Time to move to a glycated haemoglobin-based algorithm for diabetes screening and diagnosis?

A different approach may provide more effective early detection of diabetes

Diabetes poses a considerable health threat in Australia and is predicted to soon become the largest contributor to the burden of disease in this country.[1] There are an estimated 1 million Australians with diabetes, and another 2 million at high risk of developing the disease.[2] Many people with diabetes remain undiagnosed and an important strategy for reducing the disease burden is to detect and treat it earlier in order to minimise the risk of its devastating complications.

The current glucose-based protocol endorsed by the National Health and Medical Research Council (NHMRC) for screening for undiagnosed diabetes is cumbersome, time-consuming and inconvenient, and it impedes the widespread implementation of diabetes screening programs.[3] This protocol requires large numbers of individuals to have oral glucose tolerance tests (OGTTs), but fewer than 1 in 3 of those who should complete an OGTT do so.[4] In 2011, the World Health Organization endorsed the assessment of glycated haemoglobin (HbA_{1c}) levels as a diagnostic test for diabetes,[5] a recommendation adopted by the Australian Diabetes Society (ADS) in 2012.[6] While the HbA_{1c} test is more user-friendly and does not require fasting, there are clinical situations in which it may not provide an accurate assessment of diabetes, such as people with certain haemoglobinopathies or conditions that alter red blood cell turnover.[6]

HbA_{1c} testing in remote communities

An important question is how well HbA_{1c} testing detects undiagnosed diabetes in real-life contexts. The study by Marley and colleagues in this issue of the Journal[7] compared the glucose-based algorithm recommended by the NHMRC with an HbA_{1c}-based algorithm as applied in a remote Australian Aboriginal community. The HbA_{1c}-based algorithm used an initial point-of-care (POC) HbA_{1c} assessment followed by laboratory HbA_{1c} assay if needed. Participants were significantly more likely to receive a definitive result within 7 days and to be diagnosed with diabetes using the HbA_{1c} algorithm than with the glucose-based protocol. The study also highlighted the increased likelihood of follow-up with HbA_{1c} testing; only 42% of participants with an equivocal glucose result underwent an OGTT as recommended by the NHMRC guideline. Since not all participants had undergone both HbA_{1c} and OGTT assessments, a comparison of the accuracy of the two procedures for diagnosing diabetes was not possible. Nevertheless, the study clearly showed that the HbA_{1c}-based algorithm detected more cases of diabetes, is more likely to be completed as recommended, and delivered more rapid results.

Can the findings of this study be applied more broadly in Australia? Potentially, but not, unfortunately, while the current Medicare Benefits Schedule (MBS) restrictions on diagnostic HbA_{1c} tests apply.[8] The costs of POC HbA_{1c} testing for diabetes diagnosis are not reimbursed by the MBS. This is a major problem, not only for remote communities with restricted access to laboratory services, but also in any situation where POC testing could be used to exclude the likelihood of undiagnosed diabetes. The accuracy of POC testing is often raised as a concern, but an established quality control program operates in the Aboriginal Medical Services, and a similar program could be extended to other settings.[9] The Marley et al study could have provided more information on the comparative accuracy of POC and laboratory HbA_{1c} assays had all participants undergone both POC and laboratory HbA_{1c} assessments. In this regard, it should be remembered that there are many inherent inaccuracies in glucose testing related to methodological and procedural techniques, as well as substantial intra-individual biological variability.

A second restriction is that an MBS reimbursement is available for only one diagnostic HbA_{1c} test in a 12-month period. This has implications for performing a second, confirmatory HbA_{1c} test before an asymptomatic person is diagnosed with diabetes, as recommended by Australian and international guidelines.[3,5,6] Confirming an initial result is essential in light of the significant lifelong implications of being diagnosed with diabetes, especially when the laboratory result is close to the diagnostic cut-point. This MBS restriction is a missed opportunity, as not all individuals who receive an initial abnormal blood glucose result have follow-up tests, meaning that some individuals are incorrectly diagnosed with diabetes.

Stephen Colagiuri
MBBS, FRACP

Boden Institute of Obesity, Nutrition and Exercise, University of Sydney, Sydney, NSW.

stephen.colagiuri@sydney.edu.au

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Practical questions that need to be resolved

According to the MBS regulations, a single elevated laboratory HbA_{1c} test result establishes the diagnosis of diabetes. Once diagnosed with diabetes, the individual can have up to four MBS-reimbursed HbA_{1c} tests in a 12-month period to monitor their diabetes. This provides a possible solution to the dilemma of making a diabetes diagnosis based on only one abnormal HbA_{1c} result, especially if the result is borderline positive and the individual is asymptomatic. The second HbA_{1c} test (the first post-diagnosis monitoring HbA_{1c} test) could be performed within a short time, before any changes in the management of the patient, and could be used to confirm the diabetes diagnosis.

Another point worth noting is that neither the WHO nor the ADS endorse a particular HbA_{1c} range for diagnosing prediabetes. While the American Diabetes Association suggests that an HbA_{1c} value of 39–47 mmol/mol (5.7%–6.4%) is equivalent to prediabetes as defined by glucose testing,[10] this remains an area of ongoing debate, particularly concerning the appropriate lower HbA_{1c} cut-point.

For many years, we have struggled to implement glucose-based diabetes screening and case detection algorithms. As shown by Marley and colleagues,[7] HbA_{1c} testing provides an opportunity to overcome many of the barriers to implementing effective screening programs. Although there are certain clinical limitations to HbA_{1c} testing that doctors must bear in mind, the pragmatic approach adopted by Marley and colleagues would facilitate the earlier detection of diabetes in many people, and provide the opportunity to intervene earlier to reduce the personal, family and societal burden of diabetes.

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