Diabetes AUSTRALIA

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

Submission to the PBAC Review of Products and Medicines used in the Treatment of Diabetes

Phase 2: Review of the Clinical Benefits of Insulin Pump Therapy for Type 1 Diabetes

From

Diabetes Australia

and the

Juvenile Diabetes Research Foundation

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CONTENTS

Executive Summary

Type 1 diabetes (formerly known as insulin dependent diabetes or juvenile diabetes) is a chronic, autoimmune condition, affecting almost 130,000 Australians. It can be diagnosed at any age, although is most commonly diagnosed in childhood or adolescence. It results from an autoimmune destruction of insulin-producing beta cells in the pancreas and is treated with exogenous insulin. Optimal management of type 1 diabetes is required to reduce the risk of long-term diabetes-related complications (e.g. retinopathy, neuropathy, nephropathy, heart attack, amputations and stroke) and short-term complications (e.g. severe hypoglycaemia, diabetic ketoacidosis).

Insulin pumps are electronic devices, which deliver small amounts of rapid-acting insulin throughout the day, minimising variability in insulin absorption and enabling better matching of insulin to food intake. Consequently, insulin is delivered in a more precise manner (mimicking the body's own insulin production) than that achieved with multiple daily injections (MDI).

Latest official figures indicate that there are 10,510 insulin pump users in Australia (around 10% of people with type 1 diabetes), and this number is growing each year. By comparison, the USA has considerably higher rates of insulin pump therapy (IPT) use, where it is estimated that up to 25% of people with type 1 diabetes use IPT. From 2004 to 2010 in Australia, the number of people commencing IPT increased from 104 per month to 140 per month. In addition, people with type 1 diabetes are commencing IPT sooner after diagnosis. Almost half of insulin pump users are under 25 years old and a disproportionate number live in areas of high socioeconomic status.

There are currently three insulin pumps available to people with diabetes in Australia, the purchase costs of which vary from $9,000 to $9,500. There are also various indirect costs associated with initiation and ongoing pump use. To date, private health insurance has been the major funding source for the purchase of insulin pumps (80% of pumps), which are listed on the prosthesis schedule but this has been threatened by the policies of various insurers.

The Australian Government's Type 1 Diabetes Insulin Pump Program administered by the Juvenile Diabetes Research Foundation (JDRF) provides a means-tested subsidy to assist with the cost of an insulin pump. Since the Insulin Pump Program commenced in 2009, 439 pumps have been supplied with a total expenditure of $2,560,000 for insulin pump subsidies. However, Program funding has been allocated to consumables (already supported by the National Diabetes Services Scheme; NDSS) as well as the costs of the pump, significantly limiting the availability of pumps through the Program. This anomaly needs to be rectified with separate streams of funding, independent of each other.

The Insulin Pump Program is currently available only to people with diabetes under the age of 18 years who meet the eligibility criteria. Thus, 112,578 adults (representing some 87% of all people with type 1 diabetes) are currently excluded from the Program. Furthermore, the current age-based eligibility criteria is not consistent with the evidence of equivalent benefit of pump therapy for adults with type 1 diabetes as for children/adolescents in terms of glycaemic control; for those who experience recurrent severe hypoglycaemia; women with type 1 diabetes

planning for and during pregnancy; and for older people, many of whom may have impaired awareness of hypoglycaemic symptoms.

Summary of evidence

Compared with MDI, the available evidence indicates that IPT:

- is a reliable, safe and valuable management tool for people with diabetes;
- can assist in reducing HbA1c, particularly for those with higher HbA1c using MDI, thus reducing the likelihood of developing long-term diabetes-related complications;
- is associated with a four-fold reduction in frequency of severe hypoglycaemia, thus enabling lower HbA1c to be targeted, and reducing costs associated with ambulance use, emergency department presentations and hospital admissions;
- can reduce fear of hypoglycaemia, diabetes-related distress and depressive symptoms; can increase satisfaction with treatment, and improve health status and quality of life;
- is best supported by a multidisciplinary team;
- requires education and regular follow-up care to ensure the person with diabetes is gaining the most benefit from IPT;
- benefits can be enhanced when it is used in combination with continuous glucose monitoring, i.e. sensor-augmented pump therapy;
- is beneficial to both adults and children with type 1 diabetes, and is of particular benefit to women with type 1 diabetes when planning for and during pregnancy.

Recommendations

Diabetes Australia and the JDRF believe that the Insulin Pump Program can do more to achieve the Government's goal of providing improved diabetes care and outcomes for Australians with type 1 diabetes. Diabetes Australia and the JDRF call for a fully funded and enhanced Insulin Pump Program for Australia with broader access dependent on evidence-based clinical criteria, and make the following recommendations:

- IPT should be made available to people of all ages with type 1 diabetes as an effective tool for the management of this chronic condition;
    - In relation to the Insulin Pump Program, the age-related criterion, which currently defines that only children and adolescents up to 18 years old can access the Insulin Pump Program, needs to be removed on the basis that it is inequitable given current evidence;
- Eligibility for insulin pumps under the Insulin Pump Program should be determined by diabetes specialists in concert with the person with diabetes, on the basis of evidence-based clinical need. In addition to existing criteria, eligibility should be expanded to include the following important groups:

    - People with recurrent severe hypoglycaemia, or
    - Women planning for and during pregnancy, or
    - People with sub-optimal HbA1c, or
    - People with fear of hypoglycaemia, diabetes related distress or ability for IPT to improve their satisfaction with treatment and/or quality of life.
- The current Insulin Pump Program budget as included in forward estimates should be fully applied to support the purchase cost of insulin pumps only, with insulin pump consumables subsidised separately through the NDSS;
- The Insulin Pump Program should provide 100% subsidy to those people in the lowest income bracket (annual income up to $67,389 pa);
- IPT initiation should be supported by an appropriately trained multidisciplinary team, with sufficient funding, staff and resources made available for effective education of the person with diabetes at IPT initiation, as well as for ongoing support and education to maximise the clinical benefits of IPT;
- Every person with diabetes registered with the NDSS to receive subsidised insulin pump consumables should be contacted through the Registrant Support Service program at least once per year to encourage regular review by the diabetes centre to ensure optimal pump use, optimal use of consumables, ongoing education updates and optimal health outcomes.

1. Introduction

1.1 Type 1 diabetes

Type 1 diabetes (formerly known as insulin dependent diabetes or juvenile diabetes) is a chronic, autoimmune condition, affecting almost 130,000 Australians. It can be diagnosed at any age, although is most commonly diagnosed in childhood or adolescence. It results from an autoimmune destruction of insulin-producing beta cells in the pancreas and is treated with exogenous insulin. Each year, 2,100 new cases of type 1 diabetes are diagnosed, half of which are in those aged under 15 years [1, 2]. In the past decade, incidence has increased by 30% [2], at an average rate of 2.8% per year [3].

The long-term complications of type 1 diabetes are devastating, including renal failure, neuropathy and retinopathy. The burden of such complications on the Australian health system is enormous and disproportionate to the prevalence of T1DM. The annual cost of type 1 diabetes is at least $570M [4]. The average annual cost per person with T1DM is AU$4,669 (ranging from $3,468 with no complications to $16,698 for both microvascular and macrovascular complications [4]). Despite type 1 diabetes affecting less than 1% of the general population, its complications alone are responsible for 4% of all ambulatory care or hospital admissions and 5% of all hospital bed days - more than angina or asthma [4].

Acutely, the immediate life-threatening consequences of insulin deficiency are managed with use of exogenous insulin and lifelong, continual attention to blood glucose levels. In 2011, the National Health and Medical Research Council (NHMRC) published Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults [5], which emphasised that achieving excellent glycaemic control is by far the most critical factor in reducing diabetes complications. The risk of these complications increases by about 30% for every 1% increase in glycated haemoglobin (HbA1c; average blood glucose) above 7% [6]. Intensive insulin therapy reduces HbA1c and, thereby, the risk of long-term complications but is associated with a threefold increase in severe hypoglycaemia [6]. Thus, intensive blood glucose management is necessary for long-term health but, unsurprisingly, is difficult to achieve in routine practice.

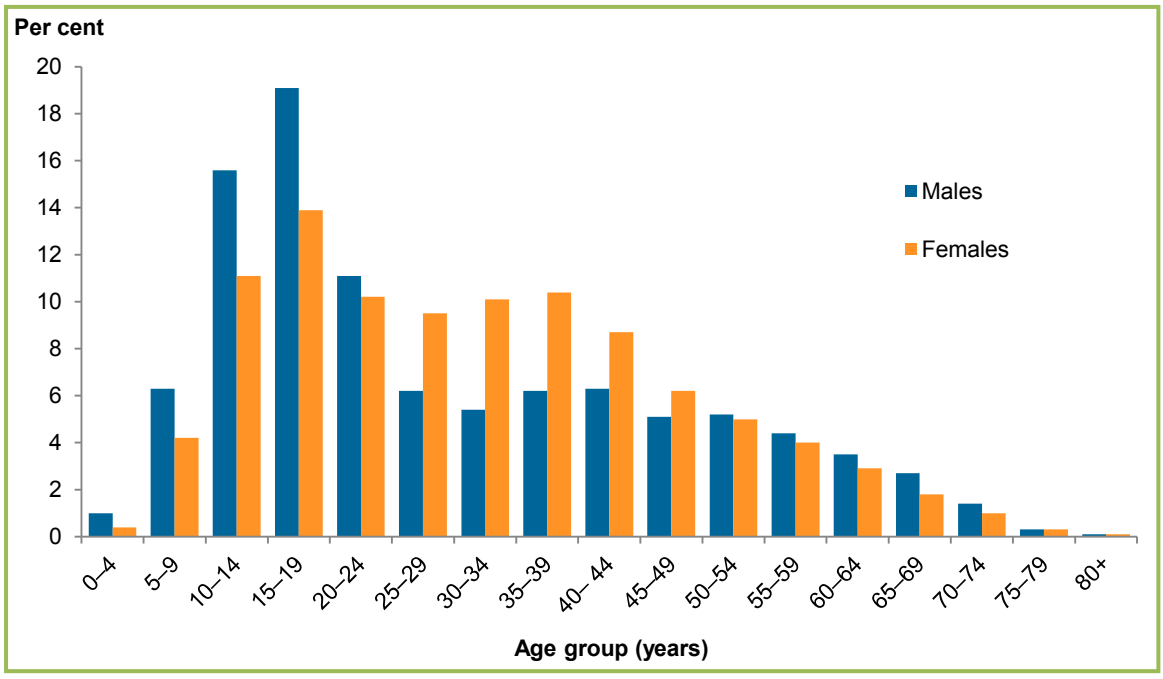
1.2 Insulin pump therapy

Traditionally, type 1 diabetes has been managed with multiple daily injections (MDI) but advances in the past twenty-five years mean that insulin can now be delivered by means of a small electronic device, providing continuous subcutaneous insulin infusion (CSII), also known as an insulin pump. Insulin pumps deliver small amounts of rapid-acting insulin throughout the day (the basal rate). A bolus dose of insulin, programmed by the person with diabetes, is delivered at meal-times and additional boluses can be administered to correct high blood glucose levels. Thus, insulin pump therapy (IPT) delivers insulin in a more precise manner compared with multiple daily injections; there is less variable insulin absorption and the ability to better match insulin to food intake[7]. The initiation of IPT requires extensive training and ongoing support from a multidisciplinary team consisting of an endocrinologist, pump-trained diabetes nurse educator and a dietitian.

1.2.1 Insulin pump therapy in Australia

The Australian Institute for Health and Welfare (2012) report examining insulin pump use among people with type 1 diabetes indicates that, at 30 June 2011, there were 10,510 insulin pump users in Australia (around 10% of people with type 1 diabetes) [8], and this number is growing each year. From 2004 to 2010, people commencing IPT increased from 104 people per month to 140 per month. In addition, people with type 1 diabetes are commencing IPT sooner after diagnosis. In 2009 18% commenced IPT within 2 years of diagnosis as compared with 1% in 1997 [8]. By comparison, the USA has considerably higher rates of insulin pump use where it is estimated that up to 25% of people with type 1 diabetes use IPT [9]. Almost half of Australian insulin pump users are under 25 years old (see Figure 1) [8]. A disproportionate number live in areas of high socioeconomic status [8]. Approximately 80% of insulin pump users obtained a private health insurance rebate for the purchase of their insulin pump [8].

Figure 1: Insulin pump use by age and sex in Australia (Jan 2004 – June 2011)



Source: AIHW. Insulin Pump Use in Australia 2012 [8].

1.2.2 The Type 1 Diabetes Insulin Pump Program

There are currently three insulin pumps available to people with diabetes in Australia, the cost of which vary from $9,000 to $9,500. There are also various indirect costs associated with initiation and ongoing pump use. The Australian Government's Type 1 Diabetes Insulin Pump Program is administered by the Juvenile Diabetes Research Foundation (JDRF). It provides a means-tested subsidy to assist with the cost of an insulin pump. The Insulin Pump Program is currently available only to people with type 1 diabetes under the age of 18 years who meet the eligibility criteria.

Since the Program commenced in 2009, 439 pumps have been supplied with a total expenditure of $2,560,000 for insulin pump subsidies. More than 85% of subsidy recipients had an annual income less than $67,389, with the mean average annual family income being $44,576.

In 2010/11, the Program was not receiving sufficient uptake from the lower income bracket families as the remaining 20% of the cost of the pump was still unaffordable for the majority. As a result, the co-payment initiative was introduced in the 2011/12 financial year with the support of the then Minister for Health and Ageing, where insulin pump manufacturers agreed to provide co-payment support to ensure that the full 100% cost of the pump was provided to those families in the lower income bracket.

Over the period of the Program, 73% of all recipients of the subsidy received the full subsidy amount of $6,400, and had an income below the means testing threshold of $67,389. However, since the establishment of the co-payment initiative, the percentage of families receiving a fully funded pump (80% subsidy plus co-payment support) increased to 86%.

These data reaffirm that families in the lowest income bracket require a 100% subsidy in order to afford an insulin pump, as 20% of the cost of the pump may be too much for such families to afford.

Without a readily accessible and fully funded subsidy program, IPT may be a clinical need but unattainable for many Australians with type 1 diabetes who cannot afford private health insurance.

Unfortunately, Program funding has been allocated to consumables (already supported by the National Diabetes Services Scheme[a]; NDSS) as well as the costs of the pump, significantly limiting the availability of pumps through the Program. This anomaly needs to be rectified with separate streams of funding, independent of each other.

The current age-based eligibility criterion means that 112,578 adults (representing some 87% of all people with type 1 diabetes) [10] are currently excluded from the Program solely on the basis of their age. Furthermore, this criterion is inconsistent with the evidence of equivalent benefit of IPT for adults with type 1 diabetes as for children/adolescents (see Sections 2 – 4) in terms of glycaemic control; for those who experience recurrent severe hypoglycaemia; women with type 1 diabetes planning for and during pregnancy; and for older people, many of whom may have impaired awareness of hypoglycaemia.

In the following pages, this submission refers to the terms of reference of the PBAC review, specifically relating to evidence for the benefits of IPT in type 1 diabetes.

[a] The NDSS is an initiative of the Australian Government administered by Diabetes Australia

2. Clinical indicators and evidence

PBAC term of reference: The clinical outcomes (e.g. HbA1c, 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 particular reference to those under 18 who may be eligible for the Insulin Pump Program which is funded by the Australian Government.

The clinical benefits of IPT have been evaluated in numerous clinical trials and summarised in several reviews and meta-analyses. In our synthesis of the evidence, we have prioritised research published since 2000, focusing on modern insulin pump devices and, in particular, newer forms of the technology, such as sensor-augmented pump therapy (SAPT)[b] and progress towards the closed loop or so-called 'artificial pancreas'. The technological advances in diabetes care are progressing at such a pace that, in the next few years, they have the potential to become more common management tools in Australia. Thus, the evidence relating to SAPT is highly relevant to this review.

2.1 Glycaemic control

Most studies and reviews have focused on the impact of IPT (compared with MDI) on glycaemic control, typically measured by glycated haemoglobin or HbA1c. Other short-term outcomes, severe hypoglycaemia and diabetic ketoacidosis (DKA) also warrant attention.

2.1.1 Glycated haemoglobin (HbA1c)

Glycated haemoglobin is a measure of average blood glucose control over the past 2-3 months and a strong predictor of the risk of developing long-term diabetes-related complications, e.g. retinopathy, neuropathy, nephropathy, cardiovascular disease and stroke. *The risk of these complications increases by about 30% for every 1% increase in glycated haemoglobin (HbA1c; average blood glucose) above 7%* [11].

The 2011 National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults published by the Australian Diabetes Society (ADS) and Australian Paediatric Endocrine Group (APEG) concluded that across all individuals with type 1 diabetes, there is 'Level 1' evidence demonstrating a small but statistically significant reduction in HbA1c with IPT compared with MDI [5].

The 2010 Cochrane review by Misso *et al* reported on the results of 23 randomised studies, seven of which involved children/adolescents while 16 involved adults [12]. Of the 23 studies, 20 reported HbA1c as a primary outcome, 15 of which were parallel of cross-over studies using appropriate statistical rigour. a statistically significant difference between IPT and MDI favouring IPT (weighted mean difference -0.3%); -0.2% for children/adolescents and -0.3% for adults. The authors concluded that there may be benefit to using IPT over MDI for improving HbA1c. This review

[b] i.e. insulin pump combined with continuous glucose monitoring

indicates that the benefits of IPT are at least equivalent if not slightly more favourable for adults with type 1 diabetes compared with children/adolescents.

A meta-analysis by Pickup et al (2008) of studies in children, adolescents and adults reported a significant improvement in HbA1c of -0.62% with IPT compared with MDI [13]. This synthesis of 22 studies (published from 1996-2006) identified that the greatest improvements in HbA1c were observed in real-world clinic-based before/after studies (-0.72%) than in randomised controlled trials (RCTs; -0.21%). Furthermore, the greatest improvement in HbA1c was in those with the highest HbA1c at baseline [13], i.e. those with worse glycaemic control on MDI achieved the greatest benefit in this respect. The authors noted that those in clinic-based before/after studies are more likely to have problematic glycaemic control than those recruited into RCTs.

Interpretation of findings should take into account the baseline HbA1c since floor effects limit improvements in HbA1c. Secondly, if the HbA1c does not improve with use of IPT compared to MDI, it does not mean that the IPT is 'failing' but that other barriers could be the cause of suboptimal HbA1c [13]. Adult pump users who felt 'in control' of their diabetes (high internal locus of control) had lower HbA1c while those attributing control to external factors had higher HbA1c [14].

A meta-analysis by Weissberg-Benchell et al (2003) of studies in children, adolescents and adults concluded that there is a significant improvement in HbA1c when using CSII for over 12 months; with no significant improvement found when the pump was used for less than 12 months [15].

The evidence for improvements in HbA1c with IPT compared with MDI is particularly strong when sensor-augmented pump therapy (SAPT) is used, with reported improvements in HbA1c of 1.21% [16]. The ADS/APEG Guidelines also conclude that studies of SAPT demonstrate greater benefits for HbA1c than MDI [5].

Some studies have shown no significant difference in HbA1c with IPT compared to MDI, but have shown other benefits, such as reduction in severe hypoglycaemic episodes (see Section 2.1.2) and improvements in quality of life and other psychological outcomes (see Section 2.2). Even where small statistically significant improvements in HbA1c are found these are beneficial, and vital in reducing the likelihood of developing long-term diabetes-related complications. Evidence suggests when comparing IPT to MDI, the reductions in HbA1c attributed to IPT can lead to significant savings for the healthcare system due to the reduction in incidence of diabetes-related complications [17].

2.1.2 Severe hypoglycaemia

Another very important marker of glycaemic control is rate of severe hypoglycaemia (or very low blood glucose). Severe hypoglycemia affects approximately 30% of individuals with established type 1 diabetes each year [18]. An internationally agreed definition is that a severe event is one 'requiring assistance of another person to actively administer carbohydrate, glucagon or other resuscitative actions' [19]. Severe hypoglycaemia remains one of the most serious and feared complications of insulin therapy, as it can result in collapse without warning, fits or even sudden death.

Severe hypoglycaaemia is widely regarded as the single greatest limiting factor to achieving optimal diabetes outcomes, as HbA1c goals may be relaxed in order to avoid such events [20].

The Cochrane review by Misso *et al* found that severe hypoglycaemia data had been collected and recorded in different ways in different trials, rendering them data inappropriate for a meta-analysis. However, the authors concluded that IPT "may be better than multiple injections for reducing the incidence of severe hypoglycaemic events" [12].

In their meta-analysis, Pickup et al (2008) found that IPT was associated with a four-fold reduction in the frequency of severe hypoglycaemia (a mean 2.9-fold reduction for RCTs; 4.3-fold for before/after studies) [13]. This finding was despite the mean HbA1c being significantly lower on IPT. Similarly to the finding for HbA1c, the authors demonstrated the greatest reduction in severe hypoglycaemia occurred in those who had the most severe / frequent hypoglycaemia on MDI, those who were older, and those with the longest duration of type 1 diabetes [13]. Tight blood glucose control is known to increase the rate of hypoglycaemia, but this meta-analysis showed no evidence of an increase in hypoglycaemia with improvements in HbA1c. In fact, the improvements in HbA1c were associated with reduced rates of severe hypoglycaemia.

A study by Plotnick et al (2003) specifically compared the effectiveness of IPT versus MDI in children and adolescents and found improvements in rate of severe hypoglycaemic episodes. They investigated 95 children with a mean age of 12 years, who had been using IPT for a median of 28 months. Results showed that there were fewer hypoglycaemic events following commencement of IPT (12 versus 17, rate ratio 0.46, 95% CI 0.21-1.01) [21].

There are also studies that report no significant benefit on occurrence of hypoglycaemic episodes (severe or otherwise). However, most studies are powered only to detect changes in glycaemic control rather than in hypoglycaemic episodes.

Severe hypoglycaemia is associated with serious morbidity, including neurological events (coma, convulsions, and cognitive impairment), cardiac events (arrhythmias, MI) and accidents (fractures, soft-tissue injuries, road accidents). It is difficult to capture what this means in terms of cost, but Frier (2011) reports the costs associated with hypoglycaemia to be a major economic burden on the healthcare system, with the highest proportion of direct costs resulting from the small number of patients admitted [22]. Costs can be directly related to ambulance services, emergency department presentations, hospital admissions, and/or primary care services. By reducing the overall incidence of severe hypoglycaemic events, IPT has the potential to save considerable healthcare costs while improving quality of life for people with diabetes.

2.1.3 Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a serious complication of diabetes and is caused by absolute or relative lack of insulin. As IPT only uses short-acting insulin, i.e. there is no background insulin available, there is a greater risk of DKA if delivery of insulin is compromised.

Reports documenting the development and early use of IPT in the 1980s described an increased incidence of DKA during IPT compared with MDI [23,24]. During a feasibility study of the use of IPT [24], 11 participants who had experienced episodes of DKA over a period of 2.5 years were matched for age, sex and duration of diabetes with 11 who had not developed DKA. No differences were found between groups in terms of any clinical or demographic characteristics, except that those with DKA had significantly fewer year of full time education. Of the psychological variables measured, those who experienced DKA felt less personally in control of their diabetes and attributed more responsibility for their diabetes management to the technology [25]. The authors commented that those who experienced DKA seemed to be "looking for a medical solution to their diabetes" and that "over optimistic expectations [of IPT] may have encouraged patients to assume that less personal responsibility for their diabetes would be required than with injection treatment" [25].

Fortunately, lessons have been learned since these early experiences and clinical criteria for IPT are more appropriate. In our review of the evidence, only two studies of modern IPT were identified (one in adolescents and one in adults) in which DKA was noted, with one event reported in each study [26, 27]. Over a median period of 20.5 months, a clinical audit in a specialist service noted that IPT was associated with a statistically significant reduction in DKA (from 1.8±4.5/year to 0.3±1.1/year; $p<0.05$) [28].

2.1.4 Barriers to better glycaemic control for insulin pump users

Motivation and self-care skills are mediating factors to be taken into account when evaluating the benefits of any therapy. Glycaemic benefits for those using pumps or MDI are likely to be limited by ineffective self-management, and strategies are needed to promote engagement and prolonged motivation [29]. The education received at IPT initiation is intensive but largely focused on the technical skills needed to use the insulin pump, with less attention to matching carbohydrate to insulin doses, and dose adjustment. The 2011 AIHW Insulin Pump Survey found that 72% of respondents had last had contact with a specialist diabetes doctor or educator within the past three months but, for 10%, it had been more than six months [8]. No indication is given in that report of the extent to which people feel well trained in the skills required for optimal insulin pump use to maximise glycaemic benefits. Anecdotally, many insulin pump users seek out further training (e.g. from the OzDAFNE program[c]). Currently, the government subsidises the cost of insulin pumps and consumables (through the Insulin Pump Program (for children / adolescents) and the NDSS). However, there is no subsidy or funding for intensive management support and education for those using IPT.

[c] The Dose Adjustment For Normal Eating (DAFNE) program in Australia is coordinated by Diabetes Australia – Vic. DAFNE is a structured education program for adults with type 1 diabetes, which provides skills-based training enabling a range of benefits, including improved HbA1c, reduced frequency of severe hypoglycaemia, reduced diabetes-related distress and improved quality of life. Over 2,000 adults with type 1 diabetes have been trained in the OzDAFNE. It is not subsidised by the Australian Government, with centres in each state and territory making their own arrangements to fund the program.

2.2 Quality of life and other psychological outcomes

The clinical benefits of IPT are inextricably linked with the individual's treatment preferences, lifestyle, lifestage and with how people use new technologies. If an individual is not satisfied with a given treatment, or finds it impairs their quality of life, it will be more difficult for them to stay motivated, engaged and make optimal use of new devices [30].

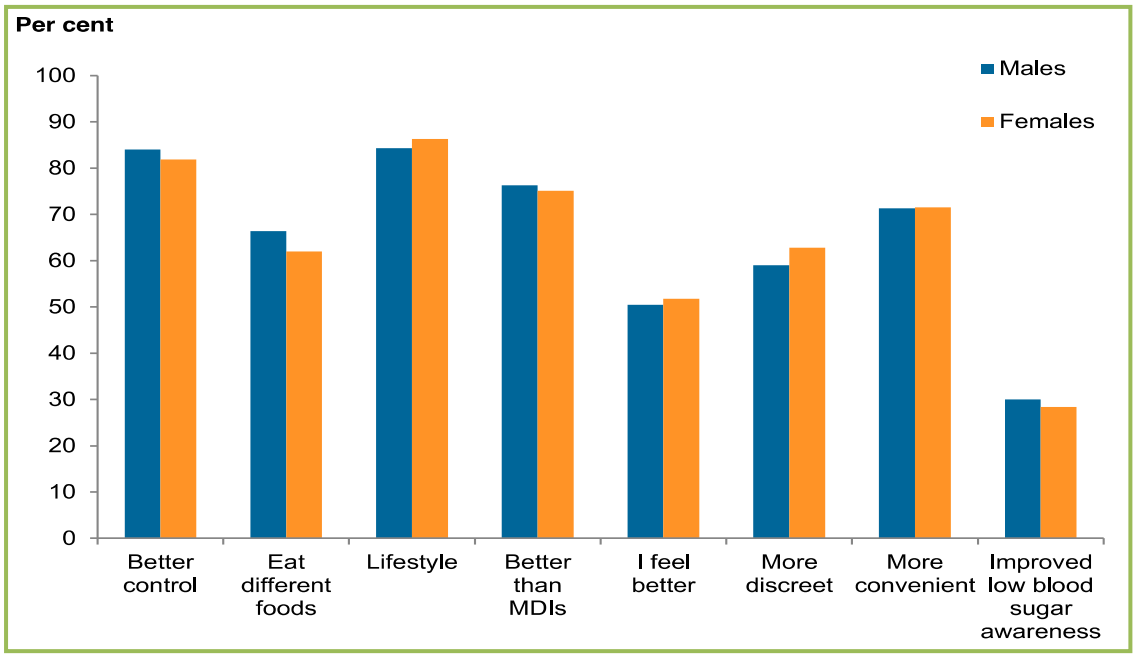
Generally, the findings with regards to the impact of IPT on quality of life (QoL) appear, at face value, less convincing than for biomedical outcomes. However, this is often due to the study design, or the complexity of so-called 'quality of life assessment' - the validity and wide range of assessment tools used [31], and the way in which the concept of QoL is defined is often problematic [32]. For example, the Cochrane review by Misso et al (2010) identified 15 studies using different instruments to assess 'quality of life' and reported that there may be benefit to using IPT over MDI in this respect [33]. The psychological outcomes measured in these studies actually included a range of related but distinct outcomes (i.e. 'treatment satisfaction', 'diabetes-specific quality of life', and 'health status'), and are reported in the sub-sections below. Before reviewing the evidence from clinical trials and observational studies in which validated measures of psychological outcomes have been used, we consider the findings of recent surveys[d].

The benefits of IPT are wide-ranging and numerous, as indicated by broad clinical criteria (see Section 4) and the reports of insulin pump users themselves [8]. Figure 2 (overleaf) shows the benefits of IPT reported by insulin pump users, with an average of five out of eight benefits cited by each of the 5,860 survey respondents [8]. Importantly, at least five of the eight cited benefits relate directly to psychological outcomes, including lifestyle benefits (86%), convenience (71%) and dietary freedom (64%). Importantly, different benefits are associated with different lifestages. For example, 12-24 year olds (the single largest user group by age; Figure 1) are more likely than older adults to highlight 'quality of life' benefits of the pump fitting in with their lifestyle, being discreet and more convenient [8].

These findings are supported by a survey initiated by JDRF in 2010 (and run throughout 2011 and 2012), which quantified the effect of the Insulin Pump Program on subsidy recipients. Pump subsidy recipients answered questions rating the level of change in various lifestyle areas, on a scale from 1 (much worse) to 5 (large improvement). Results from 133 subsidy recipients showed overwhelmingly positive responses, indicating that they experienced significant improvements in their independence and confidence, overall mood, quality of sleep, lifestyle freedom and mealtime flexibility. These are outlined in Figure 3 (overleaf).

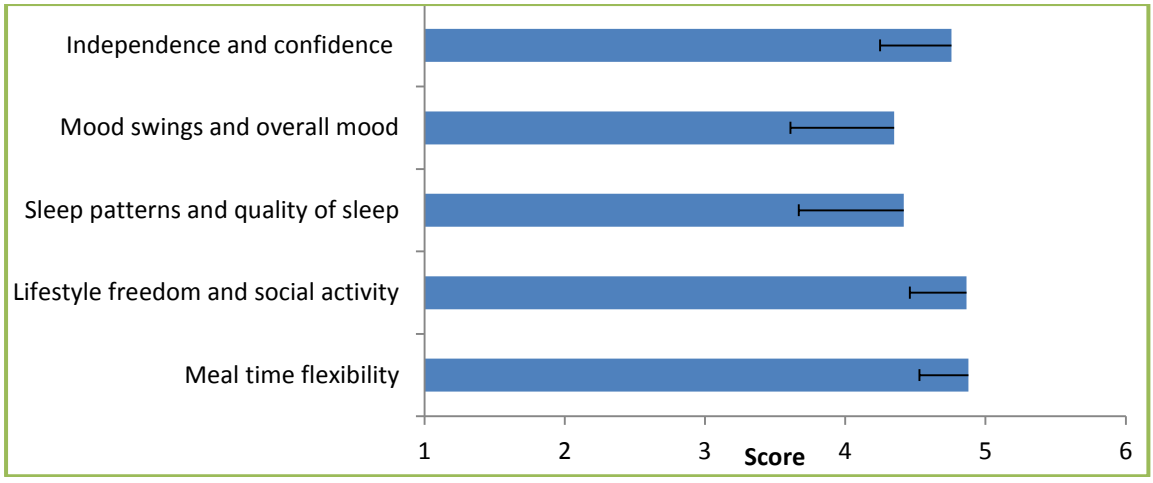
[d] Such surveys typically use unvalidated, study-specific questions but provide a useful overview of the impact of IPT in ways that are important to people with type 1 diabetes and their families.

Figure 2: Benefits of IPT reported by 5,860 insulin pump users by sex



Source: AIHW. Insulin Pump Use in Australia 2012 [8].

Figure 3: Average changes in quality of life since pump usage



Each bar represents the mean±sSD of quality of life measurements from 133 subsidy recipients, where 1=Much worse, 2 slightly worse, 3 no change, 4 some improvement, 5 large improvement

Source: JDRF Insulin Pump Program Quality of life Survey

2.2.1 Fear of hypoglycaemia

It is widely acknowledged that many people with type 1 diabetes live with a fear of hypoglycaemia that is more pervasive than their actual experience of hypoglycaemia and can have significant consequences for their glycaemic control and QoL [34]. Compared to MDI users, adults with type 1 diabetes using IPT were less worried about hypoglycaemia and undertook fewer avoidant behaviours, i.e. actions designed to avoid hypoglycaemia but limiting QoL in other ways [35].

The most recent clinical trials using SAPT demonstrate lower fear of hypoglycaemia among this group compared with MDI [36]. On the other hand, fear of hypoglycaemia might be a barrier for achieving optimal blood glucose levels, and be a reason for suboptimal HbA1c with IPT.

2.2.2 Treatment satisfaction

Overall, insulin pump users are more satisfied with their treatment than MDI users. Higher satisfaction with IPT compared to MDI is consistent in many studies, both in adults [28,35,37,38,39,40] and in children/adolescents [41]. More specifically, satisfaction was significant higher among the IPT compared to MDI in respect to less interference with daily life, less diabetes worries and social burden, higher satisfaction with treatment and clinical efficacy [42]. These findings have also been confirmed in an observational study [35].

In addition, qualitative studies provide an in-depth understanding of why some people prefer MDI or why they do not experience clinical improvement with IPT. Adults with type 1 diabetes who held realistic expectations about IPT and who took an active approach in their self-care management achieved lower HbA1c compared to those who were more passive in regards to their self-care and who perceived the pump as a panacea [43].

In adolescents and adults using IPT, frequent glucose monitoring has been shown to be a prerequisite for improved clinical outcomes [44]; findings that are confirmed in recent trials with SAPT [16,45]. This underlines the impact of the beliefs and behaviours of people with diabetes when comparing treatments. People with diabetes who choose IPT as their preferred treatment are more likely to be satisfied with this treatment than those who preferred MDI [46], and some still prefer MDI over IPT [47].

The beneficial effects of any new technology will be more pronounced when it fits with the person expectations and preferences, and individualized education and support for optimal use of the devices. Weighing the advantages and disadvantages of IPT for diabetes management, and more broadly on lifestyle, is highly idiosyncratic. As people with diabetes tend to have strong preferences about whether to use IPT or MDI, their benefits are best evaluated in preference-based trials (i.e. in which the individual is able to indicate whether or not s/he has a strong preference for a given treatment group [30].

2.2.3 Diabetes-related distress and depression

The most recent clinical trials demonstrate that those using SAPT, compared to MDI, experience less diabetes-related distress [16].

Barnard and colleagues have undertaken a review of the impact of IPT on depressive symptoms, which revealed mixed findings (Prof Jane Speight, personal communication, paper in preparation). Significantly lower depression scores were reported for pump users in three longitudinal studies [48, 49, 50] including one cross-over clinical trial (effect size 0.34-0.73) [50]. Higher depression scores were reported for pump compared to MDI users in the two most recent studies but these were both cross-sectional [51, 52]; although in both studies, symptoms were below a clinically significant threshold for depression. Other cross-sectional studies reported no significant difference. Thus, while the most recent studies demonstrate higher

depressive symptoms for those using IPT or no difference between groups, these are limited by a cross-sectional design. While considerably older, the longitudinal studies provide more robust designs for assessing impact and reveal significant improvements in depressive symptoms.

2.2.4 Health status

General physical and mental health are typically assessed with measures such as the SF-36 and SF-12. Such measures are not specific to diabetes or its treatment. Thus, scores on such measures can be insensitive to the benefits of new treatments and cannot necessarily be expected to improve following a switch to IPT. Two studies have demonstrated improved physical and mental health in the IPT group compared to the injection group [27, 55]. However, these results were not confirmed in other studies using the same measures [38].

2.2.5 Quality of life

As discussed above, it can be difficult to the capture changes in QoL associated with IPT using measures not specifically designed for evaluating new diabetes treatments. As indicated above (see Section 2.2.2), the impact of IPT will largely depend on whether or not the expectations of the users are met. The findings gathered through research using specific methods adapted for evaluating pump therapy are highly consistent.

Both children and their parents, as well as adults with type 1 diabetes. agree that ‘uncontrolled blood glucose’ is one of the main reasons for switching to an insulin pump. When this expectation is met, it will optimize the QoL of the person with diabetes [53].

The first National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes for Children Adolescents and Adults published in 2011 [5] reviewed several studies examining the impact of IPT versus MDI, on general and diabetes-specific. This analysis showed that, on average, there are advantages for pump therapy over the MDI in terms of QoL. Compared to MDI, insulin pump users report better QoL overall [35,54,55]. Reported benefits include greater flexibility of lifestyle (including more variety in food and eating at any time during the day and not eating when one does not wish to do so) 8’[55,56]. It should be noted here that food restrictions are considered by many as one of the most negative consequence of diabetes [53, 57].

These results underline also the benefit for the caregivers. For those close to the person with diabetes, improved health of the person with diabetes and increased flexibility in life style were highly appreciated [56,58]. One study showed increased self-efficacy with diabetes in both the children and their parents [59].

2.3 Specific populations

IPT has proven benefits for people with type 1 diabetes in terms of glycaemic control (see Section 2.1) and psychological outcomes (see Section 2.2). Based on these criteria, there appear to be specific sub-populations that may benefit from use of IPT

(see Sections 2.3.1, 2.3.2, 2.3.3) and also others that warrant consideration here for sake of equity despite a paucity of evidence (see Section 2.3.4 and 2.3.5).

2.3.1 Children and adolescents

Guidelines developed by the Australian Paediatric Endocrine Group (APEG) state that insulin pumps should be considered as a treatment option for children and adolescents with type 1 diabetes [60]. The guidelines also propose that IPT should be initiated and supervised by an expert multidisciplinary team.

Insulin requirements can change rapidly with growth and during puberty when significant insulin resistance may occur. As such, children and adolescents using IPT should have the insulin doses on their pump reviewed and adjusted at regular intervals [60].

Preliminary studies suggest that IPT may be associated with improved behaviour and cognitive performance [61, 62], providing evidence of further benefit particular to this population.

2.3.2 Women planning for and during pregnancy

For women with type 1 diabetes, pregnancy demands careful preconception planning and management throughout gestation. Intensive management is required to achieve and maintain optimal glycaemic management prior to conception in the planning stages of the pregnancy and throughout the duration of the pregnancy. Once pregnant, IPT may help women manage morning sickness and make increasing insulin requirements easier to negotiate.

Evidence from controlled trials demonstrates IPT to be an effective means of managing diabetes during pregnancy, though the authors did not conclude that women using IPT had better diabetes management than women using MDI [63].

There are very few studies of SAPT in pregnant women. Petrowski et al compared women using SAPT continually with those using SAPT intermittently and showed that the former had a lower HbA1c in the first trimester of pregnancy [64].

For women with type 2 diabetes, the optimisation of blood glucose levels before and during pregnancy are as important as in type 1 diabetes, with MDI often used to achieve optimal glycemic control. IPT, however, is not used in Australia for this population, with no reimbursement available for either the pump or consumables. The evidence is limited for the use of IPT in pregnant women with type 2 diabetes. Few clinical trials have been undertaken on the use of IPT in pregnant women with type 2 diabetes, although a study from New Zealand concluded that IPT in pregnant women with gestational diabetes (GDM) or type 2 diabetes is safe and effective [65]. However, improvements in HbA1c were not quantified, the women were primarily of Polynesian or South Asian background, and the data were combined for GDM and type 2 diabetes.

2.3.3 Older adults

For older adults with type 1 diabetes, there is evidence to support IPT may benefit their diabetes management, specifically for those who experience severe hypoglycaemia [66].

2.3.4 Women with gestational diabetes

GDM is a type of diabetes that exists only during pregnancy and is the result of metabolic changes and a reduction in glucose tolerance. Pregnant women undergo an oral glucose tolerance test at approximately 26 weeks of pregnancy to exclude or confirm the development of GDM. If GDM is confirmed, optimisation of blood glucose levels for the remainder of the pregnancy is vital to ensure a successful outcome, as with pregnancies in type 1 and type 2 diabetes. Insulin administration is often required to treat high blood glucose levels.

There is very little evidence available comparing the use of MDI to IPT in GDM. The study by Simmons et al did not differentiate between the women with type 2 diabetes or GDM but concluded that IPT is safe and effective for women with GDM/type 2 diabetes [65]. Although women with GDM are eligible to receive subsidised pump consumables from the NDSS, data from 2012 reveals that no pump consumables were purchased for / by women with GDM [67]. From a practical perspective, this is not surprising considering that diagnosis of GDM occurs more than half way through a pregnancy, and insulin administration is no longer required once the baby is born.

2.3.5 People with type 2 diabetes

Currently, the Insulin Pump Program, NDSS and private health insurance subsidies relating to the purchase of insulin pumps and consumables are all restricted to type 1 diabetes. Historically, type 1 diabetes was the only type of diabetes for which insulin treatment was required, hence it was formerly known as insulin-dependent diabetes. However, since the landmark UK Prospective Diabetes Study demonstrated that intensive treatment (including insulin) could delay or prevent the complications of diabetes [68], insulin use has become a recognised if not clinically preferable treatment option for many people with type 2 diabetes. There are now more people with type 2 diabetes using insulin in Australia than there are with type 1 diabetes (204,188 vs. 128,986) [69].

While studies of IPT in type 2 diabetes are very few, the lack of evidence should not be construed to indicate a lack of benefit in subgroups of this population such as those with longstanding type 2 diabetes and minimal residual islet cell function or those on substantial daily doses of insulin. IPT in people with type 2 diabetes is associated with significantly improved HbA1c and no severe hypoglycaemia [70], as well as significant improvements in several patient-reported outcomes [71].

3. Cost-effective use of different insulin pumps

PBAC term of reference: Investigate the cost-effective use of different insulin pumps available under the Insulin Pump Program.

There are currently three insulin pumps available to people with type 1 diabetes, the cost of which vary from $9,000 to $9,500. No single insulin pump is considered to be better than any other, as each has features and benefits that may suit different individuals. The Insulin Pump Program does not prescribe which pump should be used by the person with diabetes. Insulin pumps available in Australia are selected by a Therapeutic Goods Association approval process. Approved pumps are added to the Private Health Insurance Prosthesis List, which provides rebates for the purchase price of the pump for people with PHI.

Diabetes Australia and the JDRF recommend that the ultimate decision of which insulin pump is chosen should be left to the person with diabetes, in consultation with his/her healthcare team. There is currently little difference in overall cost between insulin pumps but people with diabetes may have clear preferences regarding the features and benefits of the devices that are important to them. Furthermore, the technological advances in this area are so rapid that it would not be sensible to make such recommendations because, for example, the costs change as new technologies come to market. Thus, we recommend that people with diabetes need to be made aware of all the insulin pumps available on the market, with a comprehensive explanation of their features and the benefits of each pump, to assist in the decision-making process.

Program funding has been allocated to consumables (already supported by the National Diabetes Services Scheme; NDSS) as well as the costs of the pump, significantly limiting the availability of funds for pumps through the Program. This anomaly needs to be rectified with separate streams of funding, independent of each other.

4. Clinical criteria and eligibility

PBAC term of reference: Consider the clinical criteria and eligibility under the Insulin Pump Program to ensure those who would most benefit from insulin pump therapy receive support to assist in their care.

In Australia, a person with type 1 diabetes may be considered for a pump by his/her multidisciplinary team (including physician, credentialled diabetes educator - RN, dietitian, and possibly a psychologist) if they meet an extensive set of criteria (see Figure 1). These criteria provide for equitable access based upon clinical need and ensuring the safety and clinical support of the person with diabetes. We would recommend that QoL and related issues are also considered when determining suitability for IPT (see Section 2.2).

Figure 3: Victorian CSII Working Party (2009) criteria to determine suitability for insulin pump therapy

- Person confirmed as having Type I diabetes
- Lifestyle allows for wearing of a pump
- Lifestyle choices to facilitate adequate time for initial stabilization and education
- Person requires less than 300 Units of insulin per 2-3 days
- Consistent home blood glucose monitoring and recording or is willing to increase monitoring (and subsequently demonstrates has done so)
- Ability to measure blood or urine ketone levels
- Basic numeracy
- Willing and able to learn how to count carbohydrates and to calculate doses of insulin
- Willing to communicate on a regular basis with the health care team
- Able to comply with treatment plans or scheduled visits
- 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
- Reasonable level of motivation and able to accept responsibility for care of diabetes
- No significant visual impairment
- No major restriction in manual dexterity, or lack of required assistance
- Adequate condition of subcutaneous tissue and skin
- Satisfactory hygiene
- Funds available to purchase pump and consumables.

Source: Victorian CSII Working Party: *Guidelines for Continuous Subcutaneous Insulin Infusion Pump Therapy* 2009

The government-funded Type 1 Diabetes Insulin Pump Program currently assists Australians with low income to purchase an insulin pump. The program provides a

subsidy of up to 80% of the cost of purchasing an insulin pump. However, *it is only accessible to the family of those under 18 years only in need of financial assistance*. The current Insulin Pump Program [72] outlines the following clinical eligibility criteria:

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

Means testing appears to be an equitable solution for ensuring that those who most need financial assistance receive it. **However, high level evidence indicates that clinical need does not cease at the end of adolescence.** At December 2010, only 116 children with type 1 diabetes had received a subsidy from the Insulin Pump Program [8]. JDRF confirms that as of December 2012 439 pumps and associated consumables have been supplied with a total expenditure of $2,560,000. Of the 5,860 respondents to the 2011 Insulin Pump User Survey (representing 59% of insulin pump users), 88% received some kind of financial assistance (97% of whom received a rebate through private health insurance). However, no information is available concerning the proportion of people who would like to use an insulin pump but do not have the financial means to do so. People without private health insurance and who do not qualify for government subsidy do not have equitable access to IPT, instead relying on opportunistic access through enrolment in clinical trials or donations from charity / fundraising; some people pay the full cost of IPT themselves [8].

Fundamentally, Diabetes Australia and the JDRF believe that **all people with type 1 diabetes, regardless of age, should have equitable access to IPT and that eligibility for the Insulin Pump Program needs to be broadened to include adults, as well as children, with clinical need**

Furthermore, we recommend mandatory annual contact with all people registered to receive NDSS insulin pump consumables subsidy to encourage the registrant to receive follow up care so as to optimise clinical benefit.

5. Summary and recommendations

Summary of evidence

Compared with MDI, the available evidence indicates that IPT:

- is a reliable, safe and valuable management tool for people with diabetes;
- can assist in reducing HbA1c, particularly for those with higher HbA1c using MDI, thus reducing the likelihood of developing long-term diabetes-related complications;
- is associated with a four-fold reduction in frequency of severe hypoglycaemia, thus enabling lower HbA1c to be targeted, and reducing costs associated with ambulance use, emergency department presentations and hospital admissions;
- can reduce fear of hypoglycaemia, diabetes-related distress and depressive symptoms; can increase satisfaction with treatment, and improve health status and quality of life;
- is best supported by a multidisciplinary team;
- requires education and regular follow-up care to ensure the person with diabetes is gaining the most benefit from IPT;
- benefits can be enhanced when it is used in combination with continuous glucose monitoring, i.e. sensor-augmented pump therapy;
- is beneficial to both adults and children with type 1 diabetes, and is of particular benefit to women with type 1 diabetes when planning for and during pregnancy.

Recommendations

Diabetes Australia and the JDRF believe that the Insulin Pump Program can do more to achieve the Government's goal of providing improved diabetes care and outcomes for Australians with type 1 diabetes. Eligibility based on age alone is not evidence-based and is indefensible. However, Program funding has been allocated to consumables (already supported by the National Diabetes Services Scheme; NDSS) as well as the costs of the pump, significantly limiting the availability of pumps through the Program. This anomaly needs to be rectified with separate streams of funding, independent of each other. Diabetes Australia and the JDRF call for a fully funded and enhanced Insulin Pump Program for Australia with broader access dependent on evidence-based clinical criteria.

The choice to use an insulin pump rather than MDI is ultimately the choice of the person with diabetes, in consultation with their medical practitioner, who will take into account their glycaemic control (including frequency of severe hypoglycaemia), and their quality of life (including factors such as body image, dietary freedom, confidence). However, given the costs of insulin pump purchase and consumables, the low uptake (10% among people with type 1 diabetes) and the disproportionate

usage in higher SES areas, Diabetes Australia and the JDRF make the following recommendations:

- IPT should be made available to people of all ages with type 1 diabetes as an effective tool for the management of this chronic condition;
    - In relation to the Insulin Pump Program, the age-related criterion, which currently defines that only children and adolescents up to 18 years old can access the Insulin Pump Program, needs to be removed on the basis that it is inequitable given current evidence;
- Eligibility for insulin pumps under the Insulin Pump Program should be determined by diabetes specialists in concert with the person with diabetes, on the basis of evidence-based clinical need. In addition to existing criteria, eligibility should be expanded to include the following important groups:
    - People with recurrent severe hypoglycaemia, or
    - Women planning for and during pregnancy, or
    - People with sub-optimal HbA1c, or
    - People with fear of hypoglycaemia, diabetes related distress or ability for IPT to improve their satisfaction with treatment and/or quality of life.
- The current Insulin Pump Program budget as included in forward estimates should be fully applied to support the purchase cost of insulin pumps only, with insulin pump consumables subsidised separately through the NDSS;
- The Insulin Pump Program should provide 100% subsidy to those people in the lowest income bracket (annual income up to $67,389 pa).
- IPT initiation should be supported by an appropriately trained multidisciplinary team, with sufficient funding, staff and resources made available for effective education of the person with diabetes at IPT initiation, as well as for ongoing support and education to maximise the clinical benefits of IPT;
- Every person with diabetes registered with the NDSS to receive subsidised insulin pump consumables should be contacted through the Registrant Support Service program at least once per year to encourage regular review by the diabetes centre to ensure optimal pump use, optimal use of consumables, ongoing education updates and optimal health outcomes.

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