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Horizon scanning prioritising summary

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Diatest™: Point-of-care diagnostic test for detection of insulin resistance in patients at risk of Type 2 diabetes.

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PRIORITISING SUMMARY

REGISTER ID: **000172**

NAME OF TECHNOLOGY: **DIATEST™**

PURPOSE AND TARGET GROUP: **POINT-OF-CARE DIAGNOSTIC TEST FOR DETECTION OF INSULIN RESISTANCE IN PATIENTS AT RISK OF TYPE 2 DIABETES.**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☒	No	

The Diatest™ insulin resistance test is currently not available in Australia.

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Canada	✓		

IMPACT SUMMARY:

Isodiagnostika Inc. a division of Isotechnika Diagnostics has developed the Diatest™ for the detection of insulin resistance in patients who may be at risk of developing Type 2 diabetes. The Diatest™ is licensed for used in Canada and is not currently available in Australia or the United States.

BACKGROUND

Insulin resistance occurs when there is an impaired insulin secretory response to glucose and decreased insulin effectiveness in stimulating glucose uptake by muscle and in restraining hepatic glucose production. Insulin resistance may be a precursor for the development of Type 2 diabetes and is associated with obesity, hypertension, hyperlipidaemia and cardiovascular disease (Beers and Berkow 1999).

In normal individuals, glucose is metabolised in the presence of insulin by a process of glycolysis. The normal metabolic by-product of glycolysis is CO_2, which is expelled via the lungs into the atmosphere. In individuals with either Type 2 diabetes or insulin resistance, glucose uptake is

impaired, therefore the amount of CO_2 produced is reduced or impaired. By utilising a radioactive glucose marker patients may be tested for impaired glucose metabolism or insulin resistance (Lewanczuk et al 2004).

The Diatest™ is a non-invasive breath test that uses a radioactive labelled carbon 13 (^{13}C) glucose marker. After an overnight fast, the patient provides a baseline breath sample into a specimen tube. This is followed by the ingestion of the ^{13}C glucose formulation (test drink) and a second breath sample is taken 90 minutes later (Isotechnika Diagnostics 2005). The expired $^{13}CO_2$ following ingestion of the test drink is compared to the baseline value and results are expressed as an increases in $^{13}C0_2$ (δ/‰). Levels of expelled CO_2 will be lower in individuals with Type 2 diabetes or insulin resistance when compared to normal individuals (Isotechnika Diagnostics 2005). A Diatest™ result of less than 9.0 δ/‰ over baseline is consistent with insulin resistance as measured by the gold standard, the hyperinsulinaemic-euglycaemic clamp (personal communication Isotechnika Inc. representative). Breath samples are stable for up to 90 days and required no specialised handling (Lewanczuk 2004).

The $^{13}CO_2$ samples are analysed by an isotope ratio mass spectrometer. The same apparatus and method for testing is commonly used in other breath tests such as the ^{13}C urea breath test for *Helicobacter pylori* (personal communication, Isotechnika Inc. representative). Isodiagnostika Inc. has also developed a point-of-care Diatest™ that permits analysis in a clinician's office.

CLINICAL NEED AND BURDEN OF DISEASE

The World Health Organization has classified a specific clustering of risk factors as the Metabolic Syndrome (Syndrome X). The underlying defect in this syndrome is thought to be insulin resistance. Individuals with Metabolic Syndrome will typically have two or more of the following: glucose intolerance (impaired glucose tolerance or diabetes), dyslipidaemia, high blood pressure, central obesity and microalbuminuria. In addition to insulin resistance, Metabolic Syndrome may greatly increase a person's risk of developing Type 2 diabetes or cardiovascular disease (AIHW 2002).

It is difficult to estimate the number of individuals in Australia with insulin resistance, as the gold standard for its detection, hyperinsulinaemic-euglycaemic clamp, is not suitable for routine clinical use. As insulin resistance is a risk factor for the development of Type 2 diabetes, the prevalence of Type 2 diabetes may be an indicator of the number of individuals with insulin resistance. It should be noted, however, that patients with insulin resistance may be detected years before developing Type 2 diabetes (Rao 2001). There is currently a lack of reliable incidence and prevalence data for diabetes in Australia. Type 2 diabetes is most common among people aged 40 years and over, and accounts for 85–90% of all people with diabetes. It is estimated that approximately one million people suffer from the three types of diabetes (Type-1, Type-2 and gestational diabetes) in Australia (AIHW 2002). A 1999–2000 survey estimated that more than 7% of Australians aged 25 years or over have Type 2 diabetes.

DIFFUSION

The Diatest™ insulin resistance test is currently not available in Australia. An inexpensive, point-of-care test may be a useful tool in the primary care setting for general practitioners working with patients at risk of developing diabetes. It is likely, therefore, to receive rapid uptake.

COMPARATORS

The gold standard in directly measuring insulin resistance is the hyperinsulinaemic-euglycaemic clamp test commonly referred to as the insulin clamp test. This quantifies both beta-cell sensitivity to glucose (hyperglycaemic clamp technique) and tissue sensitivity to insulin (euglycaemic insulin clamp technique) (DeFronzo et al 1979).

The procedure takes about 2 hours. Insulin is infused at 0.06 units per kg body weight per minute through a peripheral vein. In order to compensate for the insulin infusion, 20% glucose is infused to maintain blood sugar levels between 5 and 5.5 mmol/l. The rate of glucose infusion is determined by checking the blood sugar levels every 5 minutes.

The rate of glucose infusion during the last 30 minutes of the test determines insulin sensitivity. If high levels (7.5 mg/min or higher) are required, the patient is insulin-sensitive. Very low levels (4.0 mg/min or lower) suggest that the body is resistant to insulin action. Levels between 4.1 and 7.4 mg/min may indicate impaired glucose tolerance, considered an early form of insulin resistance.

The hyperinsulinaemic-euglycaemic clamp test is complicated and expensive and is therefore used for research purposes rather than in clinical practice (Lewanczuk et al 2004). To provide clinically useful measurements, fasting insulin, glucose and triglycerides blood tests and/or a combination of tests and risk factors may be used to determine insulin resistance. The analyses may include the homeostasis model assessment (HOMA), a mathematical model of fasting blood glucose and insulin levels, and/or the quantitative insulin sensitivity check index (QUICKI), the calculation of body mass index (BMI) and waist-to-hip ratios, the presence of gestational diabetes or a family history of diabetes.

EFFECTIVENESS AND SAFETY ISSUES

The only published study to date assessed results from the Diatest™ compared with measures of insulin sensitivity from the gold standard hyperinsulinaemic clamp test, and the HOMA and QUICKI indexes of insulin sensitivity (Lewanczuk et al 2004).

In this study (level III-2 diagnostic evidence) 26 adults, including ten healthy non-obese people, seven obese people and nine people with known Type 2 diabetes, underwent the Diatest™ breath test and the hyperinsulinaemic clamp test within two days of each other. The study reports that the Diatest™ measurements of insulin sensitivity correlated well with results from the hyperinsulinaemic clamp tests for all patient types ($r=0.69$, $p<0.0001$). The correlation between the QUICKI index and the Diatest™ was also high ($r=0.73$, $p<0.0001$). There was a strong association between BMI and insulin resistance although an ANOVA analysis demonstrated that the Diatest™ detected differences among the three patient groups beyond that which was predicted by BMI. ANOVA analysis of Diatest™ demonstrated statistically significant differences between the obese and diabetic groups from the non-obese group, although numbers in this study were small ($p=0.0003$) (Lewanczuk et al 2004).

There are two further studies of the Diatest™ awaiting publication (personal communication Isodiagnostika Inc.).

COST IMPACT

There are no studies of the cost impact of using the Diatest™ to guide clinical practice in detecting and/or managing insulin resistance in patients. It is not possible to predict an increase in

prescription medication to manage insulin resistance and the likely cost impact has not been examined. In the first instance, insulin resistance is managed by increasing physical activity and promoting weight loss.

The cost of the test is approximately $US 20 utilising the existing equipment employed for ^{13}C urea breath testing for *Heliobacter pylori* (Isodiagnostika Inc. company representative).

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

The breath samples are stable for up to 90 days and require no specialised handling, which may make the Diatest™ more suitable for use in rural and remote areas. Large numbers of samples may be taken and shipped to a central point for analysis without the requirement of a cold chain (Lewanczuk 2004).

OTHER ISSUES

The Diatest™ has not been used to assess effectiveness of interventions designed to alter insulin sensitivity such as medication (Lewanczuk 2004).

CONCLUSION:

The early detection of insulin resistance could allow patients to begin preventive lifestyle interventions to delay or avoid the development of diabetes. However, as it is known that obesity and lack of physical activity (associated with insulin resistance) are risk factors for diabetes, and that lifestyle modification are preventive, it is unclear as to the clinical utility of an additional marker for diabetes. It is difficult to assess the benefits of incorporating the use of the Diatest™ into clinical practice without evidence of how it could guide therapy.

HEALTHPACT ACTION:

It is difficult to ascertain the extent that the Diatest™ will add to the diagnosis of Type II diabetes. Therefore it is recommended that this technology be archived.

LIST OF STUDIES INCLUDED	TOTAL
Total number of studies	
Level III-2 diagnostic evidence	1

SOURCES OF FURTHER INFORMATION:

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Association, A. D. (1998). 'Consensus Development Conference on Insulin Resistance. 5-6 November 1997. American Diabetes Association', *Diabetes Care*, 21 (2), 310-314.

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Grundy, S. M., Hansen, B. et al (2004). 'Clinical management of metabolic syndrome: report of the American Heart Association/National Heart, Lung, and Blood Institute/American Diabetes Association conference on scientific issues related to management', *Arterioscler Thromb Vasc Biol*, 24 (2), e19-24.

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Rao, G. (2001) *Insulin Resistance* [Internet] Available from: http://www.aafp.org/afp/20010315/1159.html [Accessed 2nd June 2005]

Sjoholm, A. & Nystrom, T. (2005). 'Endothelial inflammation in insulin resistance', *Lancet*, 365 (9459), 610-612.

Streja, D. (2004). 'Metabolic syndrome and other factors associated with increased risk of diabetes', *Clin Cornerstone*, 6 Suppl 3, S14-29.

SEARCH CRITERIA TO BE USED:

Diabetes Complications
Diabetes Mellitus/physiopathology/therapy
Diabetes Mellitus, Type 2/etiology/ prevention & control
Insulin Resistance
Metabolic Syndrome X/complications/ diet therapy/ drug therapy/therapy