

Pharmaceutical Benefits Scheme  
**Post-market Review**  
**Products Used in the Management of Diabetes**  
Report to Government

**Stage 2: Insulin Pumps**

**Version 5**

# Contents

Report Structure.....	4
Glossary .....	5
Executive Summary.....	8
Part 1 Review background and context .....	11
1.1 Diabetes Post-market Review.....	11
1.2 Insulin Pumps Review .....	11
1.3 Context for the Diabetes Post-market Review .....	15
Part 2 Diabetes mellitus: treatment and access to insulin pumps.....	17
2.1 Diabetes mellitus .....	17
2.2 Prevalence of diabetes in Australia .....	17
2.3 Complications .....	18
2.4 Diagnosis.....	19
2.5 Monitoring blood glucose and glycaemic control .....	20
2.6 Treatment options and technologies for type 1 diabetes .....	21
2.7 Access to insulin pumps via the Type 1 Diabetes Insulin Pump Programme .....	24
2.8 Access to insulin pumps via private health insurance .....	26
2.9 Regulation of insulin pumps in Australia.....	28
Part 3 Stakeholder consultation outcomes.....	30
3.1 Public consultation processes .....	30
3.2 Key issues raised in written submissions by stakeholders.....	30
3.3 Key issues raised by stakeholders at the Stakeholder Forum .....	31
3.4 Public consultation on the draft Insulin Pumps Review Report .....	32
3.5 Internal Working Group.....	32
3.6 Reference Group .....	32
3.7 Advice from the Australasian Paediatric Endocrine Group (APEG) .....	33
Part 4 – ToR 8 Benefits and safety of insulin pump therapy.....	34
4.1 Key findings for ToR 8 .....	34
4.2 Introduction.....	36
4.3 First literature review: Randomised controlled trials (RCTs) .....	37
4.4 Second literature review: Observational studies.....	42

4.5	Recent additional evidence.....	46
4.6	Potential safety risks associated with insulin pump therapy .....	47
4.7	Potential safety risks associated with multiple daily injections .....	48
Part 5 – ToR 9 Costs and comparative effectiveness of insulin pumps.....		49
5.1	Key findings for ToR 9 .....	49
5.2	Introduction.....	51
5.3	Effectiveness of insulin pumps available under the Insulin Pump Programme	52
5.4	Cost of insulin pump therapy.....	53
5.5	Insulin pump use under the Programme .....	57
5.6	Issues identified .....	60
Part 6 – ToR 10 Programme eligibility criteria .....		62
6.1	Key findings for ToR 10.....	62
6.2	Introduction.....	63
6.3	Literature review: RCTs and observational studies.....	64
6.4	Literature review: Australian and international clinical guidelines.....	65
6.5	Government subsidised access to insulin pump therapy in other countries .....	69
6.6	Issues identified .....	70
References .....		72
Appendices .....		78
Appendix A - Insulin pumps available under the Protheses List as at February 2014 .....		78
Appendix B – Insulin pumps no longer available under the Protheses List.....		85
Appendix C – Breakdown of insulin pump brands supplied under the Insulin Pump Programme from commencement to 31 March 2013.....		86
Appendix D – National and international guidelines for the management of type 1 diabetes using insulin pump therapy .....		87
Appendix E – Current Guidelines hosted by the NHMRC Clinical Guidelines Portal in relation to type 1 diabetes .....		91

## 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).

DRAFT

## Glossary

AADE	American Association of Diabetes Educators
ADEA	Australian Diabetes Educators Association
AIHW	Australian Institute of Health and Welfare
APEG	Australasian Paediatric Endocrine Group
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 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 \$6.97 million over the four years to 2015-16.

It is estimated that there are approximately 118,600 Australians with type 1 diabetes (ABS 2013), of which 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 any of the pumps on the Prostheses List, which is primarily designed for private health insurance purposes and is also managed by the Department, or any other eligible and clinically recommended pump.

### Review findings

ToR 8 focussed on clinical outcomes of insulin pump therapy. The systematic literature review of randomised controlled trials (RCTs) showed that the 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 evidence 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 *et al.* 2010; Cummins *et al.* 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 *et al.* 2012). No trials 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> with insulin pump therapy and have a lower risk of severe hypoglycaemia. Some long term studies showed statistically

significant reductions in HbA<sub>1c</sub> ranging from 0.3–0.5% in children and adolescents using insulin pump therapy at 2-5 years follow-up. In addition, a recently published case-control study undertaken in children and adolescents in Australia showed a significant reduction in HbA<sub>1c</sub> of 0.6% with insulin pump therapy and reduced rates of severe hypoglycaemia and hospitalisation for ketoacidosis (Johnson *et al.* 2013). In adults, before-and-after studies showed statistically significant reductions in HbA<sub>1c</sub> in most studies, with mean decreases of 0.17–1.9%. The largest cohort study in adults, showed a statistically significant reduction in HbA<sub>1c</sub> with insulin pump therapy of 0.2% at five years (Carlsson *et al.* 2013). The observational studies lack randomisation and have a high risk of selection and publication bias and results should be interpreted cautiously. However, the patients included in these studies may be more reflective of the patients in which insulin pumps are used in Australia, such as those with diabetes complications or hypoglycaemia unawareness, who were generally excluded from RCTs.

As the literature reviews demonstrated only minimal benefits of insulin pump therapy over multiple daily injections, a cost-effectiveness analysis was not undertaken. In addition, the literature search showed that there is no evidence available on the comparative effectiveness of different insulin pump brands and no evidence was provided on this through the stakeholder consultation process. ToR 9 subsequently focussed primarily on Programme costs to consumers and Government, utilisation, and affordability and access issues.

On average, insulin pump consumables (excluding insulin) cost consumers \$310 per annum. In terms of costs, 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).

A brief review of the available cost-effectiveness models indicates that insulin pumps are unlikely to be cost-effective assuming an HbA<sub>1c</sub> reduction of around 0.5% relative to multiple daily injections, but are likely to be cost-effective assuming an HbA<sub>1c</sub> reduction of around 1.2% (Cummins *et al.* 2010, Cohen *et al.* 2007). The incremental cost-effectiveness ratio for insulin pump therapy is likely to be \$A110,000–\$150,000 per quality-adjusted life year assuming a reduction in HbA<sub>1c</sub> of 0.5–0.6% (Cummins *et al.* 2010, Cohen *et al.* 2007). This suggests that patient selection is important to ensure cost-effective use of insulin pumps, but the lack of sub-group analyses makes this difficult. The literature review of observational evidence indicated that people with high initial HbA<sub>1c</sub> generally showed greater improvements in HbA<sub>1c</sub> with insulin pump therapy. Use in patients with severe and/or unpredictable hypoglycaemia requiring hospitalisation at least once a year may also be cost-effective (Scuffham & Carr 2003).

The investigation of the Programme's usage and financial eligibility criteria highlighted several issues with affordability for the eligible population. [Figure 1](#) in Part 2.7.2 summarises the relationship between family income, the amount of the Government subsidy and cost of the patient co-payment for the most used insulin pump under the Programme. After JDRF made agreements in 2011 with some manufacturers to cover the patient co-payment to aid access for the lowest income families, Programme uptake

increased. This led to the development of a waiting list in 2012-13, which has since been addressed with new funding from the Government. As at February 2014, the delivery of insulin pumps through the Programme has now recommenced.

The Prostheses List pump prices increased on 1 August 2012, which led to a subsequent increase in the patient co-payment as the Programme's maximum subsidy remained capped. Families on the lowest eligible incomes of under \$71,230 (2013-14) per annum are now less likely to be able to afford the co-payment without further subsidy or continued assistance from insulin pump manufacturers. For the majority of other eligible families, private hospital insurance is likely to be a more affordable option than to access the Programme, at least for their first insulin pump. The median family income data indicates that families on eligible incomes between \$71,230-\$101,653 (2013-14) rarely access the Programme (JDRF data). This raises the issue of the affordability of the Programme for low- and middle-income families.

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, which makes it difficult to define clinical criteria to restrict use of the Programme to patients in which insulin pumps are most likely to be effective and cost-effective.

The Australasian Paediatric Endocrine Group (APEG) advised, via direct written input, 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. For the healthcare systems examined, most provided full or partial subsidy arrangements for an insulin pump, with a focus on providing access for children or young adults.

### **Stakeholder input**

The overall sentiment from stakeholders was that there are clinical (effectiveness and safety) and quality of life benefits to insulin pump therapy. Stakeholders were supportive of the continuation of the Programme and suggested expansion to pregnant women and to all ages. Clinical groups expressed that while the evidence does not conclusively support the clinical benefits of insulin pump therapy, there is some benefit in particular patient sub-groups, including high-risk patients. It was explicit that success with either therapy was dependent on the level of motivation and compliance of the patient/carers. It was also suggested that access to a range of insulin pumps assisted health professionals to tailor products to individualise patient needs.

# 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. Reports will be provided to the Pharmaceutical Benefits Advisory Committee (PBAC) and to Government for consideration in a staged approach 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 Internal 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.

### **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 and consumer groups, industry organisations, non-government organisations, peak professional bodies, a government organisation, and an individual professional.

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 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 Internal Working Group**

An Internal 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. The Reference Group includes experts from a range of fields including endocrinology, diabetes education, general practice, consumer advocacy, clinical epidemiology, pharmacy, health economics, nutrition, and psychology. Reference Group meetings at which the Insulin Pumps Review was discussed, were held on: 17 April 2013, 17 July 2013, and 16 January 2014.

Reference Group advice has been used to guide the development of the Insulin Pumps Review and this Report. Following public consultation on the draft Insulin Pumps Report and further consideration by the Reference Group, the final Report will be provided to the PBAC for noting and 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 Department presented the findings of the literature review, which considered evidence from randomised controlled trials (RCTs), to the Reference Group. The trial evidence did not conclusively support the superior effectiveness or safety of insulin pump therapy over multiple daily injections, particularly for children and adolescents. 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, or sub-populations that may benefit from insulin pump therapy. The Department subsequently engaged the QUMPRC to conduct a second literature search to include observational studies.

As a part of addressing the ToRs, the literature reviews considered studies that assessed the effects of each therapy on: HbA<sub>1c</sub> levels, quality of life 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, as there is currently no literature available on these issues.

The full literature review reports are available on a case-by-case basis on request from the Department.

The Department and Reference Group also considered the following in addressing ToR 8:

- written stakeholder submissions and comments received at the Stakeholder Forum;
- 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).

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

### **1.3.1 The National Medicines Policy (NMP)**

The NMP is a broad framework that aims to improve health outcomes for all Australians through improving both access to, and appropriate use of, medicines.

The four central objectives of the policy are:

- timely and affordable access to medicines for all Australians;
- appropriate standards of quality, safety, and efficacy of medicines;
- quality use of medicines; and
- maintenance of a responsible and viable medicines industry in Australia.

Post-market reviews contribute to the quality use of medicines objective of the NMP.

*Quality use of medicines* is defined as:

- selecting management options wisely;
- choosing suitable medicines if a medicine is considered necessary; and
- using medicines safely and effectively.

The definition of quality use of medicines applies equally to decisions about medicine use by individuals and decisions that affect the health of the population.

### **1.3.2 The Pharmaceutical Benefits Scheme (PBS)**

The PBS provides reliable, timely, and affordable access to a wide range of medicines for all Australians. Under the PBS, the Australian Government subsidises medicine costs to help people afford prescription medicines for most medical conditions. The PBS is part of the Australian Government's broader NMP.

### **1.3.3 The Pharmaceutical Benefits Advisory Committee (PBAC)**

The PBAC is an independent expert body appointed by the Australian Government, comprised of doctors, health professionals, health economists and consumer representatives. The PBAC meets three times a year, usually in March, July and November. Additional special meetings may be held as required.

The PBAC is responsible for evaluating the clinical and cost-effectiveness of medicines in order to make recommendations relating to listing on the PBS. Recommendations for new listings are informed by evidence of a medicine's clinical effectiveness, safety, and cost-effectiveness ('value for money') compared with other treatments.

The PBAC has a broad statutory function under the *National Health Act 1953*, to advise the Minister on any matters concerning the operation of the PBS. This includes making further recommendations regarding the safety, effectiveness and cost-effectiveness of medicines after they have been listed. Therefore, the PBAC considers the need for, and provides recommendations on, post-market reviews. The advice of the PBAC will be

sought on the Insulin Pumps Review Report to provide consistency across the Diabetes Review.

The PBAC has two sub-committees to assist with analysis and advice: the Drug Utilisation Sub-Committee (DUSC) and the Economics Sub-Committee (ESC). Information relating to the PBS, and the PBAC, DUSC and ESC meeting dates, and agendas and outcomes are available on the [PBS website](#).

#### **1.3.4 Post-market monitoring**

Post-market reviews are a systematic and formal approach to monitoring the use of medicines listed on the 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.

Applications to list a medicine on the PBS are considered by the PBAC on a case-by-case basis at the time a submission for listing is made. This means that a medicine is only considered in the context of treatments and evidence available at that time. Over time, new medicines are listed on the PBS, more data on medicine safety and efficacy becomes available, and treatment guidelines change. As a result, the actual use or health outcomes of a medicine may be different to what was considered by the PBAC at the time of listing. The post-market review process provides a mechanism for medicines to be considered in the full and current treatment context, including actual utilisation, comparative efficacy, treatment guidelines and health outcomes.

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.

Post-market reviews are initiated due to concerns related to safety, cost-effectiveness, clinical-effectiveness, higher than predicted use and/or international differences in use, of a medicine or a group of medicines. A full post-market review will only proceed following either PBAC agreement or 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 10% of people with diabetes (AIHW 2013). The cause of type 1 diabetes is not known, there are no known cures, and it is not preventable with current knowledge (Misso *et al.* 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) (AIHW 2013). 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 *et al.* 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 *et al.* 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 Impact in Australia**

Diabetes significantly affects the health of many Australians and can result in a range of complications. In 2005, diabetes was associated with cause of death for nearly 11,900 people in Australia or 9% of all deaths that year. Approximately half of these deaths involved coronary heart disease (47%), while hypertensive and cerebrovascular diseases accounted for 30% and 20% of diabetes deaths, respectively (AIHW 2013). 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 Humblert 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2011, Cavalot 2013, Gordin *et al.* 2008, Pena *et al.* 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 *et al.* 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 *et al.* 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).

According to the AIHW report, *Diabetes Among Young Australians* (2012a), insulin pump use is most common among people under the age of 19. Data from the NDSS indicates that there are 9,971 children aged between 0-18 with type 1 diabetes in Australia. Of these, 3,402 have been recorded as using insulin pump therapy for their form of treatment; meaning approximately 6,500 children (0-18 years) with type 1 diabetes are currently not using insulin pump therapy. These figures represent a 34% uptake rate of insulin pump therapy in the 0-18 year demographic in Australia. This 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 blood glucose testing and insulin administration at school. This raises questions as to whether children, particularly in early primary school, have the developmental capacity to self-administer blood glucose testing or 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 *et al.* 2013).

There is limited published literature regarding diabetes treatment in Australian schools. An unpublished study conducted in Australia in 2008, indicated that 87% of children with type 1 diabetes under the age of 12 were receiving insulin at school. Teachers, school administration staff and nurses provided assistance in some cases. However, a parent attended the school to assist with insulin administration in 28% of cases, mostly for children using insulin injections and under the age of 8. After 8 years of age most

children administered blood glucose testing and insulin themselves (Middlehurst & Morrison 2008).

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 *et al.* 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 *et al.* 2010).

The ability of a child to administer insulin at school may also affect their treatment. In an Australian study, whilst 60% of children with type 1 diabetes surveyed used insulin injections, only 47% received insulin injections at school. In contrast, of the 40% of children using insulin pump therapy, 98% received a bolus dose at school. Furthermore, children with insulin pumps were less likely to require a parent to attend the school to assist with treatment and teachers were more willing to assist with bolus administration through an insulin pump (Middlehurst & Morrison 2008). Taken together, these data indicate 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 an 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. When used in conjunction with a compatible insulin pump, 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, *et al.* 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 Prosthesis List and associated reimbursement through private health insurers is to use existing Prosthesis 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 Prosthesis 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 Prostheses 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. This enables patients under the Programme to access subsidised consumables at the same rate as all other NDSS 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 Prostheses 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 Prostheses List available to access. If a clinically recommended insulin pump is not listed on the Prostheses 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 Prostheses List.

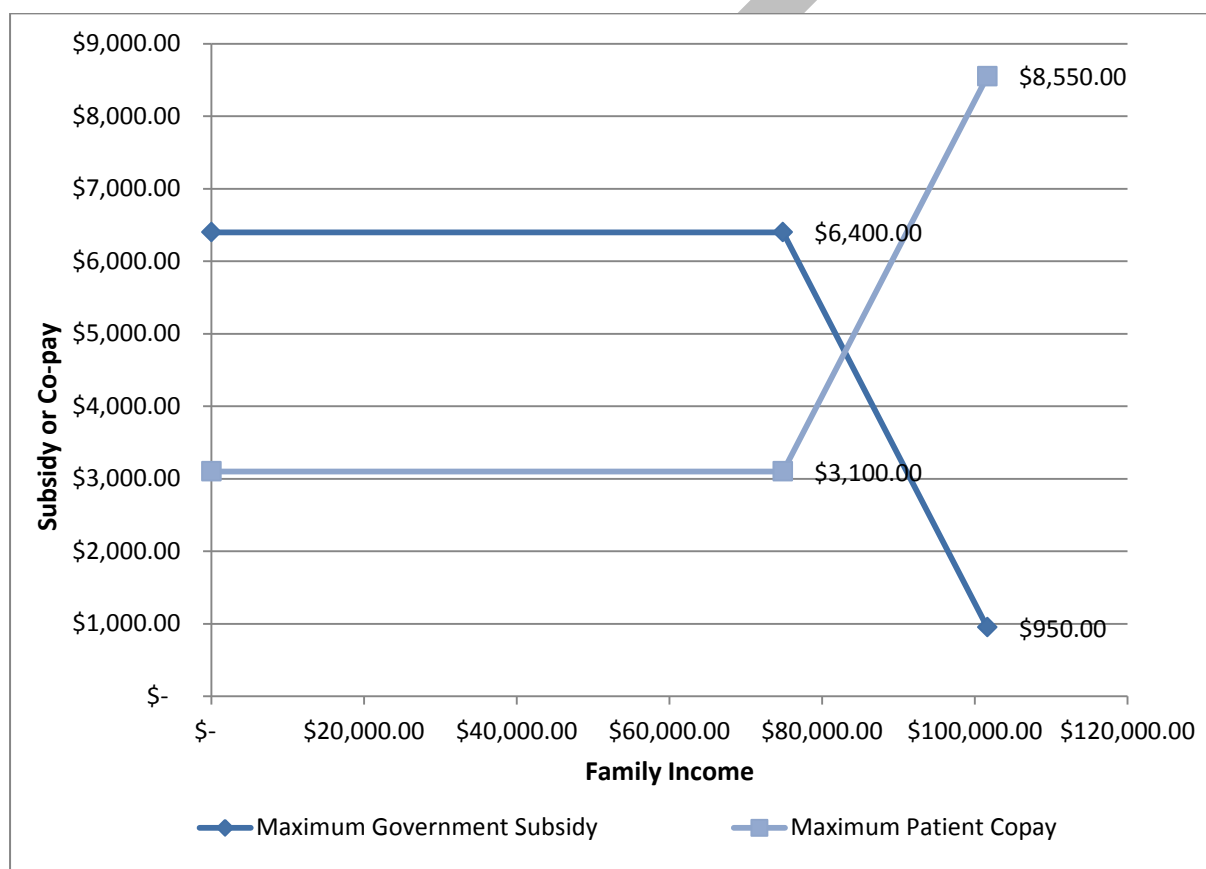
The Programme provides a subsidy between \$500 and \$6,400 for families that meet the means-tested income requirements. The applicant's family income determines the level of subsidy for the insulin pump on a sliding scale up to a maximum of 80% of the listed minimum benefit amount on the Prostheses List 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 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](#).

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

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 \$6.97 million over four years from 2012-13 to 2015-16. As at February 2014, the delivery of insulin pumps has now recommenced with 466 insulin pumps now 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% indicated a private health insurance rebate and around 3% indicated funding through the Insulin Pump Programme or an Australian Government subsidy.

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.

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## 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 Internal 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, along with all other comments contributed, will be provided to the Diabetes Review Reference Group for consideration.*

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

- Stakeholders were unanimously supportive of the advantages of insulin pump therapy. Any restrictions to current access arrangements would be 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.
- Consumers, consumer groups, industry organisations and sponsors expressed that improvements in glycaemic control, including lower HbA<sub>1c</sub> levels, from 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.

### **Breakdown of submissions by stakeholder type:**

<i>Individual Professional = 1</i>	<i>Industry Organisation = 2</i>
<i>Non-Government Organisation = 6</i>	<i>Other Government Organisation = 1</i>
<i>Peak Professional Body = 4</i>	<i>Individual Consumer = 19</i>

### **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. risk level), 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 sub-groups of patients should be considered for eligibility for the Insulin Pump Programme.
- It was noted that there are numerous issues regarding access to insulin pumps through private health insurance, including those patients who are denied an insulin pump through their private health insurance provider. *Note: This issue is*

*outside the scope of the Insulin Pumps Review and has been referred to the correct area of the Department.*

- Some patients may not receive an insulin pump subsidy, but they can be adequately managed on insulin 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 Public consultation on the draft Insulin Pumps Review Report**

*Note: This section will be completed following the public consultation process.*

### **3.5 Internal Working Group**

Key issues discussed by the Internal 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 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.

### **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 consulted the TGA regarding the ARTG listing of insulin pumps. Advice received is included in [Part 2.9](#).
- 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 *et al.* (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. Further analysis of this study is explored in [Part 4.5.1](#).

## 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

##### ***First literature review: Randomised controlled trials***

- The outcomes of the systematic literature review of RCTs showed that the trial evidence could not conclusively support superior efficacy (HbA<sub>1c</sub> levels) or safety (hypoglycaemic events) of insulin pump therapy over multiple daily injections in any age group. None of the trials assessed long-term health outcomes.
- The observed benefit of insulin pump therapy compared to multiple daily injections for adults, adolescents and children, showed a modest improvement in HbA<sub>1c</sub> levels. In children and adolescents the improvement in HbA<sub>1c</sub> ranged from -0.22% to -0.1%, however only one of the four meta-analyses demonstrated a statistically significant significance. 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 *et al.* 2010; Cummins *et al.* 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 *et al.* 2012).
- There is inconclusive evidence for HbA<sub>1c</sub> improvements in adults, and the RCTs for children had small sample sizes, low evidence strength, and were mostly funded 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. However, only two of the five RCTs showed a statistically significant increase favouring insulin pump therapy.
- In adults, the literature review found that the reported quality of life outcomes scored, on average, higher with insulin pump therapy compared to multiple daily injections. A number of assessment tools were used with five of the eight outcome measures reporting statistically significant differences.
- No sub-group analyses in the systematic reviews considered characteristics of children other than age.

### ***Second literature review: Observational studies***

- There are a number of important limitations to observational studies including a lack of randomisation and blinding, and high risk of selection and publication bias, which mean that the results should be interpreted cautiously. 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 20 observational studies in children and adolescents, fourteen showed statistically significant reductions or end of study differences in HbA<sub>1c</sub> favouring insulin pump therapy.
- The reductions in HbA<sub>1c</sub> were shown to be greater in patients with high initial HbA<sub>1c</sub> levels, and two studies reported that insulin pump therapy seems more beneficial when initiated in children under six years old.
- 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 four observational studies of glycaemic variability, all demonstrated statistically significant results favouring insulin pump therapy.
- A recently published case-control study undertaken in children and adolescents in Australia showed a significant reduction in HbA<sub>1c</sub> of 0.6% with insulin pump therapy and reduced rates of severe hypoglycaemia and hospitalisation for DKA (Johnson *et al.* 2013).

### ***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 to insulin pump therapy. Improvements in effectiveness, safety and quality of life were reported in the public submissions.
- Clinical groups expressed that while the 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 subgroups that would benefit more from insulin pump therapy.

In the 2010 Cochrane Collaboration Report, Misso *et al.* 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 *et al.* 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.

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 *et al.* 2007, DeVries *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2010), and one review restricted the analysis to RCTs that had used short-acting insulin analogues in the insulin pump therapy groups (Yeh *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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 questionnaires. 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 five trials. All trials had small sample sizes of fewer than 40 participants.

Three RCTs assessed treatment satisfaction using the Diabetes Treatment Satisfaction Questionnaire. All found a statistically significant and clinically relevant improvement with insulin pump therapy compared to multiple daily injections, defined as a  $\geq$  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 *et al.* 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 *et al.* 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%) (Fatourechi *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 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.

Two RCTs assessed quality of life with the Medical Outcomes Study 12-Item Short-Form Survey (SF-12) and the Medical Outcomes Study 36-Item Short-Form Survey (SF-36). They both found significant improvements on 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 *et al.* 2002).

Three RCTs assessed quality of life with the Diabetes Quality-of-Life questionnaire. A significant difference was evident only in the largest trial involving 272 participants (Hoogma *et al.* 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. 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 *et al.* 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 *et al.* 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 *et al.* 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 *et al.* 2012).

One meta-analysis did not find a difference between insulin pump therapy and multiple daily injections in nocturnal hypoglycaemia (Fatourehchi *et al.* 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.

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 (Fatourehchi *et al.* 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 group differences.

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 *et al.* 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 *et al.* 2012).

One systematic review did not perform a meta-analysis because studies used different scales to report hypoglycaemia (Misso *et al.* 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 May 2013. 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 regards 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 regards 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 lack of randomisation. In before-and-after studies, there is no comparison group so it is 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. 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 *et al.* 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 may also add difficulty to the interpretation of the synthesised results. 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 significance (Clar *et al.* 2010; Cummins *et al.* 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 *et al.* 2012).

#### **4.4.2 Results**

A total of 33 observational studies were identified, including 22 before-and-after studies, seven retrospective cohort studies and four prospective cohort study. The studies were conducted in 24 different countries and the majority (64%) had a follow-up period of two or more years (range of three months to nine years).

There were 19 studies in children and adolescents under 18 years old, one study in adolescents and adults, 12 studies in adults, and one study including all age groups. The number of patients included in the studies varied between 10 and 2709, with six studies including over 200 patients.

A variety of pumps were used in the studies; most studies (17) did not report the type of insulin pumps used. Twenty studies did not report the source of funding, seven received public funding, three industry funding, and three 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 12 before-and-after studies, 11 showed a decrease in HbA<sub>1c</sub> (0.1-1.04%) with insulin pump therapy that was statistically significant in eight studies. Long term studies generally showed positive results for insulin pump therapy, with statistically significant HbA<sub>1c</sub> reductions of 0.3-0.5% at two to five years follow-up in four studies, a non-significant reduction in one study (Abaci *et al.* 2009), and no reduction in a sixth study (Knight *et al.* 2011).

Of eight cohort studies, six 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 significant (Cummins *et al.* 2010). Most studies did not explicitly adjust for pre-study HbA<sub>1c</sub>. One study of around 100 children found a 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).

One prospective cohort study showed lower glycaemic variability in HbA<sub>1c</sub> with insulin pump therapy (0.73, SD 0.45) compared to multiple daily injections (0.84, SD 0.54), which was of borderline statistical significance (p=0.049) (Fendler *et al.* 2012).

##### ***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 *et al.* 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, four reported decreases in severe hypoglycaemia, which were statistically significant in three studies (Campbell *et al.* 2009; Hasanbegovic & Hasanbegovic 2009; Rabbone *et al.* 2009). Only one study of 17 adolescents reported an increase in the rate of severe hypoglycaemia with insulin pump

therapy (Abaci *et al.* 2009). Six cohort studies found a decrease in the rates of severe hypoglycaemic events with the use of insulin pump therapy, which was statistically significant in two studies (Berghaeuser *et al.* 2008; Jakisch *et al.* 2008).

One study reported significant decreases in the rates of symptomatic and nocturnal hypoglycaemic events with insulin pump therapy (Çamurdan *et al.* 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 mean decreases ranging from 0.17-1.9%. 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>.

Two cohort studies, involving 220 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 *et al.* 2009; Carlsson *et al.* 2013). 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.

Aberle (2008) examined variability in blood glucose levels and found a significant decrease in variance from before insulin pump therapy to after insulin pump therapy. Lin (2011) and Gimenez (2010) used three-day long continuous glucose monitoring at the start and end of a three-month and two-year study of insulin pump therapy, respectively. The glucose variability, determined by standard deviation of plasma glucose, and the mean amplitude of glycaemic excursions, decreased significantly in both studies.

#### **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. Four before-and-after studies reported decreased rates of severe hypoglycaemic events with insulin pump therapy in adults; two with significant results (Marmolin *et al.* 2012; Shalitin *et al.* 2010).

## 4.5 Recent additional evidence

### 4.5.1 Results of a large Australian case-control study

In 2013, Johnson *et al.* published 'Long-term outcome of insulin pump therapy in children with type 1 diabetes assessed in a large population-based case-control study'. This study is considered valuable as it reports outcomes from long-term use of insulin pumps in Australian clinical practice. It is one of the largest studies of insulin pump use in children, has the longest follow-up period of any study to date, and may be one of the best sources of evidence on the effectiveness of insulin pump therapy in the real patient setting (Tamborlane & Sherr 2013).

The study showed an average reduction in HbA<sub>1c</sub> in those using insulin pumps of 0.6% (6.6 mmol/mol), which remained significant through seven years follow-up. There was a significant reduction in severe hypoglycaemic events from 14.7 to 7.2 events per 100 patient-years in the insulin pump group, while in the injection group, severe hypoglycaemic events increased from 6.8 to 10.2 events per 100 patient-years. The rate of hospitalisation for DKA was also significantly lower in the insulin pump group compared to the injection group at 2.3 versus 4.7 hospitalisations per 100 patient-years (p=0.003) (Johnson *et al.* 2013).

This study has a number of limitations including the:

- Potential for bias due to substantial loss to follow-up over time (i.e. n=324 at the start of the study and n=25 at seven years follow-up).
- Potential for selection bias as little information is provided about selection criteria for initiating pump therapy and those using insulin pumps had significantly higher rates of severe hypoglycaemia prior to initiation. The Department of Health has requested the selection criteria for this study and is awaiting a response.
- Differences in education and support, which was more intensive for those on insulin pump therapy than injections and is likely to bias the results in favour of insulin pump therapy (Tamborlane & Sherr 2013). For example, a pooled analysis of ten studies identified a 0.5% reduction in HbA<sub>1c</sub> in children and adolescents following psychological interventions, although there was significant heterogeneity in the study results (Craig *et al.* 2011). In adults, self-management education delivered in conjunction with intensive diabetes management is associated with significant reductions in HbA<sub>1c</sub> of 0.5–1.0%, although again with significant heterogeneity in study results (Craig *et al.* 2011).

The Department and Reference Group considered this study as a part of the evidence for the potential benefits of insulin pump use in children and adolescents.

#### **4.5.2 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.

#### **4.6 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 *et al.* (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](#).

#### **4.7 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).

DRAFT

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

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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).

- 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 available analyses, the cost-effectiveness of insulin pump therapy relative to multiple daily injections is likely to be around \$A110,000–\$150,000 per quality-adjusted life year assuming a reduction in HbA<sub>1c</sub> of 0.5–0.6% (Cummins *et al.* 2010, Cohen *et al.* 2007). Models did not generally consider productivity costs and some quality of life factors, and were highly sensitive to assumed HbA<sub>1c</sub> reductions.
- Patient selection is important to ensure cost-effective use of insulin pumps. Use is likely to be cost-effective in patients with high initial HbA<sub>1c</sub> or, severe and/or unpredictable hypoglycaemia leading to hospitalisation at least once per year (Scuffham & Carr 2003), who are highly motivated to intensively manage their diabetes.

### ***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. As at February 2014, the delivery of insulin pumps through the Programme has now recommenced.
- Data from the NDSS used in the AIHW *Insulin Pump Use in Australia* (2012) report indicates that there are 9,971 children aged between 0-18 years with type 1 diabetes in Australia. Of these, 3,402 have been recorded as using insulin pump therapy for their form of treatment, which represents 34% uptake.
- The *Insulin Pump Use in Australia* survey indicates that of the 88% of insulin pump users in Australia who received financial assistance to purchase a pump, 3% received funding through the Insulin Pump Programme and 97% received funding through private health insurance (AIHW 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 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.

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.

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.

The evidence examining the use of different bolus types to reduce postprandial hyperglycaemia (e.g. single short bolus, two boluses, delayed or square bolus, and combination or dual wave bolus) is limited to a small number of studies, most of which have shortcomings in study design. These studies indicate that postprandial glycaemia is controlled best by use of a combination bolus for high fat meals that may delay glucose absorption in the gastrointestinal tract, and low glycaemic index meals. High glycaemic index meals were shown in one study to cause significant postprandial glycaemic excursions irrespective of bolus type (Heinemann 2009). The results of these studies should be interpreted cautiously; however, the ability to provide a combination bolus may be a useful feature of insulin pumps.

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.

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. Programme funding now totals \$6.97 million over four years from 2012-13 to 2015-16.

### 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.

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 *et al.* 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**

Product	Benchmarked price	Patient co-payment (2014)
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.**

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**

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 Associated costs with the Insulin Pump Programme

Cost of consumables over four years per patient	\$8,379.29
Median subsidy amount 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 year per patient	\$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 life of a pump is four years (the average warranty period).
- 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 JDRF). 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.

#### 5.4.3 Potential costs other than insulin pumps and consumables

The potential costs of the Programme are not limited to the insulin pump and the consumables. There may also be additional 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 number of severe hypoglycaemic episodes);
- 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).

#### 5.4.4 Cost-effectiveness studies of insulin pumps

A recent Australian study estimated that the mean discounted lifetime direct medical costs associated with insulin pump therapy were \$34,642 higher in adults and \$41,779 higher in adolescents compared to multiple daily injections (Cohen *et al.* 2007). This translates into a cost per life-year gained of \$88,220 for adults and \$77,851 in adolescents. This study was based on modelling the reduction in complications from an assumed 1.2% reduction in HbA<sub>1c</sub> with the use of insulin pump therapy. The study did not consider non-medical costs such as lost productivity, and assumed an eight-year lifespan for each insulin pump (twice the standard warranty length). A sensitivity analysis based on an HbA<sub>1c</sub> reduction of 0.51%, closer to the evidence seen in the RCTs and observational studies, gave an incremental cost-effectiveness ratio of \$124,201 per quality-adjusted life-year (or around \$146,000 in 2013 dollars). Cohen *et al.* concluded that patient selection is critical for cost-effective use of insulin pumps and that it was unlikely that the use of insulin pumps in those already well controlled on multiple daily injections would be cost-effective (2007). The literature review of observational studies indicated that greater HbA<sub>1c</sub> reductions were generally achieved with insulin pump therapy in those with higher baseline HbA<sub>1c</sub> levels.

Cummins *et al.* undertook a review of the cost-effectiveness of insulin pump therapy and found that most studies assumed an HbA<sub>1c</sub> reduction of 1.2% as the base case, and concluded that insulin pump therapy was cost-effective with an anticipated survival gain of 0.8–0.9 years. However, the models were highly sensitive to assumed HbA<sub>1c</sub> reductions and did not generally consider productivity costs and some quality of life factors (2010). In their model, Cummins *et al.* estimated the incremental cost-effectiveness ratio at £53,788 per quality-adjusted life year for insulin pump therapy assuming an HbA<sub>1c</sub> reduction of 0.6%. This is equivalent to >\$A110,000 in 2013.

A UK study looking at hypoglycaemia and DKA only, over a period of eight years, concluded that insulin pumps were most cost-effective in patients with severe and/or unpredictable hypoglycaemia requiring hospitalisation at least once a year (Scuffham & Carr 2003).

## 5.5 Insulin pump use under the Programme

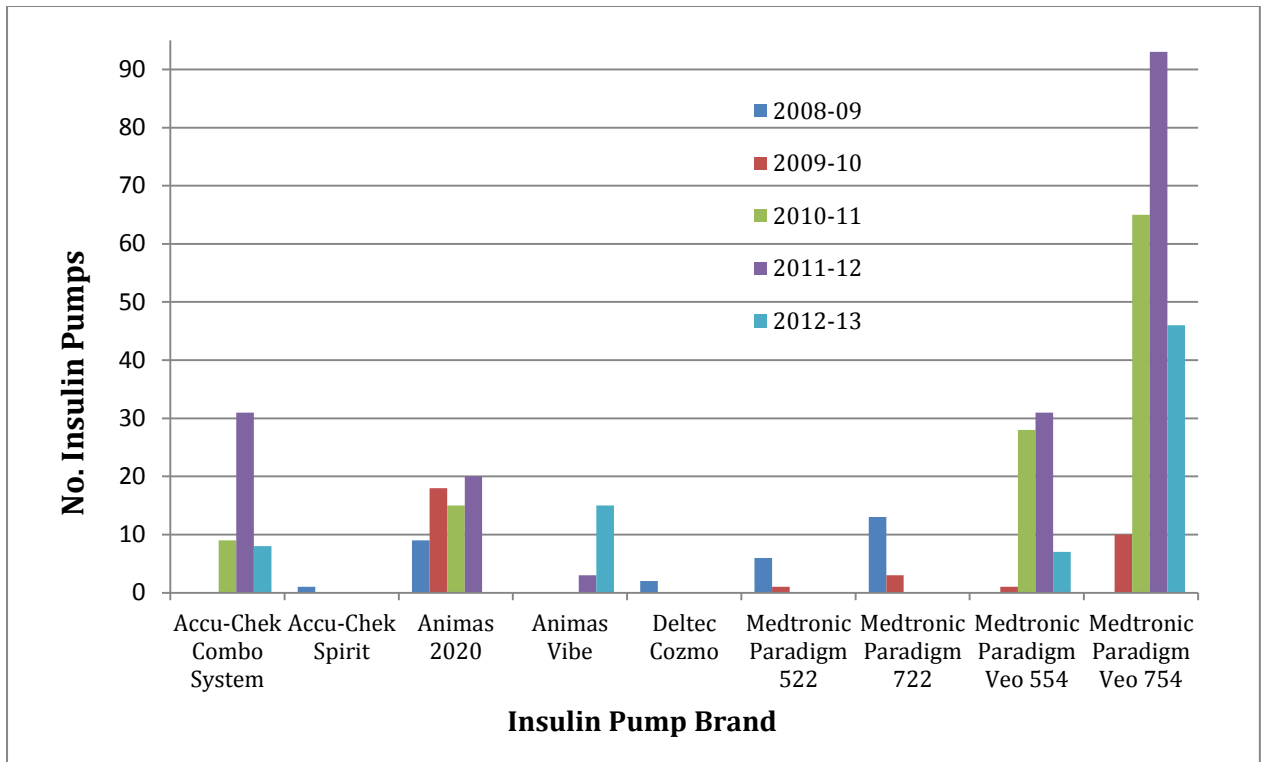
The following figures are derived from the data collected and supplied by JDRF on the Insulin Pump Programme. The data collected includes:

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

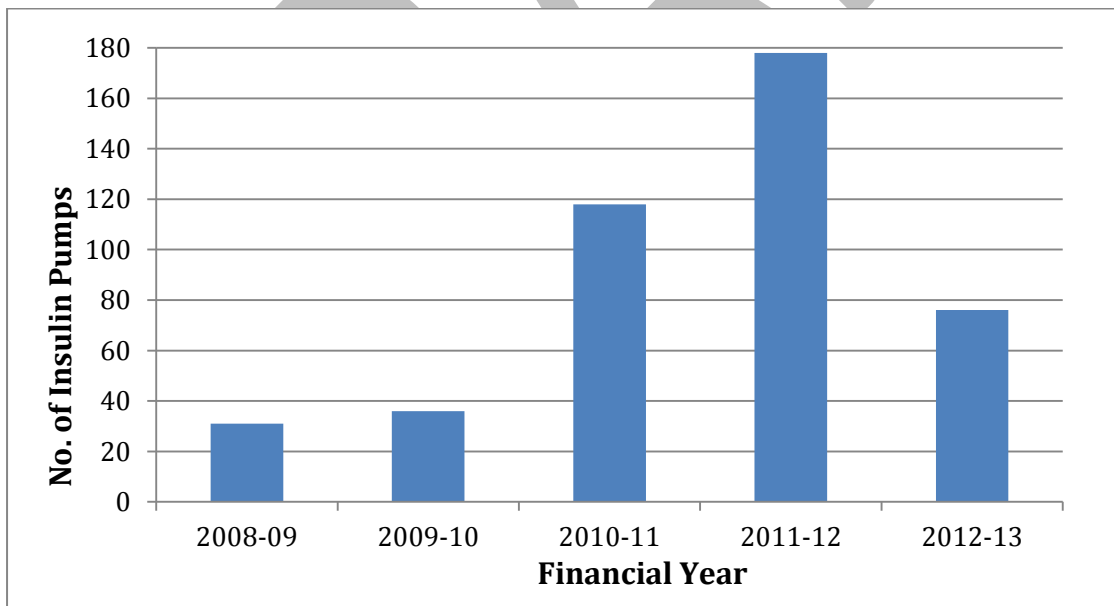
Up to 31 December 2012, 439 insulin pumps had been provided to eligible patients under the Programme (JDRF 2013). [Figure 2](#) shows the number of insulin pumps provided by brand each year under the Programme. The Medtronic Paradigm Veo 754 is the most commonly supplied pump at 47%.

[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](#).

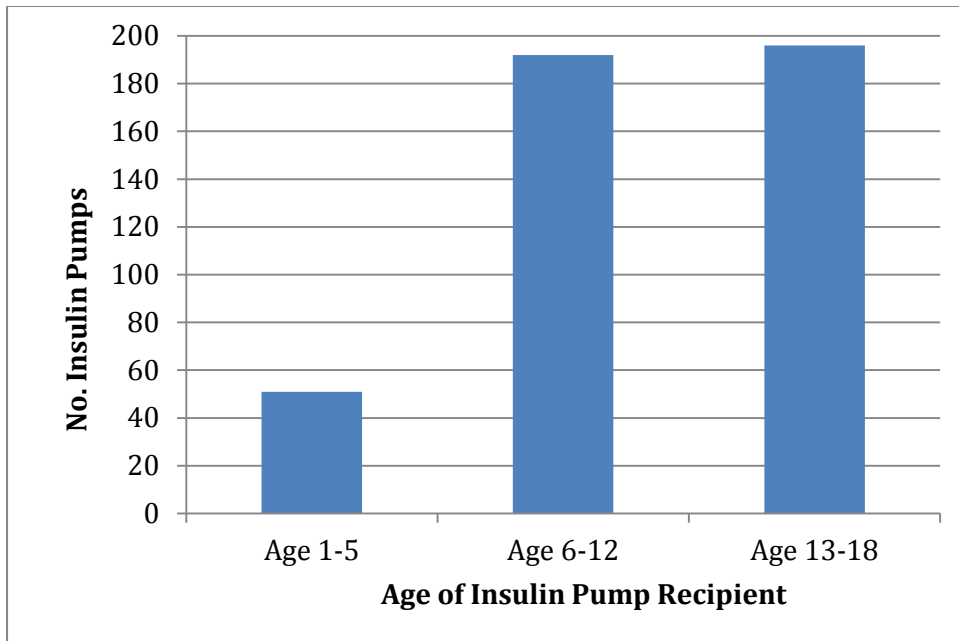
[Figure 4](#) shows the age distribution of insulin pump recipients under the Programme. Further information on the breakdown of insulin pump brand utilisation is detailed in [Appendix C](#).



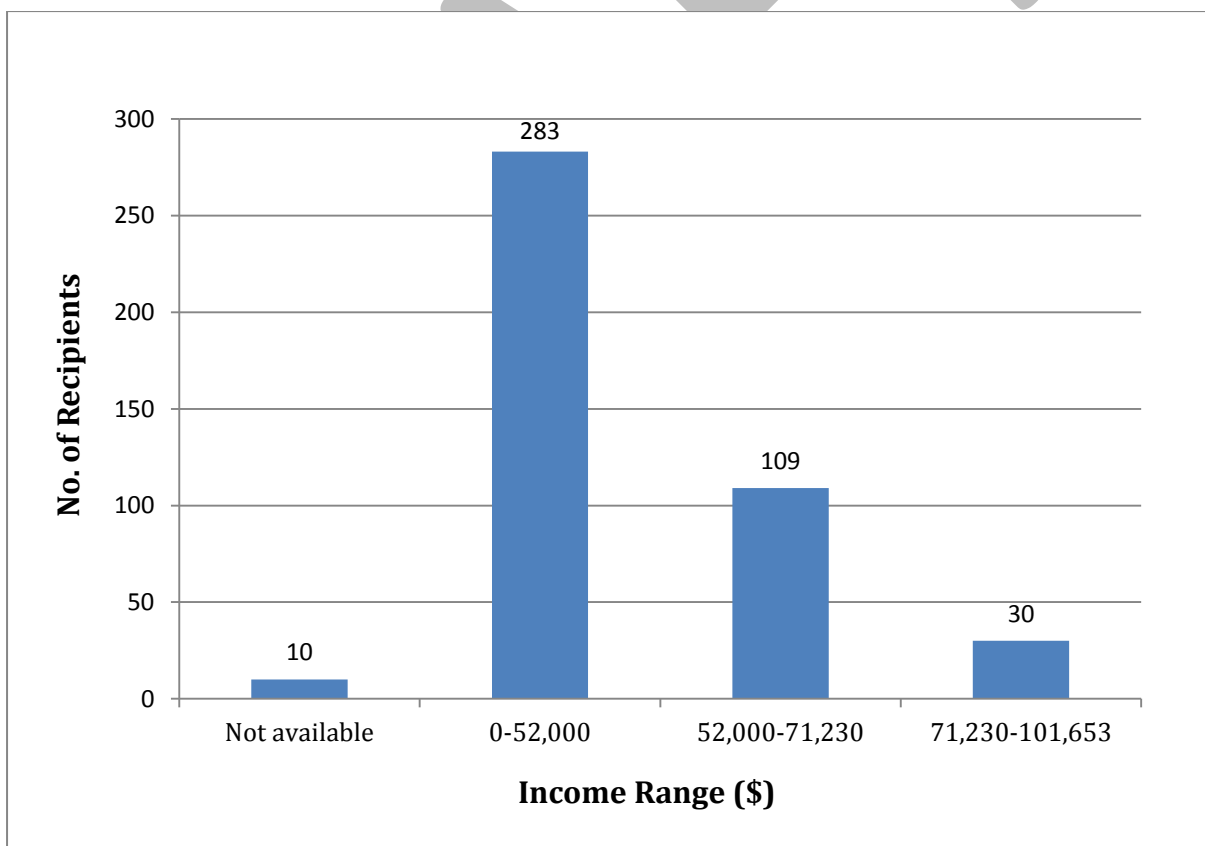
**Figure 2. Number of insulin pumps administered under the Programme by brand and financial year.**



**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.**

## 5.6 Issues identified

### 5.6.1 Patient affordability

Due to 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 effect of subsidy and pump loan schemes (AIHW 2012b).

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

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.

### **5.6.2 Dependency on the Prostheses List**

The Programme 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's increased focus is on assessing new listing 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.

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.

## 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 evidence does not specifically define a particular sub-group in the type 1 diabetes population that receives greater benefit from insulin pump therapy.
- 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***

- With regard to children and adolescents, the Programme's eligibility criteria and the practice points for initiation of insulin pump therapy under the Australian clinical guidelines for type 1 diabetes (Craig *et al.* 2011) are similar and include technological and cognitive capacity to manage use of the pump, and high levels of patient/carer motivation to intensively manage diabetes.
- Most guidelines indicate 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 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 from creating eligibility criteria without strong clinical evidence and that there is insufficient evidence on which to base any additional criteria. APEG advised that, ideally, there would not be age-limits for the Programme.
- Stakeholders were unanimously supportive of the benefits of insulin pump therapy and also recommended expanding the Programme to all ages.

### ***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. This latter group could be problematic because potential behavioural issues may not have been addressed.

### ***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 or 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 waiting list: 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 Internal 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 can access the Programme.
- A number of 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 which method of insulin delivery is superior 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, for those who would benefit most.

The literature reviews of RCTs and observational studies undertaken by the QUMPRC aimed to identify sub-groups who may benefit more 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. The studies generally showed significant decreases in HbA<sub>1c</sub>, though often not of a level considered clinically significant, and lower rates of severe hypoglycaemic events, with insulin pump therapy compared to multiple daily injections in children, adolescents and adults. There was more evidence for reduced rates of severe hypoglycaemia in children and adolescents than adults, due to a larger number of observational studies.

There were no sub-group or sensitivity analyses in the systematic reviews that considered children's characteristics other than age. The search included low health

literacy and low socio-economic status. Two small observational studies suggest that insulin pump therapy may be more beneficial in children under 6 years old (Hughes *et al.* 2012), or when initiated in children under 6 years old (Levy-Shagra *et al.* 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 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 first literature review 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 with a high risk of bias. 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 *et al.* 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 *et al.* 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 *et al.* 2011).

The Victorian CSII Working Party *Guidelines for Continuous Subcutaneous Insulin Infusion (CSII) Pump Therapy* (2009) are centralised around insulin pump therapy rather than type 1 diabetes management as a whole. 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;
- 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 *et al.* 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 *et al.* 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 *et al.* 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**

District Health Boards receive annual funding on a population based formula to subsidise insulin pumps. Funding is distributed at the discretion of the District Health Boards in order of application. There is variability in insulin pump services in different regions as some District Health Boards fund both pumps and consumables, while others fund only pumps. Clinical eligibility is generally determined according to the *NZSSD Position Statement on Insulin Pump Therapy* (2008) (see 6.4.3.2).

### **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 *et al.* 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 Programme (International Diabetes Federation Europe *et al.* 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 Internal Working Group raised the issue of ensuring that Aboriginal and Torres Strait Islander children and adolescents have 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.

#### **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 *et al.* 2011).

The NZSSD position statement (2008) and Australian guidelines (Victorian CSII Working Party 2009, Craig *et al.* 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.

The Programme does not currently subsidise insulin pumps for use during pregnancy or preconception, and as such the literature reviews did not address comparative effectiveness in this sub-group. A Cochrane Review comparing insulin pumps with multiple daily injections for pregnant women with diabetes, based on randomised trial data, found that there was insufficient evidence to say which method is better for the woman or infant (Farrer *et al.* 2011).

Observational studies generally show small numbers of participants and little difference between multiple daily injections and insulin pump therapy on maternal or foetal outcomes (Bruttomesso *et al.* 2011, Chen *et al.* 2007, Chico *et al.* 2010, Gabbe *et al.* 2000). Two studies showed significantly lower HbA<sub>1c</sub> during pregnancy with insulin pump therapy, but this did not translate to significant improvements in maternal or foetal outcomes (Bruttomesso *et al.* 2011, Gabbe *et al.* 2000), while another study found significantly higher rates of maternal DKA and neonatal hypoglycaemia with pump therapy (Chen *et al.* 2007). A recent observational study in 269 pregnant women with type 1 diabetes found that good glycaemic control could be achieved using either therapy and that pregnancy planning was significantly associated with lower HbA<sub>1c</sub> levels, particularly in the first trimester (Cyganek *et al.* 2010).

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.

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## Appendices

### Appendix A - Insulin pumps available under the Protheses List as at February 2014

Model Name/No.	DANA IIS Diabecare 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 Protheses 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 delivery capable of remotely receiving and acting on information about blood glucose levels.	Insulin delivery, automatic adjusting, 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 Protheses 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 Diabecare 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	30 min – 24 hours	30 min – 24 hours	10% - 200% for 30 min – 24 hours
<b>Max # of basal rates programmes / 24 hours</b>	24	24	8	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.	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 additional insulin).

<b>Model Name/No.</b>	<b>DANA IIS Diabecare 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>Additional features</b>	Not available	Blood glucose measurement in remote controller.  Bluetooth communication to Android mobile phone. Can utilise the mobile phone for all pump settings and to discreetly deliver boluses.	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.  Date reminders (e.g. infusion set change) and alarm clock reminders (up to 8 per day).	Activity guard available to protect the pump from disconnecting.  CGM using 6-day disposable sensors connected to transmitter. Transmitter provides readings to pump at 5-minute intervals.	Activity guard available to protect the pump from disconnecting.  CGM using 6-day disposable sensors connected to transmitter. Transmitter provides readings to pump at 5-minute intervals.	High-contrast colour screen.  Trends and rates.  CGM with Animas® Vibe™ is only indicated for patients 18 years or older.
<b>Safety - Maximum Qty delivered at a single fault condition</b>	Yes, customisable for patient doses.	Yes, customisable for patient doses.	≤1.0 units	Maximum Bolus – customisable to 75U. Maximum Basal Rate – customisable. Maximum Delivery Exceeded – to prevent multiple small boluses within one hour.	Maximum Bolus – customisable to 75U. Maximum Basal Rate – customisable. Maximum Delivery Exceeded – to prevent multiple small boluses within one hour.	Maximum prime dose is 20U. Total Daily dose is set by patient. A maximum 2 hour dose limit is set. Bolus & Basal limits are user selected. Response to single fault condition depends on circumstances.
<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.	Child block - disables buttons to prevent accidental delivery. Keypad lock – prevent accidental button pressing.	Child block - disables buttons to prevent accidental delivery. Keypad lock – prevent accidental button pressing.	Tamper resistant "Locked" feature.

Model Name/No.	DANA IIS Diabecare 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>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 blockage in infusion set.</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. *Alerts 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. *Alerts available only with pump and glucose monitor turned on.</p>	<p>High/low blood glucose*.</p>

<b>Model Name/No.</b>	<b>DANA IIS Diabecare 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 faulty. Next day delivery for metropolitan areas. 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. 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. 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>User manuals and handbooks. Quick reference guides. 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. Online learning modules are available for patients.</p>	<p>User manuals are available online. 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>Repair/replace ment policy</b>	<p>Any impact damage may be deemed as negligent and the manufacturer can decline warranty repair.</p>	<p>Any impact damage may be deemed as negligent and the manufacturer can decline warranty repair.</p>	<p>Repair of minor issues, otherwise replacement.</p>	<p>Repair or replace. Does not cover dropping, improper storage or submersion in water.</p>	<p>Repair or replace. Does not cover dropping, improper storage or submersion in water.</p>	<p>Faulty pumps are replaced and not repaired.</p>

<b>Model Name/No.</b>	<b>DANA IIS Diabecare 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>Warranty length</b>	4 years	4 years	4 years	4 years	4 years	4 years
<b>Product Recalls</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.</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>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>Model Name/No.</b>	<b>DANA IIS Diabecare 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>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 remote 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.	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>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

\*Requires use of continuous glucose monitoring.

## Appendix B – Insulin pumps no longer available under the Prostheses List

Pump Sponsor/ Manufacturer	Australasian Medical & Scientific Pty Ltd	Roche Diagnostics Australia Pty Ltd	Medtronic Australasia Pty Ltd	Medtronic Australasia Pty Ltd	Australasian Medical & Scientific Pty Ltd
<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>

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

Reference	Recommendation	Difference
<p>(Craig, Twigg <i>et al.</i> 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> </ul>	<p>Details more specific clinical requirements to Craig <i>et al.</i>, 2011, as well as financial suitability.</p>

Reference	Recommendation	Difference
	<ul style="list-style-type: none"> <li>• Adequate condition of subcutaneous tissue and skin</li> <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>	CSII therapy is associated with modest improvements in glycaemic control and should be considered for patients unable to achieve their glycaemic targets (Grade A)	
	CSII therapy should be considered in patients who experience recurring episodes of severe hypoglycaemia (Grade B)	
(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
<p>(Grunberger, Bailey <i>et al.</i> 2010)  <b>United States</b></p>	<p>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 <math>\geq 4</math> times per day during the previous 2 months. Patient must also meet <math>\geq 1</math> of the following criteria:  - HbA<sub>1c</sub> &gt; 7.0%  - History of recurrent hypoglycaemia  - Wide fluctuations in blood glucose before mealtime  - Dawn phenomenon with fasting plasma glucose concentration frequently &gt; 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 <math>\geq 4</math> times per day during the month before enrolment.</p>	
<p>The New Zealand Society for the Study of Diabetes (NSSD). NSSD Position Statement on Insulin Pump Therapy, June 2008:  <b>New Zealand</b></p>	<p>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:</p> <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> <p>Practice Guidelines:</p> <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>	
<p>Agence d'évaluation des technologies et des modes d'intervention en santé</p>	<p>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</p>	

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 in relation to type 1 diabetes

Title	Publication year	Primary developer	Recommendations in relation to T1DM Or Insulin Pump use	Comparative analysis – quantitative guidelines
<u>Australian Diabetes Society position statement. Individualisation of HbA<sub>1c</sub> targets for adults with diabetes mellitus</u>	2009	Australian Diabetes Society	<p>General target HbA<sub>1c</sub> ≤7.0, based on United Kingdom Prospective Diabetes Study (UKPDS) demonstrated improved outcomes with median HbA<sub>1c</sub> ≤7%, supported by NHMRC systematic review This target will vary with specific clinical situations.</p> <p>Practitioners need to individualise the HbA<sub>1c</sub> target for people with type 2 diabetes, taking into consideration the presence of CVD, diabetes duration, diabetes medication(s) taken, comorbidities, and problems with severe hypoglycaemia. Prevention of hypoglycaemia does not rely purely on adjustment of medication, but also on patient education, including blood glucose monitoring.</p>	General target HbA <sub>1c</sub> ≤7.0 However, HbA <sub>1c</sub> targets however, need to be individualised to a tighter or lesser degree, with a recommended target HbA <sub>1c</sub> level of ≤6.0% in some people, or up to ≤8.0% in others.
<u>Dietary management in diabetes</u>	2010	Collaborating Authors		
<u>Guidelines for the management of diabetic retinopathy</u>	2008	Australian Diabetes Society	The Guidelines recognise that the mainstay of current treatment involves risk factor reduction by controlling blood glucose, blood pressure and serum lipids	
<u>National evidence based clinical care guidelines for type 1 diabetes in children, adolescents and adults</u>	2011	Australasian Paediatric Endocrine Group and Australian Diabetes Society		
<u>Type 1 diabetes in children - emergency management</u>	2010			

<u>Diabetes management in general practice. Guidelines for type 2 diabetes (17th edition) 2011/12</u>	2011	Diabetes Australia		References insulin pumps
<u>Peri-operative diabetes management guidelines</u>	2012	Australian Diabetes Society		References insulin pumps

**Note 1**

**Definition of NHMRC grades of recommendations**

**A** Body of evidence can be trusted to guide practice

**B** Body of evidence can be trusted to guide practice in most situations

**C** Body of evidence provides some support for recommendation(s) but care should be taken in its application

**D** Body of evidence is weak and recommendation must be applied with caution