What's new in diabetes monitoring?

Ronda Greaves

Overview

- Prevalence
- Diagnostic Criteria – glucose
- Monitoring Diabetes – HbA1c
  - Harmonisation: New HbA1c units
- The Diabetes Clinic at RCH

Prevalence

Prevalence of diabetes

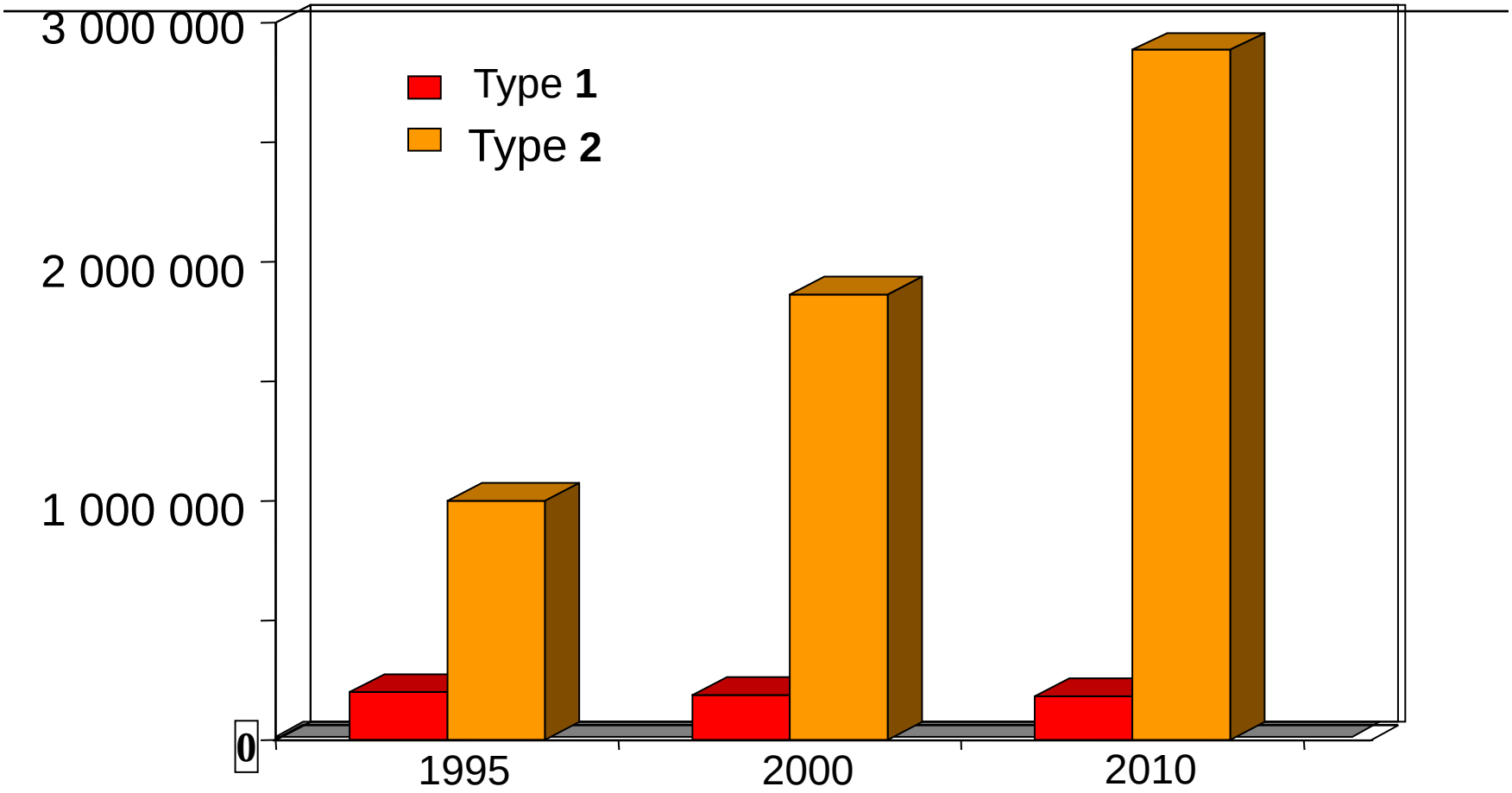
- Worldwide 246 million people have diabetes

- AUSTRALIA population 21+ million
  - Diabetes is Australia's fastest growing chronic disease
  - An estimated 2.1 million Australians are at risk of diabetes
  - One person is diagnosed every seven minutes
  - About 1 million Australians are diagnosed with diabetes. However, for every one diagnosed, another is undiagnosed
  - By 2014 the expected number of people with diabetes will be 4.5 million
  - Type 2 diabetes costs Australia $3+ billion per year

- VIETNAM population 86+ million
  - "With 5 million sufferers, Vietnam is one of the countries which have the highest rates of diabetes in the world"
  - 67% of people only discover they have the disease because of complications
  - One of the four fastest developing diseases (next to cancer, cardiovascular disease and obesity)
  - Expected to reach 10 million in next decade.

http://www.diabetesnsw.com.au/about_diabetes/factsheet.asp
http://www.lookatvietnam.com/2009/11/five-million-vietnamese-have-diabetes.html

Increasing prevalence of diabetes in UK



Type 1 diabetes	Type 2 diabetes
autoimmune destruction of insulin producing pancreatic beta islet cells	insulin resistant condition with inadequate insulin secretion
Australian prevalence 1% and rising	Australian prevalence 8% (4% overt) and rising (2-4 x higher in indigenous population)
typical onset < 30 years	typical onset > 20 years
sudden onset	gradual onset
severe symptoms	may be no symptoms
usually thin	usually obese
spontaneous ketosis	not ketotic
insulin low or absent	insulin low, normal or high
absent C-peptide	detectable C-peptide
islet cell antibodies	no islet cell antibodies

Type 2 diabetes mellitus

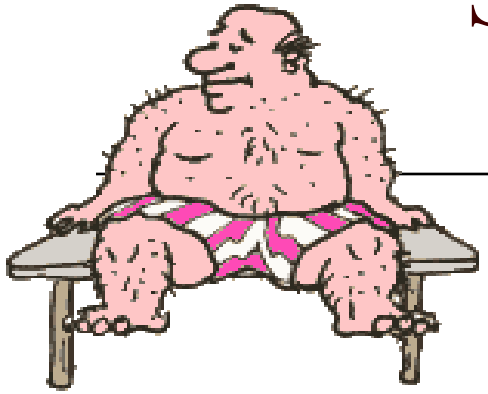
- usually insulin resistant with inadequate insulin production to maintain normal glucose levels
- onset (usually gradual) at any age, usually >20 years
- usually overweight or obese but not ketotic and often no symptoms at presentation
- worldwide very high prevalence in rural to urban migrant communities

Underlying insulin resistance
- genetic and ethnicity
- obesity
- inactivity / low physical fitness
- intrauterine & childhood factors
- smoking & drugs

Impaired insulin secretion
- worsens with time (b-cell exhaustion)

Syndrome of insulin resistance

AKA syndrome X, metabolic syndrome



microalbuminuria

high blood pressure

hyperuricaemia

abdominal obesity

insulin resistance

PAI-1 -
fibrinogen -
factor VII -

HDL cholesterol –
VLDL triglyceride -
small dense LDL -

hyperinsulinaemia
glucose intolerance
diabetes

Diabetes in pregnancy

- Increased risk of neonatal morbidity with maternal diabetes
- Gestational diabetes
  - normal pregnancy associated with increased insulin resistance
  - GD develops if failure to increase insulin secretion
  - Screening at 24-28 weeks with 50g OGTT
- Pre-existing diabetes
  - Excellent glycaemic control required to reduce risks

Diagnosing Diabetes: Glucose

2 hour Glucose Tolerance Test

DIAGNOSES

- Diabetes Mellitus if:
  - Fasting plasma glucose is ≥ 7.0 mmol/L

    and/or
  - 2 hour plasma glucose is ≥ 11.1 mmol/L

- Impaired glucose tolerance
- Impaired fasting glucose

Impaired Fasting Glucose

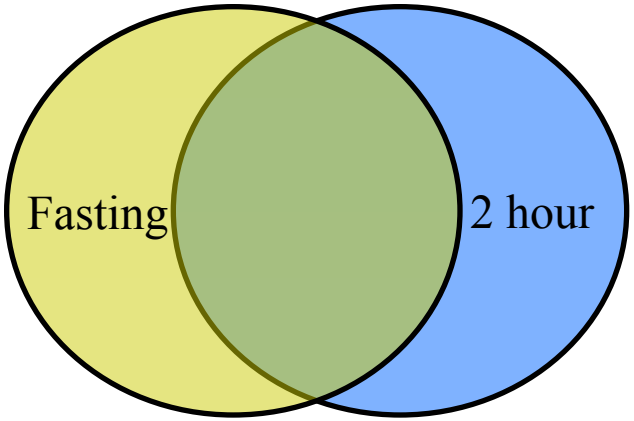
DIAGNOSED if:

- Fasting plasma glucose is 5.6 to 6.9 mmol/L
  According to the American Diabetes Association

Or

- Fasting plasma glucose is 6.1 to 6.9 mmol/L
  According to NHMRC, WHO, IDF, ADS, RCPA and AACB

Interpretation of GTT results

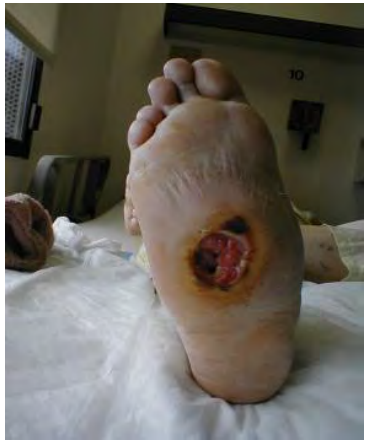


- The 2 tests (GTT v Fasting glucose) do not define identical populations (i.e. do not give same results)
- GTT – More abnormals in older, heavier population
- Fasting glucose – more abnormals in younger, thinner population

Monitoring diabetes: HbA1c

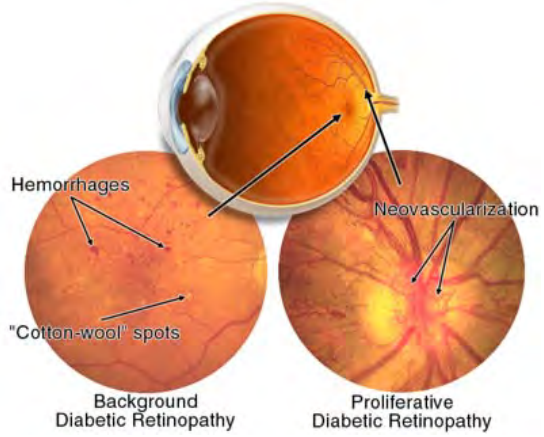
Monitoring diabetes - why

- Improving blood glucose control reduces risk of microvascular complications in Type 1 and Type 2 DM



medicine.ucsd.edu/clinicalmed/extremities.htm

- Complications include:
  - Neuropathy
  - Retinopathy
  - Nephropathy
  - CVD



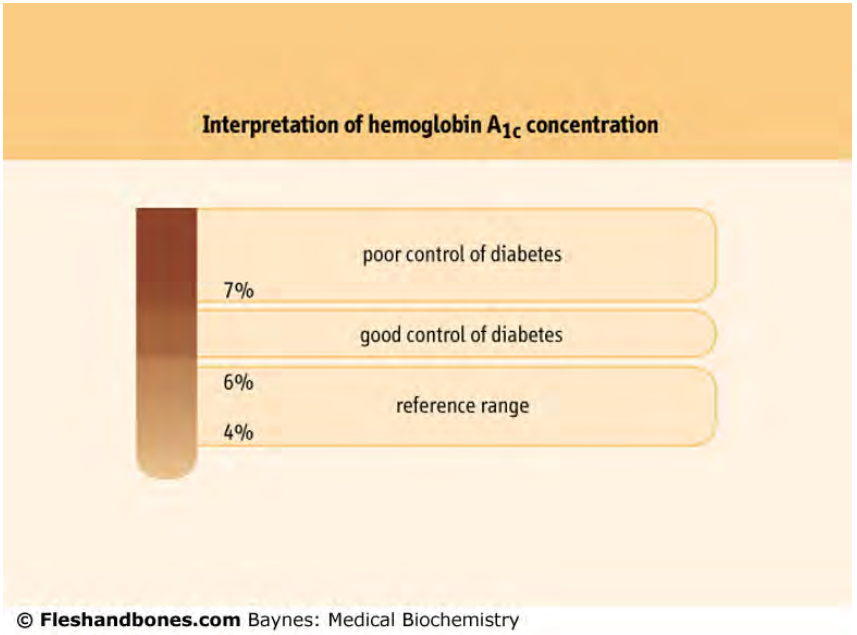
http://www.stlukeseye.com/Conditions/DiabeticRetinopathy.asp

Glycated Haemoglobin

- Haemoglobin A (97%) a_2b_2
- Haemoglobin A_2 (2.5%) a_2d_2
- Haemoglobin F (0.5%) a_2g_2

6% of HbA is HbA_1

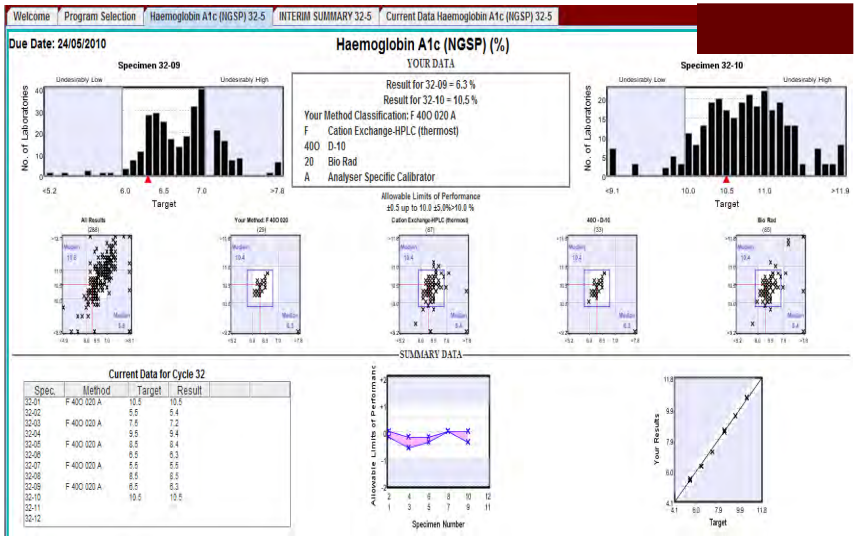
- HbA_{1a} fructose-1,6-diphosphate 0.2%
- HbA_{1b} glucose-6-phosphate 0.2%
- HbA_{1b} pyruvate 0.4%
- HbA_{1c} glucose 5%



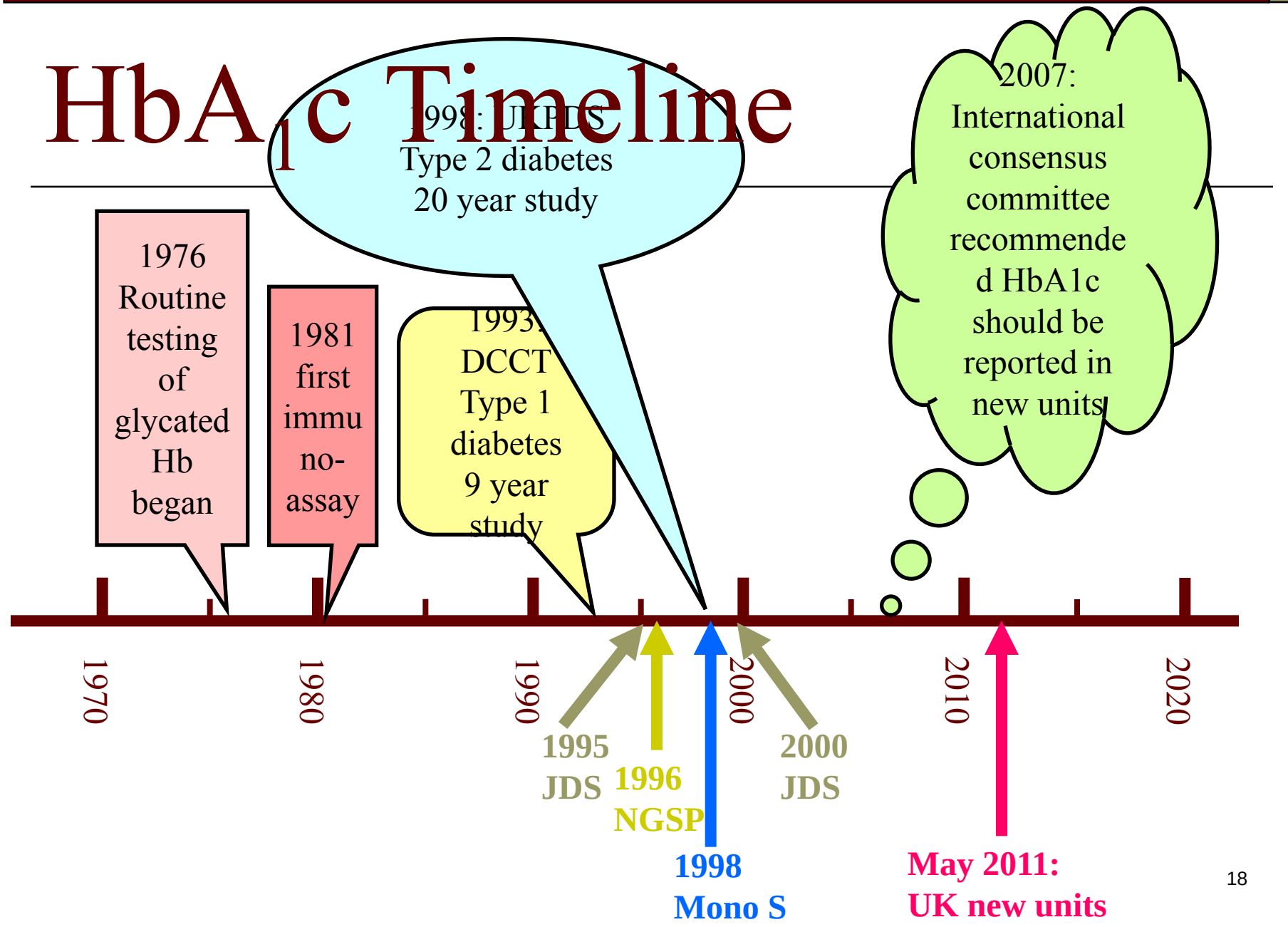
HbA_{1c} methods in use in Australia

From RCPA QAP Glycated Hb 2010

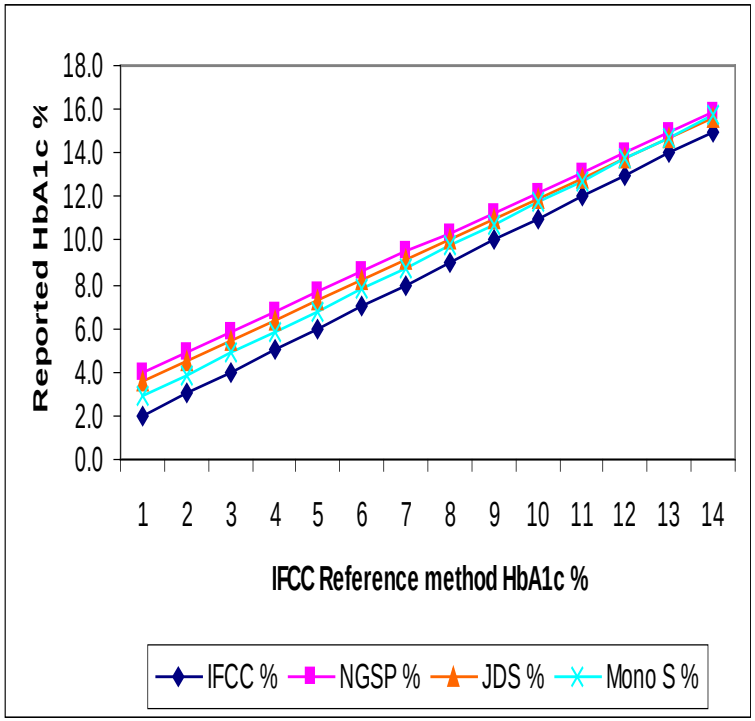
- Total labs = 288
  - Immunoassay = 158
  - HPLC
    - Cation exchange = 93
    - Affinity = 32
  - 12 labs also reporting new IFCC units



HbA$_1$c Timeline



Comparison of HbA1c measured with nationally designated methods



IFCC %	NGSP %	JDS %	MonoS %
2.0	4.0	3.6	2.9
3.0	4.9	4.5	3.8
4.0	5.8	5.4	4.8
5.0	6.7	6.4	5.8
6.0	7.6	7.3	6.8
7.0	8.6	8.2	7.8
8.0	9.5	9.1	8.8
9.0	10.4	10.1	9.8
10.0	11.3	11.0	10.8
11.0	12.2	11.9	11.8
12.0	13.1	12.9	12.7
13.0	14.0	13.8	13.7
14.0	15.0	14.7	14.7
15.0	15.9	15.6	15.7

NGSP HbA_1c = 0.915 (IFCC HbA_1c) + 2.15
JDS HbA_1c = 0.927 (IFCC HbA_1c) + 1.73
Mono S HbA_1c = 0.989 (IFCC HbA_1c) + 0.88

Equations: Clin Biochem Rev. 2007 November; 28(4): 163–168.

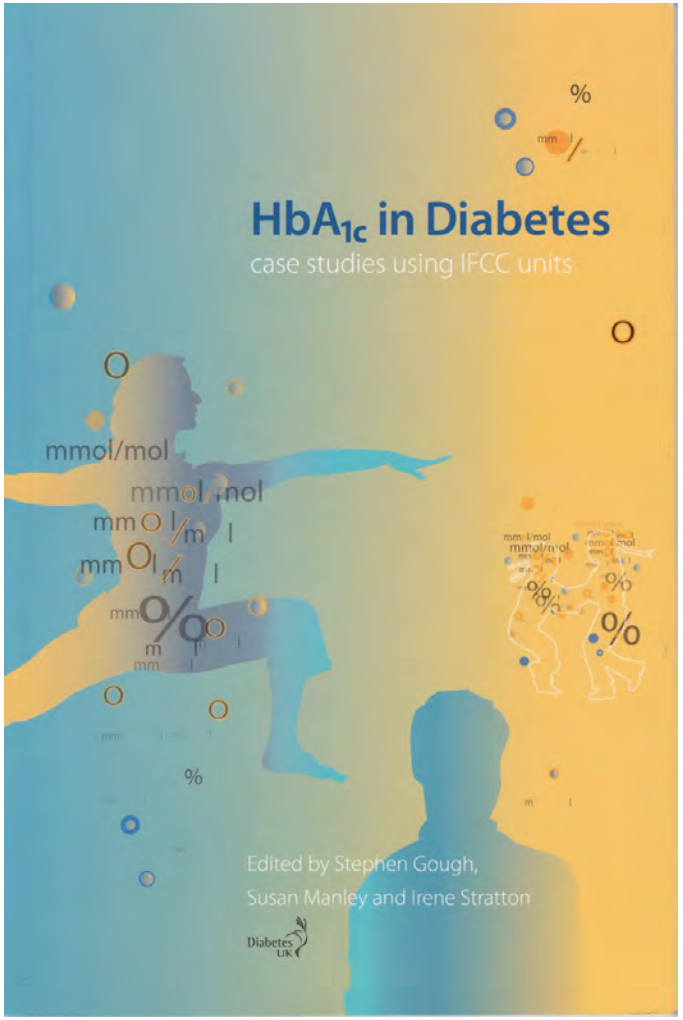
HbA1c: Reporting of results

- NGSP/DCCT/UKPDS - Report as a percentage of total haemoglobin
- IFCC - Report as mmol/mol
- Denominator is HbAo + HbA1c

IFCC HbA_1c (mmol/mol)
= 10.93 * NGSP HbA_1c (%) – 23.5

NGSP %	IFCC mmol/mol
3.0	9
4.0	20
5.0	31
6.0	42
7.0	53
8.0	64
9.0	75
10.0	86
11.0	97
12.0	108
13.0	119
14.0	130
15.0	140
16.0	151
17.0	162
18.0	173
19.0	184
20.0	195

2010 Diabetes UK booklet



Case Example 14 – Diabetes UK

Case notes	**IFCC HbA_1c mmol/mol** **NGSP%**
Presentation: Previously well controlled 14yo girl with T1 DM had lost 3 kg over 3 months	59 to 81 **7.5 – 9.6%**
Insulin regime: Pre-prandial rapid acting insulin analogue + once daily long acting analogue given in the evening.	
Treatment plan: Change insulin regime, gentle enquiries about weight and mental assessment	
3 weeks later: She was admitted to hospital with DKA pH=6.9; glucose = 33.5 mmol/L; ketones 5.6 mmol/L	96 **10.9%**
Post recovery: Weight drop and admitted to skipping insulin doses for weight control	
Next two years	92 – 111 **10.6-12.3%**
Age 17	72 **8.7%**

RCPA Quality Assurance Programs Pty Limited

Chemical Pathology

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LAB. NUMBER

GLYCOHAEMOGLOBIN PROGRAM 2010

RESULT SHEET

DUE DATE FOR RESULTS	SAMPLE NUMBER		UNITS
HAEMOGLOBIN A1c			%
			mmol/mol

CHANGE OF METHOD CLASSIFICATION

IMPORTANT!	ANALYTE	NEW METHOD CODE	ADDITIONAL INFORMATION IF REQUIRED
PLEASE COMPLETE IF YOU HAVE ALTERED OR DELETED A METHOD. CHANGE EFFECTIVE FROM: CYCLE No. SAMPLE No.	HAEMOGLOBIN A1c		

HBRS/10

ADAG Study

- ADAG = A1c Derived Average Glucose
- Equating Haemoglobin A1C results with estimated average glucose concentrations
- ADAG Study
  - 507 participants, each with about 2700 glucose measurements
  - e.g. HbA1c 6% = 42 mmol/mol = average glucose of 7.0 mmol/L
- Some consensus statements recommend reporting both % and mmol/mol, as well as estimated average glucose!
- Case Study 30 from Diabetes UK booklet:
  - Example of a 66 y.o. women with type 2 DM for 11 years without complications.
  - "The patient's GP was aware that although the mean glucose (eAG) for a patient with an IFCC HbA1c of 53 mmol/mol (NGSP 7.0%) was around 8.6 mmol/L it can vary between individuals from 6.8 – 10.3 mmol/L."

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