SUBMISSION ON THE REVIEW OF INSULIN PUMPS

February 2013

MTAA Medical Technology ASSOCIATION OF AUSTRALIA

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1. EXECUTIVE SUMMARY

The Medical Technology Association of Australia (MTAA) welcomes the opportunity to respond to the Pharmaceutical Benefit Advisory Committee (PBAC) Terms of Reference for the review of diabetes management.

The purpose of this submission is to address the Terms of Reference 8 to 10 relating to the clinical benefits of insulin pump therapy for type 1 diabetes.

MTAA recommends that the use of insulin pumps for children and adolescents with type 1 diabetes remains funded. Insulin pump therapy should continue to be offered as a treatment option to children and adults with type 1 diabetes as part of the treatment and management of diabetes services. There is considerable evidence showing insulin pump therapy is more beneficial and cost-effective in comparison to the multiple daily injections (MDI). These benefits include reduction in the incidence and severity of complications of diabetes, and attaining a better quality of life. Therefore, the use of insulin pumps would lead to substantial cost savings for the Australian Government by reducing the incidence and severity of diabetes-related complications, and hospitalisation costs due to diabetes.

2. ABOUT THE MEDICAL TECHNOLOGY ASSOCIATION OF AUSTRALIA

The Medical Technology Association of Australia (MTAA) represents the manufacturers, exporters, and suppliers of medical technology products in Australia. Medical technology companies manufacture a range of devices that can be used for the treatment and management of diabetes including insulin pumps and continuous glucose monitoring devices with or without real-time capabilities.

3. BACKGROUND

The Australian Government developed the post-market diabetes review program to focus on diabetes management including medicines used in the management of type 2 diabetes, blood glucose test strips and insulin pumps subsidised for use in juveniles with type 1 diabetes.

In 2012, the Pharmaceutical Benefits Advisory Committee (PBAC) agreed to a complete review of diabetes management. The PBAC endorsed the Terms of Reference for the review of diabetes management in August 2012. The purpose of the Terms of Reference is to examine and characterise the complexity and heterogeneity of Pharmaceutical Benefits Scheme (PBS) listings for drugs used in type 2 diabetes and to review self-monitored blood glucose testing for people with type 2 and insulin pumps for people with type 1 diabetes mellitus to inform an assessment of their effectiveness in terms of clinical outcomes and cost.

The purpose of this submission is to address Terms of Reference 8 to 10, relating to the clinical and economic benefits of insulin pump therapy for type 1 diabetes.

Terms of Reference:

8. Determine 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 a particular reference to

those under 18 who may be eligible for the Insulin Pump Program which is funded by the Australian Government.

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

10. 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.

4. DIABETES MELLITUS

Diabetes mellitus is a chronic disease characterised by high glucose levels in the blood that is caused by the inability of the pancreas to produce enough insulin or the body's inability to effectively use the insulin it produces or both. Insulin is a hormone that regulates the body's use of glucose and without insulin, the body cannot use most of the energy in the form of glucose that is obtained from food.

Diabetes, if left untreated or poorly controlled, can lead to a range of complications including coronary heart disease, peripheral vascular disease, stroke, diabetic neuropathy (nerve disease), kidney failure, limb amputations and blindness.[1]

Type 1 and 2 diabetes and gestational diabetes are the main types of diabetes.

- Type 1 diabetes or juvenile-onset diabetes, commonly manifests in children and adolescents and usually accounts for approximately 10% of all cases of diabetes. Although it was previously known as insulin-dependent diabetes, it can occur at any age. This type of diabetes involves immune-mediated destruction of insulin producing cells in the pancreas. Due to the loss of these cells, individuals with type 1 diabetes require external insulin therapy.

- Type 2 diabetes is the most common form of diabetes and accounts for about 90% of the total diabetes population. Individuals with type 2 diabetes are characterised by lack of insulin production or insulin resistance. The risk of developing type 2 diabetes increases with age, obesity and lack of physical activity. Type 2 diabetes usually develops over several years and may remain undiagnosed. Approximately 30% of individuals with type 2 diabetes will eventually require insulin therapy.

- Gestational diabetes is a type of diabetes that may develop in women during pregnancy. It involves increased blood glucose levels during pregnancy in women not previously diagnosed with other forms of diabetes and usually disappears after birth.

4.1 Burden of disease in Australia

According to the 2007–08 National Health Survey, around 900,000 Australians have diabetes (4% of the Australian population).[2] Most have type 2 diabetes (90%). However, the common form in children and adolescents is type 1 diabetes.

According to the National Diabetes Services Scheme (NDSS) in 2010:[3]

- In those aged 30 years and under with diabetes, 79% have type 1 diabetes. The rate of persons with type 1 diabetes was highest in those aged 25–30 (371 per 100,000 persons) followed by those aged 19–24 (351 per 100,000) and 12–18 (339 per 100,000).

- The proportion of persons aged 0–30 years registered with NDSS with type 2 diabetes was lower (19%). The rate of type 2 diabetes rises with age and was highest in those aged 25–30 (197 per 100,000).

For individuals with diabetes, hospitalisation and medical care are often needed, and mortality rate is high.

- In 2009, diabetes was the sixth leading cause of death.[4]

- One in every 25 hospitalisations in Australia is due to diabetes (these were a total of 344,680 hospitalisations for diabetes and diabetes-related diagnosis in 2009).[5]

- Average length of stay (ALOS) in hospitals is longer for principal diagnosis of diabetes and diabetes-related diagnosis compared with all other hospitalisations (4.3 and 8.0 days, respectively, vs 3.1 days).[3]

- Diabetes hospitalisations are mainly due to poor blood glucose control and diabetes-related complications such as renal, eye, neurological and circulatory complications. Diabetes is the leading cause of:
  - non-traumatic lower limb amputation[6]
  - end stage kidney disease[7]
  - eye disease, particularly diabetic retinopathy.[8]

- In people with diabetes, cardiovascular disease is the most common cause of death.[9] The risk to stroke and heart attack is increased in those with diabetes compared to those with normal blood glucose levels.[10]

4.2 Cost of diabetes in Australia

Diabetes places a large economic burden on the Australian healthcare system in terms of expenditure on hospitalisations, aged care, medications, diagnostic services and other out-of-hospital medical care, including General Practioners (GPs) and community health services.[11] Non-health care and indirect costs borne by governments, private health insurers and people with diabetes can also be substantial.

The Australian Institute of Health and Welfare (AIHW) reported the total direct costs of treating diabetes in Australia during 2004–05 were around **$990 million** (approximately 1.9% of all healthcare expenditure).[12]

A recent report on the global health expenditure on diabetes estimated the **total annual Australian healthcare expenditure for diabetes to range between US$4.1 to US$7.7 billion** in 2010, and reach **US$10.9 billion by 2030**.[13]

According to a recent review, DiabCo$t Type 1[14], which described the cost of type 1 diabetes in direct healthcare costs, indirect costs and quality of life (QOL), **hospitalisation accounts for nearly half of the direct healthcare costs (47%) for the treatment and management of diabetes.** In total, insulin, blood glucose testing strips, insulin-administering equipment such as insulin pumps, and pump consumables only account for 18.5% of the overall costs. The study also reported the total average annual cost per person with type 1 diabetes without complications to be around $3468 (2006). However, the average total annual cost

increases to $16,698 (2006) depending on the severity of the diabetes-related complications (i.e. microvascular and macrovascular complications[i]).

5. INSULIN THERAPY FOR DIABETES

Current diabetes treatment is to regulate blood glucose levels using insulin. Insulin therapy mimics the natural function of the pancreas by maintaining a near normal level of blood glucose.

Tight control of blood glucose level (HbA1c) using intensive insulin therapy has been shown to be effective in reducing the risk of complications of diabetes.[15-17] However, only around 50% of Australians with diabetes are reaching the recommended glycaemic target (HbA1c <7%).[18] The individuals not reaching the recommended glycaemic target are likely to have higher risks to developing complications such cardiovascular disease and kidney failure.

During pregnancy, tight glycaemic control is also recommended to avoid maternal, foetal and neonatal complications.[19]

Despite the clinical benefits of intensive insulin therapy, it is however associated with increased risk of hypoglycaemia and glycaemic instability. Hypoglycaemia occurs when blood glucose drops below normal levels, which can cause confusion or fainting. If left untreated, severe hypoglycaemia can lead to seizures, coma and even death.

Several insulin treatment programs are available for individuals with diabetes. The conventional therapy programs for diabetes require injection of insulin once or twice a day with combination of short- and long-acting insulin preparations. Some patients however require intensive insulin therapy using multiple daily injections (MDI), in which insulin is injected three or more times a day or by external continuous subcutaneous insulin infusion (CSII) via pump.

6. INSULIN PUMP THERAPY

Insulin pump therapy is currently the only treatment type that replicates normal insulin secretion by a healthy pancreas, which is especially important for individuals with type 1 diabetes, in which insulin therapy is necessary for their survival.

Insulin pumps are smaller than most mobile phones and worn external to the body, 24 hours a day and can be removed for short periods such as when the person wants to shower or go swimming. Insulin pumps deliver fast-acting insulin continuously through a small needle or cannula inserted and left in place under the skin. The amount of insulin delivered can be determined by the clinician and programmed according to the pump user's needs. Additional doses of insulin (bolus) can be given through the cannula by the pump user at meal times or when their blood glucose level is too high.

6.1 Clinical benefits of insulin pump therapy

There are numerous benefits for individuals with type 1 diabetes of using CSII (insulin pump therapy) compared with MDI. The benefits include reduction in HbA1c, reduction in the frequency of hypoglycaemia, reduction in insulin dosage and glycaemic variability, and improvement in the individual's QOL.[20]

[i] Diabetes microvascular complications include diabetic nephropathy, neuropathy and retinopathy. Diabetes macrovascular complications include coronary artery disease, peripheral arterial disease and stroke.

Children and adolescents with type 1 diabetes

Evidence on the benefits of using CSII compared with MDI includes:

- A systematic review of randomised controlled trials (RCTs) performed by the US Agency for Healthcare Research and Quality (AHRQ)[21] reported on the use of CSII in children with diabetes to be associated with reduced HbA1c, reduced incidence of hypoglycaemia and improved QOL compared with MDI.

- The UK's National Institute for Health and Clinical Excellence (NICE) (2011) reported on the following evidence from a number of sources:[22]
  - 'statistically greater reduction in HbA1c levels following CSII therapy compared with MDI therapy'
  - 'statistically significant fewer episodes of severe hypoglycaemia with CSII therapy compared with MDI therapy'
  - Large quantity of evidence from observational trials in children and adolescents 'showed significant and larger benefits from the initiation of CSII therapy...observational studies would more closely resemble the population in routine clinical practice that would be considered as likely candidates for CSII therapy. In addition these studies included a larger number of people and ran over longer periods of time.' NICE concluded that it was appropriate to use evidence from observational studies as well as from the RCTs to inform its decision.

- The National Health and Medical Research Council (NHMRC) reported 'some advantage for CSII over MDI in terms of HbA1c levels, especially in the paediatric population, and QOL for many people receiving CSII compared with MDI'.[23]

- Pankowska et al. (2009)[24] performed a meta-analysis and systematic review of six RCTs involving 165 children with type 1 diabetes. The study results showed that the CSII group compared with the MDI group experienced a significant reduction in the level of HbA1c.

- Jeitler et al. (2008)[25], performed a systematic review and meta-analysis on 22 RCTs, showed CSII therapy in adolescents with type 1 diabetes resulted in a greater reduction of HbA1c.

- Misso et al. (2010)[26], a Cochrane review of 23 RCTs, found CSII to be better than MDI in reducing HbA1c levels and incidence of severe hypoglycaemic events. QOL measures were also better with CSII over MDI.

- A meta-analysis by Fatourechi et al. (2009)[27] demonstrated some evidence for a reduction in severe hypoglycaemia with CSII.

- Pickup and Sutton (2008)[28] conducted a meta-analysis of 22 studies comparing severe hypoglycemia and glycaemic control in children and adolescents on CSII or MDI. The rate of severe hypoglycemia in type 1 diabetes was markedly less during CSII than MDI. The greatest reduction was in those with most severe hypoglycemia.

- An HTA review conducted by Colquitt et al. (2004)[29], which included 20 studies comparing CSII with MDI, found some evidence of lower HbA1c and insulin dose in adolescents with CSII.

- Many studies have found statistically significant improvement in the QOL of children and adolescents using CSII compared with MDI.[30, 31] The improved QOL outcomes included

avoidance of the fear of hypoglycaemia, reduced incidence of depression and avoidance of cognitive impairment in children. Fox et al. (2005)[32] measured diabetes-related QOL separately in mothers and fathers, with mothers of children on MDI reporting a greater negative impact of diabetes on family life, and fathers in the MDI group reporting significantly higher scores on the stress index.

Adults with type 1 diabetes

Evidence on the benefits of using CSII compared with MDI includes:

- According to a systematic review by AHRQ 'CSII is superior to MDI in lowering HbA1c in adults with type 1 diabetes.....adults with type 1 diabetes treated with CSII reported better overall QOL than those treated with MDI'.[21] The review also found evidence on tighter glycaemic control in adults with type 1 diabetes using CSII compared to MDI. These include:
  - Reduction in HbA1c levels
  - Reduced daily mean blood glucose levels
  - Decreased glucose variability
  - Fewer episodes of severe hypoglycaemia
  - Improvement in general and diabetes-specific QOL measures.

- Jeitler et al. (2008)[25] examined HbA1c as a primary outcome measure by reviewing six RCTs of CSII pumps compared to MDI for use among adults with type 1 diabetes. The authors found the between-treatment difference in HbA1c levels in favour of CSII pumps. Total insulin requirements were found to be lower with CSII pump treatment than MDI therapy.

- Fatourechi et al. (2009)[27] concluded that CSII pumps slightly reduced HbA1c levels compared with MDI.

- Four RCTs also reported CSII as compared with MDI in adults with type 1 diabetes, provides the following clinical benefits:[33-36]
  - Reduction in HbA1c levels
  - Reduction in glucose variability
  - Less frequent episodes of hypoglycaemic events
  - Improvement in QOL outcomes
  - Lower insulin requirements
  - Minimal or no adverse events.

Adults with type 2 diabetes

Only a few studies have assessed the comparative effectiveness of CSII versus MDI in individuals with type 2 diabetes. There is some evidence that CSII compared with MDI reduces HbA1c.[37, 38]

Reviews by UK's NICE, Ontario Health and US' AHRQ also reported on the few studies showing the comparative effectiveness of CSII compared with MDI and found that no clear conclusions could be deduced from the current available evidence.[21, 22, 39] These reviews also strongly recommended future research to show better comparisons between CSII and MDI in adults with type 2 diabetes.

Pregnant women with gestational diabetes

There are few studies that have compared CSII with MDI in pregnant women with gestational diabetes.[21,22,39]

According to AHRQ, there is 'a need for more RCTs on CSII versus MDI in pregnant women with gestational diabetes'.[21]

6.2 Economic value and cost-effectiveness

Multiple studies have shown insulin pump therapy to be cost-effective compared to MDI therapy, where the costs per quality-adjusted-life-years (QALY) ranged from US$16,992 for the US to £34,330 for the UK.[40]

An Australian study reported the incremental cost effectiveness ratio (ICER) of insulin pump therapy compared to MDI therapy to be around $74,147 per QALY and $74,661 per QALY for adults and adolescents with type 1 diabetes, respectively. Thus suggesting that the use of CSII is 'good value for money' in Australia.[41]

Most cost analyses support the assumption that initiating insulin pump therapy is more expensive than MDI. However, the benefits of insulin pump therapy such as improving glycaemic control and prevention of complications (one of the main cost drivers for diabetes is the cost of hospitalisation) can lower long-term costs.

- A study by Lynch et al. (2010)[42] showed that the number of emergency department visits and inpatient hospital admissions decreased after using an insulin pump.

- The AIHW Insulin Pump Survey[43] found that the proportion of insulin pump users (23%) who required a hospital visit in a year was less than those who were not using a pump (28%).

6.3 Other benefits

Benefits of pump use according to pump users

According to the AIHW Insulin Pump User Survey[43], of 5,860 respondents:
- The main factors for choosing to use a pump include better control of diabetes (88%) and the prevention of long-term complications (66%)
- Insulin pump therapy fitted in with the lifestyle of the user (86%).

Advancement in insulin therapy for diabetes management

Recent studies have shown that there are many advantages in using an insulin pump linked to a continuous glucose monitoring (CGM) system (these are also known as sensor-augmented pumps) compared to the use of the conventional insulin pump alone. These include:[44-52]
- Alarming the patient regarding rate of change of glucose concentrations (i.e. alarms for impending or actual hypoglycaemia and hyperglycaemia)
- Highly significant reduction in HbA1c levels
- Hyperglycaemia episodes were less in the sensor-augmented pump group than the MDI/self-monitoring blood glucose (SMBG) intervention group
- Weight gain (a side effect of insulin therapy) was less in the group using a sensor-augmented pump compared to the group using MDI/SMBG

- User acceptance and overall diabetes treatment satisfaction were greater in the sensor-augmented pump group than the MDI/SMBG group.

In addition, data from most current insulin pumps can be downloaded and shared between the person with type 1 diabetes and their healthcare team, which allows easier management of diabetes (during overnight) for patients especially children and adolescents.

7. ACCESSIBILITY AND UTILISATION OF INSULIN PUMPS IN AUSTRALIA

7.1 Accessibility to insulin pumps

From February 2010, funding from the Australian Government Type 1 Diabetes Insulin Pump Program[53], was raised from $2,500 to $6,400 (or 80% of the pump price) and made available to applicants under the age of 18 years who have an annual family income of less than $69,496 or receive income support payments from Centrelink. Some assistance with the 20% co-payment is available for applicants that qualify for the full 80% subsidy.

The level of the subsidy operates on a sliding scale, gradually reducing to $500 or 10% of the pump cost (whichever is greater), for a family with an annual income of $101,458.

According to the AIHW report on insulin pumps:[43]
- Majority of insulin pump users (89%) received financial assistance for the purchase of their pump, with almost all of these obtaining a private health insurance rebate (97%)
- Insulin pump use was more common among people with type 1 diabetes living in areas of high socioeconomic status (14%) than among those in low socioeconomic status areas (6%).

For people with diabetes who are not eligible to receive funding under the Program, only those with private health insurance and appropriate cover are able to access the benefit covering the cost of insulin pumps.

In rare cases, people with diabetes who do not have private health insurance and do not qualify for a government subsidy, may be able to obtain a pump through enrolment in clinical trials or donations from charitable organisations. Some people cover the entire cost of the pump out-of-pocket.

7.2 Utilisation of insulin pumps in Australia

As of 30 June 2011, there were 10,510 insulin pump users in Australia (representing 10% of people with type 1 diabetes).[43]

Since the inclusion of insulin pump consumables on the NDSS[54] in September 2004, there was a slight growth in the use of insulin pumps in Australia. However, the proportion of Australians with type 1 diabetes who use insulin pumps (around 10% in 2011) is still below the NICE recommendations of 12% of individuals with type 1 diabetes.[55]

8. RECOMMENDATIONS FOR INSULIN PUMP USE

8.1 In Australia

The recent NHMRC National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults recommended that '**insulin pump therapy should be**

considered for use in individuals in whom the expected magnitude of benefit is clinically significant in terms of reducing HbA1c, reducing hypoglycaemia, or improving quality of life'.[23]

8.2 Other recommendations

The UK's NICE recommends insulin pump therapy as a treatment option for patients with type 1 diabetes:[22]

- For children (under 12 years), if 'MDI therapy is considered to be impractical or inappropriate'.

- For adults and children (12 years and over), if 'attempts to achieve target HbA1c levels with MDIs result in the person experiencing disabling hypoglycaemia' or 'HbA1c levels have remained high (that is, at 8.5% or above)'.

The European Society for Paediatric Endocrinology/Lawson Wilkins Pediatric Endocrine Society/International Society for Pediatric and Adolescent Diabetes made recommendations regarding the use of insulin pump therapy in children with diabetes. These recommendations are endorsed by the American Diabetes Association and the European Association for the Study of Diabetes.[56] The recommendations include:

- CSII should be considered for individuals with diabetes who have these conditions:
  - Recurrent severe hypoglycemia
  - Wide fluctuations in blood glucose levels regardless of HbA1C
  - Suboptimal diabetes control (i.e. HbA1C exceeds target range for age)
  - Microvascular complications and/or risk factors for macrovascular complications
  - Good metabolic control but insulin regimen that compromises lifestyle.

- Other circumstances in which CSII may be beneficial include:
  - Young children (especially infants and neonates)
  - Adolescents with eating disorders
  - Children and adolescents with a pronounced 'dawn phenomenon'
  - Children with needle phobia
  - Pregnant adolescents, ideally preconception
  - Competitive athletes.

9. CONCLUSION

Insulin pump therapy should continue to be available to children and adults with type 1 diabetes as recommended by their endocrinologist, as part of the treatment and management of diabetes services. Most recent studies have shown that insulin pump therapy is a more beneficial and more cost-effective treatment method in comparison to MDI.

With around half of Australians with diabetes unable to attain the normal glycaemic target (i.e. HbA1c<7%), this means that there are around half a million Australians with diabetes (or 50,000 people with type 1 diabetes) who do not have blood glucose levels within the target and who are at higher risk of developing diabetes-related complications. Use of insulin pump therapy would lead to substantial cost savings for the Australian Government and healthcare system by reducing the incidence and severity of diabetes-related complications (where hospital costs for diabetes and diabetes-related complications accounts for 50% of overall healthcare expenditure for diabetes).

The use of insulin pumps for diabetes treatment and management has great potential to improve patient compliance, quality of life and provide better health outcomes for Australians with diabetes. Furthermore, use of insulin pumps with CGM is especially clinically beneficial for people with diabetes living in rural and regional locations.

MTAA agrees with the recommendations made by NHMRC and other reviews (e.g. NICE) relating to the benefits of using insulin pumps for children and adults with type 1 diabetes. MTAA also agrees with NICE relating to the large quantity of evidence from observational trials in children and adolescents showing significant and larger clinical benefits from the initiation of insulin pump (CSII) therapy.

Based on the large amount of evidence showing the many benefits to using insulin pumps, MTAA recommends that the use of insulin pumps for children and adolescents with type 1 diabetes remains funded, and that there is some subsidy for the use of insulin pumps for adults with diabetes with one of these conditions:

- Individuals with poorly controlled blood glucose levels
- Individuals with severe hypoglycaemia who suffer frequent episodes
- Individuals who live in rural and remote regions (via remote monitoring using insulin pump/CGM system)
- Pregnant women who require tight glucose control with respect to the outcome of pregnancy.

REFERENCES

1. Ceriello A and Colagiuri S. International Diabetes Federation guideline for management of postmeal glucose: A review of recommendations. Diabetic Medicine. 2008. 25(10): 1151–1156.

2. Australian Institute of Health and Welfare. Diabetes. Available at: http://www.aihw.gov.au/diabetes/. Accessed on February 1, 2013.

3. Australian Institute of Health and Welfare 2012. Diabetes among young Australians. Diabetes Series no. 18. Cat. no. CVD 59. Canberra: AIHW.

4. Australian Bureau of Statistics. Diabetes in Australia: A Snapshot, 2007-08. 2011. ABS cat no. 4820.0. Available at: http://www.abs.gov.au/ausstats/abs@.nsf/mf/4820.0.55.001. Accessed on February 1, 2013.

5. Australian Bureau of Statistics. Australian Health Survey: First Results, 2011-12. 2012. ABS. cat no. 4364.0. Available at: http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4364.0.55.001main+features12011-12. Accessed on February 1, 2013.

6. The Global Lower Extremity Amputation Study Group. Epidemiology of lower extremity amputation in centres in Europe, North America and East Asia. British Journal of Surgical. 2000. 87(3): 328-337.

7. Australia & New Zealand Dialysis & Transport Registry: Annual Reports. Available at: http://www.anzdata.org.au/v1/annual_reports_download.html. Accessed on February 8, 2013.

8. Tapp RJ, Shaw JE, Harper CA, de Courten MP, Balkau B, McCarty DJ, Taylor HR, Welborn TA, Zimmet PZ. The prevalence of and factors associated with diabetic retinopathy in the Australian population. Diabetes Care. 2003. 26(6):1731-1737.

9. Australian Institute of Health and Welfare. Diabetes deaths. Available at: http://www.aihw.gov.au/diabetes-indicators/deaths/. Accessed on February 1, 2013.

10. Barr EL, Zimmet PZ, Welborn TA, Jolley D, Magliano DJ, Dunstan DW, Cameron AJ, Dwyer T, Taylor HR, Tonkin AM, Wong TY, McNeil J, Shaw JE. Risk of cardiovascular and all-cause mortality in individuals with diabetes mellitus, impaired fasting glucose, and impaired glucose tolerance: the Australian Diabetes, Obesity, and Lifestyle Study (AusDiab). Circulation. 2007. 116(2):151-157.

11. Australian Institute of Health and Welfare: Dixon T 2005. Costs of diabetes in Australia, 2000–01. Bulletin No. 26. Cat. no. AUS 59. Canberra: AIHW.

12. Australian Institute of Health and Welfare. Diabetes: Australian Facts 2008. Diabetes Series no. 8. Cat. no. CVD 40. Canberra: AIHW.

13. Zhang P, Zhang X, Brown J, Vistisen D, Sicree R, Shaw J, Nichols G. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Research and Clinical Practice. 2010. 87(3):293-301.

14. Colagiuri S, Brnabic A, Gomez M, Fitzgerald B, Buckley A, Colagiuri R. 2009. DiabCo$t Australia Type 1: Assessing the burden of Type 1 Diabetes in Australia. Canberra: Diabetes Australia.

15. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. New England Journal of Medicine. 2005. 353(25):2643-2653.

16. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). Guidelines on diabetes, pre-diabetes, and cardiovascular diseases. European Heart Journal. 2007. 28(1):88-136.

17. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus. Endocrine Practice. 2007. 13 (Suppl 1):1-68.

18. The Mapping Glycaemic Control Across Australia (MGCAA) project. Available at: www.glycomate.com/changingdiabetes/. Accessed on February 1, 2013.

19. Kitzmiller JL, Block JM, Brown FM, Catalano PM, Conway DL, Coustan DR, Gunderson EP, Herman WH, Hoffman LD, Inturrisi M, Jovanovic LB, Kjos SI, Knopp RH, Montoro MN, Ogata ES, Paramsothy P, Reader DM, Rosenn BM, Thomas AM, Kirkman MS. Managing preexisting diabetes for pregnancy: summary of evidence and consensus recommendations for care. Diabetes Care. 2008. 31(5):1060-1079.

20. Cummins E, Royle P, Snaith A, Greene A, Robertson L, McIntyre L, Waugh N. Clinical effectiveness and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes: systematic review and economic evaluation. Health Technology Assessment. 2010. 14(11):iii-iv, xi-xvi, 1-181.

21. Agency for Healthcare Research and Quantity. Methods for Insulin Delivery and Glucose Monitoring: A Comparative Effectiveness Review, July 2012. Available at: http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=749. Accessed on February 6, 2013.

22. National Institute for Health and Clinical Excellence. Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus. NICE technology appraisal guidance 151. 2011. Available at: http://guidance.nice.org.uk/TA151. Accessed on February 6, 2013.

23. Craig ME, Twigg SM, Donaghue KC, Cheung NW, Cameron FJ, Conn J, Jenkins AJ, Silink M, for the Australian Type 1 Diabetes Guidelines Expert Advisory Group. National evidence-based clinical care guidelines for type 1 diabetes in children, adolescents and adults, Australian Government Department of Health and Ageing, Canberra 2011. Available at: http://www.apeg.org.au/portals/0/guidelines1.pdf. Accessed on February 6, 2013.

24. Pańkowska E, Błazik M, Dziechciarz P, Szypowska A, Szajewska H. Continuous subcutaneous insulin infusion vs. multiple daily injections in children with type 1 diabetes: a systematic review and meta-analysis of randomized control trials. Pediatric Diabetes. 2009.10(1):52-58.

25. Jeitler K, Horvath K, Berghold A, Gratzer TW, Neeser K, Pieber TR, Siebenhofer A. Continuous subcutaneous insulin infusion versus multiple daily insulin injections in patients with diabetes mellitus: systematic review and meta-analysis. Diabetologia. 2008. 51(6):941-951.

26. Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J. Continuous subcutaneous insulin infusion (CSII) versus multiple insulin injections for type 1 diabetes mellitus. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD005103. DOI: 10.1002/14651858.CD005103.pub2.

27. Fatourechi MM, Kudva YC, Murad MH, Elamin MB, Tabini CC, Montori VM. Clinical review: Hypoglycemia with intensive insulin therapy: a systematic review and meta-analyses of randomized trials of continuous subcutaneous insulin infusion versus multiple daily injections. Journal of Clinical Endocrinology and Metabolism. 2009. 94(3):729-740.

28. Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in Type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabetic Medicine. 2008. 25(7):765-774.

29. Colquitt JL, Green C, Sidhu MK, Hartwell D, Waugh N. Clinical and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes. Health Technology Assessment. 2004. 8(43):iii, 1-171.

30. Weintrob N, Schechter A, Benzaquen H, Shalitin S, Lilos P, Galatzer A, Phillip M. Glycemic patterns detected by continuous subcutaneous glucose sensing in children and adolescents with type 1 diabetes mellitus treated by multiple daily injections vs continuous subcutaneous insulin infusion. Archives of Pediatrics and Adolescent Medicine. 2004. 158(7):677-684.

31. Wilson DM, Buckingham BA, Kunselman EL, Sullivan MM, Paguntalan HU, Gitelman SE. A two-center randomized controlled feasibility trial of insulin pump therapy in young children with diabetes. Diabetes Care. 2005. 28(1):15-19.

32. Fox LA, Buckloh LM, Smith SD, Wysocki T, Mauras N. A randomized controlled trial of insulin pump therapy in young children with type 1 diabetes. Diabetes Care. 2005. 28(6):1277-1281.

33. DeVries JH, Snoek FJ, Kostense PJ, Masurel N, Heine RJ. Dutch Insulin Pump Study Group. A randomized trial of continuous subcutaneous insulin infusion and intensive injection therapy in type 1 diabetes for patients with long-standing poor glycemic control. Diabetes Care. 2002. 25(11):2074–2080.

34. Bruttomesso D, Crazzolara D, Maran A, Costa S, Dal Pos M, Girelli A, Lepore G, Aragona M, Iori E, Valentini U, Del Prato S, Tiengo A, Buhr A, Trevisan R, Baritussio A. In Type 1 diabetic patients with good glycaemic control, blood glucose variability is lower during continuous subcutaneous insulin infusion than during multiple daily injections with insulin glargine. Diabetic Medice. 2008. 25(3):326-332.

35. Hanaire-Broutin H, Melki V, Bessieres-Lacombe S, Tauber J. Comparison of continuous subcutaneous insulin infusion and multiple daily injection regimens using insulin lispro in type 1 diabetic patients on intensified treatment. Diabetes Care. 2000. 23(9):1232–1235.

36. Hoogma RP, Hammond PJ, Gomis R, Kerr D, Bruttomesso D, Bouter KP, Wiefels KJ, de la Calle H, Schweitzer DH, Pfohl M, Torlone E, Krinelke LG, Bolli GB: 5-Nations Study Group. Comparison of the effects of continuous subcutaneous insulin infusion (CSII) and NPH-based multiple daily insulin injections (MDI) on glycaemic control and quality of life: results of the 5-nations trial. Diabetic Medicine. 2006. 23(2):141-147

37. Wainstein J, Metzger M, Boaz M, Minuchin O, Cohen Y, Yaffe A, Yerushalmy Y, Raz I, Harman-Boehm I. Insulin pump therapy vs. multiple daily injections in obese Type 2 diabetic patients. Diabetic Medicine. 2005. 22(8):1037-1046.

38. Berthe E, Lireux B, Coffin C, Goulet-Salmon B, Houlbert D, Boutreux S, Fradin S, Reznik Y. Effectiveness of intensive insulin therapy by multiple daily injections and continuous subcutaneous infusion: a comparison study in type 2 diabetes with conventional insulin regimen failure. Hormone and Metabolic Research. 2007. 39(3):224-229.

39. Health Quality Ontario. Continuous Subcutaneous Insulin Infusion (CSII) Pumps for Type 1 and Type 2 Adult Diabetic Populations: An Evidence-Based Analysis. Ontario Health Technology Assessment Series. 2009. 9(20):1-58.

40. Roze S, Valentine WJ, Zakrzewska KE, Palmer AJ. Health-economic comparison of continuous subcutaneous insulin infusion with multiple daily injection for the treatment of Type 1 diabetes in the UK. Diabetes Medicine. 2005. 22(9):1239-1245.

41. Cohen N, Minshall ME, Sharon-Nash L, Zakrzewska K, Valentine WJ, Palmer AJ. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin: economic comparison in adult and adolescent type 1 diabetes mellitus in Australia. Pharmacoeconomics. 2007. 25(10):881-897.

42. Lynch PM, Riedel AA, Samant N, Fan Y, Peoples T, Levinson J, Lee SW. Resource utilization with insulin pump therapy for type 2 diabetes mellitus. American Journal of Managed Care. 2010. 16(12):892-896.

43. Australian Institute of Health and Welfare. 2012. Insulin pump use in Australia. Diabetes series no. 18. Cat. no. CVD 58. Canberra: AIHW.

44. Langendam MW, Luijf YM, Hooft L, DeVries JH, Mudde AH and Scholten RJ. Continuous glucose monitoring systems for type 1 diabetes mellitus. Cochrane Database Systematic Review. 2012. 1:CD008101.

45. Szypowska A, Ramotowska A, Dzygalo K, Golicki D. Beneficial effect of real-time continuous glucose monitoring system on glycemic control in type 1 diabetic patients: systematic review and meta-analysis of randomized trials. European Journal of Endocrinology. 2012. 166(4):567-574.

46. Kordonouri O, Hartmann R, Pankowska E, Rami B, Kapellen T, Coutant R, Lange K, Danne T. Sensor augmented pump therapy from onset of type 1 diabetes: late follow-up results of the Pediatric Onset Study. Pediatric Diabetes. 2012. 3(7):515-518.

47. Peyrot M, Rubin RR. Patient-reported outcomes for an integrated real-time continuous glucose monitoring/insulin pump system. Diabetes Technology and Therapeutics. 2009.11(1):57-62.

48. Weinzimer SA, Steil GM, Swan KL, Dziura J, Kurtz N, Tamborlane WV. Fully automated closed-loop insulin delivery versus semiautomated hybrid control in

pediatric patients with type 1 diabetes using an artificial pancreas. Diabetes Care. 2008. 31(5):934-939.

49. Bergenstal RM, Tamborlane WV, Ahmann A, Buse JB, Dailey G, Davis SN, Joyce C, Peoples T, Perkins BA, Welsh JB, Willi SM, Wood MA; STAR 3 Study Group. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. New England Journal of Medicine. 2010. 363(4):311-320.

50. Kordonouri O, Pankowska E, Rami B, Kapellen T, Coutant R, Hartmann R, Lange K, Knip M, Danne T. Sensor-augmented pump therapy from the diagnosis of childhood type 1 diabetes: results of the Paediatric Onset Study (ONSET) after 12 months of treatment. Diabetologia. 2010. 53(12):2487-2495.

51. Raccah D, Sulmont V, Reznik Y, Guerci B, Renard E, Hanaire H, Jeandidier N, Nicolino M. Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study. Diabetes Care. 2009. 32(12):2245-2250.

52. Hirsch IB, Abelseth J, Bode BW, Fischer JS, Kaufman FR, Mastrototaro J, Parkin CG, Wolpert HA, Buckingham BA. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. Diabetes Technology and Therapy. 2008. 10(5):377-383.

53. Juvenile Diabetes Research Foundation Australia: Type 1 Diabetes Insulin Pump Program. Available at: http://www.jdrf.org.au/our-community/insulin-pump-grants/pumps-information. Accessed on February 6, 2013.

54. National Diabetes Services Scheme. Available at: http://www.ndss.com.au/. Accessed on January 31, 2013.

55. National Institute for Health and Clinical Excellence. Available at: http://www.nice.org.uk/media/87F/E2/InsulinPumpsToolDevelopmentUpdate.pdf. Accessed on January 31, 2013.

56. Phillip M, Battelino T, Rodriguez H, Danne T, Kaufman F. Use of insulin pump therapy in the pediatric age-group:consensus statement from the European Society for Paediatric Endocrinology, the Lawson Wilkins Pediatric Endocrine Society, and the International Society for Pediatric and Adolescent Diabetes, endorsed by the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2007. 30(6):1653-1662.