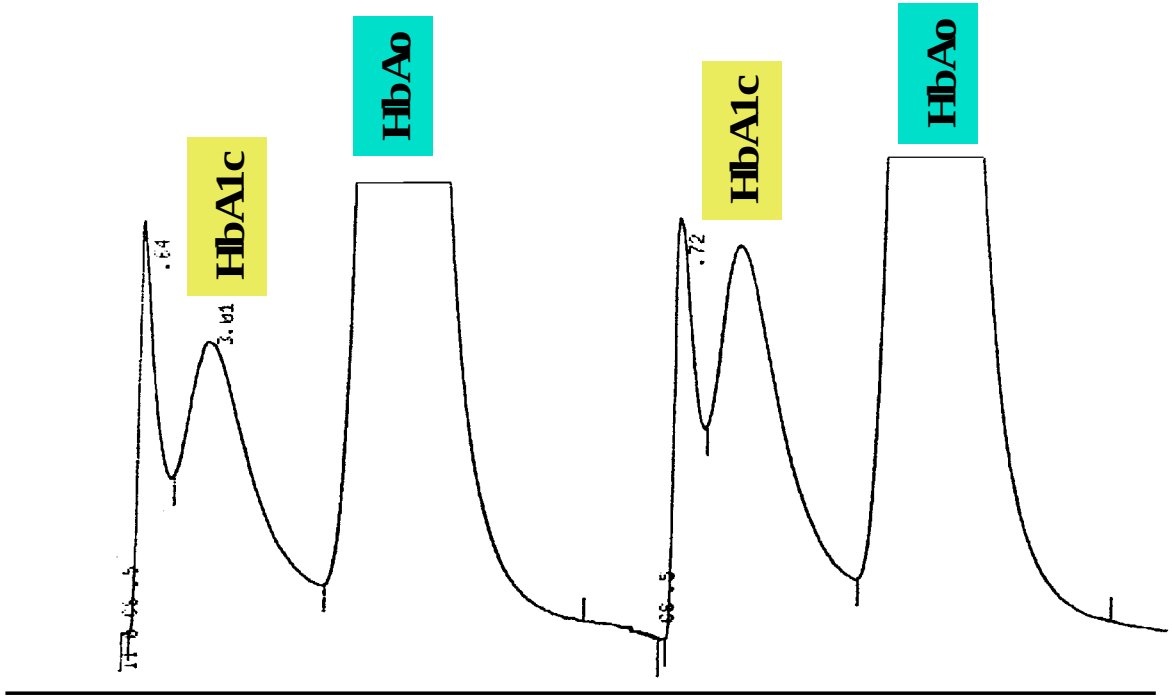
USA	NGSP	Biorex 70 HPLC Method 1983 (DCCT)
JAPAN	JDS/JSCC	National Calibrators (1995) Tosoh / Kyoto Daiichi. HPLC mean
		Now KO500 HPLC (2000) (Set to 1995 values)
SWEDEN	Swedish Clinical Chem Soc JO Jeppsson	
		Mono S Cation Exchange HPLC

REST OF THE WORLD
Mainly NGSP, based on commercial methods calibrated to DCCT / NGSP and includes

Australia and New Zealand
Europe (except Scandinavia)
Asia (except Japan)
Africa, South and Central America

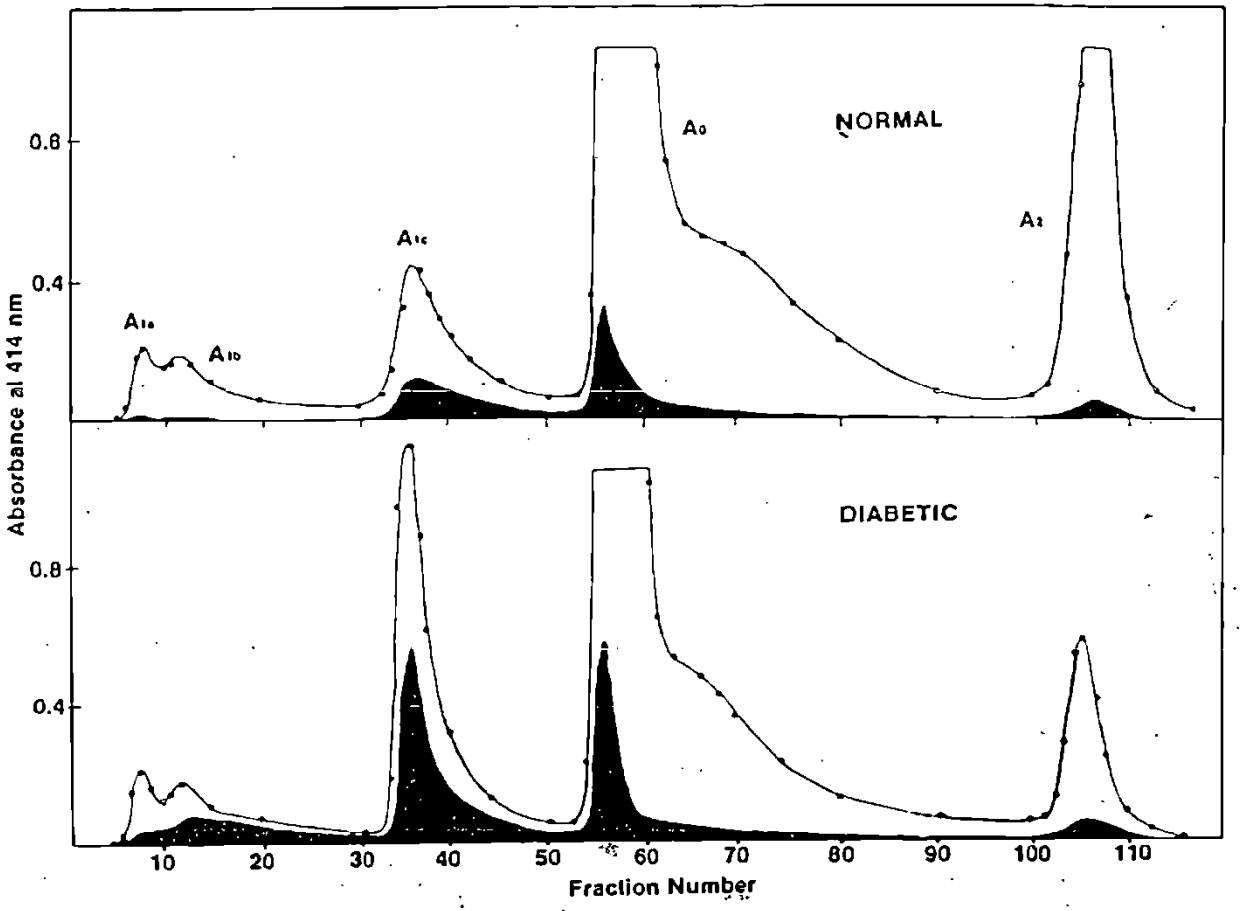
NGSP DESIGNATED COMPARISON METHOD

Typical Chromatograms of BioRex 70 (DCCT) Method



Reference of the method:
Goldstein et al. in Clark WL, LarNER J, Pohl SL eds.
Methods of Diabetes Research, Vol 2. Clinical Methods. New York 1986: 475-504

Figure 5 Chromatography of Normal and Diabetic Pools on BIO-REX 70.



Hemolysate pools (≈ 25 mg Hb) prepared from red blood cells of 5 normal and 5 diabetic individuals were dialyzed vs. 0.04 M sodium phosphate, pH 6.7, and applied to (1 × 30 cm) Bio-Rex 70 columns equilibrated with the same buffer at room temperature. Minor hemoglobin components were resolved using a step gradient: 0.08 M sodium phosphate, pH 6.5 (started at column fraction 30) and 0.3 M sodium phosphate, pH 6.5 (fraction 50). Fraction size: 2.0 ml. Flow rate: 10 ml/hr. Individual fractions were dialyzed and run on 1.0 ml boronate affinity columns to determine glycosylated components indicated by the shaded area.

NGSP TRACEABILITY / UNCERTAINTY

Method	Biorex 70 Cation Exchange HPLC Used for DCCT 1983 – 1993 Interference from abnormal Hb variants
Non Specific HbA1c	40% of HbA1c glycation HbF Minor Hb Forms Carbamylated Hb (Uraemic Adduct)

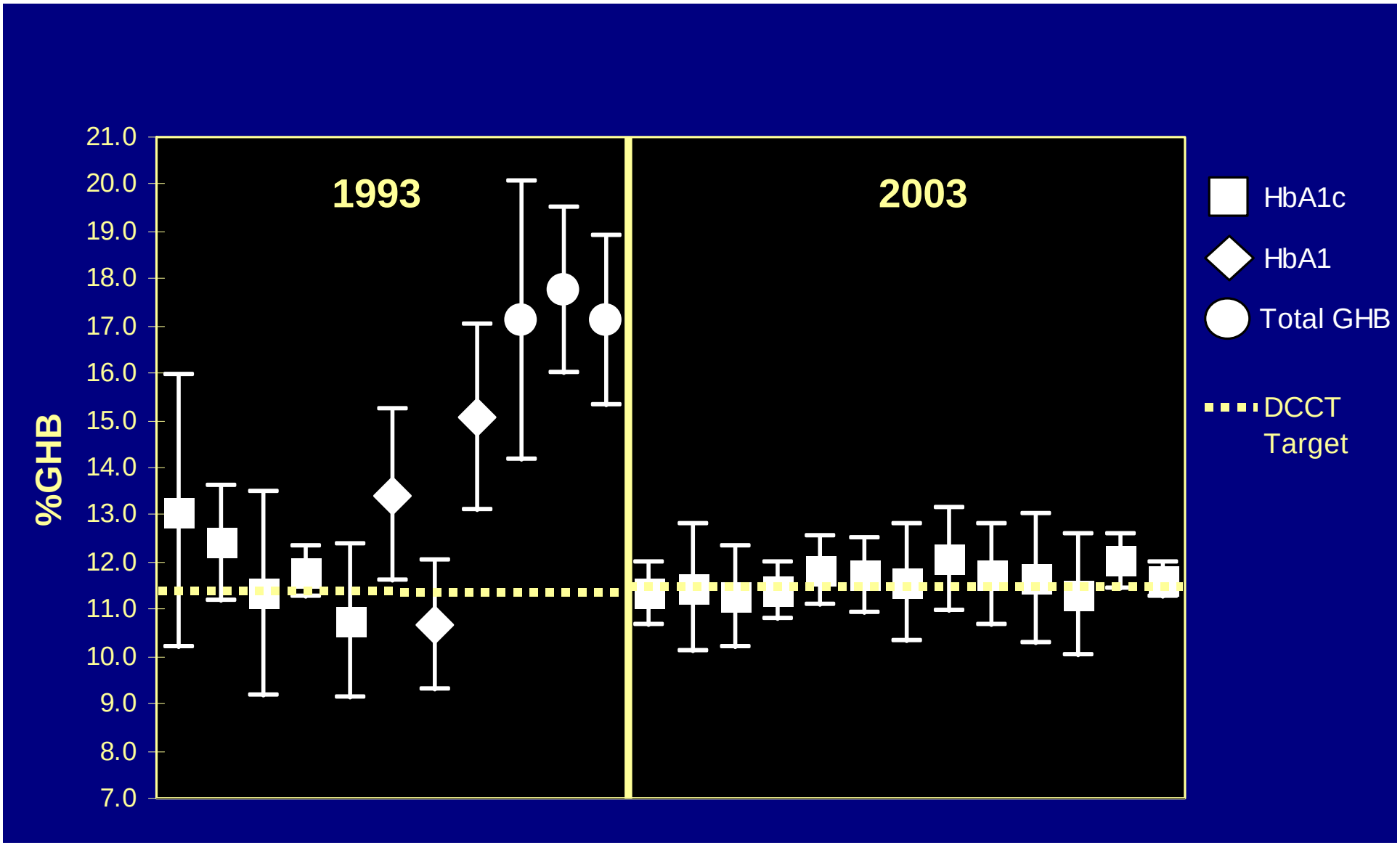
Poor Separation of Peaks HbA1a / HbA1b and HbA1c / HbF / Carb Hb

Non HbA1c peaks (HbA1a, HbA1b and HbAO) contain some Glycated Hb. Also HbA1c peak contains some Non Glycated Hb.

TRACEABILITY - Non specific peak on a 1980's HPLC Chromatogram

UNCERTAINTY - High

CAP SURVEY (mean ± 2SD)



MASTER EQUATIONS IFCC HbA1c v DCM HbA1c

- HbA1c-*NGSP* = 0.915 HbA1c-*IFCC* + *2.15* (r^2= *0.998*)
- HbA1c-*Japan* = 0.927 HbA1c-*IFCC* + *1.73* (r^2= *0.997*)
- HbA1c-*Sweden* = 0.989 HbA1c-*IFCC* + *0.88* (r^2= *0.997*)

Reference: Clinical Chemistry 50: 166-174 (2004)

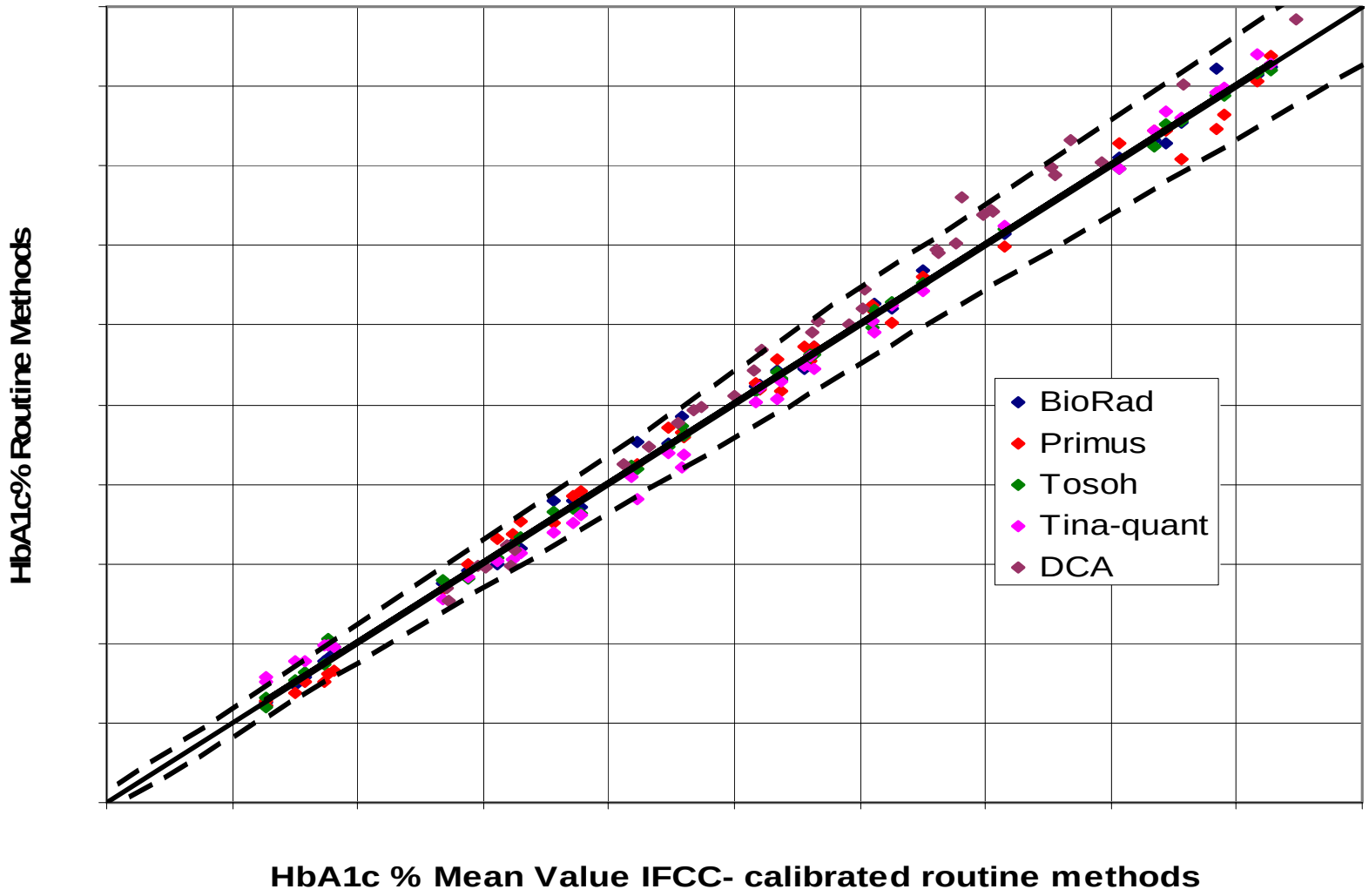
Clinical Chemistry 50:1
166–174 (2004)

Endocrinology and Metabolism

IFCC Reference System for Measurement of Hemoglobin A_{1c} in Human Blood and the National Standardization Schemes in the United States, Japan, and Sweden: A Method-Comparison Study

WIELAND HOELZEL,[1] CAS WEYKAMP,[2] JAN-OLOF JEPPSSON,[3] KOR MIEDEMA,[4*] JOHN R. BARR,[5] IAN GOODALL,[6] TADAO HOSHINO,[7] W. GARRY JOHN,[8] UWE KOBOLD,[1] RANDIE LITTLE,[9] ANDREA MOSCA,[10] PIERLUIGI MAURI,[11] RITA PARONI,[12] FRANSISCUS SUSANTO,[13] IZUMU TAKEI,[14] LINDA THIENPONT,[15] MASAO UMEMOTO,[16] and HSIAO-MEI WIEDMEYER,[9] on behalf of the IFCC WORKING GROUP ON HbA_{1c} STANDARDIZATION

COMPARABILITY OF RESULTS OF IFCC-CALIBRATED HbA1c ROUTINE METHODS



Clinical use of HbA1c

- Quality of patient care (long term monitoring)
- Outcome risk (complications)
- In USA, used for monitoring diabetes services/clinicians and programmes
- Non-diabetics –cardiovascular and stroke risk stratification
- Diabetes diagnosis (USA-ADA)

The A1C-Derived Average Glucose (ADAG) Study

International study designed to:

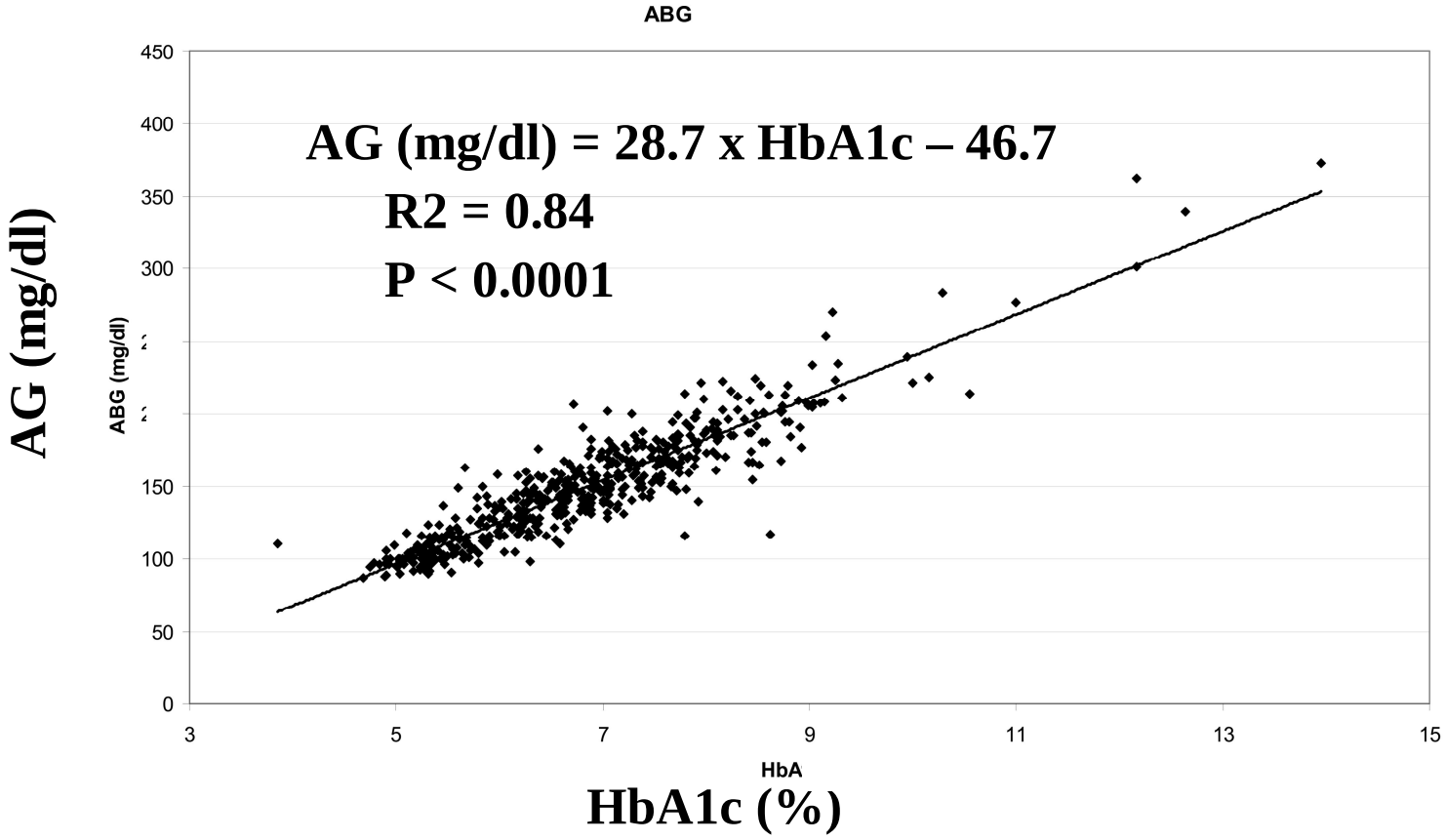
- Carefully look at relationship between HbA1c and average glucose
- Determine the mathematical relationship between the two for reliable conversion
- Establish that the relationship is valid across:
  - Diabetes types
  - A wide range of HbA1c levels and age
  - Different races/ethnicities

Nathan et al, Diabetes Care 31:1473, 2008

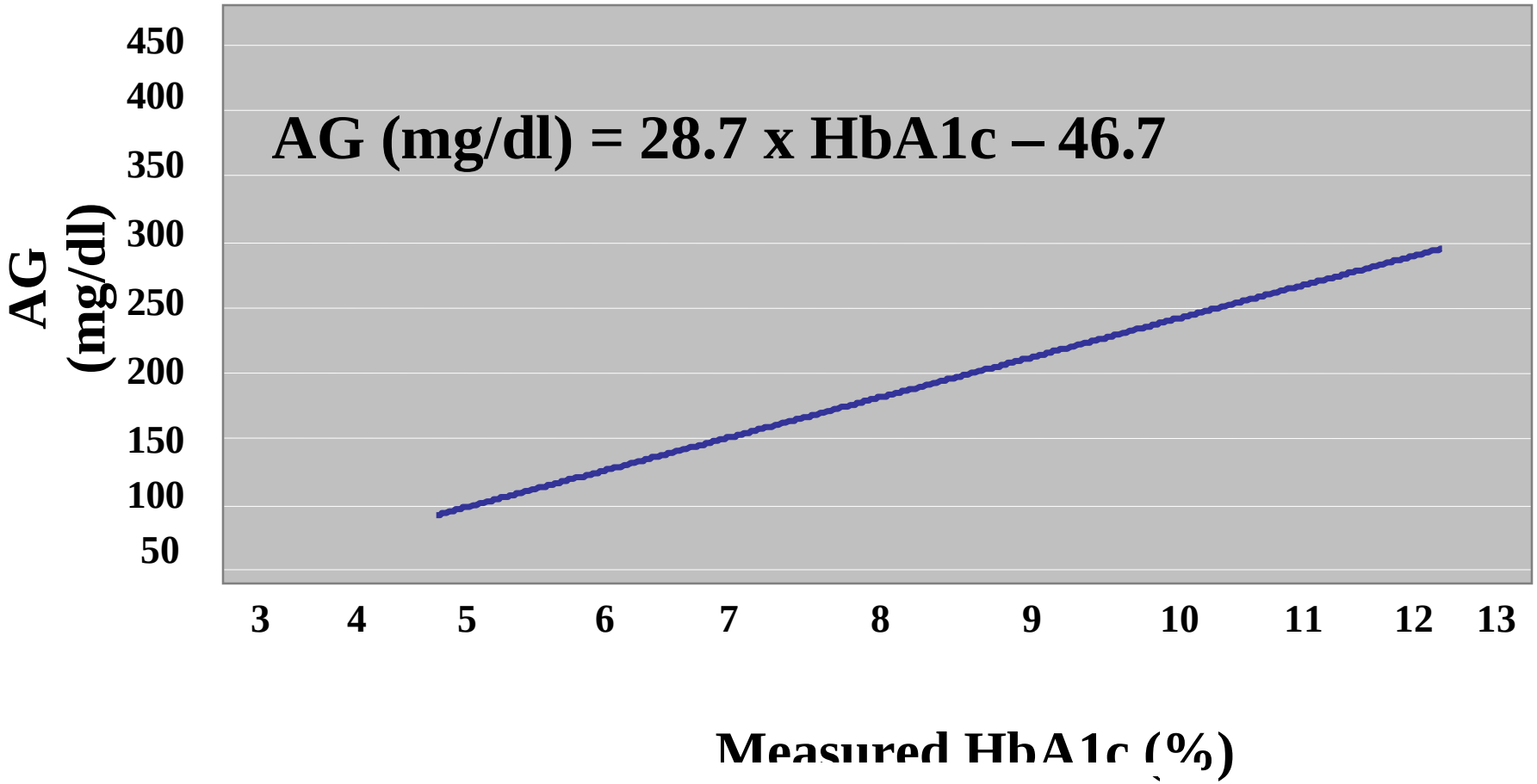
ADAG Study Centers

- Cameroon
- Denmark
- Italy
- The Netherlands
- United States
  - Boston
  - New York
  - San Antonio
  - Seattle
- India (site dropped due to specimen handling issues)

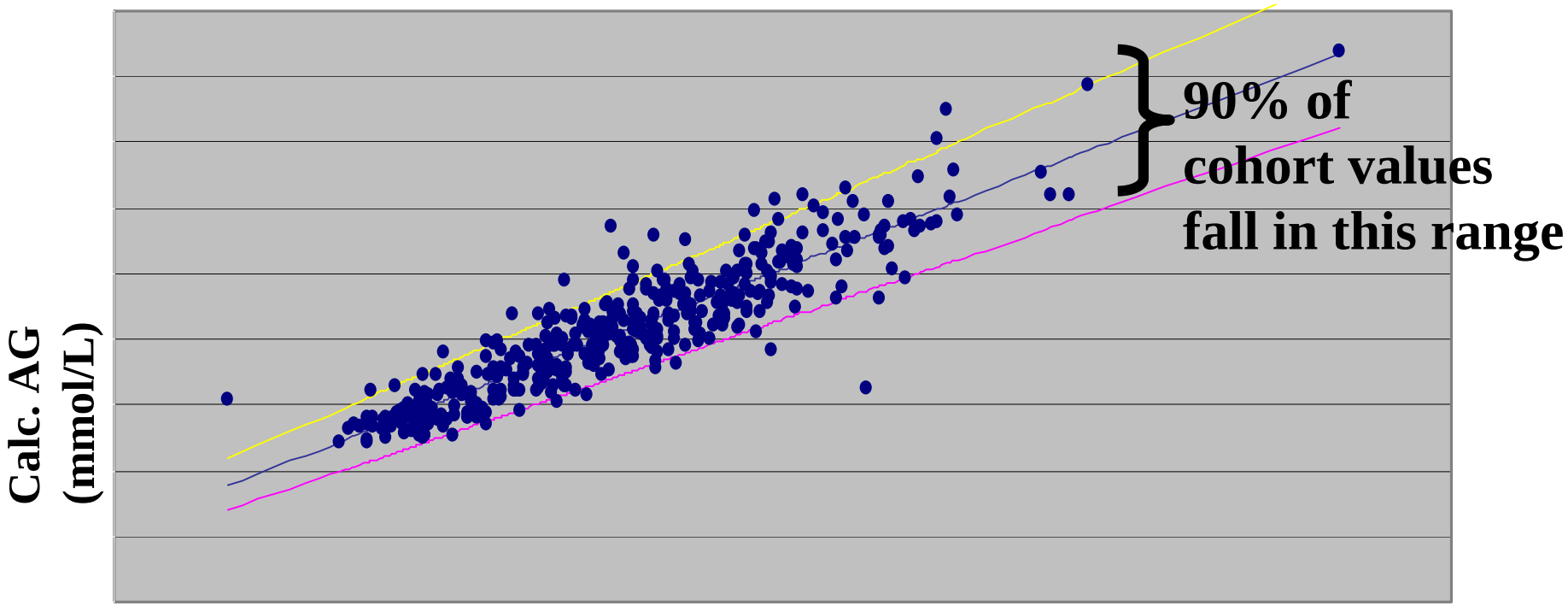
ADAG Study: Correlation of AG With HbA1c



ADAG Study Conclusion: HbA1c Correlates Highly With AG



ADAG Study: Study Success



90% of values fell within +/- 15%

eAG Study Negatives

- Only 507 patients worldwide
  - 268 Type 1, 159 Type 2, 80 non Diabetics
- Few patients with poor control
- Very limited ethnic groups
- No children
- Correlation results show imprecision and wide scatter

Correlation equivalents	HbA1c	eAG
ULN Level	6.0%	7.0 mmol/l
Poor Control Level	8.0%	10.2 mmol/l

Consensus Statements – Global HbA1c Units

2007 IFCC is only valid anchor for standardisation ADA/EASD/IFCC/IDF.

To report IFCC mmol/mol + NGSP/DCCT % (master equation) + ADAG (if passes criteria)

2009 ADA/EASD/IFCC/IDF/ISPAD

To report IFCC mmol/mol + NGSP/DCCT % (master equation) + eAG locally

2010 International HbA1c Consensus Committee

To report IFCC mmol/mol + NGSP/DCCT % (master equation)

To December 2011

2010 Reference CCLM 2010; 48: 775-6 (also ACB, Clin. Chem., CCLM, Diab. Care, Diabetologia, Diab. Med., Ped. Diab., Diab. Res & Clin. Pract.)

Comparison between HbA1c values under old and new reporting units

Current DCCT/NGSP aligned HbA1c (%)	New IFCC HbA1c (mmol/mol)
4.0	20
5.0	31
6.0	42
6.5	48
7.0	53
7.5	59
8.0	64
9.0	75
10.0	86
12.0	108

HbA_1c as indicator of Diabetes Control

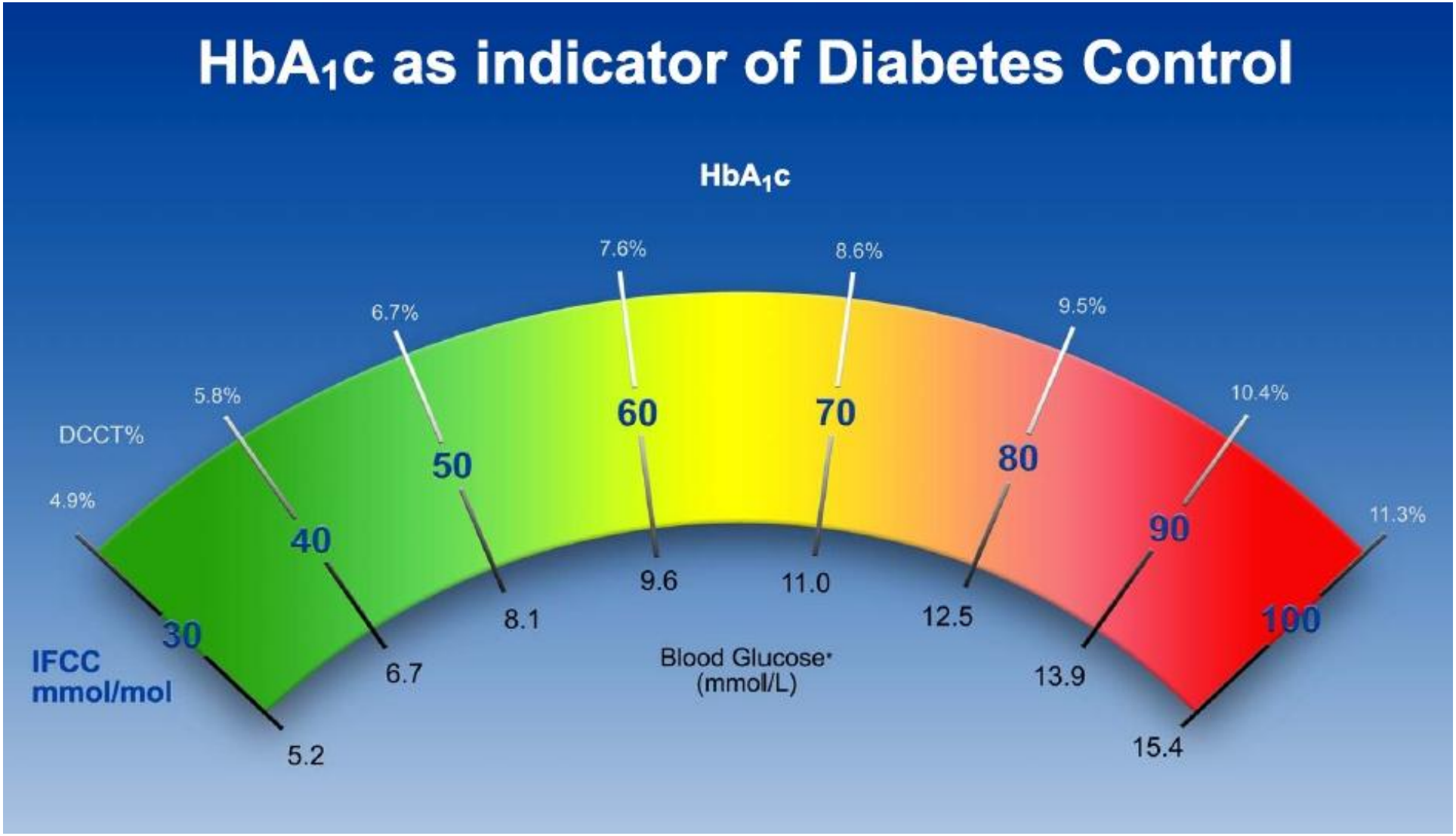


Table 2. Summary of progress made by selected countries for change in HbA1c reporting units

Country	Old Units %DCCT	Reporting of Dual Units %DCCT, mmol/mol Commencement date	Global Unit mmol/mol - Commencement date	eAG/ADAG - to be reported
Australia	%DCCT	To be confirmed	To be confirmed	No
Austria	%DCCT	No dates yet	No dates yet	No
Denmark	%DCCT	1/1/2010*	No dates yet	Yes
Finland	%DCCT	3/3/2010**	No dates yet	No
Germany	%DCCT	1/1/2009	1/1/2010	No
Italy	%DCCT	1/1/2010	1/1/2012	No
Netherlands	%DCCT	6/4/2010	1/1/2011	No
New Zealand	%DCCT	1/8/2009	1/8/2011	No
UK	%DCCT	1/6/2009	1/6/2011	No
Sweden	%Mono S	Mono S, mmol/mol 1/9/2010	mmol/mol 1/1/2011	No
USA* **	%DCCT	%DCCT	%DCCT	****

AACB website: "www.aacb.asn.au"

Footnotes to table:

* Denmark is reporting dual units (%DCCT, mmol/mol) as from 1/1/2010, together with automatic eAG to produce all three units on laboratory reports.

** Finland is reporting dual units (%DCCT, mmol/mol) as from 3/3/2010. eAG can be reported but is not mandatory. eAG must be requested separa tely to HbA1c.

*** The USA has not announced any changes in their HbA1c Units. They do not report any pathology in SI Units at all.

**** The USA Position on eAG is detailed as "the American Diabetes Association (ADA) and the American Association for Clini cal Chemistry (AACC) have determined that the correlation (r=0.92) obtained in the ADAG study (Reference 4) is strong enough to justify reporting both an A1c result and an estimated average glucose (eAG) when a clinician orders the A1c test." Diabetes Care 2010; 33 (Supplement 1): S19 .

AACB Position Statement on HbA1c Reporting Units (2)

Conversion Formula

- DCCT/NGSP % = 0.09148 X IFCC mmol/mol + 2.152
- IFCC mmol/mol = 10.93 X DCCT/NGSP – 23.50

- DCCT target of 7.0% = 53 mmol/mol
- DCCT change of therapy level of 8.0% = 64 mmol/mol
- Old DCCT RR of 4.0-6.0% HbA1c = 20-42 mmol/mol
- GTT Diagnosis of >6.5% HbA1c = >58 mmol/mol

2002 Consensus Statement

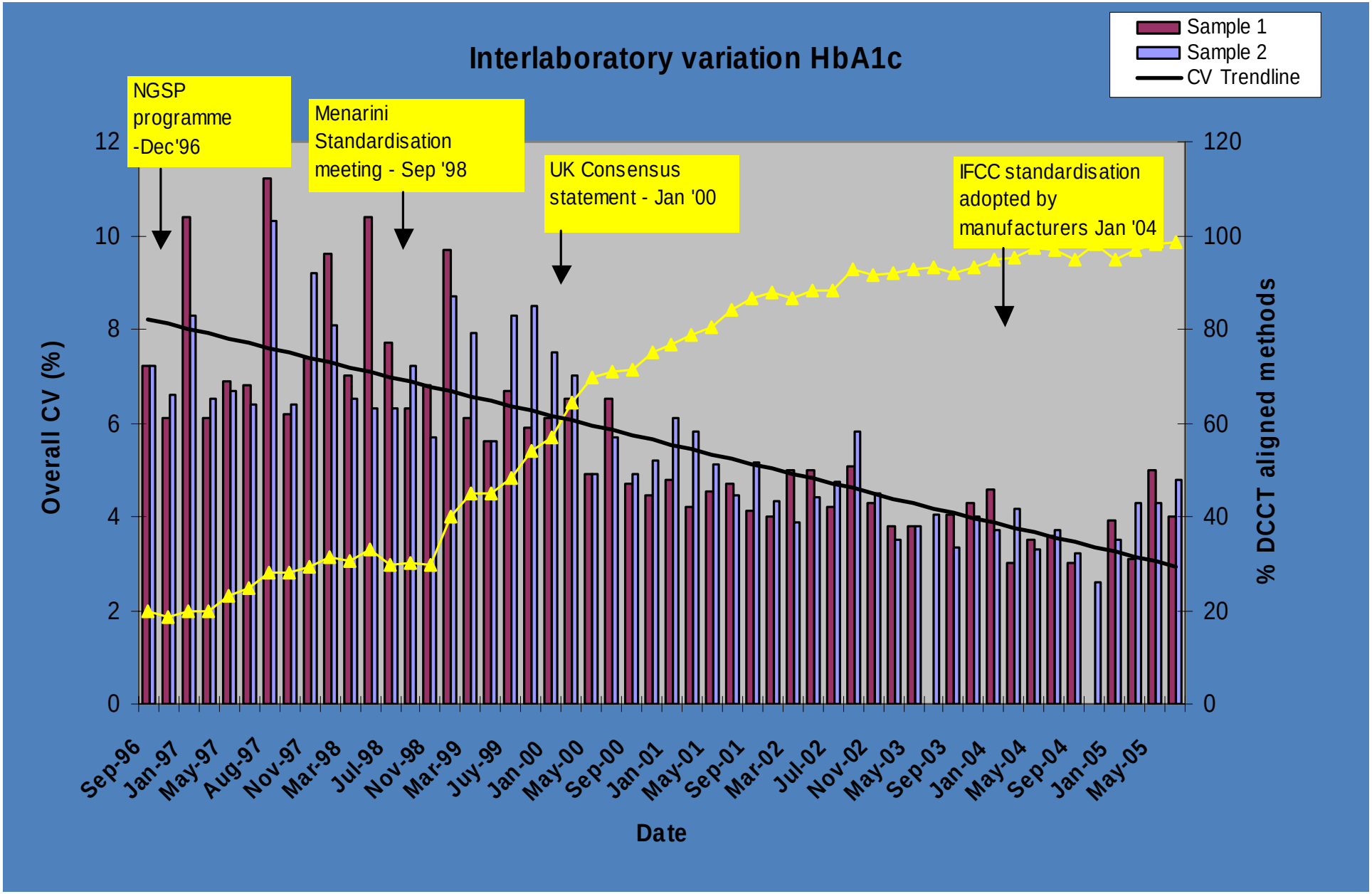
EASD, IDF, IFCC, AACC, ADA, CEN (Dusseldorf 2002)

Clinical requirements of a HbA1c test include:

- Low individual variance
- Precision that justifies clinicians acting on differences of 0.35% to 0.5% as being significant.
- HbA1c assays with CV < 2% for combined, between and within run.

(Diabetologia 2002;38:R19-21)

Between Laboratory Variability for HbA_{1c} results



HbA1c methods in use in Australia*

- Immunoassay (169 labs)
- HPLC (cation exchange) (98 labs)
- HPLC (affinity chromatography) (28labs)

* RCPA-AACB QAP 2009

Factors Effecting HbA1c

- Average blood glucose
- Standardisation - IFCC
- Red cell life span (haemolytic anaemia)
- Precision
  - Recomendation < 2% CV, Poor >3% CV
- Interferences
  - Abnormal Hb variants
  - Homozygous Hb variants (no HbA1c)
  - HbF (HPFH)
  - Ureamic adduct (Method dependant)

HbA1c methods and Hemoglobin Variants (Interference from HbS and HbC traits)

NGSP website (www.ngsp.org)

Method	Interference from HbS	Interference from HbC
Abbott Architect/Aeroset	**Yes**	**Yes**
Axis-Shield Afinion	No	No
Bayer (Siemens) Advia	**Yes**	**Yes**
Bayer (Siemens) DCA 2000	No	No
Beckman Synchron System	No	No
Bio-Rad D-10	No	No
Bio-Rad DiaStat	**Yes**	No
Bio-Rad Variant A1c	No	No
Bio-Rad Variant II A1c	No	No
Bio-Rad Variant II Turbo A1c	No	No
Dade Behring Dimension	No	No
Metrika A1cNOW	**Yes**	**Yes**
Olympus AU system	**Yes**	**Yes**
Ortho-Clinical Vitros	No	No
Primus HPLC (affinity)	No	No
Roche Cobas Integra *	**Yes**	**Yes**
Roche Cobas Integra Gen.2	No	No
Roche/Hitachi (Tina Quant II)	No	No
Tosoh A1c 2.2 Plus	No	No
Tosoh G7 Auto HPLC	No	No

*This method will be replaced by the Roche Cobas Integra Gen 2 by the end of 2007

Germany

Enacted a law which states that HbA1c assays must be reported only in SI units

1/1/2009 DCCT → DCCT + IFCC

1/1/2010 DCCT + IFCC → IFCC (mmol/mol)

eAG NOT to be reported

United Kingdom

Consensus Meeting ACB, London 23/1/2008

Convened by Dr Sue Roberts, National Director for Diabetes, UK Department of Health

19 Associations (Medical/Scientific/Diabetes/QC)

ACB/Assoc Clin Path/ Ass Brit Diabetologists/ Dept of Heath/ Diabetes UK/ Eur Fed Clin Chem/ IDF/ IFCCLM/ Medicine/ AACB/ Prim Care Diab Soc/ RC Path/ RC Phys/ RCGP/ RC Nursing/ RC Obstrets and Gynaec/ UK NEQAS/ Wales WEQAS

1/6/2009 DCCT → DCCT + IFCC

1/6/2011 → IFCC (mmol/mol)

eAG NOT to be reported

Publication – Diab. Med. 2008; 25: 381-2.

New Zealand (No Meetings)

NZSSD – NZ Society for Study of Diabetes

All professionals involved in the care of people with diabetes, 250 members

-Diabetes physicians, specialist nurses, podiatrists, dieticians, opthalmologists, general physicians, family doctors, community health, allied industries, medical scientists.

1/8/2009 DCCT → DCCT + IFCC

1/8/2011 → IFCC (mmol/mol)

eAG NOT to be reported

Italy

Working Group (20 Delegates/National Associations) meeting in Milan (2009)

Ital Soc Clin Bio/Clin Molec Biol (SIBioC) (Umbrella Org)

Publication – CCLM 2010; 48: 625-6

Changes in reporting units/new units

Relationship old vs new units

Timeline for Changes

Definition of analytical goals

1/1/2010 DCCT → DCCT + IFCC

1/1/2012 → IFCC (mmol/mol)

eAG NOT to be reported

Netherlands

Several meetings 2009. Ten associations

Assoc. Manufacturers Diagnostic Devices/ Assoc. GP specialising in Diabetes/ Foundation Diab and Nutrition/ Org. Professionals Diabetes Care/ Nat. Assoc. of Dieticians/ Org. Patients with Diabetes/ Nat. Org. Internists/ Assoc. Pediatricians/ Assoc. Of Biochemists/ Nat. Diabetes Fed. (Umbrella Org.)

6/4/2010 DCCT → DCCT + IFCC

1/1/2011 → IFCC (mmol/mol)

eAG NOT to be reported

70, 000 Euro from government

Sweden

Collaboration between clinical chemists and five medical associations, diabetic nurses association and diabetes patients association.

1/9/2010 Mono S → Mono S + IFCC

1/1/2011 → IFCC (mmol/mol)

eAG NOT to be reported

Note- Dual Units only for four months

Japan

JSCC Jap. Soc. Clin. Chem.

JDS Jap. Diab. Soc.

% JDS → JDS + 0.4 % → IFCC

(JDS + 0.4% = DCCT/NGSP)

Will report in % JDS in clinical practice

15/5/2011 JDS to report HbA1c as JDS + 0.4% and IFCC (mmol/mol)

No dates of implementation

Australia

- Teleconferences and emails
- RCPA/ AACB/ Aust. Diab. Soc./ Aust. Diab. Educ. Assoc.
- www.aacb.asn.au – AACB website - Position Statement
  - Home page → Resources (bottom left) then → Position Statement (upper right)

Approx.	4/7/2011	DCCT → DCCT + IFCC
	4/7/2013	→ IFCC (mmol/mol)

eAG NOT to be reported

Publication – Med. J. Aust. (MJA) 2011; 195: July

USA

- No Changes to current % DCCT units
- USA does not use any SI units
- eAG to be reported with every HbA1c
- Diabetes Care 2010, 33 (supp. 1): 519-
- ADA/AACC have determined that the correlation (r=0.92) obtained in the ADAG (eAG) study is strong enough to justify both an A1c result and an eAG whenever a clinician orders the A1c test

Typical Plan of Action

- Convene a working group of official representatives, preferably representing National Associations (diabetes clinicians, scientists, pathologists, diabetes organisations and Department of Health etc.)
- Convene a national meeting, teleconference, or email correspondence.
- Discuss concepts of units (IFCC or DCCT) and select units and future dates for implementation.
- Prepare educational material for laboratories, clinicians and patients

IFCC Reference System for HbA1c

- New precise definition of HbA_{1c}
- The IFCC has defined HbA_{1c} as (β-N-(1-deoxy)- fructosyl Hb), a hexapeptide, representing the major glycation site of the HbA1c molecule.
- Preparation of primary reference materials
  - HbA_0 and HbA_{1c}, six calibrators with 3-15% HbA_{1c}
- IFCC reference methods
  - Electrospray ionisation MS or capillary electrophoresis detection
  - Unanimous adoption as Approved IFCC Reference Method
- IFCC National Reference Laboratories
  - 15 laboratories, 6 countries, 2 reference methods (MS/CE)

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

Adapted from Hoelzel *et al Clin Chem* 2004; 50: 166-74

Rationale for Reporting in SI Units

- Scientists and clinicians have been working for more than 10 years to produce a gold-standard, interference free method for HbA_{1c}
- The new calibration method, without interferences, gives values approximately 1.5% lower than the DCCT values
- Unfortunately the two numbers are still similar enough in appearance to cause confusion, so a decision has been taken to change the units of reporting the new values in order to avoid any problems
- The new 'IFCC standardised' results will be written in units of mmol/mol

IFCC
International Federation of Clinical Chemistry and Laboratory Medicine

International Consensus Statement: 2007 ADA/EASD/IFCC/IDF

1. HbA_{1c} results should be standardised worldwide including the reference system and results reporting
2. The new IFCC reference system represents the only valid anchor to implement standardisation of the measurement
3. HbA_{1c} results are to be reported worldwide in IFCC units (mmol/mol) and derived NGSP units (%)
4. If the ongoing average plasma glucose study fulfils its a priori specified criteria an HbA_{1c}-derived average glucose (ADAG) value calculated from the HbA_{1c} result will also be reported
5. Glycaemic goals appearing in clinical guidelines should be expressed in IFCC units, derived NGSP units and as ADAG

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

Diabetologia 2007; 50: 2042-3

UK Consensus Statement Summary (2008)

- HbA_{1c} test results should be standardised using the IFCC reference method (already completed by manufacturers)
- Extensive education programmes should be developed for all healthcare professionals (completed)
- HbA_{1c} results should be reported in IFCC (mmol/mol) units and DCCT (%) units
- Parallel reporting will start from June 2009 and continue for 2 years (commenced)
- After this time it is envisaged that laboratories will report only IFCC units (planning under way)

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

Ann Clin Biochem 2008; 45: 343-4

International Consensus Statement 2010 ADA/EASD/IFCC/IDF

1. HbA_{1c} results standardised worldwide
   - Reference system and results reporting
2. IFCC reference system is the only valid anchor for standardisation
3. HbA_{1c} reported in IFCC (mmol/mol) and derived NGSP (%) units
4. HbA_{1c} conversion tables (IFCC-NGSP) easily accessible
5. Editors to recommend publication in both IFCC and NGSP units
6. Reportable term is HbA_{1c}
   - Other terms (e.g. A1C may be used in guidelines and educational material
7. Further discussion at IDF meeting in December 2011

Note: *Estimated average glucose (eAG) not included in statements.*

Recognize may add value to consultation process. Local

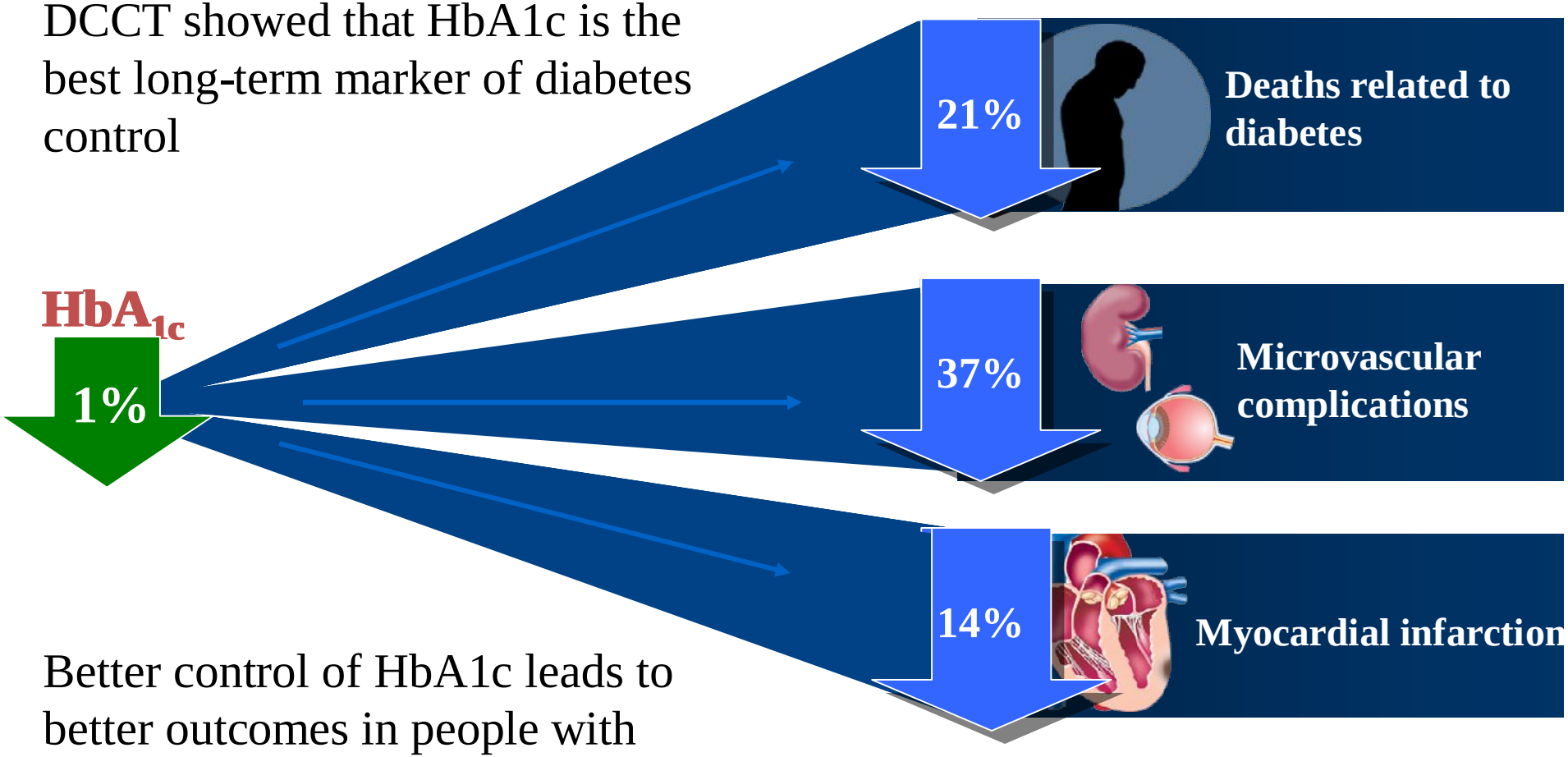
n on implementation

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

Ann Clin Biochem 2010; 47: 290-1

Why is HbA1c so important?

DCCT showed that HbA1c is the best long-term marker of diabetes control



Better control of HbA1c leads to better outcomes in people with diabetes

Stratton IM, *et al*. *BMJ* 2000; 321:405–412.

INTERLABORATORY VARIABILITY

International, National and between Provinces / Cities / Laboratories

- Both accuracy and precision are ultimately and totally dependent on routine laboratory assays in every laboratory.

- There are very good and very poor commercial assays.

- Good assays are good everywhere, poor assays are poor everywhere

- HbA1c assays need tight precision and high specificity.

- The choice of HbA1c instrumentation and assays is crucial in all laboratories.