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# Point-of-care blood test for ketones in patients with diabetes:

## primary care diagnostic technology update

### Clinical Question

In patients with diabetes, does a point-of-care test for blood ketones improve the diagnosis and management of diabetic ketoacidosis compared to standard practice?

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### ADVANTAGES OVER EXISTING TECHNOLOGY

Earlier diagnosis of capillary blood ketones associated with hyperglycaemia facilitates the prevention of ketoacidosis, as well as prompt treatment.[1] Urine ketone strips are semi-quantitative and measurements do not accurately reflect current conditions if the urine has been in the bladder for several hours (for example, overnight) before testing. Bottled strips can lose their accuracy if the bottle has been open for several months. Results can also be affected by medications, giving false-positive results in the presence of drugs containing sulphydryl groups, or false-negative reactions in the presence of ascorbic acid. In some cases, patients may also be unable to provide a urine sample (for example, due to confusion).

### DETAILS OF TECHNOLOGY

Three portable point-of-care (POC) blood ketone meters were identified, which require ~1 µl of blood and a test time of ~10 seconds: the Precision Xtra® (called Optium Xceed in the UK; Abbott Diabetes Care; detection range 0.1–6 mmol/l); the Nova Max® PLUS blood glucose and beta-ketone monitoring system (Nova Biomedical; detection range 0.1–8 mmol/l), and the GlucoMen® Lx Plus (A. Menarini Diagnostics; detection range 0.1–8 mmol/l).

### PATIENT GROUP AND USE

- Patients with type 1 or type 2 diabetes mellitus in whom diabetic ketoacidosis (DKA) is suspected clinically.
- Monitoring and management of patients with DKA.

### IMPORTANCE

DKA remains a leading cause of hospitalisation and the main cause of morbidity and death in children and adolescents with both type 1 and type 2 diabetes.[2–6] There were 2.5 million people diagnosed with diabetes in the UK in 2008 (3.8% prevalence). A recent study reported an increase in the incidence of diabetes among children in Europe, with an average annual increase of 3.9%.[3] The study also predicted a 70% increase in the incidence among children younger than 15 years by 2020.

### PREVIOUS RESEARCH

#### Accuracy compared to existing technology

The POC blood ketone test meter measures the ketone 3-beta-hydroxybutyrate (beta-OHB) in the blood of patients with diabetes. In comparison to the standard laboratory enzymatic method the ketone sensor accurately measured beta-OHB concentrations in patients with DKA (limits of agreement [LOA] 0.9 to 1.0 mmol/l) or starvation-induced ketonaemia (LOA –0.5 to +0.5 mmol/l).[7]

In an emergency department (ED) study of 173 hyperglycaemic patients, POC blood ketone tests were compared to urine dipstick analysis.[8] Several cut-off points were evaluated. At a beta-OHB value <3 mmol/l or ketonuria ≤1+, ketoacidosis could be excluded (negative predictive value 100%). At 2+ cut-off points for ketonuria and at the 3 mmol/l cut-off point for ketonaemia the two tests had the same sensitivity (100%), but the specificity of beta-OHB (94%) was significantly higher ($P$<0.001) than that of ketonuria (77%). Overall the study showed that measurement of beta-OHB in capillary blood was faster and more effective than the use of urine dipsticks to detect ketoacidosis. A follow-up study by the same group on the correlation between urine and capillary blood ketones showed a good correlation for low values, but a poor correlation for high values. The study concluded that either test could be used to exclude ketosis, but that the capillary blood ketone test is more accurate to confirm ketoacidosis.[9]

A prospective observational study in an ED comparing ketone dipstick testing with capillary blood ketone testing, showed that the positive likelihood ratio (LR+) for DKA was

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## What this technology adds

Point-of-care blood tests for ketones allow for rapid and accurate diagnosis and monitoring of diabetic ketoacidosis. A clear role of the ketone blood test in primary care is as yet uncertain; however, it may be useful in the assessment of a patient with known diabetes who is unwell, and/or has very high glucose levels.

3 using urine ketone dipstick testing, and 4 for capillary blood ketone testing. In determining hyperketonaemia (both in diabetic ketosis and diabetic ketoacidosis) the LR+ was 1.8 and 2, respectively.[10]

A study in an ED setting compared the results of this POC with standard clinical criteria for predicting DKA[11] in 160 patients presenting with blood glucose levels of >6.4 mmol/l. The study concluded that the POC test for beta-OHB was as sensitive as more established indicators of DKA and more useful than glucose alone.

Another study investigated the performance of the POC blood ketone test in the diagnosis of DKA in 450 patients with type 2 diabetes in the ED. DKA was diagnosed in 50 of these patients, with capillary ketonaemia (beta-OHB >3.0 mmol/L) providing the best accuracy for the diagnosis of DKA, compared with serum ketonaemia or ketonuria.[12]

Management and monitoring of DKA using a POC meter has also been investigated.[13] Sixty-eight children with type 1 diabetes presenting to an ED with DKA were treated using a standard protocol while also measuring venous beta-OHB levels using standard laboratory measures as well as the POC blood ketone meter. The meter readings significantly correlated with pH, bicarbonate, and $pCO_2$ at all points of measurement and may replace repeat laboratory measurement.

## IMPACT COMPARED TO EXISTING TECHNOLOGY

One study evaluated the utility of blood beta-OHB testing in children during days when they were ill or generally unwell;[14] 123 children and young adults with type 1 diabetes (3–22 years) were randomised into two groups. Participants were randomised to receive either a blood glucose monitor that also measures blood beta-OHB (blood ketone group) or a monitor plus urine ketone strips. At 6-months follow-up, there were 11 episodes of acute complications (eight ED visits and three hospitalisations) in the blood ketone group and 22 episodes (14 ED visits and eight hospitalisations) in the urine ketone group. The authors concluded that sick days guidelines with careful monitoring of capillary glucose and beta-OHB associated with adequate supplemental insulin may prevent or reduce the occurrence of DKA episodes compared to ketonuria guidelines.

## COST-EFFECTIVENESS AND ECONOMIC IMPACT

Use of the POC meter could potentially avoid the need for ED assessments and hospitalisations. However, there is limited evidence to support this. As mentioned above, in the study of 123 children and young adults comparing blood ketone with urine testing, the need for emergency assessment, treatment, and hospitalisation was reduced by almost 50% in the blood ketone group and the authors highlighted the potential cost savings.[14] Further research is required to assess the cost-effectiveness of implementing POC blood ketone tests within a UK general practice setting and to study self-assessment and self-management.

### Methodology

Standardised methodology was applied in writing this report, using prioritisation criteria and a comprehensive, standardised search strategy, and critical appraisal. Full details of this are available from www.madox.org.

### Relevant guidelines

The guideline on the management of DKA in adults published by the Joint British Diabetes Societies Inpatient Care Group in March 2010 recommends measurement of blood ketones and now represents best practice for DKA monitoring. The Scottish Intercollegiate Guidelines Network (SIGN) recommend that for monitoring during sustained hyperglycaemia, blood ketone monitoring with increased healthcare professional support is preferable to urine ketone monitoring in young adults with type 1 diabetes (SIGN 116, March 2010).


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