Key messages

- To test for diabetes, use HbA₁c instead of fasting plasma glucose or glucose tolerance testing EXCEPT in pregnancy, presence of acute symptoms and in some other circumstances.

- Diabetes is confirmed with HbA₁c ≥48mmol/mol (6.5%), on two occasions in an asymptomatic individual. If symptomatic, a single HbA₁c test will suffice if 48mmol/mol or above.

- Diabetes can be diagnosed using glycated haemoglobin (HbA₁c) or glucose tests.

Aim of the guideline

This guidance aims to support the use of HbA₁c as a diagnostic test for diabetes to replace the use of blood glucose in most circumstances.
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Error

A mistake on p3 has been corrected: code for pre-diabetes should be C11y5

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1. Reason for the change

Diagnosis of diabetes has been dependent on glucose tests for a number of years, and case finding relied on fasting glucose values, augmented by oral glucose tolerance testing (OGTT) if fasting glucose levels were abnormal.

A World Health Organisation (WHO) consultation has concluded that glycated haemoglobin (haemoglobin A1c or HbA1c) can be used to diagnose diabetes. The rationale for this is the observation that the cut point of 48 mmol/mol (6.5%) correlates with a significant increase in risk for the development of diabetic retinopathy, and the correlation is stronger than that for fasting plasma glucose.

It is now recommended to use HbA1c rather than fasting or random glucose testing, or OGTT to diagnose diabetes in patients whom you suspect of having the condition. Random glucose testing is rarely helpful unless the patient is symptomatic, and should be discouraged. (Diabet Med 2012;29:1350–1357)

2. Diagnosis of diabetes

HbA1c ≥48mmol/mol (6.5%), on two occasions in an asymptomatic individual, diagnoses diabetes.

If symptomatic, a single test will suffice.

Diagnostic criteria are outlined in Table 1.

HbA1c should not be used in the following circumstances:

- Abnormal haemoglobins (haemoglobinopathies/traits) However, most haemoglobin traits do not affect the level of HbA glycation or its analytical quantitation. In particular, Sickle Cell trait and HbA/HbC, HbA/HbD, HbA/HbE heterozygotes do not interfere with HbA1c analysis and the result is valid.

Thalassaemia α and β do not interfere with HbA1c analysis and the result is valid.

Rarer haemoglobinopathies including homozygous sickle cell and complex thalassaemia/haemoglobinopathy hetereozygotes may interfere and blood glucose/OGTT are advised.

3. Raised HbA1c without diabetes

Elevated HbA1c of 42–47 mmol/mol (6.0–6.4%) should be coded as “Pre-diabetes” – and undergo yearly HbA1c testing.

Where testing is in asymptomatic individuals, diagnosis of diabetes should depend on two readings both of which should be 48mmol/mol. If one is above and one below this level then calssify as ‘Pre-diabetes’.

This group should receive vigorous lifestyle advice, weight reduction support where appropriate, smoking cessation, increasing physical activity and control of other cardiovascular risk factors.

The Read code for pre-diabetes is C11y5 which is scheduled to be avaliable from April 2013. In the meantime EMIS havea temporary code , EMISNQPR215.
4. Issues when using HbA1c

There are some potential problems with using HbA1c to diagnose diabetes. HbA1c reflects prevailing glycaemia over the preceding two or three months, so may not be elevated if glucose levels have risen acutely, or where there is abnormal haemoglobin metabolism.

Clinicians need to be aware of certain clinical situations where HbA1c may not be suitable for diagnostic use in diabetes, and where glucose tests must be undertaken (above).

Most abnormal haemoglobins will be picked up by standard HbA1c assays, but a frequently encountered important clinical situation in which HbA1c may be raised is in the presence of iron deficiency anaemia (haemoglobin under 10 g/dl). The WHO guideline does not suggest undertaking a full blood count in all patients undergoing HbA1c testing to diagnose diabetes.

Other factors influencing HbA1c include carbamylated haemoglobin (seen in end stage renal failure) which increases HbA1c, as does hypertriglyceridaemia and hyperbilirubinaemia. Anti-retroviral therapy, pregnancy and chronic liver disease all modestly lower HbA1c.

Glucose tests and HbA1c may detect different populations of people with diabetes, with many studies showing significant discordance between glucose and HbA1c tests. Some ethnic groups have modestly higher HbA1c (eg. black African/Caribbeans and South Asians by around 0.4%). Some studies suggest that HbA1c is a more specific, but less sensitive test for diagnosis of diabetes, therefore potentially missing some patients with diabetes diagnosed on glucose tests. Other studies suggest that in some ethnic groups, especially South Asians, HbA1c may increase the diagnosis of diabetes. Proponents for the test, however, suggest that HbA1c of 48 mmol/mol (6.5%) is the level at which risk for complications rises and HbA1c is a better predictor of CVD events than glucose tests. Hence this level is one at which intervention to improve glycaemia might be instituted.

HbA1c has been used for population based screening for diabetes in some studies. When compared to the OGTT, the performance of HbA1c ≥48mmol/mol (6.5%) for T2D diagnosis is variable, and may be influenced by ethnicity. For population based screening of diabetes, a more cost effective and efficient option is to undertake screening using a risk score to identify people at high risk of developing diabetes followed by the use of HbA1c to identify diabetes in people found to be at high risk.

Tuomilehto has clearly set out the pros and cons of HbA1c testing. IFCC are the new units for HbA1c and a converter is available at http://www.diabetes.co.uk/hba1c-units-converter.html. Table 2 tabulates some common HbA1c values.

A second HbA1c test would usually be taken 2-4 weeks after the first test.
5. Diagnostic criteria and IFCC values

### Table 1. Diagnostic criteria for diabetes mellitus and abnormal glucose tolerance

<table>
<thead>
<tr>
<th></th>
<th>Fasting plasma glucose mmol/L</th>
<th>2 hour plasma glucose mmol/L</th>
<th>Random plasma glucose mmol/L</th>
<th>HbA1c mmol/mol (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≤ 6.0</td>
<td>&lt; 7.8</td>
<td>&lt; 11.1</td>
<td>&lt; 42 mmol/mol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt; 6.0%</td>
</tr>
<tr>
<td>Impaired fasting glucose (IFG)</td>
<td>6.1 – 6.9 and &lt; 7.8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Impaired glucose tolerance (IGT)</td>
<td>&lt; 7.0 and 7.8 - 11.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pre-diabetes</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>42–47 mmol/mol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6.0 – 6.4%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>≥ 7.0 or ≥ 11.1</td>
<td>≥ 11.1</td>
<td>≥ 11.1</td>
<td>≥ 48 mmol/mol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>≥ 6.5%</td>
</tr>
</tbody>
</table>

### Table 2. HbA1c in DCCT and IFCC units

<table>
<thead>
<tr>
<th>DCCT aligned (%)</th>
<th>IFCC HbA1c (mmol/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.0</td>
<td>42</td>
</tr>
<tr>
<td>6.5</td>
<td>48</td>
</tr>
<tr>
<td>7.0</td>
<td>53</td>
</tr>
<tr>
<td>7.5</td>
<td>58</td>
</tr>
<tr>
<td>8.0</td>
<td>64</td>
</tr>
<tr>
<td>9.0</td>
<td>75</td>
</tr>
<tr>
<td>10.0</td>
<td>86</td>
</tr>
</tbody>
</table>
6. Diagnostic pathway for diabetes – not to be used in pregnancy

Any of the following?
- Acute Symptoms (polyuria, polydipsia, weight loss)
- Possibly Type 1 diabetes
- Age under 18 years
- Short duration of symptoms
- Acutely unwell
- On steroids
- Abnormal haemoglobin
- Anaemia

Use HbA1c:
\[ \geq 48 \text{ mmol/mol (6.5\%)} \]
Confirm on repeat test
= Diabetes

Use glucose tests:
- Fasting glucose \( \geq 7.0 \text{ mmol/L} \)
- Random glucose \( \geq 11.1 \text{ mmol/L} \)
- Check urine for ketones

= Diabetes

NO

YES
References


