Diagnosing type 2 diabetes and identifying high-risk individuals using the new glycated haemoglobin (HbA1c) criteria

INTRODUCTION
Up to 30% of people with type 2 diabetes remain undiagnosed in the UK on average for 7 years, and complications are already present at diagnosis in about 50% of people.1,2 Furthermore, impaired glucose regulation or high risk of diabetes’ (pre-diabetes, impaired glucose tolerance, and/or impaired fasting glucose)3 is highly prevalent, at around 15% in adults, and carries an increased risk of progression to type 2 diabetes and vascular complications. Early initiation of lifestyle and therapeutic measures significantly reduces long-term complications of diabetes. Furthermore, intensive lifestyle intervention and/or pharmacotherapy reduce progression to diabetes by 40–60% in individuals at high risk of diabetes. Accurate diagnosis of diabetes and routine screening to identify high-risk individuals is important to improve outcomes. Availability of a simple, accessible, and reliable diagnostic test is crucial.

LIMITATIONS OF CONVENTIONAL GLUCOSE-BASED DIAGNOSTIC TESTS
Diagnosis of diabetes has been traditionally based on plasma glucose measurements.4 The fasting plasma glucose (FPG) test is more commonly used on pragmatic grounds but still involves overnight fasting and has modest sensitivity for detecting diabetes compared to the oral glucose tolerance test (OGTT).4 In contrast, the OGTT is sometimes considered as the ‘gold standard’ test but has poor test reproducibility and is inconvenient and costly.5 Furthermore glucose measurement can be affected by factors such as instability of glucose in blood samples at room temperature and fluctuations in glucose levels during periods of illness.5 Measured glucose levels therefore may not always accurately reflect true blood glycaemia.

HOW TO USE THE NEW HbA1c CRITERIA
Here we provide algorithms giving practical stepwise advice on interpretation of HbA1c results and further care that partly incorporate UK guidelines published recently6,8 (Appendix 1). The algorithms are for use mainly in the setting of clinical practice in UK.

Algorithm A should be followed when an individual presents with suspected diabetes. In someone with symptoms of diabetes, HbA1c \( \geq 6.5\% \) (\( \geq 48 \text{ mmol/mol} \)) on a single occasion confirms diagnosis of diabetes. In the absence of symptoms, the HbA1c test should be repeated in 2 weeks to rule out laboratory errors with diagnosis confirmed if repeat HbA1c is also \( \geq 6.5\% \) (\( \geq 48 \text{ mmol/mol} \)).
Algorithm B should be used while considering routine identification of individuals with undiagnosed diabetes or those at high risk. The National Institute for Health and Clinical Excellence (NICE) recommends risk identification for all non-pregnant adults aged ≥40 years, non-pregnant adults of South Asian and Chinese descent aged 25–39 years, and adults with conditions that increase the risk of type 2 diabetes, using a two-step, targeted screening strategy. The strategy involves initial risk stratification using validated diabetes risk assessment tools followed by either the HbA1c or FPG test. However the HbA1c test alone can be used after the initial risk assessment. HbA1c is a strong predictor of risk of developing diabetes and cardiovascular events, independent of FPG. Moreover inconvenience of performing an FPG test can affect the screening uptake.

PRACTICAL ISSUES IN USING THE HbA1c CRITERIA

HbA1c test may not diagnose the same individuals as the glucose-based tests. However the criteria for diagnosing diabetes relates to prediction of the risk of microvascular disease, in particular diabetes-specific retinopathy. In that regard HbA1c performs at least as well as fasting and 2-hour plasma glucose. Confirmation of diabetes using glucose tests is therefore only needed when HbA1c is <6.5% (≤48 mmol/mol) but a strong clinical suspicion of diabetes remains. Certain clinical conditions preclude use of HbA1c for diagnostic purpose and warrants use of glucose tests (Appendix 1). In the following clinical situations HbA1c must not be used to diagnose diabetes:

- pregnancy;
- all symptomatic children and young people (aged <18 years);
- symptoms suggestive of type 1 diabetes (any age);
- short duration of diabetes symptoms for <2 months;
- medication use that may cause rapid glucose rise: for example, corticosteroid, antipsychotics; and
- acute pancreatic damage/pancreatic surgery.

Furthermore the following conditions may preclude accurate measurement of HbA1c:

- anaemia or haemoglobinopathies (check haemoglobin and mean corpuscular volume);
- chronic renal/liver failure (check urea and electrolytes/liver function tests);
- hypertriglyceridaemia (check lipid profile); and
- use of drugs: erythropoietin/antiretroviral drugs/chronic opiate use, or chronic alcoholism (take drug history).

There are no specific cut-points defined for the above-mentioned haematological and biochemical tests that preclude the use of HbA1c in these conditions. Clinicians need to look at each case individually and discuss with the local laboratory. In case of uncertainties plasma glucose should be used to diagnose diabetes.

Finally it is important that HbA1c is measured on a venous blood sample in the laboratory; point-of-care assays [near testing machines] may not be accurate and should be avoided for diagnostic purpose.

CONCLUSIONS

The traditional glucose-based tests for diagnosis of type 2 diabetes have shortcomings including inconvenience of fasting, limited sensitivity, and poor test reproducibility. In comparison, an HbA1c test is simple, convenient, and reliable. Use of HbA1c as the preferred diagnostic test may improve early and accurate diagnosis of type 2 diabetes and high-risk individuals. It is crucial that clinicians remain aware of some of the limitations and practical issues in using the HbA1c-based diagnostic criteria.

Provenance

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Appendix 1. Algorithm for using HbA1c in diagnosing diabetes or identifying people at high risk of diabetes.

A. Diagnosing diabetes if patient present with clinical suspicion

**Urgent situation**
- For significantly symptomatic and/or clinically unwell patients, urgent testing and treatment may be needed. Perform an immediate finger capillary glucose and send off a venous laboratory random glucose, if either of them are > 11.0 mmol/L, diabetes is likely: consult same day referral to specialist diabetes team.

**Non-urgent situation**
- Use HbA1c**b,c** to confirm glycaemic status, otherwise proceed as below.
- Refer to intensive structured lifestyle intervention programme & Annual monitoring with HbA1c.

- If symptomatic present consider glucose test to confirm glycaemic status, otherwise proceed as below.

- < 6.0% (< 42 mmol/mol)
- 6.0 - 6.4% (< 42 - 47 mmol/mol)
- ≥ 6.5% (< 48 mmol/mol)

- No Symptoms*  
  - Repeat HbA1c in 2 weeks
  - Reassess risk at 5 years

- Symptoms*  
  - Repeat HbA1c in 6 - 12 months or sooner if symptoms develop
  - High risk of diabetes
  - Diagnosis is Diabetes
  - Refer to intensive structured lifestyle intervention programme & Annual monitoring with HbA1c

B. Routine identification and early structured intervention for individuals with undiagnosed diabetes or at a high risk

**High Risk**
- (Risk score in the top 50% of the rank)
- Use the computer based risk assessment tool, to calculate risk scores on all adults on practice register age ≥40 years. Rank the individuals according to their risk scores and categorise them as below.

**Intermediate Risk**
- (Risk score in the intermediate 25% of the rank)

**Low Risk**
- (Risk score in the bottom 25% of the rank)

- Lifestyle advice on:
  - Risk of developing diabetes & the benefits of a healthy lifestyle.
  - Modifying individual risk factors.
  - Reasses risk at 5 years

- The self assessment risk score is available online at the Diabetes UK website:  

**Notes**

**Note a. Symptoms of diabetes include**
- Increased thirst, polyuria; extreme fatigue; unexplained weight loss or burned vision.

**Note b. Clinical situations where HbA1c must not be used as a sole test to diagnose diabetes**
- Pregnancy
- All symptomatic children and young people (<18 years)
- Symptoms, suggestive of Type 1 diabetes (any age)
- Short duration of diabetes symptoms for less than 2 months
- Medication use that may cause rapid glucose rise: e.g., corticosteroid, antipsychotics
- Acute pancreatic damage/pancreatic surgery

**Note c. Exclude conditions that may preclude accurate measurement of HbA1c**
- Anaemia / Haemoglobinopathies
- Chronic renal failure (check Urea & Elect electrolytes / Liver function tests)
- Hypothyroidism / hypoglycaemia
- Use of drugs: Erythropoietin / antiretrovirals / antineoplastic drugs / Chronic Opiate use / Chronic Alcoholism / (take drug history)

There are no specific cut points defined for these haematological and biochemical tests that preclude the use of HbA1c. Clinicians need to look at each case individually and discuss with local laboratory. In case of uncertainties plasma glucose should be used to diagnose diabetes as advised.

**Note d. Leicester Practice Risk Score**

The Leicester Practice Risk Score is calculated using routinely available information in the general practice computer databases and incorporates variables including age, sex, BMI, ethnicity, family history, BP, diabetes, and history of CVD. To implement screening strategies in a cost-effective manner, a pragmatic approach is to rank people from high to risk score and allocate the top 50% of this rank to high-risk category. Other risk scores are available for example: Cambridge Diabetes risk score.

**Note e. Leicester Self Assessment Risk Score**

Leicester Self Assessment Risk Score is intended for use by lay persons where individuals calculate their own risk and then attend the GP practice for further action. Variables include age, sex, BMI, waist circumference, smoking, alcohol intake, BP, cholesterol status, physical activity, family history, other conditions. Instructions are given on how to calculate Body mass index and waist circumference.

Other risk score are available for example FINDRISC score.