



MINISTRY OF HEALTH

Republic of Marshall Islands

Diabetes Management Guidelines

December, 2016

REPUBLIC OF MARSHALL ISLANDS DIABETES MANAGEMENT GUIDELINES

Table of Contents

	Торіс	Page
	Acknowledgements	2
1	Message from the Ministry of Health	3
2	Introduction	4
	2.1 Types of Diabetes	4
	2.2 Diagnosis of Diabetes Mellitus	4
	2.3 Pre-Diabetes	5
3	Management of diabetes in adults	6
	3.1 The Diabetes Care Process	6
	3.2 Therapeutic Lifestyle Changes	9
	3.3 Targets for Control	13
	3.4 Therapeutic Medications	13
	3.5 General approach to control of blood sugar	18
	3.6 Special situations	20
4	Treatment of associated metabolic conditions	21
	4.1 Hypertension	22
	4.2 Hyperlipidemia	22
	4.3 Anti-platelet therapy	22
5	Management of acute complications of diabetes	23
	5.1 Hypoglycemia	23
	5.2 DKA	24
	5.3 Hyperosmolar Hyperglycemic state	26
6	Management of chronic diabetic complications	28
	6.1 Retinopathy	29
	6.2 Nephropathy	32
	6.3 Neuropathy	33
	6.4 Diabetic foot disease	34
	6.5 Periodontal disease	38
7	Diabetes in pregnancy	42
8	Family Planning in Diabetes	50
9	Tuberculosis Screening	51
10	Cancer Screening	56
11	References	59
12	Annexes	62

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Kommol tata!

1. MESSAGE FROM THE MINISTRY OF HEALTH

Diabetes is the top cause of morbidity and mortality in the Republic of the Marshall Islands. Thus improving diabetes prevention and care is essential.

These diabetes management guidelines aim to allow the following:

- Recognize early, diagnose and manage Diabetes effectively.
- Give clear guidelines on diagnosing pre-diabetes, and diabetes
- Give clear targets of control in the management of diabetes
- Raise awareness of diabetes complications, and the need for screening of complications, at least annually
- Help defer or delay the onset of complications.
- Manage complications effectively with the available resources.
- Have an effective referral system for optimum intervention at every level.

These guidelines recommend diabetes screening for all adults aged 30 and above, accessing any clinical service. This change from the previous practice will detect diabetes and prediabetes and allow earlier prevention or treatment. The guideline also addresses insulin adjustment in more detail. As Tuberculosis is a high burden disease and associated with diabetes, these guidelines incorporate TB-DM Management according to the modified Pacific Standards. In addition Cancer screening guidelines and Family Planning options are included.

Since these guidelines have been developed to help health care providers – physicians, dental staff, medex, health assistants, nurse practitioners and nurses in providing **QUALITY MEDICAL CARE** and standard clinical practice to people with diabetes or pre-diabetes, I hope you will refer to these guidelines frequently, and let us all do our part in reducing the diabetes burden!

Honorable Minister of Health Kalani Kaneko 15th March, 2017

2. INTRODUCTION

Diabetes mellitus is defined as a metabolic disorder caused by a variety of factors, and is characterized by chronic hyper-glycaemia due to impaired insulin secretion, and or insulin sensitivity.

The 3 major types of primary diabetes mellitus are:

- Type 1 diabetes
- Type 2 diabetes (T2DM)
- Gestational diabetes (GDM)

2.1 TYPES OF DIABETES

Type 1 diabetes results from severe insulin deficiency. Symptoms can appear rapidly and ketones are usually present (see *Diabetic ketoacidosis*). Patients require insulin therapy for survival. Patients with Type 1 are usually younger, and have marked weight loss and dehydration. Type 1 diabetes is now also being seen in older patients. If the diagnosis is uncertain between Type 1 and Type 2 diabetes, **C-peptide levels** can be tested on island, and refer to internal medicine specialist.

Type 2 diabetes is much more common type of diabetes. Symptoms and hyperglycemia occur gradually and patients may have <u>complications at diagnosis</u>, since it can remain undiagnosed.

Signs and symptoms of Diabetes:

 weight loss 	 polyphagia
• polyuria	 lethargy
 polydipsia 	 genital candidiasis

Conditions suggestive of diabetes:

Foot sepsis, multiple abscesses, delayed wound healing, neuropathy, poor vision

Gestational diabetes is characterized by hyperglycemia developing only in pregnancy. These women are at high risk of future Type 2 diabetes so need to be followed up, ideally at NCD clinic.

2.2 DIAGNOSIS OF DIABETES MELLITUS

Any of the following criteria can be used to diagnosis DM

• Fasting plasma glucose (FPG) level of 126 mg/dL or greater after 8 hours of no calorie intake

- Symptoms of uncontrolled DM with a random plasma glucose level of 200 mg/dL or greater
- Plasma glucose (PG) level of 200 mg/dL or greater 2 hours after ingesting 75-g oral glucose load in the morning after an overnight fast of at least 8 hours
- A1_c level of 6.5% or higher

Finger stick capillary glucose can be substituted for plasma glucose when the plasma glucose is not available. If no symptoms are present then **two positive results** on two different days are recommended. **A single positive result** is significant if there is unequivocal hyperglycaemia with metabolic decompensation or is accompanied with symptoms of diabetes.

Test	Results	Diagnosis	
	70-89	Ideal glucose level	
	90-99	Mild elevation in FPG	
Fasting plasma glucose, mg/dl	100-109	Moderate elevation- impaired fasting glucose	
	110-125	Severe elevation- Impaired fasting glucose	
	≥ 126	Diabetes	
Glucose, mg/dL, (oral glucose	≤139	Normal	
tolerance test, 2 hours after	140-199	Impaired glucose tolerance	
ingestion of 75-g glucose)	≥200	Diabetes	
	<5.7	Normal	
Hemoglobin A1 _c % as a	5.7 – 6.4	High risk/pre-diabetes	
screening test (minimize use	≥6.5	Diabetes	
as it is costly)			

Interpretation of Glucose test Results:

2.3 PRE-DIABETES

Pre-diabetes signals that the pancreas is unable to produce enough insulin due to insulin resistance caused by excess body weight of the patient. It increases a patients' risk of developing T2DM 5-fold, and also increases cardiovascular (CVD) risk.

Pre-diabetes is defined by the following blood sugar levels:

- FBG of 100 -125mg/dL,
- Oral glucose tolerance test of 140 199mg/dL or a
- Hemoglobin A1_c of 5.7 6.4%.

T2DM can be prevented or delayed by intervening in persons who have pre-diabetes. <u>The</u> <u>primary goal of pre-diabetes management is **weight loss**</u>, which reduces insulin resistance, and can improve blood lipids and blood pressure.

Patients with pre-diabetes must be offered therapeutic lifestyle changes (TLC) and pharmacotherapy. Due to the elevated risk of CVD, achieving targets for lipid and blood pressure by both TLC and medications is essential. *Metformin and Acarbose can reduce the risk of developing T2DM by 25-30%*, and both are considered relatively well-tolerated, safe and reduce cardiovascular risk.

FPG should be monitored at least every 6 months in pre-diabetics.

DM screening should be done for all Pacific islanders over 30 years of age. Screening can be considered in overweight and obese children who have two or more additional risk factors for diabetes (such as being Marshallese, and having a family history of diabetes).

These risk factors also suggest a need for screening:

• Age > 30	Hypertension	
 High Risk Ethnicity – Pacific Islander, or Asian 	 Overweight/Obese(BMI>27mg/m2) 	
 First degree relative with Diabetes Mellitus (family history) 	 Increased triglyceride(>150mg/dL) and low HDL (< 35mg/dL) 	
Sedentary lifestyle	• A1C \geq 5.7%, IGT or IFG on previous	
Cardiovascular disease	testing	
• Previous history of Gestational Diabetes	 Polycystic ovarian syndrome 	
Mellitus (GDM) or delivering babies weighing > 9 lb	 Acanthosis nigricans – darkened skin folds especially in neck area 	

If the results are normal, testing should be repeated at a minimum of 3-year intervals, or more frequently depending on risk status, and initial results.

3. THE MANAGEMENT OF DIABETES IN ADULTS

Over 90% of patients seen in RMI have Type 2 diabetes. The management of diabetes requires a multi-factorial approach to prevent the development of cardiovascular and micro-vascular disease. A practical approach to the management of type 2 diabetes in adults is considered below.

3.1 DIABETES CARE PROCESS

The following patients should be referred to the staff at NCD Clinic:-

- ✓ Patients with suspected type 1 diabetes
- ✓ Patients with suspected Type 2 diabetes
- Pregnant patients with diabetes or abnormal glucose challenge test results, as early as possible
- ✓ Patients with diabetes complications presenting with new symptoms
 - To start insulin therapy as in acute illness (foot sepsis, pneumonia), and gestational diabetes
 - Poor control of diabetes.

The following patients must be referred to ER, stabilized and before discharge must be referred to the NCD Clinic staff for follow up of blood glucose control and education:-

- ✓ **Poor Control of other conditions**, such as hypertension and heart failure.
- ✓ Indications for urgent referral within minutes: Septicemia, foot sepsis, severe pneumonia, DKA, and Hypoglycemia.
- Acute conditions needing urgent investigations: abdominal pain, nausea and vomiting, injuries etc.

Patients with pre-diabetes should be followed by their usual health care provider, and weight reduction should be the focus of their treatment.

3.1.1 Initial Visit

On the first visit after diabetes is diagnosed, a thorough assessment with review of history, physical examination, and investigations needs to be done (see Table below).

Education on the following points is essential:

- ✓ Diabetes and its long term complications
- ✓ Treatment goals for self-management
- ✓ Diet and exercise
- ✓ Medications and their common side effects given so as to increase compliance
- ✓ Hypoglycemia signs and symptoms and treatment advice.

Review of History	Physical examination	Investigations
 Severity and duration of Symptoms Duration of diabetes General health & comorbidities Family history of diabetes and complications Social history Current medications and history of drug allergy Interview form* to screen for TB symptoms 	Vitals: Pulse and blood pressure (BP), respiration & temperature (if indicated). BP measurement should include any postural drop. Height & Weight (BMI calculated) Capillary blood glucose Alertness and hydration Pallor Heart and lung examination Examination of the extremities for oedema, peripheral pulsation and neuropathy Visual acuity and fundoscopy Oral cavity inspection Ketones - if RBS is above 250	 Complete Blood Count: A low Hb may indicate an underlying chronic kidney disease Biochemistry: urea, electrolytes, creatinine, lipid profile, FBS or RBS, HbA1c Urine for micro-albuminuria (if test not possible, do proteinuria) – albumin creatinine ratio (ACR) spot testing Radiology- baseline CXR* to screen for TB Sputum* for AFB if patient has TB symptoms

All newly diagnosed patients should be screened for complications. If no complications exist, perform screening annually. If complications are present, they must be managed appropriately – refer to Sections 5 and 6 of this guideline.

*Only patients with no TB disease who are close contacts of sputum TB positive cases or close contacts of laryngeal TB cases should receive isoniazide (INH) preventive treatment for 9 months. Refer to Section 8 of this guideline.

3.1.2 Subsequent Visits

In follow up the acronym **ABCDEF** can be used, and assessment will also depend on presenting clinical status of the patient:-

- 1. A: A1c to be assessed (every 3 months while adjusting medications, then yearly)
- 2. B: Blood pressure, BMI, fasting blood glucose
- 3. C: Cholesterol to be assessed at least annually, and assess Creatinine Clearance

Also assess medications, compliance and any adverse effects

- 4. **D**: Diet follow up and give brief advice
- 5. E: Exercise to be assessed, advice given and goal to be set
- F: Feet check in those with past amputation and past foot ulcer; and arrange Follow up. (Frequency of clinic visits may be every few day to every few weeks while blood sugar levels are stabilized)
- 7. Immunizations for Influenza (yearly), and pneumococcal vaccine (once in a lifetime).
- 8. TB screening- for patients who are initially TB negative, CXR should be repeated every 2 years. * (note: this replaces the PPD test which was done in the past)

3.1.3 Coordinated NCD Care Team Process

Diabetes care requires teamwork among different health care providers in different health disciplines each with their own expertise and ability to care for the patient with diabetes. Members of the One Stop Shop – Dental, Eye, Rehabilitation and Foot Care Team, Health promotion and self-management goal setting team, Tobacco Cessation counselors, Nutritionists, Internists, Information technology and medical records, Surgical and Orthopedics teams including inpatient ward staff and those referring patients to NCD Clinic such as ER, OPD, OBGYN, TB Clinic and so forth are all members of the team.

Coordination with community organizations, churches, and community leaders is also essential in enabling healthier lifestyles for patients as this is beyond the capacity of the medical care team.

Advocacy for policies which can change the environment outside of the clinic is also strongly needed. For instance policies that are proven effective are increased tobacco taxes, salt reduction, improved diets and physical activity- increased price of unhealthy foods, improved spaces for physical activity, and increase in alcohol taxes.

3.1.4 Data management and tracking system

Clinical and Public health providers involved in the management of diabetic patients should enter and access data using the *Chronic Disease Electronic Management System (CDEMS)* which is in use. *This ensures quality of care for individual patients, giving prompts to health care providers, and also provides vital surveillance* – allowing the compilation of periodic reports of diabetes chronic care performance indicators used for program planning, monitoring and evaluation.

3.2 THERAPEUTIC LIFESTYLE CHANGES

Therapeutic lifestyle changes are imperative in the management and prevention of diabetes. The risk factors targeted have been collectively termed as "SNAP" - smoking, nutrition, alcohol and physical inactivity (SNAP). Stress management is helpful as well.

3.2.1 Smoking

Any level of smoking harms; smoking increases insulin resistance by 40%. ASK all patients about tobacco use and ACT to help them quit. Research shows that advice from health providers can more than double smoking cessation success rates. Even brief advise given by the health provider, such as *"The best thing that you can do for your health is to give up tobacco"* at every clinic visit is useful.

Smokeless tobacco – like snus, snuff Copenhagen, and chewed tobacco and betel nut as well is addictive, and risks include high blood pressure, heart disease, increased risk of stroke and CAD and cancers. In fact, a recent study by Lin et al. links betel nut with metabolic syndrome, chronic kidney disease, certain cancers, and T2DM and increased risk of cardiovascular disease. As smokeless tobacco use is increasing in RMI, always ask your patients about its use as well.

Brief clinical interventions such as the five A's (see below) can be used. Tobacco users can also be advised to tell friends and family that they are quitting, and avoid occasions where they would be tempted, and to follow the 4 D's – Delay, Deep breathing, Drink water and Do something else and not to be discouraged by relapse- relapse can strengthen resolve to stay quit.

The Five A's to Quit Tobacco:

- Ask (about smoking status)
- Advise (the patient to quit)
- Assess (determine willingness to quit)
- Assist (help the patient with a plan to quit)
- Arrange (a follow up contact)

3.2.2 Nutrition

Diabetes is associated with obesity, so weight reduction using a diet restricted in calories, rich in fiber and whole foods such as fresh fruit and vegetables, whole grains, and legumes is encouraged.

Dyslipidemia is also associated with diabetes, and patients can be advised to avoid frying and shellfish such as prawns, organ meats, eggs and full cream milk and cheeses. Baked confectionery and candies should be avoided.

The diet should also be limited in calories and include foods with low glycaemic index (e.g. substitute brown rice for white rice, and whole meal or whole wheat flour for white flour). To increase sustainability, encourage local foods such as breadfruit, green banana, markinin jojo, pumpkin leave tops.

The diet recommended for diabetic people is the same as a healthy diet recommended for the general population.

Ideally all patients should be referred for individualized medical nutrition therapy with a locally available dietician or nutritionist.

The Healthy Plate model

- This can help patients portion their foods in a healthy way based on an 8-9 inch plate.
- ✤ (½ ¼- ¼ portions).
- Half of the plate is filled with non-starchy vegetables, such as green beans, tomatoes, lettuce; and
- One quarter is filled with a healthy protein source, such as fish, chicken, cooked beans, lentils, or tofu.
- The last one-quarter of the plate is filled with healthy grains and starches such as brown rice, whole-wheat bread, taro, breadfruit or boiled green banana.
- In addition, every day 2-3 small servings of fruit should be eaten.

3.2.3 Alcohol

Patients can be advised on the following points about alcohol.

- Alcoholic drinks contain sugar and will cause the blood glucose level to rise quickly
- Extra energy (calories) can increase body weight
- o It can interact with diabetes medications
- It can hide symptoms of hypoglycaemia

• Other medical conditions may be worsened

It is recommended that only 1-2 standard drinks per day are consumed. Patients can also be assessed and counseled if their drinking is excessive, or problematic.

3.2.4 Physical inactivity

Regular physical activity is important and needs to be assessed during the clinic visit – ask about whether any activity is being done, the type of activity, and duration and frequency.

Exercise improves insulin sensitivity, reduces fasting and postprandial blood glucose levels. It decreases cardiovascular risk factors, improves functional capacity and sense of well-being.

The current recommendation is for 150 minutes a week of moderately intense exercise such as brisk walking spread over at least 3 days per week. Education and local community support groups are very helpful in assisting patients in achieving their exercise goals. Flexibility and strength training are also recommended.

During exercise, patients must drink a lot of water, and be alert for and treat hypoglycemia if it arises. Patients with proliferative diabetic retinopathy must avoid heavy lifting and jogging; and patients with high risk feet and or active foot ulcers must avoid walking and standing on their feet so can be advised to do resistance exercises, and cycling. Patients with active foot ulcers should avoid swimming until ulcers have healed.

3.2.5 Stress

Stress can result in elevated blood sugar levels by the breakdown of the body's fat and glucose stores. Also stress may result in non-compliance to medications and diet, and reduced physical activity.

Patients can be advised on **positive stress management** -:

- ✓ replacing bad thoughts with positive ones, and
- ✓ relaxation techniques like
 - o deep breathing exercises,
 - o yoga,
 - o exercising or dancing, and
 - Listening to calming music.

Patients should be advised to share their worries and talk to someone – who may help to change their perspective as it may not be really as bad as the patient thinks. Starting a new hobby can also be helpful.

By relaxation, the body's need for energy is decreased, thus blood glucose levels are also lowered.

3.3 TARGETS FOR CONTROL

These targets need to be discussed between the patient and the doctor before initiating treatment and during each follow –up visit.

	GOOD CONTROL	FAIR CONTROL	POOR CONTROL
Fasting Blood sugar	80 - 110	<u><</u> 130	<u>≥</u> 130
Random Blood Sugar	80- 144	<u><</u> 162	<u>></u> 162
Body Mass Index	<u><</u> 27	<u>></u> 27	<u>></u> 32
Blood Pressure	< 130/80	>130/80, <140/90	<u>></u> 140/90
Total Cholesterol	< 200	200-239	<u>></u> 240
HDL-C	<u>></u> 60	40-59	< 40
LDL-C	<100 <70 ideal	100-129	>130
Triglycerides	<u><</u> 150	<150-199	<u>≥</u> 200
HgbA1c	<7%	>7%, <7.5%	<u>≥</u> 7.5%

3.4 THERAPEUTIC MEDICATIONS

The ultimate goal of management is to *minimize long term complications while avoiding severe hypoglycemia*. Results of various randomized trials in diabetic patients have shown that control of hyperglycaemia delays the onset and slows the progression of microvascular complications but the effect on macrovascular disease is still uncertain.

The first step in the control of hyperglycemia is setting an appropriate glycaemic target in each individual. In younger patients an HbA1c of < 6.5% is acceptable, whereas older patients with co

morbidities and thus higher risk of adverse hypoglycemia effects may need a target HbA1c set at 7-8%. Thus glycemic targets must be individualized.

In a few patients, therapeutic lifestyle changes (SNAP) may be sufficient to control hyperglycemia, but <u>the majority of patients will require medications</u>. Metformin is the first recommended drug of choice, unless contraindicated.

When to start medications for hyperglycemia

• All newly diagnosed diabetic patients should be started on medications, in addition to lifestyle interventions as many are unable to control blood sugars with lifestyle changes

The following medications are used to manage hyperglycemia:

3.4.1. Biguanides

Metformin is a biguanide; brand names include Glucophage, Diabex. It lowers blood glucose by suppressing hepatic gluconeogenesis and increasing tissue sensitivity to insulin. It is the first line of treatment for Prediabetes and T2DM and since one of the side effects can be weight loss, it is suitable for overweight/obese patients. When used alone, there is no risk of hypoglycemia. Start with a smaller dose and increase gradually in order to facilitate compliance. Metformin can reduce HbA1c by 1-1.5%.

It is cleared from the body predominantly by renal excretion. It accumulates in renal impairment and should be used with caution in patients with eGFR of <45ml/min. It can cause **lactic acidosis** in situations such as ischemic heart disease, congestive heart failure and renal impairment. It should be stopped for 48 hours before surgery or administration of contrast radiography and only resumed once urine output and renal function have returned to acceptable level.

Side-effects: Nausea, vomiting, diarrhea, lactic acidosis.

Adult starting dose: 500mg bid-tid. May be increased to 1g bid a day.

Maximum daily dose: 2-3 g (Most physicians limit to 2g daily since gastrointestinal side effects are more common with higher doses)

Patient counseling: Take after food. Return to clinic if you get loss of appetite, nausea, vomiting, abdominal pain, cramps, diarrhea or weight loss.

3.4.2. Sulphonylureas

Glibenclamide, glyburide and *glipizide*, are available on the RMI EMF. They stimulate the pancreatic beta-cells and to produce insulin. In older patients, renal function deteriorates and since *Glibenclamide* is excreted by the kidneys and it is recommended in younger patients. In contrast, *glipizide* is cleared by the liver and the kidneys and it is the recommended drug in older patients and in patients with renal impairment. As one of the side effects is weight gain, they are recommended in lean T2DM patients. They can be combined with metformin if the diabetes control is inadequate.

Sulphonylureas are not recommended in pregnancy and in lactating mothers.

The main adverse effect is hypoglycemia, and this is more likely if there is significant renal impairment, and if patients are taking longer acting drugs such as glibenclamide. They should be taken 30 minutes before meals. Either of these drugs can reduce HbA1c by 1-1.5%.

Glyburide can be started at 2.5-5mg qd, and increased no more frequently than 2.5mg/week up to a maximum of 20 mg/day. Glipizide can be started at 2.5mg qd and increased to twice daily up to a 20mg per single dose and a maximum dose of 40mg daily. Glibenclamide can be started at 2.5mg once daily to two doses of 10mg and a daily maximum dose of 20mg. Glimeperide can also be used.

3.4.3. Other Newer Drugs

Thiazolidinediones – Example is *Pioglitazone*. The common side effect of these drugs include oedema, weight gain and precipitation of heart failure, hence these drugs are contraindicated in heart failure. Risk of fracture should be considered in the long term in females treated with *pioglitazone*. They increase tissue sensitivity to insulin. *Pioglitazone* can be used as monotherapy but can be combined with dual or triple therapy in combination with *metformin, sulphonlyurea* or *insulin*. The dose of *pioglitazone* is 15-30 mg as a single dose.

Alpha glucosidase Inhibitors –These inhibit alpha glucosidase enzymes on the brush border of the small intestine and thus interfere with the digestion of complex carbohydrates. *Acarbose* belongs to this group and can be used as monotherapy or combined. Alone it can reduce HbA1c by upto 0.5%. The common side effects include abdominal discomfort, gas and bloating due to fermentation of undigested carbohydrate by colonic bacteria. When used alone, it cannot cause hypoglycemia. It is contraindicated in chronic intestinal disease, intestinal obstruction and cirrhosis. Start the dose with 25 mg three times a day to 100 mg tds as required. It should be taken with the first bite of a meal.

Other newer hypoglcemic drugs include *Peptyl peptidase -4 Inhibitors, Meglitinides and Glucagon like Peptide- 1 Agonists (GLP-1).*

3.4.4. Insulin

There are three insulin preparations available on the RMI EMF and are discussed below. Recommended sites of injection are the abdominal wall, the deltoids and the thighs and these sites should be rotated regularly.

Characteristics of available Insulins			
Types	Onset of Effects	Maximum Effect	Duration
	(In Hours)	(In Hours)	(In Hours)
Short-acting soluble insulin	0.5	2 - 5	6-8
(Actrapid HM, Humulin R)			
Intermediate-acting isophane	1 – 2.5	4 - 12	16-24
insulin (Protaphane HM, Humulin			
NPH)			
Biphasic isophane insulin	0.5 - 1	2-12	16 - 24
(Mixtard 70/30)			

There are other types and brands of Insulin available such as the long acting preparations detemir and glargine. Lantus insulin – which is basal insulin with a long duration of action, is also available.

Insulin treatment in type 2 diabetes

(i) Deciding when to start Insulin

- Failure of oral hypoglycaemic agents insulin therapy should not be delayed. About 50% of patients after 5-10 years of T2DM will require insulin therapy in addition to oral medications. Early treatment delays complications and preserves beta cell function.
- Patients undergoing major surgery,
- Critically ill patients, and infections
- Pregnancy

(ii) Adding insulin to the oral hypoglycemic drugs (basal control)

- As outpatient treatment, start with Isophane or NPH Insulin 10- 12 Units at bedtime and adjust dose according to fasting blood sugar levels. To reach glycemic goals, insulin titration every 2-3 days is recommended.
- Total daily dose (TDD) of NPH or Isophane Insulin is 0.1-0.3 Units/kg.

- Insulin doses are adjusted accordingly:
 - FBS > 180mg/dL: Add 20% of TDD
 - FBS > 140-180mg/dL: Add 10% of TDD
 - FBS 110-139 mg/dL: add 1 unit
- If hypoglycemia occurs, reduce TDD by
 - o RBS < 70mg/dL : Reduce 10-20%</p>
 - RBS <40mg/dL : Reduce 20-40%

<u>Oral hypoglycaemic agents</u> **should not be stopped** with the commencement of intermediate (basal) acting insulin therapy, but the doses can be adjusted. Combining oral hypoglycemic medications with insulin minimizes the amount of insulin required.

Triple B- Basal/Bolus and Booster insulin protocol

(iii) Intensifying Insulin (prandial control)

- If glycemic control is not at goal then insulin must be intensified by adding prandial insulin (insulin containing regular insulin such as 70/30).
- At first, a dose of 5 Units of regular insulin given before the biggest meal can be added to the regimen of bedtime NPH insulin and oral hypoglycemic agents
- Stop sulfonylureas once you start prandial insulin due to the risk of hypoglycemia

(iv) Switching to Insulin 70/30 (pre-mixed insulin), or Basal-Bolus (4 times a day injections)

If glycemic control is not achieved with one dose of regular insulin in addition to the NPH insulin and oral hypoglycemic agents, then the patient can be started on either the basal-bolus regimen (4 times a day injections) or the twice a day injections of pre-mixed insulin eg. 70/30.

- The TDD (total daily dose) is 0.3-0.5 Units/kg.
- **Pre-mixed regimen:** If the insulin is given twice daily then 2/3rd is given during the morning dose and 1/3rd at night.
- **Basal –bolus regimen:** However, if the basal bolus regimen is used then the TDD can be divided as follows;
 - Breakfast: 20% of TDD as Regular Insulin (Soluble insulin)
 - \circ $\;$ Lunch : 13% of TDD as Regular Insulin (Soluble insulin)
 - Dinner: 17% of TDD as Regular Insulin (Soluble insulin)
 - Bedtime: 50% of TDD as Intermediate Insulin (NPH Insulin)

(Another option is to give 50% of TDD divided equally and given before each meal, and the remaining 50% of TDD given at bedtime)

How to alter the insulin dose

- Insulin dosage must be **titrated every 2-3 days to reach the glycemic goal** using the following:
 - Premixed: Increase TDD by 10% if fasting/premeal blood glucose is >180mg/dL.
 - If the 2-hr post-prandial or the next pre-meal glucose is >180mg/dL, then Increase prandial dose by 10% for that meal
 - In event of hypoglycemia
 - BG < 70 mg/dl : reduce TDD by 10-20%
 - BG < 40 mg/dl: reduce TDD by 20-40%
 - If fasting AM hypoglycemia- reduce basal insulin (i.e. NPH Insulin or Lantus)
 - If nighttime hypoglycemia reduce basal and pre-dinner regular insulin
 - If between meal daytime hypoglycemia, reduce previous pre-meal regular insulin

(v) Correction doses

Insulin sliding scale is now considered ineffective in proactive management of hyperglycemia and as much as possible, section (iii) should be used, with additional correction boluses given as below. Correction doses can be calculated in different ways

- 1. 10% of TDI
- 2. 1 unit for every 50mg over the target
- 3. 1,700 Rule (Bode, Tamborlane, Davidson 2002)
 - 1,700 ÷ TDI = (Insulin Sensitivity Factor) ISF
 - Blood glucose (BG) Target glucose (TG) = excess glucose
 - Excess glucose ÷ ISF = extra units of glucose needed
 - ISF = how many mg/dl 1 unit of insulin will decrease the blood glucose level
- o Example
- Patient's glucose level is 300mg/dl; target level is 140mg/dl
- 300mg/dl 140mg/dl = 160mg/dl excess glucose
- Calculated TDI = 50 units of insulin
- 1,700 ÷ 50 = 34 ISF
- Corrected insulin dose: 160mg/dl ÷ 34 md/dl/ unit
 - 4.7 units of insulin

Management of Severe or Acute Hyperglycemia – Inpatient Care

For hospitalized patients with diabetes treated with insulin, a proactive approach that includes basal, bolus and correction (supplemental) insulin, along with pattern management, should be used to reduce adverse events and improve glycemic control, instead of the reactive sliding-scale insulin approach that uses only short- or rapid-acting insulin (Harper et al, 2013).

Section 3.4.4 can be used as a guide for inpatient care, with particular attention to sub-section (iii).

3.5 GENERAL APPROACH TO CONTROL OF BLOOD SUGAR

Drug therapy should be considered initially- with the first line as Metformin (provided there are no contraindications), and if HbA1c is available at diagnosis, this can help decide if other medications are needed. The decision to commence glucose lowering medications is based on the degree of hyperglycaemia and the presence or absence of symptoms. The first step in the control of hyperglycemia is setting an appropriate glycaemic target in each individual. In younger patients an HbA1c of < 6.5% is acceptable, whereas older patients with co morbidities and thus higher risk of adverse hypoglycemia effects may need a target HbA1c set at 7-8%. Thus glycemic targets must be individualized with more stringent targets on younger patients.



The general approach to the management of diabetes is outlined in **Figure 1**.

Figure 1

3.6 SPECIAL SITUATIONS

3.6.1 PHYSICAL ACTIVITY/ EXERCISE

Patients should be advised to check blood sugars before and after exercise.

If FBS > 120, take food first before exercise

If FBS > 250, do not exercise as blood sugar levels will increase further with increase. These patients should have their diabetes controlled, and then reassess after 2 weeks; if FBS < 250 mg/dl then they may exercise.

Physical activity carries additional risks in diabetic patients on insulin therapy. Hypoglycaemia is a major concern. For mild to moderate physical activity (e.g. fast walking on a flat surface, mopping the floor) for 30 minutes, extra carbohydrates should be taken beforehand. For "short bursts" or longer strenuous physical activity (e.g. scrubbing the floor, moving heavy furniture), it is advisable to reduce dosage of short-acting insulin.

3.6.2 FASTING

Many patients with diabetes fast for religious or other reasons. Continue to give oral medications, but only with the main meals.

For those on insulin, prandial doses should be stopped but basal insulin (e.g. Lantus or NPH insulin) can be continued, but the dose may be reduced by 30%.

Once meals resume, medications can be resumed.

3.6.3 ILLNESS

Illness can affect blood sugar levels thus there should be close monitoring of the levels. Every patient should make a plan of what to do if illness affects their diabetes control.

Insulin doses should be adjusted according to blood sugar levels and changed to shortacting insulin for better control. Insulin must not be stopped but if need be, can be reduced by up to 30%. Oral hypoglycaemic drugs should not be stopped unless the patient cannot eat.

Fluid intake is extremely important and must be maintained. If the patient is unable to take in solid food, substitute with coconut juice, fruit juices, regular soft drinks, or other fluids containing glucose. Those patients with vomiting must seek medical assistance early to avoid complications such as diabetic ketoacidosis (DKA) and hyperosmolar- hyperglycemic state (HHS).

3.6.4 TRAVELING

Trips require careful planning, with adequate supply of medications. A medical report from the doctor with details of treatment is useful for customs clearance, and in case of emergency. Insulin must be stored cool in an insulated bag. In case of hypoglycemia, advise the patient to carry some candies, and snacks.

3.6.5 PRE-OPERATIVE STATE

A day prior to operating room (OR) procedure/surgery, give oral medications in the evening. Change intravenous fluid to dextrose saline (D5NSS) when the patient is nil per oral (NPO). Prior to OR; check FBS and then during and after surgery. If on insulin, blood sugars are to be more closely monitored. Surgery tends to raise blood sugar levels.

4.0 TREATMENT OF ASSOCIATED CONDITIONS

4.1 HYPERTENSION

Elevated blood pressure (BP) in patients with T2DM increases risk of cardiovascular events. A blood pressure **target of less than 130/80 mmHg** is recommended. The Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP) trial also showed that a systolic blood pressure at this target decreased nephropathy and all cause mortality.

Several studies have demonstrated the value of the following:

- Weight loss can improve blood pressure
- Exercise is also helpful
- Sodium restriction is essential
- The Dietary Approaches to Stop Hypertension (DASH) diet, which is low in sodium and high in potassium and recommends 8-10 serves of fruits and vegetables daily- has been proven to lower blood pressure.

If BP is over 130/80 mmHg, medications such as an Angiotensin-Converting Enzyme Inhibitor (ACEi) e.g. Enalapril or an Angiotensin-Receptor Blocker (ARB) e.g. Losartan or Irbesartan (Avapro) is recommended. (ACEi and ARB cannot be combined.)

If blood pressure is moderately elevated (> 160/90 mm Hg), it is preferable to start on **combination antihypertensive agents (more than one)** as studies show that increasing monotherapy dose will only have a minimal effect of blood pressure.

Priority in Blood pressure lowering medications

- 1. Renin-angiotensin-aldosterone system blockers (ACEi or ARBs)
- 2. Calcium channel blockers
- 3. Thiazide diuretic
- 4. B-adrenergic blocker
- 5. Additional therapy: Aldosterone receptor blockers, direct renin inhibitor, selective α_1 -adrenergic inhibitors, Central α_1 , agonists, direct vasodilators

A combination of the above drugs might be needed to achieve desired blood pressure control. It is essential to monitor to also monitor kidney function and presence of hyperkalemia when using ACEi, ARBs, and diuretics. A slight increase in serum creatinine is generally expected and is usually less than 30% of baseline values. If there is more than 30% rise in serum creatinine from the baseline values, it is recommended that ACEIs should be stopped and replaced by another anti-hypertensive drug.

Patients may also be started on Enalapril 5mg daily if microalbuminuria is present, regardless of whether blood pressure or renal function is normal. This will delay progression of renal impairment. Patients can also be started on Enalapril if there is presence of renal impairment. A common side effect of ACEi is cough and ACEi can be replaced with ARBs.

4.2 DYSLIPIDEMIA

This condition is common in patients with diabetes, thus all patients should be screened for dyslipidemia at least annually. Therapeutic lifestyle changes should be advised. Lipid lowering drug therapy with simvastatin 20 mg or atorvastatin 10 mg or 10mr rosuvastatin is recommended for primary prevention in patients with type 2 diabetes aged > 40 yrs regardless of baseline cholesterol.

*Statins should be started to all patients with Type 2 diabetes aged >40 years with at least one other risk factor.

Patients under 40 years and other important risk factors should also be considered for anti-lipid treatment.

- Overt CVD
- > Hypertension
- Smoking
- > Family history of CVD
- > Dyslipidemia
- > Albuminuria

The common side effects of lipid lowering drugs are muscle and liver problems. Liver function should be checked before commencement, and one month after starting statins, and then annually afterwards. Combination therapy of statins with bile acid sequestrants, niacin, or cholesterol absorption inhibitors may be considered if patients fail to reach the target lipid goal.

4.3 ANTIPLATELET AGENTS

Aspirin is not routinely used for low risk <50 males and < 60 females. Aspirin (ASA) 81mg can be considered for **men over 50 years and women who have an additional major risk factor for CVD**. These risk factors are:

- Hypertension
- Smoking
- Family history of CVD
- Dyslipidemia
- Albuminuria

However all patients with CVD due to their high risk status, unless contraindicated, must receive ASA.

Common contraindications to ASA include:

- History of peptic ulcer disease,
- GI bleed, low platelet states,
- Intracranial bleed, and or
- Bleeding disorder.

For those with allergy to ASA- use Clopidogrel 75mg.

In patients with Acute Coronary Syndrome, combination of ASA and Clopidogrel should be used for up to 1 year.

5.0 MANAGEMENT OF ACUTE COMPLICATIONS OF DIABETES

5.1 HYPOGLYCEMIA

The term 'hypoglycemia' refers to a low blood sugar level below 80mg/dL. It can be both symptomatic and asymptomatic, depending on individual patient threshold for symptoms. A patient with persistently elevated blood sugar levels may experience symptoms if the blood sugar level falls rapidly but is still above the normal range.

Common signs and symptoms are: sweating, tremor, tachycardia, pallor, hunger, and can proceed to mental confusion, coma and seizures.

The factors that can cause hypoglycaemia include:

- high insulin dose
- high doses of sulphonylureas
- presence of renal failure
- liver failure
- septicaemia
- missed or delayed meals
- hormonal disturbances, and
- Vigorous physical activity.

Urgent treatment is required!

If the patient is conscious and able to swallow, give a sugary food or drink followed by foods that take longer to be absorbed e.g. crackers.

If the patient is unable to swallow or becomes unconscious at home, give sugar paste, jam jelly or honey into the side of the mouth and transfer immediately to the nearest health care facility for intravenous glucose therapy. At the health care facility, if the patient is unconscious or unable to swallow:

• Give 50 ml of 50% dextrose intravenously followed by continuous intravenous infusion of 5% dextrose for up to 24 hours.

In elderly patients, hypoglycemia may reoccur for several days after stopping the sulphonylureas due to slowed renal drug clearance.

Prevention of hypoglycemia:

Educate all patients on signs and symptoms, and how to treat and prevent hypoglycemia. Advise relatives to seek immediate hospital care to avoid irreversible brain damage

5.2 DIABETIC KETOACIDOSIS (DKA)

5.2.1 Diagnosis

Diabetic ketoacidosis (DKA) is characterized by ketosis, hyperglycemia and acidosis. DKA occurs predominantly in Type 1 diabetic patients but can occur in Type 2 diabetes.

The common precipitating factors of DKA are omission of insulin, infection or sepsis, drugs such as corticosteroids, and recent trauma or acute coronary event.

Symptoms include:

٠	vomiting,	dehydration,
•	abdominal pain,	 ketotic breath,
•	Kussmaul's breathing,	 mental confusion progressing to coma.

Patients also notice rapid weight loss which can be a marker for dehydration. It is necessary to test urine for moderate to large ketone bodies.

5.2.2 Management

Management should be undertaken urgently, and the most important intervention is **FLUID REPLACEMENT**. Insulin therapy can be started subsequently.

Transfer patient to the major hospital once he/she is stable.

a. Fluids: Administer intravenous infusion of normal saline as follows:

•	First liter for 30 minutes
•	Second liter for one hour
•	Third liter for 2 hours
•	Fourth liter for 4 hours

Further infusion should be administered according to clinical assessment of the patient.

Once the blood sugar level reaches 250mg/dL, change intravenous fluid to 5% dextrose (**Note 10% dextrose** fluid preferred). If 5% dextrose is not available, use dextrose saline.

It is important to continue normal saline to correct circulatory volume along with dextrose infusion if necessary. Caution is required in the elderly, pregnant, and those with renal and/or cardiac dysfunction.

b. Insulin

A fixed rate **IV insulin infusion 0.1 Unit per kilogram body weight per hour** (estimated if necessary) is recommended.

*If insulin infusion is started, there must be one dedicated staff nurse to look after the patient

Insulin Infusion: Mix 100 units (1ml) of regular insulin in 100 ml of normal saline in an IV giving set or chamber and hook up to an IV infusion pump.

Monitor:

- 2 hourly- Blood sugar
- 4 hourly- Urine ketones ; Venous bicarbonate; and serum sodium and potassium
- Arterial blood gases

The fixed rate may need to be adjusted if:

- the ketone concentration is not falling fast enough
- The venous bicarbonate level is not rising by 3mmol/L per hr.
- The capillary blood glucose level does not decrease by 55 mg/dL per hr

Once blood glucose level reaches 250mg/dL, the insulin dose can be halved.

Following that, insulin can be changed to multiple –dose insulin regimen subcutaneously followed by twice- daily dosing.

Alternatively, the patient can be placed on intermittent IV insulin of 0.1U/kg every hour.

In the case that an IV access cannot be established, give:

• Short acting insulin IM 8 units/hour

Do not give insulin subcutaneously in DKA, as absorption is poor when patient is in shock

c. Electrolytes and Acid Base Disturbance

(i). Potassium

(i) Insulin takes glucose and potassium into the cells, so serum levels of both glucose and potassium fall.

Replacement Potassium should be administered as follows:

- \circ if it remains above 5.5 mmol/L do not give potassium
- if Potassium level is between 3.5 5.5 mmol/l
 - Initiate intravenous potassium at a rate of no more than 10 20 mmol/hour (added to IV infusion fluid bag) once insulin and fluids have been started and renal function and urinary output have been assessed as satisfactory.
- If level is below 3.5 mmol/L
 - Review potassium requirement.
 - A separate potassium infusion line should be started

*Be cautious when giving Potassium – monitor the levels

Potassium infusion should not exceed 20mmol per hour.

(ii). Bicarbonate

Measure venous rather than arterial bicarbonate and PH. Sodium bicarbonate should not be given routinely. It is only given when the blood pH is less than 7.0. In such cases, infuse 50 mmol

of sodium bicarbonate over one hour.

d. Underlying cause

Do a CXR, EKG, Urinalysis for culture, Blood culture routinely for cases of DKA and HHS as infections are also a common cause. Investigate for and treat the underlying cause.

e. Other measures

- An indwelling catheter should be inserted to monitor urine output.
- Oxygen therapy if required
- Insertion of nasogastric tube if paralytic ileus develops.

f. Post DKA Management

Patient Education

- On blood sugar monitoring, and compliance.
- On sick day management need to seek early hospital care if patients are unwell.
- On early warning signs and symptoms.

Changing IV insulin to SC insulin

• Patients must be switched from IV route to insulin SC; and then attempt to place back on usual medications based on blood sugar control.

5.3 HYPEROSMOLAR, HYPERGLYCAEMIC STATE (HHS)

This was previously referred to as "Hyperosmolar Non- Ketotic State" or HONK. It is seen more commonly than DKA, and the main feature that differentiates it from DKA is the absence of ketones. HHS is seen commonly in elderly patients above 60 years old, and present with a history of thirst, polyuria, and progressively impaired consciousness as the condition develops more gradually and patients present with marked dehydration.

Blood sugar levels are usually very high, above 540 mg/dL. Serum sodium is often elevated and the calculated serum osmolality >320 mOsm/l.⁶

Management- Treat as for DKA; IV Normal saline therapy, IV insulin low dose (4-6 Units/hour by infusion) and potassium monitoring are the key strategies. On discharge, patients may be controlled with oral medications and diet.

6.0 MANAGEMENT OF CHRONIC DIABETIC COMPLICATIONS

The chronic complications of diabetes are both microvascular and macrovascular. Microvascular complications are: retinopathy, nephropathy, and neuropathy. Good diabetes control is proven to

reduce the risk of these microvascular complications. Macrovascular complications are: coronary heart disease, cerebrovascular disease, and peripheral vascular disease.

Major risk factors for complications include:		
Younger age at onset Family history of complications		
Longer duration of diabetes	Hypertension	
Poor glycaemic control	Smoking	
Dyslipidaemia		

6.1 RETINOPATHY

Diabetic retinopathy (DR) commonly causes loss of vision, but this can be avoided if it is detected and treated early. Nearly all patients with type 1 diabetes have some degree of retinopathy after 20 years, as do more than 60% of with type 2 diabetes. Moreover, in up to 21% of individuals with type 2 diabetes, retinopathy is found at the time of diagnosis. Thus, screening recommended for Type 2 is at time of diagnosis, and for Type 1 is after 5 years of diagnosis.

- Diabetic Retinopathy is asymptomatic in its early stage
- Diabetic Retinopathy can progress rapidly without warning
- Screening is the only way to identify people with diabetic retinopathy
- Timely treatment can prevent vision loss from diabetic retinopathy

6.1.1 Risk factors for diabetic retinopathy

Poor glycaemic control	Dyslipidemia
Elevated blood	Longer duration of diabetes
pressure	
Pregnancy	Micro-albuminuria & proteinuria

The presence of multiple risk factors amplifies the risk of diabetic retinopathy.

6.1.2 Eye Screening

Screening should be **done at least annually and every 2-3 years if patients had a normal eye exam more than once**. The recommended screening tool in order of preference is a fundus or retinal camera, followed by an indirect ophthalmoscope and lastly a direct ophthalmoscope. For the latter two, the pupils have to be dilated. Screening can be done by trained nurses who take fundus photographs, grade retinopathy and only refer to ophthalmologists cases that need further assessment.

In diabetic patients who are pregnant, they should be screened at booking, preferably in the first trimester regardless of previous screening history. If no retinopathy is present, screening can be annually. In patients with minimal retinopathy, frequent screening throughout the pregnancy is indicated.

Patients can be booked to the Eye Clinic, or await visiting Eye team if this is appropriate.

6.1.3 Eye Assessment

- Check visual acuity with Visual Acuity (Snellen's) chart unaided or aided (with present glasses). *Check with pinhole if visual acuity 20/40 or worse.*
- Check pupil reaction in both eyes [direct and consensual]
- Check depth of anterior chamber with light directed from the lateral limbus
- Check red reflex with ophthalmoscope; if present, do fundus photography.

IF FUNDUS CAMERA NOT AVAILABLE OR POOR RED REFLEX

- Dilate pupils with tropicamide eye drop. Add phenyephrine eye drop if available.
- Check for cataract or vitreous bleed/opacity
- Assess Retina using an indirect ophthalmoscope or a direct ophthalmoscope.

8.1.4 Management of diabetic retinopathy

Diabetic retinopathy can be classified as proliferative, or non-proliferative." Proliferative" indicates presence of new blood vessels, and these can bleed resulting in vitreous hemorrhage and macular edema which can lead to blindness. Laser treatment can slow the progression of proliferation. There is also an increased risk of cataract in diabetic patients.

In patient with *active proliferative retinopathy*, strenuous exercise may precipitate vitreous hemorrhage or traction retinal detachment. These patients should avoid weight lifting, vigorous sexual activity, high-impact aerobic activities and head-down positions.

Laser treatment is available and can slow down the progression of DR and can stabilize vision. Anti-vitreous endothelial growth factor (Anti-VEGF) is also another treatment option available.

Classification of retinal findings

Early Nonproliferative Retinopathy (NPDR) Non-proliferative diabetic retinopathy Aneurysm Hemorrhage Hard exudate	Microaneurysms; dot hemorrhages; hard (lipid) exudates	Establish and maintain HbA1c 1.5% above upper limit of normal to slow progression; treat hypertension if present.	Refer to Ophthalmologist within 1 year.
Moderate or Severe Nonproliferative Diabetic Retinopathy (NPDR)	Intraretinal microvascular abnormalities; severe dot and blot hemorrhages; cotton wool spots; venous dilation	Establish and maintain HbA1c 1.5% above upper limit of normal to slow progression of retinopathy; treat hypertension if present.	Refer to Ophthalmologist within 1- 3 months.
Proliferative Diabetic Retinopathy (PDR) Proliferative diabetic retinopathy	New vessels on disc and/or elsewhere; retinal detachment; vitreous hemorrhage; macular edema		Refer to Ophthalmologist within 48 hours.

8.2 NEPHROPATHY

Diabetic nephropathy usually takes 10-15 years to develop after the onset of hyperglycemia if hyperglycemia is long standing.

Microalbuminuria is the earliest manifestation of diabetic nephropathy and is a marker of progressive deterioration of renal function. Microalbuminuria is defined as urinary albumin loss to between 30 and 300 mg per day. In practice a more practical assessment is based on albumin/creatinine ratio (ACR), >2.5mg/mmol in men and >3.5 mgs/mmol in women is often used to define microalbuminuria.

Proteinuria is present with raised urinary albumin excretion of >300 mg/day. An ACR >30 mg/mmol in a spot urine is consistent with a diagnosis of diabetic nephropathy.

Glomerular filtration rate (GFR). This is often calculated by using Cockcroft and Gault formula as shown below and useful in assessing kidney function. A calculator on <u>www.mdcalc.com</u> can be accessed easily to calculate estimated GFR and can be adjusted to account for overweight and obesity with an additional input of height measurement.

Creatinine Clearance:

 $Cr Cl = \frac{(140 - age in years) x weight (kg) x [0.85 if female]}{72 x Serum Creatinine (in mg/dL)}$

8.2.1 Five Stages of Chronic Kidney Disease (CKD):

Stage	Renal Function	GFR (ml/min)
1	Normal GFR	≥90
2	Mild impairment	60-90
3	Moderate renal impairment	30-59
4	Severe renal impairment	15-29
5	End stage renal disease	<15

Refer to Internist if eGFR < 30 ml/min</p>

8.2.2 Assessment

Perform an annual test for urine albumin excretion for all Type 2 diabetic patients from time of diagnosis. If the UACR is positive, then the test is repeated after 4 weeks and 3 months apart and microalbuminuria is only diagnosed after 2 or 3 out of 3 tests are positive.

Serum Creatinine should be measured at least annually in all patients with DM regardless of the degree of urine albumin excretion to estimate GFR and stage of kidney disease.

8.2.3 Management

Use ACEi or ARBs for non-pregnant patients with micro- or macro-albuminuria. An appropriate starting dose is Enalapril 2.5-5mg daily.

For patients with established Diabetic Nephropathy the following is recommended:

- Control of protein intake at 0.8-1.0g /kg is recommended for CKD stages 1 and 2
- For CKD Stages 3-4 a protein intake of 0.8g/kg is needed
- Control of blood pressure
 - Blood pressure lowering is associated with a reduced rate of chronic kidney
 - disease progression with ACEi or ARBs, and other antihypertensives.
 - If eGFR is < 30ml/min then stop giving ACEi.

Ideally patients should be seen by a nutritionist. For end stage renal disease, renal replacement therapy in the form of dialysis or renal transplant needs to be considered. Refer to consultant physician for advice.

Remember that good control of A, B, C: - A1C, Blood pressure, and Cholesterol helps to reduce progression of complications

8.3 NEUROPATHY

Patients can experience peripheral neuropathy, and or autonomic neuropathy. Peripheral neuropathy is also an important cause of diabetic foot ulcers.

6.3.1 Peripheral sensory-motor neuropathy

Symptoms of peripheral sensory-motor neuropathy include:

- numbness,
- paraesthesia,
- pain, and
- weakness.

If pain is prominent, several treatments have been shown to be effective and improving the quality of life.

- > OR
- Amitriptyline 50-150 mg orally at bedtime
- Carbamazepine 100 mg twice daily up to 600 mg orally daily
- Gabapentin 300mg qid x 1 day then 300mg bid x 1 day then 300mg tid
 - Pregabalin (Lyrica) 50-100mg tid

Good glycaemic control is essential for control of symptoms.

6.3.2 Autonomic neuropathy

Autonomic neuropathy can present as:

- postural hypotension,
- dysphagia, gastroparesis
- cardiac autonomic neuropathy
- intermittent diarrhea impotence, and
- bladder atony.

Postural hypotension requires specialist assessment but the patient may respond to:

• Fludrocortisone 0.1 to 0.3mgs orally daily.

6.4 DIABETIC FOOT DISEASE

Foot problems account for much of the morbidity, hospitalization and amputations in people with diabetes. Most foot problems are preventable with education, early detection and treatment. **Examine patients yearly and every 3 months if a problem is identified**. All patients with T2DM require foot education and regular follow up.

6.4.1 Foot Assessment

- Ask about previous foot problems, neuropathic symptoms, rest pain and intermittent claudication
- Inspect the feet (including nails, between the toes) to identify active foot problems such as corn and callus, toe deformities such as claw toes, hammer toes, bony prominences, any fungal infection in between the toes, and poor perfusion
- Examine for neuropathy by testing for protective sensation using the 10g monofilament
- Check peripheral pulses
- Check Ankle Brachial Index (ABI)
- Assess footwear

6.4.2 Risk Factors for Diabetic Foot Problems

The major risk factors for diabetes foot problems are:

- *Peripheral Neuropathy* sensory loss is a significant risk
- *Peripheral Arterial Disease* poor arterial blood supply is also a significant risk factor for diabetic foot ulceration and contributes` to poor wound healing

- *Poor Glycaemic Control* poor blood glucose level control increases the risk of neuropathy, vascular disease and infection;
- *Foot Deformities* Foot deformity is a risk factor for ulceration. Hammer toe, claw toes and bony deformities subject the foot to high pressure and trauma that can lead to ulceration;

6.4.3 Risk Classification and Management for the Diabetic Foot

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The risk level will determine how frequently the patient's foot should be reviewed.

Risk Classification and Management for the Diabetic Foot							
<u>Risk Status</u>	Clinical Findings	Clinical review	What to Do				
Category 0 Low Risk	 No increased risk of foot problems No signs of peripheral neuropathy No peripheral vascular disease No foot deformity No loss of protective sensation → All "+" responses to the 10gram filament 	Annual review	Provide foot care education, inspect and advise on foot wear. Routine foot care as needed.				
Category 1 Some Risk	Loss of protective sensation → requires at least 1 "-" to the 10 gram filament. No foot deformity or plantar ulcer history.	Every 6 months	Patient education, proper footwear, routine foot care as needed, soft molded insoles, daily self- inspection.				
Category 2 Medium Risk	 Peripheral vascular disease and/or peripheral neuropathy Impaired sensation Foot deformities No history of foot ulcers (plantar ulceration) 	Every 3 months	Provide foot care education, advice on appropriate foot wear, consider therapy for symptomatic neuropathy, consider further vascular assessment if indicated; examine feet every 3-6 months				

1

Category 3 High Risk	 Peripheral neuropathy Peripheral vascular disease History of previous foot ulcers or amputation 	Every 1 month	As above and review every 3 months by foot specialist
Acute Foot Problems	 Acute foot problems, e.g. ulceration Ischemia Infection Acute Charcot foot 	<u>Refer to specialist</u> . May review every 1- 7 days depending on need	Urgent foot care by foot specialist service and treat problem, or foot infection with antibiotics, advise on pressure relief and provide education and regular follow up as directed. <u>Systemic signs</u> <u>of infection require</u> <u>hospital admission</u> and debridement or amputation.

(Adapted from International Consensus on the Diabetic Foot. 1999; Frykberg et al,2006)

6.4.4 Foot Care

Education

All persons with diabetes must be advised to do the following:

- Check and wash their feet every day;
- Avoiding walking around bare feet- even indoors;
- Apply oil or lotion to avoid dry and cracked feet;
- Avoid burning the feet;
- Wear proper fitting shoes- adjustable Velcro sandals or lace- up are preferred;
- Buy shoes in the afternoon and stand up to fit both shoes;
- New shoes should be worn in slowly- 1hr daily for a week or two before wearing new shoes outdoors to avoid blisters. Never wear shoes for more than 8 hours at a time.
- Always feel the inside and check shoes before wearing them.
- Cut toe nails straight across and file sharp edges;
- Quit cigarette smoking immediately.
- Seek medical care immediately for any foot wounds.

i. Aggressive Treatment of Infection

Clinical manifestations of infection	Infection severity
 Wound with <u>no signs of inflammation</u> (i.e., erythema, pain, tenderness, warmth, or induration) 	Not infected- ADVISE WOUND CARE & WHEN TO RETURN
 Presence of pus and/or two or more signs of inflammation, but any cellulitis or erythema extends 2 cm or less around the ulcer; infection is limited to the skin or superficial subcutaneous tissues; <u>no</u> <u>systemic illness</u> 	 Mild- FLUCLOXACILLIN 500mg q6h + METRONIDAZOLE 500mg q8h Wound care/ debridement
	Duration: 1-2 weeks
 Infection in a patient with <u>no systemic illness</u> but has at least one of the following characteristics: cellulitis extending more than 2 cm around the ulcer; lymphangitic streaking; spread beneath the superficial fascia; deep tissue abscess; gangrene; involvement of muscle, tendon, joint, or bone("sausage toe") 	• Moderate- AMOXYCILLIN/CLAVULANIC ACID 500/125mg q8h CIPROFLOXACIN 500mg bd Wound care/ debridement regularly Duration: 2-4 weeks or longer 8-12 weeks if residual infected bone
 Infection in a patient with <u>systemic toxicity or</u> <u>metabolic instability</u> (e.g., fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycemia) 	 Severe- REFER FOR URGENT ADMISSION (see medications below)

Recognize and treat infection early and aggressively with proper antibiotics. Have a high index of suspicion for infection as **50% of diabetic patients will not show classic signs of infection.** Diabetic infections are often caused by a mixture of organisms (aerobes and anaerobes).

- For severe infections, refer to the surgical department. Start on
 - IV Ceftriaxone 1g q12h
 - IV Cloxacillin 1g q6h
 - PO Clindamycin 300mg q6h

ii. Wound Care

Early and regular debridement of dead and devitalized tissues will provide an effective wound bed for healing. Sharp debridement by a skilled practitioner is very useful and can reduce pressure on the wound by up to 25%.

A moist wound environment will encourage healing. A wound bed that is too wet or too dry will delay wound healing. Moist dressings with normal saline are preferred over dry gauze dressings.

Avoid excessive dressing materials, and consider off-loading the wound with felt dressings, a boot, or adjusted shoes, and other off loading equipment.

Hyperbaric therapy can be used.

iii. Multidisciplinary Approach

The benefit of multidisciplinary approach is well established. The contributions from Surgeons, Physicians, Foot Clinic Nurses, Physiotherapist and health educators must be sought to enhance the care for diabetic feet.

6.5 PERIODONTAL DISEASE

Periodontal disease refers to a group of oral health problems that arise in the gingival sulcus, (the gap between the gum and the tooth). Diabetes causes abnormalities in blood vessels, and high levels of specific inflammatory chemicals such as interleukins, weakened immune response that significantly increase the chances of periodontal disease. High levels of triglycerides (which are common in type 2 diabetes) and obesity also, are also linked to poor gum health.

Controlling both type 1 and 2 diabetes may help reduce periodontal problems.

There is a strong relationship of adult periodontitis with the following health conditions:

- Respiratory infections
- Severe osteopenia
- Pre-term or low birth weight babies
- Stroke
- Heart disease and
- Uncontrolled diabetes.

Patients need regular oral exams, so refer to the Dental Clinic at least once a year. Every 6 months people with diabetes' teeth need cleaning. They should also be advised about proper tooth brushing and flossing and mouth rinsing.

Periodontitis which characterized by the following:

- Gum inflammation, with redness and bleeding.
- Deep pockets (greater than 3 mm in depth) form between the gum and the tooth.
- Loose teeth, caused by loss of connective tissue structures and bone.

Periodontal diseases are generally divided into two groups:

- Gingivitis which only affects the gingival tissues (gums) without loss of attachment and bone. Treatment is very effective if initiated early in the course of gingivitis. Without good management of gingivitis, however, the problem can progress further to periodontitis
- 2. Periodontitis which involves loss of the bone and connective tissue which supports the teeth.

Symptoms:

In general, symptoms of periodontal disease progress over time if left untreated at the initial stages and include:

- Red and swollen gingivae.
- *Gingival Bleeding*. (Bleeding of the gums, even during brushing, is a sign of inflammation and the major marker of periodontal disease.)
- **Bad Breath** : Debris and bacteria can cause a bad taste in the mouth and persistent bad breath.
- **Gingival Recession and mobile teeth**. (Occurs in Periodontitis): As the disease advances the gums recede, and supporting structure of bone is lost. Loose teeth, sometimes causing a change in the occlusion (way the upper and lower teeth fit together) when biting down or a change in the fit of dentures (false teeth).

CLASSIFICATION OF PERIODONTAL DISEASE

I. Gingival diseases

- a) Dental plaque- induced gingival diseases
- b) Non plaque induced gingival diseases
- II. Chronic periodontitis
 - a) Localized
 - b) Generalized
- III. Aggressive periodontitis
 - a) Localized
 - b) Generalized
- IV. Periodontitis as a manifesting of systemic disease
- V. Necrotizing periodontal diseases
- VI. Abscesses of the periodontium
- VII. Periodontitis associated with endodontic lesions
- VIII. Developmental or acquired deformities and conditions

ASSESSMENT

These features should be noted during the periodontal examination:

1. VISUAL	Deposits: supra-gingival plaque, calculus Gingivae: erythema, hyperplasia, recession Occlusal abnormalities
2. PROBING	Pocket depths Bleeding on probing Sub-gingival calculus Furcation defects
3. PALPATION	Mobility

The stages of periodontal disease



Healthy Gums HEAL THY GUMS ARE FIRM AND PINK.



Gingivitis

THE EARLY

THE ENKLI STAGE OF PERIODONTAL DISEASE - GUMS BECOME RED,

SWELL, AND BLEED EASILY



Periodontitis

THE BEGINNING

OF BONE AND TISSUE LOSS AROUND THE TOOTH.



Moderate Periodontitis MORE BONE AND TISSUE DESTRUCTION.



Severe Periodontitis EXTENSIVE BONE AND TISSUE LOSS. TEETH MAY BECOME LOOSE.

STAGING OF PERIODONTITIS

	Slight (mild)	Moderate	Severe(Advanced)			
Probing depths	>3 & <5 mm	≥5 & <7 mm	≥7 mm			
Bleeding on probing	Yes	Yes	Yes			
Radiographic bone	Up to 15% root length	16% to 30% or	> 30% or > 5mm			
loss						
	≥2mm&,	>3mm & <u>≤</u> 5mm				
Clinical attachment	1 to 2mm	3 to 4mm \geq 5mm				
loss						
(Source: American Academy of Periodontology,						
AAP Classification)						

MANAGEMENT OF PERIODONTAL DISEASE

Prioritizing oral hygiene and having regular dental checkups is just as important as watching cholesterol levels. Management of periodontal disease is as follows:

1. Hygiene phase	Comprises of:
	 Oral health education Oral health instructions in plaque control (tooth brushing, flossing use, Chlorhexidine gluconate 0.12% mouth rinses) Tooth brushing technique Elimination of obstacles in effective oral hygiene Non surgical sub-gingival scaling
2. Re assessment	 Conducted 4 – 6 weeks after completion of hygiene phase.
	 Full periodontal assessment (Includes plaque, gingivitis and pocket charts)
3. Corrective phase	Treatment of any oral health disease following hygiene phase
	 Root planning or surgery (Involves removal of sub- gingival plaque, calculus and infected cementum) Advisable to have it once a year.
4. Supportive periodontal care / maintenance phase	 Patients should be reviewed at regular intervals to monitor oral hygiene and permit early detection of recurrent disease. (Usually 6 – 8 weeks) and then gradually extended provided the periodontium remains stable. Careful probing of all tooth surfaces is required to detect bleeding pockets (reliable indicator of active periodontitis.) Long-term follow up is required to monitor the success of therapy.

7.0 DIABETES IN PREGNANCY

When a person with diabetes becomes pregnant, this is referred to as **pre-existing diabetes** or **pre-gestational diabetes**.

When a woman with no history of diabetes becomes pregnant and develops elevated blood sugars levels above the normal, this is called **gestational diabetes**.

7.1 PRE-EXISING DIABETES

Initial work up for all cases diagnosed with diabetes for the first time during pregnancy

- 1. Assess for complications of Diabetes
 - a. Baseline Ophthalmic review for Retinopathy
 - b. Renal Function Test
 - 2. Get a baseline dietary assessment and counselling
 - 3. Counsel on:
 - a. Impact of Diabetes on Pregnancy outcome,
 - b. Self Glucose monitoring,
 - c. Logistics of ongoing care

7.2 GESTATIONAL DIABETES MELLITUS (GDM)

- Defined as any degree of glucose intolerance with the onset or first recognition during pregnancy
- Diabetes diagnosed in the second or third trimester of pregnancy that is not clearly overt diabetes
- Women with diabetes in the first trimester would be classified as having preexisting diabetes
- Associated with increased perinatal morbidity and mortality

Complications of GDM include the following: Macrosomia, preterm delivery, respiratory distress syndrome, Infant hypoglycemia after delivery.

Maternal Complications		Fetal Complications		Neonatal Complications	
•	Infection:	•	Fetal Macrosomia	٠	Respiratory Distress
	Chorioamniotis,	٠	Early pregnancy loss		Syndrome
	endometritis,	٠	Fetal Acidosis, Hypoxia	•	Hypoglycemia
	pyelonephritis	•	Stillbirth	•	Hypocalcemia
٠	Pregnancy Induced	•	Long term complications:	٠	Hyperbilirubinemia
	Hypertension		obesity		

•	Postpartum bleeding	•	Congenital malformation
٠	Ketoacidosis		
٠	Caesarian Section and		
	Birth Trauma		

In GDM, the monitoring of blood sugars is so important so all patients with GDM should be encouraged to monitor their blood sugars as diet alone can control it. Also, since GDM has important complications, if GDM is suspected, check for it.

7.2.1 What are the risk factors for GDM?

HIGH RISK FOR GDM

- Maternal age >35 years
- Marked Obesity (BMI > 40)
- Personal history of GDM
- Previous infant weight > 8.8 lbs
- Prediabetes
- Glycosuria
- Polycystic ovarian syndrome
- Strong family history of DM (parents/ siblings)
- Hypertension before pregnancy or in early pregnancy
- Ethnic Group: African Americans, Asian -Americans, Hispanic Americans, Native Americans, and PACIFIC ISLANDERS

7.2.2 Universal screening – test all patients with fasting plasma glucose

- Screen for undiagnosed Type 2 diabetes at the first prenatal visit in those with risk factors, using the standard diagnostic criteria (see Table High Risk for GDM)
- Request for Fasting Plasma glucose (FPG) for all clients at first prenatal visit, if result indicate overt diabetes (FPG ≥ 126) then follow up for further diagnosis of preexisting diabetes
- If FPG is <92mg/dL, retest for GDM at 24-28 weeks of gestation using One Step 75 gram Oral Glucose Tolerance Test (Note: Overnight Fast of at least 8 hours)
- An FPG result of 92 125mg/dl during pregnancy indicates GESTATIONAL DIABETES

7.2.3 Check OGTT if fasting plasma glucose is elevated

- Do an oral glucose tolerance test (OGTT). After an 8 hour fast give 75 grams of glucose then check a plasma glucose at one and two hours. <u>Note that one gram of glucose is</u> <u>equivalent to 4 calories therefor three hundred glucose calories in juice or soda is</u> <u>approximately 75 grams.</u>
- Diagnosis confirmed if FBG > 92 125 mg/dl, one hour glucose > 180mg/dl, 2 hour blood glucose > 153 mg/dl. At least 2 abnormal readings out of the 3 are needed to confirm diagnosis of GDM.

Diagnostic Criteria for Pre-existing Diabetes and Gestational Diabetes

Pre-Existing Diabetes	Gestational Diabetes (After 75 gram Oral Glucose Tolerance Test)		
$FPG \ge 126 \text{ mg/Dl}$ OR	FPG >92mg/DI (5.1 mmol/L) OR		
Random Blood Sugar (RBS) >200mg/dl PLUS symptoms of Polyuria, Polydipsia, and	One Hour OGTT of >180mg/dl (10mmol/L) OR		
Unexplained weight loss OR			
Hba1c \geq 6.5% (using a NSGP certified analyzer)	Two Hour OGTT of >153 (8.5 mmol/L)		
Source: American Diabetes Association Standards of Medical Care (Diabetes Care 2016, 39 (Supp 1) S13-S22			

7.2.4 What steps should be taken when the diagnosis is confirmed?

7.2.4.1 Dietary Assessment and Advice

Start a low sugar healthy diet with more fruits, vegetables, whole grains and fiber. Breakfast should be only 10-15% carbohydrates.

- Ideally, therapy should be Individualized, based on diet history, prepregnancy weight, and activity level
- Aim to achieve normoglycemia- Use food and blood glucose monitoring records
- Graph weight gain
- Modify carbohydrate intake at breakfast
- Smaller meals, more frequent snacks
- Prevent or correct ketosis
- Contribute to fetal well being

Nutritional advice should be culturally appropriate and individualized to incorporate each client's specific needs. The advice should cover both diabetic diet recommendations and specific pregnancy requirements. Recommended calorie intake differs for all trimesters, and time should be spent discussing diet with patients.

Adequate dietary intake is important to avoid foetal growth retardation – ketonuria may help detect inadequate carbohydrate intake. Lack of material weight gain (particularly in non- obese women) may also indicate excessive restriction of food intake.

In Clinical practice, women often require 1800 to 2500 kcal per day.

Recommended Daily Caloric Intake

Pre-pregnancy weight status	Kcal/kg/day
Ideal body weight (IBW or desirable body weight –	30
DBW))	
120-150% DBW (overweight)	22-25
>150% DBW (morbidly obese)	12-18
<90% DBW (Underweight)	35-40

REFER TO Dietitian or Nutritionist for their meal plan with the Recommended Calorie Distribution as follows:

Carbohydrate	<mark>40-50</mark> %
Protein	20%
Fat	30-40%

In case Dietitian is not available, may give simple advise:

- Limit sweets
- Eat three small moderate meals and two -three snacks daily
- Be careful about amount of carbohydrate rich food in the meal
- Include fiber in meals in the form of fruits, vegetables, whole grain, limit consumption of flour based products (such as bread, donut) and potatoes
- Advise to eat only small amount of Carbohydrates (10% of total computed grams of Carbohydrates) during breakfast.

Optimal pattern of weight gain

1 st trimester	2-5 lbs
2 nd trimester	0.5-1 lb/week
3 rd trimester	0.5-1 lb/week

7.2.4.2 Exercise Daily

Benefits	Improve blood glucose control
Exercise may cause	Fetal Distress
	Hypertension

If there is no contraindication, encourage simple activities such as upper body exercise, walking, and swimming.

7.2.4.3 Pharmacologic Therapy

• Use of Metformin in Gestational Diabetes

In selected cases Metformin can be used in Pregnancy for GDM cases however this will be based on consultation with the specialist. Start on Metformin 500mg per orally once a day and gradually titrate up to a maximum of 2000mg daily in two divided doses .

Metformin is not to be used in people with type 1 Diabetes.

• If FBS>95mg/dL after 2 weeks of diet, start insulin therapy (see guidelines on starting insulin- Section 7.1.5)

7.1.5 Insulin Therapy in GDM

- Monitor FPG closely;
 - o monthly during first trimester,
 - every 2 weeks during 2nd trimester and
 - weekly during 3rd trimester
 - Monitor A1c every 4 to 6 weeks
 - If FPG >95mg/dL or 2 hour PPG (postprandial glucose) >120mg/dL, and if HbA1C is > 7%, refer to Internal Medicine to start Insulin Therapy

Duration category	Insulin type	Onset of	Peak	Duration
		action(hours)	activity	(hours)
Short acting	Regular	0.5	2 to 3	6 to 8
Intermediate acting	NPH	1 to 2.5	4 to 12	16 to 24
Mixed	30% regular; 70% NPH	0.5 to 1	2 to 12	16 to 24

Levemir and Humalog can be used if available.

Insulin Dose and Regimens

Empiric	20-30 units/day
Once Daily	NPH; NPH/Regular
Twice Daily	NPH; NPH/Regular; Premixed
Multiple Daily Insulin	

OR initial dose of 0.7 units/kg for 1st trimester, 0.8 units for 2nd trimester, and 0.9-1.0 units/kg for 3rd trimester

Initiation of Insulin in GDM

- 1. Admit patient if self-blood glucose monitoring is not possible.
- Give basal insulin 10 units either NPH or glargine at 10pm, at 0.1-0.2 units/kg/day. Then add regular insulin before meal depending on the result of 2hr post prandial blood glucose then titrate depending on the target blood glucose.
- 3. Give **regular insulin** with each meal, the usual starting dose is **5-10 units** with each meal.
- 4. If 2-hours post-meal blood glucose > 140 mg/dl, increase insulin dose in increments of 5 units.
- 5. Continue to monitor 2-hrs post-meal blood glucose with each insulin increase. Monitor blood sugar 7x (premeal, postmeal, and bedtime).
- 6. Monitor fetal movements.
- 7. Once blood sugar is stable, and patient is well educated, you may discharge the patient and resume prenatal checkup.
- 8. Readmit patient once on labor or at 38 weeks AOG
- 9. If diabetes is controlled by diet alone, induce labor at 40 weeks.
- 10. If on insulin, induce labor at 38 weeks. If cervix is not ripe, ripen it with Misoprostol (100micrograms inserted into vagina every 12 hours – if available), followed by artificial rupture of membrane and augmentation of labor with oxytocin as per our labor ward protocol.
- 11. Give IV glucose/insulin infusion for prolonged labor or caesarean section.
- 12. Advise **breastfeeding postpartum immediately** as baby might develop hypoglycemia.
- 13. For GDM, you may stop insulin post-partum
- 14. For pre-existing diabetes, continue insulin and encourage breastfeeding. Oral antihyperglycemic agents may have an effect to breastfed baby hence should be avoided.
- 15. Do **diabetes education** (lifestyle change, diet counseling, smoking cessation) prior to discharge.
- 16. Encourage mothers to have tubal ligation as soon as she has sufficient children. Diabetics are more likely to have pregnancy complications and should be encouraged to limit their children to 2 or 3.
- 17. Repeat OGTT (75g glucose) after 6 weeks for GDM patient.

<u>If resources do not permit</u> the 4 times a day insulin regimen (regular insulin at each meal, and NPH insulin at bedtime), then premixed insulin (70/30 or 30/70 which is 30% regular or short acting insulin, and 70% NPH or intermediate acting insulin) can be started . for this, give $2/3^{rd}$ of the daily dose in the morning before breakfast, and $1/3^{rd}$ of the dose before dinner.

Note that patients usually require higher doses of insulin as the pregnancy progresses from 24 weeks to term.

Recommendation for Patients with Diabetes and Chronic Hypertension

Treatment:

- In pregnant patients with diabetes and chronic hypertension, blood pressure target goals of 110-129/65-79 mmHg are suggested in interest of long term maternal health and minimizing fetal growth
- ACE inhibitors (e.g. Enalapril), ARBs (e.g. Losartan) are contraindicated during pregnancy

DIABETES EDUCATION

Initial education should cover the implications of GDM for the mother and her baby, blood glucose monitoring, overview on diet and recommendations regarding exercise and the importance of postpartum follow-up. Women with GDM should also be provided with positive encouragement to minimize their emotional stress.

BLOOD GLUCOSE MONITORING

Once diagnosed with GDM, women need to monitor their BGL fasting (pre- breakfast) and 2 hour after meals timed from the beginning of the meals for the rest of the pregnancy.

Therefore **all women with GDM should be encouraged to purchase a blood glucose meter**. Meters can be purchased from Wellness Centre at below \$20 for the set. Blood glucose monitoring can also take place in the ante-natal clinic.

BGLs in pregnancy are approximately 20% lower than outside pregnancy therefore, women should be given the following BGL target ranges.

Fasting: 70 – 94 mg/dL 2 hour postprandial: 90 – 120 mg/dL At night: should not be < 70 mg/dL

HbA1c levels may provide additional information regarding the adequacy of the glycaemic control. In general, HbA1c should be measured at diagnosis and monthly thereafter.

HbA1c can be used to determine if DM pre-existed prior to pregnancy. It should be noted that HbA1c results are approximately 20% lower by mid pregnancy compared to outside pregnancy.

URINARY KETONES

Check urinary ketones, at least once per week (fasting), and in the following situations:

- FBS > 180mg/dL
- During illness
- If there are symptoms of nausea, vomiting, or abdominal plain (suspect ketoacidosis)
- If there are signs of **dehydration**

LABOUR AND DELIVERY

"Gestational Diabetes is not an indication for Caesarian Section"

Requirements for pregnancy to proceed to 40 weeks

- 1. Excellent metabolic control throughout pregnancy
- 2. Normal Antenatal Testing
- 3. No severe complications (e.g. pregnancy induced hypertension, growth retardation

INTRAPARTUM MANAGEMENT

- IV Fluid: D5 LRS at 100cc/hr
- <u>CBG monitoring every 1-4 hours</u>
- Target CBG: 70-120 mg/dL
- For CBG >120mg/dL
 - \circ Insulin infusion at 0.5 1 unit/hr OR
 - SC insulin 2-4 units/hr
 - Give subcutaneous regular insulin as needed. Maintain normoglycemia by giving <u>1</u> <u>unit sc for each 20 mg/dL increase in glucose above 120 mg/dL</u>

FOR PATIENTS UNDERGOING CAESAREAN SECTION

For patients who need to undergo caesarean section, please note: "Gestational Diabetes is not an indication for Caesarian Section".

- Procedure should be scheduled in the morning
- Give the last insulin dose subcutaneously the night before
- Do not give the morning maintenance insulin dose
- Measure RBS immediately prior to caesarean section
- Give regular insulin subcutaneously depending on RBS according to rule of 1 unit for each 20 mg/dL above 120 mg/dL

POSTPARTUM MANAGEMENT OF WOMEN WITH GDM

Women with GDM are at marked increase risk of future diabetes and should be advised regarding optimum lifestyle and appropriate follow-up. Some women will continue to have abnormal glucose tolerance in the early postpartum period.

Therefore, women should be advised to visit the clinic 6 weeks postpartum to undergo a repeat OGTT, and OGTT should be performed annually thereafter.

- Recheck FPG 24-48 hours postpartum, if result > 126mg/dL manage as Type 2
 DM
- Encourage breastfeeding
- Encourage achievement of ideal body weight
- Use of contraceptives may be appropriate
- Continue with self monitoring of blood glucose
- Counsel regarding complications in children born to mothers with preexisting
 - Increased frequency of obesity
 - Increased incidence of diabetes
- OGTT 6 weeks postpartum for GDM

8.0 FAMILY PLANNING IN DIABETES

8.1 Unintended Pregnancy and Increased Health Risk

Diabetes is a condition that might make pregnancy an unacceptable health risk. Thus longacting, highly effective contraceptive methods may be the best option to avoid unintended pregnancy. So the use of barrier methods and behaviour-related methods, due to higher rates of failure, should be discouraged.

Other conditions in the categorized as increasing risk for adverse health events as a result of pregnancy include the following:

- Diabetes: insulin dependent; with nephropathy, retinopathy, or neuropathy or other vascular disease; or of >20 years' duration
- Hypertension (systolic ≥160 mm Hg or diastolic ≥100 mm Hg)
- Ischemic heart disease & stroke
- Complicated valvular heart disease
- Cancers breast, endometrial or ovarian, liver
- Epilepsy
- Tuberculosis
- HIV: not clinically well or not receiving antiretroviral therapy
- Systemic lupus erythematosus



8.2 Effectiveness of family planning methods FIGURE. Effectiveness of family planning methods*

Sources: Adapted from World Health Organization (WHO) Department of Reproductive Health and Research, Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs (CCP). Knowledge for health project. Family planning: a global handbook for providers (2011 update). Baltimore, MD; Geneva, Switzerland: CCP and WHO; 2011; and Trussell J. Contraceptive failure in the United States. Contraception 2011;83:397–404.

9.0 TUBERCULOSIS SCREENING

9.1 The Association between TB and DM

Much evidence points out that **DM increases the risk of developing TB three-fold**, compared to non-diabetics. DM also has an adverse effect on TB outcomes. This is because immunological function is depressed in diabetes, and infections for which cell-mediated immunity has a pivotal role, such as tuberculosis, are more likely in uncontrolled diabetes.

Infections, including tuberculosis, usually worsen control of blood sugars and in turn poorly controlled DM can worsen the severity of infections. Some studies have suggested that TB can also cause DM in those not previously known to have diabetes. The drugs used to treat TB themselves may also worsen blood sugar control in patients with diabetes.

This highlights the need for vigilant screening for both diabetes and TB when one of the two is present.

In addition, there are several pharmacological issues to be considered:

- **Tuberculosis drug treatment affects diabetes treatment** Treatment with isoniazide can cause peripheral neuropathy
 - So pyridoxine should be given with isoniazide during TB treatment in patents with diabetes
- Treatment with rifampicin can cause hyperglycemia as it induces metabolising enzymes and accelerates drug metabolism – for instance, studies show that serum concentrations of glyburide and glipizide fall by 39% and 22% respectively, when given with rifampicin.
- **Diabetes can also alter the pharmacokinetics of TB drugs** diabetes can cause changes in oral absorption, decreased protein binding of drugs, and impaired drug clearance with renal insufficiency or fatty liver.

9.2 Standards for the management of Tuberculosis and DM in Marshall Islands

The United States Affiliated Pacific Islands (USAPI) through their membership with Pacific Islands Tuberculosis Controllers Association (PITCA) and Pacific Chronic Disease Coalition (PCDC) have developed a guideline document regarding the management of tuberculosis and diabetes, given their close association and the high prevalence of both diseases on the islands. This was initially put together in December 2010.

This document has since been revised, and in November 2015 the TB-DM Working group in Ebeye decided on the following working document to further guide practitioners in the care of both TB and DM in the Republic of the Marshall Islands.

Standards	Timeline	Responsible Person
Screening for DM in persons with TB		
 <u>Standard 1 : Every person with tuberculosis (TB) over</u> <u>the age of 18 should be screened for diabetes</u> <u>mellitus (DM)</u> 1.1 The diagnosis of DM may be made using one of the following criteria: Fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l), Random plasma glucose ≥ 200 mg/dl(11.1 mmol/l), Hemoglobin A1C ≥ 6.5 % (48 mmol/mol). 1.2 Abnormal glucose values should be verified in patients who have no symptoms of DM. 	Screening for DM done at diagnosis of TB. Abnormal glucose values can be verified by HbA1c test and referred to NCD Clinic within 1 week of diagnosis. Within 4 weeks of TB treatment, repeat screening for DM.	All admitted patients with TB will be screened by ward nurses. TB Physician to verify. All newly diagnosed patients must be referred to the NCD Clinic within 1 week of diagnosis. TB clinic will have glucometer and supply of
1.3 Rifampin can elevate blood glucose in TB patients. Glucose testing may be repeated after 2-4 weeks of TB treatment, or if symptoms of hyperglycemia develop during TB treatment.	DM Screening can be done earlier than 4 weeks of TB Rx if there are any symptoms.	strips. TB Clinic nurse will refer to TB Physician if values are abnormal.
Screening for TB in persons with DM		
 <u>Standard 2 : Every person with DM should be</u> <u>screened for TB disease and TB infection</u> 2.1 Persons with TB symptoms or TB disease should be referred to the local TB Program for TB management. 2.2 A test for TB infection should be done at the time of DM diagnosis. 	All patients should be asked about symptoms of TB using the interview form. All newly diagnosed DM should be evaluated for TB disease	TB Clinic staff comes to DM Clinic and arranges referral for symptom positive patients. If symptomatic request sputum. TB Clinic staff will use the interview form & order CXR and sputum if need be.
2.3 Screening should be repeated as often as the local TB epidemiology may warrant.	For those patients who are TB negative previously, repeat CXR every 2 years.	TB Program Manager to ensure adequate X-ray supplies. CDEMS Data person to generate list of all patients due for CXR on each NCD Clinic visit. NCD Clinic staff to order

		CXRs.
Standard 3 : Persons with DM and TB infection should be encouraged to take preventive therapy 3.1 Persons with DM are at increased risk of peripheral neuropathy. If INH is used for prevention, give B6 to prevent neuropathy (10 –25 mg/day). 3.2 Monitor for adherence and side effects of preventive treatment.	Only DM patients with no TB disease who are <u>close contacts of sputum</u> <u>TB positive or laryngeal</u> <u>TB should receive INH</u> Preventive Rx for 9 months. Do not do PPD test – assume that all patients with DM are high risk DOTS workers should check patients for side effects every day and if present, refer to TB Clinic manager who informs TB Physician.	TB Program Manager order INH and B6 to cover both TB patients and contacts of sputum positive or laryngeal TB cases. TB Clinic managers to send in timely request every quarterly. TB Clinic manager to oversee DOTS workers verification of adherence & side effects
Treating TB in Persons with DM		
Standard 4 : Clinicians may need to adjust TB treatment in persons with DM 4.1 Make sure that TB medications are properly dosed. Check creatinine for diabetic nephropathy, and if present, adjust the frequency of PZA and EMB according to ATS-CDC guidelines. Administer B6 to prevent INH-induced neuropathy (10 –25 mg/day).	Upon TB diagnosis, full workup should be done (if not already) including Creatinine; TB Physician to adjust dosages of PZA and EMB and gives B6- follow 2015 RMI National Guidelines	For outpatients, TB Clinic staff can order work up. For inpatients- TB Physician does work up TB Physician adjusts meds
4.2 Observe closely for TB treatment failure in persons with DM. Be aware of poor absorption of some TB meds in DM. Manage the many interactions between TB and DM meds. Some programs follow INH or RIF levels in persons with DM.	Rx duration in DM patients is 9 months (3 months of intensive and 6 months of continuation phase). Be aware of interaction of Rifampicin and Sulphonylureas. Retest sputum at 3 months of Rx - Consider MDR-TB if sputum is still positive. <i>Treatment</i> <i>failure if sputum is still</i> <i>positive after 5 months.</i>	TB Physician/ TB Clinic managers and DOTS workers are aware of difference in Rx for DM patients TB Clinic staff are responsible for arranging sputum collection. Refer to TB Physician if MDR- TB or treatment failure is suspected.

 4.3 "Assure the Cure" Consider extending treatment to 9 months for persons with DM, especially persons with cavitary disease or delayed sputum clearance. Upon completion of therapy, obtain sputum for AFB smear and culture. Evaluate at one year after treatment for evidence of relapse. 	Inpatient- Check sputum at 2 weeks and if positive then check weekly until negative. Patients cannot be discharged if they are sputum positive. In follow up- check sputum at 3 months (after intensive phase) and at the end of the continuation phase (in the 9 th month). Cure is assured if sputum for AFB smear and culture is negative after 3 months intensive phase (IP) and 6 months continuation phase (CP) of Rx. Do symptom screening interview, CXR and sputum check (culture & smear)	TB Clinic staff must order tests and document results for cure at the end of the IP and CP. TB Clinic staff and TB Physician must evaluate patients one year after they complete the full nine months of treatment.
Managing DM in persons with TB	smear)	
Standard 5 : Use TB clinic visits to help persons manage their DM 5.1 There should be a glucometer in every TB clinic for monitoring glucose. 5.2 TB patients with DM should have their glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if diabetes is controlled. Monthly glucose testing during treatment is recommended.	Agreed Weekly check of RBS for the first 4 weeks > Week 1 > Week 2 > Week 3 > Week 4 Then monthly check during treatment of TB > Month 2 > Month 3 > Month 4 > Month 5 > Month 5 > Month 6 > Month 7 > Month 8 > Month 9 At every TB clinic visit	Glucometer and strips to be in TB Clinic; TB Program manager to ensure adequate supplies. DOTS workers and refer to TB Physician for cases of uncontrolled diabetes during the Intensive phase. During the continuation phase, refer to NCD Team.

 5.3 All clinic staff should reinforce lifestyle changes at TB clinic visits. 5.4 If available, refer persons with DM to the Diabetes Clinic for diabetes care. Ensure DM clinician is aware of TB diagnosis and TB medications. 	During continuation phase of treatment, refer patient to NCD Team	TB Clinic staff – use ARC flipcharts and health promotional material TB Physician/ TB Clinic staff referral to NCD Team – use referral form
<u>Standard 6 : Use DOT visits to help persons manage</u> their DM		
6.1 DOT workers should encourage lifestyle changes at every encounter. DOT workers should use structured and culturally-appropriate diabetes educational materials.*Dietary changes and physical activity are the most important in this effort.	Every home visit and TB clinic visit should be an encounter to promote diet and exercise. Use the ARC flipcharts and health promotion material.	TB Program Manager to supervise DOTS workers and supply them with tools Need translated ARC flipcharts
6.2 Consider delivering DM meds with TB meds via DOT for persons with poorly-controlled DM who have non-adherence to diabetic medications.	DOT workers should be able to deliver refills of DM meds. For patients with poorly controlled DM, TB programme to include one NCD staff once a month to reinforce DM management.	DM med prescriptions to be written by TB Physician in the IP and by NCD Physician in the CP and adjusted based on DOT workers blood sugar monitoring.

10.0 CANCER SCREENING

10.1 The Association between Cancer and Diabetes

Current evidence shows that people with diabetes have a significantly higher risk for developing many forms of cancer. Thus all health care practitioners must encourage all their patients with diabetes to undergo the appropriate cancer screening as recommended by the guidelines below.

People with diabetes are at higher risk of developing the following cancers:

- Liver
- Pancreas
- Endometrium
- Colon and rectum
- Breast, and
- Bladder

However diabetes is associated with a decreased risk of prostate cancer. For other cancers, evidence of association is still inconclusive. Type 2 diabetes and cancer also share many of the same risk factors yet the biological link is not fully understood. The link between cancer and diabetes may be

hyperinsulinemia, hyperglycemia, and inflammation. The shared risk factors are aging, obesity, diet, and physical inactivity.

Thus there is a role for healthy diets, physical activity, and weight management as it can improve outcomes of diabetes, and reduce the risk of developing some forms of cancers.

Medications used to treat diabetes can also apparently affect cancer risk- early evidence points to metformin as reducing cancer risk, and that exogenous insulin is associated with increased cancer risk (evidence may be needed to prove that glargine insulin has a stronger cancer association as compared with other insulins). However as mentioned earlier, the evidence for this is still very limited and so the choice of therapy should not be based on cancer risk.

10.2	Cervical	Cancer	Screening	Guideline

Resource Levels	Services
Core	Screen with VIA (Visual Inspection with Acetic Acid) Screen women age <u>30-49 at least once in their lifetime with VIA</u> (WHO 2013 Minimum Screening)
Expanded	 Screen women between 30-49 with VIA at least every 5 years, but no more frequently than every 3 years (WHO 2013 Guidelines #4) Treat abnormal lesions (that are appropriate for cryotherapy*) in either single visit or two-step. → Follow-up VIA in 1 year
	*If lesion is not appropriate for cryotherapy (i.e., too large, overt cancer), refer for LEEP or surgical treatment
Desirable	Screen with Pap test Screen women age 21-65 with Pap test every 3 years (USPSTF 2013 Guidelines) OR HPV DNA testing (when available) every 5 years for women 30-60, followed by and treat with cryotherapy (or LEEP when not eligible for cryotherapy) (WHO 2013 Guidelines #8) OR Screen women age 30-65 with both Pap and HPV DNA testing (co- testing) every 5 years (USPSTF 2013 Guidelines)
Stop	No further screening for: Women age > 60 if no abnormal test in the preceding 10 years Women with total hysterectomy if indication for removal was not related to treatment of cervical dysplasia

10.2.1 What if the woman is >60 and never screened?

Unless the woman has a high likelihood of passing away within the next year*, then they should receive screening. *Requires discussion with a physician, family, goals of care discussion. Examples might include Symptomatic congestive heart failure despite treatment with available medicines, Stage 4 kidney disease, Presence of ascites (from any cause), Severe dementia (completely dependent for all ADLs), Bed ridden (from any cause), Disseminated TB resistant to treatment / unable to further treat

Resource Levels	Services
Core	Breast Health Awareness: education with breast self-examination (BSE) Monthly BSE beginning at age 20
	Clinical Breast Examination (CBE)
	Every year starting at age 20
	Target Outreach/education encouraging CBE for at-risk groups (with family history)
Expanded	Expanded education to women of reproductive age emphasizing community approach and including ultrasound and mammography
	Diagnostic Ultrasound
	Diagnostic Mammography
	Mammographic screening age 40-75, every 2 yrs.
Desirable	Population-based mammographic screening
	Age 40-75, every 2 yrs.

10.4 Breast Cancer Screening Guideline

10.5 Colorectal Cancer Screening Guidelines

Resource Levels	Services
Core	FOBT (standard) or FIT (fecal immunochemical testing), every 1-2
	years, age 50-75
	Education about risk factors (as well as preventative measures
	including food, activity) to insure high compliance
Expanded	FOBT (standard) or FIT (fecal immunochemical testing), every year,
•	age 50-75
	For those with risk factors begin screening at age 40
	Flexible Sigmoidoscopy every 5 years, with FOBT every year age 50-75
	Colonoscopy every 10 years, age 50-75
Desirable	Increased training of personnel to perform endoscopy

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12.0 ANNEXES

Annex 1

KEY INTERVENTION POINTS AND ASSOCIATED ACTION REQUIRED

KEY INTERVENTION POINTS	ACTION – KEY TASKS
No Diabetes*	Keep the healthy, healthy. Prevent the healthy population from developing risk factors.
	risk factor reduction strategies.
Pre-diabetes (At –risk people)	Reduce risk factors in the 'at risk' population* SNAP intervention to reduce risk factors. Support goal directed research into causes of and preventative interventions.
Undiagnosed Diabetes*	Active NCD Tool Kit Screening for people over 30 years of age. Provide avenues for opportunistic screening as well (workplaces, festivals, etc.) Increase public awareness of symptoms, risk factors and where people can go for screening.
KNOWN DIABETES	
• At Diagnosis	 Provide services for: Clinical care according to guidelines (DMG, IECs) Education in self –care & monitoring (PDRB) Information about recommendations for clinical care (personal targets for control)
 Established uncomplicated Diabetes 	 Provide services for: Routine monitoring of diabetic and general health status Regular screening for complications Management of problems as they arise Reinforcement of self-care education Affordable therapies and supplies. Implement programs for:
	 Identification and reduction of risks for diabetes complications Self –care education and psycho-social support Support goal directed research aimed at curing diabetes.
• Diabetes with complications	 Provide services for: Prevention of the progression of complications Self –care education and psycho-social support Rehabilitation of people with disabilities Palliation for people with end stage complications Support goal directed research aimed at the reversal of complications.

*Until modifiable risk factors are identifiable and effective interventions available, these interventions cannot be applied to Type 1 diabetes. Adapted from the Australian National Diabetes Strategy and Implementation Plan