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Measuring change

The experts explain what you need to know about the new method for reporting HbA_{1c}.

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A CHANGE in the reporting of HbA_{1c} is being adopted globally, including in Australia.

It's anticipated that this change will, among other things, make it easier for doctors to educate their patients about the importance of glycaemic control. However, to understand how this change will help in practice, it's useful to firstly understand what HbA_{1c} is and to know something of the history of how laboratories have measured the HbA_{1c} assay.

What is HbA_{1c}?

Glycated haemoglobin is formed by the binding of glucose to the protein component of haemoglobin in red blood cells. The most common of these glycated haemoglobins is haemoglobin A1c (HbA_{1c}).

The HbA_{1c} result reflects the patient's glycaemic control over the 120-day lifespan of red blood cells. The result is time weighted with 50% of the HbA_{1c} result reflecting the glycaemic control in the month prior to specimen collection. The remaining 50% reflects the two month period from one to three months prior to specimen collection.

Assays over time

In the 1970s, a relationship between long-term diabetes complications and glycated haemoglobins was identified. The process of glycation was found to occur slowly, meaning that acute fluctuations in blood glucose levels would not impact significantly on the HbA_{1c} result.

From the late 1970s to the early 1980s, HbA_{1c} assays took several days to perform in the laboratory. A range of other glycated fractions were measured as well as HbA_{1c} and analysers were not very precise, leading to significant interlaboratory variation.

By the mid-to-late 1980s, the HbA_{1c} assay was increasingly used in the routine monitoring of glycaemic control. However, standardisation of HbA_{1c} assays was rarely performed and the same blood sample would give very different results when analysed by different laboratories.

There was a global recognition of the need for different laboratories to use a standardised reference method.

Between 1983 and 1993, the landmark Diabetes Control and Complications Trial (DCCT) was conducted in the US. This trial highlighted the importance of the HbA_{1c} test as the 'gold standard' marker of diabetes control — particularly in relation to the reduction in diabetes complications in patients with type 1 diabetes.

In the trial, all HbA_{1c} assays were performed in one central laboratory using a single method.

Following the success of this trial, the National Glycohemoglobin Standardization Program (NGSP) was established in the US in 1996. The measurement system used to per-

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form all the HbA_{1c} assays in the DCCT central laboratory was chosen as the NGSP reference method in the US; this system was subsequently adopted for use in Australia and many other countries.

However, Japan and Sweden developed separate national systems. Clearly there was a need for an international standardisation program.

International reference system

To address the lack of standardisation between countries, the International Federation of Clinical Chemistry (IFCC) spent more than a decade developing an international reference system for HbA_{1c} analysis.

This reference system is consistent with modern analysers, which measure HbA_{1c} more precisely than the DCCT method, which measured other glycated fractions as well as HbA_{1c} and therefore overestimated the true HbA_{1c} value.

In 2007, there was international agreement that HbA_{1c} test results should be standardised worldwide using the IFCC reference system with results reported in a different unit.

All manufacturers now calibrate HbA_{1c} analysers using the IFCC reference system and all HbA_{1c} methods used in Australia are now standardised using this system.

The new HbA_{1c} result has a very different number value and is reported in a unit known as mmol/mol — stated as millimoles per mole (table 1).

For example 6% in the 'old' DCCT unit is equivalent to 42 mmol/mol in the 'new' IFCC unit.

The numbers from the two systems can be converted as follows:

HbA_{1c} (mmol/mol) = $10.93 \times HbA_{1c}$ (%) - 23.50

HbA_{1c} (%) = HbA_{1c} (mmol/mol) $\times$ 0.091 + 2.15

A calculator that quickly

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allows you to convert the old to new units is available at the Quality Assurance for Aboriginal and Torres Strait Islander Medical Services website (www.qaams.org.au).

There's also an easier way to convert the old reporting method to the new that works for HbA_{1c} (DCCT) results in whole numbers from 4% to 14%. Let's call it the 'minus two minus two' rule.

For example, for an HbA_{1c} of 7.0%, minus 2 from 7 = 5, and then minus 2 from 5 = 3, giving a result of 53 mmol/mol.

Why change?

The new reporting method is in keeping with the recent international consensus and is a contemporary and scientifically valid measure of HbA_{1c}.

International standardisation was needed because:

- Patients and clinicians need the most accurate measure of HbA_{1c} to assess glycaemic control.
- Diabetes centres and facilities are often assessed on the basis of patients achieving HbA_{1c} targets and therefore we need to be able to measure these as accurately as possible.
- Certain diabetes medications can only be prescribed on the basis of the patient's HbA_{1c} result.
- There is now also a move internationally to employ HbA_{1c} measurements as a tool for diagnosing diabetes.

While there is no change in the performance of the current assays, the new standardisation allows for future improvement to ensure the highest quality result.

The change will reduce confusion associated with the current reporting system. In practice, many patients have assumed that the HbA_{1c} result is an average of the blood glucose levels obtained on their blood glucose meters, namely that an HbA_{1c} of "7" means their average blood glucose is 7mmol/L. This is clearly incorrect.

Further, the use of "%" units can make some significant changes seem trivial, in that a change of HbA_{1c} of 1% may appear insignificant.

The new IFCC system reduces any confusion associated with the closeness in numerical value between the HbA_{1c} and the blood glucose level.

Further, the number values reported in the new system are larger, making variations in HbA_{1c} results over time appear more significant.

Additionally, the relationship with average blood glucose is more closely aligned — halving the glucose will lead to halving of the HbA_{1c}.

This should make it easier for doctors and other health professionals involved in diabetes care to help their patients understand the significance and difference of the results obtained by both methods.

This change is similar to the introduction of the metric system.

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What is happening overseas?

A number of countries are already reporting the new units. These countries include France, Denmark, Japan, New Zealand, UK, Germany, Holland, Italy and Sweden.

A small number of countries, including the US and Canada, have chosen not to introduce the new units at this time.

What is happening in Australia?

The HbA_{1c} Reporting Unit Working Party (HbA_{1c} RWP) convened with representation from the Australasian Association of Clinical Biochemists, the Australian Diabetes Educators Association, the Australian Diabetes Society and the Royal College of Pathologists of Australasia. It released a position statement addressing this change earlier this year.

In short, the HbA_{1c} working party recommended that for two years from July 2011 to July 2013, HbA_{1c} results in Australia should be reported in both percentage units (NGSP) and mmol/mol (IFCC), for example, HbA_{1c} 6.0% (NGSP); HbA_{1c} 42 mmol/mol (IFCC).

This will allow time to implement the new reporting units slowly and provide opportunities to develop and disseminate educational information about the change to doctors, diabetes health professionals and patients.

After the two-year period expires, only the new IFCC units will be reported.

How have the goals changed?

The reference interval for patients without diabetes using the new system will be 20-42 mmol/mol (equivalent to 4.0-6.0% in the old units).

The target range for adults with diabetes should still be individualised with a recommended target HbA_{1c} level less than or equal to 42mmol/mol (6.0%) in some people, or up to 64mmol/mol (8.0%) in others. However, for most it will be less than 53mmol/mol (<7.0%).

HbA_{1c} targets for children and adolescents with type 1 diabetes are less than 59mmol/mol (<7.5%) and with type 2 diabetes are less than 53mmol/L (<7.0 %).

What is the eAG?

In the current literature, you may also see reference to the term 'estimated average glucose value' or eAG.

The eAG is a further estimate of long-term glucose control. The evidence for reporting eAG has been based on a small study known as the ADAG study. ADAG is an acronym for 'an HbA_{1c}-derived average glucose'. The purpose of the study was to attempt to define a relationship between HbA_{1c} and self-managed blood glucose results.

The HbA_{1c} RWP does not endorse the routine reporting of the eAG and most other countries have also resolved not to report the eAG, with the exception of the US and Denmark.

For example, the American Diabetes Association and the American Association for Clinical Chemistry believe that the reporting of the HbA1c result with an eAG result is justified when a clinician orders the HbA_{1c} test.

While it is acknowledged some Australian clinicians will choose to use the eAG as an educational tool, they should be aware of its limitations as well as its benefits.

It is suggested that reporting of eAG would make it easier for patients with diabetes to understand their results, as they directly relate to their own blood glucose levels obtained from their blood glucose meter.

However, blood glucose levels measured by a blood glucose meter vary considerably during the day. So although the units are the same, the eAG gives no indication of a patient's daily range of glucose values.

Further, there is considerable controversy about the strength of this evidence for use of this surrogate measure from the ADAG study with concern, among other things, about the relatively small, selected population studied.

What can you do?

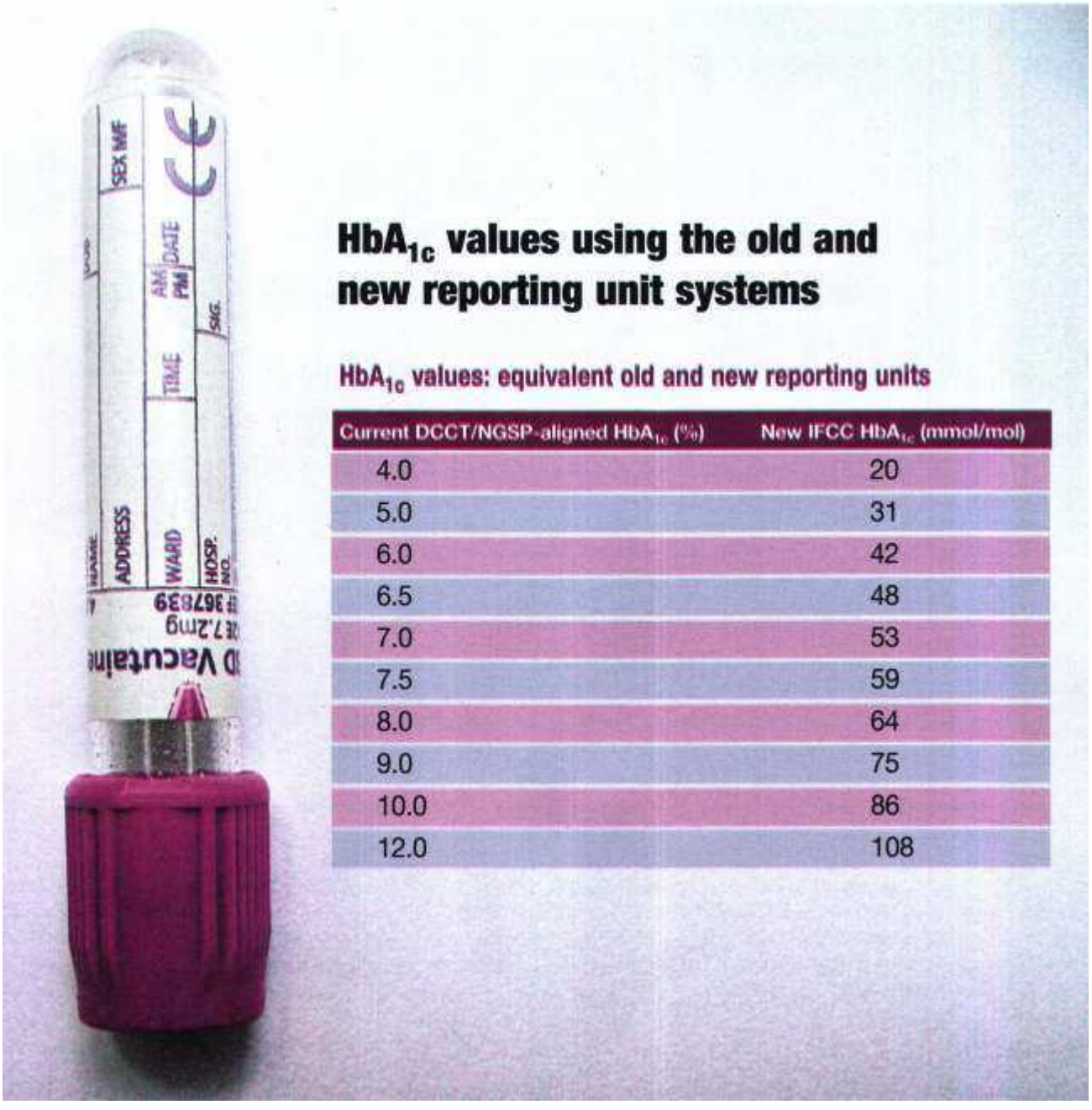
This change is similar to the introduction of the metric system. It will only work if all participants in diabetes management actively change their ways. Just as laboratories will report in the new units, doctors and diabetes educators should use the new units in discussions with patients and in correspondence and other communication.

The medical software suppliers are being approached to allow the new units to be transmitted automatically to desktop software.

Training and further information

The International Diabetes Federation recommends that self-monitoring of blood glucose should be used only when individuals with diabetes (and/or their caregivers) and/or their healthcare providers have the knowledge, skills and willingness to incorporate it and therapy adjustment into their diabetes care plan in order to attain agreed treatment goals.

The target range for adults with diabetes should still be individualised … However, for most it will be less than 53mmol/mol (<7.0%).



HbA_{1c} values using the old and new reporting unit systems

HbA_{1c} values: equivalent old and new reporting units

Current DCCT/NGSP-aligned HbA_{1c} (%)	New IFCC HbA_{1c} (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

Diabetes educators accredited through the Australian Diabetes Educators Association can help your patients learn how to use blood glucose meters effectively and to understand the changes to the new HbA_{1c} reporting system. ●

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References available on request