PHC Chapter 9: Endocrine conditions

9.1 TYPE 1 DIABETES MELLITUS

DESCRIPTION

Type 1 diabetes mellitus, previously known as juvenile onset diabetes mellitus and as insulin-dependent diabetes mellitus (IDDM), occurs because of a lack of insulin. The result is an increase in blood glucose concentration.

CLINICAL PRESENTATION

- » hunger
- » polyuria
- » ketoacidosis
- » thirst
- » unexplained weight loss
- » tiredness

DIAGNOSIS

Type 1 diabetes mellitus is diagnosed when the classic symptoms of polyuria and polydipsia are associated with hyperglycaemia:

- » Random blood glucose ≥ 11.1 mmol/L.
- » Random is defined as any time of day without regard to time since last meal.

OR

- » Fasting blood glucose ≥ 7.0 mmol/L.
- » Fasting is defined as no caloric intake for ≥ 8 hours.

OR

- » 2-hour plasma glucose in a 75 g oral glucose tolerance test ≥ 11.1 mmol/l. *LoE:III*[1]

GENERAL MEASURES

- » Education regarding diabetes and its complications.
- » Even and regular meal consumption.
- » Dietary emphasis should be on regulating carbohydrate, fibre and fat intake (See Section 9.2.2: Type 2 Diabetes mellitus, in adults for recommended diet plan).
- » Increased physical activity: aim for 30 minutes 5 times a week.
- » Appropriate weight loss if body mass index > 25 kg/m2.
- » Education about foot care.
- » Monitor for development of depression.
- » All patients should wear a notification bracelet.

REFERRAL

All patients.

9.1.1 TYPE 1 DIABETES MELLITUS, IN CHILDREN AND ADOLESCENTS

E10.9

MEDICINE TREATMENT

Oral anti-diabetic medicines should not be used to treat children with type 1 diabetes mellitus.

REFERRAL

All children with confirmed or suspected type 1 diabetes mellitus must be referred to a hospital immediately for management.

9.1.2 TYPE 1 DIABETES MELLITUS, IN ADULTS

E10.9

Type 1 diabetes mellitus is a rare condition and should be diagnosed and monitored at hospital level. Only stable patients may be down referred for chronic medicines.

MONITORING FOLLOWING DOWN REFERRAL

At every visit:

» Finger-prick blood glucose.
» Weight.
» Blood pressure.

Annually:

» HbA1c, one month before next hospital appointment.

TARGETS FOR CONTROL

Glycaemic targets for control:

Patient type	Target HbA1c	Target FBG*	Target PPG*
» Young, low risk » Newly diagnosed » No CVS disease	< 6.5%	4.0–7.0 mmol/L	4.4–7.8 mmol/L
» Majority of patients	< 7.0%	4.0–7.0 mmol/L	5.0–10.0 mmol/L
» Elderly » High risk » Hypoglycaemic unawareness » Poor short-term prognosis	< 7.5%	4.0–7.0 mmol/L	< 12.0 mmol/L

***FBG: fasting blood glucose; PPG: post-prandial blood glucose.**

Non-glycaemic targets:

» Body mass index ≤ 25 kg/m2.
» BP < 140/90 mmHg.

The increased risk of hypoglycaemia must always be weighed against the potential benefit of reducing microvascular and macrovascular complications.

MEDICINE TREATMENT

As type 1 diabetes mellitus usually presents with diabetic ketoacidosis, treatment is usually initiated with insulin and the patient is stabilised at hospital level. Oral anti-diabetic medicines should not be used to treat type 1 diabetics.

Insulin dose requirements will decrease as kidney disease progresses.

Types of insulin

- Insulin, short acting, SC, three times daily, 30 minutes before meals.
  - Regular human insulin.
  - Onset of action: 30 minutes.

  - Peak action: 2–5 hours.
  - Duration of action: 5–8 hours.
- Insulin, intermediate acting, SC, once or twice daily usually at night at bedtime, approximately 8 hours before breakfast.
  - Intermediate acting insulin.
  - Onset of action: 1–3 hours.
  - Peak action: 6–12 hours.
  - Duration of action: 16–24 hours.
- Insulin, biphasic, SC, once or twice daily.
  - Mixtures of regular human insulin and intermediate acting insulin in different proportions, e.g. 30/70 (30% regular insulin and 70% intermediate acting insulin).
  - Onset of action: 30 minutes.
  - Peak action: 2–12 hours.
  - Duration of action: 16–24 hours.

Insulin regimens

Basal bolus regimen

All type 1 diabetics should preferentially be managed with the "basal bolus regimen" i.e. combined intermediate acting (basal) and short acting insulin (bolus). This consists of pre-meal, short acting insulin and bedtime intermediate acting insulin not later than 22h00.

The initial total daily insulin dose:

  - 0.6 units/kg body weight.

The total dose is divided into:

  - 40–50% basal insulin
  - The rest as bolus insulin, split equally before each meal.

Adjust dose on an individual basis.

Pre-mixed insulin

Twice daily pre-mixed insulin, i.e. a mixture of intermediate- or short acting insulin provides adequate control when used with at least daily blood glucose monitoring. It is a practical option for patients who cannot monitor blood glucose frequently.

Education related to insulin therapy

» Types of insulin.
» Injection technique and sites of injection.
» Insulin storage.
» Recognition and treatment of acute complications, e.g. hypoglycaemia and hyperglycaemia.
» Diet:
  - Meal frequency, as this varies according to the type and frequency of insulin, e.g. patients may need a snack at night, about 3–4 hours after the evening meal.
  - Consistent carbohydrate intake for patient receiving fixed mealtime doses of insulin.
» Self-monitoring of blood glucose and how to self-adjust insulin doses.

Drawing up insulin from vials
» Clean the top of the insulin bottle with an antiseptic swab.
» Draw air into the syringe to the number of marks of insulin required and inject this into the bottle; then draw the required dose of insulin into the syringe.
» Before withdrawing the needle from the insulin bottle, expel the air bubble if one has formed.

Injection technique
» The skin need not be specially cleaned.
» Repeated application of antiseptics hardens the skin.
» Stretching the skin at the injection site is the best way to obtain a painless injection. In thin people, it may be necessary to pinch the skin between thumb and forefinger of one hand.
» The needle should be inserted briskly at almost 90□ to the skin to almost its whole length (needles are usually 0.6–1.2 cm long).
» Inject the insulin.
» To avoid insulin leakage, wait 5–10 seconds before withdrawing the needle.
» Injection sites must be rotated to avoid lipohypertrophy.

Prefilled pens and cartridges
In visually impaired patients and arthritic patients, prefilled pens and cartridges may be used.

Home blood glucose monitoring
Patients on basal/bolus insulin should measure glucose 3-4 times daily.
Once patient is stable, reduce the frequency of monitoring. *LoE:III*

REFERRAL
All patients.

9.2 TYPE 2 DIABETES MELLITUS

9.2.1 TYPE 2 DIABETES MELLITUS, IN ADOLESCENTS
E11.9

DESCRIPTION
The majority of adolescent diabetics are of type 1. However, an increasing number of adolescents are being diagnosed with type 2 diabetes mellitus.

Criteria for screening for diabetes in children
» Body mass index > 85th percentile for age and sex.
» Family history of type 2 diabetes mellitus.
» Presence of hyperlipidaemia, hypertension or polycystic ovarian syndrome.

AND
» Physical signs of puberty or age > 10 years of age.

DIAGNOSIS
» Symptoms of diabetes plus a random blood glucose ≥ 11.1 mmol/L.
  - Random is defined as any time of day without regard to time since last meal.

- Classic symptoms of diabetes mellitus include polyphagia, polyuria, polydipsia.

OR

» Fasting blood glucose ≥ 7.0 mmol/L.
- Fasting is defined as no caloric intake for ≥ 8 hours.

OR

» 2-hour plasma glucose in a 75 g oral glucose tolerance test ≥ 11.1 mmol/l. *LoE:III*[2]

It is difficult to distinguish type 2 from type 1 diabetes mellitus, as many type 1 diabetics may be overweight, or have a family history of type 2 diabetes mellitus, given the increasing prevalence of both obesity and type 2 diabetes mellitus. The diagnosis of type 2 diabetes mellitus in adolescents should be made in consultation with a specialist.

REFERRAL
All patients.

9.2.2 TYPE 2 DIABETES MELLITUS, ADULTS
E11.9

DESCRIPTION
Type 2 diabetes mellitus is a chronic debilitating metabolic disease characterised by hyperglycaemia with serious acute and chronic complications. It is an important component of the metabolic syndrome (see Section 9.5.1: Obesity in diabetes).
Most type 2 diabetes mellitus adults are overweight with a high waist to hip ratio.
In adults, the condition might be diagnosed when presenting with complications, e.g.:

» ischaemic heart disease
» peripheral artery disease
» stroke
» deteriorating eyesight
» foot ulcers
» erectile dysfunction

CLINICAL PRESENTATION
Symptoms of hyperglycaemia are:

» thirst, especially noticed at night
» polyuria
» tiredness
» periodic changes in vision due to fluctuations in blood glucose concentration
» susceptibility to infections, especially of the urinary tract, respiratory tract and skin

Note: It is important to distinguish type 2 diabetes mellitus from type 1diabetes mellitus. Suspect type 1 diabetes mellitus among younger patients with excessive weight loss and/or ketoacidosis.

DIAGNOSIS
» Symptoms of diabetes plus a random blood glucose ≥ 11.1 mmol/L.
- Random is defined as any time of day without regard to time since last meal.

OR

» Fasting blood glucose ≥ 7.0 mmol/L.
- Fasting is defined as no caloric intake for ≥ 8 hours.

OR

» 2-hour plasma glucose in a 75 g oral glucose tolerance test ≥ 11.1 mmol/l.

Note: If screening and not symptomatic: 2 positive tests done on separate days are required for diagnosis. *LoE:III*[3]

MONITORING

At every visit:
» Finger-prick blood glucose.
» Weight.
» Blood pressure.

Baseline:
» Serum creatinine concentration (and calculate eGFR).
» Serum potassium concentration, if on ACE-inhibitor or eGFR < 30 mL/min.
» Urine protein by dipstix.
  - If dipstix negative, send urine to laboratory for albumin: creatinine ratio, unless already on an ACE-inhibitor. (See Section 9.4.3: Diabetic nephropathy).
  - If dipstix positive, see Section 9.4.3: Diabetic nephropathy.
» BMI for cardiovascular risk assessment if appropriate (See Section 4.1: Prevention of ischaemic heart disease and atherosclerosis).
» Blood lipids (fasting total cholesterol, triglycerides, HDL and LDL cholesterol).
» Foot examination.
» Eye examination to look for retinopathy.
» Abdominal circumference.

Annually:
» Serum creatinine concentration (and calculate eGFR).
» Serum potassium concentration, if on ACE-inhibitor or eGFR < 30 mL/min.
» Urine protein by dipstix.
  - If dipstix negative, send urine to laboratory for albumin: creatinine ratio, unless already on an ACE-inhibitor. (See Section 9.4.3: Diabetic nephropathy.)
» HbA1c, in patients who meet treatment goals (3–6 monthly in patients whose therapy has changed, until stable).
» Eye examination to look for retinopathy.
» Foot examination.

TARGETS FOR CONTROL

Glycaemic targets for control:

Patient type	Target HbA1c	Target FBG*	Target PPG*
» Young, low risk » Newly diagnosed » No CVS disease	< 6.5%	4.0–7.0 mmol/L	4.4–7.8 mmol/L
» Majority of patients	< 7.0%	4.0–7.0 mmol/L	5.0–10.0 mmol/L
» Elderly » High risk » Hypoglycaemic unawareness » Poor short-term prognosis	< 7.5%	4.0–7.0 mmol/L	< 12.0 mmol/L

***FBG: fasting blood glucose; PPG: post-prandial plasma glucose.**

» In the elderly, the increased risk of hypoglycaemia must be weighed against the potential benefit of reducing microvascular and macrovascular complications.
» Prevent acute complications, e.g. hyperglycaemic and hypoglycaemic coma.

Non-glycaemic targets:
» Body mass index ≤ 25 kg/m2.
» BP ≤ 140/90 mmHg and ≥ 120/70 mmHg.

Management of type 2 diabetes mellitus includes:

» Treatment of hyperglycaemia.
» Management of chronic conditions associated with diabetes. For treatment of hypertension and dyslipidaemia after risk-assessment, see Section 4.7: Hypertension and Section 4.1: Prevention of Ischaemic heart disease and atherosclerosis.
» Prevention and treatment of microvascular complications. See Section 9.4: Microvascular complications of diabetes.
» Prevention and treatment of macrovascular complications. See Section 9.5: Cardiovascular risk in diabetes.

GENERAL MEASURES

» Lifestyle modification, including self-care practices.
» Refer to a dietician if available for annual follow-up.
» Refer to a support group if available.
» Education about diabetes and its complications.
» Increased regular physical activity, aim for 30 minutes 5 times a week.
» Appropriate weight loss if weight exceeds ideal weight.
» Discourage smoking.
» Moderate or no alcohol intake (≤ 2 standard drinks per day for males and ≤ 1 for females).
» Education about foot care.
» All patients should wear a notification bracelet.

Diet

Encourage: *LoE: III*[4]

» regular, evenly-spaced meals, with small portions
» nutritionally balanced meals, with a variety of healthy foods
» meals that consist of one meat dish option with an option of vegetarian for those who are vegetarian, one starch option, two vegetable options, one fruit option and water

Carbohydrates

» Strict control of carbohydrate intake:
  - encourage small portions of healthy carbohydrates, such as vegetables, fruits, whole grains (e.g. whole wheat bread, oats, brown rice, pearled wheat, maise meal porridge, sorghum porridge, samp, wheat rice), legumes (lentils, beans), and dairy products
  - discourage intake of less healthy, highly processed/refined carbohydrate foods, especially those with added fats, sugars, or salt (e.g. takeaways, deep-fried foods, pies, doughnuts, cakes, biscuits, white bread, sugary drinks)

Fruit and vegetables

» Aim for 5 servings of fruit or vegetables per day (e.g. vegetables: spinach, morogo, cabbage, tomato, imifino (amadumbe, amaranth, cowpea, pumpkin and sweet potato leaves); fruit: apple, orange, naartjie, banana, mango, pear, peach)
» Limit fruit to 2 servings per day, preferably in small portions throughout the day rather than all at one meal
» Limit intake of starchy vegetables like potatoes, sweet potatoes, mielies, butternut, and pumpkin
» Limit intake of concentrated fruit sources such as dried or tinned fruit, or juices.

Legumes

» Soy beans, dry beans, chickpeas, lentils, and split peas are an economical source of protein and fibre
» They do contain starch, so contribute to total carbohydrate intake (see portion sizes below)

Dairy

» Advise fat-free or lower fat options.

Meat, fish, and eggs

» Encourage less fatty cuts of meat if possible.
» Encourage low fat cooking methods such as baking, grilling, or steaming. Trim excess fat from meat and remove skin from chicken before cooking.
» Encourage patients to eat oily fish e.g. sardines and pilchards 2-3 times a week.
» Limit eggs to 1 per day.
» Avoid processed meats such as polony and viennas.

Fats

» Replace unhealthy animal fats (fatty beef, pork, lamb and chicken) and tropical oils (e.g. coconut and palm kernel oil) with healthier fats (e.g. avocado pear, fatty fish such as pilchards and plant oils such as canola, olive, sunflower, or peanut butter).
» Do not reheat oil, and use softer margarines where possible.
» Limit intake of takeaway foods, and rather prepare food at home most of the time.

Sugar

» Avoid sugar and sugary foods and drinks, such as: table sugar, honey, sugary drinks (fizzy drinks, fruit juices, energy drinks, sport drinks, sweetened flavoured milk/drinking yoghurt, flavoured water), sweets, desserts and baked goods.
» If eaten on special occasions, advise in very small portions.

Salt

» Do not exceed a half teaspoon of salt per day. This includes hidden salt in processed foods (e.g. stock cubes, gravy and soup powders, deli meats like polony and viennas, take-away foods, chips/crisps).
» Avoid adding salt to food.
» Use less salt when preparing food. Use herbs and spices to enhance the flavour of foods instead of salt.

Portion control guide:

A portion is the amount of food that a person eats at one time, for a meal or snack. Advise the following portion sizes:

» Make protein (e.g. fish, chicken, or meat) food portions the size of the palm of your hand (about 90 g or 1/2 cup).
» Make fruit, vegetables and starchy food (such as rice, pasta and potatoes) portions no greater than the size of your clenched fist (1 cup).
» Make healthy fat portions the size of the tip of your thumb (1 teaspoon).
» Make hard cheese or peanut butter portions the length of your thumb (1 tablespoon).

MEDICINE TREATMENT

Oral blood glucose lowering agents

Stepwise approach:

» Add metformin to the combination of dietary modifications and physical activity/exercise.
» Combination therapy with metformin plus a sulphonylurea is indicated if therapy with metformin alone (together with dietary modifications and physical activity/exercise) has not achieved the HbA1c target.
» For persisting HbA1c above acceptable levels and despite adequate adherence to oral hypoglycaemic agents: add insulin and withdraw sulphonylurea.
» Ensure patient is adherent at each step.
» Oral agents should not be used in type 1 diabetes mellitus, renal impairment or clinical liver failure.

STEP 1

Lifestyle modification plus metformin

Entry to Step 1	Treatment and duration	Target
» Typical symptoms - thirst, tiredness, polyuria. **AND** » Random blood glucose >11.1mmol/L. **OR** » Fasting blood glucose ≥ 7 mmol/L.	» Lifestyle modification for life. » Appropriate diet. » Weight loss until at ideal weight. Initiate drug therapy with: • Metformin. » Assess monthly.	» 2-hour post-prandial finger-prick blood glucose: 8–10 mmol/L. **OR** » fasting finger-prick blood glucose: 6–8 mmol/L. **AND/OR** » HbA1c:7–8%.

- Metformin, oral, 500 mg daily with meals.
  - Titrate dose slowly depending on HbA1c and/or fasting blood glucose concentrations to a maximum dose of 850 mg 8 hourly.
  - Contraindicated in:
    - uncontrolled congestive cardiac failure
    - severe liver disease
    - patients with significant respiratory compromise
    - renal impairment i.e. eGFR <30 mL/minute,

In patients with renal impairment, adjust dose according to table:

eGFR	Metformin dose
» eGFR >60 mL/min	Normal daily dose (see above).
» eGFR 45–60 mL/min	Standard dose, measure eGFR 3–6 monthly.
» eGFR 30–45 mL/min	**Maximum dose 1 g per day**; measure eGFR 3–6 monthly.
» eGFR <30 mL/min	Stop metformin.

LoE:III[5]

STEP 2

Add sulphonylurea:

Entry to Step 2	Treatment and duration	Target
» Failed step 1: HbA1c > 8 % or fasting finger-prick blood glucose >8 mmol/L despite adherence to treatment plan in step 1 and maximal dose of metformin for 2–3 months. **OR** » 2-hour post-prandial finger-prick blood glucose >10 mmol/L despite adherence to treatment plan in step 1 and maximal dose of metformin for 2–3 months.	» Lifestyle modification. **AND** » Combination oral hypoglycaemic agents, i.e.: • Metformin, oral. **AND** • Sulphonylurea.	» 2-hour post-prandial finger prick blood glucose < 8–10 mmol/L. **OR** » fasting finger prick blood glucose: 6–8 mmol/L. **AND/OR** » HbA1c:7–8%.

- Sulphonylurea derivatives
- Glimepiride, oral, daily with breakfast.
  - Titrate the dose by 1 mg at weekly intervals up to 6 mg daily (according to blood glucose levels). *LoE:III*[6]
  - Usual dose: 4 mg daily.
  - Maximum dose: 8 mg daily.
  - Preferred in the elderly.

OR

- Glibenclamide, oral, 2.5 mg daily 30 minutes with breakfast.
  - Titrate dose slowly depending on HbA1c and/or fasting blood glucose levels to a maximum of 15 mg daily.
  - When ≥ 7.5 mg per day is needed, divide the total daily dose into 2, with the larger dose in the morning.
  - **Avoid in the elderly and patients with renal impairment.**

All sulphonylureas should be avoided in patients with renal impairment i.e. eGFR < 60 mL/minute.

Sulphonylureas are contraindicated in:
» severe hepatic impairment
» pregnancy

Missing meals while taking sulphonylureas may lead to hypoglycaemia.

STEP 3

Insulin therapy: See Section 9.1.2: Type 1 diabetes mellitus, in adults.

» Insulin is indicated when oral combination therapy fails.
» Continue lifestyle modification.
» Insulin therapy must be initiated and titrated by a doctor until stabilised.
» Stop sulphonylurea once insulin therapy is initiated but continue metformin.

LoE: III[7]

Education for patients on insulin therapy:

» Types of insulin.
» Injection technique and sites of injection.
» Insulin storage.
» Self-monitoring of blood glucose and how to self-adjust insulin doses.
» Diet:
  - Meal frequency, this varies according to the type and frequency of insulin, e.g. patients may need a snack at night about 3–4 hours after the evening meal.
  - Consistent carbohydrate intake for patients receiving fixed mealtime doses of insulin.
» Recognition and treatment of acute complications, e.g. hypoglycaemia and hyperglycaemia.

Insulin type	Starting dose	Increment
Add on therapy: • Insulin, intermediate to long acting, SC	10 units in the evening before bedtime, but not after 22h00.	If 10 units not effective: increase gradually to 20 units (2–4 units increase each week).
Substitution therapy: • Insulin, biphasic, SC	Twice daily. Total daily dose: Start with 0.3 units/kg/day* divided as follows: *LoE: III*[8] o 2/3 of total daily dose, 30 minutes before breakfast. o 1/3 of total daily dose, 30 minutes before supper.	4 units weekly. First increment is added to dose before breakfast. Second increment is added to dose before supper.

*Example of a dose calculation:

- For a 70 kg adult: 0.3 units x 70 kg = 21 units per day; divided as 14 units 30 minutes before breakfast and 7 units 30 minutes before breakfast.

REFERRAL

Urgent (same day)

» Acidotic breathing.
» Dehydration and hypotension.
» Nausea, vomiting and abdominal pain.
» Ketonuria (more than 1+).
» Hyperglycaemia >25 mmol/L.

» Gangrene.
» Sudden deterioration of vision.
» Serious infections.

Note: Consider IV infusion with sodium chloride 0.9%, before transferring very ill patients.

Non-urgent

» Pregnancy.
» Failure of step 3 to control diabetes.
» eGFR< 30 mL/minute.
» Ischaemic heart disease.
» Cerebrovascular disease.
» Refractory hypertension.
» Progressive loss of vision.

9.3 DIABETIC EMERGENCIES

DESCRIPTION

Diabetics may present with a decreased level of consciousness owing to:

» hyperglycaemia diabetic ketoacidosis (DKA) or hyperosmolar hyperglycaemic state (HHS), or
» hypoglycaemia.

DIAGNOSIS

Check blood glucose concentration and test urine for ketones, immediately.

	Hyperglycaemia		Hypoglycaemia
	DKA	HHS	
Blood glucose	≥ 11.1 mmol/L	Usually > 40 mmol/L	< 4 mmol/L
Urine test for ketones	Usually positive and > 1+	Usually negative	Usually negative

If a diagnosis cannot be made, treat as hypoglycaemia and refer urgently.
Low blood glucose presents the most immediate danger to life.

9.3.1 HYPOGLYCAEMIA IN DIABETICS

E10.0/E11.0/E12.0/E13.0/E14.0

DESCRIPTION

Diabetic patients on therapy may experience hypoglycaemia for reasons such as intercurrent illness (e.g. diarrhoea); missed meals; inadvertent intramuscular injections of insulin or miscalculated doses of insulin or progressive renal failure leading to decreased insulin clearance; alcohol ingestion; and exercise without appropriate dietary preparation.

Risk factors include age < 6 years of age, low HbA1c, and longer duration of diabetes.

Hypoglycaemia in diabetic patients can be graded according to the table below:

Mild/moderate hypoglycaemia	Severe hypoglycaemia
» Capable of self-treatment*.	» Semi-conscious

	or » Unconscious/comatose.
» Conscious, but requires help from someone else.	» Requires medical help.

**Except children < 6 years of age.*

Autonomic symptoms/signs	Neurological symptoms/signs
» Tremors » Palpitations » Sweating » Hunger » Fatigue » Pallor	» Headache » Mood changes » Low attentiveness » Slurred speech » Dizziness » Unsteady gait » Depressed level of consciousness/ convulsions

***Note:**

» Children, particularly < 6 years of age, generally are not capable of self-management and are reliant on supervision from an adult.

» Patients may fail to recognise that they are hypoglycaemic when neuroglycopenia (impaired thinking, mood changes, irritability, dizziness, tiredness) occurs before autonomic activation.

DIAGNOSIS

» Blood glucose < 4mmol/L with symptoms in a known diabetic patient.

» Blood glucose concentrations should be measured with a glucometer to confirm hypoglycaemia.

Hypoglycaemia must be managed as an emergency.
If a diabetic patient presents with an altered level of consciousness and a glucometer is not available, treat as hypoglycaemia.

EMERGENCY TREATMENT

» Measure blood glucose concentration with glucometer/testing strip, immediately.

Conscious patient, able to feed

Breastfeeding child

- give breast milk

Older children

- a formula feed of 5 mL/kg

OR

- oral sugar solution

dissolve 3 teaspoons of sugar (15 g) in 200 mL cup of water, administer 5 mL/kg

OR

- sweets, sugar, glucose by mouth

Adults

- sweets, sugar, glucose by mouth

OR

- oral sugar solution
  - dissolve 3 teaspoons of sugar (15 g) in 200 mL cup of water, administer 5 mL/kg

Conscious patient, not able to feed without danger of aspiration

Administer via nasogastric tube:

- Dextrose 10%, 5mL/kg
  - Add 1 part 50% dextrose water to 4 parts water to make a 10% solution.

OR

- milk

OR

- sugar solution
  - dissolve 3 teaspoons of sugar (15 g) in 200 mL of water; administer 5 mL/kg

Unconscious patient

Children

- Dextrose 10%, IV, 2–5 mL/kg.

IV administration of dextrose in children with hypoglycaemia:

» Establish an IV line. Do not give excessive volumes of fluid: usually can keep line open with 2mL/kg/hour.

» Take a blood sample for emergency investigations and blood glucose.

» Check blood glucose.

- **If low, i.e. < 2.5 mmol/L or if testing strips are not available, administer 2–5 mL/kg of 10% dextrose solution IV rapidly.**
  In the majority of cases, an immediate clinical response can be expected.

» Re-check the blood glucose after infusion.

- If still low, repeat 2 mL/kg of 10% dextrose solution.

» After recovery, maintain with 5–10% dextrose solution until blood glucose is stabilised.

» Feed the child as soon as conscious.

Adults

- Dextrose 10% solution, IV, 2–5 mL/kg.
  - Do not give unless hypoglycaemic or hypoglycaemia strongly suspected.
  - Do not give excessive volumes of fluid.
  - If hypoglycaemia is treated:
    - re-check blood glucose 10–15 minutes later;
    - if still low, give a further bolus of dextrose 10%, IV, 2 mL/kg, and commence dextrose 5 or 10%, infusion, 3–5 mL/kg/hour to prevent blood glucose dropping again.

Assess continuously until the patient shows signs of recovery. *LoE:III*[9]

Alcoholics (or where alcohol intake cannot be excluded)

- Thiamine, IV/IM, 100 mg immediately.

CAUTION

Thiamine should preferably be administered prior to intravenous glucose to prevent permanent neurological damage.
Do not delay the dextrose administration in a hypoglycaemic patient.

REFERRAL

Urgent

» All hypoglycaemic patients on oral hypoglycaemic agents.
» Hypoglycaemic patients who do not recover completely after treatment.
» All children with documented hypoglycaemia unless the cause is clearly identified and safe management instituted to prevent recurrence.

9.3.2 SEVERE HYPERGLYCAEMIA (DIABETIC KETOACIDOSIS (DKA) & HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS)

E10.0-1/E11.0-1/E12.0-1/E13.0-1/E14.0-1

DESCRIPTION

Clinical features of severe hyperglycaemia include:

» dehydration
» abdominal pain
» vomiting
» deep sighing respiration
» drowsiness, confusion, coma
» acetone/fruity-smelling breath
» elevated blood glucose

MEDICINE TREATMENT

Adults

Average fluid deficit 6 L, and may be as much as 12 L.
Be cautious in renal and cardiac disease.
In the absence of renal or cardiac compromise:

- Sodium chloride 0.9%, IV, 15–20 mL/kg in the first hour.
  - Subsequent infusion rate: 10 mL/kg/hour with 20 mL/kg boluses if shocked.
  - Do not exceed 50 mL/kg in the first 4 hours.
  - Correct estimated deficits over 24 hours.

Refer urgently with drip in place and running at planned rate.

When referral will take more than 2 hours and a diagnosis of diabetes with hyperglycaemia is confirmed:

- Insulin, short acting, IM, 0.1 unit/kg.
  - When giving insulin IM, do not use insulin needle.

CAUTION

Do not administer short acting insulin if the serum electrolyte status, especially potassium, is not known.
Continue with fluids, but delay giving insulin in these cases in consultation with referral facility as this delay should not negatively affect the patient, but hypokalaemia with resultant cardiac dysrhythmias definitely will.

Children

If in shock:

- Sodium chloride 0.9%, IV, 20 mL/kg as a bolus.
  - If shock not corrected, repeat the bolus.

- If a 3rd bolus is required, consult with a paediatrician.

If no shock or aftershock is corrected:

- Sodium chloride 0.9%, IV.

Fluid rates of sodium chloride 0.9%, IV (if no shock) in children awaiting transfer.	**Check regularly for shock or increasing dehydration**
Weight range kg	**Rate**(mL/hr) (2–10 kg: 6 mL/kg/hr) (>10-–20 kg: 5 mL/kg/hr) (>20–40 kg: 4 mL/kg/hr)
>4–6	25
>6–10	40
>10–15	60
>15–20	85
>20–30	100
>30–45	150
>45–80	200

Refer urgently with drip in place and running at planned rate.

When referral will take > 2 hours and a diagnosis of diabetes with hyperglycaemia is confirmed and provided glucose is monitored hourly:

- Insulin, short acting, IM, 0.1 units/kg after 1st hour of infusion of saline
  - When giving insulin IM, do not use insulin needle.

9.4 MICROVASCULAR COMPLICATIONS OF DIABETES

9.4.1 DIABETIC NEUROPATHY

E10.4/E11.4 + (G63.2*/G99.0*/G59.0*)

DESCRIPTION

Neuropathies are a common complication of diabetes. They play an important role in the morbidity and mortality suffered by people with diabetes.

There are three major categories:

» peripheral neuropathy
» autonomic neuropathy
» acute onset neuropathies

GENERAL MEASURES

» Educate patient regarding appropriate footwear and good foot care.
» Patients with neuropathy should have their feet examined at every visit.

MEDICINE TREATMENT

Ensure appropriate glycaemic control.

Exclude or treat other contributory factors e.g.:

» alcohol excess
» vitamin B12 deficiency, if suspected
» uraemia
» HIV infection

Pain

- Amitriptyline, oral, 10–25 mg at night increasing to 100 mg, if necessary.

AND/OR

- Paracetamol, oral, 500 mg to 1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

Gastroparesis:

- Metoclopramide, oral, 10 mg 8 hourly before meals.

REFERRAL

For further treatment, if the above measures do not control symptoms adequately.

9.4.2 DIABETIC FOOT ULCERS

L97/L08.8 + (E10.5/E11.5/E12.5/E13.5/E14.5)

DESCRIPTION

Ulcers develop at the tips of the toes and on the plantar surfaces of the metatarsal heads and are often preceded by callus formation.
If the callus is not removed, then haemorrhage and tissue necrosis occur below the plaque of callus, which leads to ulceration. Ulcers can be secondarily infected by staphylococci, streptococci, coliforms, and anaerobic bacteria which can lead to cellulitis, abscess formation, gangrene, and osteomyelitis.

DIAGNOSIS

The three main factors that lead to tissue necrosis in the diabetic foot are:

» neuropathy,
» infection, and
» ischaemia.

GENERAL MEASURES

» Metabolic control.
» Treat underlying comorbidity.
» Relieve pressure: non-weight bearing is essential.
» Smoking cessation is essential.
» Frequent (e.g. weekly) removal of excess keratin by a chiropodist with a scalpel blade to expose the floor of the ulcer and allow efficient drainage of the lesion.
» Cleanse with sodium chloride 0.9% solution daily and apply non-adherent dressing.

MEDICINE TREATMENT

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 10 days.

<u>Severe penicillin allergy:</u>
Z88.0
Refer.

REFERRAL

Urgent

Threatened limb, i.e. if the ulcer is associated with:

» cellulitis,
» severe hyperglycaemia,
» abscess,
» discolouration of surrounding skin, or
» crepitus.

Non-urgent

» Claudication.
» Ulcers not responding to adequate treatment.
» Severe penicillin allergy.

9.4.3 DIABETIC NEPHROPATHY

E10.2/E11.2/E12.2/E13.2/E14.2 + (N18.1-5/N18.9)

DESCRIPTION

Screening

» Check annually for proteinuria using dipstix.
» A diagnosis of nephropathy can be made on either a positive dipstix or, if dipstix negative, send urine to laboratory for albumin: creatinine ratio. If ratio > 30 mg/g (3 mg/mmol), diagnose nephropathy.
» Measure serum creatinine annually and estimate eGFR. *LoE: III[10]*

Diet and lifestyle

» Limit protein intake < 0.8 g/kg daily, if proteinuric.
» Advise smoking cessation.

MEDICINE TREATMENT

Start treatment with an ACE-inhibitor and increase gradually to maximal dose if tolerated.

- ACE-inhibitor, e.g.:
- Enalapril, oral, initiate with 5 mg 12 hourly.
  - Increase to maximum daily dose of 20 mg.
  - Monitor potassium, at baseline, within 1 month, and annually. *LoE: I[11]*

Persistent proteinuria

See Chapter 8: Kidney and urological disorders.

Hypertension

Target BP: < 140/90 mmHg. See Section 4.7: Hypertension.

Diabetes mellitus

Target HbA1c < 7.5%.

Intensify other renal and cardiovascular protection measures (not smoking, aspirin therapy, lipid-lowering therapy).

REFERRAL

To specialist: When eGFR<30 mL/minute or earlier if symptomatic.

9.5 CARDIOVASCULAR RISK IN DIABETES

E10.5-9/E11.5-9

See section 4.1: Prevention of ischaemic heart disease and atherosclerosis.

9.5.1 OBESITY IN DIABETES

E66.0/E66.8-9 + (E10.5-9/ E11.5-9)

DESCRIPTION

Abdominal obesity is a waist circumference >94 cm in men, and > 80 cm in women. BMI is determined by weight in kg/height in m2.

BMI (kg/m^2)	
18.5–24.9	normal
25.0–29.9	overweight
30.0–34.9	mildly obese
35.0–39.9	moderately obese
>40	extremely obese

GENERAL MEASURES

A decrease in food intake together with an increase in physical activity is crucial to losing weight.

MEDICINE TREATMENT

Treat the metabolic risk factors, i.e. dyslipidaemia, hypertension, and hyperglycaemia.

9.5.2 DYSLIPIDAEMIA IN DIABETES

E78.0-6/E78.8-9

DESCRIPTION

Dyslipidaemia in type 2 diabetes is usually characterised by increased fasting plasma triglycerides (> 1.7 mmol/L), decreased HDL cholesterol (< 1.0 mmol/L in men and < 1.3 mmol/L in women) and to a lesser extent, increased LDL cholesterol. In those with type 1 diabetes, triglycerides, and to a lesser extent cholesterol concentration, are usually increased.

MONITORING

See Section 9.2.2: Type 2 diabetes mellitus in adults.

MEDICINE TREATMENT

Dyslipidaemia may successfully be treated through lifestyle modifications alone.

- HMGCoA reductase inhibitor (statin) therapy should be added to lifestyle modifications, regardless of baseline lipid concentrations, for all type 2 diabetic patients, who:
  - are > 40 years of age;
  - have had diabetes for > 10 years;
  - have existing cardiovascular disease (for example angina pectoris, previous myocardial infarction, peripheral vascular disease or stroke);
  - have chronic kidney disease (eGFR < 60 mL/minute);

- type 1 diabetes with microalbuminuria *LoE:I*[12]
- e.g., Simvastatin, oral, 10 mg at night.

In patients < 40 years of age, risk assess as for dyslipidaemia; patients on protease inhibitors or amlodipine, see Section 4.1: Prevention of ischaemic heart disease and atherosclerosis.

REFERRAL

Random cholesterol > 7.5 mmol/L.
Fasting (14 hours) triglycerides > 10 mmol/L.

9.5.3 HYPERTENSION IN DIABETES

I10

BP lowering in hypertensive patients reduces cardiovascular risk. The diagnosis of hypertension is confirmed if the blood pressure remains > 140/90 mmHg on two separate days. See Section 4.7: Hypertension.

9.6 HYPOTHYROIDISM

9.6.1 HYPOTHYROIDISM IN NEONATES

E03.0-5/E03.8-9

DESCRIPTION

Congenital deficiency of thyroid hormone due to aplasia/hypoplasia of the thyroid gland, defects in thyroid hormone biosynthesis or intrauterine exposure to antithyroid medicines. Congenital hypothyroidism is one of the common treatable causes of preventable mental retardation in children. Congenital hypothyroidism must be treated as early as possible to avoid intellectual impairment.

DIAGNOSIS

Clinical

- » prolonged jaundice
- » feeding difficulties
- » lethargy
- » constipation
- » swollen hands, feet and genitals
- » decreased muscle tone
- » delayed achievement of milestones
- » enlarged tongue

REFERRAL

All patients for investigation and initiation of therapy.

9.6.2 HYPOTHYROIDISM IN CHILDREN AND ADOLESCENTS

E03.0-5/E03.8-9

DESCRIPTION

Hypothyroidism in children causes decreased growth, lethargy, cold intolerance and dry skin. Physical signs may include goitre, short stature, bradycardia and delayed deep tendon reflexes.

Congenital hypothyroidism may present in childhood. Acquired hypothyroidism in children and adolescents may be caused by:

» chronic lymphocytic thyroiditis
» iodine deficiency
» surgery
» radioactive iodine
» infiltrations

DIAGNOSIS

Elevated TSH and low T4 concentrations.

MEDICINE TREATMENT

- Levothyroxine, oral, 100 mcg/m2 once daily, preferably on an empty stomach (Doctor initiated).

REFERRAL

All cases for investigation and initiation of therapy.

9.6.3 HYPOTHYROIDISM IN ADULTS

E03.0-5/E03.8-9

DESCRIPTION

Hypothyroidism causes general slowing of metabolism, which results in symptoms that include fatigue, slow movement and speech, hoarse voice, weight gain, constipation, cold intolerance, depression and impaired memory. Physical signs may include bradycardia, dry, coarse skin, hair loss and delayed relaxation of deep tendon reflexes.

Common causes of primary hypothyroidism are:

» thyroiditis
» amiodarone
» post-surgery
» radio-active iodine

Secondary hypothyroidism (< 1% of cases) may be due to any cause of anterior hypopituitarism.

DIAGNOSIS

» Check TSH concentration. If elevated, check T4 concentration.
» If TSH is elevated, and T4 is low, diagnose hypothyroidism.

MEDICINE TREATMENT

- Levothyroxine, oral, 100 mcg daily, preferably on an empty stomach.
  - If there is a risk of ischaemic heart disease, start at 25 mcg daily and increase by 25 mcg every 4 weeks.
  - In the elderly, start at 50 mcg daily, increased by 25 mcg at 4 week intervals, according to response.
  - Check TSH and T4 after 2–3 months and adjust dose if required.
  - Once stable, check TSH andT4 annually.

REFERRAL

» Suspected hypopituitarism.
» Hypothyroidism in pregnancy.

9.7 HYPERTHYROIDISM

9.7.1 HYPERTHYROIDISM IN CHILDREN AND ADOLESCENTS

E05.0-5/E05.8-9

DESCRIPTION

Hyperthyroidism is a pathological syndrome in which tissue is exposed to excessive amounts of circulating thyroid hormones. The most common cause is Grave's disease, although thyroiditis may also present with thyrotoxicosis.

DIAGNOSIS

Clinical

- » fatigue
- » nervousness or anxiety
- » weight loss
- » palpitations
- » heat insensitivity
- » tachycardia
- » warm moist hands
- » thyromegaly
- » tremor

REFERRAL

Urgent

All patients.

9.7.2 HYPERTHYROIDISM IN ADULTS

E05.0-5/E05.8-9

DESCRIPTION

Most common cause of hyperthyroidism is Graves' disease, which is an autoimmune condition resulting from the presence of thyroid stimulating autoantibodies. Other common causes are toxic single or multinodular goitre and sub-acute thyroiditis.

DIAGNOSIS

Suppressed TSH and elevated T4.
Note: T4 may be normal in hyperthyroidism.

REFERRAL

Urgent

All patients.

References:

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HMGCoA reductase inhibitor (indications - CKD, albuminuria): Qin X, Dong H, Fang K, Lu F. The effect of statins on renal outcomes in patients with diabetic kidney disease: A systematic review and meta-analysis. Diabetes Metab Res Rev. 2017 Sep;33(6). https://www.ncbi.nlm.nih.gov/pubmed/28477396

SOUTH AFRICAN PRIMARY HEALTHCARE ESSENTIAL MEDICINES LIST
CHAPTER 9: ENDOCRINE CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020)

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the complete chapter for endocrine conditions
Note: This primary healthcare chapter has been updated to align to previous NEMLC recommendations as well as the recent NEMLC-approved Adult Hospital Level STGs and EML, 2019 edition and Paediatric Hospital Level HIV and AIDS chapter (2020 draft).

MEDICINE/ MANGEMENT AMENDMENTS

SECTION	MEDICINE/ MANAGEMENT	ADDED/DELETED/AMENDED
9.1 Type 1 Diabetes mellitus		
-Diagnosis	Oral glucose tolerance test	Added
9.1.2 Type 1 Diabetes mellitus, in adults		
- Monitoring	Home glucose monitoring	Amended
9.2.1 Type 2 Diabetes mellitus, in adolescents		
- Diagnosis	Oral glucose tolerance test	Added
9.2.2 Type 2 Diabetes mellitus, in adults		
- Diagnosis	Oral glucose tolerance test	Added
-Treatment	Glimepiride, oral	Maximum dose added
	Metformin, oral	Dose amended in renal impairment
9.5.2 Dyslipidaemia		
-Treatment	HMGCoA reductase inhibitors	Indication extended to include microalbuminuria

9.1 DIABETES MELLITUS *and* 9.2.1 TYPE 2 DIABETES MELLITUS, IN ADOLESCENTS *and* 9.2.2 TYPE 2 DIABETES MELLITUS, IN ADULTS

Diagnosis
Oral glucose tolerance test: *added*
The 2-hour plasma glucose in a 75g oral glucose tolerance test ≥ 11.1 mmol/l was added as an option to diagnose diabetes mellitus, aligned with guidelines.
Level of Evidence: III Guidelines[1]

9.1.2 TYPE 1 DIABETES MELLITUS, IN ADULTS

Home glucose monitoring: *amended*
Frequency of monitoring for patients on basal/bolus insulin was amended from "at least once daily" to "3-4 times a day" for correctness.
Level of Evidence: III Expert opinion

9.2.2 TYPE 2 DIABETES MELLITUS, IN ADULTS

Glimepiride, oral: *maximum dose added*
Maximum dose of 8 mg per day was added to the text of the STG, aligned with the SAMF 2016; though the approximate equivalent dose of glimepiride to gliclazide is 2:160 mg.
Level of Evidence: III Guidelines[2]

[1] The Society for Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee. The 2017 SEMDSA Guideline for the Management of Type 2 Diabetes Guideline Committee. JEMDSA 2017; 21(1)(Supplement 1): S1-S196.
http://www.jemdsa.co.za/index.php/JEMDSA/article/view/647/937
[2] SAMF, 2016

Metformin, oral: *dose amended in renal impairment*
Aligned with Guidelines.
Level of Evidence: III Guidelines[3]

9.5.2 DYSLIPIDAEMIA IN DIABETES

HMGCoA reductase inhibitors: *indication extended to include microalbuminuria*

Aligned with Adult Hospital STGs and EML, 2019 to include microalbuminuria as an indication for HMGCoA reductase inhibitors in diabetic patients regardless of baseline lipid levels.
Rationale: Available evidence suggests that statins are beneficial in reducing major cardiovascular events, coronary events, cardiovascular or all-cause death in patients with CKD. However, statins were shown to reduce albuminuria and not overt proteinuria or eGFR, in diabetic kidney disease patients.[4]
Level of Evidence: I Systematic reviews

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