Why is type 1 diabetes different? Key messages from the guidelines

HELEN PHELAN RN, BA, CDE
STEPHEN M. TWIGG MB BS(Hons-I), PhD, FRACP
MARIA E. CRAIG MB BS, MMedSc(ClinEpid), PhD, FRACP

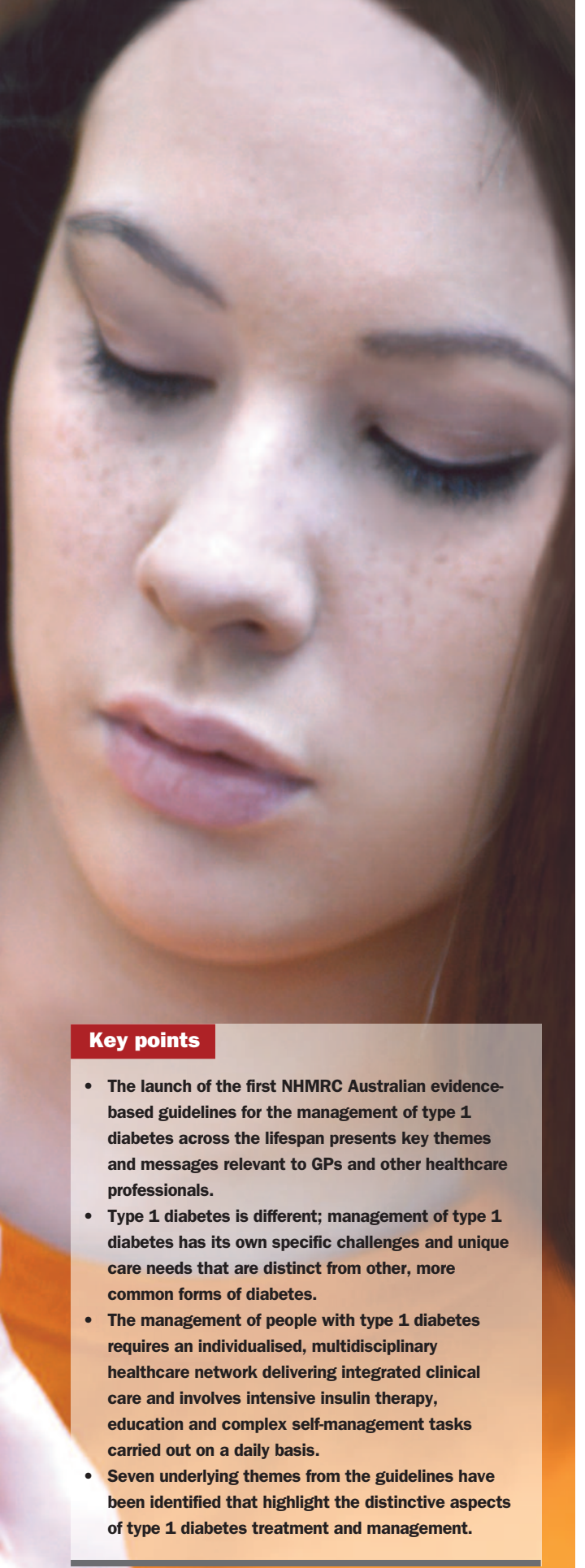
It is important to recognise that type 1 diabetes has its own specific challenges and unique care needs that are distinct from other, more common forms of diabetes. Management requires a multidisciplinary healthcare network delivering integrated clinical care, which is individualised to the patient.

Type 1 diabetes is an increasingly common condition in Australia. Following diagnosis, the demands in managing type 1 diabetes have a major effect on the individual's and the family's lifestyle, both in the short and long term. These demands include the burden of intensive self-care (including diet and exercise regimens), monitoring the disease, taking insulin safely and controlling blood glucose levels. The management of type 1 diabetes requires a multidisciplinary healthcare network delivering integrated clinical care, which should be individualised, and involves intensive insulin therapy, education and complex self-management tasks carried out on a daily basis.

The launch of the first National Health and Medical Research Council (NHMRC) Australian evidence-based guidelines for the management of type 1 diabetes across the lifespan presents key themes and messages relevant to GPs and other health professionals. The guidelines are for use in both

ENDOCRINOLOGY TODAY 2012; 1(1): 8-16

Ms Phelan is a Clinical Nurse Consultant and Diabetes Educator at the John Hunter Children's Hospital, Newcastle, NSW. Professor Twigg is an Adult Endocrinologist and Deputy Head, Department of Endocrinology at the Royal Prince Alfred Hospital, Sydney and Professor of Medicine, Sydney Medical School, The University of Sydney, NSW. Associate Professor Craig is a Paediatric Endocrinologist at the Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead and Associate Professor, Paediatrics and Child Health, The University of Sydney and The School of Women's and Children's Health, University of New South Wales, Sydney, NSW.



Key points

- **The launch of the first NHMRC Australian evidence-based guidelines for the management of type 1 diabetes across the lifespan presents key themes and messages relevant to GPs and other healthcare professionals.**
- **Type 1 diabetes is different; management of type 1 diabetes has its own specific challenges and unique care needs that are distinct from other, more common forms of diabetes.**
- **The management of people with type 1 diabetes requires an individualised, multidisciplinary healthcare network delivering integrated clinical care and involves intensive insulin therapy, education and complex self-management tasks carried out on a daily basis.**
- **Seven underlying themes from the guidelines have been identified that highlight the distinctive aspects of type 1 diabetes treatment and management.**

Seven distinctive aspects of treatment and management for type 1 diabetes

Type 1 diabetes is different because it:

- cannot be prevented
- can present diagnostic difficulties
- requires a specialist multidisciplinary diabetes team approach
- requires intensive management that includes intensive insulin therapy, intensive education and complex self-management tasks carried out on a daily basis
- requires therapy that is individualised to the age and situation of the person with diabetes
- may result in particular life-threatening medical emergencies and long-term complications
- is associated with a high prevalence of psychological distress and psychological conditions.

hospital and ambulatory-based settings, and target not only multidisciplinary specialist healthcare professionals but also primary care physicians. The guidelines provide a comprehensive resource for the GP in the modern clinical care of people with type 1 diabetes.

National evidence-based guidelines

The *National Evidence-based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults* are the culmination of three years of collaboration between the Australasian Paediatric Endocrine Group (APEG) and the Australian Diabetes Society (ADS), on behalf of the Australian Government Department of Health and Ageing.[1] The aim was to update the current APEG guidelines for children and adolescents[2] and extend their scope to address the needs of adults with type 1 diabetes. An expert advisory group (EAG) was formed representing specialist societies and organisations, with the active participation of consumer groups and the community. Systematic review of the best available scientific evidence was undertaken, with the EAG developing and grading recommendations based on a structured assessment of the evidence (Table 1).[3-5] Where insufficient evidence was available, practice points based on consensus-decision making were used. There are some aspects of type 1 diabetes that were not systematically reviewed and narrative text is included in the guidelines to provide context.

There are many potential barriers to the effective dissemination of clinical guidelines. A key message that emerged from expert consultation with stakeholders, and which was identified as having relevance across the medical, allied health and consumer audience was, type 1 diabetes is different. Management of the disease has its own specific challenges and unique care needs that are distinct from other, more common forms of diabetes, and these needs can be misunderstood by healthcare professionals, policy makers and the community. Workshop participants identified seven underlying themes from the guidelines that highlight distinctive aspects of type 1 diabetes (see the box above).

Table 1. Definitions of National Health and Medical Research Council (NHMRC) grades for recommendations[4]*

Grade	Definition
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
D	Body of evidence is weak and recommendations must be applied with caution

*Adapted from NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra, Australia: NHMRC; 2009.[4]

Unpreventable

Type 1 diabetes, unlike type 2 diabetes, cannot be prevented by following a healthy lifestyle. This point is often misunderstood in the community. At diagnosis, parents of children and adolescents may experience feelings of guilt because they feel responsible for causing their child's diabetes. It is therefore important that appropriate information is provided regarding the aetiology and risk factors for type 1 diabetes based on the best available evidence. Adults with type 1 diabetes and parents of children with the disease may be concerned about the risk of diabetes in the other siblings or offspring, and advice may be sought regarding treatments that may prevent or delay diabetes onset. Accordingly, the guidelines provide currently available evidence to address these concerns, and the role of interventions to prevent type 1 diabetes is systematically reviewed. Multicentre, randomised controlled trials (RCTs) aimed at secondary prevention of type 1 diabetes (in antibody-positive first-degree relatives of individuals with type 1 diabetes) have used:

- antioxidant therapy
- immunomodulating therapies, such as nicotinamide
- low-dose parenteral insulin, oral insulin or intranasal insulin (as the intervention compared with placebo).

None were effective in delaying the onset of diabetes.

As early exposure to complex dietary proteins may increase the risk of beta-cell autoimmunity and type 1 diabetes, the Trial to Reduce the Incidence of Diabetes in the Genetically at Risk (TRIGR) pilot primary prevention RCT examined the hypothesis that supplementing breast milk with highly hydrolysed cow's milk formula during infancy would decrease the cumulative incidence of diabetes-associated autoantibodies in at-risk children.[6] The authors reported a 50% risk reduction (hazard ratio, 0.51; 95% confidence interval, 0.28 to 0.91) in positivity for one or more diabetes-associated autoantibodies in the group randomised to hydrolysed formula compared with the control group.[6] However, the primary outcome for this study was islet autoimmunity and not type 1 diabetes.

EAG RECOMMENDATIONS

- 'No interventions are recommended for use in clinical practice to delay or prevent the onset of type 1 diabetes (Grade A).'
- Currently, 'interventions aimed at delaying or preventing the onset of type 1 diabetes should only be used in a research setting.'

Diagnostic difficulties

The clinical picture at diagnosis of type 1 diabetes can vary widely; factors such as younger age, presence of intercurrent illness, socioeconomic status and timeliness of referral all influence the risk of presentation with acute metabolic compensation and diabetic ketoacidosis (DKA).[7,8] Classic symptoms of polyuria, polydipsia and weight loss are often present, but atypical presentations can occur and the diagnosis may be missed or delayed. When the presentation is atypical, it may be difficult to determine the type of diabetes. Other clinical or laboratory information may be helpful. Signs of insulin resistance, such as acanthosis nigricans and obesity, would favour a diagnosis of type 2 diabetes. The presence of antibodies associated with type 1 diabetes (including anti-GAD, IAA, ICA and ZnT-8) or a family history of type 1 diabetes may also assist with the diagnosis.

Diabetic ketoacidosis

The symptoms and signs of the emergency condition DKA, which include abdominal pain, vomiting, dehydration and hyperventilation, may be mistaken for asthma, pneumonia, an 'acute abdomen', gastroenteritis or sepsis. In very young children, severe DKA may be the first presentation of type 1 diabetes because of the more rapid onset of severe insulin deficiency. Prompt referral of patients with suspected type 1 diabetes for investigation and management is essential because delayed diagnosis of type 1 diabetes in a young person is associated with an increased risk of DKA.[7,9]

EAG RECOMMENDATIONS

- 'Children and adolescents presenting with newly diagnosed type 1 diabetes should be managed in an appropriately resourced ambulatory care or inpatient hospital setting (Grade B).'
- Although most patients with type 1 diabetes at diagnosis can be managed in an ambulatory setting, hospital admission may be indicated. Groups for whom inpatient management is typically necessary at diagnosis of diabetes include: individuals with DKA, significant comorbidities, inadequate social support or mental health issues; children under 2 years of age; those in geographically remote areas and non-English speakers.

Specialist multidisciplinary team approach

The care of individuals with diabetes requires the input of a specialist team of healthcare professionals who have expertise in the management of type 1 diabetes. The specialist multidisciplinary diabetes team includes:

- the person with diabetes and his or her family or carer
- an endocrinologist or another physician trained in the care of people with type 1 diabetes
- a credentialed diabetes educator
- an accredited practicing dietitian trained in medical nutrition therapy
- a psychologist or social worker.

This specialist team takes responsibility for the patient's diabetes care, including making changes to diabetes management, scheduling regular reviews, screening for diabetes complications and managing diabetic emergencies.

The GP is a key member of the healthcare team and can play a key role in:

- facilitating access to diabetes services through the Chronic Diseases Management and Team Care schemes
- supporting mental health and arranging for access to Medicare services
- providing systems for recall or reminders for diabetes reviews
- managing intercurrent medical conditions
- preventive health issues, such as immunisation
- ensuring continuity of care, particularly for young people transitioning from paediatric to adult services.

Not all members of the diabetes team may be available in rural and remote areas. In this situation, primary care may be provided by a locally based paediatrician, physician or GP. These doctors should have ready access to facilities and advice provided by the diabetes care team in regional centres. Telemedicine is an option to support the delivery of healthcare to remote and geographically isolated sites, although currently there is insufficient evidence to determine efficacy.[1]

Intensive management

'Intensive glycaemic control' refers to an implemented strategy of intensive glycaemic management and is achieved by a 'package' of methods. These include:

- a multiple daily injection regimen (i.e. three or more injections per day) or an insulin pump (continuous subcutaneous insulin infusion)
- frequent insulin dose adjustment (taking into account the carbohydrate content of meals, blood glucose levels and physical activity)
- blood glucose level monitoring at least four times per day
- weekly measurement of the blood glucose level at 3 am
- intensive formal diabetes education
- medical nutrition therapy
- physical activity advice.

Clinical judgement should be used to determine the most appropriate insulin regimen for each patient. This should be continually reappraised to maximise outcomes for the individual with diabetes. Intensive control of blood glucose levels can prevent and slow the onset of microvascular and macrovascular complications.

Individuals with diabetes and/or their parent/carer must make multiple decisions on a daily basis regarding their diabetes therapy. The demands in managing type 1 diabetes have a major effect on their lifestyle in the short and long term due to the burden of monitoring the disease, taking insulin safely and controlling blood glucose levels. Intensive self-management education and psychological support are therefore fundamental to this method of diabetes management.

EAG RECOMMENDATIONS

- 'Intensive glycaemic control should be implemented to reduce the risk of onset or progression of microvascular and development of macrovascular diabetes complications (Grade B).'
- 'Education and psychological support are an essential component of standard diabetes care. Intensified education and psychological support programs should be considered when treatment goals are not being met (Grade B).'

Individualised therapy

Type 1 diabetes can occur at any age or stage of life. It is crucial that treatment is individualised to the age and situation of the person with diabetes. As children and adolescents grow and progress through puberty, insulin doses and regimens must be adapted with the aim of maintaining glycaemic targets and ensuring normal growth and psychological or cognitive development.

The young person with diabetes and his or her family must be supported to help successfully transfer self-management skills and knowledge from the parent to the young person. Gender is also an important consideration and the updated guidelines specifically address the needs of women with type 1 diabetes.

EAG RECOMMENDATIONS

- 'Females of childbearing age with type 1 diabetes should be aware of the need for pregnancy planning and receive preconception care (Grade B).'
- Key points are that poor glycaemic control in pregnancy is associated with an increased risk of congenital malformations, miscarriage and perinatal morbidity and that pregnancy may increase the predisposition to both hypoglycaemia and ketoacidosis. This delivers an important message that is an underlying theme throughout the guidelines: each person with diabetes will need his or her therapy adapted in response to the person's age, life stage, diabetes duration and comorbidities; and this requires regular review by the specialist healthcare team.

Associated medical emergencies and long-term complications

Type 1 diabetes may result in life-threatening medical emergencies and long-term complications. The acute medical emergencies arising from type 1 diabetes pose a significant threat to the individual with diabetes. An intercurrent illness, missed insulin doses or delivery problems with an insulin pump can quickly evolve into life-threatening severe DKA. Likewise, an episode of mild hypoglycaemia can progress to a severe episode, resulting in loss of consciousness and/or seizure. It is imperative that individuals with diabetes receive a plan that includes:

- education and advice on managing medical emergencies that is reinforced at regular intervals
- a written plan for the management of sick days, providing guidance for the adjustment of insulin, frequency of monitoring blood glucose and ketone levels and frequency and type of fluid intake
- advice about when to seek medical attention, which should be revised with the patient at regular intervals.

The sick-day management plan derived from the guidelines is shown in Table 2.[1]

EAG RECOMMENDATIONS

- 'Blood ketone measurement should be available as part of a comprehensive sick-day management plan (Grade C).'
- The practice points indicate that 'blood ketone measurement is preferred, because it gives a more timely result. However, where blood ketone measurement is not available, urine ketone measurement is the alternative test as part of a comprehensive sick-day management plan.'

Severe hypoglycaemia

Severe hypoglycaemia is much more common in people with type 1 diabetes and occurs, on average, about 10 times more often than in people with type 2 diabetes. Episodes of severe hypoglycaemia also tend to cluster in certain individuals. The care team should thus help identify and discuss the risk factors for severe hypoglycaemia, which include:

- a history of severe hypoglycaemia (especially over recent months)
- reduced hypoglycaemia awareness
- a lower HbA_{1c} level
- longer duration of diabetes
- younger age (younger than 6 years).

Education on how to avoid and manage hypoglycaemia (including the availability of glucagon) should be provided with structured education programs to help reduce rates of severe hypoglycaemia. Reduced hypoglycaemia awareness is linked to increased diabetes duration of usually more than 10 years, and recent severe hypoglycaemia. Reduced hypoglycaemia awareness is characterised by a lack of early warning autonomic symptoms of hypoglycaemia, such as tremor or sweats, and therefore the first symptoms of hypoglycaemia are manifestations of neuroglycopenia with cognitive dysfunction or confusion, which occur at capillary blood glucose levels well below 4 mmol/L. This may lead to an inability of the person with diabetes to treat his or her hypoglycaemia.

EAG RECOMMENDATION

- 'Risk factors for severe hypoglycaemia should be identified (Grade B).'

Microvascular and macrovascular complications

The microvascular and macrovascular complications of diabetes can be detected at a very early stage with timely screening (Table 3).[1] The annual cycle of care is a fundamental component of management for the individual with type 1 diabetes. Hypertension is a pathogenic factor in macrovascular and microvascular events in diabetes; therefore, tight control of blood pressure is of critical importance, particularly in slowing progression of retinopathy and nephropathy. The general blood pressure target is below 130/80 mmHg and below 125/75 mmHg in the presence of 1 g daily or more of proteinuria.

A diet low in saturated fat and high in fruit and vegetables, a healthy body weight and regular physical activity are important for reducing macrovascular risks. As global macrovascular risk in type 1 diabetes is high in adults, statins should be commenced early in the disease course and before the development of cardiovascular disease.

EAG RECOMMENDATIONS

- 'ACEI [angiotensin converting enzyme inhibitor] therapy should be used to prevent progression of diabetic nephropathy (Grade B).'
- 'Statins are recommended for use in adults with type 1 diabetes, to reduce total and LDL cholesterol, and to reduce cardiovascular risk (Grade B).'

Table 2. Guidelines for sick-day management for people with type 1 diabetes[1]*

Blood glucose level (BGL; mmol/L)	Ketones – blood (mmol/L)† or urine	Supplemental insulin dose (can be given up to 2 hourly)‡	Timing of review	Fluid intake
<4.0	<1.0 Negative	Insulin dose reduction may be required. Consider mini-dose glucagon to prevent hypoglycaemia if vomiting, diarrhoea or reduced carbohydrate intake	Check every 20 to 30 minutes until BGL is >4. Supervised medical care required if ketones remain positive and BGL remains low	Take sweetened fluids or fast-acting carbohydrate (or both); hospital admission for IV fluids may be needed if BGL cannot be maintained
	⩾1.0 Positive	Priority is to increase blood glucose level (BGL) with fluid and carbohydrate		
4 to 8	<1.0 Negative/trace	No change to insulin	Two hourly	Give sweetened fluids or extra carbohydrate to maintain or increase BGL
	1.0 to 1.4 Small	No change to insulin. Ketones indicate carbohydrate and insulin deficiency	Two hourly	
	>1.5 Moderate/large	5% supplemental insulin may be required	Two hourly	
8 to 15	<1.0 Negative/trace	May fall without extra insulin. If persistently elevated, consider 5% supplemental insulin	Two hourly	Sweetened fluids recommended
	1.0 to 1.4 Small	If persistently elevated ketones, consider 5 to 10% supplemental insulin	Two hourly	
	>1.5 Moderate/large	10% supplemental insulin dose	Hourly	
>15	<1.0 Negative/trace	5 to 10% supplemental insulin dose	Hourly	Unsweetened fluids recommended
	1.0 to 1.4 Small	10 to 15% supplemental insulin dose	Hourly	
	>1.5 Moderate/large	15 to 20% supplemental insulin dose	Hourly	

* Reproduced from the type 1 diabetes guidelines.[1] Refer to these guidelines for further information.[1] If health professional support is not readily accessible to provide ongoing sick-day management advice then prompt presentation to hospital is recommended.
† Blood 3-hydroxybutyrate.
‡ Refers to percentage of total daily insulin dosage given as rapid or fast-acting supplemental insulin dose. Caution is advised with supplemental insulin doses in the presence of blood glucose levels less than 8 mmol/L and increasing sweetened fluid intake first is advised.

Autoimmune diseases

Individuals with type 1 diabetes are at increased risk of other autoimmune diseases, such as thyroid disease and coeliac disease.

EAG RECOMMENDATIONS

- 'Screening for coeliac disease should occur at diagnosis of type 1 diabetes in children and adolescents; individuals with negative tests at diagnosis should be rescreened (Grade B).'
- 'Screening for thyroid dysfunction and testing for antibodies to thyroid peroxidase (TPO Ab) should be performed at diagnosis of type 1 diabetes; screening for thyroid dysfunction should be performed regularly thereafter (Grade B).'

Associated psychological conditions

Type 1 diabetes is associated with a high prevalence of psychological distress and psychological conditions. Psychological distress or 'diabetes distress' can stem from the burden of the daily self-management tasks, fear of hypoglycaemia and diabetes complications experienced. There is an increased rate of depression and anxiety in young people with type 1 diabetes.

Importantly, psychological problems can affect the ability to carry out daily diabetes self-management tasks, which in turn leads to poor metabolic control. Every member of the diabetes care team can provide support and advice for these issues and there are tools available that can be used by healthcarers to detect psychological problems. Families should be assessed and supported in their communication around diabetes-related tasks because this can often be a source of stress, particularly during adolescence.

Table 3. Suggested frequency of screening for complications in people with type 1 diabetes[1]*

	When to commence screening	Frequency	Method of screening
Retinopathy	After two years of diabetes duration in adolescents and adults; and after five years' duration and from age 9 years in children	Bi-yearly or annually if high risk, long duration, high HbA_{1c}, nonprolific background retinopathy	Slit lamp biomicroscopy Retinal photography Mydriatic fundoscopy Visual acuity
Nephropathy	After two years of diabetes duration in adolescents and adults; and after five years' duration and from age 9 years in children	Annually	Timed albumin excretion rate First morning albumin to creatinine ratio Spot urinary albumin to creatinine ratio
Neuropathy	Annually	Annually	Physical examination Monofilament Vibration and thermal threshold Autonomic nerve tests
Lipids	At diagnosis if family history or from 12 years of age	Every five years until puberty, then annually	Fasting cholesterol, LDL cholesterol
Blood pressure	At diagnosis	At least annually	Sphygmomanometer 24-hour blood pressure measurements
Macrovascular disease	In adulthood	At least annually	Clinical assessment and consider resting ECG

* Reproduced from the type 1 diabetes guidelines.[1]

EAG RECOMMENDATIONS

- 'Clinicians should be aware that the co-occurrence of psychological disorders in type 1 diabetes is common (Grade A).'
- In the accompanying practice points to the guidelines, clinicians were advised to 'consider the co-occurrence of psychological disorders, including clinical and subthreshold eating disorders, when assessing people with type 1 diabetes and suboptimal glycaemic control, insulin omission, disordered eating behaviours, unexplained weight loss or recurrent DKA admissions.'

Conclusion

The *National Evidence-based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults* provide a comprehensive resource for multidisciplinary healthcare teams in the clinical care of people with type 1 diabetes in Australia. Effective dissemination of these guidelines will inform the best management of type 1 diabetes, with the aim of achieving positive outcomes for the individual with diabetes. Partnership and collaboration with all stakeholders, incorporation of the key messages into the medical literature and publications, and active communication with healthcare professionals, individuals with diabetes and their families and/or carers are essential for successful dissemination.

In particular, achieving awareness that type 1 diabetes is different from other types of diabetes and that it demands a different approach to management to optimise care for the individual is a major objective of the guidelines.

The guidelines and the technical report on the systematic review of the scientific evidence can be downloaded from the websites of APEG (www.apeg.org.au), ADS (www.diabetessociety.com.au), and the NHMRC clinical guidelines portal (www.clinicalguidelines.gov.au). **ET**

References

1. Craig ME, Twigg SM, Donaghue KC, et al. National evidence-based clinical care guidelines for type 1 diabetes in children, adolescents and adults. Canberra: Australian Government Department of Health and Ageing; 2011. Available online at: www.diabetessociety.com.au/downloads/Type1guidelines14Nov2011.pdf (accessed March 2012).
2. Australian Paediatric Endocrine Group (APEG); National Health and Medical Research Council. Clinical Practice Guidelines: Type 1 diabetes in children and adolescents. Canberra: NHMRC; 2005.
3. National Health and Medical Research Council. A guide to the development, implementation and evaluation of clinical practice guidelines. Canberra: NHMRC; 1999.
4. National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009.
5. National Health and Medical Research Council. Standards and procedures for externally developed guidelines. Canberra: NHMRC; 2007. Available online at: www.nhmrc.gov.au/publications/synopses/nh56syn.htm (accessed March 2012).
6. Knip M, Virtanen SM, Seppa K, et al. Dietary intervention in infancy and later signs of beta-cell autoimmunity. N Engl J Med 2010; 363: 1900-1908.
7. Craig ME, Wong CH, Alexander J, Maguire AM, Silink M. Delayed referral of new-onset type 1 diabetes increases the risk of diabetic ketoacidosis. Med J Aust 2009; 190: 219.
8. Wolfsdorf J, Craig ME, Daneman D, et al. Diabetic ketoacidosis in children and adolescents with diabetes. Pediatr Diabetes 2009; 10 Suppl 12: 118-133.
9. Sundaram PC, Day E, Kirk JM. Delayed diagnosis in type 1 diabetes mellitus. Arch Dis Child 2009; 94: 151-152.

COMPETING INTERESTS: None.