NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Type 1 diabetes: Integrated sensor-augmented pump therapy systems for managing blood glucose levels (The MiniMed Paradigm Veo System and the Vibe and G4 PLATINUM CGM system)

Final scope

September 2014

1 Introduction

The MiniMed Paradigm Veo System is manufactured by Medtronic. The Medical Technologies Advisory Committee identified the MiniMed Paradigm Veo System as potentially suitable for evaluation by the Diagnostics Assessment Programme on the basis of a briefing note. The final scope was informed by discussions at the scoping workshop held on 29 July 2014 and at the assessment subgroup meeting held on 13 August, 2014.

A glossary of terms is provided in appendix A.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE by the manufacturer and NHS professionals and on information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technologies

The MiniMed Paradigm Veo System and the Vibe and G4 PLATINUM CGM system are integrated sensor-augmented insulin pump systems that are intended to be used in people with type 1 diabetes. Diabetes is a chronic

metabolic disorder which causes a person's blood glucose to become too high. To prevent this, insulin is often administered to reduce the blood glucose level but sometimes this can cause blood glucose levels to become too low and lead to hypoglycaemia. The integrated sensor-augmented pump systems are designed to measure interstitial glucose levels on a continuous basis (every few minutes) and allow immediate adjustment of insulin therapy in real-time. The systems produce alerts if the glucose levels become too high or low and the MiniMed Paradigm Veo system can also suspend insulin delivery automatically if there is no response to a low glucose warning. Using these systems may improve glucose control and consequently, may reduce the number of diabetes-related complications and improve the quality of life for people with type 1 diabetes. It may also make it easier for them to adhere to treatment. The ability of the MiniMed Paradigm Veo system to automatically suspend insulin delivery may be beneficial in reducing the incidence of nocturnal hypoglycaemia and the associated anxiety. Both systems may also offer benefits to the NHS through cost and resource savings by reducing the number of hospital admissions associated with diabetes-related complications, and by achieving optimum therapy more quickly.

2.2 The MiniMed Paradigm Veo System

The MiniMED Paradigm Veo system (Medtronic) is a type of sensor-augmented pump therapy which comprises 3 components:

- a glucose sensor placed under the skin that continuously measures blood glucose levels,
- an insulin pump which delivers insulin continuously,
- and a non-implanted transmitter which sends glucose level readings wirelessly from the monitor to the pump.

The system produces alerts if glucose levels become too high or low, if levels are rapidly changing, or if the system predicts glucose levels will be too high or too low in the near future. The automated low glucose suspend function of

the system operates independently of user action and stops insulin delivery for 2 hours if there is no response to the alert.

The system is intended for use in conjunction with standard capillary blood glucose tests because the MiniLink glucose sensor is situated under the skin and therefore, measures the glucose levels in the fluid between blood capillaries and the body's cells (interstitial fluid) rather than capillary blood glucose levels. There is a lag between blood and interstitial glucose levels of at least 15 minutes and therefore, a minimum of 2 capillary blood glucose tests per day may be needed. The lag increases when blood glucose levels are changing rapidly so although trends in interstitial glucose are representative of blood glucose changes, absolute interstitial glucose values do not always coincide with blood glucose levels. Further confirmatory capillary blood glucose tests may therefore be required to confirm the value displayed by the continuous glucose monitor before making any adjustments to diabetes therapy.

The insulin pump in the system delivers insulin continuously from a refillable storage reservoir by means of a subcutaneously placed infusion set. The pump can be programmed to deliver a basal rate of insulin throughout the day, with higher infusion rates triggered by pushing a button on the pump at meal times. This may be a bolus dose (that is one taken specifically at meal times to keep glucose levels under control following a meal) or over a period of time. It can also deliver different basal rates of insulin at different times of the day and night. The manufacturer information for use document states that the infusion set should be replaced every 3 days.

The MiniMed Paradigm Veo system is compatible with the CareLink software platform (Medtronic) which is designed to allow users to upload their data from the MiniMed Paradigm Veo system so that clinicians can evaluate the patient's glycaemic control, notice any trends and adjust their therapy as appropriate.

2.3 The Vibe and G4 PLATINUM CGM system

This integrated sensor-augmented pump system is a continuous glucose monitoring (CGM)-enabled insulin pump (Animas), integrated with the G4 PLATINUM sensor (Dexcom). It is similar to the MiniMed Paradigm Veo system in that the glucose sensor is placed under the skin and measures interstitial glucose levels rather than capillary blood glucose levels. Confirmatory capillary blood glucose tests are also required to confirm the value displayed by the continuous glucose monitor before making any adjustments to diabetes therapy. The sensor is approved for up to 7 days of wear.

The insulin pump in the Vibe and G4 PLATINUM CGM system also delivers insulin continuously from a refillable storage reservoir by means of a subcutaneously placed cannula and the pump can be programmed to deliver a basal rate of insulin throughout the day, with the option of triggering higher infusion rates at meal times either as a bolus dose or over a period of time. The pump can be programmed to enable different basal rates of insulin at different times of the day and night.

The system produces glucose level readings in real-time, alerts for high and low readings, and glucose trend information. It does not have an automated low glucose suspend function.

3 Target conditions

3.1 Diabetes

Background

Diabetes is a chronic metabolic disorder which causes a person's blood sugar level to become too high (hyperglycaemia). Blood sugar (glucose) levels are regulated by a hormone called insulin, which is produced by the pancreas. Glucose is released into the blood when food is digested and insulin stimulates the cells of the body to break down the glucose to produce energy.

As the glucose is broken down, the levels of sugar in the blood reduce. In diabetes, the activity or levels of insulin are not sufficient to regulate blood glucose levels effectively which can lead to high and even toxic levels of glucose (hyperglycaemia). Hyperglycaemia is defined as blood glucose levels greater than 7.0 millimoles/litre when fasting and greater than 11.0 millimoles/litre 2 hours after meals. Hyperglycaemia in diabetes can cause short-term problems like diabetic ketacidosis and long-term problems including retinopathy and blindness, peripheral and autonomic nephropathy, renal failure, ischaemic heart disease, stroke, neuropathy and foot ulceration.

Diabetic ketoacidosis is a life-threatening short-term problem of diabetes which occurs when a lack of insulin prevents the body from using glucose for energy. The body starts to break down other body tissue, such as fat, as an alternative energy source. This leads to the production of ketones as a by-product. Ketones also need insulin to enter cells and if there is not enough they build up in the blood causing it to become acidic. The presence of ketones is an early sign of diabetic ketoacidosis. Symptoms include frequent passing of urine, thirst, lethargy, blurry vision, nausea and vomiting, smell of ketones on breath and collapse and unconsciousness. A person with diabetic ketoacidosis may need to be admitted to hospital for the condition to be treated with insulin and intravenous fluids. Ketone testing and early detection is therefore important in the management of diabetes.

There are 2 types of diabetes: Type 1 diabetes which is an autoimmune disorder caused by the destruction of insulin-producing cells in the pancreas, leading to an absolute lack of the hormone; and type 2 diabetes which is characterised by insulin resistance and is often associated with obesity.

The focus of this assessment is the use of integrated sensor-augmented insulin pump therapy systems in people with type 1 diabetes.

Type 1 diabetes

Type 1 diabetes typically develops in children and young adults and has an estimated prevalence of approximately 0.42% (250,000) people in the UK in 2005 (NICE technology appraisal 151). The incidence is increasing, with the greatest increase in children younger than 5 years.

If left untreated, lack of insulin in type 1 diabetes leads to hyperglycaemia and complications such as diabetic ketoacidosis in the short-term and long-term complications such as retinopathy and blindness, nephropathy and renal failure, ischaemic heart disease, stroke, neuropathy and foot ulceration. Hyperglycaemia can be controlled by injecting insulin to maintain biological glucose levels. However, high levels of circulating insulin can lead to hypoglycaemia (low blood glucose levels).

Hypoglycaemia occurs when the level of glucose present in the blood falls below 4 millimoles per litre (diabetes.co.uk). Hypoglycaemia can be mild, which is corrected by oral intake of sugars, or severe, which is defined by the need for assistance from another person for recovery. The main symptoms associated with hypoglycaemia are blurred vision, dizziness, fatigue, hunger and sweating. More severe symptoms include confusion, convulsions, coma and death. In children, especially those younger than 5 years, severe hypoglycaemia can cause long-term cognitive impairment. In addition, fear of recurrent hypoglycaemia not only decreases quality of life in the short term but can also hinder adherence to treatment and the achievement of good glycaemic control.

Nocturnal hypoglycaemia is hypoglycaemia that occurs during sleep and is common in people who manage their diabetes with insulin (Brunton, 2007). It is particularly serious because people with diabetes are unable to detect its symptoms while sleeping and may not awaken during an episode. Symptoms of nocturnal hypoglycaemia include waking up with a headache, feeling unusually tired and experiencing unprovoked sleep disturbance. Death is rare as a result of nocturnal hypoglycaemia because the body usually reacts to the

low by producing adrenaline, which causes profuse sweating, shaking, and a strong/rapid heartbeat (Scheiner, 2012). Adrenaline also stimulates the liver to release some of its stored-up sugar into the bloodstream.

Nocturnal hypoglycaemia may also lead to an impaired awareness of hypoglycaemia, where people with type 1 diabetes are frequently unable to notice when they have hypoglycaemia. Symptoms of hypoglycaemia become less obvious after having diabetes for several years because repeated hypoglycaemia episodes impair the body's release of stress hormones Nocturnal hypoglycaemia occurs in approximately 20% of people with type 1 diabetes and is associated with compromised safety in attempting to achieve optimal diabetes control, and reduced quality of life (Otway, 2014).

Type 1 diabetes in pregnancy

Diabetes that complicates pregnancy is becoming more common worldwide. Up to 5% of the approximately 700,000 women who give birth in England and Wales each year have pre-existing or gestational diabetes. Less than 1% of this 5% of pregnant women have pre-existing diabetes. The duration of diabetes before conception also varies but is increasing because the average age of onset of type 1 diabetes is declining. This is important because duration of diabetes is one of the strongest factors associated with microvascular complications and it is, therefore, more likely that women with a long duration of diabetes will enter pregnancy with established retinopathy, nephropathy and neuropathy.

Maternal risks of pre-existing diabetes include recurrent hypoglycaemia, progression of retinopathy, nephropathy, increased incidence of pre-eclampsia (especially in women with microvascular disease) and operative delivery. Fetal risks of pre-existing maternal diabetes include structural congenital abnormality, pathological fetal growth (macrosomia) and 'unexplained' fetal death. Neonatal complications include premature delivery, respiratory distress syndrome, transient tachypnoea, birth trauma,

hypoglycaemia, hypomagnesaemia, hypocalcaemia, polycythaemia and neonatal death.

3.2 Patient issues and preferences

Diabetes is a life-long condition in which both morbidity and treatment affect quality of life. Daily life activities need to be arranged around a relatively inflexible structure of meal times and insulin injections. Many factors can cause fluctuations in glucose levels, such as examination-associated stress, diet, mental and physical exercise, which can make it difficult for a patient to maintain good glucose control. With increasing duration of illness and the onset of complications, people with diabetes and their carers may experience occupational difficulties, and in children difficulties in school performance.

Diabetes in children can cause intense parental anxiety and stress for all members of the family. The burden on carers of children with diabetes who are under 12 years old can be high and can substantially impact on their quality of life. Nocturnal hypoglycaemia, particularly, can cause substantial anxiety for parents and may result in them becoming sleep deprived because they stay up all night to monitor their children's glucose levels.

Other patient issues related to the technologies in the scope include alarm fatigue (especially when related to false alarms) and scarring on the skin in the areas where sensors are worn, causing users to seek alternative areas to wear the sensor.

People with diabetes also report that the requirement from the Driver and Vehicle Licensing Agency to test glucose levels before driving results in having to perform many additional capillary blood glucose tests, particularly for those in occupations that involve driving. The fear of losing a driving licence may also dissuade a person with diabetes from reporting a hypoglycaemic episode which may mean that the number of episodes of hypoglycaemia in people with diabetes may be underestimated.

3.3 Diagnostic and care pathway

Management of type 1 diabetes consists of frequent testing of blood glucose levels and either multiple daily insulin injections or continuous subcutaneous insulin infusion. In addition, ketone testing is undertaken if a person has sustained high blood glucose levels.

Measuring blood glucose

Blood glucose concentrations vary widely during a 24 hour period and from day to day in diabetes. In the management of diabetes, glycemic control is assessed by measuring blood glucose levels as well as by measuring HbA1c levels. Blood glucose measurements are taken after several hours of fast, usually in the morning before breakfast (fasting blood glucose level), and before and after each meal to measure the change in glucose concentration (post prandial blood glucose level).

Blood glucose is measured in 3 ways:

a) Firstly, blood glucose can be checked at any time by testing a drop of blood with a glucose meter (capillary blood glucose testing), also known as self-monitoring of blood glucose.

b) Secondly, continuous glucose monitors provide frequent automated testing of interstitial tissue glucose, calibrated to reflect blood plasma glucose.

c) Thirdly, longer-term control is measured by glycated haemoglobin (HbA1c), which reflects the average blood glucose levels over 2 to 3 months.

a) Self-monitoring of blood glucose by capillary blood glucose testing

Self-monitoring of blood glucose involves the measurement of blood glucose concentration by people with diabetes or their carers. This involves pricking a part of the body (usually the finger) with a lancet device to obtain a small blood sample at certain times of the day. The drop of blood is then applied to

a reagent strip which is inserted into a blood glucose meter for automated determination of the glucose concentration in the blood sample at the time of the test. A 7-point self-monitoring of blood glucose regimen may also be used by people with diabetes. This involves measuring blood glucose levels 7 times during the day (before and after each meal and at bedtime).

Self-monitoring of blood glucose should be viewed as part of the self-management of diabetes, not a standalone intervention. It is used to inform the person of their blood glucose to allow decision making regarding treatment and to inform the person on the impact of changes in lifestyle, diet and physical activity which could influence the longer term control of their diabetes (Arnott and Currie, Date unknown).

NICE Clinical Guideline 15; "Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults (2004)" states:

- *Self-monitoring of capillary blood glucose levels, normally via a fingertip or 'fingerprick' test, is dependent upon the specific insulin treatment regimen, personal preference and the specific characteristics of a person's blood glucose control. Optimal targets of short term control around mealtimes are recommended at 4.0-7.0millimoles/litre before meals and less than 9.0 millimoles/litre after meals. Typical testing for multiple daily injection therapy involves a minimum of 4 tests (before meals and before night time sleep) but this is supplemented depending on symptoms of feeling being at high or low blood glucose; 8 to 10 tests per day is not uncommon.*

This guideline is currently being updated and the updated guideline is scheduled to be published in 2015.

For pregnant women, NICE clinical guideline 63; "Diabetes in pregnancy: Management of diabetes and its complications from pre-conception to the postnatal period" recommends:

- *Individualised targets for self-monitoring of blood glucose should be agreed with women who have diabetes and are planning to become pregnant, taking into account the risk of hypoglycaemia.*

- *Women with diabetes who are planning to become pregnant should be offered a meter for self-monitoring of blood glucose.*

- *Women with diabetes who are planning to become pregnant and who require intensification of hypoglycaemic therapy should be advised to increase the frequency of self-monitoring of blood glucose to include fasting and a mixture of pre- and postprandial levels.*

b) Continuous glucose monitoring

Continuous glucose monitoring generates an average glucose value every few minutes. Continuous glucose monitors are inserted under the skin and measure interstitial fluid glucose. They require calibration and are therefore used in conjunction with self-monitoring of blood glucose. NICE clinical guideline 15 states:

- *Continuous glucose monitoring systems have a role for individuals who have repeated hyper- or hypoglycaemic episodes at the same time each day or who have hypoglycaemic unawareness which is unresponsive to insulin dose adjustment.*

For pregnant women; the Scottish Intercollegiate guidelines Network guideline 116 on the management of diabetes states:

- *Continuous glucose monitoring may be considered in women with type 1 or type 2 diabetes who are pregnant.*

c) Measurement of glycated haemoglobin (HbA1c) level

Long-term monitoring of blood glucose control is achieved by measuring glycated haemoglobin (HbA1c levels), which reflect average blood glucose levels over the preceding 3 months. Good control is indicated by an HbA1c

value of 58.5 millimole/mole (7.5%) or less. The normal range for people who do not have diabetes is 25.7-43.2 millimole/mole (4.5-6.1%). For people with diabetes, the higher the HbA1c value, the greater the risk of developing diabetes-related complications.

NICE Clinical Guideline 15 recommends:

- *Children and young people with type 1 diabetes and their families should target long-term glycaemic control at an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia. Similarly, adults with type 1 diabetes should maintain a diabetes control and complications trial - harmonised HbA1c below 7.5% to minimise their risk of developing diabetic eye, kidney or nerve damage in the longer term".*

For pregnant women, NICE clinical guideline 63 recommends:

- *If it is safely achievable, women with diabetes who are planning to become pregnant should aim to maintain their HbA1c below 6.1%. Women should be reassured that any reduction in HbA1c towards the target of 6.1% is likely to reduce the risk of congenital malformations.*

- *Women with diabetes whose HbA1c is above 10% should be strongly advised to avoid pregnancy.*

- *Women with diabetes who are planning to become pregnant should be offered monthly measurement of HbA1c.*

Ketone testing

Early detection of ketones in the blood allows prompt action to be taken and prevents the person from developing diabetic ketoacidosis. Ketone testing is crucial if a person has sustained high blood sugar readings which can often occur during periods of illness and when there is difficulty in controlling glucose levels.

Ketone testing involves measuring the amount of ketones in either urine or blood. Blood ketone testing is considered to be more accurate and more up to date. Moreover, the accuracy of urine testing is affected by medication and the amount of liquid a person drinks. Dilute urine can lead to false negatives and if the person is dehydrated, a falsely high ketone measurement.

NICE Clinical Guideline 15 recommends:

- *Children and young people with type 1 diabetes should have short-acting insulin or rapid-acting insulin analogues and blood and/or urine ketone testing strips available for use during intercurrent illness.*

For pregnant women, NICE clinical guideline 63 recommends:

- *Women with type 1 diabetes who are planning to become pregnant should be offered ketone testing strips and advised to test for ketonuria or ketonaemia if they become hyperglycaemic or unwell.*

Management with Insulin

a) Multiple daily insulin injections

In Type 1 diabetes, blood glucose control is achieved by insulin injection, with the treatment being required throughout the person's life. There are various types of insulin distinguished by their rate of onset and duration of action. Insulin requirements change depending on food intake and/or exercise. Insulin types with varying times to onset and durations of action are combined in treatment regimens, which are then delivered by multiple injections timed to coincide with requirements. Achieving good control of blood glucose through an intensive regimen reduces the risk of complications. Intensive insulin regimens attempt to reproduce the normal secretion of insulin by the pancreas. However, exogenously administered insulin lacks the feedback mechanism that the pancreas uses to regulate insulin secretion, whereby insulin production decreases as blood glucose levels fall. Therefore, people taking insulin need to self-monitor their blood glucose level. Regular

measurements enable short-term control of blood glucose levels by adjusting the insulin dose.

NICE Clinical Guideline 15 recommends:

- *Use multiple insulin injection regimens in adults who prefer them in an integrated package with education, food, skills training and appropriate self-monitoring.*

b) Continuous subcutaneous insulin infusion

Continuous subcutaneous insulin infusion makes use of an external pump that delivers insulin continuously from a refillable storage reservoir by means of a subcutaneously placed cannula. The pump can be programmed to deliver a basal rate of insulin throughout the day, with higher infusion rates triggered by the push of a button at meal times.

NICE technology appraisal 151; "Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus" recommends:

1. Continuous subcutaneous insulin infusion therapy *as a treatment option for adults and children 12 years and older with type 1 diabetes mellitus provided that:*

- *attempts to achieve target HbA1c levels with multiple daily injections result in the person experiencing disabling hypoglycaemia. For the purpose of this guidance, disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life.*

or

- *HbA1c levels have remained high (that is, at 8.5% or above) on multiple daily injection therapy (including, if appropriate, the use of long-acting insulin analogues) despite a high level of care.*

2. *Continuous subcutaneous insulin infusion therapy is recommended as a treatment option for children younger than 12 years with type 1 diabetes mellitus provided that:*

- *multiple daily injection therapy is considered to be impractical or inappropriate, and*

- *children on insulin pumps would be expected to undergo a trial of multiple daily injections therapy between the ages of 12 and 18 years.*

3. *It is recommended that continuous subcutaneous insulin infusion therapy be initiated only by a trained specialist team, which should normally comprise a physician with a specialist interest in insulin pump therapy, a diabetes specialist nurse and a dietician. Specialist teams should provide structured education programmes and advice on diet, lifestyle and exercise appropriate for people using continuous subcutaneous insulin infusion.*

4. *Following initiation in adults and children 12 years and older, continuous subcutaneous insulin infusion therapy should only be continued if it results in a sustained improvement in glycaemic control, evidenced by a fall in HbA1c levels, or a sustained decrease in the rate of hypoglycaemic episodes. Appropriate targets for such improvements should be set by the responsible physician, in discussion with the person receiving the treatment or their carer.*

5. *Continuous subcutaneous insulin infusion therapy is not recommended for the treatment of people with type 2 diabetes mellitus.*

4 Scope of the evaluation

Table 1: Scope of the evaluation

Decision question	Does the use of the MiniMed Paradigm Veo System and, the Vibe and G4 PLATINUM CGM system for managing blood glucose levels in type 1 diabetes represent a clinically- and cost-effective use of NHS resources?
Populations	People with type 1 diabetes If evidence permits, the following sub-populations may be included: • Women who are pregnant and those planning pregnancy (not including gestational diabetes) • People who need to self-monitor their blood glucose level more than 10 times a day. • People who are having difficulty managing their condition. These difficulties include: o not maintaining the recommended HbA1c level of 69.4 millimoles/mole (8.5%) or below o nocturnal hypoglycaemia o impaired awareness of hypoglycaemia. o severe hypoglycaemia defined as having low blood glucose levels that requires assistance from another person to treat.
Interventions	• The MiniMed Paradigm Veo System • The Vibe and G4 PLATINUM CGM system
Comparator	• Capillary blood testing with continuous subcutaneous insulin infusion • Capillary blood testing with multiple daily insulin injections • Continuous glucose monitoring with continuous subcutaneous insulin infusion (non-integrated)

	• Continuous glucose monitoring with multiple daily injections
Healthcare setting	Self-use supervised by primary or secondary care
Outcomes	Clinical outcomes for consideration may include: • Adverse events from testing, false results, treatment and sequelae • Mean blood glucose levels including fasting glucose levels • Postprandial glucose level • Amount of insulin being administered • Number of ketone tests • Episodes of diabetic ketoacidosis • Episodes of hyperglycaemia (mild and severe) • Episodes of hypoglycaemia (mild and severe including nocturnal) • Frequency of hypoglycaemic episodes • HbA1c levels • Long term complications of diabetes and treatment including retinopathy, neuropathy, cognitive impairment and end stage renal disease. • Morbidity and mortality In pregnant women, additional type 1 diabetes-related clinical outcomes may include: • Premature birth • Macrosomia (excessive birth weight) • Respiratory distress syndrome in newborn
	Patient-reported outcomes for consideration may include: • Acceptability of testing and method of insulin administration

	• Anxiety about experiencing hypoglycaemia • Health related quality of life
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Cost of consumables (glucose testing strips, sensors, infusion sets, ketone testing strips) • Cost of technology • Cost of insulin • Cost of staff and training of staff and users. • Costs of NHS treatment for episodes of diabetic ketoacidosis • Costs of NHS treatment for severe hypoglycaemic episodes • Medical costs arising from ongoing care and treatment diabetes and associated sequelae • Costs of managing clinical outcomes arising from diabetes during pregnancy. This may include: o Premature birth o Macrosomia (excessive birth weight) o Respiratory distress syndrome in newborn
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

5 Modelling approach

5.1 Existing models

Searches undertaken during scoping identified the following existing models.

a) The Centre for Outcomes Research (CORE) model which is the main model used in NICE technology appraisal 151. The CORE model is an internet model which is based upon 15 sub-models which stimulate the main complications of diabetes. Each sub-model is a Markov model that employs Monte Carlo simulation which incorporates the time, state, the time in state and transition probabilities.

   The 15 sub-models of the CORE model are: angina, cataract, congestive heart failure, foot ulcer with possible amputation, hypoglycaemia, ketoacidosis, lactic acidosis, macular oedema, myocardial infarction, nephropathy, neuropathy, peripheral vascular disease, retinopathy, stroke and general mortality.

b) The Sheffield Type 1 Diabetes Policy Model which is a patient-level simulation model of type 1 diabetes and its associated complications. The model is highly flexible and has broad potential application to evaluate the Dose Adjustment For Normal Eating programme (DAFNE), other diabetes structured education programmes, and other interventions for type 1 diabetes (Thokala *et al*, 2013).

6 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Some potential equality issues which may be addressed are:

- People with cognitive disorders and people whose vision or hearing does not allow recognition of pump signals and alarms may have difficulty in using the technologies.
- People with a disability may have difficulty in self- administering insulin injections.
- Glucose levels should be more tightly controlled in pregnancy.
- Impaired awareness of hypoglycaemia is more common in older people.

7 Potential implementation issues

NICE technology appraisal 151 recommended continuous subcutaneous insulin infusion for people with diabetes who met the clinical criteria stated in the guidance. However, the UK-wide Insulin Pump Audit (2013) which was commissioned jointly by Diabetes UK, the Association of British Clinical Diabetologists and the Juvenile Diabetes Research Foundation, reported that approximately half of sites that deliver continuous subcutaneous insulin infusion have to submit separate funding applications for each person who requires continuous subcutaneous insulin infusion. The audit also reported that 18% of clinical commissioning groups have a fixed quota for continuous subcutaneous insulin infusion in adults.

Anecdotally, people with diabetes and patients organisations also report that it is difficult to gain access to continuous glucose monitors because of a lack of funding.

Other potential implementation issues include:

- Lack of capacity and training for healthcare professionals. Half of diabetes specialist nurses delivering continuous subcutaneous insulin infusion services have attended training; only 1 consultant per centre has attended training (UK-wide Insulin Pump Audit, 2013).

- Less experience in continuous glucose monitoring among healthcare professionals.

- Training and educational tools are needed to teach users and their carers how to manage glucose levels. Some users and carers may find interpreting the data challenging and becoming competent at managing glucose levels can involve a lot of time and dedication.

- Lack of whole time equivalent diabetes specialist nurses with continuous subcutaneous insulin infusion expertise

Difficulty with compatibility in IT software and IT systems at home for people with diabetes and for healthcare professionals in the NHS. Users and their carers report that some sensors fail and that the supply of sensors from manufacturers can be inconsistent. Both of these can cause the user to run out of sensors.

Appendix A Glossary of terms

Diabetic ketoacidosis: occurs when the body is unable to use blood glucose because of inadequate insulin. Instead, fat is broken down as an alternative source of fuel; a process that leads to a build-up of a by-product called ketones.

Hypocalcaemia: this is a term that refers to low blood calcium level.

Hypomagnesaemia: this is a term that refers to low levels of magnesium in their blood.

Impaired awareness of hypoglycaemia: a term used to describe a situation where people with diabetes, usually type 1 diabetes, are frequently unable to notice when they have low blood sugar.

Ketonaemia: this is a term that refers to the presence of an abnormally high concentration of ketone bodies in the blood.

Ketonuria: this is a term that refers to the presence of abnormally high amounts of ketones and ketone bodies (a by-product of the breakdown of cells) in the urine. Ketonuria is a sign seen in badly controlled diabetes.

Macrosomia: this is a term that refers to a condition characterised by foetuses being too large for their gestational age.

Nephropathy: this is a term that refers to damage to or disease of a kidney.

Neuropathy: this is a term that refers to disease or dysfunction of one or more peripheral nerves, typically causing numbness or weakness.

Polycythaemia: this is a term that refers to an abnormally increased concentration of haemoglobin in the blood, either through reduction of plasma volume or increase in red cell numbers.

Pre-eclampsia: this is a term that refers to a condition in pregnancy characterized by high blood pressure, sometimes with fluid retention and proteinuria.

Respiratory distress syndrome: It is an acute lung disease present at birth, which usually affects premature babies. The lungs are said to be "airless" and without treatment, the infant will die within a few days after birth. However, if oxygen can be provided, and the infant receives treatment in a neonatal intensive care unit, complete recovery with no after-effects can be expected.

Retinopathy: Diabetic retinopathy is a common complication of diabetes. It occurs when high blood sugar levels damage the cells at the back of the eye (known as the retina). If it isn't treated, it can cause blindness.

Transient tachypnoea: it is a respiratory disorder usually seen shortly after delivery in full- or near-term babies. **Transient** means it is short-lived (usually less than 24 hours). **Tachypnea** means rapid breathing (most healthy newborns take 40 - 60 breaths per minute).

Appendix B Related guidance

NICE guidance

- **Published NICE guidance**

Diabetes. NICE Pathway. (2013). Available from: http://pathways.nice.org.uk/pathways/diabetes

Preventing type 2 diabetes. NICE Pathway. June 2013. Available from: http://pathways.nice.org.uk/pathways/preventing-type-2-diabetes

Diagnosis and management of type 1 diabetes in children, young people and adults: NICE clinical guideline CG15 (2004). Available from: http://www.nice.org.uk/CG15 Date for review: Reviewed in August 2011 and decision was made to update the guideline. Update scheduled to be published in

Diabetic foot – inpatient management of people with diabetic foot ulcers and infection: NICE clinical guideline CG119 (2011). Available from: http://guidance.nice.org.uk/CG119. Date for review: TBC

Type 2 diabetes: the management of type 2 diabetes (update): NICE clinical guideline CG66 (2008). Available from: http://guidance.nice.org.uk/CG66. Date for review: Following a review in 2011 an update of this guideline is currently in the process of being scheduled into the work programme.

Type 2 diabetes: prevention and management of foot problems: NICE clinical guideline CG10 (2004). Available from: http://guidance.nice.org.uk/CG10. Date for review: An update of this guideline is underway to coincide with publication of the four diabetes guidelines currently being updated.

Type 2 Diabetes - newer agents (partial update of CG66) (CG87): NICE clinical guideline CG87 (2009). Available from: http://guidance.nice.org.uk/CG87 Date for review: Following the recent review recommendation, an update of this guideline is in progress

Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period: NICE clinical guideline (2008). Available from: http://guidance.nice.org.uk/CG63 Date for review: This guideline is currently being updated. Further information can be found on the Diabetes in pregnancy guideline in development page.

Neuropathic pain - pharmacological management: the pharmacological management of neuropathic pain in adults in non-specialist settings: NICE clinical guideline CG173 (2013). Available from: http://guidance.nice.org.uk/CG173 Date for Review: TBC

Hyperglycaemia in acute coronary syndrome: NICE clinical guideline CG130 (2011) Available from: http://www.nice.org.uk/guidance/CG130 Date for review: TBC

The clinical effectiveness and cost effectiveness of long acting insulin analogues for diabetes: NICE technology appraisal guidance TA53 (2002). Available from: http://www.nice.org.uk/guidance/TA53 Date for review: The recommendations in this technology appraisal relating to type 2 diabetes have been replaced by recommendations in the Diabetes - type 2 (update) clinical guideline published in May 2008. Please note that the recommendations in this technology appraisal relating to type 1 diabetes have not changed.

Continuous subcutaneous insulin infusion for the treatment of diabetes (review). NICE technology appraisal guidance TA151 (2008). Available from: http://guidance.nice.org.uk/TA151 Date for review: TBC

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- **NICE guidance under development**

Diabetes in children and young people (update) NICE clinical guideline (publication expected August 2015)

Type 1 diabetes (update) NICE clinical guideline (publication expected August 2015)

Type 2 diabetes (update) NICE clinical guideline (publication expected August 2015)

Diabetes in pregnancy (update) NICE clinical guideline (publication expected February 2015)

Diabetic foot problems (update) NICE clinical guideline (publication expected June 2015)

NICE pathways

The guidance: "Type 1 diabetes: Integrated sensor-augmented pump therapy systems for managing blood glucose levels (The MiniMed Paradigm Veo System and the Vibe and G4 PLATINUM CGM system)" will be included in the NICE diabetes pathway.

Relevant guidance from other organisations

Management of diabetes. Scottish Intercollegiate guidelines Network guideline 116 (2010). Available from: http://www.sign.ac.uk/guidelines/fulltext/116/

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