MINISTRY OF HEALTH

CLINICAL PRACTICE GUIDELINES

TYPE 2 DIABETES

A continuum of care for diabetes patients both with and without complications at NCD clinics/RHs

Bureau for NCD Prevention & Control

DEPARTMENT OF PREVENTIVE MEDICINE

2015

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Forward

Diabetes is on the increase worldwide, especially in Western Pacific countries. In 1995, there were 135 million people with diabetes worldwide, with the number expected to rise to 330 million by 2025, with the majority of cases being type 2 diabetes. Most of this increase will occur in developing countries where an increase of 170% is expected, compared with an increase of 42% in the developed world. This indicates that over 60% of the world's diabetic population resides in the Western Pacific region. The living and eating habits of the people in our region are significantly different from those of Europe and elsewhere.

The Asian-Pacific region is the forefront of the type 2diabetes mellitus epidemic, with consequences to health which threaten to be devastating. Younger members of our communities are not spared from this disease, with a significant problem emerging in the urbanized young in more affluent parts of the region. Lifestyle changes and urbanization appear to be the underlying causes of this problem, and continue to accelerate in this new millennium.

People at risk of premature death from cardiovascular disease and diabetes usually have multiple risk factors, which can be modified through behaviour change or medications. The most cost-effective way to deliver secondary prevention to these people, is by treating people at medium-high risk with an integrated package of interventions: advice and medications.

This Clinical Practice Guidelines for type 2 diabetes management is intended for health professionals who are working to provide a continuum of care for diabetes patients both with and without complications at NCD clinics and RHs. Its main objective is to guide them in the appropriate process of the management of the most common health problems of Cambodian Diabetics encountered at the referral hospital including unhealthy diet, smoking, physical inactivity and particularly neglected foot care management.

I strongly believe that our guidelines provide for appropriate and affordable needs within our country according to our limited resources and the suggested treatment will benefit health professional while prescribing diabetes patients. I have no doubt that these guidelines will play a prominent role in reaching a recognized process of care and our own appropriate treatment goals for Diabetics at NCD clinics.

Finally, I would like to acknowledge those individuals who contributed to reviewing this guidelines, and to take this opportunity to express my gratitude for their generous contributions.

Phnom Penh, 2015

Minister of Health

Acknowledgements

The initial guideline, developed by "Diabetes Working Group" of the ministry of health of the kingdom of Cambodia with the support of WHO was based on "Type 2 Diabetes. Practical Targets and Treatments," published by the Asian- Pacific Type 2 Diabetes Policy Group.

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CLINICAL PRACTICE GUIDELINES FOR THE TREATMENT OF TYPE 2 DIABETES at NCD clinics/RHs

Introduction

The latest WHO Global Burden of Disease estimates the worldwide burden of diabetes in adults to be around 173 million in the year 2002. Around two thirds of these live in developing countries. It is predicted that there will be at least 350 million people in the world with type 2 diabetes by the year 2030. Equally alarming and less well known is the fact that, of these people, only around one half are known to have the condition. This has been shown repeatedly in epidemiological surveys. An added concern is that half of those who do present with type 2 diabetes clinically already have signs of the complications of the disorder.

The countrywide survey, WHO STEPS 2010, to assess risk factors of non-communicable diseases in Cambodia has shown the prevalence of Diabetes was 2.9% and the urban was 2.4 time higher than the rural areas (5.6 vs.2.3%). This study revealed that 33.7% used tobacco daily, 20.7% had raised total cholesterol, 15.4% ware overweight or obese, 11.2% had high blood pressure and 19.0% with heavy episodic alcohol drinking

Diabetes is a chronic condition that can result in disability, impoverishment and early death. The aim of this publication is to provide guidelines and standards of care for the management of diabetic patients in Cambodia as well as providing a frame work for diabetes services.

Guiding principles

Evidence based, cost effective and adapted to local circumstances

A continuum of care for diabetes patients both with and without complications

Promoting access to quality and affordable diabetes services

Empowering and enabling patients in self-management

Creating a team approach centered on the patient and involving health professionals, peer educators, health facilities

Ongoing evaluation of services

Key Interventions

Summary of Key interventions - Overall clinical Care for people with diabetes

- Improving blood glucose control reduces the risk of developing the microvascular complications of diabetes in people with both Type 1 and Type 2 diabetes
- Improving blood glucose control may reduce the risk of people with diabetes developing cardiovascular disease
- Controlling raised blood pressure in people with diabetes reduces their risk of developing both microvascular complications and cardiovascular disease
- Smoking cessation in people with diabetes who smoke reduces their risk of both cardiovascular disease and microvascular complications
- Regular recall and review of people with diabetes can improve the quality of diabetes care and outcomes for people with diabetes

Summary of Key interventions - Detection and management of long term complications

- Regular surveillance for diabetic retinopathy and early laser treatment of those with sight-threatening retinopathy can reduce incidence of new visual impairment and blindness
- Treatment of people with microalbuminuria with ACE inhibitors can reduce progression to diabetic nephropathy
- Tight blood pressure and blood glucose control in people with diabetic nephropathy can reduce deterioration in renal function and risk of cardiovascular disease
- People at increased risk of lower limb complications can reduce risk by participating in foot care programme and wearing protective footwear
- In people with diabetes who develop foot ulceration, prompt intervention can minimize risk of disability and amputation
- People with diabetes who have other CVD risk factors or previous CVD can benefit from tight blood pressure control, a statin, ACE inhibitors, low dose aspirin (if no contraindication) and lifestyle advice – ESPECIALLY SMOKING CESSATION

TARGETS FOR CONTROL

GLYCAEMIC CONTROL	HbA1c (DCCT aligned)	<7%

BLOOD PRESSURE	Systolic Diastolic	< 140 < 90
	If proteinuria (>1g/day) Systolic diastolic	 < 130 < 80

WEIGHT/HEIGHT	BMI	18.5–22.9

PHYSICALACTIVITY	Moderate intensity	150min/week

SMOKING	NONE	NONE

LIPIDS*(if available) (after10-12hour fast)	Total cholesterol	<174mg/dl(4.5mmol/L)
	LDL	<97mg/dl(<2.5mmol/L)
	HDL	>39mg/dl(>1mmol/L)
	TG	<133mg/dl(<1.5mmol/L)

*based on Asian-Pacific Type 2 Diabetes Policy Group guidelines. Type 2 Diabetes.

Check every visit	Check annually unless abnormal
Blood glucose	Eye examination (1-2years)
Weight & lifestyle factors	Renal function (Proteinuria/creatinine)
Blood Pressure	Lipids (if available)
Feet at risk	Thorough foot examination

Framework for diabetes care

ROLE OF CLINICIAN

Usually at referral hospital

- Clinical care based on guidelines but individualized
- Risk factor management
- Empowering patients in self-management
- Documentation of patient information
- Coordination with other health professionals, peers and CBO
- Form part of the Provincial working group on NCD

ROLE OF EDUCATOR

- Empower patients in self-management and lifestyle changes
- Impart knowledge and skills to enable optimal self-care and prevent complications
- Regular monitoring and support
- Inform patients about access to health services and expectations
- Liaise regularly with other health providers (including other health professionals or peer educators)
- Train health center staff especially in lifestyle management
- Form part of provincial network

Diabetes self-management Education

Diabetes self-management education has been shown to improve metabolic control, self image, depression and other outcomes. It should be a major component of the management of all people with diabetes.

Education can be provided by a diverse group of people including doctors, nurses, educators, peer educators and other health professionals.

Education is ongoing and needs to continue for the rest of a person's life.
Diabetes knowledge and especially self-care skills (blood glucose monitoring, foot care and insulin administration) need to be assessed regularly.
Individuals should not only be provided with adequate education but also be equipped in problem solving skills.
Techniques could include peer education or group work
Any programme should be evaluated to help us understand which techniques are most effective in Cambodia.

A PERSON WITH DIABETES SHOULD KNOW.....

- Nature of diabetes, that it is a lifelong disorder and that regular review is essential
- Understand symptoms
- Risk of complications-reduced with effective care
- Individual targets of treatment
- Self monitoring–how and what it means
- Importance of foot care
- Interaction of food, physical activity and medication
- Individual life style requirements and meal planning
- Medications–how they work, generic medications, importance of compliance
- How to cope with emergencies such as illness or hypoglycaemia
- Know when they should seek urgent medical advice eg infections

Screening and diagnosis of Type 2 diabetes

At the time of diagnosis over 50% of patients have one or more diabetic complications. It is therefore recommended to screen high–risk people with the hope of diagnosing people earlier and decreasing the risk of complications.

1) Identify those who should be screened:

THOSE WHO SHOULD BE SCREENED

FOR TYPE 2 DIABETES

- Overweight (BMI>23, waist circumference in men ≥85cm and in women≥80cm)
- Family history of diabetes
- Hypertension (BP>140/90), dyslipidaemia
- History of stroke or ischaemic heart disease
- Women with a previous history of gestational diabetes
- Women who have given birth to a large baby(>3500g)
- Age over 35

2) Measure fasting glucose in venous or capillary blood (glucometer).

3) **If fasting plasma venous glucose is ≥126mg/dl (7mmol/L) or random venous glucose is ≥ 200mg/dl (11.1mol/L)= diabetes**

The patient is likely to have diabetes and this should be confirmed by a repeat test on another occasion unless there are obvious symptoms.

4) **If fasting plasma glucose is 100–125mg/dl = impaired fasting glucose**, and in some countries an OGTT would be done at this stage.

If someone is found to have impaired fasting glucose then they are at increased risk of developing diabetes and other cardiovascular complications. Therefore assess and give advice regarding metabolic risk factors. (This should include advice re healthy diet, physical activity, appropriate weight management and smoking cessation). Retest in one year.

Venous plasma is the preferred test however the blood must be collected and stored appropriately (collected in preservative or tested within the hour). Corresponding capillary values are similar for fasting samples and differ only for the 2 hours.

If venous blood is taken and cannot be analyzed immediately, it should be collected in a sodium fluoride tube to inhibit glycolysis and then the tube should be placed in ice-water until analyzed.

If glycosuria has been detected on urinary dipstick, the patient is likely to have diabetes and this should be confirmed on capillary or venous blood.

Remark1:

The 2006 WHO recommendations for the diagnostic criteria

for Diabetes and intermediate hyperglycaemia

Diabetes	
Fasting plasma glucose	≥7.0mmol/l (126mg/dl)
2-h plasma glucose*	**Or**
	≥11.1mmol/l (200mg/dl)
Impaired Glucose Tolerance (IGT)	
Fasting plasma glucose	<7.0mmol/l (126mg/dl)
2-h plasma glucose*	**And**
	≥7.8 and <11.1mmol/l
	(140mg/dl and 200mg/dl)
Impaired Fasting Glucose (IFG)	
Fasting plasma glucose	6.1mmol to 6.9mmol/l
2-h plasma glucose*	(110mg/dl to 125mg/dl)
	And (if measured)
	<7.8mmol (140mg/dl)

* Venous plasma glucose 2-h after ingestion of 75 g oral glucose load

* If 2-h plasma glucose is not measured, status is uncertain as diabetes or IGT cannot be excluded

Note: a random (casual) plasma glucose cannot be used to diagnose IFG or IGT

Remark2:

WHO diagnostic criteria for diabetes

	Glucose concentration, mmol/l (mg/dl)		
	Whole blood		Plasma venous
	Venous	Capillary	
Diabetes mellitus			
Fasting	≥ 6.1 (110)	≥ 6.1 (110)	≥ 7.0 (126)
or			
2-hour post glucose load	≥ 10.0 (180)	≥ 11.1 (200)	≥ 11.1 (200)
or both			
Impaired glucose tolerance			
Fasting concentration	≤ 6.1 (110)	≤ 6.1 (110)	≤ 7.1 (126)
(if measured)			
and			
2 hours after glucose load	6.7-9.9 (120-179)	7.8-11.0 (140-199)	7.8-11.0 (140-199)
Fasting hyperglycaemia			
Fasting	5.6-6.0 (100-109)	5.6-6.0 (100-109)	6.1-6.9 (110-125)
2 hours (if measured)	≤ 6.7 (120)	≤ 7.8 (140)	≤ 7.8 (140)

Care delivery

Involve the patient in decision making and making an action plan.

Every clinic should offer annual surveillance of all aspects of diabetes control and complications and more regular review for specific aspects.

Initial visits should include an overall assessment:

HISTORY	EXAMINATION	BLOOD TESTS
History of diagnosis Risk factors - Eating habits - Physical activity - smoking - alcohol Background history including cardiovascular and renal disease	Height and weight (BMI) Waist circumference Blood pressure Cardiovascular Detailed foot exam Eye–VA and fundoscopy (formal testing with dilated pupils–normally will need to be done at eye clinic) Teeth inspection	HbA1c Glucose Creatinine, sodium, potassium ALT Urine analysis (glu/ketones/protein) Lipids(if available and affordable)

All patients and their family should be provided with diabetes education and made aware of other available support structures such as peer education or patient associations.

It must be emphasized that diabetes is not curable and requires lifelong lifestyle changes and management.

Followup visits:

HISTORY	EXAMINATION	BLOOD TESTS
Relevant history, Review symptoms Risk factor review– discourage smoking	Height and weight(BMI) Waist circumference Blood pressure Foot inspection As indicated	HbA1c (3–6monthly) Glucose As indicated

Patients should be initially seen more frequently depending on control and if taking insulin. This may need to be everyone to two weeks if unstable.
Then every 1 - 3months.

Most patients should be seen 3 monthly once stable

If patient is on minimal medication and has excellent control and understanding, then patients can be seen 3 – 6 months.

Annual visit: Summary of Assessments that should be performed at least annually for each person with Type 2 diabetes

HISTORY	EXAMINATION	BLOOD TESTS
Self-care knowledge and beliefs Lifestyle factors and Body weight trends Blood glucose control History of hypoglycaemia Any significant events	Height and weight (BMI) Waist circumference Blood pressure Cardiovascular Detailed foot exam Eye–VA and fundoscopy Teeth inspection General exam Self-monitoring skills and equipment	HbA1c, Glucose Creatinine, sodium, potassium Urine analysis (glu/ketones/protein) Lipids (if available and affordable) Others as indicated

Life style management

All health professionals including health centre staff should be able to provide lifestyle advice and risk factor management.

Calculate the person's BMI (see below). Together with clinical examination and waist circumference, BMI gives a rough estimate of adiposity.

Inform people of their target weight

BMI	Classification
<18.5	Underweight
18.6-22.9	Normal
23-24.9	Overweight
≥25	Obese

Normal Waist circumference	
Men	<85 cm
Women	<80cm

MEASUREMENT AND DEFINITIONS

BMI (Body mass index)
BMI=weight in kgs / height in metres 2

Waist circumference
Stand patient with abdomen relaxed, arms loose at the sides, feet together. Use non Stretchable measure and do not compress the skin. Measure the narrowest section between the lower ribs and iliac crest.

Maximum Heart Rate
MHR=220 – age in years

HEALTHY DIET

Eat a variety of foods at each meal.

Eat smaller but regular portions of starchy carbohydrate at each meal eg rice, noodles or beans.

Increase the amount of vegetables and fruit everyday and eat a variety. Eat one or two serves of fruit (especially low GI) per day.

Most people in Cambodia do not eat enough protein. Good sources of protein include tofu, beans, fish, eggs and chicken.

Avoid foods with high amounts of sugar such as soft drinks (coca-cola), sweets or condensed milk.

Reduce saturated fat and high fat foods such as fried foods (eg deep fried banana), prohok and pork fat.

Use unsaturated vegetable oils such as sunflower, soya bean oil, olive or canola during cooking, rather than saturated oils (palm oil or coconut oil) or pork fat. Cut off fat before cooking.

Decrease salt intake, limit intake of prohok, MSG, fish sauce, soy sauce and salted meat or fish. Use other flavours (eg lemon juice, pepper) and herbs.

Reduce alcohol, especially strong alcohols like rice wine, whisky. Have 2 alcohol free days per week

It is recommended 50 – 65% of calories come from carbohydrate (see below for details).

WHAT ABOUT CARBOHYDRATES IN DIABETES??

The amount and type of carbohydrate greatly influences blood glucose levels and so monitoring of carbohydrate amount is very important.

Carbohydrate is necessary for brain and nervous system function–it is recommended that 50 – 65% of calories come from carbohydrate. In Cambodia usually at least 80% of the meal consists of carbohydrate because people eat a lot of rice. Rice (especially polished rice) is a very quickly absorbed carbohydrate that can cause glucose levels to dramatically increase very quickly.

Therefore:

HAVE SMALLER PORTIONS OF QUICKLY ABSORBED CARBOHYDRATE (IE WHITE RICE) AND SPREAD IN MORE EVENLY THROUGH THE DAY

Some carbohydrates like polished rice increase the glucose level very quickly, others are slower acting and do not cause the blood glucose to rise so much–examples include brown rice, grains, beans, most vegetables except potatoes, tofu.
Try and replace white rice with slower absorbed carbohydrates and increase protein in the diet.

Patients can see how particular foods influence their sugar levels themselves if they measure their blood sugar level before and 2 hours after they start eating a meal.

This is an excellent way for people to understand how different foods can affect their glucose control.

Try and spread the carbohydrates through the day by having smaller portions at each meal and snacks between if necessary.

IF high blood pressure (BP>130/80):
Decrease salt intake, limit intake of prohok, MSG, fish sauce, soy sauce and salted meat or fish. Use other flavours (e.g.lemon juice, pepper) and herbs.
Limit to1tsp of table salt per day or equivalent

IF trying to lose weight (BMI≥23or abdominal obesity):
Decrease portion sizes particularly rice.
Eat slowly. Exercise frequently.
Use smaller plates/bowls
Limit unhealthy snacks and fast food (high in sugar and fat). Eliminate soft drinks.

IF the patient is underweight:
Usually this will improve once the patient is appropriately treated with oral Hypoglycaemics or insulin.
Advise the patient to eat more frequently and eat healthy foods.

If the patient is using insulin:
For people using insulin it is best to advise consistent carbohydrate intake at Meals and adjust insulin accordingly

GENERAL PHYSICAL ACTIVITY ADVICE

Physical activity plays an important role in the management of type 2 diabetes. Physical activity improves insulin sensitivity, thus improving glycaemic control, and may help with weigh reduction

Introduce physical activity gradually and set individual goals. Try and help patients think of easy ways to fit physical activity into their normal life activities e.g. walking or bicycling instead of catching a motorcycle

The best activity is brisk walking 30 minutes per day on most days of the week is recommended (>150 min/week). Walking should be brisk, so that they are puffed but can still have a conversation (increase heart rate 50-70% of maximum heart rate). Exercise should be more gradual if unfit or older. People should try and build this into their normal routine. These recommendations apply to the general population as well.

If weight loss is desired then this may require longer periods of activities such as 50 – 60 minutes of moderate intensity on most days and avoid sedentary activities such as TV.

Those who have peripheral neuropathy should do other activities such as cycling or resistance exercise.

Care with physical exercise must be taken in those treated with insulin or secretagogues – patients should have a ready store of carbohydrate and if available glucose monitoring is useful before and after exercise.

Physical activity should not be undertaken if uncontrolled blood sugar level or blood pressure. Avoid strenuous exercise if glycaemia >250mg/dl, the patient has ketonuria or blood glucose is less than 80mg/dl.

Proper foot wear must be worn

Look for opportunities to walk or bicycle instead of using a motorbike/car.

SMOKING

The 2010 STEPS survey revealed that 33.7% used tobacco daily

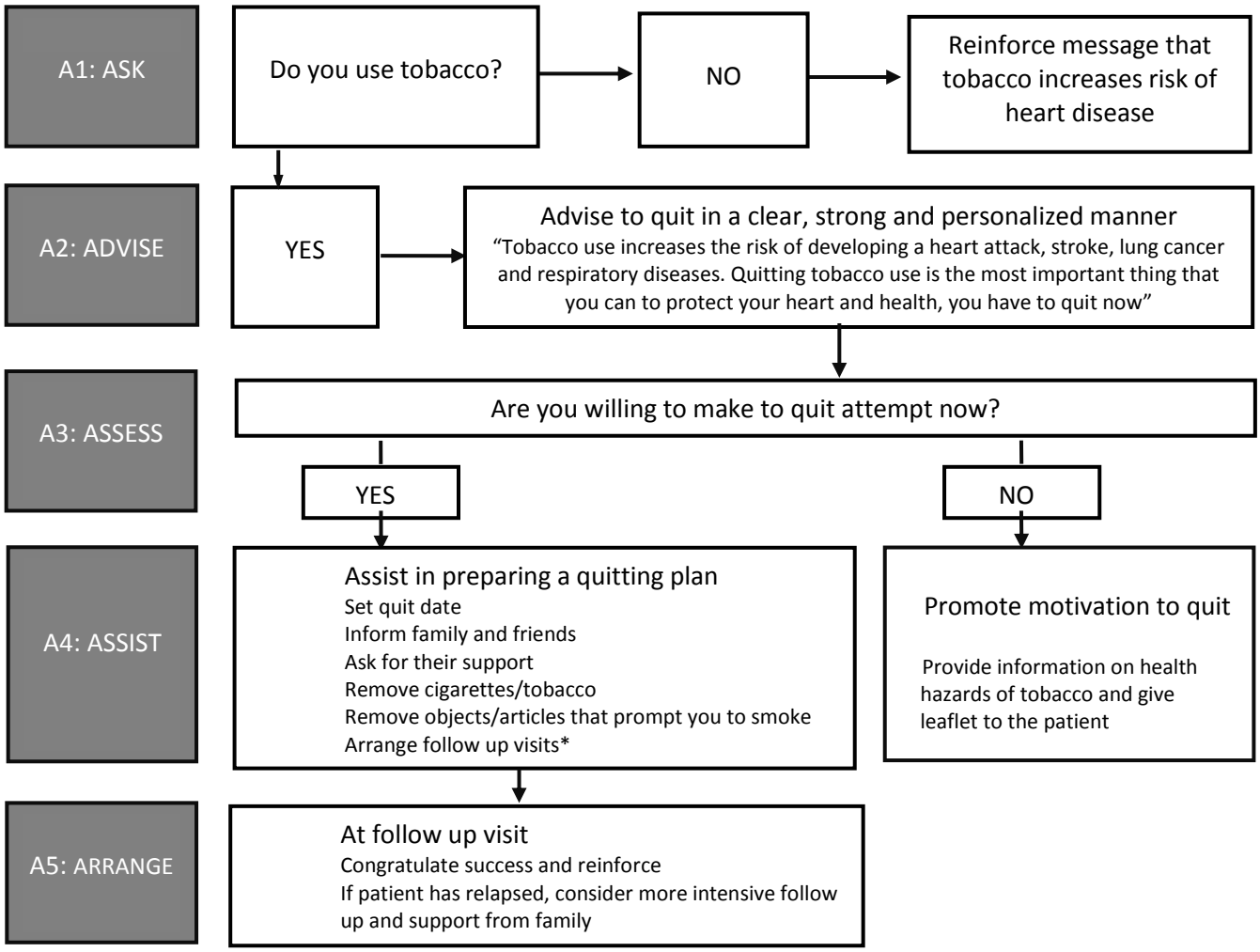
The effects of smoking are particularly severe if patients have diabetes and include:

- High risk of cardiovascular disease and death (myocardial infarction and stroke)
- Poorer glycaemic control
- Increased risk of neuropathy
- Increased risk of end-stage renal disease
- Peripheral vascular disease which is a risk factor for amputation

Smoking also leads to chronic respiratory disease, increase blood pressure, impotence and certain cancers including lung, oral, stomach and oesophagus

Smoking cessation is one of the most important and effective treatments in people with diabetes

Counseling on Cessation of Tobacco use (WHO PEN protocol 2)



*Ideally follow up visit is recommended within the same month and every month thereafter for 4 months and evaluation after 1 year, reinforce counseling whenever the patient is seen for blood pressure monitoring

Blood glucose control and self- monitoring

Glucose control has been clearly established to be important in the prevention of microvascular complications and more recently for macrovascular complications. HbA1c reflects the degree of glycaemic control over the preceding 2 – 3 months.

HbA1c should be measured at least every 6 months with a target of <7%. Aim to improve lifestyle measures and titrate therapy if HbA1c >7%. The patient should be informed of his or her HbA1c result and the target level.

Timed glucose levels can also provide some picture of control. Targets for blood glucose:

*Before meals: 80-130mg/dl

*2 hours after meals: 130-180mg/dl

*The strictness of control should be influenced by the patient's age, duration of diabetes, family support, comorbidity, financial support, history of hypoglycaemia. For example strict control may be dangerous in a new insulin dependent diabetic who lives far from a health centre or may not be justified in the elderly.

Look at the pattern of glucose if available to help determine interventions-eg what time of the day is the level usually high or after what type of foods.

Glucometers are an excellent way for people to learn how lifestyle factors such as diet and exercise affect their sugar levels. Patients should check blood sugar levels before and 2hours after starting a meal. This can help people understand how meals with different compositions can affect their glucose levels.

Every effort should be made to provide those who are taking insulin with their own glucometer or a borrowed one; especially at initiation or changes in treatment.

If the blood sugar levels are very high, the urine dipstick glucose is consistently positive or the patient is symptomatic then the patient should be seen frequently until the blood sugar levels are under control. Telephoning could be helpful if transport is an issue.

Currently glucometers are too expensive for most patients–therefore consider:

1) Advocate for the clinic to have glucometers which can be lent out for a period of time
2) Peer educators with glucometers can check blood sugar levels in the community
3) Use urine strips –urinary glucose is not very sensitive but can be a cheap and useful method as long as its limitations are known. The aim is to keep the urine free of glucose. Advise People to test urine before eating and 3 hours after eating.
   Positive glucose urinary dipsticks Are roughly equivalent to glucose level of greater than 180mg/dl (10mmol/l.). However urine testing does not detect hypoglycaemia and is not useful in certain situations such as where the renal threshold is elevated (eg in the elderly) or low (eg in pregnancy).

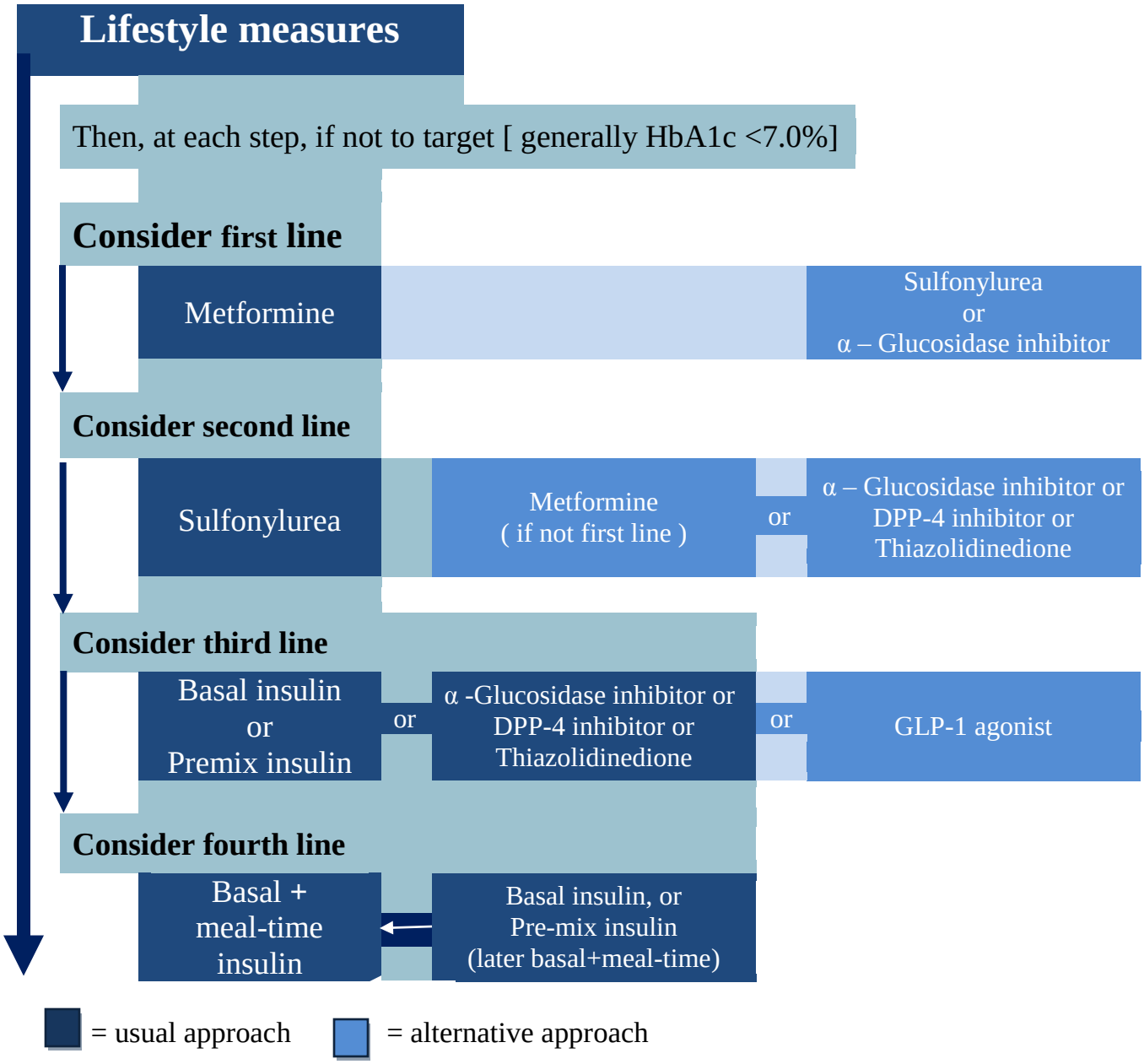
Glucose control: oral therapy

Lifestyle interventions should remain the underlying theme throughout the treatment.

If the patient the blood glucose level is very high (eg fasting BSL>180 or postprandial >360 or HbA1c>9%) then medication needs to be used early to decrease glucose levels and relieve symptoms AND TITRATE to a second agent more rapidly if sugars not falling

Type 1 diabetics need insulin immediately and for life. Suspect in lean patients who have had rapid weight loss. Check for ketones.

Treatment algorithm for people with type 2 Diabetes



Metformin: Start with low dose and increase gradually every few weeks or so. If the dose is increased too rapidly then people can suffer gastro-intestinal effects and compliance maybe difficult. Metformin is available on the essential drug list. It is contra indicated in renal impairment (see table) and liver disease (ie ALT>2.5xN) or septic shock.

Sulphonylureas: All sulphonylureas can cause hypoglycaemia and also should be avoided in those with sulphur allergies. Glibenclamide and gliclazide are currently available on the essential drug list. Glibenclamide is cheaper and recommended as first line treatment-although great care should be taken if the patient is elderly or has renal impairment, where it is more likely to cause hypoglycaemia. In the elderly or those with glucose levels that are not too high start with lower doses (eg 2.5mg of glibenclamide or 40mg gliclazide) and increase gradually.

The cardiovascular benefits of one sulphonylurea over another have not yet been adequately researched in large clinical trials. Metformin was the only oral medication that had clear cardiovascular benefits in a large clinical trial (UKPDS) and this was among those classified as overweight or obese.

Remember to carefully review diet and carbohydrate intake before adding further medication. It may be more appropriate to make dietary/lifestyle changes.

Thiazolidinediones

Pioglitazone or rosiglitazone can be added to help control levels to those on oral medication. The dose should be increased slowly. Improved glucose levels are not usually seen for a number of weeks or months. Generic Pioglitazone is now available in the market and maybe preferable as the next step instead of adding insulin. This is because glitazones do not cause hypoglycaemia and therefore maybe a safer option when patients cannot afford glucometers and strips. Thiazolidinediones should not be used in those with active liver disease or transaminase levels 2.5 times the upper limit of normal or in those with significant cardiac failure.

Some medicines are currently available on the essential medicine list and therefore should become available free through referral hospitals. Cheap generic versions are also available in pharmacies. There is no need to use the other medications if adequate control is obtained with those highlighted as they have been used for many years and are low cost.

Elderly

Aim for less aggressive targets. The aim should be to avoid hypoglycaemia with reasonable Control of hyperglycaemia. Metformin is often contraindicated in elderly patients, because of coexisting renal, liver or cardiovascular impairment. Sulphonylureas should be used with caution because of the risk of hypoglycaemia. If using glibenclamide then start with a dose of 1.25mg and slowly titrate.

Table of oral glucose lowering agents

On essential drug list

Drugs	Daily dose	Mode of action	Efficacy	Advantages	Disadvantage
Biguanide*					
Metformine	500-2000mg daily in 2-3 times with/after meals	Reduce hepatic glucose output	Reduce A1c 1% - 2%	No weight gain, may reduce triglycerides	GIT symptoms. Avoid in renal impairment (Cr>1.5 in males or >1.4mg/dL in females or CrCl < 60-70), age>80 years, chronic heart failure and in those with hepatic disease or heavy alcohol intake,
Sulfonylureas (SFUs, second generation)**					
Glibenclamide (glyburide)	2.5 – 20mg 1-2 with meals	Stimulate insulin Release by receptor mediated, glucose independent mechanism	Reduce A1c 1% - 2%	Well tolerated	Hypoglycemia, weight, gain, allergy. Use with precaution in elderly or in patients with liver or renal insufficiency.
Gliclazide	40-320mg 1-2 with meals				
Glimepiride (amaryl)	2-8mg once daily				

Others

Meglitinides**					
Repaglinide	1.5-16mg 3 times a day	Short acting insulin secretagogue	Reduce A1c 1% - 1.5%	Well tolerated, may have less risk of hypoglycemia compare to sulfonylureas	Hypoglycemia, 3 times a day. More expensive than sulfonylureas
Nateglinide	60-120mg 3 times a day				
Thiazolidinediones (TZDs)*					
Pioglitazone (actos)	15 – 45 mg Once daily	Insulin sensitizer; reduces insulin resistance peripherally	Reduce A1c 0.8% -1.8%	Neutral to Positive effect on CV outcome, carotid IMT	Weight gain, fluid retention, congestive heart failure, anemia; fracture in women; variable lipid effects; rare liver toxicity, increase risk of bladder cancer
Alpha-glucosidase inhibitors (AGIs)					
Acarbose (precise)	50-100mg 3 time a day before meals, start with lower doses	Inhibit gut enzymes that break down carbohydrate	Reduce A1c 0.6% -1.2%	No weight gain	GI side effects, including flatulence, diarrhea, and cramping; rare liver toxicity
Miglitol (Glyset)					

* Insulin Sensitizer ** Secretagogues

Clinician should give enough generic medication to patients so that they will not run out before seen again. This may mean giving a 1-2 month supply. If not available in the hospital then patients must be encouraged and supported if possible to purchase their own and take regularly.

Glucose Control: insulin therapy

Start insulin therapy when optimized glucose-lowering drugs and lifestyle interventions are unable to maintain blood glucose at target levels.

Lifestyle measures should continue.

Poor use of insulin can cause weight gain and continuing poor control and therefore should be supervised by a health practitioner specializing in diabetes.

Patients taking insulin –especially those taking more than one injection per day should preferably have a glucometer or at least have access to one regularly and have a good understanding of insulin and glucose control.

An initial step is to check the morning fasting glucose. If this is greater than 126mg/dL then commence evening intermediate acting insulin such as protaphane or long acting insulin before the patient goes to bed. Start for example with 8 –10 units (~0.1-0.2 units/kg) and increase by 2-4 units every 4-5 days or so until the fasting glucose is about 80– 126 mg/dl. Both Metformin and sulphonylurea can be continued. Remember aim for less tight control if the patient does not have access to glucometer or lives far away from health services.

Uninterrupted supply is vital as is insulin of consistent quality and type.

If blood sugar is still high despite night time insulin then twice daily intermediate acting insulin or twice daily mixed insulin maybe required. If mixed insulin is being used then it is often easier to stop sulphonylureas which may cause difficulties in interpreting peaks and troughs. Metformin can be continued. Clinicians with experience with diabetes should be involved especially when doses are being titrated.

Both carbohydrate and physical activity need to be regular so that blood glucose levels are easier to predict.

Insulin needs to be appropriately stored and people need to be trained in injection techniques. The importance of rotating injection sites so that fatty deposits are avoided needs to be emphasized.

Abdominal wall is the usual site for injection and has the most uniform rate of absorption. Insulin can also be injected into the thigh area but this has slower absorption (unless exercising). Insulin should not be injected into arms.

Patients should be involved in the interpretation of glucose levels and in decision making.

Hypoglycaemia

Hypoglycaemia is usually due to excessive insulin or sulphonylurea dose, deficient carbohydrate intake, unusual physical activity or excessive alcohol intake.

Common warning signs: hunger, sweating, palpitations, tremor, tingling. Some may develop behavioural changes such as aggression or have slurred speech. Severe hypoglycaemia can cause unconsciousness and seizures
Early morning headaches maybe a symptom of hypoglycemia overnight.

IT is important that those taking insulin have a stable amount of food, regular starchy carbohydrate and be able to adjust dose if extra physical activity or decreased intake.

Patients who are taking insulin or sulphonylureas should be taught to recognize the warning signs aware of symptoms and management.

Patients should be instructed to check their glucose if they have a meter as sometimes anxiety from other causes can mimic the symptoms.

Mild symptoms can be treated with oral glucose eg 3 heaped teaspoons of sugar, a glass of soft drink and should be followed with a longer acting carbohydrate (starchy).

If the patient is unconscious then intravenous dextrose (50%) is the treatment of choice (10-25ml). do not give oral glucose, as they may aspirate.
Honey can be smeared around the teeth and buccal mucosa but be careful as the patient may bite.
Monitor glucose for at least 24 hours.

It is important that the patient and doctor explores what may have caused the episode and discuss ways of preventing further episodes. Remember that hypoglycaemia can be prolonged with the longer acting sulphonylureas and so the patient should be observed for a longer period.

STORAGE TIPS FOR INSULIN

- Do not use expired insulin.
- Store unopened vials in a refrigerator. Do not freeze.
- Insulin can be stored inside a sealed container or bag in a ceramic water storage pots in a cool area
- May store opened vials at room temperature or in refrigerator.
- Protect opened vials from heat and light.
- Insulin which contains ‘clumps’ should not be use

Blood pressure control

- Blood pressure is elevated in many people with type 2 diabetes and can be associated with many health problems in people with diabetes including stroke, ischaemic heart disease, kidney damage and eye damage.
- Therefore blood pressure should be intensively treated to prevent macrovascular and microvascular complications.
- Blood pressure should be measured at every clinic visit.
  Measure BP at least 3 monthly for people on medication and more regularly when titrating the dose of medications.

  Check BP at least 6 monthly for those with normal blood pressure.

Measurement of blood pressure

Measure after patient has been sitting for at least 5 minutes with arm at heart level

Use a mercury sphygmomanometer or validated meter in good working order and an appropriately sized cuff

Record all values in patient notes and on patient's own record card.

RISK FACTOR MANAGEMENT for EVERYONE WITH DIABETES ESPECIALLY THOSE WHO HAVE HIGH BLOOD PRESSURE

- Aim for target weight
- Decrease salt intake
- Regular moderate physical activity
- Avoid alcohol (excessive increases blood pressure)
- STOP SMOKING

TARGET BP <140/90

If Proteinuria < 130/80

CHECK RESTING BP ON AT LEAST 2 OCCASIONS
(rule out acute causes such as pain, anxiety)

Patients with persistent
BP values > 130/80mmHg should be treated,
with the aim of achieving BP < 130/80 mmHg, and
reducing the risk of both CVD and microvascular complications.

Review BP every 2 weeks to 3 months

Titrate medication

And add 2nd drugs and titrate

Add 3rd drugs if necessary

Continue risk factor management

NOTES

Most Diabetes patients will need at least 2 drugs

Usually start with **HYDROCHLOROTHIAZIDE** and then add **ACE inhibitor**
Choice will depend on individual factors and contraindication

ACE Inhibitor considered first line treatment if AER elevated
or
a history of myocardial infarction.

Consider BB in those with angina or history of AMI
but avoid in those with claudication.

Some Angiotensin II Receptor Blockers (ARB: losartan) are available
now in essential drug list and can be used instead of ACEI
if patients are troubled by cough

Cardiovascular disease(CVD) is the major cause of mortality and morbidity in people with Type 2 diabetes.The term includes ischaemic heart disease (IHD), stroke and peripheral vascular disease (PVD).

Drug	Daily Dose	Advice for patients	Contre indication
Diuretic			
Hydrochloro-thiazide	Start at 12.5mg once daily and Increase to 25mg once daily	Eat fruit and vegetable everyday	Absolute: GOUT
Furosemid	20-80mg in 2 divided doses especially useful in those with renal impairment		
ACE inhibitor			
Captopril	Start at12.5mg twice a day and gradually increase to 50mg three times daily (Start 6.25mg if elderly)	If persistence cough → See doctor	Absolute :Pregnancy :Bilateral renal artery stenosis :Hyperkalemia
Enalapril	Start at 5mg once daily and increase to 40mg once daily		Relative :If creatinine> 2mg/dL
Beta Blocker			
Atenolol	Start at 25mg once daily and increase to 50mg once daily		Absolute :Asthma :Chronic obstructive airway disease :heart block :Bradycardia Relative :Peripheral vascular disease
Calcium Channel Blockers			
Nifedipine (slow release)	Start at 30mg once daily and increase 120mg once daily		Absolute :congestive cardiac failure :Aortic stenosis
Verapamil	Start at 30mg three times daily and increase to 60mg 2-3 times daily		:Bradycardia :Sino atrial block :Atrio ventricular Block
Amlodipine	5mg (or 2.5 in elderly) and titrate to 10mg		Decrease dose with hepatic or renal impairment

Cardiovascular risk Protection

Aggressive management of risk factors is important and includes blood pressure, blood glucose control and lifestyle measures as previously discussed as well as lipids and anti-platelet therapy

Cardiovascular risk factors should be checked at diagnosis and annually thereafter:

- Current or previous cardiovascular disease
- Age > 40
- BMI>23
- Smoking
- Hypertension
- Family history
- Raised lipids (raised Total cholesterol, LDL or decreased HDL)
- Micro or macro albuminuria

KEY POINTS

CARDIOVASCULAR DISEASE IS A MAJOR CAUSE OF MORBIDITY AND MORTALITY IN PEOPLE WITH DIABETES

In those with a history of CVD or risk factors:

- Aggressive management of blood pressure
- Aspirin
- Statin
- ACE Inhibitor or
- ARBs
- Lifestyle measures: especially NOSMOKING, physical activity, diet low in saturated fat, low salt

Provide aspirin 75 – 100mg daily (unless aspirin intolerant or uncontrolled blood pressure) to people with evidence of CVD, atrial fibrillation or CVD risk factors as listed.

Measurement of lipids (total cholesterol and TG) .
However there is sufficient evidence to use statins in diabetic patients who have CVD or who are older than 40 even if levels are unknown.

Generic statins (eg simvastatin) and ACE inhibitor should be used in people with known cardiovascular disease (IHD, stroke or PVD) or those with additional risk factors.

Be on the alert for cardiovascular disease. Remember people with diabetes and cardiac ischaemia may have atypical symptoms or ‘silent’ angina or myocardial infarction.

Eye Screening

Diabetic retinopathy is a major cause of visual loss. Measures to control blood glucose and blood pressure can help prevent onset and delay worsening of retinopathy but most people with retinopathy will be asymptomatic until damage is far advanced.

Therefore early detection by regular surveillance is essential if people with sight-threatening retinopathy are to be identified and offered treatment in time.
It is very important to screen patients at diagnosis as studies have shown between 21 – 39% already have some retinopathy.

Screen patients at diagnosis and 1–2 yearly or more frequently if retinopathy
Patients should be advised that they could help reduce the risk of eye damage developing or worsening through good control of blood pressure, Blood glucose and blood lipids.

Cataract is another important cause of visual loss in people with diabetes and is twice as common as in people without diabetes.

Examination of eyes of people with Type 2 diabetes should be performed around the time of diagnosis and should include documentation of visual acuity corrected with glasses or pinhole and an assessment for retinopathy with dilated pupils.

This examination should be done by someone with appropriate training or an ophthalmic specialist.

If the eye exam is normal then less frequent exams (every1 -2years) is reasonable, otherwise annually or more frequently if retinopathy is progressing.
It is important that results are recorded, with feed back to primary care giver and patient (write on patient's card).

Only a few ophthalmologists are experienced in the use of laser therapy. Patients who have macular oedema, severe non proliferative retinopathy or any proliferative retinopathy should be referred to an ophthalmologist who is experienced in laser use.

Patients should also be referred to an ophthalmologist if the clinician cannot visualize the retina or there is unexplained reduction in visual acuity.

Kidney Damage

Diabetic nephropathy occurs in 20 – 40% of patients. There is clear evidence that blood glucose control and blood pressure control reduces risk of renal impairment, there is also evidence that worsening impairment and progression to renal failure can be delayed.

With decreasing renal function there is a significant increase in cardiovascular disease even at the stage of microalbuminuria.

Screen patients annually for proteinuria and creatinine.

1. Check annually for proteinuria in an early morning urine sample using a dipstick.
    - If positive – exclude urinary tract infection
    - If negative check for urine microalbuminuria using semi quantitative methods (Micral II or clinitek) or albumin: creatinine ratio when available.

Microalbumin can be falsely elevated exercise, infection, fever, heart failure and so avoid screening in these circumstances

If either is raised then confirm with repeat test.

2. Measure serum creatinine annually and estimate GFR– only if stable Creatinine

$$\text{CrCl (ml/min)} = \frac{(140\text{-age}) \times \text{body weight [kg]}}{\text{Cr [mg/dl]} \times 72} \times 0.85 \text{ (for females)}$$ (Cockcroft-Gault)

In patients with proteinuria/microalbuminuria or reduced eGFR (<90ml/min/1.73m^2) management should include:

- ACE inhibitor titrated to maximum dose (check serum creatinine and potassium levels within1–2 weeks of starting)
- Intensive management of blood pressure (aim<130/80) with drugs and low salt intake
- Intensify management of blood glucose
- Intensify other renal and cardiovascular protection measures (not smoking, aspirin therapy, lipid–lowering therapy)
- Monitor progression

If renal impairment measure serum creatinine, urea and potassium every 3-6 months

Foot Care

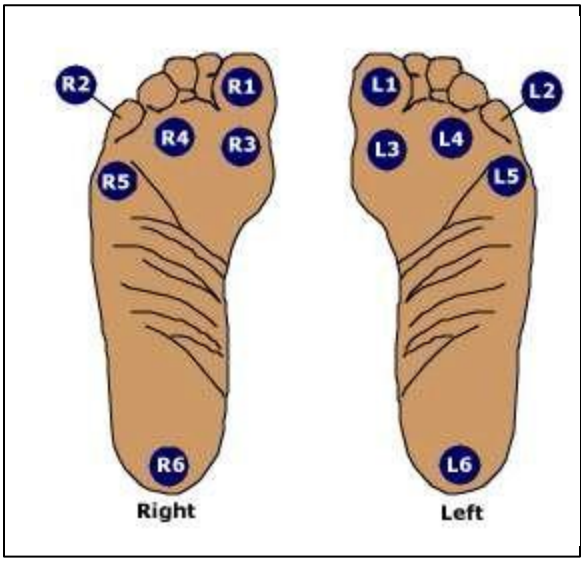
Clinicians should inspect patient feet at diagnosis and then at least annually as per classification.

Ask about history of symptoms or ulceration
Check for signs of possible neuropathy including dry skin, callus, clawed toes, and deformities.
Check pedal pulses and capillary return.
Check foot sensation using a 10g monofilament and vibration using128Hz on dorsum of greater toe just below the nail bed.

1) No risk: if no loss of sensation, no signs of peripheral arterial disease
    - Check feet annually
    - Advise re prevention with good glucose control

2) At risk: Evidence of neuropathy or decreased capillary return
    - Teach patients daily self care
    - Provide information on foot wear and general advice
    - Review feet 3 – 6 monthly
3) High risk: current or previous ulceration or amputation
    - Review feet 3 monthly
    - Intense foot education
    - Check callus removal

Are there other causes for the neuropathy? (alcohol, renal dysfunction, drug, leprosy)
Check patient is eating a healthy balanced diet. Multivitamin supplementation has not yet been tested adequately in randomized trials. However it is recommended by some clinicians and because vitamin B1 deficiency is common in Cambodia and then patients should also be offered vitamin B complex. (50mg B1/day)



TESTING PRESSURE SENSATION WITH 10G

- Check in a quiet setting.
- First apply to patients arm so that they know what to expect
- Patient closes eyes
- Apply monofilament perpendicular to skin with sufficient force to cause the filament to buckle.
- Ask patient to point to area or say yes
- Should take ~2 seconds
- Do not apply over callus, ulcer or scar

How to care for feet with neuropathy

1) Always wear protective foot wear, even inside your house you should keep special shoes
2) Avoid long walks or standing for long periods
3) Check feet regularly through the day
4) Don't sit for too long in the same position
5) Soak and scrape your feet everyday
6) DO NOT SMOKE
7) Control glucose, blood pressure

LOOK AT YOUR FEET REGULARLY

Choosing good shoes!

- Resilient on the inside to cushion the foot during walking
- Strong on the underside to prevent stones or thorns from going through the shoe
- Has a heel strap
- Comfortable and the correct size to prevent rubbing
- New shoes should only be worn for short times and check carefully for blisters
- Choose a shoe for inside the house as well as outdoors

Care of neuropathic skin (soak and scrape)

1) Soak feet in <u>room temperature</u> water every day for15-20min, so that any callus becomes white and soft
2) Examine feet for hard skin, wounds or blisters
3) Gently scrape off any hard skin/callus with a rough stone (not crumbly) or pumice
4) Apply oil (vegetable, lanolin, animal oil, hair oil) while the feet are still moist to keep the moisture in

REMEMBER – NO CALLUS = NO ULCER

Foot ulceration

Decide if the ulcer is simple or complicated

SIMPLE ULCERS
Teach patients to care for simple ulcers at home. Try and establish a cause

THE MOST IMPORTANT MEDICINE IS REST-NOT ONE STEP A DAY
(If a person with normal sensation injured their foot and developed an ulcer, pain would stop them from walking on their foot)

Advise people to use a crutch or walking stick if needing to walk around the house.

Soak the ulcer in clean water every day to which a coffee spoon of salt has been added. Clean the ulcer with clean salted water. (1 coffee spoon to 1 litre)
Cover the ulcer with a clean compress or cloth and bandage with a kroma or cloth. Treat with oral antibiotic if signs of infection.

REST

The patient should measure the size of the ulcer every week to ensure that it is getting smaller.

If not getting smaller check whether the patient is resting enough or has developed signs of complications.

COMPLICATED ULCER

This is indicated by significant swelling, cellulitis, smell, pus or any systemic symptoms like temperature or anorexia.

Admit to hospital and start systemic antibiotics if indicated. Oral metronidazole should be considered if bony involvement suspected. Do not assume heat and swelling are due to osteomyeltis. Think about neuropathic bone disintegration– do an x ray.

Rest is still the most important treatment with foot elevated–not one step a day. Not even to the bathroom.

Simple cleaning and dressings are appropriate. Sugar solution is a cheap and good for cleaning infected wounds (boil 500ml of water and add 1 kg of white sugar, bring to boil and cool). Dress daily while wound discharging.

A back slab plaster can be useful to keep the foot immobile and allow daily checking of the wound. Be careful of pressure areas.

Monitor the size of the ulcer. Consider x ray.

Amputation should rarely be required if ulcers are being managed appropriately.

Consider total contact cast when the wound, swelling and discharge is settling, usually after 7 – 10 days

Advice can be sought from KienKhleang Rehabilitation unit which has much experience in treating neuropathic feet.

NEUROPATHIC JOINT DAMAGE

Neuropathic bone disintegration (NBD) is sometimes mistaken for infection in people with diabetes.
There is usually atypical history of a red, warm, swollen foot which settles with rest. The patient often reports a number of 'flares' which settle down.

An x ray should be obtained.

If there is evidence of bone fracture or disintegration then the patient will need a total contact cast. This needs quite specialized application usually by a trained physiotherapist. This needs to usually be worn for 6months or so.

The KienKhleang CIOMAL hospital in PP has along history of treating this problem and so should be contacted for assistance if NBD is suspected.

Painful diabetic neuropathy

Stabilize glycaemic control.
Rule out other causes of pain. Naturopathic pain related to diabetic neuropathy tends to affect the feet more than the calves, is worse at rest and at night and improves with walking.
Reassure patient that the pain is usually self limiting although can take time to settle.
Try simple analgesia first such as panadol, tramadol.

If the person is still bothered by pain, a number of antidepressants/anticonvulsants can be trialed. Most have side effects and therefore should be used cautiously especially in the elderly or those with renal impairment. For example:
Amitryptylline –start with 25mg at bed time and increase dose as tolerated to 100–125mg/evening. Side effects include dizziness, low blood pressure, ataxia, confusion, urinary retention and is contraindicated in people with cardiac disease.
Gabapentin and others can be considered but be sure to check contraindications and dosing instructions as most have significant side effects.

Other issues

Erectile Dysfunction

Erectile problems occur in up to 50% of men with diabetes.
Erectile dysfunction increases in prevalence with age.
The common causes include medications, neurological, vascular and psychogenic
Consider possible contributions of other medications (eg BB) or disease.

Pregnancy

Gestational Diabetes

Women with any of the below high risk factors for diabetes should be screened for diabetes at the first visit with a fasting glucose.

- History of GD,
- Family history of diabetes,
- BMI> 23,
- History of large baby (>3500g)
- age > 35 years

Check again between 24–28 weeks of gestation if first test negative. Current

Screening test is 75g OGTT: usually not available

Gestational Diabetes if-
Fasting BGL ≥ 92mg/dl (5.1mmol/L) or 2 hour BGL ≥ 153mg/dl (8.5mmol/L)

[Note: Type 2 diabetes in pregnancy woman: fasting BGL ≥ 126 mg/dl (7mmol/L)]

Until OGTT becomes available in Cambodia, test all high risk mothers with fasting venous glucose if possible at first visit:
If fasting venous BGL ≥ 92 then manage as for gestational diabetes.

Do not use urine tests to diagnose gestational diabetes as the renal threshold is lowered. Encourage monitoring with glucometer if possible. If resources are limited then clinics should consider lending machines to pregnant women.

Women with diabetes in pregnancy should aim for a fasting glucose of ≤ 92mg/dl (5.1mmom/L) and ≤ 153mg/dl (8.5mmol/l) at 2 hours after the meal.

Trial a diet for 1 -2 weeks particularly focused on decreasing carbohydrate intake. Consider insulin if not reaching targets with diet. Expect a rise in insulin requirements as pregnancy proceeds.

Oral agents are not currently recommended for use in pregnancy (although there are ongoing trials). Remember ACEI and statins are contraindicated in pregnancy.

Mother and baby should be closely monitored by an obstetrician. Monitor BP. If she lives far from the hospital it is probably best for her to stay with friends or relatives near the hospital during her last trimester

Immediately after delivery of baby and placenta the insulin requirement usually drops to normal and there is danger of hypoglycemia. The baby should be kept under close observation for the first 24-48 hours because of the danger of hypoglycaemia and fed early. Blood glucose should be checked immediately after birth.

Mother should be checked for diabetes with a fasting glucose (or OGTT if available) at 6 – 12 weeks and then yearly. She should be advised on high risk for future diabetes (approx 50% at10 years) and given education about preventative life style measures.

In-patient Care

Referral hospitals should designate an individual in charge of matters relating to in-patient diabetes, to coordinate training in awareness of the needs and provision of in-patient care to people with diabetes. Systems of care and protocols need to be put in place and staff trained to ensure effectiveness.

Ensure laboratory support–plasma glucose, basic hematology and biochemistry.
Quality assurance must be up-to-date in laboratories to ensure accuracy of glucose and other tests.

There is an opportunity to screen individuals who are admitted with high risk factors for diabetes such as myocardial ischaemia, stroke.

HIGH RISK INDIVIDUALS FOR TYPE 2 DIABETES

- Overweight (BMI>23,waist circumference in men >=85cm and in women >= 80cm)
- Family history of diabetes
- **Hypertension**
- **History of stroke or ischaemic heart disease**
- Women with a previous history of gestational diabetes
- Women who have given birth to a large baby (>3500g)
- Age over 35

Each hospital should have a protocol for managing diabetes patients around the time of procedures or surgery and for significant hyperglycaemia.

During hospital admissions, aim to maintain near-normoglycaemia. (100– 180mg/dl)