

**Post-market Review**  
**Products Used in the Management of Diabetes**

**Report to Government**

**Stage 2: Insulin Pumps**

**February 2015**

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## Report Structure

This report is separated into seven parts, as briefly outlined below. The Report structure is designed to clearly address the Terms of Reference on insulin pumps and the Insulin Pump Programme for Stage 2 of the Diabetes Post-market Review.

**Executive Summary** – This summary is a stand-alone document that summarises the process and results of the Insulin Pumps Review.

**Part 1** – Review background and context.

**Part 2** – Diabetes background including prevalence, impact in Australia, complications, diagnosis, monitoring, and treatment options. This section also contains information on access to insulin pumps including detail on the Insulin Pump Programme and the regulation of insulin pumps in Australia.

**Part 3** – Stakeholder consultation and input.

**Part 4** – Benefits and safety of insulin pump therapy (Terms of Reference 8).

**Part 5** – Costs and comparative effectiveness of insulin pump therapy (Terms of Reference 9).

**Part 6** – Examination of the Insulin Pump Programme eligibility criteria (Terms of Reference 10).

## Abbreviations and Glossary

AADE	American Association of Diabetes Educators
ADEA	Australian Diabetes Educators Association
AIHW	Australian Institute of Health and Welfare
APEG	Australasian Paediatric Endocrine Group
APGAR score	A simple method to assess the health of a newborn baby that considers appearance/complexion, pulse rate, reflex irritability, activity and respiratory effort, to determine if immediate medical attention is required.
ARTG	Australian Register of Therapeutic Goods
CADTH	Canadian Agency for Drugs and Technologies in Health
CGM	Continuous Glucose Monitoring
CHD	Coronary Heart Disease
CI	Confidence Interval
Commonwealth	Commonwealth of Australia as represented by the Department of Health
CSII	Continuous subcutaneous insulin infusion (insulin pump therapy)
DAEN	Database of Adverse Event Notifications
Dawn phenomenon	Long-acting insulin analogues may cause a trough of insulin dosing before breakfast resulting in fasting hyperglycaemia, known as the dawn phenomenon.
Department	Department of Health
DCCT	Diabetes Control and Complications Trial
DHS	Department of Human Services
Diabetes	Diabetes Mellitus
DKA	Diabetic Ketoacidosis
DUSC	Drug Utilisation Sub-Committee (of the PBAC)
DVA	Department of Veterans' Affairs

ESC	Economics Sub-Committee (of the PBAC)
HbA <sub>1c</sub>	Glycated Haemoglobin, measured as a per cent or in mmol/mol, 1% HbA <sub>1c</sub> is equivalent to 11mmol/mol.
Insulin Pump	A small computerised device that delivers small amounts of continuous rapid acting insulin throughout the day
IPC	Insulin pump consumable
IU	International Units
JDRF	Juvenile Diabetes Research Foundation (Australia)
Macrovascular complications	Damage to large blood vessels of the heart, brain, and legs leading to heart attack and stroke
MDI	Multiple daily injections (multiple insulin injections (MII))
Microvascular complications	Damage to small blood vessels causing problems in the eyes, kidney, feet and nerves
NDSS	National Diabetes Services Scheme
NICE	National Institute for Health and Clinical Excellence, United Kingdom
NHMRC	National Health and Medical Research Council
NMP	National Medicines Policy
NPS Medicinewise	National Prescribing Service Medicinewise
NZSSD	New Zealand Society for the Study of Diabetes
PBAC	Pharmaceutical Benefits Advisory Committee
PBS	Pharmaceutical Benefits Scheme
PLAC	Prostheses List Advisory Committee
Programme	Type 1 Diabetes Insulin Pump Programme
Prostheses List	A determination under Section 72-10 (5) of the <i>Private Health Insurance Act 2007</i> which lists devices that are provided as part of an episode of hospital treatment (or hospital substitute treatment) where a Medicare benefit is payable for the associated professional services (surgery) which private health insurers are required to pay mandatory benefits for.

PVD	Peripheral Vascular Disease
QoL	Quality of Life
QUM	Quality Use of Medicines
QUMAX	Quality Use of Medicine Maximised for Aboriginal and Torres Strait Islander People
QUMPRC	Quality Use of Medicines and Pharmacy Research Centre (University of South Australia)
RCT	Randomised Controlled Trial
RPBS	Repatriation Pharmaceutical Benefits Scheme
SARA	System for Australian Recall Actions
SF-12	Medical Outcomes Study 12-Item Short-Form Survey
SF-36	Medical Outcomes Study 36-Item Short-Form Survey
SIGN	Scottish Intercollegiate Guidelines Network
TGA	The Therapeutic Goods Administration
ToR	Terms of Reference
UKPDS	United Kingdom Prospective Diabetes Study
WHO	World Health Organization

## Executive Summary

### Background and context

This Report contains the findings of Stage 2 of the Post-market Review of Products used in the Management of Diabetes focussing on insulin pumps (the Insulin Pumps Review). The objective of the Insulin Pumps Review, in line with the Diabetes Review Terms of Reference (ToR 8-10), was to evaluate the clinical outcomes and cost-effectiveness of insulin pump therapy for people with type 1 diabetes, and the clinical and financial eligibility criteria for the Insulin Pump Programme. The Insulin Pumps Review was conducted according to the Post-market Review Framework (as at February 2014).

The Type 1 Diabetes Insulin Pump Programme (the Programme) aims to increase the affordability of insulin pump therapy for children up to 18 years of age from low-income families without private health insurance by subsidising the cost of an insulin pump. The Programme also provides funding for part of the cost of pump consumables, including infusions sets, cannulas, and tubing. The Juvenile Diabetes Research Foundation (JDRF) administers insulin pumps under the Programme, while consumables are supplied through the National Diabetes Services Scheme (NDSS) administered by Diabetes Australia. Programme funding totals approximately \$7.1 million over the four years from 2012-13 to 2015-16.

There are approximately 118,600 Australians with type 1 diabetes (ABS 2013), of whom approximately 10,510 are currently using an insulin pump (AIHW 2012b). As at February 2014, 466 pumps were supplied under the Programme. Families accessing a subsidised insulin pump under the Programme are able to choose different brands of pumps. Subsidised pumps are generally those on the Department of Health Protheses List, which is designed for private health insurance purposes and is managed by the Department. As continuous glucose monitoring sensors and transmitters are not currently subsidised under the Insulin Pump Programme or by private health insurers, sensor-augmented pump therapy was considered outside of the scope of the Review.

### Review findings

ToR 8 focussed on clinical outcomes of insulin pump therapy and the Review considered evidence from randomised comparative trials and observational studies. The systematic literature review of randomised controlled trial (RCT) evidence showed that this evidence does not conclusively support the superior efficacy or safety of insulin pump therapy over multiple daily injections in any age group. The overall strength of this evidence for decision-making was low to very low, with minimal benefit from insulin pump therapy on HbA<sub>1c</sub> and no effect on hypoglycaemia. The observed benefit of insulin pump therapy compared to multiple daily injections showed a reduction in HbA<sub>1c</sub> levels, ranging from 0.1–0.22% in children and adolescents, and 0.19–0.30% for adults. The difference did not reach the 0.5% reduction generally accepted to be of clinical significance (Clar 2010; Cummins 2010). However, there is no consensus on the best minimum clinical difference and a smaller reduction may be considered important from a public health perspective if achieved by most people using pumps in place of multiple

daily injections (Farmer 2012). No trials were identified that assessed long-term health outcomes.

The systematic review of observational evidence indicated that children, adolescents, and adults appear to achieve greater reductions in HbA<sub>1c</sub> and have a lower risk of severe hypoglycaemia with insulin pump therapy compared to multiple daily injections. Some long term studies showed statistically significant reductions in HbA<sub>1c</sub> ranging from 0.4-0.7% in children and adolescents using insulin pump therapy at 2–5 years follow-up. A retrospective cohort study undertaken in children and adolescents in Australia showed a significant reduction in HbA<sub>1c</sub> of 0.7% with insulin pump therapy over 5 years and reduced rates of severe hypoglycaemia and hospitalisation for ketoacidosis (Johnson 2013).

Before-and-after studies showed statistically significant reductions in HbA<sub>1c</sub> of 0.4–2.6% in adults using insulin pump therapy at 2–6 years follow-up, with the majority showing reductions of 0.4-0.7%. The largest cohort study of adults showed a statistically significant reduction in HbA<sub>1c</sub> with insulin pump therapy of 0.2% at five years (Carlsson 2013). For women with type 1 diabetes who are pregnant or planning a pregnancy, the majority of observational studies did not show a significant difference between insulin pump therapy and multiple daily injections on diabetes management, maternal pregnancy outcomes or newborn outcomes. There were similar results from systematic reviews of trial evidence (Farrar 2007; Mukhopadhyay 2007).

The observational studies lacked randomisation of the choice of selected treatment resulting in a high risk of selection and publication bias. Therefore, results should be interpreted cautiously. Despite the limitations of observational studies, the Review considered these studies as the patients included may be more reflective of the patients currently using insulin pump therapy in Australia, such as those with diabetes complications or hypoglycaemia unawareness, who were generally excluded from RCTs.

A review of cost-effectiveness studies of insulin pump therapy was undertaken consistent with ToR 9. Programme costs, utilisation, and affordability and access issues were also considered. The literature review did not identify any studies on the comparative effectiveness of different insulin pump brands.

On average, insulin pump consumables (excluding insulin) cost consumers \$310 per annum. The average cost to Government for each insulin pump supplied through the Programme is \$14,779 over four years (the warranty period), or \$3,695 per annum. This estimate is based on the median pump subsidy amount (\$6,400) and the cost of consumables for four years (\$2,098 per annum).

Four cost-effectiveness studies in Australia, Canada, UK and US comparing insulin pumps to multiple daily injections were identified. All studies used the CORE model (Palmer 2004). The cost-effectiveness studies, while assuming a large reduction in HbA<sub>1c</sub> with insulin pump therapy of 0.9% in one study and 1.2% in three studies, suggest a cost per quality-adjusted life year (QALY) gained of AUD\$28,874 to AUD\$96,220 at 2013 prices, with the UK study providing the upper estimate.

Sensitivity analyses showed that the incremental cost-effectiveness ratios (ICERs) were most sensitive to the estimated reductions in HbA<sub>1c</sub>. Assuming reductions in HbA<sub>1c</sub> of 0.51%–0.675% with insulin pump therapy compared to injections, the ICERs per QALY ranged from AUD\$63,274 in the US study to AUD\$292,952 in the UK study (converted to 2013 prices). The US, Canadian and Australian studies assumed a pump life span of seven or eight years, while the standard warranty length for an insulin pump is four years. These studies may have overestimated the cost-effectiveness of insulin pump therapy compared to multiple daily injections if the average pump life span is less than that assumed. In the US study, reducing the pump life span to four years increased the ICER by 54%. The ICERs were sensitive to changes in severe hypoglycaemic events only when the cost of severe hypoglycaemia was high (2007 USD\$1,234). The studies did not consider improvements in quality of life with the exception of fear of hypoglycaemia. Stakeholders considered quality of life to be a key benefit of insulin pump therapy.

The investigation of the Programme's usage and financial eligibility criteria highlighted several issues with affordability for the eligible population. JDRF made agreements in 2011 with some manufacturers to cover the cost of the patient co-payment for families on the lowest eligible incomes of under \$71,230 (2013-14) per annum. This aided Programme access and led to the development of a waiting list in 2012-13, which was addressed by additional funding. The Prostheses List insulin pump prices increased on 1 August 2012, which subsequently increased the patient co-payment, as the maximum subsidy is capped. Families on the lowest eligible incomes are now less likely to be able to afford the co-payment without further subsidy or continued assistance from insulin pump manufacturers. For many other eligible families, private hospital insurance may be a more affordable option than to access the Programme. Median family income data indicates that families on eligible incomes between \$71,230-\$101,653 (2013-14) rarely access the Programme (JDRF data).

ToR 10 examined the clinical eligibility of the Programme, as well as a comparison of Australian and international guidelines for insulin pump therapy, and subsidy arrangements in other countries. This showed that most guidelines recommend that the decision to initiate insulin pump therapy should be at the discretion of a healthcare professional in consultation with the patient or carer. The literature shows that there is limited evidence regarding sub-groups that receive greater benefit from insulin pump therapy. This makes it difficult to define clinical criteria to ensure that the Programme is available to patients for whom insulin pumps are most likely to be effective and cost-effective.

The Australasian Paediatric Endocrine Group (APEG) advised that the current Programme eligibility criteria are appropriate for children, and that there is not enough evidence on which to base any additional criteria. Australian and international clinical guidelines often recommend insulin pump therapy for: children under 12 years where multiple daily injections are impractical; women who are pregnant or trying to conceive; and people with poor glycaemic control. In the healthcare systems examined, most provided full or partial subsidy arrangements for an insulin pump, with a focus on providing access for children and young adults.

## **Stakeholder input**

Stakeholders generally consider that there are clinical (effectiveness and safety) and quality of life benefits to insulin pump therapy. The main quality of life benefits associated with insulin pump use raised by stakeholders were: greater flexibility with meals and sleeping times; enhanced participation in social, school and sporting activities; and enhanced participation in employment, including for carers of children with type 1 diabetes.

Stakeholders were supportive of the continuation of the Programme and suggested expansion to pregnant women and those planning a pregnancy, and to adults with high initial HbA<sub>1c</sub> or disabling hypoglycaemia (severe and/or unpredictable hypoglycaemia). Clinical groups acknowledged that the evidence does not conclusively support the clinical benefits of insulin pump therapy. However, they consider there is additional benefit from using insulin pumps rather than multiple daily injections in particular patient sub-groups. With the exception of the age criterion, stakeholders generally agreed that the current Programme eligibility criteria were appropriate.

Stakeholders noted that success with either insulin pump therapy or multiple daily injections is dependent on the level of motivation and compliance of the patient/carer. They suggested that access to a range of insulin pumps allowed health professionals to tailor products to individual patient needs. Stakeholders considered that insulin pumps should be fully subsidised for those on the lowest eligible incomes under the Programme.

## Part 1 - Review background and context

### 1.1 Diabetes Post-market Review

Appropriate medication and treatment management is a significant National Medicines Policy (NMP) issue and the Department of Health (the Department) is working with key partners to improve the management of diabetes in Australia, including a focus on medicines, devices and the delivery of support services to consumers. The Post-market Review of Products used in the Management of Diabetes (Diabetes Review) aims to ensure that patients are using the most appropriate medicines and products, effectively, and safely, to achieve optimal health outcomes and support quality use of medicines.

The Diabetes Review has three stages:

1. Blood glucose test strips use in people with type 2 diabetes not using insulin;
2. Insulin pumps for people with type 1 diabetes, and the Insulin Pump Programme; and
3. Medicines used in the management of type 2 diabetes.

Each stage is being progressed separately with the findings presented in an associated written report. Each report is designed to be read as a stand-alone document and may contain some shared information with previous reports. This report will be provided to the Government for consideration in the context of the broader Diabetes Review. The findings will be published on the [Diabetes Review](#) website.

Each stage will be progressed in line with work being undertaken across other NMP partners including the Therapeutic Goods Administration (TGA), the National Health and Medical Research Council (NHMRC), and the National Prescribing Service Medicinewise (NPS Medicinewise).

The Review aligns with the objectives of the current National Diabetes Strategy as it aims to improve patient outcomes by ensuring that the use of medicines and products in clinical practice reflects best evidence and guidelines. The Department will work via the Review's Inter-Departmental Working Group to ensure that outcomes align with the new National Diabetes Strategy, currently in development.

### 1.2 Insulin Pumps Review

#### 1.2.1 Review purpose and Terms of Reference (ToR)

In August 2012, the PBAC endorsed the following Terms of Reference (ToR) for the Insulin Pumps Review (Stage 2). The Insulin Pumps Review comprises ToR 8–10 of the Diabetes Review:

8. Determine the clinical outcomes (e.g. HbA<sub>1c</sub>, health-related quality of life), and other potential benefits and harms for people with type 1 diabetes of insulin pump therapy. In this, consideration should be given to different age groups, with a particular reference to those under 18 who may be eligible for the Insulin Pump Programme, which is funded by the Australian Government.

9. Investigate the cost-effective use of different insulin pumps available under the Insulin Pump Programme.
10. Consider the clinical criteria and eligibility under the Insulin Pump Programme, to ensure those who would most benefit from insulin pump therapy receive support to assist in their care.

The purpose of the Insulin Pumps Review is to examine the use of insulin pumps for people with type 1 diabetes, to inform an assessment of their effectiveness in terms of clinical outcomes and cost. Ongoing representations from the Juvenile Diabetes Research Foundation (JDRF), Diabetes Australia, and consumers regarding the current Insulin Pump Programme parameters, eligibility criteria and funding, lead to a review of the Programme. The Insulin Pumps Review was incorporated into the overarching Diabetes Review to provide an established framework that includes opportunities for public consultation and expert input, and to ensure that the Programme was not considered in isolation.

Although a number of the insulin pumps listed on the Prosthesis List are compatible with sensor-augmented pump therapy, the sensors and transmitters required for continuous glucose monitoring are not currently subsidised under private health insurance or any Australian Government programme. Therefore, sensor-augmented pump therapy was considered outside of the scope of the Review.

### **1.2.2 Overview of the Insulin Pumps Review process**

Post-market reviews follow a standard process detailed on the [Post-Market Review website](#) (as at February 2014).

#### **1.2.2.1 Process for written stakeholder submissions**

Direct stakeholder input was sought by announcing a call for submissions to address ToR 8–10, along with information about the Insulin Pumps Review, on the [PBS website](#). The call for submissions was open between 20 December 2012 and 13 February 2013. Thirty-three submissions were received from a range of stakeholders including: consumers/carers (19), health professionals (1), professional peak bodies (4), non-government organisations (6), government organisations (1), and industry (2).

In particular, the Department requested information regarding the current clinical outcomes for patients with type 1 diabetes on insulin pump therapy; the range of insulin pumps available including their differences, advantages and disadvantages; and how investment in the Insulin Pump Programme should be directed to achieve the most benefit.

The full submissions were published on the [Diabetes Review webpage](#), except where requested to be withheld by the author. A summary of key issues raised by stakeholders is in [Part 3.2](#).

### **1.2.2.2 Process for the Stakeholder Forum**

A Stakeholder Forum was held in Canberra on 12 September 2013. The Forum was a further opportunity for stakeholders to contribute to Stage 2 of the Diabetes Review. Prior to the Forum, attendees were provided with a discussion paper that included background information, the ToR, a summary of the literature review undertaken by the University of South Australia, and issues and themes raised by stakeholders through the public submission process. Discussion focussed on four questions posed by the Department, with opportunities for additional comments.

The main themes of the Forum were:

- consumer and clinician views on the advantages and disadvantages of insulin pump therapy (manufacturer views were well expressed via the written submissions to the ToRs);
- differences between brands or types of insulin pumps, including aspects that might be important for clinical outcomes or desirable to patients; and
- the eligibility criteria for the Insulin Pump Programme and types of patients that should be prioritised to receive a subsidised pump.

The Forum Summary was published on the [Diabetes Review webpage](#). A summary of key issues raised by stakeholders is in [Part 3.3](#).

### **1.2.2.3 Process for the Departmental Working Group**

An Inter-Departmental Working Group was formed consisting of key Australian Government agencies and relevant divisions of the Department to provide a forum to discuss potential interactions with other Government programmes and priorities.

The Working Group assisted in steering the Review and worked in parallel to the Reference Group. The Group convened three times on: 23 October 2012, 10 April 2013, and 10 October 2013.

A summary of key issues raised by Working Group members is in [Part 3.5](#).

### **1.2.2.4 Process for the Reference Group**

A Reference Group was formed to provide a platform for expert advice to inform the Diabetes Review. Reference Group advice was used to guide the development of the Insulin Pumps Review and this Report. The Reference Group included experts from a range of fields including endocrinology, diabetes education, general practice, consumer advocacy, clinical epidemiology, pharmacy, health economics, nutrition, and psychology. The Reference Group membership will be published on the [Diabetes Review website](#) following completion of all stages of the Diabetes Review.

The Reference Group discussed the Insulin Pumps Review at meetings on 17 April 2013, 17 July 2013, and 16 January 2014, and provided out-of-session comments on the draft Report. In addition to the results from the commissioned literature reviews, the Reference Group also considered the:

- written stakeholder submissions, comments received at the Stakeholder Forum, and public comments on the draft Report;
- literature on potential safety risks associated with insulin pump therapy and multiple daily injections;
- the Australian Institute of Health and Welfare (AIHW) Insulin Pump User Survey (2012b); and
- the regulatory requirements for insulin pumps to be included on the Australian Register of Therapeutic Goods (ARTG).

Following public consultation on the draft Insulin Pumps Report and further consideration by the Reference Group, the final Report will be provided to the Minister for Health for consideration.

#### **1.2.2.5 Process for literature searches**

The Department engaged the Quality Use of Medicines and Pharmacy Research Centre (QUMPRC) of the University of South Australia to conduct a literature review on the efficacy and safety of insulin pump therapy versus multiple daily injections. Further detail on the literature review findings is included in [Part 4](#), [Part 5](#), and [Part 6](#).

The Reference Group considered the literature review. The evidence from randomised controlled trials (RCTs) did not conclusively support superior effectiveness or safety of insulin pump therapy over multiple daily injections. The Reference Group suggested expanding the scope of the literature review to assess whether other sources of evidence such as observational studies, would be able to provide any further information about the benefits of insulin pump therapy in people with type 1 diabetes or subsets of this population. The Department subsequently engaged the QUMPRC to conduct a second literature search to include observational studies.

The literature reviews considered studies that assessed the effects of each therapy on: HbA<sub>1c</sub> levels, quality of life measures in all age groups, and hypoglycaemia. The literature searches did not identify any RCTs or studies comparing the different types of insulin pumps or long-term health outcomes of insulin pump therapy.

In response to stakeholder comments on the draft Insulin Pumps Report, the QUMPRC was further contracted to update the draft Report and literature reviews. This work included:

- Extending the review of observational studies to include literature published between May 2013 and October 2014.
- Extending the review of observational studies to include women who are pregnant or planning to conceive. Diabetes-related, and perinatal and maternal outcomes were considered.

- Undertaking a literature review of full cost-effectiveness studies of insulin pumps compared to multiple daily injections published between 2007 and October 2014.

The literature review reports are available by email to the [Review Secretariat](#).

### **1.2.2.6 Process for consultation on the draft Review Report**

The draft Insulin Pumps Report contained the considerations of the Reference Group, stakeholder comments collected at the Stakeholder Forum and through the public submission process addressing ToR 8–10 of the Diabetes Review, and key findings from the literature reviews. The draft Report was published on the [Diabetes Review website](#) between 7 and 21 July 2014, for a two-week period of public consultation. Sixteen submissions were received from a range of stakeholders including: government organisations (4); health professionals and professional peak bodies (4); consumers and consumer organisations (4); industry (3); and a joint submission (1).

In addition to providing general comments on the draft Report, stakeholders were asked to address six focus questions:

1. Should the Insulin Pump Programme prioritise any age groups in providing subsidised access to insulin pumps, and why?
2. Should the Programme be expanded to provide access to women with type 1 diabetes who are pregnant or planning a pregnancy and meet the financial eligibility requirements?
3. Do you consider it a greater priority to provide expanded access to the Programme in terms of age ranges covered and pregnant women, or more affordable access for the currently eligible population, i.e. children and adolescents aged 18 years and under?
4. In your experience in dealing with service providers, is the delivery of type 1 diabetes products particularly insulin pumps and consumables, satisfactory? Do you have any suggested improvements?
5. Are the clinical eligibility criteria for the Insulin Pump Programme appropriate? If not, what should the criteria be?
6. What are the most important features of an insulin pump that assist in achieving optimal health outcomes or impact greatly on quality of life?

The submissions were reviewed and themes checked in order to update stakeholder views on the ToR. [Part 3.4](#) contains a summary of the key stakeholder viewpoints on the draft Report. The draft Report was updated in response to stakeholder comments and the final Report includes the key findings from the updated literature reviews.

## **1.3 Context for the Diabetes Post-market Review**

### **1.3.1 Post-market monitoring**

Post-market reviews are a systematic and formal approach to monitoring the use of medicines listed on the Pharmaceutical Benefits Scheme (PBS). The Post-market Review Programme was established to improve patient safety and quality use of medicines, in addition to supporting the ongoing evidence-based cost and clinically effective use of PBS listed medicines.

The Post-market Review Programme aims to achieve four main goals:

- improved patient safety through better understanding of adverse events and medicine-related harms;
- ensuring the ongoing viability of the PBS through better targeting of medicines use and avoiding preventable wastage or inappropriate prescribing;
- developing a better understanding of medicines use, to validate intended clinical benefit and inform medicines evaluation processes; and
- strengthened medicines pricing management, including through better management of clinical and economic uncertainty.

A full post-market review will only proceed following Ministerial approval.

## **Part 2 - Diabetes mellitus: treatment and access to insulin pumps**

### **2.1 Diabetes mellitus**

Diabetes mellitus (diabetes) is a chronic disease characterised by high levels of glucose in the blood. Insulin, a hormone produced by the beta-cells of the pancreas, controls blood glucose levels. Diabetes occurs when the pancreas is unable to produce enough insulin, or the body becomes resistant to insulin, or both (World Health Organization (WHO) 2013). There are three main types of diabetes: type 1 diabetes, type 2 diabetes, and gestational diabetes (WHO 2013).

#### **2.1.1 Type 1 diabetes**

Type 1 diabetes is an autoimmune disease characterised by the progressive destruction of the insulin producing beta-cells of the pancreas. People with type 1 diabetes cannot produce insulin and require lifelong insulin injections for survival (WHO 2013). Type 1 diabetes is sometimes referred to as juvenile onset diabetes or insulin dependent diabetes. Type 1 diabetes affects about 12% of people with diabetes (AIHW 2013a). The cause of type 1 diabetes is not known, there are no known cures, and it is not preventable with current knowledge (Misso 2010, WHO 2013).

#### **2.1.2 Type 2 diabetes**

People with type 2 diabetes produce insulin, but may not produce enough of it or cannot use it effectively (insulin resistance). It is associated with hereditary factors and lifestyle risk factors, including poor diet, insufficient physical activity and being overweight or obese (Shaw & Chisholm 2003). Some people with type 2 diabetes may be able to manage their condition through lifestyle changes, others may require diabetes medications or insulin injections to control blood glucose levels. Type 2 diabetes occurs mostly in people aged over 40 years. However, the disease is becoming increasingly prevalent in younger age groups, including children (WHO 2013).

#### **2.1.3 Gestational diabetes**

Gestational diabetes occurs during pregnancy and usually resolves after birth. However, a history of gestational diabetes increases a woman's risk of developing type 2 diabetes later in life. It is estimated that gestational diabetes affects women in about 3-8% of pregnancies. Additionally, certain populations including Aboriginal or Torres Strait Islander, Indian, Vietnamese, Chinese, Middle Eastern and Polynesian, are at increased risk of gestational diabetes (Diabetes Australia 2012).

### **2.2 Prevalence of diabetes in Australia**

Diabetes mellitus was endorsed as a National Health Priority Area at the Australian Health Minister's Conference in 1996, in recognition of the high prevalence of the disease in Australia, its impact on morbidity and mortality, and its potential for health improvements through prevention and treatment programmes.

According to the *Australian Health Survey: Updated Results (2011-12)*, the total number of people in Australia aged 2 years and older that have ever been diagnosed with diabetes (excluding gestational diabetes) is 999,000, around 4.6% of the population (Australian Bureau of Statistics (ABS) 2013).

The prevalence of diabetes in Australia has almost doubled since 1995 (407,900 people). This substantial increase has been attributed to more people developing the disease, but also people with diabetes living longer and improved detection of the disease. However, the prevalence of diabetes in terms of percentage of the Australian population, remained stable between 2007-08 and 2011-12 (4.5% in 2007-08) (ABS 2013).

The *Australian Health Survey: Updated Results (2011-12)* show that, of persons aged 2 years and older who reported having diabetes: 84.9% had type 2 diabetes, 11.9% had type 1 diabetes, and 3.3% had an unspecified type of diabetes. More men reported having diabetes than women (5.1% of all men compared with 4.2% of all women) (ABS 2013).

Type 1 diabetes can occur at any age, although new cases mostly occur in children and young adults. While many childhood diseases are declining in Australia, it is estimated that the prevalence of type 1 diabetes in the 0-14 year old demographic will increase by 10% between 2008 and 2013, from 5,700 to 6,300 (AIHW 2012a).

## **2.3 Complications**

In type 1 diabetes, a lack of insulin elevates blood glucose levels (hyperglycaemia) and creates disturbances in carbohydrate, lipid and protein metabolism. Subsequently, because the body cells are not receiving a source of energy through glucose (sugar), the body responds by using fats as an energy source. This causes accumulation of ketones (an acidic molecule) in the blood, a by-product of abnormal lipid metabolism, lowering the blood pH to a point that is more acidic than normal and leading to diabetic ketoacidosis (DKA) (AIHW 2012b). If not treated, there are many potentially life threatening diabetes complications (Misso 2010).

For people with diabetes, low blood glucose levels (hypoglycaemia) can be brought on by delaying or missing a meal, eating an insufficient amount of carbohydrates, unplanned physical activity, alcohol consumption, and mismanagement of insulin administration or diabetes medicines. In the short-term, hypoglycaemia can lead to loss of coordination, slurred speech, confusion, loss of consciousness, seizure and death (Diabetes Australia 2010).

### **2.3.1 Long-term complications**

As the disease progresses over time, diabetes macrovascular and microvascular complications can damage the heart, blood vessels, eyes, kidneys and nerves, as well as diminishing quality of life (WHO 2006). Diabetes increases the risk of:

- heart disease and stroke;

- diabetic neuropathy (nerve damage), and reduced blood flow and blood vessel damage, resulting in foot ulcers and limb amputation;
- diabetic retinopathy, which can cause blindness resulting from long-term accumulated damage to the small blood vessels in the retina (microaneurysms);
- nephropathy (kidney disease), which can lead to kidney failure; and
- death.

After 15 years of having the disease, approximately 2% of people become blind and 10% develop severe visual impairment. Diabetes is one of the leading causes of kidney failure and this condition is the cause of death in 10-20% of people with diabetes. Diabetic neuropathy affects up to 50% of people with diabetes with common symptoms including tingling, pain, numbness, or weakness in the feet and hands (WHO 2013). Cardiovascular disease is the major cause of death in people with diabetes, accounting for approximately 50% of all fatalities (International Diabetes Federation 2011).

Early age of onset of type 1 diabetes is associated with a minor, but statistically significant reduction in IQ, presumably due to poor glycaemic control (Craig 2011). Serious complications of diabetes including nerve damage, foot ulcers, and eye and kidney disease, are already evident in some people aged 19-30 years; many of these conditions may have been preventable by improved glycaemic control (AIHW 2012a).

### **2.3.2 Diabetes-related deaths**

In 2010, diabetes was associated with cause of death for nearly 7,750 people in Australia or 5.4% of all deaths that year (AIHW 2013b). However, these data may underestimate death caused by diabetes as it is not always recorded as a contributory cause on the death certificate (Yorkshire and Humber Public Health Observatory 2008). Diabetes was the underlying cause of death in 88 people with type 1 diabetes aged 0-30 years in 2001-07 (AIHW 2012a).

## **2.4 Diagnosis**

The current WHO (2006) diagnostic criteria for diabetes include:

- Fasting plasma glucose  $\geq 7.0$ mmol/l (126mg/dl); or
- 2-hour plasma glucose  $\geq 11.1$ mmol/l (200mg/dl).

HbA<sub>1c</sub> (glycated haemoglobin) is a laboratory test that shows the average level of blood glucose over the previous three months. HbA<sub>1c</sub> has recently been accepted as an additional test to diagnose diabetes, provided that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values. An HbA<sub>1c</sub> of  $\geq 48$  mmol/mol (6.5%) is recommended as the cut off point for diagnosing diabetes. However, a value less than 6.5% does not exclude diabetes, if a diagnosis of diabetes is indicated using the glucose tests above (WHO 2011).

## **2.5 Monitoring blood glucose and glycaemic control**

### **2.5.1 Self-monitoring of blood glucose**

Self-monitoring of blood glucose using blood glucose test strips and a blood glucose meter is recommended for people using insulin. In type 1 diabetes and gestational diabetes it is usually recommended that blood glucose levels be tested at least four times daily (early morning, plus other tests before and/or after meals). Less frequent testing is usually recommended for people with type 2 diabetes. Frequent consultation with health care professionals is important. Self-monitoring should be individualised and assist people with diabetes to understand the impact of insulin, food, physical activity, and other factors on blood glucose control. Frequency of monitoring should be determined according to the individual's self-management goals.

### **2.5.2 HbA<sub>1c</sub>**

In addition to its use as a diagnostic tool, HbA<sub>1c</sub> testing is also used to provide an indication of how well a patient's diabetes is being controlled. High levels of HbA<sub>1c</sub> indicate poor glycaemic control. The Diabetes Control and Complications Trial (DCCT) in Type 1 diabetes and the UK Prospective Diabetes Study (UKPDS) in Type 2 diabetes both showed that, as HbA<sub>1c</sub> increases, the risk of microvascular and macrovascular complications of diabetes increases (Craig 2011).

The Australian Diabetes Society recommends a general target HbA<sub>1c</sub> of  $\leq 7.0\%$  (53 mmol/mol) for most patients (Australian Diabetes Society 2009). However, HbA<sub>1c</sub> targets should be individualised and may need to be higher for some people including children and the elderly (Craig 2011).

HbA<sub>1c</sub> testing provides clinicians with a reliable indication that therapy is working appropriately and the risk of long-term complications, particularly microvascular complications, is reduced (Saudek & Brick 2009).

It should be noted that glycation of haemoglobin occurs only as the erythrocyte (red blood cell) circulates in serum. Therefore, anything that alters the erythrocyte survival will influence HbA<sub>1c</sub> independent of glycaemia. In people with conditions associated with altered erythrocyte survival (e.g. thalassaemia, portal hypertension, haemolytic anaemia), HbA<sub>1c</sub> is less reliable and self-monitoring of blood glucose or fructosamine testing, which measures the glycation of all serum proteins, may be of more value (Saudek & Brick 2009).

### **2.5.3 Glycaemic variability**

Glycaemic variability has been suggested as a factor that may increase the risk of diabetes complications independent of HbA<sub>1c</sub>. A systematic review examined glycaemic variability and its impact on diabetes complications and found that of eight studies in patients with type 1 diabetes, only two studies demonstrated a significant association with microvascular complications, and none showed an association with macrovascular complications (Nalysnyk 2010). Diabetes complications are proposed to result from increased mitochondrial oxidative stress induced by hyperglycaemia (Giacco & Brownlee 2010). One study showed that there was no association between glycaemic

variability and urinary markers of oxidative stress in people with type 1 diabetes (Wentholt 2008). Though it remains uncertain, other studies also do not support glycaemic variability as an important independent factor in the development of diabetes complications in people with type 1 diabetes (Borg 2011, Cavalot 2013, Gordin 2008, Pena 2011). Therefore, due to this uncertainty, this report concentrates primarily on HbA<sub>1c</sub> as a measure of glycaemic control and predictor of diabetes complications, and frequency of hypoglycaemic episodes as a measure of safety.

## **2.6 Treatment options and technologies for type 1 diabetes**

People with type 1 diabetes are required to manage their condition with lifelong insulin therapy and blood glucose level monitoring. Insulin is administered subcutaneously where it is absorbed into the blood stream. The two main forms of insulin administration are the conventional method of multiple daily injections, and continuous subcutaneous insulin infusion using an insulin pump (insulin pump therapy) (Misso *et al.* 2010).

### **2.6.1 Multiple daily injections**

Multiple daily injection insulin therapy consists of administering around three or four insulin injections per day. There are five different types of insulin currently available to treat diabetes in Australia: ultra-short acting, short-acting, intermediate-acting, long-acting, and pre-mixed. These types differ in both their speed of onset, time to peak, and duration of glucose-lowering action.

Ultra-short acting analogues and short-acting insulins are designed to supply the bolus level of insulin needed after a meal, while intermediate-acting insulin and long-acting analogues do not need to be injected with a meal and are used to help mimic the basal level of insulin excreted by the pancreas (Diabetes Australia 2008).

### **2.6.2 Insulin pumps**

Insulin pumps are small, computerised, portable devices that deliver continuous, small doses of fast-acting insulin 24-hours a day, known as the basal insulin dose (Misso 2011). Basal insulin controls blood glucose at night and between meals (Diabetes Queensland 2009). A bolus dose, also of fast-acting insulin, is initiated manually by the individual before meals and when correcting hyperglycaemia (high blood glucose) (Diabetes Australia 2008).

Insulin is delivered through a small tube and cannula, and an infusion set inserted subcutaneously, usually in the abdomen or hip region (Misso 2011). These sets are changed on average every three days, depending on the type of infusion set.

Insulin dose adjustments may be based on food intake, exercise and other factors, and in-built algorithms may assist users with these calculations. The insulin pump can only be disconnected for short periods of time (for exercise or showering), usually not more than two hours (Diabetes Queensland 2009).

Insulin pumps do not measure blood glucose levels and levels must be monitored throughout the day with the use of blood glucose test strips and a blood glucose meter,

similar to those using multiple daily injection therapy. Insulin pump users should perform four or more blood glucose tests a day to ensure insulin administration from the pump is correct. There are insulin pumps with the capability of continuous glucose monitoring with the addition of a glucose sensor (Diabetes Queensland 2009). However, continuous glucose monitoring does not replace the need for independent testing of blood glucose with a blood glucose meter, and for some insulin pumps is not indicated for use in patients under 18 years of age (Animas Corporation 2012; Medtronic MiniMed Inc. 2009).

### **2.6.3 Insulin pump use in Australia**

The *Australian Health Survey: Updated Results, 2011-12*, indicates there are approximately 118,600 people with type 1 diabetes (ABS 2013). The AIHW report, *Insulin Pump Use in Australia* (2012b), states that there are approximately 10,510 people with type 1 diabetes in Australia currently using an insulin pump, or around 10% of all people with type 1 diabetes. It is unclear how the affordability of insulin pumps and the associated consumables influences their usage in Australia. However, the most commonly identified issue for insulin pump users in Australia, identified by 32% of survey respondents, was the cost of insulin pump consumables (AIHW 2012b).

Data from the NDSS indicates that in 2010 there were 10,285 children and adolescents aged between 0-18 years with type 1 diabetes in Australia (AIHW 2012a). NDSS data also indicates that almost one-third of people with type 1 diabetes aged under 20 years used an insulin pump (AIHW 2012b). Therefore, an estimated 3,400 people aged 0–18 years in Australia are using an insulin pump.

Insulin pump uptake in Australia is similar to the modelled uptake of insulin pumps in the United Kingdom, where the National Institute for Health and Clinical Excellence (NICE) estimated a 12.4% uptake across all age groups, and 33% uptake for those under 12 years of age (NICE 2009).

### **2.6.4 Diabetes management at school**

For children using injections, the recommended treatment for type 1 diabetes usually involves four insulin injections a day, and therefore requires insulin administration at school. This raises questions as to whether children, particularly in early primary school, have the developmental capacity to self-administer insulin. Whilst children can be managed with two insulin injections a day, which eliminates the need for insulin administration at school, this treatment regimen is not considered ideal (Marks 2013). Children using insulin pump therapy would receive insulin continuously at a basal rate throughout the day, with additional bolus doses of insulin delivered via the pump at meal times or to correct high blood glucose levels. Bolus doses need to be programmed by the user.

The type of treatment and ability of a child to self-administer insulin at school may affect their treatment. A recent Australian study on children with type 1 diabetes attending kindergarten–year 2 (aged 4–8) found that children using insulin pump therapy were significantly more likely to receive insulin at school than those using injections (97%

versus 55%). This may be because children who were able to self-administer insulin were more likely to receive treatment at school than those unable to self-administer (93% versus 65%), and children using insulin pumps were more likely to self-administer insulin than those using injections (63% versus 23%) (Marks 2014).

Attending school to assist with blood glucose testing and insulin administration can limit parents' ability to work, leading to financial stress. An international survey showed that 46% of parents had to alter their work to manage their child's diabetes at school (Lange 2009). As younger children may not have the ability to recognise the symptoms of hypoglycaemia or ask for assistance, this also poses a higher risk. One study indicated that 20% of parents were called to the school on a regular basis (Schwartz 2010).

In Australia, an unpublished study by Middlehurst and Morrison (2008) found that a parent attended school to assist with insulin administration in 28% of cases, most commonly for children using insulin injections and under the age of eight. After eight years of age most children administered blood glucose testing and insulin themselves. Teachers, school administration staff and nurses provided assistance with insulin administration in some cases, with teachers more willing to assist with administration through an insulin pump (as cited in Marks 2013). Also in Australia, Marks (2014) found that around 19% of children had insulin administered by a parent at school. Insulin injections at school were most commonly administered by the parent or child, while insulin delivered by an insulin pump was most commonly administered by the child, teacher or teacher's aide. This research indicates that insulin pump therapy may improve diabetes treatment in young children at school and alleviate some of the pressure on carers.

### **2.6.5 New technologies**

Continuous glucose monitoring devices consist of a glucose sensor that is inserted under the skin. They can be used in conjunction with a compatible insulin pump, and provide real-time monitoring of blood glucose levels throughout the day. Generally, glucose levels are displayed at 1-5 minute intervals. The devices can sound alarms to warn patients of impending hypoglycaemia or hyperglycaemia. Some pumps have the ability to suspend delivery of insulin once the sensor reaches a threshold of low blood glucose and sounds an alarm (Ly 2013).

Tubeless closed loop system insulin pumps consist of two components: a waterproof patch that holds and delivers insulin, and a device that connects wirelessly that programs insulin delivery and calculates insulin doses. It also features an in-built glucose meter.

The above sensor technologies are not currently funded by any Australian Government subsidy programme or through private health insurance. The pathway for new insulin pump technologies to request listing on the Prostheses List and associated reimbursement through private health insurers is to use existing Prostheses List Advisory Committee (PLAC) processes. These technologies will be assessed by the PLAC

as applications are submitted by sponsors. Further information on PLAC and the Protheses List is in [Part 2.8](#).

## **2.7 Access to insulin pumps via the Type 1 Diabetes Insulin Pump Programme**

### **2.7.1 Type 1 Diabetes Insulin Pump Programme**

The Type 1 Diabetes Insulin Pump Programme (the Programme) is managed by the Department of Health and administered by the Juvenile Diabetes Research Foundation (JDRF). The Programme, introduced in 2008-09, aims to increase the affordability of insulin pump therapy for low-income families without private health insurance that have children under 18 years of age who would benefit from insulin pump therapy to control their type 1 diabetes. JDRF offered an insulin pump programme prior to 2008, which provided about 20 pumps per year, and submitted the proposal for the current Programme. The pumps available under the Programme are generally those on the Protheses List, which is managed by the Department.

The Programme also funds part of the cost of insulin pump consumables for pumps provided under the Programme. These are supplied through the National Diabetes Services Scheme (NDSS), which is funded by the Australian Government and administered by Diabetes Australia. All NDSS registrants with type 1 diabetes are able to access subsidised insulin pump consumables through the NDSS, with the cost of consumables being the same for Programme recipients and other registrants.

### **2.7.2 Programme access arrangements**

Families accessing a subsidised insulin pump under the Programme are able to choose any of the insulin pumps on the Protheses List as recommended by an endocrinologist or specialist physician who has been approved by JDRF. As at February 2014, there were six<sup>1</sup> insulin pumps on the Protheses List available to access. If a clinically recommended insulin pump is not listed on the Protheses List, the cost of the pump, and the subsequent subsidy amount, will take into account the recommended retail price of the pump, and the minimum benefit amount for comparable pump on the Protheses List.

The Programme provides a subsidy between \$500 and \$6,400 for families that meet the means-tested income requirements. The applicant's family income determines the level of subsidy for the insulin pump on a sliding scale up to a maximum of 80% of the listed minimum benefit amount on the Protheses List or \$6,400, whichever is less. Conversely, the minimum subsidy is 10% of the cost of the pump or \$500, whichever is greater. For example, families with an income equal to or less than \$71,230 (2013-14, indexed annually) will receive a subsidy amount between \$3,200 and \$6,400, depending on the insulin pump selected. Families with an income of \$101,653 (2013-14, indexed annually) will receive a subsidy amount between \$500 and \$950, depending on the

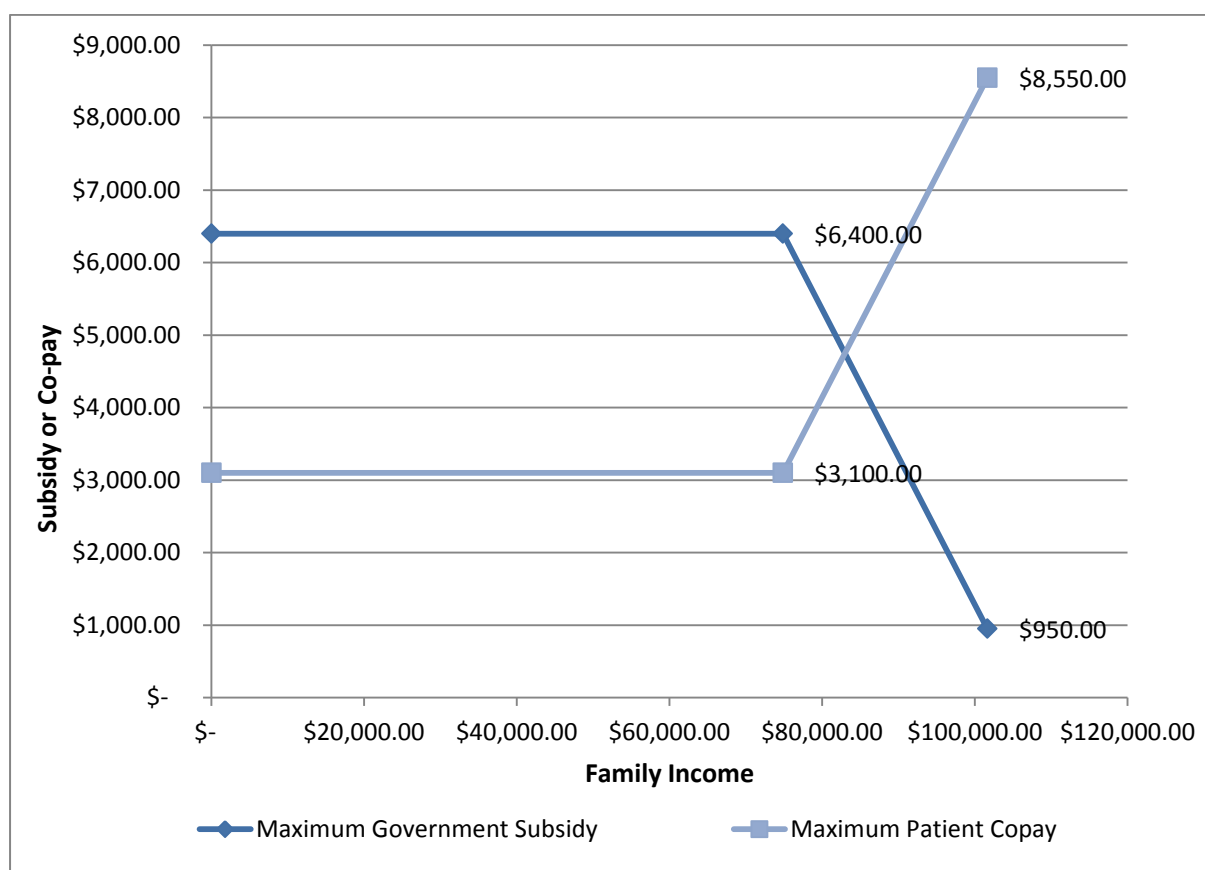
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<sup>1</sup> *There are currently still seven insulin pumps listed on the February 2014 edition of the Protheses List. However, the Animas 2020 insulin pump has been discontinued by the manufacturer, but still maintains a listing (Department of Health 2014).*

insulin pump selected. Families with a household income over \$101,653 (2013-14) are not eligible for subsidy. [Figure 1](#) describes the subsidy and co-payment relationship to the family income for the most commonly supplied insulin pump valued \$9,500. Further detail on the Prostheses List is outlined in [Part 2.8](#). Discussion on the limitations of the Programme link to the Prostheses List is detailed in [Part 5.6.2](#).

Low-income is defined from the base rate of *Family Tax Benefit Part A* with one child between 13 and 15 years of age. This low-income figure is currently \$71,230 (2013-14) household income per annum and does not vary with the number of children in the family. However, the Programme provides a concession for families with more than one child with type 1 diabetes by applying the calculated subsidy for the first child and the maximum subsidy for subsequent children. The low-income salary benchmark has been indexed in line with the changes to the *Family Tax Benefit Part A* since the Programme commenced.

**Figure 1. Relationship between the patient co-payment, subsidy amount, and family income for the most commonly supplied insulin pump under the Programme valued at \$9,500.**



### 2.7.3 Patient co-payment

When the Programme began, the maximum subsidy provided under the Programme was \$2,500 per pump. Due to low uptake, this was increased in February 2010 to \$6,400, to meet consumer expectations, and to reach the Programme’s objectives.

The maximum-capped subsidy of \$6,400 was based on 80% of the cost of the most expensive (and most clinically recommended) insulin pump available, prior to an increase in the minimum benefit cost of the insulin pumps on the Prostheses List on 1 August 2012. Subsequently, the cap of \$6,400 no longer equals 80% of the most expensive pump, which currently costs \$9,500. The patient co-payment, was designed to be equal to or greater than the cost of holding private health insurance for 13 months (just over the period necessary to qualify for an insulin pump under private health insurance). The median co-payment paid by recipients under the Programme is \$1,600 (JDRF data).

To aid families in covering the patient co-payment, JDRF signed agreements with the Princess Margaret Hospital in Perth, the Canberra Hospital, Diabetes Queensland, and the Australian Diabetes Council in March 2011. They agreed to provide funding to cover the co-payment gap, the remaining 20% of the cost, for eligible families. In October 2011, two key insulin pump manufacturers commenced subsidising the co-payment gap amount for families in the lowest income bracket, which was an annual income below \$67,398 in 2011-12, and is currently \$71,230 (2013-14).

#### **2.7.4 Programme funding status**

The original Programme funding amount of \$5.5 million was approved for pumps and consumables for the four-year period to 2011-12. This was continued with additional funding for the four-year period to 2015-16.

The uptake for the Programme was greater than predicted in 2012-13. On 18 October 2013, the Australian Government provided an additional \$870,400 in funding for 2013-14 for the Insulin Pump Programme, to clear the waiting list of up to 136 families waiting to have their application processed for financial support to purchase a pump. Programme funding now totals \$7.1 million over four years from 2012-13 to 2015-16. As at February 2014, the delivery of insulin pumps had recommenced with 466 insulin pumps provided under the Programme since it began.

This Review aims to explore long-term measures to maintain the ongoing efficient and effective use of funds under the Programme. JDRF has campaigned since September 2012 to increase funds for insulin pumps and made a joint submission with Diabetes Australia to the Insulin Pump Review.

According to a survey included in the AIHW report, *Insulin Pump Use in Australia* (2012b), 88% of respondents indicated that when purchasing their current or previous insulin pump, they received some sort of financial assistance; while the remaining 12% borrowed an insulin pump, paid for the entire cost of the pump themselves, or were unsure of the funding arrangements for their pump. Of those who received financial assistance, 97% had private health insurance, 3% indicated a Commonwealth Government subsidy and 2% a JDRF grant. A number of respondents indicated more than one type of funding. It is likely that the government subsidy and JDRF grant both relate to funding through the Insulin Pump Programme.

Specific aspects of the Programme are discussed further in [Part 4](#), [Part 5](#) and [Part 6](#).

## **2.8 Access to insulin pumps via private health insurance**

### **2.8.1 Prostheses List**

Under the *Private Health Insurance Act 2007*, private health insurers are required to pay mandatory benefits for a range of products on the Prostheses List that are provided as part of an episode of hospital treatment (or hospital substitute treatment) where a Medicare benefit is payable for the associated professional service. There are more than 9,000 products on the Prostheses List including cardiac pacemakers, hip and knee replacements, and intraocular lenses; as well as human tissues, such as human heart valves and corneas.

In order to obtain an insulin pump through private health insurance, patients usually have a 12-month waiting period before they are eligible to apply for a benefit from their health insurance provider. Insulin pumps are listed under Schedule C of the Prostheses List and have a minimum benefit amount listed. The minimum benefit amount listed on the Prostheses List dictates the minimum benefit insurers are required to pay for a specific insulin pump where the pump is provided as part of an episode of hospital or hospital-substitute treatment during a professional attendance by a consultant physician for which a Medicare benefit is payable (i.e. a certified Type C procedure). Insurers may not pay benefits less than this amount, such as a percentage of the minimum benefit. However, the hospital may charge more for the insulin pump than the minimum benefit and in this case, the remainder would need to be covered by either the insurer or the patient.

Insulin pumps fitted in a clinic are considered part of general rather than hospital treatment, and the insurer is not required to pay the minimum benefit for the pump. Some insurers provide cover for insulin pumps as part of general treatment, but the amount covered and level of cover required varies. Some insurers require patients to maintain their cover at a certain level in the intervening years between receiving one insulin pump and the next.

The benefit amount is negotiated between the insurer and manufacturer of the product, mediated by the Department. [Appendix A](#) contains information on insulin pumps available under the Prostheses List as at February 2014 and [Appendix B](#) provides information on insulin pumps that have been discontinued or are no longer available on the Prostheses List.

### **2.8.2 Prostheses List Advisory Committee (PLAC)**

The Prostheses List Advisory Committee (PLAC) was established on 4 October 2010, replacing the Prostheses and Devices Committee. Its primary role is to advise the Minister for Health about the listing of prostheses and their appropriate benefits on the Prostheses List. In making recommendations, the PLAC considers advice from Clinical Advisory Groups, members of the Panel of Clinical Experts and the Negotiating Oversight Committee (Department of Health 2010).

In order to provide advice to the Minister, when considering a new prosthesis listing, the PLAC considers the cost, clinical function, effectiveness and safety of the prosthesis in comparison to other products included on the Prostheses List intended to treat similar clinical conditions. For the item to be listed it must also fit within the classification criteria of a prosthesis as defined in the Department's *Guide to listing and setting benefits for prostheses* (Department of Health 2010).

The Prostheses List arrangements and the PLAC were established to control inflation in private health insurance benefits paid for prostheses. The Prostheses List plays an important role in ensuring the sustainability of the Australian private health insurance system, and helps to achieve the Government's policy objective of ensuring private health insurance remains affordable and accessible.

The PLAC is comprised of an independent Chair, with members having expertise in clinical practice, health insurance, consumer health, health economics, health policy, private hospitals, and the medical device industry (Department of Health 2010).

Since the establishment of PLAC in 2010, there has been an increasing focus on the comparative effectiveness for new listings on the Prostheses List, which includes the clinical advantages over the already listed comparators in the therapeutic group.

## **2.9 Regulation of insulin pumps in Australia**

The TGA is Australia's regulatory authority for therapeutic goods. Medical devices must be included on the Australian Register of Therapeutic Goods (ARTG) before they may be supplied in, or exported from, Australia.

There are currently six insulin pump listings included on the ARTG ([Table 1](#)). Each ARTG entry covers all models of ambulatory insulin infusion pumps made by that manufacturer and supplied by that sponsor.

**Table 1. Insulin pumps on the ARTG as of 1 November 2013.**

ARTG No.	Sponsor	Manufacturer	Classification	Global Medical Device Nomenclature Term
98469	Medical Specialties Australia Pty Ltd	Smiths Medical ASD Incorporated	Class IIb	Infusion pump, insulin, ambulatory
96120	Australasian Medical & Scientific Ltd	Animas Corporation	Class IIb	Infusion pump, insulin, ambulatory
169095	Closing the Loop Pty Ltd	Insulet Corporation	Class IIb	Infusion pump, insulin, ambulatory
95763	Medtronic Australasia Pty Ltd	Medtronic Minimed	Class IIb	Infusion pump, insulin, ambulatory
212526	Roche Diagnostics Australia Pty Limited	Roche Diagnostics GmbH Diabetes Care	Class IIb	Infusion pump, insulin, ambulatory
99868	Managing Diabetes Pty Ltd	SOOIL Development Co Ltd	Class IIb	Infusion administration set, insulin pump

Class IIb devices such as insulin pumps are required to meet certain criteria to be included on the ARTG. This requires the manufacturer to implement and have assessed a Quality Management System in accordance with the ISO 13485:2003 standard for the design, production, packaging, labelling, and final inspection of the devices. The manufacturer must make a *declaration of conformity*, which includes a statement that the insulin pump complies with the provisions of the Essential Principles. This includes the requirement that the device is fit for purpose, designed considering the current 'state-of-the-art', and that sufficient clinical evidence exists for the device. A full list of the Essential Principles can be found in *Schedule 1 of the Therapeutic Goods (Medical Devices) Regulations 2002*.

Generally, the TGA would not conduct any specific reviews of an insulin pump prior to inclusion of the device on the ARTG. This type of device is not required to undergo a pre-market application audit of product or technical information by the TGA.

The TGA's website contains the Database of Adverse Event Notifications (DAEN) and the System for Australian Recall Actions (SARA), which contains information on adverse events and recall actions, respectively, for medical devices in Australia since 1 July 2012.

Information regarding adverse events or recalls of insulin pumps is included in [Appendix A](#).

## Part 3 – Stakeholder consultation outcomes

### 3.1 Public consultation processes

The public consultation processes involved three main milestones:

1. a written public submission process addressing the Terms of Reference;
2. a Stakeholder Forum; and
3. public consultation on the draft Insulin Pumps Report.

An Inter-Departmental Working Group and an expert Reference Group were established by the Department to provide advice and information to the Diabetes Review.

***Disclaimer:** Parts 3.2–3.4 are intended to provide a broad summary of the views expressed by stakeholders and only information provided in the submissions or at the Stakeholder Forum has been included. No attempt was made to reach consensus and the views and opinions should not be considered as medical advice or the views of the Department. This Summary and all other comments contributed were provided to the Diabetes Review Reference Group for consideration.*

### 3.2 Key issues raised in written submissions by stakeholders

- Stakeholders were unanimous in considering that insulin pump therapy has advantages for people with type 1 diabetes. Any restrictions to current access arrangements are strongly opposed.
- Consumers and consumer groups strongly expressed that transitioning from multiple daily injections to insulin pump therapy provides a significant improvement in the quality of life of paediatric type 1 diabetes patients, including a reduction in physical and mental stress, and greater independence and flexibility for the child and family. In terms of clinical outcomes, this includes lower HbA<sub>1c</sub> levels, stable blood glucose levels, and reduced frequency of severe hypoglycaemic attacks.
- Consumers and consumer groups expressed strong support for the continuation of the Insulin Pump Programme, including funding to alleviate the waiting list (which has now been provided, see Part 2.7.4 for further information). Consumers and consumer groups also supported extension of the Programme to include low-income adults, or at least to continue subsidies for current paediatric patients after transitioning into adulthood to support them in continuing access to an insulin pump.
- Consumers, consumer groups, industry organisations and sponsors expressed that improvements in glycaemic control, including lower HbA<sub>1c</sub> levels, from accessing insulin via insulin pump therapy may reduce long-term diabetes-related complication rates. Lifetime use may improve the cost-effectiveness ratio of an insulin pump when the long-term health and quality of life improvements are considered.

### 3.3 Key issues raised by stakeholders at the Stakeholder Forum

- Insulin pump use can lead to benefits in clinical outcomes, including glycaemic control, reducing the frequency and severity of hypoglycaemic events, and reducing the frequency of sick days.
- Insulin pumps can greatly improve quality of life, specifically, reducing patients' and their families' anxieties, and allowing greater flexibility, independence, and insight into managing their type 1 diabetes.
- Success with insulin pump therapy depends on the type of patient (e.g. those with high risk of diabetes complications), the motivation of patients and their families, and the quality of education and support for patients, families and health professionals.
- The clinical data to date seem to compare datasets that are not comparable. By pooling data (i.e. in a systematic literature review), the context and nuance is generally lost. In the literature, there is limited evidence for the benefits of insulin pumps due to this cancellation effect, which is also apparent in the NHMRC *National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults*. There is some dissent between the literature review and on-the-ground experience. Randomised controlled trials (RCTs) are not appropriate to measure insulin pump therapy outcomes. Observational and cohort studies may provide stronger and more beneficial evidence on the use, benefits and effectiveness of insulin pump therapy.
- There are high costs associated with insulin pump therapy, such as specialised training and ongoing support. Insulin pumps may have some cost-benefits associated with reduced hypoglycaemic events and hospital admissions.
- It is necessary to support the rapidly changing technologies in this area, including avenues for government subsidy. Education and support needs to adapt to these rapid changes as well.
- All patients with type 1 diabetes should be considered for eligibility for the Insulin Pump Programme.
- Some patients with private health insurance experience problems when trying to access an insulin pump through their insurer, including denial of access to an insulin pump. *Note: This issue is outside the scope of the Insulin Pumps Review and was referred to the appropriate area of the Department.*
- Many patients are adequately managed on multiple daily injections.
- Specific insulin pump features are important, such as small dose increments for children or those requiring low amounts of insulin, waterproof casing, tubing or tubeless design, and the potential for a closed loop system.
- It is important to ensure a baseline quality control and to have a wide variety of insulin pumps available to allow adequate patient choice, and guaranteed supply and replacement of insulin pumps. Education for patients, families and health professionals with the variety of insulin pumps is critical.

### 3.4 Key stakeholder views in response to the draft Insulin Pumps Report

- Access to the Insulin Pump Programme should be based on clinical need and financial disadvantage, and should be widened to all ages. The current age restriction is inequitable as it denies access to an insulin pump to those over 18 years who are unable to afford private health insurance and who would benefit from insulin pump therapy. With the exception of age, the Programme eligibility criteria are appropriate.
- Insulin pumps under the Programme should be affordable, and the Programme should fully subsidise the cost of the pump for those in the lowest income bracket.
- The Programme should be expanded to include: women who are pregnant or trying to conceive, and people with high HbA<sub>1c</sub> (i.e.  $\geq 8.5\%$ ) or disabling (severe or unpredictable) hypoglycaemia. There is evidence for the benefits of insulin pump therapy and good glycaemic control in women who are pregnant.
- Insulin pumps reduce hospitalisations and the development of complications, reducing healthcare costs.
- Treatment should be part of a multidisciplinary team care arrangement.
- Pump consumable costs should be funded through the NDSS, to provide additional Programme funding. Insulin pump consumables should be available through local pharmacies to prevent access delays. *Note: Comments relating to the administration and delivery of insulin pump consumables were directed to the relevant area of the Department to consider as part of a broader review of the NDSS.*
- Quality of life benefits associated with insulin pump use include: greater flexibility with meals and sleeping times; enhanced participation in social and school activities; and enhanced participation in employment for carers of children with type 1 diabetes.
- Important features of insulin pumps include: continuous glucose monitoring, user-friendly software, adjustable bolus (e.g. square wave, multiwave, etc.), ability to set different basal rates and daily profiles, low glucose insulin suspension, education/training and user support, waterproofing, child lock, and the ability to download data for review.

### 3.5 Inter-Departmental Working Group

Key issues discussed by the Inter-Departmental Working Group include:

- Members noted the need for consistency between guidelines and clinical practice in the management of diabetes.
- Members considered the impacts that changes to the Insulin Pump Programme may have on private health insurance markets.
- Members discussed the possible pathway for new insulin pump technologies to request listing on the Prosthesis List through existing PLAC processes.

- Members recommended the inclusion of Aboriginal and Torres Strait Islander, and rural and remote, identifiers in the data collection for the Insulin Pump Programme.
- At the request of the Reference Group, the TGA representative provided information on the safety and regulation of insulin pumps and the listing of insulin pumps on the ARTG for inclusion in this Report (refer to [Part 2.9](#)).

### **3.6 Reference Group**

As a result of Reference Group input, the following actions were taken:

- An extension to the literature review to include observational evidence, which may be more suitable than trial evidence to identify any patient relevant outcomes from insulin pump therapy.
- The Department wrote to APEG to seek additional specialist clinician advice on:
  - what features of an insulin pump are vital in achieving the best clinical outcomes for paediatric patients and their families;
  - which patient sub-groups, from a clinical outcomes perspective, might benefit the most from insulin pump therapy in order to help to prioritise patients under the Programme; and
  - what eligibility criteria for the Insulin Pump Programme are necessary to ensure the best possible patient outcomes.
- Inclusion of an option for insulin pump discontinuation rates and reasons to be gathered in the data collection for the Insulin Pump Programme.
- Inclusion of observational studies on the use of insulin pump therapy in pregnant women with type 1 diabetes.
- Inclusion of research on the importance of glycaemic variability as an independent factor in the development of diabetes complications.
- Inclusion of research on bolus type delivered by an insulin pump and the effect on postprandial glycaemia.

### **3.7 Advice from the Australasian Paediatric Endocrine Group (APEG)**

The APEG advised that the most important features of a pump will vary based on patient needs, and therefore the treating team should be able to determine the most appropriate pump for the patient. However, features such as bolus calculators, dose increments suitable for children, and the ability to download data may have additional advantages for the paediatric population. They stated that features such as continuous glucose monitoring and algorithms to detect hypoglycaemia and suspend insulin delivery provide additional safety and efficacy advantages.

The APEG indicated that the current eligibility criteria are appropriate for children, that there is insufficient evidence on which to base any additional criteria or prioritisation rules, and ideally, there should not be an age cut-off for the Programme. There are risks to creating eligibility criteria without strong clinical evidence to support the restrictions. Without evidence, such prioritisation is likely to result in inequitable distribution of pump use.

Commenting on the system in the United Kingdom, where adolescents are required to undertake a trial of multiple daily injections sometime between the ages of 12 and 18, APEG indicated that this may restrict insulin pump use to those who fail multiple daily injections, and undervalues the potential benefits of pump therapy for those who can also successfully use multiple daily injections.

A recent study by Johnson (2013), an Australian case-control analysis of children and adolescents using pump therapy, demonstrated the benefits of pump therapy, particularly for those with poor control of their diabetes prior to initiating pump treatment. Although this is an observational study, RCTs are generally of shorter duration with fewer subjects, and therefore the case-control study represents some of the best evidence available relating to pump therapy.

## Part 4 – ToR 8

### Benefits and safety of insulin pump therapy

Determine the clinical outcomes (e.g. HbA<sub>1c</sub>, health-related quality of life, and other potential benefits) and harms for people with type 1 diabetes of insulin pump therapy. In this, consideration should be given to different age groups, with a particular reference to those under 18 who may be eligible for the Insulin Pump Programme, which is funded by the Australian Government.

#### 4.1 Key findings for ToR 8

##### *Literature review of RCTs*

- The outcomes of the systematic literature review of RCTs (n = 31) showed that the trial evidence could not conclusively support the superior efficacy (measured by HbA<sub>1c</sub> levels) or safety (measured by number of hypoglycaemic events) of insulin pump therapy compared to multiple daily injections in any age group. None of the trials assessed long-term health outcomes.
- The studies reported a modest improvement in HbA<sub>1c</sub> levels in adults, adolescents and children with the use of insulin pump therapy compared to multiple daily injections. In children and adolescents, the improvement in HbA<sub>1c</sub> ranged from -0.22% to -0.1%, but only one of the four meta-analyses located demonstrated a statistically significant difference. In adults, HbA<sub>1c</sub> improved by -0.30% to -0.19% and all three meta-analyses showed statistical significance. The difference did not reach the 0.5% reduction generally accepted to be of clinical significance (Clar 2010; Cummins 2010). However, there is no consensus on this issue and a smaller reduction may be considered important from a public health perspective if achieved on a wide scale (Farmer 2012).
- The RCTs for children had low evidence strength due to small sample size, lack of participant and personnel blinding due to the nature of the intervention, and funding by insulin pump manufacturers.
- In children and adolescents, the literature review found that the reported quality of life outcomes were better with insulin pump therapy compared to multiple daily injections in five studies. However, only two of the five RCTs showed a statistically significant increase favouring insulin pump therapy.
- In adults, the literature review (n = 6 RCTs) found that reported quality of life was better with insulin pump therapy than multiple daily injections, with statically significant differences observed in four RCTs. A number of assessment tools were used including the Diabetes Treatment Satisfaction Questionnaire, Diabetes Quality-

of-Life questionnaire, and the Medical Outcomes Study 12-Item and 36-Item Short-Form Surveys.

- No sub-group analyses in the identified systematic reviews considered characteristics of children other than age.

### ***Literature review of observational studies***

- There are a number of important limitations to interpretation of benefit from observational studies associated with the lack of randomisation and blinding, and high risk of selection and publication bias. It is not possible to compare the real difference between multiple daily injections and insulin pump therapy using observational studies independent of confounding factors. However, due to study inclusion and exclusion criteria, patients included in these studies may be more representative of use in Australian clinical practice than those in RCTs.
- The systematic literature review of observational evidence indicates that children, adolescents, and adults appear to achieve greater reductions in HbA<sub>1c</sub> with insulin pump therapy than with multiple daily injections. In the majority of studies, statistically significant reductions in HbA<sub>1c</sub> were found to be maintained over several years.
- Of the thirteen before-and-after studies and nine cohort studies in children and adolescents, sixteen showed statistically significant reductions or end of study differences in HbA<sub>1c</sub> favouring insulin pump therapy. In the before-and-after studies the significant mean difference in HbA<sub>1c</sub> ranged from -0.3% to -1.04% (where reported).
- In the fifteen observational studies in adults, twelve showed statistically significant reductions or end of study differences in HbA<sub>1c</sub> favouring insulin pump therapy. In the before-and-after studies the significant mean differences in HbA<sub>1c</sub> ranged from -0.4% to -2.6%.
- The reductions in HbA<sub>1c</sub> were shown to be greater in patients with high initial HbA<sub>1c</sub> levels (Aberle 2008; Shalitin 2010; Johnson 2013), and two studies reported that insulin pump therapy seems more beneficial when initiated in children under six years old (Hughes 2012; Levy-Shraga 2013).
- Where reported, most observational studies showed lower risks of severe hypoglycaemia with insulin pump therapy in children, adolescents and adults, with most evidence found in children.
- Of six observational studies of glycaemic variability, all demonstrated statistically significant results favouring insulin pump therapy in reducing glycaemic variability.
- Of ten retrospective cohort studies in pregnant women with type 1 diabetes, most did not show significant differences between multiple daily injections and insulin

pump therapy on diabetes management, maternal pregnancy outcomes or newborn outcomes. Limitations of the studies included low patient numbers and lack of adjustment for differences between the cohorts or confounding factors. In addition, poor glycaemic control may have been an indication for insulin pump therapy in some studies.

### ***Stakeholder input***

- Drawing on information from the written submissions and the Stakeholder Forum, the overall sentiment from consumers, consumer groups and manufacturers is that there are clinical benefits from using insulin pump therapy. Improvements in effectiveness, safety and quality of life were reported in the public submissions.
- Clinical groups expressed that while the randomised trial and observational study evidence does not conclusively support the superior outcomes of insulin pump therapy, there is some benefit in particular patient sub-groups, including high-risk patients.
- It was explicit that the success of either insulin pump or multiple daily injection therapy was dependent on the level of motivation and subsequent compliance of the patient and/or carer.

## **4.2 Introduction**

In this section, the aim is to address the differences in clinical outcomes between insulin pump therapy, also known as continuous subcutaneous insulin infusion, and multiple daily injections. Different age groups were analysed to determine if there are sub-groups that would benefit more from insulin pump therapy.

In the 2010 Cochrane Collaboration Report, Misso concluded that there may be benefits to using insulin pumps over multiple daily injections for improving glycaemic control and quality of life for people with type 1 diabetes. However, there was insufficient evidence around diabetes late complications, adverse events, mortality and costs, to make clinical recommendations regarding which form of therapy was superior. The systematic review that informed the NHMRC-approved *National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults* (Craig 2011), indicated that the slight, but statistically significant, improvement in observed benefits with insulin pump therapy may have been due to the intensive diabetes management plan, as opposed to pump therapy alone.

To clarify some of this uncertainty, the Department engaged the Quality Use of Medicines and Pharmacy Research Centre (QUMPRC) of the University of South Australia to conduct a literature review to evaluate systematically randomised controlled trial (RCT) evidence on the efficacy and safety of insulin pump therapy versus multiple daily insulin injections, the traditional method of administering insulin.

Noting the discrepancy between the trial evidence, from the first literature review, which showed only a small benefit of insulin pump therapy in terms of HbA<sub>1c</sub> and no effect on hypoglycaemia, and the stakeholder submissions, which indicated benefits to HbA<sub>1c</sub> and quality of life, the Reference Group requested an additional literature review of observational studies. Following stakeholder consultation on the draft Insulin Pumps Report, the literature review of observational studies was expanded to consider women with type 1 diabetes who are pregnant or planning a pregnancy.

Most RCTs excluded patients with diabetes complications, other chronic illnesses, pregnancy or hypoglycaemia unawareness. Baseline HbA<sub>1c</sub> in the RCTs was frequently  $\geq 8.0\%$  (64 mmol/mol) in studies of children. With some exceptions (e.g. Thomas 2007, DeVries 2002), most RCTs were not restricted to patients with severe hypoglycaemia, hypoglycaemia unawareness or persistent poor control on multiple daily injections. The paucity of data from RCTs regarding outcomes in these subgroups has made it difficult to determine if such patients receive greater benefit from insulin pump therapy than people who were previously well controlled on multiple daily injections.

In contrast, observational studies often involved a wider range of patients with indications for insulin pump therapy including high HbA<sub>1c</sub>, wide blood glucose variability, frequent or severe hypoglycaemia, dawn phenomenon (see [Glossary](#)), development of complications, pregnant or planning a pregnancy, concurrent chronic illness, needle phobia, and irregular lifestyle or need for lifestyle flexibility.

In current Australian clinical practice, initiation to insulin pump therapy often involves consideration of factors such as the capacity to pay for the pump, technological and cognitive competence to manage the pump, and a high level of patient/carer motivation to intensively monitor and manage diabetes (Victorian CSII Working Party 2009, O'Connell 2008). However, the Australian clinical guidelines for type 1 diabetes indicate that patients likely to benefit from insulin pump therapy include pregnant women (ideally preconception), some children and adolescents, and those with hypoglycaemia unawareness or microvascular complications (Craig 2011).

In general, evidence from RCTs should be given greater weight than observational studies. However, it seems likely that the populations included in observational studies may be more reflective of patients using insulin pump therapy in Australia, than patients involved in RCTs, e.g. those with complications, hypoglycaemia unawareness or who are poorly managed on multiple daily injections. An insulin pump user survey in Australia indicated that 88% of patients initiated pump therapy to better control their diabetes (to reduce hypoglycaemic or hyperglycaemic events), and around 60% were recommended to use a pump by a doctor or diabetes educator (AIHW 2012b).

## **4.3 First literature review: randomised controlled trials (RCTs)**

### **4.3.1 Methodology**

The literature review included all systematic reviews and meta-analyses focussing on insulin pump therapy versus multiple daily injections published between 2000 and July 2012, as well as additional RCTs that had not been included in the systematic reviews.

Position statements and guidelines by professional organisations that made recommendations on the use of insulin pump therapy between 2009 and July 2012, were included in the literature review. This will be discussed further in [Part 6](#) of the report addressing ToR 10.

The literature review did not specifically compare different types of insulin used in the insulin pumps.

The literature review aimed to answer three research questions that are relevant to ToR 8:

1. What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple insulin injections in children and adolescents under 18 years old?
2. What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple insulin injections in adults?
3. What is the evidence that continuous subcutaneous insulin infusion therapy is safer than multiple insulin injections?

### **4.3.2 Results**

Five systematic reviews were included in the literature review, all of which examined the efficacy and safety of insulin pump therapy compared to multiple daily injections. One systematic review restricted the analysis to RCTs that had used short-acting insulin analogues in both insulin pump therapy and multiple daily injections groups (Monami 2010), and one review restricted the analysis to RCTs that had used short-acting insulin analogues in the insulin pump therapy groups (Yeh 2012).

Overall, 31 RCTs were evaluated as part of the literature review, including 30 RCTs published between 1982 and 2009, which were included in the five systematic reviews, and one trial published afterwards. Nineteen RCTs included a total of 846 adults, 11 RCTs included a total of 361 children, and one RCT included a total of 23 adults and children. Most trials had a small sample size. There were 15 trials with 1-25 participants, 11 trials with 25-50 participants, four trials with 50-100 participants, and one trial with >100 participants.

Of the 24 RCTs for which the source of funding was reported, 19 were funded at least partly by insulin pump manufacturers who provided material or financial support to

patients. The studies were generally assessed as unclear or low risk of bias, except for participant and personnel blinding, which was not possible because of the nature of the intervention.

#### **4.3.2.1 What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple insulin injections in children and adolescents under 18 years old?**

##### ***HbA<sub>1c</sub>***

Four meta-analyses assessed HbA<sub>1c</sub> in children and adolescents less than 18 years of age. Overall, the observed benefit showed that there was modest improvement in HbA<sub>1c</sub> levels for those on insulin pump therapy, but the difference did not reach the 0.5% reduction that is usually considered a clinically significant change in HbA<sub>1c</sub>. However, it may be considered important from a public health perspective (Clar 2010). One meta-analysis of seven RCTs published between 1982 and 2008, found a statistically significant decrease in HbA<sub>1c</sub> favouring insulin pump therapy of -0.22% (95% CI -0.41% to -0.03%, P = 0.021) (Misso 2010).

Two meta-analyses found a non-significant decrease in HbA<sub>1c</sub> favouring insulin pump therapy of -0.20% (95% CI -0.43% to 0.03%) based on eight RCTs published between 2003 and 2007 (Fatourehchi 2009), and of -0.17% (95% CI -0.47% to 0.14%) based on seven RCTs published between 2003 and 2008 examining insulin analogues in insulin pump therapy (Yeh 2012).

A fourth meta-analysis found a non-significant decrease in HbA<sub>1c</sub> favouring insulin pump therapy in children with an average age of ≤10 years of -0.1% (95% CI -0.5% to 0.3%, P = 0.48) based on 4 RCTs published between 2003 and 2007 (Monami 2010).

##### ***Quality of life and treatment satisfaction***

Overall, reported quality of life was better with insulin pump therapy compared to multiple daily injections. Five trials assessed quality of life using four different assessment tools including three that were diabetes specific and one designed for measuring health-related quality of life in children and adolescents. Reported superior quality of life in insulin pump therapy over multiple daily injections was consistent; however, the difference only reached statistical significance in two of the scales/scores out of the five trials (the satisfaction scale in Cohen 2003 and the change in worry score in Opipari-Arrigan 2007). All trials had small sample sizes of fewer than 40 participants.

Three RCTs assessed treatment satisfaction using the Diabetes Treatment Satisfaction Questionnaire (Bradley 1994). All found a statistically significant and clinically relevant improvement with insulin pump therapy compared to multiple daily injections, defined as a ≥ five-point difference in score. In another RCT, participants assigned to insulin pump therapy reported significantly greater convenience, ease and flexibility of

treatment, leading to increased treatment satisfaction with insulin pump therapy compared to multiple daily injections.

### ***Patients' preferences***

Of the assessed patients' preferences in three trials published between 2003 and 2008, the majority of patients and their families preferred insulin pump therapy to multiple daily injections.

### ***Long-term health outcomes***

None of the RCTs assessed long-term health outcomes.

## **4.3.2.2 What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple insulin injections in adults?**

### ***HbA<sub>1c</sub>***

Overall, similar to the results for children and adolescents, there was a modest observed improvement in HbA<sub>1c</sub> levels with insulin pump therapy compared to multiple daily injections. The difference did not reach the 0.5% reduction usually considered a clinically significant change in HbA<sub>1c</sub> levels, but may still be considered important from a public health perspective (Clar 2010).

Three meta-analyses reported a statistically significant difference in HbA<sub>1c</sub> favouring insulin pump therapy. The Cochrane Review considered the results of 12 RCTs published between 1982 and 2005 and reported a statistically significant difference in HbA<sub>1c</sub> of -0.29% (95% CI -0.52% to -0.06%, P=0.0013) (Misso 2010). The results of a meta-analysis based on five RCTs published between 2003 and 2007 also reported a statistically significant difference in HbA<sub>1c</sub> of -0.19% (95% CI -0.27% to -0.11%) (Fatourechhi 2009).

A meta-analysis of four RCTs involving insulin analogues in the insulin pump therapy group published between 2003 and 2012, reported a statistically significant difference in HbA<sub>1c</sub> change from baseline levels favouring insulin pump therapy of -0.30% (95% CI -0.58% to -0.02%, P = 0.038) (Yeh 2012). However, this result was heavily influenced by the results of a single RCT that found a large decrease in HbA<sub>1c</sub>, which may be explained by the high baseline HbA<sub>1c</sub> level in the cohort of 9.3% (DeVries 2002). High baseline HbA<sub>1c</sub> levels may result in a greater reduction with intervention than lower initial HbA<sub>1c</sub> levels (Retnakaran 2005).

### ***Quality of life and treatment satisfaction***

Six RCTs compared quality of life between insulin pump therapy and multiple daily injections in adults. Overall, quality of life reported was better with insulin pump therapy.

One RCT assessed quality of life with the Medical Outcomes Study 12-Item Short-Form Survey (SF-12) and one RCT used the Medical Outcomes Study 36-Item Short-Form

Survey (SF-36). Both studies found significant improvements in the mental health and general health subscales with insulin pump therapy compared to multiple daily injections. One RCT did not provide detailed data. In the second RCT, there were clinically relevant improvements (defined as  $\geq$  a five-point difference) in both the SF-36 general health and mental health subscales with insulin pump therapy compared to multiple daily injections (DeVries 2002).

Three RCTs assessed quality of life with the Diabetes Quality-of-Life questionnaire (The Diabetes Control and Complications Trial Research Group 1988). A significant difference was evident only in the largest trial involving 272 participants (Hoogma 2006). In the two other RCTs, quality of life was often found to be better with insulin pump therapy compared to multiple daily injections, but the differences were not statistically significant.

Three RCTs assessed treatment satisfaction with the Diabetes Treatment Satisfaction Questionnaire (Bradley 1994). Reported treatment satisfaction was significantly greater with insulin pump therapy compared to multiple daily injections in two RCTs and the difference was clinically relevant in at least one RCT (Bruttomesso 2008).

### ***Long-term health outcomes***

None of the RCTs assessed long-term health outcomes.

#### **4.3.2.3 What is the evidence that continuous subcutaneous insulin infusion therapy is safer than multiple insulin injections?**

The main outcome considered for this question was the occurrence of hypoglycaemia. Four systematic reviews examined the occurrence of hypoglycaemia in insulin pump therapy compared with multiple daily injections. Overall, there was no statistically significant difference in the occurrence of mild, nocturnal and symptomatic hypoglycaemia, or severe hypoglycaemia, between the insulin pump therapy and multiple daily injections groups.

In RCTs, mild hypoglycaemia was often defined as a blood glucose level lower than 60 or 70 mg/dl. Severe hypoglycaemia was most often defined as requiring assistance from another person for recovery or resulting in coma or seizure.

#### ***Mild, symptomatic, and nocturnal hypoglycaemia***

Three reviews examined mild hypoglycaemia.

One meta-analysis did not find a difference between insulin pump therapy and multiple daily injections in the mean numbers of mild hypoglycaemic episodes in five crossover RCTs published between 2003 and 2008 (Fatourehchi 2009). A small significant difference favouring multiple daily injections was found in three parallel RCTs published between 2004 and 2007. This difference may be explained by the differences in study populations and hypoglycaemia data recording between trials.

One systematic review did not perform a meta-analysis because studies used different scales to report hypoglycaemia (Misso 2010). For mild hypoglycaemia, the authors concluded that the data of 17 RCTs published between 1982 and 2008 suggested there was “no relevant benefit” of one intervention over the other.

Another meta-analysis of three RCTs using insulin analogues in the insulin pump therapy groups found a higher risk of symptomatic hypoglycaemia with insulin pump therapy in adults. However, this result was influenced by the results of a single RCT that may not be generalisable to a broader population because it only included participants with at least one episode of severe hypoglycaemia in the past six months (Yeh 2012).

One meta-analysis did not find a difference between insulin pump therapy and multiple daily injections in nocturnal hypoglycaemia (Fatourechhi 2009).

### ***Severe hypoglycaemia***

Four reviews examined severe hypoglycaemia; however, it should be noted that the event rates for severe hypoglycaemia were low in all RCTs and the RCTs were not powered for this outcome. Therefore, any recorded difference is difficult to interpret.

One meta-analysis did not find a difference between insulin pump therapy and multiple daily injections in the number of people who experienced at least one severe hypoglycaemic episode, based on 12 RCTs between 2003 and 2008 (Fatourechhi 2009). The number of people who experienced at least one severe hypoglycaemic episode in each group was low, 5% and 9.4% in the insulin pump therapy and multiple daily injections groups, respectively, which affected the ability to determine the extent of difference between the groups.

Another meta-analysis of 11 RCTs published between 2000 and 2008, did not find a significant difference in severe hypoglycaemia between insulin pump therapy and multiple daily injections (Monami 2010).

The third meta-analysis of RCTs published between 2000 and 2009 with insulin analogues in the insulin pump therapy groups, found no significant difference in the rate of severe hypoglycaemia among adults (three RCTs), children less than 18 years of age (five RCTs), and above and below 12 years of age (three RCTs and two RCTs, respectively) (Yeh 2012).

One systematic review did not perform a meta-analysis because studies used different scales to report hypoglycaemia (Misso 2010). For severe hypoglycaemia, the authors concluded that, based on a summary of 15 RCTs, “...insulin pump therapy may be better than multiple daily injections”.

## **4.4 Second literature review: observational studies**

### **4.4.1 Methodology and limitations**

A systematic review was undertaken to assess the efficacy and safety of subcutaneous insulin infusion therapy versus multiple daily insulin injections in observational studies

of adults and children with type 1 diabetes published between January 2008 and October 2014. Outcomes considered were blood glucose control (HbA<sub>1c</sub> and glycaemic variability) and hypoglycaemia. Studies with a follow-up of less than three months, cross-sectional studies, and studies focussing on specific sub-groups (pregnant women, peri-operative period, cystic fibrosis) were excluded. Evidence synthesis was carried out using a narrative review for each research question.

The literature review focussed on four research questions that are relevant to ToR 8:

1. What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple daily injections for blood glucose control (HbA<sub>1c</sub>) in children and adolescents under 18 years of age with type 1 diabetes?
2. What is the evidence that continuous subcutaneous insulin infusion therapy is safer than multiple daily injections with regard to the risk of severe hypoglycaemia in children and adolescents under 18 years of age with type 1 diabetes?
3. What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple daily injections for blood glucose control (HbA<sub>1c</sub>) in adults with type 1 diabetes?
4. What is the evidence that continuous subcutaneous insulin infusion therapy is safer than multiple daily injections with regard to the risk of severe hypoglycaemia in adults with type 1 diabetes?

The results of observational studies need to be interpreted with caution because of the higher risk of bias, including publication bias, selection bias and unmeasured confounding resulting from lack of randomisation. In before-and-after studies, the changes associated with time (historical data being the comparison), make it impossible to assess whether the effect observed is due to the intervention alone (i.e. use of an insulin pump) or other factors, such as intensity of blood glucose testing or education after introduction of the insulin pump. Conversely, the increase in HbA<sub>1c</sub> levels that has been observed in patients with diabetes over time may have partially masked the potential benefit provided by insulin pumps.

In many of the cohort studies identified, the statistical tests compared the end-of-study HbA<sub>1c</sub> levels between the two treatments without explicit adjustment for baseline HbA<sub>1c</sub>. Given that with both therapies, reduction in HbA<sub>1c</sub> may progressively increase as baseline HbA<sub>1c</sub> rises (Retnakaran 2005), and that poor glycaemic control is often a selection criterion for initiation of insulin pump therapy, the improvements in glycaemic control seen with insulin pump therapy may result from higher initial HbA<sub>1c</sub>. The variation in definition of severe hypoglycaemia outcome across studies adds difficulty to the interpretation of the synthesised results for addressing any difference in benefit. Nevertheless, observational studies do provide useful data on effects observed in clinical practice.

A 0.5% reduction or more in HbA<sub>1c</sub> is generally accepted to be of clinical importance (Clar 2010; Cummins 2010). However, there is no consensus on this issue and a smaller reduction might be considered important from a public health perspective if achieved on a wide scale (Farmer 2012).

#### **4.4.2 Results**

A total of 37 observational studies were identified, including 23 before-and-after studies, nine retrospective cohort studies and five prospective cohort studies. The studies were conducted in 24 different countries and the majority (62%) had a follow-up period of two or more years (range of three months to nine years).

There were 21 studies in children and adolescents under 18 years old, one study in adolescents and adults, 14 studies in adults, and one study including all age groups. The number of patients included in the studies varied between 10 and 2709, with eight studies including over 200 patients.

A variety of pumps were used in the studies; most studies (21) did not report the type of insulin pumps used. Twenty-three studies did not report the source of funding, seven received public funding, three industry funding, and four both public and industry funding.

Indications for insulin pump therapy were broadly similar between studies: poor glycaemic control, frequent hypoglycaemia, dawn phenomenon, need for lifestyle flexibility, and needle phobia. Limited information was reported on the education provided to patients at either the time of initiating insulin pump therapy or subsequently.

##### **4.4.2.1 What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple daily injections for blood glucose control in children and adolescents under 18 years of age with type 1 diabetes?**

###### ***HbA<sub>1c</sub> and glycaemic variability***

Of 13 before-and-after studies, 12 showed a decrease in HbA<sub>1c</sub> (0.1-1.04%) with insulin pump therapy that was statistically significant in nine studies. Long term studies generally showed positive results for insulin pump therapy, with statistically significant HbA<sub>1c</sub> reductions of 0.4-0.7% at 2-5 years follow-up in four studies, a non-significant reduction in one study (Abaci 2009), and no reduction in a sixth study (Knight 2011).

Of nine cohort studies, seven showed statistically significant decreases in HbA<sub>1c</sub> with insulin pump therapy; however, the changes were less than the 0.5% decrease that is usually considered clinically meaningful (Cummins 2010) in all but one Australian study (Johnson 2013). Most studies did not explicitly adjust for pre-study HbA<sub>1c</sub>. One study of around 100 children found a statistically significant mean difference in HbA<sub>1c</sub> of 0.6% (95% CI 0.1-1.2) between the multiple daily injection group and the insulin pump group after adjusting for baseline differences in HbA<sub>1c</sub> (Senniapan 2012). The Australian study

surveyed a total of 345 children including 129 children with insulin pumps matched to 129 children with multiple daily injection. It found a mean improvement in HbA<sub>1c</sub> over a five-year period of 0.7% for those using insulin pumps. In the largest study in 868 children and adolescents a significant decrease was observed only in the first year and not in the following years (Jakisch 2008).

### ***Age***

Hughes (2012) observed that the highest HbA<sub>1c</sub> reductions occurred in children under 6 years (-0.9% at six months follow-up,  $p < 0.01$ ). In another study, the mean HbA<sub>1c</sub> levels were significantly lower for those who initiated insulin pump therapy before age 6 throughout the entire follow-up period ( $p = 0.02$ ) (Levy-Shraga 2013). These findings suggest that insulin pump therapy may be more beneficial for children under 6 years. However, these two studies included low numbers of children.

#### **4.4.2.2 What is the evidence that continuous subcutaneous insulin infusion therapy is safer than multiple daily injections with regards to the risk of severe hypoglycaemia in children and adolescents under 18 years of age with type 1 diabetes?**

Children and adolescents under 18 years of age with type 1 diabetes appear to have a lower risk of severe hypoglycaemia when using an insulin pump than with multiple daily injections.

Of five before-and-after studies identified that considered severe hypoglycaemia, four reported decreases in severe hypoglycaemia, which were statistically significant in three studies (Campbell 2009; Hasanbegovic 2009; Rabbone 2009). Only one study of 17 adolescents reported an increase in the rate of severe hypoglycaemia with insulin pump therapy (Abaci 2009). In the before-and-after studies, statistically significant differences in the rate of severe hypoglycaemia per 100 patient-years in children and adolescents using insulin pump therapy compared to multiple daily injections ranged from -6.4 to -62. The definitions of severe hypoglycaemia varied, making comparison difficult.

Seven cohort studies found a decrease in the rates of severe hypoglycaemic events with the use of insulin pump therapy, which was statistically significant in three studies (Berghaeuser 2008; Jakisch 2008; Johnson 2013). In the cohort studies, statistically significant differences in the rate of severe hypoglycaemia per 100 patient-years in children and adolescents using insulin pump therapy compared to multiple daily injections ranged from -2 to -17. Again, the definitions of severe hypoglycaemia varied.

One study reported significant decreases in the rates of symptomatic and nocturnal hypoglycaemic events with insulin pump therapy (Çamurdan 2008).

### **4.3.2.3 What is the evidence that continuous subcutaneous insulin infusion therapy is more effective than multiple daily injections for blood glucose control in adults with type 1 diabetes?**

#### ***HbA<sub>1c</sub> and glycaemic variability***

Adults with type 1 diabetes appear to achieve a greater reduction of HbA<sub>1c</sub> when using an insulin pump than with multiple daily injections.

Ten before-and-after studies assessed HbA<sub>1c</sub>. With the exception of one study, all showed a statistically significant decrease in HbA<sub>1c</sub> with insulin pump therapy at all follow-up periods with significant mean decreases ranging from 0.4–2.6%. Aberle (2008) and Shalitin (2010) showed that patients with a higher initial HbA<sub>1c</sub> at the start of insulin pump therapy showed greater decreases in HbA<sub>1c</sub>, compared to those with lower baseline HbA<sub>1c</sub>.

Three cohort studies, involving 220, 247 and 2709 patients respectively, showed statistically significant decreases in HbA<sub>1c</sub> levels with insulin pump therapy at one, two, three and five years of follow-up (Lepore 2009; Carlsson 2013) or at 6 months, 1 and 2 years of follow-up (Cohen 2013). In the largest cohort, Carlsson (2013) found that the reduction in HbA<sub>1c</sub> observed with insulin pump therapy compared to multiple daily injections was greatest in the first two years, and was estimated to be 0.20% at five years (95% CI 0.07% to 0.32%), which is less than the 0.5% reduction usually considered clinically significant. A similar trend was observed in a cohort of 247 patients where the decrease in HbA<sub>1c</sub> between the two groups declined progressively over time and was only significant up to 24 months (Cohen 2013).

Four studies found a significant decrease in glycaemic variability before insulin pump therapy to after insulin pump therapy (Aberle 2008; Lin 2011; Gimenez 2010; Maiorino 2014). Two cohort studies found a significant reduction in glycaemic variability with insulin pumps compared to multiple insulin injections (Maiorino 2014; Cohen 2013).

### **4.4.2.4 What is the evidence that continuous subcutaneous insulin infusion therapy is safer than multiple daily injections with regards to the risk of severe hypoglycaemia in adults with type 1 diabetes?**

Adults with type 1 diabetes appear to have a lower risk of severe hypoglycaemia with insulin pump therapy than with multiple daily injections. Five before-and-after studies reported decreased rates of severe hypoglycaemic events with insulin pump therapy in adults; three with significant results (Marmolin 2012; Shalitin 2010; Gimenez 2010). Statistically significant differences in the rate of severe hypoglycaemia per 100 patient-years in adults using insulin pump therapy compared to multiple daily injections ranged from -3 (where severe hypoglycaemia was defined as coma, seizures or administration of glucagon injection or intravenous glucose)(Shaitlin 2010) to -120 (where severe hypoglycaemia was defined as required assistance from another person) in a study which included patients at high risk of hypoglycaemia ( Gimenez 2010).

## **4.5 Third literature review: observational studies in pregnant women**

### **4.5.1 Background**

Reductions in the rate of adverse outcomes can be achieved by optimal care and tight glycaemic control before conception and throughout pregnancy in women with diabetes (Pearson 2007; Bismuth 2012). A Cochrane systematic review and meta-analysis, which included published literature to July 2011, identified five RCTs involving 153 women and 154 pregnancies comparing insulin pumps with multiple insulin injections (Farrar 2007). A separate meta-analysis that included literature up to April 2006 included six trials involving 213 women (Mukhopadhyay 2007). Collectively these reviews included eight trials (one trial included women with type 1 or type 2 diabetes). No trials have been published since the Cochrane review. With regards to differences in HbA<sub>1c</sub>, hypoglycaemia, hyperglycaemia, macrosomia (birth weight greater than 4 kg), preterm delivery, caesarean birth, perinatal mortality, fetal anomaly and worsening of diabetes complications, neither Farrar (2007) or Mukhopadhyay (2007) reported significant differences between women using insulin pump therapy and women using multiple insulin injections.

Observational evidence published up to 2007 supports the results of the RCTs. A review of observational studies published between 2002 and 2007 identified six studies which compared insulin pump therapy and multiple insulin injections (two published in full and four in abstract format) (Cummins 2010). Most studies found similar glycaemic control, maternal and fetal outcomes between the groups. There were small numbers of women on insulin pump therapy in all studies limiting the statistical power to detect the endpoints under study.

### **4.5.2 Methodology and limitations**

This literature review assessed the evidence for the effects of insulin pump therapy versus multiple insulin injections on diabetes management, maternal pregnancy outcomes and newborn outcomes in women with type 1 diabetes who are pregnant or planning to conceive. It included all English language, observational studies published between January 2008 and October 2014.

These observational studies had a number of limitations. They generally included a low number of women and may lack statistical power to detect significant differences. Most studies did not adjust for the differences observed between the study groups at the start of the study or other known risk factors that may impact on obstetric and perinatal outcomes. A failure to achieve therapeutic goals with multiple daily injections was an indication to switch to insulin pump therapy in some studies and could bias the results towards the null effect.

### **4.5.3 Results**

The majority of the ten retrospective cohort studies identified were small with the number of women included ranging between 14 and 113 in the insulin pump group and between 20 and 424 in the multiple insulin injection group.

The majority of studies did not show a significant difference between groups either on diabetes management, maternal pregnancy outcomes or newborn outcomes.

#### **4.5.3.1 Diabetes management**

With regards to HbA<sub>1c</sub> control, results were variable. Six studies did not show a difference between the insulin pump and injection groups for HbA<sub>1c</sub> at any time during pregnancy. Four studies showed a lower level of HbA<sub>1c</sub> with insulin pump use at the start of the study (Gonzalez-Romero 2010; Bruttomesso 2011; Kallas-Koeman 2014; Neff 2014), which was sustained throughout pregnancy in three studies. The largest study which examined 387 pregnancies (Kallas-Koeman 2014), found a significant difference in HbA<sub>1c</sub> in favour of insulin pump therapy in all three trimesters without increased risk of severe hypoglycaemia.

Most studies did not find significant differences between insulin pump and multiple insulin injection therapy for other outcomes (ketoacidosis, non-severe hypoglycaemia, severe hypoglycaemia).

#### **4.5.3.2 Maternal pregnancy outcomes**

Most studies did not find significant differences between insulin pump and multiple insulin injection therapy for the outcomes of hypertension or preeclampsia, duration of pregnancy, weight gain during pregnancy, caesarean section and preterm labour.

#### **4.5.3.3 Newborn outcomes**

Most studies did not find significant differences between insulin pump and multiple insulin injection therapy for the outcomes of hypoglycaemia in newborns, newborn weight, large-for-gestational-age infants, 5-min AGPAR score, stillbirth and congenital abnormalities.

### **4.6 AIHW Insulin Pump User Survey**

The AIHW's *Report on Insulin Pump Use in Australia* (2012) details the experiences of 5,680 insulin pump users in Australia. The survey indicates strong device satisfaction among insulin pump users with the popular benefits being good integration with the user's lifestyle (86%), better diabetes control (83%) and convenience (71%).

The survey results also highlighted the common problems experienced by insulin pump users as well as the reasons why some users decided to discontinue using the device. The biggest issue among the insulin pump users surveyed was the cost of insulin pump consumables, with 32% of respondents indicating that they were too expensive. Other

common problems included issues with relocating the cannula/tubing of the pump (16%) and others disliking wearing a pump (15%).

The most common reasons for survey respondents to have discontinued insulin pump therapy were that they did not like wearing the pump (50%), they experienced little or no improvement in diabetes control (30%), problems relocating the cannula/tubing (29%), and wanting a break (29%).

The survey found that people with type 1 diabetes living in remote and very remote areas were less likely to use an insulin pump (around 8%) than those living in major cities, inner regional and outer regional areas, which all had similar proportions of use (around 10%). This result was based on small numbers of users from remote and very remote areas (70 users or 1% of survey respondents), so it is difficult to draw firm conclusions regarding reduced access to insulin pumps for people living in these areas. The survey also indicated that insulin pump users living in remote and very remote areas had less contact with specialist diabetes doctors or diabetes educators. Around 15% of people living in rural and remote areas had last seen a diabetes specialist or educator more than six months ago, compared to 9% for those living in major cities.

#### **4.7 Potential safety risks associated with insulin pump therapy**

Aside from the reported benefits of insulin pump therapy, there are some potential safety risks associated with its use. Potential adverse events include DKA from pump malfunction, and catheter-site infection or irritation (Guinn 1988). The risk of DKA from insulin pump failure can be caused by the cannula bending, air bubbles affecting insulin delivery, unintentional misuse, or mechanical problems (Shalitin & Phillip 2008). Multiple daily injection therapy provides a reservoir of long-acting insulin, whereas insulin pump therapy provides frequent doses of short-acting insulin, and therefore, may increase the risk of rapidly developing DKA if there is an interruption to insulin supply (Pickup 2008).

Barnard (2007) found that the continual reliance on an external device, with the need to programme the pump and change over consumables, makes insulin pumps challenging for a significant number of users.

Product safety regulation of insulin pumps in Australia is managed by the Therapeutic Goods Administration. For further information, see [Part 2.9](#).

#### **4.8 Potential safety risks associated with multiple daily injections**

Long-acting insulin analogues cannot be modulated after injection and may produce a peak of insulin dosing in the middle of the night with a consequent risk of hypoglycaemia, and a waning of insulin dosing before breakfast, resulting in fasting hyperglycaemia (also known as the “dawn phenomenon”) (Pickup 2008).

There is also variability in the subcutaneous absorption of delayed-action insulin suspensions, contributing to fluctuations and unpredictability in within-day and

between-day glycaemic control. However, the differences in fluctuations between therapies may be more apparent in relative terms than in absolute terms (Pickup 2008).

## Part 5 – ToR 9

### Costs and comparative effectiveness of insulin pumps

Investigate the cost-effective use of different insulin pumps available under the Insulin Pump Programme.

#### 5.1 Key findings for ToR 9

##### *Literature review*

- The systematic literature search commissioned by the Department showed that there is currently no literature available on the comparative effectiveness of different brands of insulin pumps. The Department has compiled an information table to compare the insulin pumps available under the Protheses List at [Appendix A](#).
- The technology used in insulin pump therapy and multiple daily injections, including the types of insulin, have all improved over time. It is therefore difficult to determine the specific impact of different types of insulin pumps on outcomes over time.

##### *Costs of insulin pumps and consumables*

- The Insulin Pump Programme provides funding for the costs of both insulin pumps, administered by JDRF, and consumables, administered by Diabetes Australia through the NDSS. Programme funding totals \$6.97 million over four years from 2012-13 to 2015-16.
- Insulin pumps available under the Programme are generally those on the Protheses List, with the benefit prices ranging from \$4,000 to \$9,500. There are currently six<sup>2</sup> insulin pumps available.
- On average, consumables available through the NDSS cost \$316 per annum to the consumer, and \$2,098 per annum to the Australian Government. The prices are benchmarked and do not vary between brands. All people with type 1 diabetes are able to access subsidised insulin pump consumables through the NDSS, not just those who have received a subsidised pump through the Programme.
- The cost to Government for each insulin pump supplied through the Programme is \$14,779 over four years (the warranty period of most insulin pumps), or \$3,695 per

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<sup>2</sup> There are seven insulin pumps on the February 2014 edition of the Protheses List; however, the manufacturer has discontinued the Animas 2020. It has not been delisted at this stage (Department of Health, 2014).

annum. This estimate is based on the median pump subsidy amount and the associated cost of consumables.

- Of the 466 pumps supplied under the Programme since it began in 2008-09, the most common pump supplied is the Medtronic Paradigm Veo 754, supplied to 47% of recipients and currently valued at \$9,500.

### ***Cost-effectiveness of insulin pump therapy***

- Based on four cost-effectiveness studies available (Australia, UK, Canada and US), assuming reductions in HbA<sub>1c</sub> levels of 0.51% to 0.675% with insulin pump therapy compared to multiple daily injections, the incremental cost-effectiveness ratio (ICER) per quality-adjusted life year (QALY) converted to AUD \$ 2013 prices ranged from AUD\$63,274 in a US study to AUD\$292,952 in a UK study.
- The ICERs were highly sensitive to the level of HbA<sub>1c</sub> reduction. The modelled reductions in HbA<sub>1c</sub> with insulin pump therapy compared to multiple daily injections in the base case models (1.2% in three studies and 0.9% in one study) are greater than the reductions in HbA<sub>1c</sub> from RCT evidence for adults (0.19% to 0.3%), and adolescents and children (0.1% to 0.22%).
- All studies used the CORE model (Palmer 2004). The CORE model may overestimate the incidence of macrovascular complications in people with type 1 diabetes (Cummins 2010).
- ICERs were sensitive to changes in reductions in severe hypoglycaemia rates only when the cost of severe hypoglycaemia was valued in the high range (2007 USD\$1,234).
- With the exception of the UK study, all studies appear to underestimate the ICER by assuming a pump life span longer than the warranty period of 4 years for most insulin pumps currently marketed in Australia. In the US study, reducing the pump life span from 7 years in the base case to 4 years in the sensitivity analysis increased the ICER by 54%.
- The studies did not examine improvements in quality of life with the exception of changes to quality of life associated with fear of severe hypoglycaemia. In submissions, stakeholders emphasised the quality of life benefits of insulin pumps including greater flexibility and enhanced participation in sports, work and social activities.

### ***Use of insulin pumps in Australia***

- Uptake for the Insulin Pump Programme increased following the announcement that some key manufacturers would cover the co-payment gap for low-income

families. This has led to a waiting list. The Government announced additional Programme funding on 18 October 2013, to help clear the waiting list.

- Since the Programme commenced in 2008-09 to February 2014, a total of 466 pumps have been subsidised.
- NDSS data indicates that there are around 10,300 people aged between 0–18 years with type 1 diabetes in Australia, of which around 3,400 (33%) have been recorded as using insulin pump therapy for their form of treatment (AIHW 2012a, 2012b).

### ***Stakeholder input***

- Noting that the most important features of an insulin pump may be different for each patient, stakeholders indicated that features such as bolus calculators, dose increments suitable for children, and the ability to download data might have additional advantages for the paediatric population. Stakeholders stated that it is important to have a range of insulin pumps available to suit a range of patients.
- New features such as continuous glucose monitoring, including algorithms to detect hypoglycaemia and suspend insulin delivery, may provide additional safety and efficacy advantages. These technologies are not currently funded through any Australian Government programme and stakeholders advocated for a pathway for the evaluation and funding of new technologies.
- Other factors such as ease of use, waterproof casing, and calculators for carbohydrate content of common foods, also featured as important to improve the lifestyle benefits of insulin pumps.

### ***Reference Group input***

- Members noted a number of factors that may influence the choice between insulin pump brands, including: colour, size, waterproof casing, ease of use, low dose increments for basal and bolus insulin, continuous glucose monitoring technology, and software algorithms.
- Customer support services offered by the manufacturer were considered to be essential when choosing between insulin pump brands. When insulin pumps fail, some manufacturers will immediately send a replacement pump free of charge or arrange access to another insulin pump whilst waiting for the replacement to arrive.
- Marketing to people with diabetes, diabetes educators and health care professionals, has considerable influence on brand preference and in guiding patient choice.
- Patient factors were noted, such as adolescents being technologically savvy, but not as compliant as adults with following advice. Conversely, adult patients were

considered more compliant than adolescents with following advice, but found the insulin pump to be more technologically challenging.

### ***Issues identified***

- The current co-payment may be too expensive for many families receiving *Family Tax Benefit Part A* to afford and it may be less expensive to access an insulin pump through private health insurance.
- The Programme generally supplies insulin pumps that are available on the Protheses List. This List is primarily used for private health insurance purposes and does not consider the requirements of the Programme. Benefit amounts are not determined by cost-effectiveness and may not be appropriate for a Government-subsidised scheme.

## **5.2 Introduction**

In this section, the aim is to assess the costs of insulin pump therapy for pumps available through the Insulin Pump Programme, and investigate the difference, if any, in their effectiveness. This section also looks at the utilisation of insulin pumps supplied under the Programme and the demographics of the recipients. The QUMPRC was contracted to undertake a review of cost-effectiveness studies comparing insulin pump therapy to multiple daily injections.

Further background about the Insulin Pump Programme is detailed in [Part 2.7](#).

## **5.3 Effectiveness of insulin pumps available under the Insulin Pump Programme**

### **5.3.1 First literature review: RCTs of insulin pump comparisons**

#### ***What is the evidence for the impact of different types of continuous subcutaneous insulin infusion systems on outcomes?***

None of the RCTs directly compared different insulin pumps. The type of insulin pump has not been considered as a factor for sub-group or sensitivity analysis in systematic reviews. A range of insulin pumps have been used in RCTs. In the 21 RCTs performed between 2000 and 2011, the most frequently used insulin pumps were the MiniMed 508 and Disetronic H-TRON, neither of which are currently available under the Programme. The effectiveness of the newest insulin pumps that involve real-time continuous glucose monitoring in sensor-augmented insulin pumps has not been reviewed in this report as it is beyond the scope of the Review and is not currently funded under private hospital cover or the Insulin Pump Programme.

The difference in effectiveness between insulin pumps has not been assessed, as there is no literature analysing the differences between the insulin pumps available. There is no

evidence available to suggest that one brand of insulin pump is superior to another listed on the Prostheses List or the ARTG, and subsequently those pumps available through the Programme. No trial or observational evidence was brought forward through the public consultation process by stakeholders to demonstrate any difference in effectiveness between insulin pump brands.

It is traditionally the role of the patient or guardian and a diabetes health professional to make the decision on which brand or type of insulin pump to choose based on information provided by the manufacturer (Diabetes Queensland 2009). [Appendix A](#) compares the different features of insulin pumps available on the Prostheses List. The Insulet OmniPod is excluded as it is not on the Prostheses List and is not funded under the Programme. The appendix does not include information on efficacy of the pumps for improving glycaemic control or quality of life.

#### **5.4 Cost of insulin pump therapy**

In Australia, there are different pathways for obtaining funding for an insulin pump. Low-income families with children under 18 years of age are eligible for subsidy under the Insulin Pump Programme, while those with an appropriate level of health insurance can claim a benefit for the cost of an insulin pump. Further information about the costs of the Programme, including co-payment arrangements are detailed in [Part 2.7](#).

The benefit prices of the insulin pumps available under the Prostheses List range from \$4,000 to \$9,500. These benefit amounts are approximately market value, and have been negotiated between the manufacturer and the insurer, mediated by the Department.

Of the \$7.1 million in funding allocated between 2012-13 and 2015-16 for the Insulin Pump Programme, \$522,000 per year is allocated to insulin pump subsidies. On 18 October 2013, the Australian Government provided an additional \$870,400 in Programme funding for 2013-14, to clear the waiting list of up to 136 families waiting to have their application processed. This increased the funding for insulin pumps in 2013-14 to \$1,392,400. The remainder of the Programme funding, around \$4.1 million, is allocated to account for the expected cost of consumables through the NDSS.

##### **5.4.1 Costs of consumables supplied under the NDSS**

The Australian Government subsidises diabetes products, including insulin pump consumables, for people with diabetes through the NDSS. Consumables include reservoirs, cartridges, cannulas, and tubing lines. The NDSS is funded through an uncapped special appropriation and provides insulin pump consumables for all registrants, not just people who obtained an insulin pump through the Programme.

Diabetes Australia administers the NDSS on behalf of the Australian Government. The Department manages the product listings process, including the NDSS current product schedules, which are provided to Diabetes Australia on a monthly basis.

It should be noted that insulin pump therapy is more costly than multiple daily injections, including the ongoing costs of consumables (Cohen 2007). This is the case for both Government and patients. According to the AIHW *Insulin pump use in Australia* (2012b) report, on average, patient expenditure on consumables was \$29 per month in 2010–11 for those using insulin pump therapy, compared with \$6 per month for injection therapy.

With regard to the Insulin Pump Programme, the funding required for consumables increases each year as the Programme continues to provide funding for consumables for people who have received a pump under the Programme for the life of the insulin pump. In the first year of the Programme (2008-09), \$989,000 (GST exclusive) was allocated for consumables, while in year four (2011-12), \$1,569,000 (GST exclusive) was allocated for consumables.

Suppliers and manufacturers supply products to the NDSS at benchmarked prices. The prices are based on standard supply quantities. NDSS registrants pay a co-payment amount and the Government pays the remainder. [Table 2](#) details the NDSS benchmarked prices and co-payment amounts for insulin pump consumables. The Government also pays a Product Supply and Delivery fee for each dispensing of a consumable of \$5.10 (value for 2014). The co-payment and Product Supply and Delivery fee are indexed each year on 1 January.

Infusion sets and reservoirs/cartridges are replaced approximately every three days and come in packs of 10, i.e. around a 30 day supply. On average, consumers use 12.17 packs per annum of infusion sets and reservoirs/cartridges (NDSS data).

[Table 3](#) examines the estimated costs of insulin pump consumables to consumers and Government, annually, over a four-year period from 2012-13 to 2015-16. On average, consumers currently pay around \$316 per annum for insulin pump consumables and the Government pays \$2094 per annum. Insulin was not considered in this cost model.

**Table 2. NDSS benchmarked consumable costs and patient co-payments**

<b>Product</b>	<b>Benchmarked price</b>	<b>Patient co-payment (2014)</b>
Infusion Sets (10 cannula + 10 tubing lines)	\$145.83	\$15.60
Reservoirs/cartridges (10)	\$42.00	\$10.40

**Table 3. Costs to consumers and Government for insulin pump consumables through the NDSS for 2012-16**

**a. Annual costs to consumers (forecast to June 2016).**

Product	2012-13	2013-14	2014-15*	2015-16*	Total
Infusion Set	\$186.20	\$189.85	\$189.85	\$189.85	\$755.75
Reservoir/ cartridges	\$124.13	\$126.57	\$126.57	\$126.57	\$503.84
<b>Total</b>	<b>\$310.33</b>	<b>\$316.42</b>	<b>\$316.42</b>	<b>\$316.42</b>	<b>\$1,259.59</b>

**b. Annual costs to Government per patient (forecast to June 2016).**

Product	2012-13	2013-14	2014-15*	2015-16*	Total
Infusion Set	\$1,649.64	\$1,647.09	\$1,647.09	\$1,647.609	\$6,590.91
Reservoir/ cartridges	\$448.10	\$446.76	\$446.76	\$446.76	\$1,788.38
<b>Total</b>	<b>\$2,097.74</b>	<b>\$2,093.85</b>	<b>\$2,093.85</b>	<b>\$2,093.85</b>	<b>\$8,379.29</b>

*\* NDSS registrant co-payments and Product Supply and Delivery fees are indexed annually on 1 January. Indexation beyond 2014 has not been considered as the expected rates of indexation are not known.*

**5.4.2 Expected associated costs with the Insulin Pump Programme**

Cost of consumables over four years per patient	\$8,379.29
Median insulin pump subsidy per patient	\$6,400.00
Cost of consumables and median subsidy over 4 years per patient	\$14,779.29
Cost of consumables and median subsidy per patient per year	\$3,694.82

The estimated cost to Government associated with insulin pump use for each patient on the Insulin Pump Programme is \$14,779 over four years, or \$3,695 per annum. This estimate is based on the following assumptions:

- The average warranty period of four years was used as the lifespan of the pump.
- The price listed as a minimum benefit on the Protheses List, is approximately the commercial cost of the insulin pump as the actual commercial price could not be determined.
- The price for consumables between insulin pump brands is the same, as it could not be determined from the NDSS data.
- The cost of insulin pump consumables is \$2,093.85 annually and \$8,379.29 across four years, according to NDSS data (Table 3).
- The median subsidy income of \$42,000 per annum was used rather than the average, due to the skewed distribution. This is based on subsidy cohort incomes

ranging from \$0 to \$120,000 using the subsidy data to date (supplied by JDRC). The median subsidy amount is \$6,400 as most families receiving a benefit were under the low-income threshold of \$69,496 (2011-12) and eligible for the full, capped subsidy amount.

After the initial four years, for each additional year of pump life after expiration of the warranty, the cost to Government would be \$2,093.85 (the cost of consumables).

### **5.4.3 Additional health system costs**

The potential costs of the Programme are not limited to the insulin pump and the consumables. There may also be additional health system costs associated with the following:

- pump commencement education;
- diabetes educator;
- dietician;
- hospitalisation to install the pump (2-3 nights) or out-patient services;
- post-discharge follow-up;
- additional yearly follow-up;
- hospitalisation for complications arising from the pump;
- hypoglycaemic events (although many studies show a reduction in the number of severe hypoglycaemic episodes);
- DKA (although Johnson 2013 showed a reduction in DKA);
- cannula site infection;
- group meetings/support; and
- additional assistance with weight management (Diabetes Control and Complications Trial Group 1995).

However, there may also be a reduction in costs associated with fewer severe hypoglycaemic episodes, and reduction in the incidence of the following complications:

- diabetic retinopathy;
- end-stage renal disease;
- nephropathy death;
- cardiovascular complications;
- peripheral vascular death;
- peripheral neuropathy; and
- amputation (St Charles 2009).

## **5.5 Literature review: cost-effectiveness studies of insulin pumps**

The review assessed cost-effectiveness studies published between 2007 and October 2014 comparing insulin pump therapy to multiple insulin injections in patients with type 1 diabetes.

Four cost-effectiveness studies met the inclusion criteria: one undertaken in Australia (Cohen 2007), one in the United Kingdom (UK) (Cummins 2010), one in Canada (Charles 2009) and one in the United States (US) (St Charles 2009). Reported incremental cost-effectiveness ratios (ICERs) and selected sensitivity analyses results were converted to \$AUD prices for the year 2013 to facilitate comparison across studies.

All studies used the computer-simulation CORE model, which has been developed to estimate the long term clinical and economic consequences of interventions for type 1 and type 2 diabetes (Palmer 2004). The CORE model may overestimate the incidence of macrovascular complications in people with type 1 diabetes (Cummins 2010). In all studies, the perspective was from a public or private payer, and costs were taken from national sources. In the base cases, the time horizon was 50 or 60 years and the discount rate varied between 3% and 5% per annum applied to both costs and clinical outcomes.

The ICER per quality-adjusted life year (QALY) adjusted for purchasing power parity and converted to AUD\$ 2013 prices ranged between AUD\$28,874 in the US study and AUD\$96,220 in the UK study assuming a reduction in HbA<sub>1c</sub> level of 0.9% in one study and 1.2% in three studies. As all studies used the CORE model, with similar perspectives and time horizons, differences in results appeared to rise from differences in input variables for the benefits of insulin pump therapy, which included reductions in HbA<sub>1c</sub> level and severe hypoglycaemia episodes, and costs of diabetes complications.

Reductions in HbA<sub>1c</sub> level included in the base cases of all cost-effectiveness studies were higher than the reductions that were reported in the systematic review of RCTs (0.10–0.30%) and statistically significant results from many of the observational studies. Sensitivity analyses undertaken in the cost-effectiveness assessments demonstrated that the ICER was most sensitive to varying reductions in HbA<sub>1c</sub> levels with insulin pump therapy compared with multiple daily injections. Large increases in the ICER were observed with lower reductions in HbA<sub>1c</sub>. In the UK study, decreasing the reduction in HbA<sub>1c</sub> level from 0.9% in the base case to 0.6% increased the ICER by 43%. In the three other studies, decreasing the reduction in HbA<sub>1c</sub> level from 1.2% in the base case to 0.51% increased the ICER by 68%, 113% and 132% in the Australian, Canadian and US studies, respectively. Assuming reductions in HbA<sub>1c</sub> levels of 0.51% to 0.675% with insulin pump therapy compared to multiple insulin injections, the ICER per QALY converted to AUD\$ 2013 prices ranged from AUD\$63,274 in the US study to AUD\$292,952 in the UK study.

Studies used different assumptions (0% or 50%) for reductions in severe hypoglycaemic events avoided with insulin pump therapy compared to multiple insulin injections. All undertook sensitivity analyses varying hypoglycaemic events avoided up to 75%. ICERs were sensitive to changes in reductions in severe hypoglycaemic rates

only when the cost of severe hypoglycaemia was valued in the high range (2007 USD\$1,234).

With the exception of the UK study, all studies appear to underestimate the ICER by assuming a pump life span longer than the warranty period of 4 years for most insulin pumps currently marketed in Australia. Pump life span used in the studies was 7 years in the US study, and 8 years in the Australian and Canadian studies. In the US study, reducing the pump life from 7 years in the base case to 4 years in the sensitivity analysis increased the ICER by 54%.

With the exception of changes to quality of life associated with fear of severe hypoglycaemia, no study examined improvements in quality of life associated with insulin pump therapy. Stakeholders emphasised quality of life improvements as a key benefit of insulin pump therapy. The literature review of RCTs identified that reported quality of life was generally better with insulin pump therapy than multiple insulin injections in adults, adolescents and children.

In summary, the cost-effectiveness studies may have overestimated the cost-effectiveness of insulin pump therapy compared to multiple insulin injections by assuming larger decreases in HbA<sub>1c</sub> than the results observed in RCTs and many of the observational studies, and longer pump life spans than the standard warranty period for insulin pumps. However, improvements in quality of life associated with insulin pump therapy were not assessed in the models with the exception of fear of severe hypoglycaemia. The main limitation of all the cost-effectiveness studies related to the assumption that improvements in HbA<sub>1c</sub> observed in short term trials will generate long term morbidity benefits resulting in a decrease in diabetes complications. There are no long term trials of insulin pump therapy to support this assumption.

## **5.6 Insulin pump use under the Programme**

The following figures are derived from the data collected and supplied by JDRF on the Insulin Pump Programme. The data collected includes:

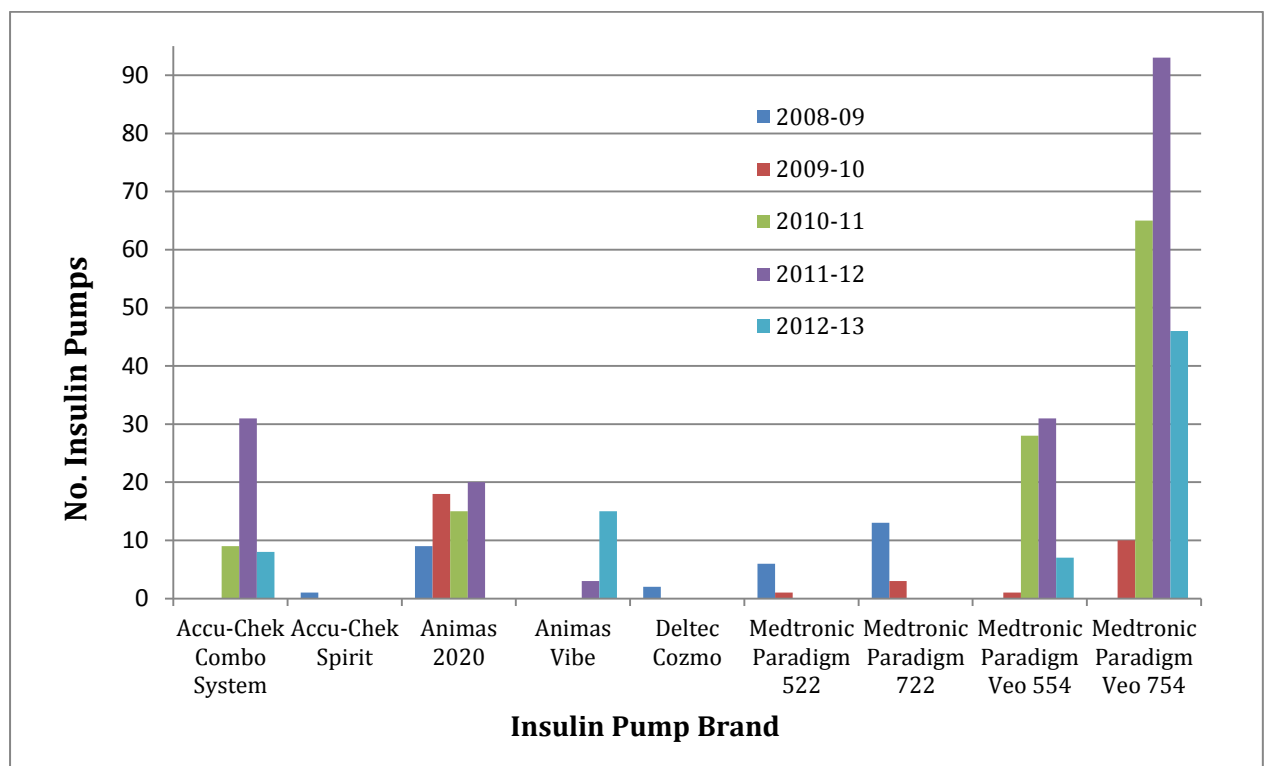
- age/sex of the recipient;
- date of receipt;
- pump brand;
- household income;
- co-payment amount; and
- co-payment assistance indicator.

Up to 31 December 2012, 439 insulin pumps had been provided to eligible patients under the Programme (JDRF 2013). [Figure 2](#) shows the number of insulin pumps provided by brand each year under the Programme. The Medtronic Paradigm Veo 754 is the most commonly supplied pump at 47%.

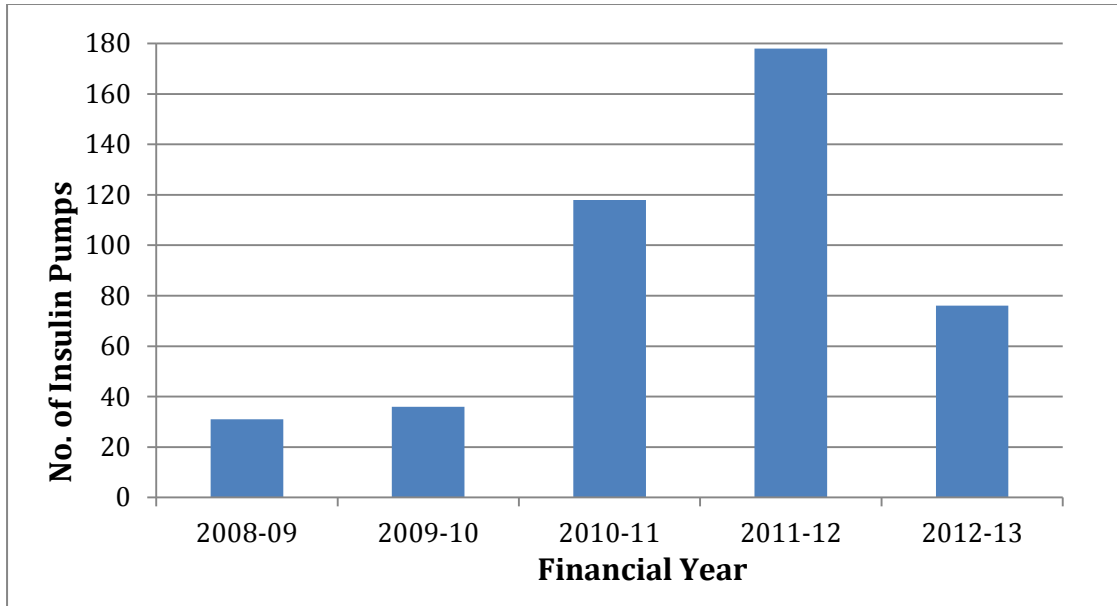
[Figure 3](#) shows the total number of pumps supplied each year under the Programme. The uptake of the Programme increased significantly due to an agreement in

October 2011 between the manufacturers and JDRF to pay the co-payment amount for families in the lowest income threshold of *Family Tax Benefit Part A*. This resulted in the lowest income families receiving a pump at no cost. Subsequently, in the 2012-13 financial year, Programme funding was exhausted by September 2012, and no more pumps were provided under the Programme beyond 31 December 2012. This explains the drop in the number of pumps supplied in 2012-13 seen in [Figure 3](#).

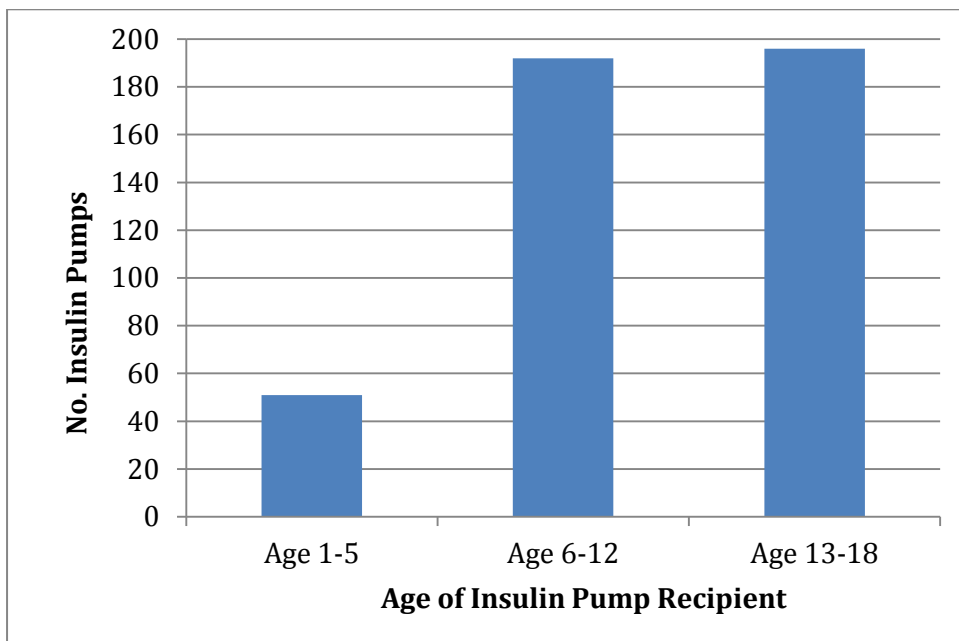
[Figure 4](#) shows the age distribution of insulin pump recipients under the Programme. Further information on the breakdown of insulin pump brand utilisation is detailed in [Appendix C](#).



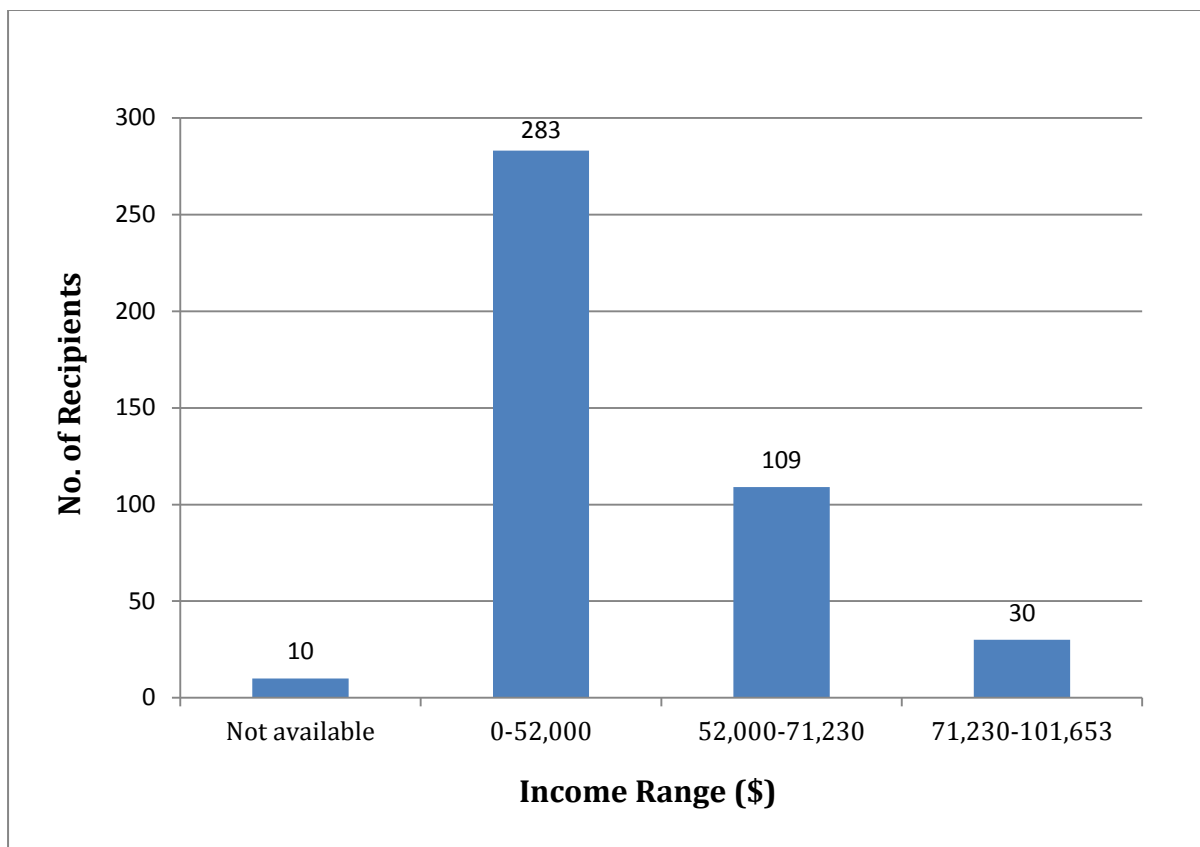
**Figure 2. Number of insulin pumps administered under the Programme by brand and financial year.**



**Figure 3. Total number of insulin pumps administered under the Programme by financial year.**



**Figure 4. Number of insulin pumps administered under the Programme by age group.**



**Figure 5. Programme recipient income ranges for 2008-09 to 2012-13.**

## **5.7 Issues identified**

### **5.7.1 Patient affordability**

Following the Health Technology Assessment Review finalised in February 2010 by the Medical Benefits Division, Department of Health, the minimum benefit amounts for insulin pumps on the Prostheses List increased from 1 August 2012. The Programme's capped subsidy is now less than 80% of the most expensive and most used pump available under the Programme, which has a minimum benefit cost of \$9,500. For this pump, the patient co-payment ranges from \$3,100 to \$8,550, dependent on family income. Families on the lowest eligible incomes of under \$71,230 (2013-14) per annum are unlikely to be able to afford the co-payment gap, which has increased from \$1,600 to \$3,100 for the most used pump, without further subsidy or the assistance of manufacturers.

In October 2011, some manufacturers agreed to cover the co-payment gap for the lowest income families, which increased use of the Programme. Most manufacturers have not confirmed their position to continue co-payment support following the increases to the minimum benefit prices on the Prostheses List. The current availability of assistance with the cost of the co-payment makes it difficult to determine whether the subsidy available is the most effective amount.

For eligible families on incomes between \$71,230 and \$101,653 (2013-14) per annum, it is likely to be less expensive to have private hospital insurance than to access an insulin pump under the Programme, particularly for the first pump. The cost of private health insurance varies between insurers, and states and territories in Australia. In general, a single parent with children up to 18 years of age can get top hospital cover for around \$1300–\$2100 per annum inclusive of the 30% Government rebate (Private Health Insurance Ombudsman, 2014).<sup>3</sup> Some insurers will allow a single child to be insured, which may further reduce costs. There is usually a 12-month waiting period for the first insulin pump. For subsequent pumps, where the pump is not fitted in a hospital or as part of hospital substitute treatment, insurers may require patients to maintain their insurance at a certain level in the intervening years.

The median family income data shown in Figure 5 indicates that families on incomes ranging from \$71,230–\$101,653(2013-14) per annum rarely access the Programme and make up less than 7% of Programme recipients (JDRF data). In addition, the AIHW's insulin pump user survey identified that for 12-17 year olds the highest proportion of insulin pump users were those in the highest socioeconomic group (46%) followed by those in the lowest socioeconomic group (39%), while for those over 17 years, the proportion of insulin pump use increased with socioeconomic status. This difference was attributed to the possible effects of subsidy and pump loan schemes (AIHW 2012b).

The co-payment gap was designed to equal the cost of private health insurance for a period of 12 months, the waiting period before a person is eligible for a rebate for an insulin pump under private health insurance. The patient co-payment for the most used pump under the Programme is now significantly more than the cost of private health insurance, even for families on the lowest eligible incomes. However, for subsequent insulin pumps, the Programme may be a less expensive option than private health insurance, depending on family income and insurance requirements regarding the level of cover and maintenance of cover in the intervening years.

### **5.7.2 Dependency on the Prostheses List**

The Programme generally supplies insulin pumps that are available on the Prostheses List. The benefit amounts on this List are negotiated between private health insurers and pump manufacturers, mediated by the Department. Although PLAC has an increased focus is on assessing new listings for devices based on comparative and cost-effectiveness, for existing products there has previously been limited information provided by manufacturers to support cost-effectiveness for insulin pump products on the Prostheses List. Maintaining the link between the Programme and the Prostheses List may not be sustainable or appropriate, although there will remain a need for evidence to be provided to inform funding decisions in relation to pumps available under the Programme.

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<sup>3</sup> Estimates assume a maximum excess of \$500, and no per day hospital co-payment.

Insulin pumps not on the Prostheses list can be recommended and in such cases the applicable cost is determined by JDRF and the Department of Health. Several factors are considered including the insulin pump manufacturer's recommended retail price, the prescribed minimum benefit payable for comparable insulin pumps listed on the Prostheses List and other information determined to be relevant at the time. Insulin pump consumables are subsidised for all patients with type 1 diabetes through the NDSS, irrespective of whether the insulin pump is on the Prostheses List or how the patient acquired their pump.

## Part 6 – ToR 10

### Programme eligibility criteria

Consider the clinical criteria and eligibility under the Insulin Pump Programme, to ensure those who would most benefit from insulin pump therapy receive support to assist in their care.

#### 6.1 Key findings for ToR 10

##### *Literature review: RCTs and observational studies*

- The trial and observational study evidence does not enable a particular sub-group in the type 1 diabetes population that receives greater benefit from insulin pump therapy to be clearly defined for the purposes of a third party operating a subsidy programme.
- Systematic reviews of RCTs comparing insulin pump therapy and multiple daily injections have not undertaken sub-group analyses of children on characteristics other than age.
- Two small observational studies suggest that insulin pump therapy may be more beneficial in children under 6 years old, or when initiated in children under 6 years old. There is also some evidence from observational studies that patients with higher initial HbA<sub>1c</sub> may achieve greater reductions in HbA<sub>1c</sub> with insulin pump therapy.

##### *Literature review: Australian and international clinical guidelines*

- Five guidelines or position statements by professional organisations that made recommendations on the use of insulin pump therapy were identified (published between 2009 and July 2012). A New Zealand position statement published in 2008 was also included in this Report. Information on eligibility criteria for Government subsidy programmes was included for Canada, New Zealand, the UK and USA.
- With regard to children and adolescents, the Programme's eligibility criteria are similar to the practice points for initiation of insulin pump therapy in the Australian clinical guidelines for type 1 diabetes (Craig 2011). Both include technological and cognitive capacity to manage use of the pump, and high levels of patient/carer motivation to intensively manage diabetes.
- Most guidelines identified in the review state that the decision to initiate insulin pump therapy is ultimately at the discretion of a healthcare professional in consultation with the patient or carer.

- Guidelines identified often recommend insulin pump therapy for: children under 12 years where multiple daily injections are impractical; women who are pregnant or trying to conceive; and anyone with poor glycaemic control as indicated by frequent severe hypoglycaemia, hypoglycaemia unawareness, dawn phenomenon, or development of microvascular complications.
- It is also generally recommended that patients/carers are supported by a team of health professionals, and have the technical and physical skills, and motivation, to use insulin pump therapy effectively.

### ***Stakeholder input***

- Advice from APEG indicates that the current Programme eligibility criteria are appropriate for children. APEG considered that there is a risk of inequitable distribution of insulin pump use in the current Programme from the creation of eligibility criteria without strong clinical evidence. There is insufficient evidence on which to base any additional criteria. However, APEG advised that, ideally, there would not be age limits for patients initiating the Programme.
- Stakeholders were unanimously supportive of the benefits of insulin pump therapy and recommended expanding the Programme so that patients of any age were eligible to commence pump therapy.

### ***Reference Group input***

- Members considered that prioritisation of patients is a difficult issue. Patients with heightened risk of hypoglycaemia, those with a significant impairment to quality of life with multiple daily injections, young children who are not yet able perform multiple daily injections, and patients who have tried other methods but are still shown to have poor glycaemic control, may be groups to target for insulin pump therapy.

### ***Issues identified***

- Reference Group members considered that continuity of care for patients who are turning 18 years old and are no longer eligible under the Programme was an important issue. These people are unlikely to be able to afford a new insulin pump outright or to be covered by private health insurance.
- With the Programme in its fifth year of operation, many recipients may now be re-applying for another subsidy. This presents the issue of whom to give priority to in the event of a waiting list developing: those who have received a pump previously, or those who have never received a subsidy through the Programme or have never used an insulin pump before.
- The Diabetes Review Inter-Departmental Working Group suggested that Programme data be collected on Aboriginal and Torres Strait Islander status and

rural and remote identifiers, to ensure that these people are accessing the Programme.

- A number of Australian and international guidelines recommend access to insulin pumps for women with type 1 diabetes who are pregnant or trying to conceive. Stakeholders also highlighted the importance of access for this group. However, there is insufficient evidence available from randomised trials to determine the superior method of insulin delivery for pregnant women.

## **6.2 Introduction**

This section of the report aims to consider clinical criteria and eligibility under the Programme to ensure these remain clinically appropriate and supported by current evidence. The aim is to provide the best possible access to insulin pump therapy under the Programme, within the funding limits, by identifying those who would benefit most as supported by clinical evidence.

The literature reviews of RCTs and observational studies undertaken by the QUMPRC aimed to identify sub-groups who may have greater benefit from insulin pump therapy. The Department also sought advice on appropriate clinical eligibility criteria for the Programme through stakeholder input, and expert advice from the Reference Group and APEG.

A number of national and international guidelines have been published on the management of type 1 diabetes and the use of insulin pumps in both paediatric and adult populations. This section summarises and compares a number of Australian and key international guidelines concerning the treatment of type 1 diabetes, with particular focus on recommendations on initiation of insulin pump therapy versus multiple daily injections. This section also compares access to, and eligibility criteria for, insulin pump subsidy programmes in other countries.

### **6.2.1 Current clinical eligibility criteria for the Insulin Pump Programme**

To be eligible for a subsidy under the Insulin Pump Programme, the patient must be under the age of 18 at the date of application, and meet the following clinical eligibility criteria:

- the child has type 1 diabetes;
- the child will benefit from a transition to insulin pump therapy;
- the child/carer has demonstrated willingness to check blood glucose levels four or more times per day;
- the child/carer has demonstrated competence at injecting insulin using pens/syringes;
- the insulin pump initiation will be conducted by a multidisciplinary team; and

- the initiating team makes a commitment to a transition and a system to ensure follow-up and ongoing support.

### **6.3 Literature review: RCTs and observational studies**

The literature reviews of RCTs and observational studies aimed to determine if there are any sub-groups of patients who may benefit more from insulin pump therapy and should be prioritised to receive a pump under the Programme (Refer to [Part 4](#) for additional detail). There were no sub-group or sensitivity analyses in the reviews of RCTs or observational studies that considered children's characteristics other than age. Two small observational studies suggest that insulin pump therapy may be more beneficial in children under 6 years old (Hughes 2012), or when initiated in children under 6 years old (Levy-Shagra 2013).

There is little evidence in the literature reviews to suggest there is a sub-group in the type 1 diabetes population that would receive significantly greater benefits from insulin pump therapy than other groups. Observational studies, which generally showed greater benefits in HbA<sub>1c</sub> reduction in patients using insulin pump therapy than the results from RCTs, often used clinical criteria when selecting patients for insulin pump therapy, including: poor glycaemic control, frequent hypoglycaemia, dawn phenomenon, need for lifestyle flexibility and needle phobia.

### **6.4 Literature review: Australian and international clinical guidelines**

The literature review for ToR 10 identified and compared recommendations for the use of insulin pump therapy from health professional and health technology assessment organisations in Australia and in countries with similar healthcare systems. Five guidelines on the use of insulin pump therapy were identified in Australia, Scotland, England, and the United States. New Zealand also has a position statement on insulin pump therapy. A summary of the guidelines is at [Appendix D](#). In addition to the Australian guidelines identified in the literature review, other notable guidelines, including those listed on the NHMRC guideline portal for the diagnosis and management of type 1 diabetes, were also considered. Information on the guidelines currently hosted by the NHMRC guideline portal is at [Appendix E](#).

The guidelines were in agreement that insulin pump therapy could be considered for improving glycaemic control, based on the results of meta-analyses and RCTs. Evidence for improving hypoglycaemia was based on the results of observational studies, primarily before-and-after studies. Evidence of this level is generally considered of low or very low quality as it has a high risk of bias resulting in the measured difference being larger due to other factors than the change to pump delivery. The guidelines provide criteria for selecting patients who may be likely to benefit from insulin pump therapy based on guideline committee members' consensus opinion.

#### 6.4.1 Australian clinical guidelines summary

The decision to commence insulin pump therapy is made in consultation with a multidisciplinary team of health professionals. People with type 1 diabetes, or their families, who wish to benefit from lifestyle improvements, may also request an insulin pump. Once accepted, patients must be fitted with their pump by a health professional and must undertake training to use the insulin pump properly. Patients must keep regular contact with a health professional to ensure the pump is being used appropriately (AIHW 2012b).

The *National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults* (Craig 2011), endorsed by APEG and the Australian Diabetes Society (ADS), addresses clinical care across the lifespan for people with type 1 diabetes. Developed by medical experts and researchers for practising health professionals, the guideline was endorsed by the NHMRC in 2011.

The guideline recommends that insulin pump therapy be “...considered for use in individuals in whom the expected magnitude of benefit is clinically significant in terms of reducing HbA<sub>1c</sub>, reducing hypoglycaemia or improving QoL [quality of life] (Grade C)”. Grade C indicates that the evidence provides some support for the recommendation(s), but care should be taken in their application (Craig 2011).

This guideline recommends that “individuals who may be likely to benefit from... insulin pump therapy, as part of intensive diabetes management are:

- some children and adolescents, including infants and young children, and pregnant women (ideally preconception);
- individuals with microvascular complications of diabetes;
- individuals with reduced hypoglycaemia awareness;
- individuals (or their supervising adults) with desirable motivational factors, for example, those seeking to improve blood glucose and having realistic expectations; and
- individuals exhibiting desirable CSII [insulin pump therapy] treatment-related behavioural factors, including those who:
  - are able to perform carbohydrate counting;
  - are currently undertaking four or more blood glucose tests per day;
  - have reliable adult supervision (in paediatrics), and a history of good self-management skills (in adults);
  - are able to master the technical skills of CSII [insulin pump therapy]; and
  - are reliable in follow-up health care” (Craig 2011).

A group of diabetes health professionals and researchers in Victoria has also developed a guideline centralised around insulin pump therapy rather than type 1 diabetes management as a whole (Victorian CSII Working Party 2009). Generally, glycaemic control, complication status, quality of management, and other co-morbidities and lifestyle factors are considered before commencement of insulin pump therapy. Patients

are expected to undergo a clinical assessment and diabetes education assessment before commencing insulin pump therapy. The guideline generally recommends insulin pump therapy use for:

- those confirmed as having type 1 diabetes or diabetes in pregnancy;
- those whose lifestyle, physical abilities, attitudes, psychiatric status, and cognitive abilities (e.g. basic numeracy and ability to undertake carbohydrate counting) allow for insulin pump therapy;
- those who demonstrate consistent home blood glucose monitoring and recording; and
- whose financial status can cover the co-payments for the insulin pump and consumables (Victorian CSII Working Party 2009).

There are a number of other guidelines for the diagnosis and management of type 1 diabetes on the [NHMRC Guidelines Portal](#). To be listed on the Portal, guidelines are assessed against specific criteria (NHMRC 2011).

#### **6.4.2 NPS MedicineWise**

The NPS MedicineWise does not provide any information on insulin pump therapy for health professionals, but does have a consumer information page: [Insulin pumps for type 1 diabetes](#) (2013).

#### **6.4.3 International clinical guidelines**

##### **6.4.3.1 England**

A NICE technology appraisal guidance (2009) states that “continuous subcutaneous insulin infusion or ‘insulin pump’ therapy is recommended as a possible treatment for adults and children 12 years and over with type 1 diabetes mellitus, if:

- attempts to reach target haemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels with multiple insulin injections result in the person having ‘disabling hypoglycaemia’; or
- HbA<sub>1c</sub> levels have remained high (8.5% or above) with multiple insulin injections (including using long-acting insulin analogues if appropriate) despite the person and/or their carer carefully trying to manage their diabetes”.

Insulin pump therapy was also recommended as a possible treatment for children under 12 years with type 1 diabetes “...if treatment with multiple daily injections is not practical or is not considered appropriate”. The guidance recommends that children who use insulin pump therapy should undergo a trial of multiple daily injections between the age of 12 and 18 years (NICE 2009).

##### **6.4.3.2 New Zealand**

The *New Zealand Society for the Study of Diabetes (NZSSD) Position Statement on Insulin Pump Therapy* (2008), is based on the results of a systematic review and economic evaluation of insulin pump therapy in the New Zealand setting, which concluded that

the improvements in glycaemic control with insulin pump therapy are of “...a small magnitude and of borderline statistical significance” (Campbell 2008).

It is recommended that insulin pump therapy should be available to people with type 1 diabetes “...who, despite optimal high level care and MDI [multiple daily injections] using a long-acting analogue, meet the following criteria:

- Recurrent severe unexplained hypoglycaemic episodes (2 or more in a 12 month period);
- Women who have suboptimal glycaemic control and wanting to conceive;
- Children (<12 years) in whom MDI is judged to be impractical;
- Poor glycaemic control (HbA<sub>1c</sub> >8.5%) demonstrated by CGM [continuous glucose monitoring] due to a prominent dawn phenomenon; and
- Other selected situations: gastroparesis, eating disorders” (NZSSD 2008).

#### **6.4.3.3 Scotland**

The Scottish Intercollegiate Guidelines Network (SIGN) state that “CSII [insulin pump] therapy is associated with modest improvements in glycaemic control and should be considered for patients unable to achieve their glycaemic targets (Grade A)” and “CSII [insulin pump] therapy should be considered in patients who experience recurring episodes of severe hypoglycaemia (Grade B)” (SIGN 2010).

#### **6.4.3.4 United States**

Two American professional organisations provide recommendations for insulin pump management. The *Statement by the American Association of Clinical Endocrinologists consensus panel on insulin pump management* provides expert advice on patient selection and the education and training of health professionals caring for patients with insulin pumps (Grunberger 2010). This statement provides the US Centre for Medicare and Medicaid Services Insulin Pump Patient Eligibility Criteria, which are:

“(a) Patient has completed a comprehensive diabetes education program and has been receiving multiple daily injection insulin with frequent self-adjustments for at least 6 months before pump initiation. Patient has documented self-monitoring of blood glucose frequency an average of  $\geq 4$  times per day during the previous 2 months. Patient must also meet  $\geq 1$  of the following criteria:

- HbA<sub>1c</sub> > 7.0%
- history of recurrent hypoglycaemia
- wide fluctuations in blood glucose before mealtime
- dawn phenomenon with fasting plasma glucose concentration frequently >200 mg/dL or history of severe glycaemic excursions

(b) Patient on pump therapy before enrolment and has documented self-monitored blood glucose an average of  $\geq 4$  times per day during the month before enrolment” (Grunberger 2010).

The *Insulin Pump Therapy: Guidelines for Successful Outcomes* provides consensus-based advice on appropriate candidates for pump therapy and guidance on associated self-management education (American Association of Diabetes Educators (AADE) 2008). This guideline states that patients should be considered for insulin pump therapy when they are not meeting treatment goals with multiple daily injections, including:

- HbA<sub>1c</sub> >7.0-7.5% with frequent severe hypoglycaemia (<55 mg/dL);
- hypoglycaemic events requiring third-party assistance or interfering with work, school or family obligations;
- frequent, unpredictable fluctuations in blood glucose levels; or
- patient perception that diabetes management is impeding the pursuit of personal or professional goals (AADE 2008).

## **6.5 Government subsidised access to insulin pump therapy in other countries**

### **6.5.1 Canada**

The Canadian Government subsidises insulin pumps in several provinces. Ontario provides a full subsidy; Saskatchewan and Newfoundland subsidise insulin pumps for people with type 1 diabetes up to 25 years of age; and British Columbia, New Brunswick, and Newfoundland subsidise up to 18 years of age.

The established eligibility criteria is that the person must have demonstrated to a diabetes assessment team an ongoing commitment to blood glucose monitoring, the safe and appropriate use of the insulin pump, participation in an insulin pump education programme and regular diabetes clinic attendance, as well as meeting certain clinical requirements.

### **6.5.2 New Zealand**

Since September 2012, the New Zealand Pharmaceutical Management Agency (PHARMAC) has been subsidising insulin pumps and consumables for people with type 1 diabetes. The expected cost of this funding is \$13.2 million over five years (2012-13 to 2016-17) to assist around 1,000 patients (PHARMAC 2012). The subsidy amount is equivalent to the listed price (ex-manufacturer, GST exclusive) of the insulin pump on Section B of the *Pharmaceutical Schedule*. The listed pumps (as at 1 October 2014) include the Animas Vibe™ listed at NZ\$4,500, and the Medtronic MiniMed Paradigm™ 522 and 722, both listed at NZ\$4,400 (PHARMAC 2014).

An Insulin Pump Panel of six clinicians assesses patient applications for subsidy. To qualify for a PHARMAC subsidised pump, a patient must either:

- Have permanent neonatal diabetes, and a trial of multiple daily injections is inappropriate.
- Have type 1 diabetes, undergone a pancreatectomy or have cystic fibrosis-related insulin, and despite adhering to an intensive multiple daily injection regimen using analogue insulins for at least six months still has either:

- Hypoglycaemia: four severe unexplained hypoglycaemic episodes (requiring assistance of another person) over a six month period due to nocturnal hypoglycaemia or hypoglycaemia unawareness.
- HbA<sub>1c</sub>: unpredictable and significant variability in blood glucose including significant hypoglycaemia affecting the ability to reduce HbA<sub>1c</sub>, and in the opinion of the clinician HbA<sub>1c</sub> could be reduced by 10 mmol/mol (1%) by initiating insulin pump therapy (PHARMAC 2012).

There are also criteria for continuing on therapy (i.e. receiving a second insulin pump) and continuing access to consumables, including:

- Hypoglycaemia: Patient has achieved a 50% reduction in hypoglycaemic events and HbA<sub>1c</sub> has not increased.
- HbA<sub>1c</sub>: Patient is maintaining a reduction in HbA<sub>1c</sub> of 10 mmol/mol (1%), and the number of severe unexplained hypoglycaemic episodes has not increased (PHARMAC 2012).

The cost-effectiveness of insulin pumps for these sub-groups was estimated at NZD\$40,000-\$90,000 per QALY.

### **6.5.3 United Kingdom**

The National Health Service provides subsidies for insulin pumps. In England and Wales it is mandatory to fund technologies approved by NICE. If a specialist team recommends insulin pump therapy for people in line with the NICE technology appraisal guidance on insulin pump therapy (2009) (see [6.4.3.1](#)) the Primary Care Trusts will fund this and there are no waiting lists.

### **6.5.4 United States**

The U.S. Centers for Medicare and Medicaid Services provides assistance for low-income families to get healthcare. Medicare may pay part of the cost of an insulin pump and insulin for some patients. With Original Medicare, Medicare pays 80% of the cost of the insulin pump and patients pay 20% of the Medicare-approved cost after the yearly Part B (medical insurance) is deducted. Patients may be required to pay coinsurance or a co-payment for diabetes supplies (U.S. Department of Health and Human Services 2012). Insulin pump patient eligibility criteria are those determined by the American Association of Clinical Endocrinologists' consensus panel (Grunberger 2010) (see [6.4.3.4](#)).

## **6.6 Issues identified**

### **6.6.1 Age restriction and continuity of access into adulthood**

Currently, the Programme provides means-tested access to people with type 1 diabetes up to 18 years of age. There may be a difficult transition for adolescents with type 1 diabetes when they turn 18 years old and their dependency status for welfare entitlements may change, with a resulting potential increase in health care costs as they

transfer into the adult healthcare system. This is a common problem internationally, and an issue with the Australian Programme (International Diabetes Federation Europe 2011).

### **6.6.2 Waiting list and prioritising applications**

At present, JDRF supplies insulin pumps chronologically according to application date. Recently, there has been a waiting list for an insulin pump subsidy due to the high Programme uptake. On 18 October 2013, the Australian Government provided an additional \$870,400 in funding for 2013-14 to clear the waiting list.

The Programme is now in its fifth year of operation with most insulin pumps supplied under the Programme having a four-year warranty period. Some people who have received an insulin pump under the Programme will now be looking at re-applying for another insulin pump subsidy, if they are still eligible.

Under the Programme, applicants may reapply for a replacement insulin pump provided that the recipient is under 18 years of age at the date of application, the manufacturer's warranty on the recipient's current insulin pump has expired, and either:

- the current insulin pump has ceased to operate as designed; or
- a replacement insulin pump has been clinically recommended by the recipient's health professional.

This raises questions about the process of assessing applications and whether access should be granted in order of application date or prioritised based on whether the patient has previously received an insulin pump under the Programme.

### **6.6.3 Access for Aboriginal and Torres Strait Islander people**

While the Indigenous Chronic Disease Package funds some medical aids such as blood glucose monitoring equipment, it does not cover expenditure for insulin pumps. However, Indigenous and Torres Strait Islander status does not preclude access to the Programme. It is not possible under the current data collection for the Programme to assess whether this population is accessing the insulin pump subsidies.

The Diabetes Review Inter-Departmental Working Group raised the issue of ensuring that Aboriginal and Torres Strait Islander children and adolescents have equal access in practice to insulin pumps under the Programme. This Group suggested collecting Programme data on Aboriginal and Torres Strait Islander status and rural and remote identifiers for all people accessing the Programme in the future.

#### **6.6.4 Access for women who are pregnant or trying to conceive**

For women with type 1 diabetes, high HbA<sub>1c</sub> levels early in pregnancy are associated with an increased risk of congenital malformations, such as cardiac and neural tube defects, miscarriage and perinatal mortality. Pregnant women may also be predisposed to severe hypoglycaemia and DKA (Craig 2011). Reductions in the rate of adverse outcomes can be achieved by optimal care and tight glycaemic control before conception and throughout pregnancy (Pearson 2007; Bismuth 2012).

The NZSSD position statement (2008) and Australian guidelines (Victorian CSII Working Party 2009; Craig 2011) recommend insulin pump therapy for women with type 1 diabetes who are pregnant or trying to conceive, ideally initiated pre-conception. The NZSSD position statement indicates women trying to conceive with suboptimal glycaemic control. Stakeholders also highlighted pregnant women as a group that could be prioritised to receive access to insulin pumps under the Programme.

Two meta-analyses of RCT evidence comparing insulin pumps with multiple daily injections for pregnant women with diabetes, found no difference in HbA<sub>1c</sub>, hypoglycaemia, hyperglycaemia, macrosomia, preterm delivery, caesarean, perinatal mortality, foetal anomaly, or worsening of diabetes complications (Farrar 2007; Mukhopadhyay 2007). The literature review of observational studies, showed that the majority of studies did not show significant differences between insulin pump therapy and multiple daily injections in diabetes management, or maternal or newborn outcomes. However, both RCTs and observational studies were small and may lack statistical power to detect differences in outcomes between insulin pump and injection therapy.

To ensure Programme value for money, patients should use their pump for at least four years (warranty period). Some manufacturers have a loan system for people seeing out the waiting period for their private health insurance, or for use when a pump under warranty has broken down. There may be scope to adapt this arrangement to suit the period of preconception and pregnancy, for those planning a single pregnancy.

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## Appendices

### Appendix A – Information on insulin pumps available under the Prostheses List as at February 2014

Model Name/No.	DANA IIS Insulin Pump	DANA R Diabecare Insulin Pump	Accu-Chek: Combo System	Medtronic Minimed Paradigm Veo MMT-554	Medtronic Minimed Paradigm Veo MMT-754	Animas: Vibe & CGM System
<b>Pump Sponsor/Manufacturer</b>	Managing Diabetes Pty Ltd / SOOIL Development CO. Ltd	Managing Diabetes Pty Ltd / SOOIL Development CO. Ltd	Roche Diagnostics Australia Pty Ltd	Medtronic Australasia Pty Ltd	Medtronic Australasia Pty Ltd	Australasian Medical & Scientific Pty Ltd/ Animas
<b>Minimum Benefit on Prostheses List<sup>4</sup></b>	\$4,000	\$8,950	\$8,950	\$9,500	\$9,500	\$8,950
<b>Main Function</b>	Continuous insulin infusion pump with 300 unit reservoir.	Insulin infusion pump with an integrated blood glucose meter and remote control via Bluetooth communication. 300 unit reservoir.	Insulin infusion pump with remote control via the blood glucose meter. Meter includes integrated bolus advisor. 3.15 mL insulin unit reservoir and occlusion detection.	Insulin delivery, automatic adjusting, and with remote control. 180 unit reservoir.	Insulin delivery, automatic adjusting, and with remote control. 300 unit reservoir.	Insulin infusion pump (incl. sensor / transmitter).
<b>CGM capable/ready</b>	No	Yes	No	Yes	Yes	Yes
<b>Basal increments (u/hour)</b>	0.01 - 0.1	0.01 - 0.1	0.01 - 0.1	0.025 - 0.1	0.025 - 0.1	0.025
<b>Max # of basal rate profiles</b>	4	4	5	3	3	4

<sup>4</sup> The **minimum benefit** listed on the Prostheses List is the minimum amount payable by insurance companies for an insulin pump under a part C consultation. The amount is agreed between the manufacturers and insurers, mediated by the Department. It is not necessarily the commercial sale price.

<b>Model Name/No.</b>	<b>DANA IIS Insulin Pump</b>	<b>DANA R Diabecare Insulin Pump</b>	<b>Accu-Chek: Combo System</b>	<b>Medtronic Minimed Paradigm Veo MMT-554</b>	<b>Medtronic Minimed Paradigm Veo MMT-754</b>	<b>Animas: Vibe &amp; CGM System</b>
<b>Temporary basal rate adjustments</b>	0-200% for 1-12 hours	0-200% for 1-12 hours	0-250% in 10% increments, for 15 min - 12 hours in 15 min intervals (-500% via Configuration Software).	30 min – 24 hours	30 min – 24 hours	10% - 200% for 30 min – 24 hours
<b>Max # of basal rate programmes / 24 hours</b>	24	24	24	48	48	12
<b>Extended or multiwave bolus available (to assist with irregular eating patterns)</b>	Extended bolus (30 min - 8 hours)	Extended bolus (30 min - 8 hours)	Extended and multiwave bolus from 15 min - 12 hours (up to 50 hours via Configuration Software).	Extended (can be cancelled) and multiwave bolus.	Extended (can be cancelled) and multiwave bolus.	Combo bolus allows some insulin to be delivered immediately (normal bolus) and remainder over time (extended bolus).
<b>Bolus algorithm</b>	Variable bolus delivery speed (1 unit bolus duration: 12 - 56 seconds).  Bolus calculator using target blood glucose, correction factor and carbohydrate to insulin ratio. Also considers active insulin from calculations.	Variable bolus delivery speed (1 unit bolus duration: 12 - 56 seconds).  Bolus calculator using target blood glucose, correction factor and carbohydrate to insulin ratio. Also considers active insulin from calculations.	Fully customisable bolus calculator. Bolus Advice function - considers 'active insulin', blood sugar level, carb intake, and additional variables such as exercise, stress, illness, premenstrual.	Allows different bolus dose rates to be set over a 24 hour period.  Active Insulin Onboard - Informs user of active insulin remaining from previous bolus.  Bolus Wizard(R) - suggests bolus dose based on personal settings, food intake and current blood glucose value.	Allows different bolus dose rates to be set over a 24 hour period.  Active Insulin Onboard - Informs user of active insulin remaining from previous bolus.  Bolus Wizard(R) - suggests bolus dose based on personal settings, food intake and current blood glucose value.	Calculate a bolus amount to cover the carbs in food (ezCarb). Automatically calculate a correction dose of insulin based on the latest blood sugar reading (ezBG).  The "Insulin on Board"* feature tracks active insulin in the body to help prevent hypoglycaemia due to "stacking" (unnecessary

<b>Model Name/No.</b>	<b>DANA IIS Insulin Pump</b>	<b>DANA R Diabecare Insulin Pump</b>	<b>Accu-Chek: Combo System</b>	<b>Medtronic Minimed Paradigm Veo MMT-554</b>	<b>Medtronic Minimed Paradigm Veo MMT-754</b>	<b>Animas: Vibe &amp; CGM System</b>
						additional insulin).
<b>Additional features</b>	Not available	<p>Blood glucose measurement in remote controller.</p> <p>Bluetooth communication to Android mobile phone. Can utilise the mobile phone for all pump settings and to discreetly deliver boluses.</p>	<p>Blood glucose meter can be used to remotely control pump and has colour display, logbook, trend graphs, target report, and standard week and standard day reports.</p> <p>Date reminders (e.g. infusion set change) and alarm clock reminders (up to 8 per day).</p>	<p>Activity guard available to protect the pump from disconnecting.</p> <p>CGM using 6-day disposable sensors connected to transmitter. Transmitter provides readings to pump at 5-minute intervals.</p>	<p>Activity guard available to protect the pump from disconnecting.</p> <p>CGM using 6-day disposable sensors connected to transmitter. Transmitter provides readings to pump at 5-minute intervals.</p>	<p>High-contrast colour screen.</p> <p>Trends and rates.</p> <p>CGM with Animas® Vibe™ is only indicated for patients 18 years or older.</p>
<b>Safety - Maximum Qty delivered at a single fault condition</b>	Customisable for patient doses.	Customisable for patient doses.	<p>Maximum bolus – customisable to 25U (50U via Configuration Software).</p> <p>Maximum basal rate – customisable to 62.5U/h (250U via Configuration Software).</p> <p>Max qty delivered at a single fault ≤1.0 units.</p>	<p>Maximum Bolus – customisable to 75U.</p> <p>Maximum Basal Rate – customisable.</p> <p>Maximum Delivery Exceeded – to prevent multiple small boluses within one hour.</p>	<p>Maximum Bolus – customisable to 75U.</p> <p>Maximum Basal Rate – customisable.</p> <p>Maximum Delivery Exceeded – to prevent multiple small boluses within one hour.</p>	<p>Maximum prime dose is 20U. Total Daily dose is set by patient. A maximum 2 hour dose limit is set. Bolus &amp; basal limits are user selected.</p> <p>Response to single fault condition depends on circumstances.</p>
<b>Safety lock to prevent accidental insulin delivery</b>	Button-Lock mode to prevent unintended operation.	Button-Lock mode to prevent unintended operation.	Key lock function and automatic shutdown (customisable 1-24 hours, 1 hour steps).	Child block - disables buttons to prevent accidental delivery. Keypad lock – prevent accidental button	Child block - disables buttons to prevent accidental delivery. Keypad lock – prevent accidental button	Tamper resistant "Locked" feature.

Model Name/No.	DANA IIS Insulin Pump	DANA R Diabecare Insulin Pump	Accu-Chek: Combo System	Medtronic Minimed Paradigm Veo MMT-554	Medtronic Minimed Paradigm Veo MMT-754	Animas: Vibe & CGM System
				pressing.	pressing.	
<b>Alerts</b>	<p>Audible reminders of bolus insulin/carbohydrate ratio for certain periods - post meal.</p> <p>Low battery, low reservoir, occlusion.</p>	<p>Audible reminders of bolus insulin/carbohydrate ratio for certain periods - post meal.</p> <p>Low battery, low reservoir, occlusion.</p>	<p>Audible and vibration notifications of blood glucose test reminders*, infusion set change, errors and occlusion in infusion set.</p> <p>Low battery, battery empty, low reservoir, reservoir empty, automatic off, temporary basal rate over, bolus cancelled, mechanical error, electronic error, bluetooth fault, power interrupt, infusion set not primed, cartridge error, data interrupted, end of warranty.</p> <p>High/low blood glucose*.</p>	<p>High and Low Glucose, Predictive, rate of change, and trend arrows alerts*.</p> <p>Low Glucose Suspend alerts – will suspend delivery for a maximum of 2 hours in times of hypoglycaemia when user does not respond to alert*.</p> <p>Auto Off – alert and Suspend feature when no button has been pressed for a pre-determined duration of time.</p> <p>Low battery, low reservoir. Missed meal bolus reminder.</p> <p>Alerts with * available only with pump and glucose monitor turned on.</p>	<p>High and Low Glucose, Predictive, rate of change and trend arrows alerts*.</p> <p>Low Glucose Suspend alerts – will suspend delivery for a maximum of 2 hours in times of hypoglycaemia when user does not respond to alert*.</p> <p>Auto Off – alert and Suspend feature when no button has been pressed for a pre-determined duration of time.</p> <p>Low battery, low reservoir. Missed meal bolus reminder.</p> <p>Alerts with * available only with pump and glucose monitor turned on.</p>	<p>High/low blood glucose*.</p>

<b>Model Name/No.</b>	<b>DANA IIS Insulin Pump</b>	<b>DANA R Diabecare Insulin Pump</b>	<b>Accu-Chek: Combo System</b>	<b>Medtronic Minimed Paradigm Veo MMT-554</b>	<b>Medtronic Minimed Paradigm Veo MMT-754</b>	<b>Animas: Vibe &amp; CGM System</b>
<b>Turnaround time for back-up or loan pump and other customer service features</b>	<p>Loan pumps are available 24/7 in Sydney, Brisbane, Newcastle, Coffs Harbour and Victoria. Outside these centres it is likely to be a next business day courier.</p> <p>Free batteries for the life of the pump.</p>	<p>Loan pumps are available 24/7 in Sydney, Brisbane, Newcastle, Coffs Harbour and Victoria. Outside these centres it is likely to be a next business day courier.</p> <p>Pump comes with batteries incl. Free batteries with every box of reservoirs.</p>	<p>Replacement pump if standard pump is not functioning.</p> <p>Next working day delivery for metropolitan areas.</p> <p>2-3 day delivery for regional areas.</p>	<p>For loan pump, dispatch is within 24 hours of receiving written notification and delivery within a further 24-48 hours.</p> <p>For other situations (e.g. pump needed for travel) turn-around time is dependent on patient requirements.</p>	<p>For loan pump, dispatch is within 24 hours of receiving written notification and delivery within a further 24-48 hours.</p> <p>For other situations (e.g. pump needed for travel) turn-around time is dependent on patient requirements.</p>	<p>Faulty product in replaced within 2 business days.</p>
<b>Training support (user manual, online training)</b>	<p>User manual and online demonstration, pre-pump training and support.</p>	<p>User manual and online demonstration, pre-pump training and support.</p>	<p>Pump experts provide pre-pump faced to face training. User manuals and handbooks. Quick reference guides.</p> <p>Online training tool with animation and quizzes. Video demos showing how to set basal rates and use the pump.</p>	<p>User manuals are available online.</p> <p>Online learning modules are available for patients.</p>	<p>User manuals are available online.</p> <p>Online learning modules are available for patients.</p>	<p>Training provided by company personnel. Diabetes Educators and user manual provided.</p>
<b>Freecall 24 Hour Hotline</b>	Yes	Yes	Yes	Yes	Yes	Yes

<b>Model Name/No.</b>	<b>DANA IIS Insulin Pump</b>	<b>DANA R Diabecare Insulin Pump</b>	<b>Accu-Chek: Combo System</b>	<b>Medtronic Minimed Paradigm Veo MMT-554</b>	<b>Medtronic Minimed Paradigm Veo MMT-754</b>	<b>Animas: Vibe &amp; CGM System</b>
<b>Repair/replace ment policy</b>	Any impact damage may be deemed as negligent and the manufacturer can decline warranty repair.	Any impact damage may be deemed as negligent and the manufacturer can decline warranty repair.	Faulty pumps are replaced and not repaired.	Repair or replace. Does not cover dropping, improper storage or submersion in water.	Repair or replace. Does not cover dropping, improper storage or submersion in water.	Faulty pumps are replaced and not repaired.
<b>Warranty length</b>	4 years	4 years	4 years	4 years	4 years	4 years
<b>Product Recalls and Safety Alerts</b>	Nil	Nil	<p><b>Roche Alert with TGA 24 October 2013</b> Software synchronization issue with ACCU-CHEK Combo system. In rare cases, when the “Manual Pump” option is chosen on the ACCU-CHEK Aviva Combo meter, there is a possibility of receiving an incorrect bolus advice recommendation that may cause a temporary under delivery of insulin. The product was not physically recalled.</p>	<p><b>TGA Medtronic paradigm insulin pump Safety Advisory 10 April 2013</b> Three rare issues required update of information manual only: - Loose drive support cap (may deliver too much insulin if pushed) - Sensor graph timeout (can delay re-start of insulin following a low glucose suspension) - water damage (can stop the pump working if immersed) The product was not physically recalled.</p>	<p><b>TGA Medtronic paradigm insulin pump Safety Advisory 10 April 2013</b> Three rare issues required update of information manual only: - Loose drive support cap (may deliver too much insulin if pushed) - Sensor graph timeout (can delay re-start of insulin following a low glucose suspension) - water damage (can stop the pump working if immersed) The product was not physically recalled.</p>	Nil

<b>Model Name/No.</b>	<b>DANA IIS Insulin Pump</b>	<b>DANA R Diabecare Insulin Pump</b>	<b>Accu-Chek: Combo System</b>	<b>Medtronic Minimed Paradigm Veo MMT-554</b>	<b>Medtronic Minimed Paradigm Veo MMT-754</b>	<b>Animas: Vibe &amp; CGM System</b>
<b>Waterproof</b>	3m for 24 hours (IPX8)	3m for 24 hours (IPX8)	2.5m for 1 hour	IPX7, rated water resistant.	IPX7, rated water resistant	3.6m for 24 hours
<b>External software that links to device</b>	No	DANA manager program (PC): download records of bolus, daily total, blood glucose and carbohydrate from insulin pump to PC and upload records to ubiquitous system server.	Supported by Accu-Check 360 Diabetes Management Software. Also supported by Accu-Check Pump Configuration Software for programming and upload of settings.	Medtronic CareLink® software allows insulin pump, CGM and blood glucose meter data to be uploaded to a secure online server and generate reports. Data can also be shared with healthcare providers remotely. Can receive readings from meters with wireless technology.	Medtronic CareLink® software allows insulin pump, CGM and blood glucose meter data to be uploaded to a secure online server and generate reports. Data can also be shared with healthcare providers remotely. Can receive readings from meters with wireless technology.	Diasend software, a customisable food database for accurate carbohydrate counting.
<b>Remote control available</b>	No	Yes	Yes – through blood glucose meter with full range of additional functions.	Yes - to deliver bolus and to suspend pump.	Yes - to deliver bolus and to suspend pump.	No
<b>Data transfer to/from blood glucose meter</b>	Not available	From blood glucose meter via radio frequency.	Two-way Bluetooth between the Spirit Combo pump and Performa Combo Blood Glucose Meter.	Data transferred from blood glucose meter via radio frequency.	Data transferred from blood glucose meter via radio frequency.	Diasend software food database upload into pump.
<b>Range of carrying devices and pouches</b>	Leather case, bra pouch, shower pouch, shoulder pouch.	Leather case, bra pouch, shower pouch, shoulder pouch, outer case, travel case and transparent case.	Various cases including bra and leg pouches.	Range of pouches and carrying devices available.	Range of pouches and carrying devices available.	Range of pouches and carrying devices available.

<b>Model Name/No.</b>	<b>DANA IIS Insulin Pump</b>	<b>DANA R Diabecare Insulin Pump</b>	<b>Accu-Chek: Combo System</b>	<b>Medtronic Minimed Paradigm Veo MMT-554</b>	<b>Medtronic Minimed Paradigm Veo MMT-754</b>	<b>Animas: Vibe &amp; CGM System</b>
<b>Personalisation (colours/skins)</b>	Five colour options.	Five colour options.	One colour and thirty 'skins' available.	Five colour options and five 'skins'.	Five colour options and five 'skins'.	Five colours available and protective skins

**Notes:** \*Requires use of continuous glucose monitoring.

Information in this table was initially gathered from publicly available sources. The relevant pump manufacturers/sponsors were then given the opportunity to provide any corrections or additional information.

**Appendix B – Insulin pumps no longer available under the Prostheses List as at February 2014**

<b>Pump Sponsor/ Manufacturer</b>	<b>Australasian Medical &amp; Scientific Pty Ltd</b>	<b>Roche Diagnostics Australia Pty Ltd</b>	<b>Medtronic Australasia Pty Ltd</b>	<b>Medtronic Australasia Pty Ltd</b>	<b>Australasian Medical &amp; Scientific Pty Ltd</b>
<b>Model Name/No.</b>	Animas: 2020	Accu-Chek: Spirit	Medtronic: Paradigm 522	Medtronic: Paradigm 722	Deltec: Cozmo
<b>Minimum Benefit on Prostheses List</b>	\$7,750	\$4,000	\$8,950	\$8,950	\$7,750
<b>Listed on Prostheses List</b>	Yes (Discontinued)	No (Delisted Feb 2013)	No (Delisted Feb 2013)	No (Delisted Feb 2013)	No (Discontinued in 2009, and delisted Feb 2014)
<b>Main Function</b>	Insulin infusion pump	Insulin infusion pump	Insulin delivery, performs bolus calculation and advice + CGM capability	Insulin delivery, performs bolus calculation and advice + CGM capability	Insulin infusion pump
<b>Reason for removal</b>	Discontinued and superseded by the Animas: Vibe insulin pump.	Manufacturer requested removal from Prostheses List. The model was superseded by a newer model.	Manufacturer requested removal from Prostheses List. The model was superseded by a newer model.	Manufacturer requested removal from Prostheses List. The model was superseded by a newer model.	Smiths Medical announced its intent to stop manufacturing and selling the Deltec Cozmo, effective 25 March 2009.

### Appendix C – Breakdown of insulin pump brands supplied under the Insulin Pump Programme from commencement to 31 March 2013

Pump Sponsor / Manufacturer	Model Name/No.	Listed on Prostheses List (Feb 2014)	Minimum Benefit (Feb 2014)	Minimum Benefit prior to Aug 2012 increase	No. provided under Programme	Share
Managing Diabetes Pty Ltd / SOOIL Development Co. Ltd	DANA IIS Diabecare Insulin Pump	Yes	\$4,000	\$4,000	0	0%
	DANA R Diabecare Insulin Pump	Yes	\$8,950	\$8,000	0	0%
Roche Diagnostics Australia Pty Ltd	Accu-Chek: Combo System	Yes	\$8,950	\$8,000	48	11%
	Accu-Chek: Spirit	No	-	\$4,000	1	<1%
Medtronic Australasia Pty Ltd	Medtronic: Paradigm Veo MMT-554	Yes	\$9,500	\$8,000	67	15%
	Medtronic: Paradigm Veo MMT-754	Yes	\$9,500	\$8,000	213	49%
	Medtronic: Paradigm 522	No	-	\$8,000	7	2%
	Medtronic: Paradigm 722	No	-	\$8,000	16	4%
Australasian Medical & Scientific Pty Ltd	Animas: Vibe	Yes	\$8,950	\$7,750	18	4%
	Animas: 2020	Yes (but discontinued)	\$7,750	\$7,750	62	14%
Medical Specialities Australia Pty Ltd / Smiths Medical	Deltec: Cozmo	No	-	\$7,750	2	<1%
<b>Total</b>					<b>439</b>	<b>100%</b>

**Note:** Insulin pump brands no longer listed on the Prostheses List or discontinued are highlighted.

## Appendix D – National and international guidelines for the management of type 1 diabetes using insulin pump therapy

Reference	Recommendation	Difference
<p>(Craig 2011)  <b>Australia – NHMRC</b>  <b>Recommended</b></p>	<p>Nonsensor-augmented CSII should be considered for use in individuals in whom the expected magnitude of benefit is clinically significant in terms of reducing HbA<sub>1c</sub>, reducing hypoglycaemia or improving quality of life</p> <p>Practice points:            Individuals who may be likely to benefit from CSII pump therapy, as part of intensive diabetes management are - some children and adolescents, including infants and young children, and pregnant women (ideally preconception,</p> <ul style="list-style-type: none"> <li>• individuals with microvascular complications of diabetes,</li> <li>• individuals with reduced hypoglycaemia awareness, - individuals (or their supervising adults) with desirable motivational factors; for example, those seeking to improve blood glucose and having realistic expectations,</li> <li>• individuals exhibiting desirable CSII treatment-related behavioural factors, including those who are able to perform carbohydrate counting, are currently undertaking four or more blood glucose tests per day, have reliable adult supervision (in paediatrics), and a history of good self-management skills (in adults), are reliable in follow-up health care</li> </ul>	
<p>Victorian CSII working party guidelines  <b>Australia</b></p>	<p>Clinical recommendations:</p> <ul style="list-style-type: none"> <li>• Patient confirmed as having Type I diabetes or diabetes in pregnancy. (For Type 1 diabetes this may include measurement of fasting C-peptide and (pre-exogenous insulin) insulin levels and anti-islet antibodies, including anti-GAD and anti-IA2 antibodies)</li> <li>• Lifestyle allows for wearing of a pump</li> <li>• Lifestyle choices to facilitate adequate time for initial stabilization and education</li> <li>• Patient requires less than 300 Units of (100 IU) insulin per 2-3 days</li> <li>• Consistent home blood glucose (BG) monitoring and recording or is willing to increase monitoring (and subsequently demonstrates has done so)</li> <li>• Ability to measure blood or urine ketone levels, or agreeable to learning to do so</li> <li>• Basic numeracy</li> <li>• Willing and able to learn how to carbohydrate count and to calculate doses of insulin</li> <li>• Willing to communicate on a regular basis with the team</li> <li>• Able to comply with treatment plans or scheduled visits</li> <li>• Absence of any severe or unstable psychiatric condition: eating disorder, psychosis, depression. It is noted that the presence of an eating disorder or depression does not preclude insulin pump use</li> <li>• Reasonable level of motivation and able to accept responsibility for care of diabetes</li> <li>• No significant visual impairment</li> <li>• No major restriction in manual dexterity, or lack of required assistance</li> <li>• Adequate condition of subcutaneous tissue and skin</li> </ul>	<p>Details more specific clinical requirements to Craig 2011, as well as financial suitability.</p>

Reference	Recommendation	Difference
	<ul style="list-style-type: none"> <li>• Satisfactory hygiene</li> <li>• Funds available to purchase pump and consumables (N.B. NDSS will not provide consumables for non-pregnant Type 2 diabetes patients using CSII therapy)</li> </ul>	
(Scottish Intercollegiate Guidelines Network (SIGN) 2010) <b>Scotland</b>	<p>CSII therapy is associated with modest improvements in glycaemic control and should be considered for patients unable to achieve their glycaemic targets (Grade A)</p> <p>CSII therapy should be considered in patients who experience recurring episodes of severe hypoglycaemia (Grade B)</p>	
(National Institute for Health and Clinical Excellence 2008) <b>England</b> <b>Wales</b>	<p>Continuous subcutaneous insulin infusion or 'insulin pump' therapy is recommended as a possible treatment for adults and children 12 years and over with type 1 diabetes mellitus if:</p> <ul style="list-style-type: none"> <li>- attempts to reach target haemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels with multiple insulin injections result in the person having 'disabling hypoglycaemia', or</li> <li>- HbA<sub>1c</sub> levels have remained high (8.5% or above) with multiple insulin injections (including using long-acting insulin analogues if appropriate) despite the person and/or their carer carefully trying to manage their diabetes.</li> </ul> <p>Insulin pump therapy is recommended as a possible treatment for children under 12 years with type 1 diabetes mellitus if treatment with multiple insulin injections is not practical or is not considered appropriate. Children who use insulin pump therapy should have a trial of multiple insulin injections when they are between the age of 12 and 18 years.</p> <ul style="list-style-type: none"> <li>- It is recommended that CSII 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 dietitian. Specialist teams should provide structured education programmes and advice on diet, lifestyle and exercise appropriate for people using CSII.</li> <li>- Following initiation in adults and children 12 years and older, CSII therapy should only be continued if it results in a sustained improvement in glycaemic control, evidenced by a fall in HbA<sub>1c</sub> 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.</li> <li>- CSII therapy is not recommended for the treatment of people with type 2 diabetes mellitus.</li> </ul>	
(American Association of Diabetes Educators 2008) <b>United States</b>	<p>Patients should be considered for insulin pump therapy when intermittent insulin injections are not meeting treatment goals and outcome measures are suboptimal, including, but not limited to:</p> <ul style="list-style-type: none"> <li>- A<sub>1c</sub> &gt; 7.0-7.5%, accompanied by frequent severe hypoglycaemia (&lt; 55 mg / dL)</li> <li>- Hypoglycaemic events requiring third-party assistance or interfering with work, school, or family obligations</li> <li>- Frequent and unpredictable fluctuations in blood glucose levels</li> <li>- Patient perception that diabetes management impedes the pursuit of personal or professional goals</li> </ul>	

Reference	Recommendation	Difference
(Grunberger 2010) <b>United States</b>	The statement provides the US Center for Medicare and Medicaid Services Insulin Pump Patient Eligibility Criteria. Patients must meet 1 of the following criteria: (a) Patient has completed a comprehensive diabetes education programme and has been receiving multiple daily injection insulin with frequent self-adjustments for at least 6 months before pump initiation. Patient has documented self-monitoring of blood glucose frequency an average of $\geq 4$ times per day during the previous 2 months. Patient must also meet $\geq 1$ of the following criteria: - HbA <sub>1c</sub> > 7.0% - History of recurrent hypoglycaemia - Wide fluctuations in blood glucose before mealtime - Dawn phenomenon with fasting plasma glucose concentration frequently > 200 mg / dL or history of severe glycaemic excursions (b) Patient on a pump therapy before enrolment and has documented self-monitored blood glucose an average of $\geq 4$ times per day during the month before enrolment.	
The New Zealand Society for the Study of Diabetes (NSSD). NSSD Position Statement on Insulin Pump Therapy, June 2008: <b>New Zealand</b>	The NZSSD Executive states that Insulin Pump Therapy should be available to people with Type 1 Diabetes who, despite optimal high-level care and MDI using a long acting analogue, meet the following criteria: <ul style="list-style-type: none"> <li>• Recurrent severe (2) unexplained hypoglycaemic episodes (2 or more in a 12 month period);</li> <li>• Women who have suboptimal glycaemic control and wanting to conceive;</li> <li>• Children less 12 years, in whom MDI is judged to be impractical;</li> <li>• Poor glycaemic control (HbA<sub>1c</sub> greater than 8.5% demonstrated by CGM to be due to a prominent dawn phenomenon; and</li> <li>• Other selected situations: gastroparesis, eating disorders.</li> </ul> Practice Guidelines: <ul style="list-style-type: none"> <li>• The person should be assessed by a physician experienced in insulin pump therapy and would include evidence of adherence to appropriate nutritional and self-monitoring practices;</li> <li>• Pump therapy should be administered through the special authority mechanism or equivalent criteria-based methodology A national panel should be developed to assess applications;</li> <li>• Pump therapy should only be commenced and supervised by a diabetic service that has the appropriate experience and resources to manage insulin pump therapy;</li> <li>• Access to treatment should be consistent throughout New Zealand;</li> <li>• Funding should apply to the pump and consumables; and</li> <li>• Response to treatment (according to predefined outcomes) should be demonstrated annually to be eligible for ongoing funding.</li> </ul>	
Agence d'évaluation des technologies et des modes d'intervention en santé	1 As set out in the Canadian practice guidelines, the preferred therapeutic approach to type 1 diabetes, in both adults and children, be based on intensive therapy with multiple daily insulin injections; 2 Therapy by continuous subcutaneous insulin infusion (insulin pump) be recognised in Quebec as a treatment modality	

Reference	Recommendation	Difference
<p>(AETMIS) 2005 Canada - Quebec</p>	<p>that might be indicated for a limited, select group of people with type 1 diabetes (various selection criteria based on expert opinion are cited in this report);</p> <p>3 The Minister consider setting up a multidisciplinary taskforce (including Diabete Quebec, and the clinical and research communities) charged with:</p> <ul style="list-style-type: none"> <li>• Identifying consensus criteria for patient selection and for prescribing and monitoring of insulin pump therapy;</li> <li>• Designating clinics that would participate in the implementation of pump therapy and determining the composition and role of the professional team required;</li> <li>• Developing common candidate selection, patient education and follow- up tools;</li> <li>• Monitoring and implementation of pump therapy; and</li> <li>• Re-evaluating the use of pump therapy in Quebec sometime after it is introduced.</li> </ul> <p>4 The consensual criteria for the use of insulin pumps to be reviewed periodically in the light of new evidence that becomes available after this report, in particular , from studies comparing the insulin pump and multiple injection therapy with glargine, it may soon be available in Canada (technology watch);</p> <p>5 A clear consistent policy governing the use of the insulin pump be developed and made part of a broader initiative for managing diabetes in Quebec that would take into account the need to increase the ability of Quebec’s health-care system to offer intensive therapy to all people with type 1 diabetes;</p> <p>6 Two options for standardising the prescription and coverage of modalities be examined:</p> <ul style="list-style-type: none"> <li>• Consider the [insulin] pump an exceptional treatment modality for exceptional patients, with access granted by the Regie de l’assurance maladie du Quebec (RAMQ) on a case by case basis according to the criteria established by the above mentioned taskforce and/or on request by a physician;</li> <li>• Institute systematic pump prescription and utilisation auditing and monitoring procedures based on set criteria in collaboration with the clinical settings concerned, possibly by creating a registry of pump-treated patients or developing tools for selecting cases on a priority basis within a predetermined budget allowance;</li> </ul> <p>7 A full range of technical service be provided in French in Quebec by the manufacturers and distributors of insulin pumps; and</p> <p>8 Research on patient selection criteria and cost-effectiveness of insulin pumps in the Quebec context be considered an important avenue of investigation by Fonds de la recherché en santé du Quebec (FRSQ).</p>	

## Appendix E – Current Guidelines hosted by the NHMRC Clinical Guidelines Portal that reference insulin pumps as at January 2015

Reference	Recommendations in relation to insulin pump use in type 1 diabetes
<p>Barclay A, Gilbertson H, Marsh K &amp; Smart C (2010), '<u>Dietary management in diabetes</u>', Australian Family Physician, Vol. 39, No. 8, pp. 579-583.</p>	<p>With regard to insulin pump therapy, notes that:</p> <ul style="list-style-type: none"> <li>• insulin pump therapy provides the greatest flexibility in meal quantity and timing, making it ideal for toddlers and teenagers</li> <li>• bolus type and dose can be adjusted to match the meal composition</li> <li>• knowledge of carbohydrate counting is essential</li> <li>• pre-prandial bolus provides best glycaemic outcomes, but the dose can be split pre-prandial and during the meal for toddlers if eating is erratic</li> <li>• the biggest contributor to poor glycaemic outcomes is a missed meal time bolus</li> <li>• hypoglycaemia should be treated with short acting carbohydrates.</li> </ul>
<p>Craig (2011), '<u>National evidence based clinical care guidelines for type 1 diabetes in children, adolescents and adults</u>', Australian Government Department of Health and Ageing, Canberra.</p>	<p><b>Evidence statements:</b> “Across all individuals with type 1 diabetes, Level I evidence demonstrates a small but statistically significant reduction in HbA<sub>1c</sub> with CSII compared to MDI. Level II evidence shows that CSII has a minor benefit for HbA<sub>1c</sub> levels compared to MDI. There is no evidence to support a reduction in hypoglycaemia in adults. There is Level I evidence of a slight, but statistically significant increase in mild hypoglycaemia in children using CSII. There is no statistically significant evidence to support a reduction in severe and nocturnal hypoglycaemia in adults and children. Level II evidence shows an improvement in QoL with CSII compared to MDI. Level II evidence consistently shows improved treatment satisfaction with CSII compared to MDI.”</p> <p>Note: Level I evidence = A systematic review of Level II studies. Level II studies = randomised controlled trial.</p> <p><b>Recommendations:</b> “Nonsensor-augmented CSII should be considered for use in individuals in whom the expected magnitude of benefit is clinically significant in terms of reducing HbA<sub>1c</sub>, reducing hypoglycaemia or improving QoL (Grade C)”.</p> <p>Note: The National Health and Medical Research Council (NHMRC) definition for evidence of Grade C level is that the body of evidence provides some support for the recommendations, but that care should be taken in their application.</p> <p><b>Practice Points:</b> “Individuals who may be likely to benefit from CSII pump therapy, as part of intensive diabetes management, are:</p> <ul style="list-style-type: none"> <li>• some children and adolescents, including infants and young children, and pregnant women (ideally preconception)</li> <li>• individuals with microvascular complications of diabetes</li> <li>• individuals with reduced hypoglycaemia awareness</li> <li>• individuals (or their supervising adults) with desirable motivational factors; for example, those seeking to improve blood glucose control and having realistic expectations</li> <li>• individuals exhibiting desirable CSII treatment-related behavioural factors, including those who:</li> </ul>

	<ul style="list-style-type: none"> <li>○ are able to perform carbohydrate counting</li> <li>○ are currently undertaking four or more blood glucose tests per day</li> <li>○ have reliable adult supervision (in paediatrics), and a history of good self-management skills (in adults)</li> <li>○ are able to master the technical skills of CSII</li> <li>○ are reliable in follow-up health care.”</li> </ul> <p><b>Results of the systematic review:</b></p> <ul style="list-style-type: none"> <li>• Did not systematically review the effectiveness of insulin pumps and continuous glucose monitoring during pregnancy.</li> <li>• Found a mean difference in HbA<sub>1c</sub> at treatment end of -0.2% (95% CI: -0.28% to -0.12%, P &lt;0.00001) favouring insulin pump therapy over multiple daily injections in all age groups. In adults, the mean difference in HbA<sub>1c</sub> was -0.16% (95% CI: -0.33% to 0.01, P=0.06) favouring insulin pump therapy, and in children under 18 years the mean difference was significantly lower with insulin pump therapy at -0.25% (95% CI: -0.46% to -0.05%, P=0.01).</li> <li>• The majority of identified studies did not show significant differences between insulin pump therapy and multiple daily injections for hypoglycaemic events. However, events rates were low in all studies and the studies were not powered for this outcome, and patients with a history of severe hypoglycaemia were often excluded.</li> <li>• There is some advantage to quality of life for patients receiving insulin pump therapy compared to multiple daily injections.</li> <li>• The level of education supplied in carbohydrate counting, self-monitoring of blood glucose and bolus correction varied between the treatment arms in some studies. This may explain some of the observed advantages of insulin pump therapy over multiple daily injections.</li> <li>• Effective intensive diabetes management regimens require motivation, routine carbohydrate counting, frequent self-monitoring of blood glucose and insulin adjustment, and support from a skilled and well-resourced multidisciplinary team.</li> <li>• One study (n=485) which randomised patients to receive either multiple daily injection therapy or sensor-augmented insulin pump therapy found a mean difference in HbA<sub>1c</sub> of 0.5% (P&lt;0.001) favouring sensor-augmented pump therapy, but no difference in severe hypoglycaemia, although rates were low.</li> </ul>
<p>Siafarikas A &amp; O’Connell S (2010), <a href="#">‘Type 1 diabetes in children - emergency management’</a>, Australian Family Physician, Vol. 39, No. 5, pp. 290-293.</p>	<p>“It is controversial whether subcutaneous (SC) insulin infusion (‘insulin pump therapy’) predisposes patients to an increased risk of DKA. It has been emphasised that this group must carry needles and syringes and an emergency plan with insulin doses in case of pump malfunction”.</p>
<p>The Royal Australian College of General Practitioners and Diabetes Australia (2014), <a href="#">‘General practice management of type 2 diabetes 2014-15’</a>, Melbourne,</p>	<p>“Insulin pumps have traditionally only been used in the management of type 1 diabetes. There is sparse literature about the benefits of using pumps in people with type 2 diabetes, however, anecdotally, these appear to be advantageous to some people.”</p>