A position statement released in September 2011 from the New Zealand Society for the Study of Diabetes (NZSSD) now recommends the use of glycated haemoglobin (HbA$_{1c}$) for the diagnosis of type 2 diabetes. In addition, HbA$_{1c}$ should also be the test of choice for opportunistic screening in the majority of people. This use, particularly for opportunistic screening, may help address the rapidly growing epidemic of type 2 diabetes in New Zealand,$^{1,2}$ and assist with the detection of the estimated 20 – 40% of all people with type 2 diabetes who remain undiagnosed.$^{1,3}$ The use of HbA$_{1c}$ for screening and diagnosis in type 2 diabetes has been widely debated in the international literature. The decision to recommend this change is based on the advantages of HbA$_{1c}$, such as the lack of need for fasting, reduced biological variability and simpler laboratory requirements. Existing glucose criteria remain valid but the statement emphasises the necessity of having two separate diagnostic readings when a patient is asymptomatic.
HbA1c is now the recommended test for the screening and diagnosis of type 2 diabetes

NZSSD has recommended that, in most cases, HbA1c should be the first-line test for screening and diagnosis of type 2 diabetes. This recommendation aims to complement and update current guidance from the New Zealand Guidelines Group and is also broadly in line with many international guidelines. Until now, the recommended diagnostic and screening tests for type 2 diabetes have been fasting plasma glucose levels or the two hour post-oral glucose tolerance test. However HbA1c has several advantages over these tests for the majority of patients.

The advantages of HbA1c for screening and diagnosis of type 2 diabetes

HbA1c testing offers several significant advantages over fasting plasma glucose. Firstly, there is no need for fasting. Research and anecdotal evidence suggests that many people are not compliant with the requirement for fasting, thereby reducing the accuracy of fasting plasma and oral glucose tolerance tests.

HbA1c is less affected by day to day variation in plasma glucose, due to exercise, smoking, medicines and diet patterns, than fasting plasma glucose testing, because it reflects the average level of glycaemia over six to eight weeks rather than measuring it at a single moment in time.

There is also less biological variability associated with HbA1c than with fasting plasma glucose testing. The variability between two tests, in the same person, is approximately four times greater with fasting plasma glucose than with HbA1c. This means that the likelihood of false negatives and positives, with repeat testing, is lower with HbA1c than with fasting plasma glucose.

HbA1c measures chronic glycaemic exposure rather than an acute value, therefore providing a more relevant view of long-term glycaemia and future risk of complications. As with fasting plasma glucose, there is a well established, and accurate relationship between HbA1c and future retinopathy risk. For example, in previously undiagnosed people with HbA1c values above 50 mmol/mol the prevalence of moderate retinopathy begins to increase exponentially. A value above this level is therefore strongly predictive of a risk of development of clinically significant retinopathy. There is also overwhelming evidence that HbA1c levels are predictive of the prevalence of other microvascular complications such as nephropathy and neuropathy. HbA1c is a superior indicator of future cardiovascular (CVD) risk than fasting plasma glucose, although the relationship is not as well defined as with retinopathy.

HbA1c has simpler sampling and analysis requirements. As it is very stable, a blood sample for HbA1c can be collected either at a laboratory or during a consultation at a general practice clinic, allowing for more opportunistic testing. While fasting plasma glucose samples can also be taken at the practice, the requirements are more complex than with HbA1c and values can be misleading if the sample is not processed immediately, due to pre-analytical instability. This is because glucose consumption continues to occur in blood after sampling, even when anti-glycolytic fixatives are applied to the tube. The pre-analytic variability of fasting plasma

PHO Performance Indicator

Diabetes detection is a PHO Performance Programme (PPP) indicator. Its purpose is to determine what proportion of the PHO population estimated to have diabetes has been diagnosed.

As HbA1c testing can be done opportunistically, ideally as part of an overall cardiovascular risk assessment, the number of people tested and diagnosed with diabetes is likely to rise, meaning that the Indicator performance should improve (along with a potential improvement in refining the estimate of people with diabetes, which forms the denominator for this indicator).

The Indicator currently comprises 9% of a PHO’s performance payment, with 3% for achieving the target in the total eligible PHO population and 6% in the high needs population (N.B. Indicator weightings are subject to change).
glucose testing is approximately 5 – 10%, with New Zealand laboratories generally accepting approximately 5% variability as inherent.\(^{10,17}\) In comparison, the pre-analytic variability of HbA\(_1c\) is negligible.

**Concerns about the use of HbA\(_1c\) for screening and diagnosis**

One of the main concerns expressed about the use of HbA\(_1c\) for screening and diagnosis is that there has previously been a lack of standardisation with the test. There is now a level of quality standardisation equal to that of fasting plasma glucose testing.\(^{10}\) This has been driven by:\(^4\)

- Improvement in the technologies used for processing and analysing samples
- An overall effort and agreement by laboratories towards international standardisation
- The change to international units (mmol/mol)

A further concern has been that the HbA\(_1c\) test is more expensive than fasting plasma glucose – although still less expensive than oral glucose tolerance testing.\(^3\) However, the long-term cost of diabetes is high, and effective screening aims to reduce the incidence of diabetes through detection of people with pre-diabetes and reduce the risk of complications post-diagnosis through early detection.\(^4\) The cost in terms of time and inconvenience to the patient is also less for HbA\(_1c\).\(^4\)

HbA\(_1c\) is not, however, suitable for patients with some haemoglobinopathies and disorders with abnormal red-cell turnover such as many anaemias, as these falsely alter the value. There is also some evidence of individual and ethnic variations in HbA\(_1c\), although local data on this is very limited.

Table 1 compares the attributes of HbA\(_1c\) and fasting glucose assays.

**Using HbA\(_1c\) for diagnosis of type 2 diabetes**

NZSSD and the Ministry of Health have recommended that the threshold for a diagnosis of diabetes using HbA\(_1c\) is ≥ 50 mmol/mol.\(^{4,5}\) This slightly differs from other international bodies and is designed to have high specificity for the diagnosis; sensitivity issues are addressed by the repeat requirements for patients with borderline levels of HbA\(_1c\).\(^4\)

All tests should be performed in an accredited laboratory, i.e. point-of-care testing is not acceptable for diagnostic purposes.\(^4\)

**In symptomatic people** a single HbA\(_1c\) ≥50 mmol/mol can be considered diagnostic of diabetes in New Zealand for the majority of people (see below for exceptions).\(^4\)

**In asymptomatic people** a HbA\(_1c\) ≥50 mmol/mol strongly indicates diabetes; however, a second test, ideally HbA\(_1c\) (at least three months later), or alternatively fasting plasma glucose, is needed for confirmation.\(^4\) Lifestyle interventions should be encouraged during the three month wait for a second HbA\(_1c\).\(^4\) If the second result is discordant, repeat testing again in three to six months is recommended.\(^4\)

Table 2 summarises diagnostic criteria for diabetes using HbA\(_1c\).

**HbA\(_1c\) results may be falsely low in people**:\(^4,5,7\)

- With a high red blood cell turnover
- Taking iron, vitamin B12 or any other product that temporarily increases red blood cell production
- Who have undergone a blood transfusion any time in the previous three months

**HbA\(_1c\) results may be falsely high in people**:\(^4,5,7\)

- Iron deficiency anaemia
- Vitamin B12 or folate deficiency
- Alcoholism or chronic renal failure
- With certain haemoglobinopathies, e.g. sickle cell anaemia, methaemoglobinemia

**Fasting plasma glucose testing remains a valuable test**

Fasting plasma glucose testing is still a valid test for diagnosing people with type 2 diabetes, including when HbA\(_1c\) is not appropriate or cannot be used.\(^4,5\) The use of fasting plasma glucose is recommended where HbA\(_1c\) results are borderline or further investigation of the result is necessary, such as in a patient with two discrepant HbA\(_1c\) results. In this situation, a fasting plasma glucose test may be used to clarify the diagnosis. Fasting plasma glucose is also the preferred initial test if the patient has a specific condition or complication that may lead to an inaccurate HbA\(_1c\) result.\(^4,5,7\)

The criteria for diagnosing diabetes using fasting plasma glucose and oral glucose tolerance testing (if indicated) remain unchanged. However, other than in pregnancy, oral glucose tolerance testing should now only be used if HbA\(_1c\) is contraindicated and fasting plasma glucose results are inconclusive.\(^4\)

* Amended 5/12/2012 from “Severe anaemia”
Table 1. Advantages and disadvantages of HbA1c and fasting glucose assays.

<table>
<thead>
<tr>
<th></th>
<th>Fasting glucose</th>
<th>HbA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient preparation</strong></td>
<td>Fasting required, this is often misunderstood or not adhered to</td>
<td>None</td>
</tr>
<tr>
<td><strong>Sample processing</strong></td>
<td>Stringent requirements for processing and separation; rarely achieved</td>
<td>Relatively simple</td>
</tr>
<tr>
<td><strong>Standardisation</strong></td>
<td>Fully standardised</td>
<td>Fully standardised</td>
</tr>
<tr>
<td><strong>Variability</strong></td>
<td>Moderate pre-analytic and biological variation</td>
<td>Little to no variation</td>
</tr>
<tr>
<td><strong>Effect of illness</strong></td>
<td>Severe illness may increase glucose concentration in hours or days</td>
<td>Severe illness may shorten red-cell lifespan, reducing HbA1c levels in days or weeks</td>
</tr>
<tr>
<td><strong>Haemoglobinopathies and disorders of red blood cell turnover</strong></td>
<td>Few problems</td>
<td>May interfere with values in some cases</td>
</tr>
<tr>
<td><strong>Cost to laboratory (approximate)</strong></td>
<td>$2.30</td>
<td>$11.40</td>
</tr>
</tbody>
</table>

Table 2. Recommended guidelines for the diagnosis of diabetes

<table>
<thead>
<tr>
<th>HbA1c results</th>
<th>Glucose Equivalent</th>
<th>Diagnosis</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50 mmol/mol, with symptoms</td>
<td>≥7.0 mmol/L, with symptoms</td>
<td>Diabetes</td>
<td>A second HbA1c test ≥50 mmol/mol is required to confirm diagnosis (after three months)</td>
</tr>
<tr>
<td>≥50 mmol/mol, no symptoms</td>
<td>≥7.0 mmol/L, no symptoms</td>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>41 – 49 mmol/mol</td>
<td>6.1 – 6.9 mmol/L</td>
<td>Pre-diabetes</td>
<td>Offer lifestyle advice. Perform CVD risk assessment and follow guidelines for treatment of risk. Repeat testing of HbA1c every 6 – 12 months</td>
</tr>
<tr>
<td>≤40 mmol/mol</td>
<td>≤6.0 mmol/L</td>
<td>Diabetes unlikely</td>
<td>Normal range. Repeat HbA1c at next CVD assessment or when clinically indicated</td>
</tr>
</tbody>
</table>
A single fasting plasma glucose result ≥7 mmol/L is indicative of diabetes in **symptomatic** people; in **asymptomatic** people two fasting plasma glucose results ≥7 mmol/L, on separate days, are required to confirm the diagnosis. A fasting glucose of 6.1 – 6.9 mmol/L indicates impaired fasting glucose/pre-diabetes.

**Testing for diabetes in women who are pregnant**

HbA1c testing is not currently recommended for diagnosis of diabetes in pregnant women because glucose tolerance is altered in pregnancy; a separate glucose-based diagnostic algorithm is used. Oral glucose tolerance testing (75 g) is still used for diagnosis of gestational diabetes in women with an abnormal initial polycose screen (50 g), although there are controversial proposals to change this.

**Monitoring glycaemic control**

HbA1c remains the preferred, and only really useful, test for monitoring glycaemic control in people with diabetes, in primary care. Glycaemic control targets should be discussed with the patient, with the aim of deciding on a realistic goal that lowers long-term risk.

New Zealand guidelines and NZSSD recommend a target HbA1c of 50 – 55 mmol/mol or as individually agreed.4, 9

<table>
<thead>
<tr>
<th>HbA1c (mmol/mol)</th>
<th>Individual targets and possible patient outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>Exceptional control, if taking insulin there is an increased risk of hypoglycaemia</td>
</tr>
<tr>
<td>50 – 54</td>
<td>Very good control, some risk of hypoglycaemia if on insulin</td>
</tr>
<tr>
<td>55 – 64</td>
<td>Acceptable in many individuals but higher than recommended. Long-term risk of microvascular complications increases exponentially from this point</td>
</tr>
<tr>
<td>65 – 79</td>
<td>Suboptimal glycaemic control. More intensive control may be required. Risk of retinopathy, CVD and other complications very high</td>
</tr>
<tr>
<td>80 – 99</td>
<td>Poor glycaemic control. More intensive control recommended</td>
</tr>
<tr>
<td>≥100</td>
<td>Extremely poor glycaemic control. Immediate action required</td>
</tr>
</tbody>
</table>

For further information see: “HbA1c targets in people with type 2 diabetes”, BPJ 30 (Aug, 2010).

**ACKNOWLEDGMENT:** Thank you to Dr Paul Drury, Clinical Director, Auckland Diabetes Centre for expert guidance in developing this article.
Who should be screened for type 2 diabetes?

Current recommendations are for asymptomatic men aged over 45 years and women aged over 55 years to be screened for diabetes as part of a joint diabetes/cardiovascular risk assessment. Screening of asymptomatic Māori, Pacific and Indo-Asian people should begin at age 35 years for men and age 45 years for women. Screening should be undertaken every three to five years depending on risk.

New Zealand Guidelines recommend screening ten years earlier in people with multiple risk factors. In addition, NZSSD recommends screening should be undertaken opportunistically at age 25 years in people with the following specific risk factors:

- Ischaemic heart disease (angina or myocardial infarction), cerebrovascular disease or peripheral vascular disease
- Long-term steroid or antipsychotic treatment
- BMI ≥30 or BMI ≥27 kg/m² for Indo-Asian peoples
- Family history of early age of onset type 2 diabetes in more than one first degree relative
- Past personal history of gestational diabetes mellitus

Additional risk factors for diabetes include:

- Central obesity
- Impaired glucose tolerance on previous assessment, e.g. HbA₁c 41 – 49 mmol/mol or fasting glucose 6.1 – 6.9 mmol/L
- Adverse lipid profile, e.g. TC/HDL ratio ≥7.0
- High blood pressure, e.g. ≥160/95 mm Hg
- Polycystic ovary syndrome
- Current smoker (or have quit within the last twelve months)

Children and young adults with BMI >30 (or >27 kg/m² in Indo-Asian children) should be screened for diabetes if:

- There is a family history of early onset type 2 diabetes or
- They are of Māori, Pacific or Indo-Asian ethnicity

References