

Risk Matters



Dear Reader,

Data published by the World Health Organisation (WHO) suggests that diabetes represents a major and growing threat to health worldwide.

Diabetes is a chronic disease of insulin production and consequently control of blood glucose. Complications of poorly managed diabetes include systemic damage to the circulatory and nervous system.

The monitoring of the control patients have over their diabetes is of key importance to improving their long-term outlook. A test to monitor glycated or glycosylated Haemoglobin (HbA_{1c}) in the blood is widely used. To establish an improved global standard for assessing diabetic control, a new reference standard and measurement system for HbA_{1c} has been introduced.

This article describes the changes to the HbA_{1c} measurement and how underwriters should interpret them. The underwriting manual CLUE will be updated to reflect these changes.

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Changes to Diabetes Monitoring

Data published by the World Health Organisation (WHO) suggests that the chronic illness of diabetes represents a major and growing public health threat.

Diabetes is characterised by either a deficiency of insulin production or the ineffective use of the insulin that is produced. Insulin is vital to the regulation of blood sugar levels, and poor control of this metabolic process causes long-term damage to blood vessels and nerves leading to complications that include heart disease, kidney failure, blindness and amputation.

Globally 5% of all deaths are as a result of diabetes, and this proportion is expected to increase by 50% over the next 10 years. It is estimated that currently 180 million people suffer from diabetes and that this figure will double by 2030. The WHO attributes the cause of this “emerging global epidemic” to increasing obesity levels and reduced physical activity. The impact of diabetes is magnified by tobacco use, a habit practiced by one billion smokers worldwide and one that has an increasing prevalence.

The surveillance and control of diabetics is core to improving the long-term outlook of individual patients and limiting the potential global impact of this epidemic. One method to monitor effective diabetic control in a clinical setting is to measure glycated or glycosylated haemoglobin (HbA_{1c}) in the blood. To help establish an improved standard for assessing diabetic control worldwide, a new global gold standard reference and measurement system for HbA_{1c} has been introduced.

Glycated or glycosylated haemoglobin (HbA_{1c}) results when glucose circulating in the blood stream binds to haemoglobin molecules that make up red blood cells. HbA_{1c} gives a measure of the average level of blood glucose over the previous 6 to 8 weeks. Monitoring the HbA_{1c} level and keeping it within an acceptable range is a key component of good diabetic management. A high level of HbA_{1c} puts a patient at increased risk of long-term diabetic complications including heart, kidney, eye and nervous system disease. Diabetic treatment aims to lower the level of HbA_{1c} and regular checks help patients modulate their treatment regimen.

The current laboratory reference range is based on results from two trials. The US-based study Diabetes Control and Complications Trial (DCCT) was one of the largest ever trials investigating the effect of good control on the incidence of complications in type 1 diabetes, a condition mainly treated with insulin. The UK-based United Kingdom Prospective Diabetes Study (UKPDS) looked at the risk of complications patients suffer with type 2 diabetes, a condition that is not controlled with insulin. The assay used in most laboratories is aligned to the assay used in the DCCT, so results are often quoted as HbA1_c (DCCT).

Underwriters are familiar with using serial HbA1_c readings to assess levels of control in diabetics. The normal reference range demonstrating good diabetic control is 6.5% to 7.5% although in risk assessment, favourable control has been represented by a slightly wider range of between 6% and 9%.

However, from 1 June 2009 the unit of measurement of HbA1_c changed. One of the key reasons for this change stems from the concern to establish an improved standard for assessing diabetic control worldwide. To address this concern, work to agree a new standard specific for HbA1_c was commenced in 1994 by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). This international body has established a global reference and measurement system for HbA1_c in collaboration with a worldwide network of reference laboratories and the manufacturers of diagnostic testing devices.

Following the release of the IFCC consensus statement in September 2007, it was agreed that all laboratories would begin reporting their HbA1_c results to the IFCC standard from October the following year. The IFCC statement recognises the status of the HbA1_c assay as the gold standard measurement for chronic glycaemia, yet it points to the limitations infrequent testing lends to calculating a true average HbA1_c level in patients.

In practice, laboratories will continue to express blood test results in DCCT numbers but in addition will report to the new IFCC standard measure. This parallel reporting will continue until 1 June 2011. The results of all laboratories to be traced back the IFCC standard allowing global tracking of HbA1_c results.

The new IFCC protocol requires that HbA1_c results be expressed as millimole of HbA1_c per mole of haemoglobin (Hb) (mmol/mol) in place of a percentage. Underwriters will need to consider good control as being represented by the range 48 - 59 mmol/mol (equivalent to 6.5% - 7.5%). The non-diabetic reference range is now 20 - 40 mmol/mol.

The new results will compare in this manner:

| Current DCCT aligned units [%] | New units [mmol/mol] |
|--------------------------------|----------------------|
| 6.0 | 42 |
| 6.5 | 48 |
| 7.0 | 53 |
| 7.5 | 59 |
| 8.0 | 64 |
| 9.0 | 75 |
| 10 | 86 |

It may be appropriate to note that any HbA1_c result may be misleading in certain circumstances. Any condition that affects the life span of a red blood cell, liver or renal disease, pregnancy or abnormal haemoglobin as in haemoglobinopathies may alter the results. In these circumstances serial blood glucose measurements may be more useful to assess control.

There may be further changes in the future as a different measure is being researched, the estimated Average Glucose level (eAG). This is derived from the HbA1_c. At this time there is no consensus that this should be used in reporting by laboratories; however there is some impetus to use this measure as it is felt that patients will understand the concept of an average level of glucose in their blood better than the HbA1_c level. We will continue to monitor this development.

Further reading

Consensus Statement on the Worldwide Standardisation of the Hemoglobin A1C Measurement; (Consensus Committee, IFCC); Diabetes Care, volume 30, number 9, September 07, 2399-2400.

www.who.int/diabetes/en/.



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