

Nurse Practitioner (Diabetes) Clinical Protocol



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Delivering a Healthy WA

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Clinical Protocol

Management of the child with type 2 diabetes

1. Local implementation of protocols & proposed Nurse Practitioner role

This protocol is based on the best available evidence and expert opinion for the management of type 2 diabetes in children and adolescents in Western Australia. It outlines the role of the Nurse Practitioner (Diabetes) in the clinical care and education of children with suspected and established type 2 diabetes. The protocol has been developed by health care professionals with expertise in diabetes and endocrinology, diabetes education, patient care, pharmacology, biochemistry, pathology and health service management.

2. Statement of intent

The information provided in this clinical protocol for type 2 diabetes in children and adolescents, is intended for information purposes only. Clinical protocols are designed to improve the quality of health care and decrease the use of unnecessary or harmful interventions. This clinical protocol provides advice regarding the care and management of the aforementioned patients by the nurse practitioner (diabetes).

While every reasonable effort has been made to ensure the accuracy of this document, no guarantee can be given that the information is free from error or omission. The recommendations do not indicate an exclusive course of action or serve as a definitive mode of patient care. Variations, which take into account individual circumstances, clinical judgement and patient choice, may also be appropriate. Users are strongly recommended to confirm by way of independent sources that the information contained within the clinical protocol is correct.

The information in this clinical protocol is NOT a substitute for proper diagnosis, treatment or the provision of advice by an appropriate health professional.

This clinical protocol may also include references to the quality of evidence used in its formulation. Where this has not been located, the clinical protocol includes references to support the recommended care. Providing a reference to another source does not constitute an endorsement or approval of that source or any information, products or services offered through that source.

The Minister for Health, the State of Western Australia and their employees and agents shall accept no liability for any act or omission occurring in reliance on this clinical protocol and for any consequences of any such act or omission.

3. Background

3.1 General

The relatively recent rise in the incidence of type 2 diabetes (T2DM) among children and adolescents is a worldwide phenomenon, which is increasing in parallel to the rise in childhood obesity.¹⁻³ Type 1 diabetes is still the predominant form of diabetes in the young, however, in certain ethnic groups type 2 diabetes is now more common⁴ and may become the predominant form within other groups.⁵⁻⁹ In a recent prevalence study of an Australian sample there was a disproportionately higher rate of type 2

diabetes among indigenous children with a significant number living in rural and remote regions. Of particular concern was the average annual increase of 27% in type 2 diabetes cases over the study period.¹⁰

The management of T2DM in Western Australian youth is based on recent, local clinical practice guidelines¹¹. There are evidenced based guidelines¹²⁻¹⁴ and consensus statements¹⁵ on how to best manage the condition in adults. However, there is a lack of such data in children and adolescents to enable application of these adult guidelines to children. Hence the establishment of local guidelines, which are based on international consensus and the best available data^{1, 2, 16, 17}.

It is known that the T2DM observed in children is often linked to obesity and insulin resistance and usually a positive family history. However, the risk factors for childhood T2DM are multiple with ethnicity, genetics and lifestyle all contributing. Insulin resistance is a feature of puberty and most cases of childhood T2DM occur at this stage¹. Interventions which target weight loss and reduce insulin resistance are considered first line treatment options, much in the same way as adults with T2DM.

3.2 Western Australia

Princess Margaret Hospital (PMH) for Children is the only tertiary referral centre for the care of child and adolescent diabetes in W.A. The Department of Endocrinology and Diabetes at PMH provides a state-wide service for the management of diabetes and other endocrine disorders. In the present model of service delivery, all new cases of diabetes are admitted to PMH for acute care, medical stabilisation and education. This model is appropriate for childhood type 1 diabetes, given the acute and symptomatic presentation. However, in contrast to the type 1 presentation, children with type 2 diabetes may present insidiously, without symptoms and may not require acute tertiary level hospitalisation.

In W.A. approximately 50% of children with type 2 live in rural and remote locations, many of whom are indigenous¹⁰. Hospitalisation in Perth for acute care and education may not be ideal given the extensive travel and cost involved. Furthermore, timely and recurrent follow-up is traditionally problematic.

Therefore, for the majority of uncomplicated presentations there is potential for the patient to be managed locally, without hospitalisation in Perth. Ideally, localised management may facilitate a timely diagnosis and improve follow-up care. Guidelines are now available to assist health care providers to make appropriate decisions about the care of T2DM in youth in order to facilitate best practice management at the local level¹¹.

For rural and remote children the Department of Endocrinology and Diabetes at PMH will provide information and clinical advice for community/primary care providers to facilitate community management for medically stable patients and where necessary, provide acute management and hospitalisation for unstable patients.

Children and adolescents living in metropolitan Perth with suspected T2DM will be referred to PMH by their primary care provider. Where necessary these children will be admitted for medical stabilisation and education or treated as an outpatient.

4. Nurse Practitioner - Diabetes (NPD) role

4.1 Children from rural and remote areas with suspected, newly diagnosed or established type 2 diabetes

For patients referred to PMH, the NPD will:

- Liaise with rural/ remote health providers (GP, Regional Paediatrician, remote area nurse) re: diagnosis and initial care (e.g. inpatient or ambulatory care).
- Assist with identification of actual or potential problems.
- Identify investigations required in collaboration with medical practitioner.
- Assess the need to visit rural/remote area to facilitate care and/or education.
- Work in collaboration to identify the need for referral to other health/allied health providers (e.g. dietitian, social worker, health worker).
- Develop management plan in partnership with primary health provider, including patient/family education and the use or non use of pharmacotherapy.
- Arrange for follow-up care

4.2 Children from metropolitan areas with suspected, newly diagnosed or established type 2 diabetes

For patients referred to diabetes outpatients at PMH, the NPD will:

- Obtain patient history and perform pertinent physical assessment.
- Identify actual and potential problems.
- Identify investigations required.
- Develop management plan including patient/family education and the use or non use of pharmacological therapy.
- Referral to other health/allied health providers within multidisciplinary team.
- Arrange for follow-up care.

5. Scope of Practice in Designated Area

The Nurse Practitioner, Diabetes will maintain an ongoing clinical and coordination role - collaborating with other members of the health care team to achieve optimal patient outcomes. Collaboration with rural and remote health care providers such as general practitioners, regional paediatricians, remote area nurses and health care workers will be particularly important, as much of this work will involve consultative advice and initiation and adjustment of therapy from a distance. Visits to rural and remote areas will facilitate the provision of community based care and provide clinical care, advice, education and support for families and health care providers.

| SCOPE OF PRACTICE | | |
|-------------------------------------|--|--|
| PRACTITIONER | SCOPE | OUTCOMES |
| Nurse Practitioner - Diabetes (NPD) | <p>Children and adolescents (including those from rural and remote areas) with suspected, newly diagnosed or established T2DM.</p> <p>Patients referred to the diabetes and endocrinology teams</p> <p>Metropolitan patients referred to the endocrinology and diabetes outpatient unit at PMH</p> | <p>Appropriate patients are identified and treated by the NPD</p> <p>Patients outside the NPD scope will be referred to a Medical Practitioner</p> |
| Medical Practitioner ± NPD | <p>Hospitalised patients with T2DM</p> <p>Patients with:</p> <ul style="list-style-type: none"> • suspected or established type 1 diabetes and/or • Other endocrine disorders. • Other suspected undiagnosed medical conditions. | <p>Patients outside the NPD Scope of Practice will be referred to a paediatric endocrinologist, members of the multidisciplinary team and other services as required</p> |

5.1 Referrals

To the Diabetes Service

New patients - whether undiagnosed or diagnosed must be referred by a medical officer. All other referrals including those from other health professionals are generally two-way for patients known to the Endocrine & Diabetes service. These are identified in **Figure 1** Referrals and therapeutic relationships.

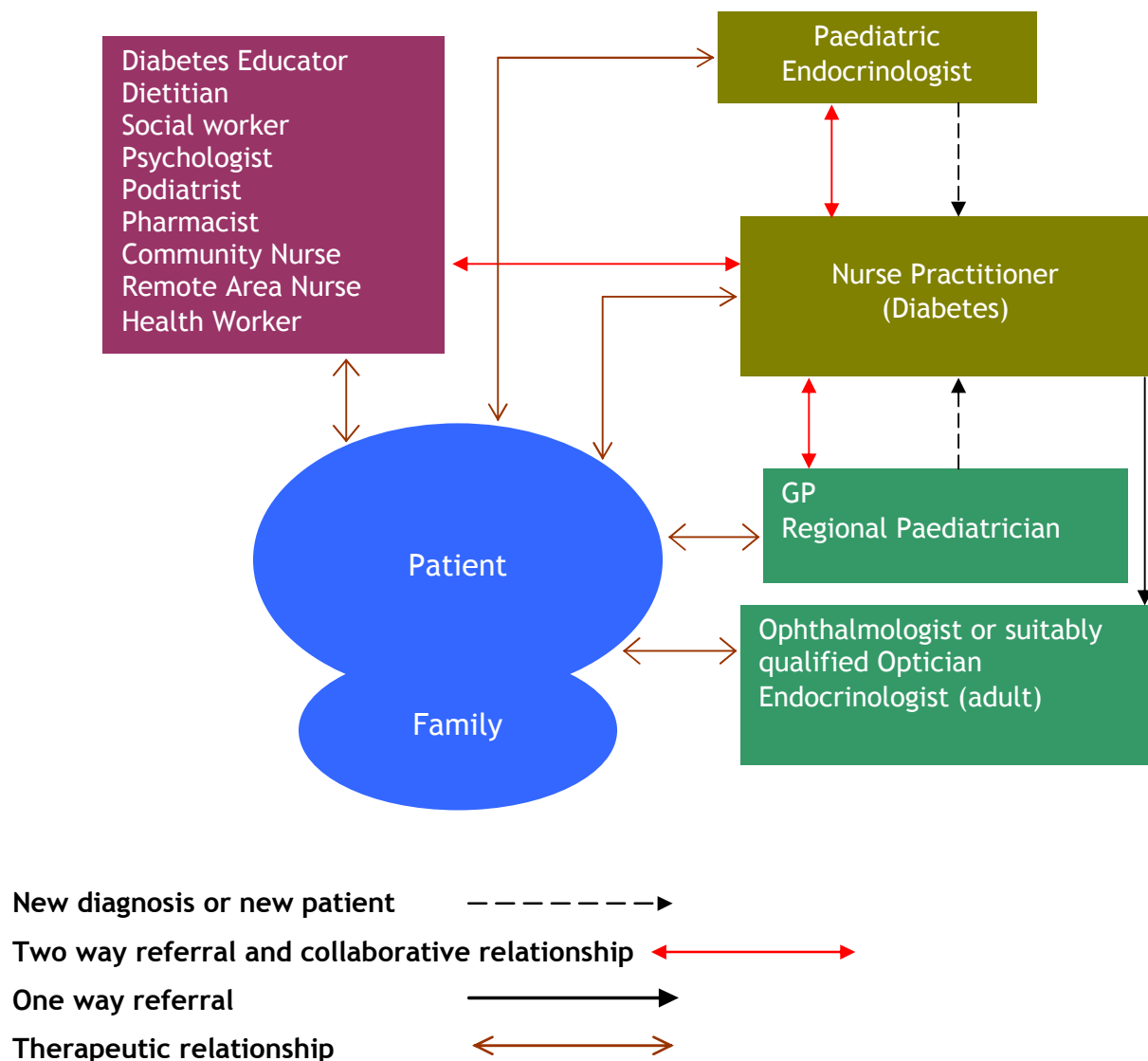
From the Diabetes Service

All patients with T2DM require multidisciplinary care and therefore all patients will be referred by the NPD to the multidisciplinary team. All patients will be referred to an ophthalmologist for retinal screening. Other circumstances requiring referral to either the **paediatric endocrinologist or other medical officer** (GP, regional paediatrician) will include patients:

- whose condition falls outside the NPD Scope of Practice
- who fail to respond appropriately to therapy (co-manage)
- with diabetes related complications or co morbid conditions (co-manage)

Rural or remote patients without an assembled multidisciplinary team will be seen by the appropriate visiting health professional or if available use alternative (e.g. telehealth services).

Figure 1. Referrals and therapeutic relationships



6. First Presentation and Patient Assessment

A detailed patient history and full physical assessment is essential. Take particular note of the type and history of symptoms (or lack thereof), evidence of weight loss/gain, evidence of acanthosis nigricans, BMI and family history. The mode of presentation, whether insidious or acute will contribute to the diagnostic picture and direct initial treatment plan. The degree of hyperglycaemia will influence, but not necessarily determine choice of initial treatment. However, the presence (or absence) of ketosis will determine the initial treatment pathway. All children and adolescents who have diabetes should have urinary or blood ketones assessed. It is a simple, inexpensive and widely available test and assists all areas, especially remote regions with decision making.

| PATIENT HISTORY | REQUIRED INFORMATION | OUTCOMES |
|---|---|--|
| Previous medical history | Determine past medical history <ul style="list-style-type: none"> ongoing medical problems any sequelae of previous health problems | Where ongoing medical problems exist the name of the care provider (e.g. GP, specialist) will be documented Ongoing sequelae of previous health problems will be documented |
| Presenting symptoms | Determine type and history of symptoms (or lack thereof) | Symptoms of hyperglycaemia, evidence of ketosis and weight change and dietary history will be documented |
| Known risk factors for the presenting condition | Determine risk factors for diabetes | Family history, BMI, ethnicity, evidence of metabolic syndrome (e.g. hypertension, dyslipidaemia) will be documented. |
| Medications | List current medications | Patient's current medications will be documented |
| Other relevant information | Determine whether development is age appropriate | Deviation from expected development will be documented. |
| Gender or age specific history | Determine age of onset if parent/s have diabetes | Incidence of parental diabetes will be documented. |
| Usual physical examination | This is presumed | Findings of comprehensive physical assessment will be recorded |
| Gender or age specific physical examination | Observe girls for signs of hyperandrogenism (PCOS) | Signs of hyperandrogenism (PCOS) will be documented |
| Supplementary physical assessment ¹⁸ | <ul style="list-style-type: none"> Skin (look for acanthosis nigricans) Infective screen (eg. Candida) Pubertal development Height, weight, BMI Blood pressure Dilated retinal examination (as soon as practicable) | Other pathology will be considered in the context of presenting condition. |

7. Investigations

Note: In contrast to newly diagnosed type 1 diabetes, complication screening in T2DM patients should begin at diagnosis.¹⁹

The ordering of the investigations listed below will be limited to PathWest (Dept of Health W.A.), as a Nurse Practitioner is not able to apply for an MBS provider number in order for tests to be processed by other laboratory service providers.

Table 1 Investigations

| INDICATIONS | INVESTIGATIONS | OUTCOMES |
|--|--|--|
| <p>To quantify symptoms suggestive of T2DM</p> | <p>Consider the need for the following investigations at first presentation</p> <ul style="list-style-type: none"> • Plasma glucose (fasting) • C-Peptide (fasting) • Islet Cell & GAD 65 antibodies • Ketones (blood or urine) • HbA1c | <p>Indications will exist for all investigations ordered</p> <p>All tests required to establish diagnosis of T2DM in children will be undertaken, where possible, at the first visit.</p> |
| <p>To identify or screen for other related conditions</p> | <p>Consider the need for:</p> <ul style="list-style-type: none"> • FBC, U&E, LFT, TFT, CRP • Coeliac screen • HLA typing • Urine microalbumin (spot ACR first morning sample or AER x3 over night collection) • Lipids (fasting) performed after 3-6 months once glycaemic control achieved | <p>Tests required to establish or confirm other diagnoses will be identified in collaboration with a medical practitioner/endocrinologist.</p> <p>Results of these tests will be used when determining the future management of the patient.</p> |

7.1 Interpretation of Results

Abnormal results will be documented and discussed with the Endocrinologist to determine the need for further consultation or investigations.

All care subsequent to an abnormal result that falls outside the NPD scope of practice will be referred to the Paediatric Endocrinologist.

8. Diagnosis

There are three accepted methods for diagnosing diabetes.²⁰ Any may be used to confirm the diagnosis.

1. Fasting plasma glucose ≥ 7.0 mmol/L (repeated)
2. Symptoms of diabetes plus casual or random plasma glucose concentration ≥ 11.1 mmol/L
3. 2-hr post load glucose ≥ 11.1 mmol/L during an oral glucose tolerance test (OGTT).

In the absence of unequivocal hyperglycaemia or DKA, the diagnosis must be confirmed on a subsequent day by one of the above methods. An OGTT should not be performed if diabetes can be diagnosed using fasting or random criteria, as excessive hyperglycaemia can result. It is rarely indicated in making the diagnosis of type 1 diabetes.

When there is marked hyperglycaemia and ketosis, treatment is urgent and should not be delayed.

Table 2 Guide to the Classification of Diabetes²

| | Type 1 diabetes | Type 2 diabetes |
|---------------------------------------|---|---|
| Onset | Acute (symptomatic) | Slow or insidious (often asymptomatic) |
| Clinical features | Weight loss Polyuria Polydipsia | Obese/overweight Strong family history of type 2 diabetes Ethnicity-high prevalence populations Acanthosis nigricans PCOS |
| Ketosis | Often present | Usually absent |
| Insulin (endogenous) | C-peptide low or absent | C-peptide normal or elevated |
| Antibodies | ICA positive Anti-GAD positive ICA 512 positive | ICA negative** Anti-GAD negative** ICA 512 negative** |
| Associated autoimmune diseases | Yes | No |

** UKPDS data revealed that 12% of type 2 subjects were ICA or GAD autoantibody positive and these subjects were more likely to require early insulin therapy²¹.

9. Recommendations for Clinical Management and education

In theory, the clinical management of type 2 diabetes in children and adolescents is similar to that of adults. Lifestyle intervention should always be the first option in asymptomatic individuals where a structured approach to improving dietary intake and improving exercise capability is required. Adolescents in particular may find this difficult, so the engagement of the family in a management program is essential. The struggle for independence and autonomy, the desire to be like their peers and risk-taking behaviours make diabetes self management difficult, particularly when dramatic lifestyle change is the cornerstone of treatment¹⁹.

Increased risk of complications of diabetes makes the management of young people who are overweight or obese particularly important. Therefore the initiation of lifestyle intervention strategies for this group may have greater urgency than that for young people with T1DM.

9.1 Treatment Goals

The management of type 2 diabetes in children and adolescents includes lifestyle intervention (physical activity and dietary education), self management education (individual and family), pharmacotherapy and psychological care. The **treatment goals** are essentially no different to that of a young person with type 1 diabetes.

That is, to promote:

- optimal long-term glycaemic control (normoglycaemia)
- self-care
- normal growth, development and adjustment
- normal lifespan
- prevent or delay of micro and macro vascular complications (control risk factors)
- social and psychological well-being

To achieve these goals, the Nurse Practitioner Diabetes will:

1. Provide optimal care within the context of available resources.
2. Where possible, facilitate a three monthly review by the GP, Regional Paediatrician or visiting NPD.
3. Adjust the patient's therapy (with regard to lifestyle) to achieve target levels (see Table 9).
4. Document findings of assessment and management outcomes in the patient's notes. A letter will be written to all relevant Health Care Professionals summarising the outcomes if seen by NPD
5. Provide written, oral and online education and resources to patients and families as required.
6. Record patient data prospectively on the WA Children's Diabetes Database.

9.2 Team Approach to Care

A team approach that includes a paediatric endocrinologist, endocrine fellow/ registrar, nurse practitioner (diabetes), diabetes educator, dietitian and social worker will assist in delivering a structured management plan. Ideally the team will also include a psychologist, physiotherapist/exercise physiologist and school nurse. Where patients live in a rural or remote location (such as an Aboriginal community) the engagement of the local community, local health providers and culturally appropriate health workers (e.g. Aboriginal Health Worker) are essential.

9.3 Education and self management

All children and adolescents with type 2 diabetes should receive comprehensive diabetes self management education with family involvement a key to achieving a successful outcome. Education should be based on an assessment of attitudes, beliefs and learning styles and where possible, educational resources should be age and culturally appropriate.

Dietary and physical activity goals need to be established early and they may have implications for more than one member of the family given the high probability of others family members having diabetes, being overweight or obese.

It will be fundamental for the child/family and/or carers to learn about the basic pathophysiology of diabetes and its complications, the role of self glucose monitoring and record keeping and the importance of regular diabetes management reviews by their relevant health professionals (see team approach). In order for the child/family to perform self glucose monitoring they will need to obtain a blood glucose meter, provided with appropriate education in its use and be registered with the National Diabetic Services Scheme (NDSS) to gain access to affordable supplies.

9.4 Education at diagnosis

Practical survival skills and basic information are essential at diagnosis as it is important not to overwhelm the child/family with excessive information but to provide necessary information.

| EDUCATION AT DIAGNOSIS | | |
|--|--|---|
| INTERVENTION | INFORMATION | OUTCOMES |
| <p>Initial patient/parent education</p> <p>Information regarding the management of the patient</p> | <p>Provide information about:</p> <ul style="list-style-type: none"> • Diabetes symptoms, • Blood glucose levels and targets, • Basic dietary advice, • Blood glucose monitoring, urine testing for ketones (only if necessary e.g. child has ketosis or DKA or type 2 diagnosis uncertain), • Insulin injections (technique) or oral medications (side-effects etc), • Storage of insulin • If taking insulin or sulphonylurea symptoms and treatment of hypoglycaemia | <p>Patients and parents/care givers will receive instruction in relevant information regarding the management of their diabetes.</p> <p>Content and presentation of Information will be individualised to meet the needs of patients and their families/care givers</p> |
| <p>Information regarding support services</p> | <p>Provide advice regarding:</p> <ul style="list-style-type: none"> • Follow-up and emergency contact numbers for PMH and/ or the NPD • the National Diabetes Services Scheme (NDSS) • Diabetes Australia • Medic alert bracelets | <p>Patients and families will be provided with information regarding resources which will assist them in the management of diabetes</p> |

9.5 Ongoing education

Diabetes education needs to be client centred. This means that the person (family) with diabetes must be involved in all aspects of the education and the depth/pace in which it is delivered. So, the ongoing education required after initial diagnosis must be delivered at a pace that is acceptable to the individual/family and the desirable outcome will be the attainment of knowledge, practical skills and empowerment to undertake diabetes self-management. The essential components of ongoing diabetes education are summarised below:

| ONGOING EDUCATION | | |
|--|---|--|
| INTERVENTION | INFORMATION | OUTCOMES |
| Dietary education (preferably by dietitian) | Provide education which includes <ul style="list-style-type: none"> • principles of healthy eating²². • Information about essential food groups, meal planning, and information for specific situations (e.g. school, exercise, alcohol). • Goal setting for dietary intake and weight management | Content and presentation of Information will be individualised to meet the needs of patients and their families/care givers Information will form the basis for continuing dietary education in the long term |
| Physical activity program | Consider including the role of a physiotherapist, exercise physiologist or family/community involvement (e.g. school or organised sport). | Goals set will form the basis for continuing physical exercise and future lifestyle management. |
| Knowledge and understanding of the pathophysiology of diabetes | Provide education which includes: <ul style="list-style-type: none"> • Delay, prevention and monitoring of diabetes related complications (the need for blood, urine tests, eye examinations and other investigations). • Role of health professionals in diabetes care and expected frequency of follow-up visits. • Sick-day management. • Problem-solving for different situations (exercise, alcohol, food) and insulin (medication) adjustment. • Health effects and other implications of smoking, alcohol and other drugs. • Sexuality and the implications for contraception, pregnancy and child birth, impotence and risk of STD's. | Ongoing education will provide the patient and family with an understanding of the pathophysiology of type 2 diabetes (insulin resistance, declining insulin secretion) and complications of diabetes. |

9.6 Blood glucose monitoring

Consensus guidelines state that self blood glucose monitoring (SBGM) is an integral part of diabetes self management and the access to blood glucose monitoring equipment should be available to all people with type 2 diabetes¹⁴. It is also important for individuals to be aware of their individualised blood glucose targets and monitoring frequency, although the ideal timing and frequency has not been established. SBGM is particularly useful for patients treated with insulin.

Other self management benefits include the ability for individuals to evaluate the blood glucose effect of:

- Oral hypoglycaemic agents or insulin
- Different foods
- Illness

Table 3. Blood Glucose Monitoring

| | Oral, diet or basal insulin therapy | Insulin therapy |
|--------------------|---|---|
| Frequency | Twice daily on 2-3 days per week. Fasting and 2 hours post prandial. | At least 4 times per day, every day until stable. Then 2-3 days per week. Pre meals, bedtime & occasional post prandial. |
| BGL Targets | Fasting < 6 mmol/L 2 hrs post-prandial < 8mmol/L | Pre-meal < 6 mmol/L 2 hrs post-prandial < 8mmol/L |

10. Pharmacotherapy (see Figure 2 for hyperglycaemic treatment algorithm)

The initial pharmacological management of children and adolescents with suspected (type 2) diabetes will depend on the severity of presentation. For those whom present symptomatic and with hyperglycaemia (>17mmol/L), ketosis or with diabetic ketoacidosis (DKA), insulin therapy should be used initially to gain metabolic control. However, if a diagnosis of T2DM is subsequently confirmed then metformin should be instituted along with an effort to cease insulin. A concerted effort to initiate and maintain healthy lifestyle choices along with weight loss will assist glycaemic control and delay the need to resume insulin therapy.^{1, 2, 16, 17, 19}

Metformin

For children who are diagnosed insidiously and/or are asymptomatic, then the lifestyle approach is the necessary first step. After 6-8 weeks of lifestyle intervention an assessment of control is required, with the introduction of Metformin at 500mg per day if glycaemic control is above target levels (HbA1c >7%).

Evaluate at next visit (up to 3 months) and increase dose over a 2-4 week period until BGL targets are achieved. Always adjust therapy in context of compliance with lifestyle changes (diet and exercise). Metformin should be adjusted up to a maximum daily divided dose of 2g or 2.5g (if tolerated)²³.

Metformin is also an optional **first line agent** for patients whom present with mild symptoms and without ketosis. Start at 500mg per day as above and adjust therapy to achieve target levels. Its use may be associated with gastrointestinal disturbances such as nausea, abdominal pain and diarrhoea. However, with slow, incremental dose increases and advice for patients to take the tablet(s) with or after food symptoms tend to reduce after the first 2-3 weeks. Metformin has been shown to be safe and efficacious when used in children and adolescents, although data is limited.^{24, 25}

Lactic acidosis is a listed adverse reaction to metformin therapy²³; however, the occurrence is rare²⁶ with the risk more often associated with acute illness (sepsis, myocardial infarction, and renal failure), predisposing patients to tissue hypoxia, hypofusion and renal insufficiency which may lead to lactic acidosis¹².

The use of metformin XR (an extended release once-daily formulation) may improve compliance²⁷ and gastrointestinal tolerability of metformin therapy.^{26, 28} The maximum dose for metformin XR is 2g daily (single dose with evening meal).²³

Sulphonylureas

The sulphonylureas are insulin secretagogues which stimulate insulin release from the β cell. This mode of action makes these drugs useful for controlling post-prandial hyperglycaemia and although this class of drug is well established, safe and effective in adults, the known side-effects of weight gain and hypoglycaemia²³ are problematic and sulphonylureas do not reduce insulin resistance, the underlying problem in type 2 diabetes. Furthermore, glycaemic control with sulphonylurea monotherapy is less durable than either, metformin or glitazone monotherapy.²⁹

Insulin Therapy and Indications

Insulin is necessary for insulin deficient type 1 diabetes but also has a major role in the treatment of insulin resistant T2DM. The early introduction and use of insulin in combination with oral agents has been shown to improve glycaemic control and therefore reduce the risk of complications.^{12, 15, 30} The two major side-effects of insulin therapy are weight gain and hypoglycaemia. However, the weight gain must be considered in context against the risk of complications with poor glycaemic control. The risk of hypoglycaemia in insulin-treated patients with T2DM is considerably less than with type 1 diabetes.¹⁵

The type of insulin and the timing of when to initiate therapy in adult or childhood T2DM has not been established, however, there is consensus that if glycaemic control is poor on max oral therapy (HbA1c > 8.5%) or patient is symptomatic (thirst, polyuria) then insulin therapy should be considered.^{1, 15} The effectiveness of insulin in lowering HbA1c over that of other therapies,¹⁵ along with the limited availability of approved therapeutic options, indicate that **insulin may be a more favourable choice as second-line therapy after metformin or stand-alone therapy in childhood diabetes**. There are many ways insulin can be used. The following list is a stepwise guide of when to initiate insulin in childhood T2DM and options for adjustment with other oral therapies.

These are summarised in **Figure 2**.

Insulin as only therapy**

Newly diagnosed individuals with hyperglycaemia (>17mmol/L) or evidence of ketosis or DKA and when patient unwell or when oral therapy has failed. Use **MDI** (multi dose insulin) or **BD pre-mixed insulin**.

1. Multi dose insulin options

Rapid-acting Novorapid ®, Humalog ® or Apidra ® insulin TDS (pre-meals) and basal insulin Lantus ®, Protophane ® or Humulin NPH ® once daily preferably at bedtime)

2. BD Pre-mixed insulin

Novomix 30 ® or HumalogMix 25 ® (twice-daily) pre breakfast and evening meal

** In newly diagnosed individuals, attempt to wean off insulin once BGL stable and **commence metformin** if type 2 diagnosis subsequently confirmed.

Insulin combined with oral therapy **

**Insulin is the preferable second-line option but options 2 (a) and 2 (b) allow for a sulphonylurea to be used as the second agent if using insulin therapy is problematic.

1. Initiated as second-line therapy when glycaemic control deteriorates.

Use basal insulin (Protophane[®], Humulin NPH[®] or Lantus[®]) in combination with metformin (preferred when HbA1c > 8.5%). Start basal insulin at bedtime (0.2-0.4 units/kg). Use fasting BGL to titrate insulin (2-4 units every 3 days) until FPG < 6 mmol/L.

2. (a) As third agent in combination with metformin and a sulphonylurea. Start with basal as above.

OR

(b) Use Pre-mixed insulin (novomix 30[®] or humalog mix 25[®]) pre-dinner only whilst continuing with metformin and/or sulphonylurea.

3. Intensive therapy using MDI with metformin.

Use rapid-acting insulin (novorapid[®], humalog[®] or apidra[®]) with meals and continue basal insulin or use mixed insulin twice daily with metformin. ** Cease sulphonylurea when using day-time rapid or BD mixed insulin

Simplified insulin/oral therapy

The previous guide is dependent on the individual/family being compliant with therapy. However, it is known that compliance with therapy, particularly complex therapy, is often suboptimal. Therefore, a simplified regimen may improve compliance with medical therapy, even if the therapy may not be entirely optimal.

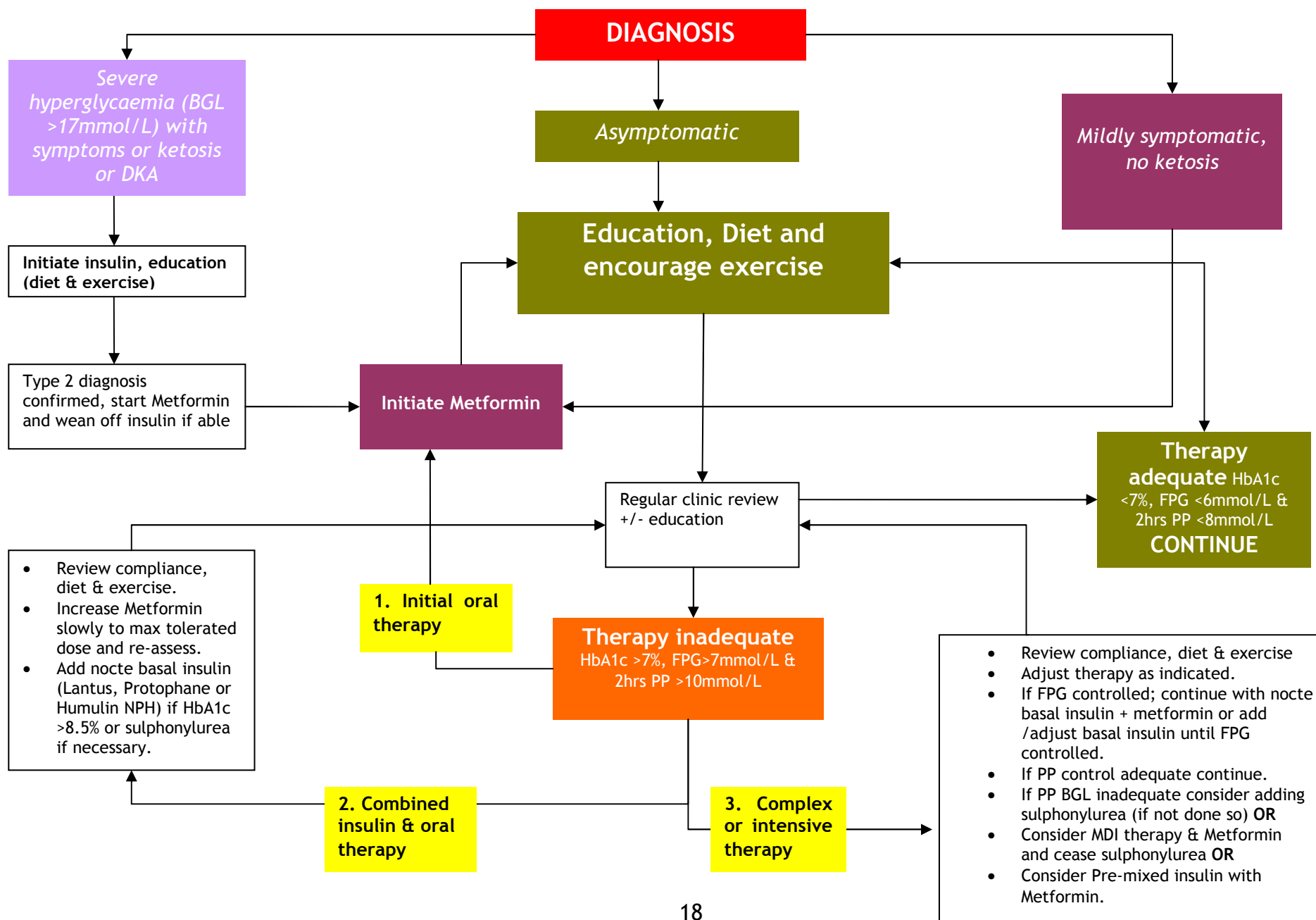
For example, the following two options allow for metformin and insulin therapy to be given at the same time once daily.

1. Metformin XR (max tolerated dose) given with evening meal along with glargine.

2. Metformin XR (max tolerated dose) given with evening meal along with pre-meal dose of pre-mixed insulin (novomix 30[®] or humalog mix 25[®]).

The above two options may enable the patient to achieve optimal fasting BGL, while the second option also assists post prandial control of the evening meal. Adherence to an appropriate diet regimen will particularly improve the success of these options.

Figure 2. Hyperglycaemic treatment algorithm



11. Table 4 Formulary of drugs to be considered for administration

All drugs are listed under the Endocrine and Metabolic therapeutic class and classified (S4) in the Poison's regulations.

| Drug Type/Class/use | Generic or brand name ® | Route/Dose/Freq | Side-effects, caution or adverse reaction | Contraindications | Comments | | | | | |
|--|--|---|---|--|--|------------------------|------------------------------|--|---------------|---------------|
| Biguanides/ (hypoglycaemic agents)/type 2 diabetes | Metformin | Oral/500mg daily up to 1000mg TDS | GI disturbances - Nausea, abdominal pain and diarrhoea/ Risk of lactic acidosis (rare). Caution Renal and hepatic dysfunction | Renal failure, Sepsis or CCF Myocardial infarction Withhold when using IV iodinated contrast media | Take with or after food to limit GI side effects | | | | | |
| | Metformin XR | Oral/ 500mg up to 2000mg daily | | | | | | | | |
| Sulphonylureas (hypoglycaemic agents)/type 2 diabetes | Gliclazide | Oral | Hypoglycaemia, hypersensitivity skin reactions | Type 1 diabetes hypoglycaemia | Take prior to meal. Risk of hypoglycaemia if meal is omitted | | | | | |
| | Glipizide | Oral | Hypoglycaemia, hypersensitivity skin reactions | Type 1 diabetes hypoglycaemia | | | | | | |
| | Glibenclamide | Oral | Hypoglycaemia, hypersensitivity skin reactions | Type 1 diabetes hypoglycaemia | | | | | | |
| Insulin (diabetes) | Insulin Aspart Novorapid® | Subcutaneous/ variable dose and frequency | Hypoglycaemia | hypoglycaemia | Given 10-20 minutes prior to meal. Risk of severe hypoglycaemia if meal omitted or carbohydrate inadequate | | | | | |
| | | | | | | Rapid-acting analogues | Insulin Lispro Humalog® | Subcutaneous/Variable dose and frequency | Hypoglycaemia | hypoglycaemia |
| | | | | | | | Insulin Glulisine Apidra® | Subcutaneous/Variable dose and freq | Hypoglycaemia | hypoglycaemia |
| Long-acting analogue | Insulin Glargine Lantus® | Subcutaneous/Variable dose/once daily | Hypoglycaemia | hypoglycaemia | | | | | | |
| Intermediate-acting insulin | Isophane Humulin NPH® & Protophane® | Subcutaneous/Variable dose and frequency | Hypoglycaemia | hypoglycaemia | | | | | | |
| Biphasic or Premixed insulin | Novomix 30® | Subcutaneous/Variable dose/once or twice daily | Hypoglycaemia | hypoglycaemia | Given 10-20 minutes prior to meal. Risk of severe hypoglycaemia if meal omitted or carbohydrate inadequate | | | | | |
| | Humalog Mix 25® | Subcutaneous/ variable dose/once or twice daily | Hypoglycaemia | hypoglycaemia | | | | | | |
| | Mixtard 30/70® and Humulin 30/70® | Subcutaneous/Variable dose/once or twice daily | Hypoglycaemia | hypoglycaemia | Given 20-30 minutes prior to meal. Risk as per above | | | | | |

12. Clinical monitoring and screening for microvascular and macrovascular complications

The prevention or delay of diabetes related end-organ complications (see also clinical management) is the primary focus and rationale for a coordinated and planned approach to ongoing clinical monitoring. Intensive management and subsequent improved glycaemic control has been shown to significantly reduce the occurrence and progression of microvascular and macrovascular complications in people with type 1 diabetes^{31, 32} and microvascular complications in adults with type 2 diabetes³³.

However, there is a lack of evidence for the effect of therapy and tight glycaemic control in young people with type 2 diabetes. It is known that diabetes is a risk factor for cardiovascular disease, which is the leading cause of mortality for people with type 2 diabetes. Therefore, a multi-factorial approach to management is required which includes efforts to control hypertension, dyslipidaemia and obesity as well as hyperglycaemia^{1, 2, 16}.

12.1 Glycaemic control

There is now a large evidence base to support the use of tight glycaemic targets in adults with type 2 diabetes¹⁴. Similar targets exist for type 1 diabetes in children and adults³⁴. Currently, the desirable HbA1c target is <7% however; tighter glycaemic targets of 6.5% have been suggested for type 2 diabetes¹⁴. In children with type 2 diabetes, a glycaemic target of normoglycaemia would be ideal but in practical terms a HbA1c of <7% as with adults, has been suggested^{2, 16}. Ideally, this relates to achieving self glucose monitoring targets of <6mmol/L (fasting) and <8mmol/L (2hrs post-prandial).

12.2 Dyslipidaemia

Children and adolescents with dyslipidaemia are more likely than the general population to have high cholesterol in adulthood. The management of dyslipidaemia in young persons with type 2 diabetes is based on relatively recent consensus-based guidelines³⁵ and are summarised in **Table 5**. Lipids can be elevated at diagnosis but it is inappropriate to evaluate in the presence of poor glycaemic control. Therefore, lipid levels should be checked soon after diagnosis (3-6months) once glycaemic control has been achieved and then 2-yearly.

First-line treatment options include lifestyle (diet and exercise) intervention strategies along with aggressively targeting blood glucose levels. If levels return to normal after 6 months of the above measures then they should be checked again on a yearly basis. Medication should be considered if LDL levels remain elevated (> 4.1 mmol/L) after the 6-month trial of lifestyle and improving blood glucose. Specialist advice should be gained prior to pharmacological treatment in children or adolescents.

12.3 Hypertension

Hypertension is defined in the paediatric population as an average of 3 measurements (systolic or diastolic blood pressure) \geq 95th percentile for age, sex and height³⁶. Blood pressure should be assessed at diagnosis and at each clinic visit using an appropriate cuff size. Targets are summarised in **table 5** below. Initial first-line therapy includes non-pharmacological treatment such as lifestyle change (weight loss, diet and exercise). The introduction of an ACE inhibitor is considered the best first-line pharmacological option^{1, 2}. Consideration should also be given to other causes of hypertension.

12.4 Clinical monitoring

Monitoring for signs of microvascular and macrovascular complications is essential and should include tests for microalbuminuria, screening for retinopathy, evaluation of blood pressure and blood lipids. Other tests will include HbA1c and foot assessment. It is uncertain how frequent these tests and assessments need to be performed. However, it has been suggested that they be performed based on the criteria for adult type 2 diabetes.

So, in contrast to newly diagnosed type 1 diabetes, complication screening should begin at diagnosis.¹⁹

Table 5 Clinical monitoring frequency and desirable levels

| Test | Frequency | Target/desirable level | Comments | |
|---|-------------------|--|--|---|
| HbA1c | 3 monthly | <7% | Used as adjunct to self glucose monitoring | |
| Dilated Retinal examination | annually | Absence of diabetes related retinal changes | Utilise tertiary and visiting Ophthalmology service | |
| Microalbuminuria | annually | a. AER <20µg/min in 2 of 3 timed overnight urine collections. or b. ACR of <2.5 mg/mmol (male) or <3.5 mg/mmol (female). | a. 3 consecutive overnight samples preferred or b. first morning specimen | |
| Blood pressure | each clinic visit | <90 th percentile normal >90 th and <95 th pre-hypertension ≥95 th hypertension | Percentile based on age, sex, height | |
| Lipids | 2 yearly | Total Chol | < 4.5 mmol/L | Interpretation ideally in context of adequate glycaemic control |
| | | HDL | >0.9 mmol/L | |
| | | LDL | <2.6 mmol/L | |
| | | TG | <1.7 mmol/L | |
| Foot assessment | annually | Check for protective sensation using 10g monofilament Reflexes, vibration. | | |
| Body Mass Index (BMI) kg/m ² | Each clinic visit | >85 th percentile (overweight) >95 th percentile (Obese) | | |

13. Authorship/review

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15. Abbreviations and Terms

| | |
|-----------------------|--|
| Acanthosis Nigricans: | Dark, thickened skin of rash appearance predominant around neck and occasionally axilla region. |
| ACR: | Albumin: Creatinine ratio. |
| AER: | Albumin excretion rate. |
| BMI: | Body mass index. |
| C-Peptide: | A biochemical marker of endogenous insulin release. |
| CRP: | c - reactive protein, a biochemical marker of infection or inflammation |
| FBC: | Full blood count. |
| FPG: | Fasting plasma glucose. |
| GAD 65: | Glutamic acid decarboxylase (diabetes antibodies). |
| HbA1c | Glycosylated haemoglobin, an estimation of the average blood glucose level of the preceding ~ 8 weeks. |
| HCP: | Health care professional. |
| Hyperglycaemia: | High blood glucose level. |
| Hypoglycaemia: | Low blood glucose level. |
| ICA: | Islet cell antibodies (diabetes antibodies). |
| LFT: | Liver function test. |
| OGTT: | Oral glucose tolerance test. |
| PCOS: | Polycystic ovarian syndrome. |
| U & E: | Urea and electrolytes. |

16. References

1. Gungor N, et.al. Type 2 Diabetes Mellitus in Youth: The complete picture to date. *Paediatric clinics of North America*. 200552:1579-609.
2. Alberti G et.al.; Type 2 diabetes in the young: The evolving epidemic. *Diabetes Care*. 200427:1798-811.
3. Goran MI, Ball GDC, L CM. Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents. *The Journal of Clinical Endocrinology and Metabolism*. 200388:1417-27.
4. Kitagawa T, et.al. Increased incidence of non-insulin dependent diabetes mellitus among Japanese school children correlates with an increased intake of animal protein and fat. *Clinical Paediatrics*. 1998, 37:111-6.
5. Sinha R, et.al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. *New England Journal of Medicine*. 2002346:802-10.
6. Ehtisham S, Barrett TG, J SN. Type 2 diabetes mellitus in UK children: an emerging problem. *Diabetetic Medicine* 200017:867-71.
7. Dabelea D. Increasing prevalence of type II diabetes in American Indian children. *Diabetologia*. 199841:904-10.
8. Macaluso CJ, et.al. Type 2 diabetes mellitus among Florida children and adolescents, 1994 through 1998. *Public Health Report*. 2002117:373-9.
9. Likitmaskul S, et.al. Increasing prevalence of type 2 diabetes mellitus in Thai children and adolescents associated with increasing prevalence of obesity. *Journal of Paediatric Endocrinology and Metabolism*. 200316:71-7.
10. McMahon SK, et.al. Increase in type 2 diabetes in children and adolescents in Western Australia. *The Medical Journal of Australia*. 2004180:459-61.
11. Department of Endocrinology and Diabetes Princess Margaret Hospital. Type 2 diabetes in children and adolescents. Clinical Practice Guidelines for Western Australia. Perth: Princess Margaret Hospital; 2007.
12. American Diabetes Association. Standards of medical care in diabetes-2007. *Diabetes Care* 200730:S4-S41.
13. McIntosh A, et.al. Clinical guidelines for type 2 diabetes mellitus: management of blood glucose. 2001 [cited; Available from: <http://www.shef.ac.uk/guidelines/>]
14. International Diabetes Federation. Global Guideline for Type 2 diabetes. 2005 [cited; Available from: <http://www.idf.org>]
15. Nathan DM, et.al. Management of hyperglycaemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. *Diabetologia*. 200649:1711-21.
16. American Diabetes Association. Type 2 diabetes in children and adolescents: consensus statement. *Diabetes Care*. 200023:381-9.
17. Bloomgarden ZT. Type 2 diabetes in the young: the evolving epidemic. *Diabetes Care*. 200427 998-1010.
18. Wein AJ, Fitzpatrick J.M, Chapple C.R, Drach GW, & Andersson KE. BPH and Male LUTS. *URO TODAY* 2007 [cited 6th March 2007]; Available from: http://www.urotoday.com/161/browse_categories/bph_male_luts/diagnosis_evaluation.html
19. Rosenbloom AL, Silverstein JH. 2003. *Type 2 Diabetes in Children and Adolescents*. Virginia: American Diabetes Association.
20. Expert committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 200124:S5-S20.
21. Turner R SI, Horton V, et al.; UKPDS 25: autoantibodies to islet-cell cytoplasm and glutamic acid decarboxylase for prediction of insulin requirement in type 2 diabetes. *Lancet*. 1997350:1288-93.
22. National Health and Medical Research Council N. Dietary guidelines for children and adolescents in Australia incorporating the infant feeding guidelines for health workers. In: Canberra, editor.: NHMRC; 2003.
23. eMims. Electronic Mims. 2007 [cited May]; Available from: www.mims.com.au
24. Jones K L AS, et al. Effect of metformin in pediatric patients with type 2 diabetes. *Diabetes Care*. 200225:89-94.
25. Gottschalk M, et.al. Glimperide versus metformin as monotherapy in pediatric patients with type 2 diabetes. *Diabetes Care*. 200730:790-4.
26. Salpeter S, et.al. Risk of fatal and non-fatal lactic acidosis with metformin use in type 2 diabetes. *Cochrane Database of Systemic Reviews* 2006.
27. Fujioka K, et.al. Efficacy, dose-response relationship and safety of once-daily extended-release metformin (Glucophage XR) in type 2 diabetic patients with inadequate glycaemic control despite prior treatment with diet and exercise: results from two double-blind, placebo-controlled studies. *Diabetes, Obesity and Metabolism*. 20057:28-39.
28. Blonde L et.al.; Gastrointestinal tolerability of extended-release metformin tablets compared to immediate release metformin tablets: results of a retrospective cohort study. *Current Medical Research and Opinion*. 200420:565-72.
29. Kahn SE, et.al. Glycemic durability of Rosiglitazone, Metformin or Glyburide monotherapy. *New England Journal of Medicine*. 2006355:2427-43.
30. UK Prospective Diabetes Study UG. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complication in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998352:837-53.
31. The Diabetes Control and Complications Trial Research Group D. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *The New England Journal of Medicine*. 1993329:977-86.
32. The Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *The New England Journal of Medicine*. 2005353:2643-5.
33. UK Prospective Diabetes Study Group U. Effect of intensive blood glucose control with metformin on complication in overweight patients with type 2 diabetes (UKPDS 34). *Lancet*. 1998352:854-65.
34. National Health and Medical Research Council and Australasian Paediatric Endocrine Group. Clinical Practice Guidelines: Type 1 diabetes in children and adolescents. In: Canberra, editor.: NHMRC, Commonwealth of Australia; 2005.

35. American Diabetes Association. Management of dyslipidaemia in children and adolescents with diabetes: consensus statement. *Diabetes Care*. 2003;26:2194-97.
36. National High Blood Pressure Education Working Group. The fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescents. *Paediatrics*. 2004; 114 (S2):555-76.