CLINICAL PRACTICE GUIDELINES

Management of Diabetes Mellitus

List of Contributors

- Prof Chandrika Wijeyaratne
- Dr Noel Somasundaram
- Prof Upali Illangasekera
- Dr Henry Rajaratnam
- Prof Riffdy Mohideen
- Dr Mahen Wijesuriya
- Dr MK Ragunathan
- Prof Rezvi Sheriff
- Dr Sarath Gamini de Silva
- Dr Bandula Wijesiriwardene
- Prof Janaka De Silva
- Prof Mandika Wijeyaratne
- Dr Thilak Weeraratne
- Dr Gnani Somasundaram
- Dr Priyankara Jayewardana
- Dr DARK Dayaratne
- Dr Aruna Lowe
- Dr MM Nawaratne
- Dr Renuka Jayatissa

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1. Introduction

There is extensive evidence that management, mainly treatment to target of diabetes improves immediate and long term quality of life. However, management of diabetes continues to be substandard throughout Sri Lanka. This consensus guideline seeks to standardize optimal management of Type 2 diabetes in diverse resource settings.

2. List of Abbreviations

ACEI	Angiotensin Converting Enzyme Inhibitor
ACR	Albumin: creatinine ratio
ALT	Alanine aminotransferase
ARB	Angiotensin Receptor Blocker
AST	Aspartate aminotransferse
A1C	Hemoglobin A1C
BMI	Body Mass Index
B12	Vitamin B12
CCB	Calcium Channel Blocker
CK	Creatinine Kinase
CVD	Cardiovascular Disease
DKA	Diabetic Ketoacidosis
EGFR	Estimated glomerular filtration rate
ESRD	End Stage Renal Disease
FPG	Fasting Plasma Glucose
HHS	Hyperosmolar Hyperglycamic state
HDL	High Density Lipoprotein
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
LDL	Low Density Lipoprotein
MI	Myocardial Infarction
MRI	Magnetic Resonance Imaging
NAFLD	Non alcoholic Fatty liver disease
NPH	Neutral Protamine Hagedorn Insulin
OHA	Oral Hypoglycaemic Agent
OGTT	Oral Glucose Tolerance Test
PDE5	Phophodiesterase 5
PPG	Post prandial glucose 2hours after 75 glucose
PAD	Peripheral Arterial Disease
RPG	Random Plasma Glucose
SMBG	Self monitoring of glucose
TG	Triglyceride
TSH	Thyroid Stimulating Hormone
UTI	Urinary Tract Infection
WHO	World Health Organization

3. Diagnosis and Screening

The natural history of Type 2 diabetes includes an asymptomatic preclinical phase which is not benign and during which it can be diagnosed. Early treatment of Type 2 diabetes reduces morbidity from long term complications. Screening for and treating Type 2 diabetes at a preclinical stage therefore seems logical although, there is no evidence (from trials) that this benefits individuals.

3.1 The diagnosis of diabetes

Minimal Care (Grade X) and
Standard care (Grade Y)

Requires two positive laboratory blood tests on separate days unless the plasma glucose is unequivocally elevated in the presence of acute metabolic decompensation or obvious symptoms (polyuria, polydipsia, weight loss). In the case of high RBS in an asymptomatic individual confirms with FPG or OGTT. (Ib)

Table 1 - Cut off values

	VenousPlasma Glucose	Capillary blood Glucose
DiabetesMellitus:		
Fasting	≥ 7.0 mmol/l≥ 126 mg/dl	≥ 6.1 mmol/l≥ 110 mg/dl
2-hr post glucose load or random	≥ 11.1 mmol/l≥ 200 mg/dl	≥ 11.1 mmol/l≥ 200 mg/dl
Impaired Glucose Tolerance:		
2-hr post glucose load	7.8-11.1 mmol/l 140-200 mg/dl	7.8-11.1 mmol/l 140-200 mg/dl
Impaired Fasting Glucose:		
Fasting	5.6-7.0 mmol/ l100-126 mg/dl	5-6.1 mmol/l 90-110 mg/dl

- Use measurement of plasma glucose, preferably fasting. (Ib)
- Perform oral glucose tolerance test# (OGTT) if: (IIb)
  - FPG 5.6-7 mmol/l (100-125 mg/dl) or
  - RPG 5.6-11.1 mmol/l (100-200 mg/dl)

- Consider tests to classify type of diabetes (e.g. islet-cell related antibodies, C-peptide, genotyping) (III)

3.2 Screening for diabetes

Who should be screened?

- Use opportunistic screening (on adults over 35 years whenever there is an opportunity) (IV)
- Individuals under 35 years should be tested if they are at high risk of developing Type 2 diabetes (III). These risk factors are:
  - impaired glucose tolerance (IGT) or impaired fasting glucose (IFG)
  - first degree relatives with diabetes
  - inactive lifestyle or overweight (BMI ≥ 25)
  - metabolic syndrome
  - hypertension or dyslipidaemia
  - cardiovascular disease (myocardial infarction, angina or stroke) and PAD
  - polycystic ovary syndrome or previous gestational diabetes
  - history of having large babies(>3.5 Kg)

 # Using 75 grams of glucose after 8-12 hour fasting.

How to screen for diabetes?

- Use venous laboratory FPG (Fasting Plasma Glucose)* (IIa)
- Capillary glucose may be used when laboratory testing is not available (values are lower and the instrument should be validated) (III)
- Glycosuria may be used for screening, When there are classical symptoms and blood testing is not available (IV)

How often to test?

Periodic testing for undiagnosed Type 2 diabetes is recommended by measuring fasting plasma glucose according to the following schedule:

- Each year for people with IGT or IFG (III)
- Every 3 years for people at high risk with a negative screening blood test (III)

People with risk factors who have a negative screening test are at risk of cardiovascular disease and the future development of Type 2 diabetes, and should be given appropriate advice on risk factor reduction (IIa)

*** FPG- fasting for 8-12 hours**

4. Prevention of Diabetes

Preventing Type 2 diabetes would result in significant public health benefits, including lower rates of cardiovascular disease (CVD), renal failure, blindness and premature mortality.

- A healthy lifestyle (regular exercise and healthy diet) with maintenance of ideal body weight (III)
- Individuals with pre-diabetes (IFG or IGT) or at high risk should be counseled on weight loss and regular physical activity (Ib)
- Weight loss is recommended for all overweight (BMI > 23 kg/m2) and centrally obese (waist circumference > 85 cm for men and > 80 cm for women).(IIb)
- Follow-up counseling is important for success (II)
- Advise and treat other CVD risk factors (e.g., tobacco use, hypertension, dyslipidaemia) (Ia)
- Drug therapy may be considered, but lifestyle modification is more effective(Ib)

Standard care as same as minimal care

5. Psychological care

Diabetes mellitus is a psychologically and behaviourally demanding disease. Stress, inadequate social and family support, inability to adjust to problems and poor coping skills may have a negative impact on self-care and glycemic control. Myths or misconceptions may also influence self-care and control.

Communication

- Adopt a wider approach and highlight the person's central role in his/her care (IV)
- Be non judgmental respecting attitudes and beliefs (IV)

Assessment of Psychological Status

- Explore the social situation, attitudes, beliefs and worries (IV)
- Be alert to signs of cognitive, emotional, behavioural and social problems (IV)
- Refer to mental health specialist according to local availability (IV)

Counseling

- Counseling should be in the context of ongoing health education and care (IV)

Standard care as for minimal care in addition

- Refer to a mental health-care professional with a knowledge of diabetes when indicated (Ib)

For Comprehensive care, principles will be as for Standard care

- Assess well-being and psychological status (including cognitive dysfunction), by questioning or validated measures (e.g. WHO-5).
- A mental health professional could be included in the multidisciplinary diabetes care team (Ib)

6. Education

- Continuous structured patient education should be an integral part of the primary care management from the time of diagnosis(Ia)
- An appropriately skilled person should be in charge of education
- Consider use of available communication technologies (Eg: patient information leaflets, audiovisuals etc;)

Standard care would be as for *minimal care* and

- An appropriately trained multidisciplinary team (including a diabetes nurse or a trained doctor) to provide education in groups or individually
- Where desired, include a family member or a friend (IV)
- Use techniques of active learning adapted to personal choices and learning styles
- Ensure that education is accessible to all people with diabetes (make relevant to culture, ethnicity, language, psychosocial, and disability issues) (III)
- Consider education at a local community level

Comprehensive care would be as for Standard care but would also include

- The availability on demand of individualized advisory service on demand. (IV)

7. Nutrition Therapy

Nutrition therapy is an integral part of the treatment and patient self-management helps to improve quality of life, nutritional status and psychological health. A reduction in glycosylated hemoglobin (HbA1C) of 1 to 2% can be achieved with nutrition therapy alone.

- Offer basic nutrition guidelines (healthy food choices)
- Advice on energy reduction (carbohydrates, fat and alcohol as appropriate)
- If the patient requests, offer non-nutritive sweeteners. (non-nutritive sweeteners are safe when consumed in acceptable daily intake levels). (Ib)
- Advise to limit alcohol intake to a moderate amount. (One drink / day or less for women and two drinks or less/day for men (one drink = 360ml beer, 150 ml wine, 45 ml distilled sprits)

- At the time of diagnosis, provide access to a dietitian or a nurse trained in principles of nutrition.
- Educate about,
  - the effect of the amount and type of carbohydrate on blood glucose
  - self monitoring of intake of total grams of carbohydrate or portions (by exchange or carbohydrate counting) (Ia)
  - use of glycemic index/ glycemic load (IIb)

- Offer individualized dietary advice by a nutritionist (One initial consultation. Two or three follow up sessions). Counseling and assessment annually or more often (III)

Table 2 - Dietary Recommendations

Total Carbohydrate

- Whole-grain cereals, vegetables, legumes and fruits as the appropriate sources of carbohydrate to form 45%- 60% of total energy (Ia)
- Carbohydrate rich, low glycemic- index foods are suitable as carbohydrate rich choices(Ia)

Dietary Protein

- Protein to contribute 10-20% of total energy(III)
- Replace red meat with chicken, fish or vegetable protein (III)
- Restriction of protein intake to 0.6 – 0.8 g / kg /day is recommended for nephropathy in diabetes (Ia) (Typical Sri Lankan diet contains approximately this quantity of protein)

Dietary Fat

- If LDL is high, reduce saturated fatty acids and trans- unsaturated fatty acids below 10% of total energy
- Total fat content should not exceed 30% of total energy (Ia)
- Regular consumption (at least twice weekly) of fish (preferably oily) and plant sources of n-3 fatty acids (e.g. Soya bean oil, nuts and some green vegetables)(IIa)
- Restrict dietary cholesterol to 300 mg or less per day (Ia)

Dietary fiber

- Naturally occurring foods that are rich in dietary fiber are strongly recommended, with a total dietary fiber intake of 40 g/day or more(Ib)
- Half of total dietary fiber should be soluble (Ib)

Free sugar

- Food items containing up to 50 g of free sugar per day may be allowed, if desired, provided glycaemic control is acceptable and the person is not overweight(Ia)

Sodium

- Restrict salt to 6g/day, with the possibility of further restriction for those with elevated blood pressure(Ia)

Antioxidants

- Encourage food rich in antioxidants, trace elements and other vitamins (range of vegetables and fruits, whole- grain cereals, and oily fish).
- There is no convincing evidence for the benefit of dietary supplements (IV)

Energy balance and body weight

- Reduce energy intake and increase energy expenditure among those who are overweight. Prevent weight gain once weight loss has been achieved (Ia)
- Maintain the BMI within 18.5 – 23 kg/ m2 (Ia)

8. Exercise

- Encourage regular physical activity (Ia)
- Advise simple ways of increasing physical activity in day-to-day life (III)
- Encourage gradual increase in duration and frequency of physical activity (Ib)
- Physical activity should be distributed over at least 5 days/week of 30 -45 min a day and with no more than 2 consecutive days with out physical activity (Ia)
- Target at least 5 sessions of minimum of 30 minutes of moderate intensity aerobic physical activity per week (eg: brisk walking) targeting all muscle groups (Ib)
- Greater activity levels of at least one hour/day of moderate activity (walking) or 30 min/day of vigorous activity (jogging) may be needed to achieve long term weight loss in the obese (Ib)
- Advice on adjusting medications (insulin) and / or adding carbohydrate for physical activity (IIa)

Standard care as for minimal care

Advice on exercise will be as for standard care.

- Exercise testing to be made available for those considering exercise programmes (IV)

9. Management of Obesity in Diabetes

About 80 to 90% of persons with type 2 diabetes mellitus are overweight or obese. Weight loss improves glycemic control, and all cause mortality, particularly cardiovascular disease.

Minimal Care (Grade X) and

Standard Care (Grade Y)

- Implement lifestyle modification, including regular physical activity and calorie reduction (Ia)
- A weight-loss goal of 5 to 10% of initial body weight over a 6-month period should be recommended (Ib)
- Energy deficit of approximately 500 kcal/day is recommended, to achieve weight loss of 1 to 2 kg/month (Ib)

Comprehensive Care, as for standard care in addition

- An organized programme for those who are obese is desirable.(Ia)
- Orlistat or sibutramine may be considered as adjuncts.(Ib)
- Bariatric surgery may be considered for individuals with class III obesity (BMI ≥40 kg/m2) or class II obesity (BMI≥35.0 to 39.9 kg/m2) with co morbidities who are unable to achieve weight-loss with lifestyle intervention.(Ib)

10. Monitoring of Glycaemic Control

There is compelling evidence that long-term complications of diabetes mellitus can be reduced by tight glycemic control. (Ia)

Table 3 - Glucose control targets

	HbA1C*(%)	FPG/ premeal PG	2-hour postprandial PG
Target	≤6.5	4.0-6.0 mmol/L (70-110 mg/dl)	5.0-8.0 mmol/ L(80-145 mg/dl)
Capillary BG		3.5-5.5 mmo/L (60-100 mg/dl)	4.0-7.2 mmol/L (70-130 mg/dl)

* UKPDS-aligned HbA1C below 6.5 %, appropriate targets to be set for other techniques

- Any improvement is beneficial in people whose targets cannot be reached. (Ib)
- In people with physical or mental impairment, the targets may be raised (when the risk of hypoglycaemia high). (III)

- The care may need to be based on measurement of plasma or capillary (visually read or meter) glucose levels alone (IV)
- The tests should be done at least once in 2 weeks (IV)
- FPG and 2hr PPG should be monitored fortnightly until glycaemic control is achieved. Thereafter, monitor monthly with FPG and PPG. (if only one measurement can be done, do PPG after the main meal) if the patient is on insulin measure blood glucose twice a week. (III)
- Site-of-care capillary blood glucose meters should be quality controlled (IIa)
- Encourage self-monitoring of blood glucose (SMBG) for those on insulin therapy (IIa)

- Perform A1C every 3 months until control is achieved and every 6 months once stabilized (Ib)
- Use fructosamine level when A1C is invalidated by haemoglobinopathy or abnormal haemoglobin turnover (Ib)
- SMBG (using strips or meter) should be encouraged whenever possible
    - for all newly diagnosed with diabetes (III)
    - for all on insulin (IIa)
- SMBG (using strips or meter) should be considered for people using oral agents (III)
- Assessment of self-monitoring skills should be made annually.(IV)

Comprehensive care, as for Standard care, it may be possible to devote more resources to achieving lower target levels.

- Perform frequent glucose monitoring in people with persistent glucose control problems, or with problems of A1C estimation (IV)

11. Glucose Control: Oral Therapy

- Begin oral glucose-lowering drugs when glycaemic control is not achieved by lifestyle interventions alone (Ia)
- The first line options are
  - Metformin start at small dose (titrate dose to minimize gastro-intestinal intolerance) (Ia)
  - Sulfonylureas (when BMI <23 kg/m2)(Ia)
- Step up doses, and add other oral glucose-lowering drugs, until blood glucose is at target levels (Ia)
- The second line options are
  - Metformin or Sulfonylurea(Ia)
  - Glitazone (thiazolidinedione) adding it to:
- metformin or sulfonylurea or (Ib)
- combination of metformin and sulfonylurea(Ib)
  - a-glucosidase inhibitors (Ib)
- Consider insulin early if rate of deterioration is rapid (Iv)

Standard care as for minimal care

- Rapid-acting insulin secretagogues may be used (as an alternative to sulfonylureas) in people with flexible lifestyles(III)

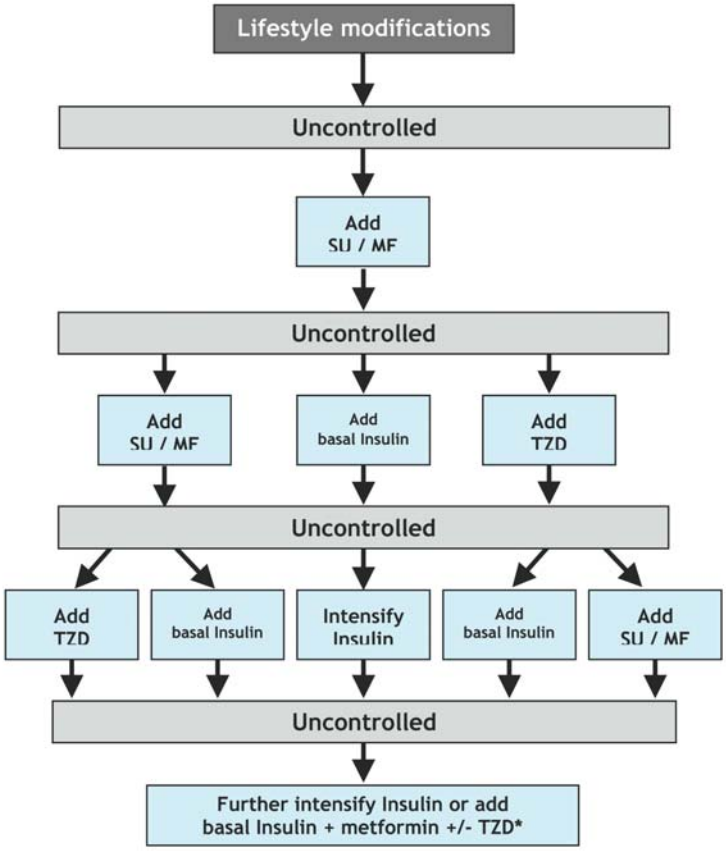
Comprehensive care as for Standard care

Table 4 - Oral Hypoglycaemic Drugs used in the treatment of Type 2 Diabetes Mellitus

Drug	Dose range	Indications	Contraindications / Caution	Common adverse effects
Biguanides Metformin	500- 3000 mg in 2-3 divided doses. Start at low dose with meals.	· First choice in obese or in insulin resistance. · Add-on therapy to SU if failing. · With insulin as insulin sparing / sensitizing agent.	Renal impairment (Creatinine > 1.5 mmol / l).Severe heart failure.Liver failure.	Diarrhoea, Dyspepsia, Bloating
Sulphonylurea Gliclazide Glimepiride Gibenclamide Tolbutamide Glipizide	40 - 320 mg in 1-3 divided doses. 1-6 mg once daily 2.5-20 mg in 1-2 divided doses. 500-3000 mg in 2-3 divided doses. 2.5-20 mg in divided doses	· First line in non obese. · Second line in obese after metformin. · (Note : Glimepiride, gliclazide cause less weight gain)	Renal failure.Poor oral intake.	Hypoglycemia
Glitazones Rosiglitazone Pioglitazone	4-8 mg once daily 15-30 mg once daily	· Non obese, add to SU / metformin. · Can be used as monotherapy in normal BMI, centrally obese. · Obese- second line after metformin. · Triple therapy after SU and metformin.	Liver disease.Heart disease (Grade iii / iv cardiac failure). Caution with insulin therapy.	Weight gain, Oedema, Worsening of cardiac failure, GI symptoms, Monitor LFT 2
		· Obese - second line after metformin. · Triple therapy after SU and metformin.		monthly in first 6 months and then yearly
α-glucosidase inhibitors Acarbose	150-300 mg in divided doses with meals	· Third line after metformin and SU. · Rarely well tolerated.		Diarrhoea, Abdominal bloating
Meglitanides Repaglinide Nateglinide	0.5-4 mg with each meal 60-180 mg with each meal	· Taken with meals - no meals, no tablet. · Control post prandial hyperglycemia.· Less weight gain in obese		Hypoglycemia

The following are generally indications for insulin at the time of diagnosis

- Type 1 Diabetes mellitus
- Diabetic ketoacidosis/Hypersomolar state
- Acute illnesses / infections
- Sever Symptoms
- Very high glucose valves (generally more than 250mg/dc)



Key : SU = sulphonylurea; TZD = thiazolidinedione
* TZD with insulin is off-label in most countries

Figure 1 - Algorithm for management of hyperglycaemia in type 2 diabetes. If HbA1C >= 7% or FPG>110 NYLDL (uncontrolled) move promptly to next level of therapy

Note : Lifestyle modification alone in asymptomatic only. OHA or insulin may be required in those symptomatic.

12. Glucose Control: Insulin Therapy

- Begin insulin when maximal OHA and lifestyle interventions are unable to achieve glycemic control (before poor control develops -when A1C has deteriorated to >7.5 %)(Ib)
- Initiation may be as a basal dose of 0.1 /units/Kg of body weight/day of long or intermediate acting insulin (IIa)
- Consider every initiation or dose increase of insulin as a trial, monitoring the response(IIa)
- Provide education, on lifestyle and self-monitoring
- Continue metformin. (IIa)
- Sulfonylureas can be continued when starting basal insulin therapy (Ia)
- Alpha-Glucosidase inhibitors may also be continued (Ia)
- Use of glitazones with insulin may worsen heart failure and should be under close clinical supervision (IIa)
- Use:
  - a basal insulin once daily such as detemir, glargine, or NPH(isophane) insulin or (IIa)
  - twice daily premix insulin (alternately mix soluble and NPH insulin prior to injection) (IIa)
- Teach self-titration (dose increases of 2 units every 3 days)(IIa)
- Aim for pre-breakfast and pre-dinner glucose levels of <6.0 mmol/l (<110 mg/dl); where these are not achievable monitor at other times to identify the glucose profile (Ia)
- Encourage subcutaneous insulin injection into the abdominal area (most rapid absorption eg. Rapid acting insulin) or thigh (slowest eg. Long acting insulin), with the gluteal area or the arm as other possible injection sites. (IIa)
- If the patient cannot self administer, teach a care giver (III)

Standard care, as for minimal care

- Provide health-care professional support by telephone until target levels are achieved (IIb)
- Consider multiple daily injections (meal-time bolus and basal insulin) where blood glucose control is sub-optimal , or meal-time flexibility is desired (Ia)
- Consider pen-injectors (prefilled or re-usable) or syringes/vials (IIa)

Comprehensive care, as for Standard care.

- Insulin analogues may be considered as alternatives. (Ia)
- Insulin pump therapy may be an additional option.(III)

13. Cardiovascular risk protection

Approximately 80% of all diabetics die of cardiovascular disease (CVD). Aggressive management of cardiovascular risk factors should take priority in the management of patients with diabetes. (Ia)

Assessment of CVD in diabetes.

- Assess CVD risk at diagnosis and annually thereafter
  - The following are high risk factors for CVD: Age > 40 years, smoking, hypertension, peripheral arterial disease (PAD), family history of CVD, obese, postmenopausal, microalbuminuria (Ia)
  - Check blood pressure, BMI, waist circumference, and peripheral pulses in feet (IIa)
  - 12 lead ECG, and Lipid profile†(IIa)(at least total cholesterol level. If cholesterol cannot be measured consider treatment with a Statin)(IIb)

Lifestyle and therapeutic risk protection
Non pharmacological measures

Reduction of dietary saturated fat and salt, regular physical activity and maintenance of ideal body weight are effective in reducing the CVD risk.(Ia)

Management of abnormal lipids.

- Those with CVD, or at high risk:
  - Should be started on pharmacological therapy (Ia)
  - A lower target of LDL<70 mg/dl (<1.8 mmol/l) is recommended (Ib)
- For those without CVD:
  - LDL target of <100 mg/dl is recommended (Ia)
  - For those over 40 years consider a statin if total cholesterol is >135 (to lower LDL despite initial LDL)(Ib)
  - In those under 40 years a 3 month trial of non pharmacological measures may be tried first.(Ia)

† 10-12 hour fasting sample

Table 5

Lipid fraction	Goal (mg/dl)	Therapeutic interventionIn order of priority
LDL	100	Statin
TG	150	Glycemic controlfibrate
HDL	50 for females & 40 for males	Lifestyle measures Nicotinic acid

Monitoring of Lipid lowering therapy

- Review lipids in 2-3 months for increase of dose of statin or addition of ezetimibe (Ib)
- Combination of statin and fibrate may be used for combined dyslipidaemia (IIa)
- Creatinine kinase (CK) should be checked if there is myalgia. Statin should be withheld if there is 10 fold increase of CK or 3 fold rise in ALT.(III)
- If lipid levels do not normalize with treatment, screen for alcohol abuse, and sub clinical hypothyroidism.
- Once target lipids are achieved life long therapy is necessary with periodic monitoring of lipid profile (twice a year) (III)

Antiplatelet therapy

- Aspirin (75-325mg daily) is recommended for
  - Secondary prevention, in all with CVD(Ia)
  - Primary prevention, in those who have an additional risk for CVD(Ia)
- Combine aspirin with clopidogrel in severe and progressive CVD (IIb)
- Aspirin is not recommended for patients under the age of 20 years because of its association with Raye's syndrome (IIb)

Smoking cessation

- Advise all with diabetes to stop smoking.(Ia)
- Arrange smoking cessation counseling and alternative therapies (e.g. nicotine patches)(IIb)

Referral for stress testing

Stress testing should be arranged for diabetic individuals with

- typical or atypical cardiac symptoms.(IIb)
- abnormal resting ECG(Ia)
- history of peripheral or carotid occlusive arterial disease (Ib)
- before starting a vigorous exercise program (IIb)

Management in special situations

- Add beta blockers (unless contraindicated) for patients with prior myocardial infarction.(Ib)
- ACE inhibitors for those (even without hypertension) at high risk of CVD(Ia)

Standard Care, as for minimal care, with more aggressive investigation of asymptomatic PVD, coronary artery disease (CAD), and carotid disease. (IIb)

Lipid profiles may be investigated more extensively to give better direct assessments of LDL cholesterol and apolipoproteins. (III)

14. Management of Hypertension in Diabetes

Hypertension contributes to the leading causes of morbidity and mortality in diabetes, including CAD, stroke, PVD, amputations and end-stage renal disease. Control of hypertension results in reduction of these complications (Ia) Cut-off values for hypertension in a patient with diabetes is lower than for a non diabetic and is set at 130/80mm Hg (Ib)

Screening and confirmation

- Measure Blood Pressure (BP) at all clinic visits.(Ib)
- If BP > 130/80mmHg recheck and confirm hypertension on a separate occasion.(Ib)

Goal

- Patients with diabetes should be treated to achieve a Systolic BP <130 and diastolic BP <80mmHg (Ia)

Treatment
SBP 130 - 139 mm Hg and DBP 80 - 89mmHg.

- Provide lifestyle and behavioural therapy for a maximum of 3 months.(Ib)
- If BP of < 130/80mmHg is not achieved commence antihypertensive therapy (Ib)

BP > 140/90mmHg

- Confirm blood pressure within 4 weeks and initiate antihypertensive therapy in addition to lifestyle measures (Ib)
- Measure blood pressure at each clinic visit(Ib)

BP > 160/100mmHg

- Initiate antihypertensive therapy immediately in addition to lifestyle advice.(IIa)

Lifestyle measures to reduce blood pressure
These include dietary sodium restriction, weight reduction in overweight and obese, aerobic exercise, and reducing alcohol consumption. (Ia)

Antihypertensive drug treatment

- Angiotensin Converting Enzyme Inhibitors (ACEIs), Angiotensin Receptor Blockers (ARBs), Thiazide diuretics, Calcium Channel Blockers (CCBs), and Beta blockers are shown to lower cardiovascular events and improve long term outcomes (Ib)
- The choice of antihypertensive agent depend on the co-morbid conditions (Ia)
- In the absence of microalbuminuria diuretics and beta-blocker can be used as first line therapy (Ia)
- In the presence of microalbuminuria
  - in Type 1 diabetes, ACEIs are recommended(Ib)
  - in Type 2 diabetes , ACEIs or ARBs are recommended (Ib)
- Multiple antihypertensives are usually required for adequate control(Ib)
- Look for a secondary cause when BP cannot be controlled with 4 or more antihypertensive agents (referral to a specialist center may be needed) (Ib)
- Where symptomatic, check for postural hypotension (IIb)
- Antihypertensive therapy is very often life long (IIb)

15. Nephropathy

Diabetic nephropathy occurs in 20–40% diabetics and is the leading cause of end-stage renal disease (ESRD). The purpose of screening for nephropathy is to delay or prevent loss of renal function by early detection and treatment.(IIa)

Screening

- Check annually for proteinuria (IIa) (in an early morning or random sample) using sulfasalicylic acid method (urine ward test) or dipstick
  - If test positive
    - Exclude urinary tract infection (UTI)
    - Once UTI is excluded repeat on two occasions over the following 3 months (proteinuria is confirmed if positive on 2 of 3 occasions)
  - If test negative
    - obtain a laboratory microalbumin: creatinine ratio (ACR)
    - test annually
- In the event where ACR cannot be tested a 24 hour urine protein excretion may be used. If neither is possible consider treating as for microalbuminuria using ACE inhibitors (Iv)
- Proteinuria can occur after major exercise, fever, UTI, congestive heart failure, acute severe elevations of blood pressure or blood glucose, or by menstruation. Screening for microalbuminuria should be delayed in the presence of these conditions.(IIa)

Manangement

- Advise to avoid risk factors (analgesic use, alcohol consumption, illicit drug use), to limit protein intake (to 0.8 g/Kg daily –typical Sri Lankan diet is about this quantity and restriction is not required in most).(IIb)

- Aim for Blood Pressure <130/75 mmHg using ACE inhibitors (maximum tolerable dose) and non hydropyridine calcium channel blockers and other agents (beta blockers, thiazides) if required(IIa)
- Aim for tight glycaemic control(Ia)
- Aim to improve lipid profile (Ia)
- Intensify cardiovascular protection (aspirin, smoking cessation)(Ia)
- Check proteinuric status/progression annually(IIb)
- Measure serum creatinine to calculate glomerular filtration rate (estimated GFR) or urea every 6 months (IIb)

$$\text{Estimated GFR} = \frac{\text{(140-Age (years) x Weight (kg)}}{\text{Serum Creatinine (µmol/l) x 72}}$$

Possible indicators of non diabetic causes of renal disease:

- Lack of retinopathy or neuropathy
- Persistent hematuria (microscopic or macroscopic)
- Signs or symptoms of systemic disease
- Rapidly rising creatinine
- High creatinine with little or no proteinuria
- Family history of nondiabetic renal disease (e.g. polycystic kidney disease, Alport syndrome)
- Short duration of diabetes
- Obstructive uropathy

- Exclude Iron deficiency periodically and treat anaemia with haematinics. Consider renal referral if still anaemic despite supplements (IIb)
- Consider Referral to a nephrologist when eGFR <60ml/min/1.73 m2 or earlier if symptomatic or biochemical problems occur (III)

Comprehensive care is in general as for Standard care

16. Retinopathy

Blindness is one of the most feared complications of diabetes with an incidence of 50-65 per 100,000 diabetic population per year. However, with good care, visual impairment can be avoided for the vast majority of patients.(IIb)

- Maintain good blood glucose and BP control (Ib)
- Refer for specialist opinion if cataracts are interfering with vision or the retina is obscured (IIb)

Screening

- Examine the eyes of at diagnosis and at least annually thereafter (including those registered blind and partially sighted).(III)
- In Type 1 diabetes screening should begin at 12 years of age (IIa)

Method of screening

- An ophthalmoscope is adequate. Use tropicamide (for mydriasis) unless contraindicated.(IIb)
- Diagnose and classify retinopathy. (IIa)

Indication for referral to an ophthalmologist

Same Day
- sudden loss of vision
- evidence of retinal detachment

Within 1 Week
- new vessel formation
- evidence of preretinal and/or vitreous haemorrhage
- rubeosis iridis

Within 1 month
- reduction in visual acuity(without evidence of above)
- hard exudates within 1 disc diameter of the fovea
- maculaoedema
- unexplained retinal findings
- pre-proliferative or more advanced (severe) retinopathy

Use retinal photography (performed and evaluated by trained personnel) or slit-lamp indirect ophthalmoscopy (Ib)

Retinal screening will be as for Standard care in most respects.

17. Foot Care

- Examine feet annually, checking
  - history of previous foot ulceration or amputation, symptoms of peripheral arterial disease, physical or visual difficulty in self-foot-care (IIa)
  - foot deformity (hammer or clawed toes, bone prominences) and footwear; features of neuropathy (dry skin, callus, dilated veins) or incipient ischaemia; nail deformity or damage (IIa)
  - detection of neuropathy by 10-g monofilament (or 128-Hz tuning fork), non-traumatic pin-prick (IIa)
  - palpation of foot pulses (dorsalis pedis and posterior tibial) and capillary return time (IIa)
- Provide foot-care education.(Ib)
- Advise a foot-care plan based on the findings.(IIb)
- Classify according to findings and manage accordingly:

Category	Criteria	Management
No Added Risk	Normal	Annual Screening, Foot Education
At Risk	Neuropathy or other single risk factor	Atleast 6 monthly review (examine feet, evaluate and arrange for foot wear)
High Risk	Diminished sensation plus foot deformities or evidence of PAD	3- 6 monthly review (examine feet, evaluate and arrange for foot wear, consider vascular referral)
Very High Risk	Previous ulceration or amputation	

- In Foot ulceration or infection: refer for specialist management.

- Sensory assessment with biothesiometer is an option (cut-off point for ulcer risk >25 volts) (IIa)
- Doppler ankle brachial pressure ratio (<0.9 for occlusive vascular disease) may be used.(IIa)
- A specialist foot-care team will include doctors with a special interest in diabetes foot care, people with educational skills, and people with formal training in foot care (usually podiatrists or trained nurses).(IIa)
- All patients with ulcers to be evaluated by a foot care team for (IIa)
  - appropriate wound management, dressings and debridement as indicated
  - consideration of systemic antibiotics for cellulitis or bone infection
  - optimal pressure distribution (casting)
  - treating vascular insufficiency
  - management of osteomyelitis
  - optimal blood glucose control
  - specialist footwear and orthotic care (e.g. insoles)
  - individualized discussion of prevention of recurrence
- Do not amputate unless:
  - a detailed vascular evaluation has been made (Ib)
  - ischaemic rest pain cannot be managed by analgesia or revascularization (Ib)
  - a life-threatening foot infection cannot be treated by other measures (Ib)

Comprehensive care is in general this will be as Standard care,

- but the foot-care team can would include vascular surgeons, orthopaedic surgeons, orthotists, social workers, and psychologists (III)
- Foot pressure distribution measurements, vascular scanning and angiography could be available to the foot-care team (III)

18. Neuropathy

- Screen annually by history of symptoms, sensory assessment by 10-g monofilament, tuning fork, non-traumatic pin-prick, and ankle reflexes
- Manage symptomatic (painful) diabetic neuropathy by,
  - excluding other causes,
  - stabilizing glycaemic control(IIb)
  - treatment with tricyclic drugs if simple analgesia is not successful(IIa)
- Assess erectile dysfunction by history and examination.
  - Consider contributions of other medication or disease
  - Give a trial of a PDE5 inhibitor (where not contra-indicated by nitrate therapy).(Ib)
- Diagnose gastroparesis by history, trial of a prokinetic drug (Metoclopramide, domperidone), and if troublesome refer for gastric emptying studies. (III)

- Check B12,TSH, creatinine, and take drug history to exclude other causes of peripheral neuropathy(III)
- Further treatment options include pregabalin / gabapentin and valproate, then tramadol (IIb)
- In erectile dysfunction exclude drugs and endocrine conditions (check prolactin and testosterone), and
  - Consider intra-urethral or intracavernosal drugs and sexual counseling, where PDE5 inhibitors fail or cannot be used.(IIa)
- Diagnose autonomic neuropathy by resting heart rate and heart rate response to provocation tests (lying-standing, Valsalva, deep breathing), and by lying and standing blood pressure. (IIb)
  - Advise anaesthetists when relevant where this is present.

Comprehensive care would be as for Standard care, but screening and diagnostic testing could also include a programme of quantitative sensory testing (vibration and temperature), electrophysiology, and autonomic function tests (III)

19. Diabetes Care in the Hospital

- Monitor blood glucose in known diabetic patients irrespective of the cause of admission. Urine sugar testing has limitations and is discouraged (Iv)
- All patients with a history of diabetes should be specially identified and labeled (Iv)
- Encourage self-management of diabetes (food choice, self-monitoring, insulin dose adjustment where appropriate) in usual ward care (III)
- Maintain near-normoglycaemia without hypoglycaemia during ward stay and procedures (IIb)

Table 6 - Goals for blood glucose levels

	Blood Glucose		
	Pre-prandial	Maximum random	Average
Patients in general wards	≤110mg/dl	≤180mg/dl	
Critically ill patients in intensive Care units		≤130mg/dl	≤110mg/dl

- In the absence of a dietician/nutritionist, provide dietary advice by a (trained) member of the health care team (III)
- Develop education plan and follow up (IIb)
- Document and arrange for follow up testing in those with hyperglycemia in the hospital (without a diagnosis of diabetes) (III)
- All patients with suspected Diabetic ketoacidosis (DKA) and Hyperosmolar (HHS) should be referred to a facility with intensive care. Intramuscular insulin may be used till transfer(IIa)

Standard Care, as for minimal care and with the following recommendations

- Services of a dietician / nutritionist should be incorporated in the patient management (IIa)
- Use of "Sliding Scale" insulin alone is discouraged as it results in unacceptably high rates of hyperglycemia, hypoglycemia and iatrogenic diabetic ketoacidosis.(IIb)
- The following 2 methods are recommended:
  - Continuous IV insulin infusions (IIa)
  - Subcutaneous doses of long-acting insulin for basal coverage, preprandial doses of rapid-acting insulin for prandial coverage & correction doses when the blood glucose concentration exceeds goal levels (IIa)
- Use a suitable protocol for blood glucose management in critical care units, in-patient procedures and surgical operations. An example of such protocol is given in the annexure (IIb)

Table 7 - Insulin infusion protocol

Blood Glucose (mg/dl)	Insulin infusion (Unit/Hr)			
	A1	A2	A3	A4
<60 Hypoglycemia				
< 70	0	0	0	0
70-109	0.2	0.5	1	1.5
110-119	0.5	1	2	3
120-149	1	1.5	3	5
150-179	1.5	2	4	7
180-209	2	3	5	9
210-239	2	4	6	12
240-269	3	5	8	16
270-299	3	6	10	20
300-329	4	7	12	24
330-359	4	8	14	28
> 360	6	12	16	28

(A = Algorithm)

Note :

- Move up to the next higher algorithm if the Blood Glucose is above the goal & does not change by at least 60 mg/dL within 1hr
- Move down an algorithm when Blood Glucose is < 70mg/dL twice

Comprehensive Care as for standard care and with the following recommendations.

- Infusion pumps should be used for delivery of insulin in patients requiring intravenous insulin. (IIa)
- All patients with DKA & HHS should be treated at intensive care facility. (IIb)
- Monitoring of blood sugar in patients undergoing IV insulin infusion should be done hourly until the patient has stable blood glucose.(IIb)

20. Diabetes Complicating Pregnancy

Close liaison between the field staff at primary antenatal care and those involved in diabetes, obstetric and neonatal care will help to achieve the desired outcome of a healthy mother and baby

Pre-pregnancy counseling

- All women between 15 and 45 should be regularly advised to have planned pregnancies to avoid problems
- Annually, discuss plans for pregnancy and re-enforce contraceptive advice (IIb)
- Pregnancy is best avoided in advanced ischemic heart disease and / or renal disease. Refer to a specialist if pregnancy is desired (IIb)
- Offer pre-pregnancy advice as appropriate:
  - Educate on intensive glucose management (usually with insulin)
  - Optimize glycemic control (pre-conception target A1C <6.0%)
  - Stop OHA and start insulin where appropriate
  - Optimize BP control (<130/80mmHg)
  - Stop ACEI and ARB drugs (convert to methyldopa, nifedipine SR)
  - Stop statins and fibrates
  - Assess and manage eye and kidney problems
  - Assess thyroid function
  - Advice to stop alcohol and smoking (III)
  - Start Folic acid

Screening for undiagnosed or new (gestational) DM in pregnancy

In women with any of the high risk factors for GDM mentioned below:

- give healthy life style advice at antenatal booking
- check a 2h PPG after a standard meal at antenatal booking

- If 2h PPG> 130 mg/dl proceed at once to an oral 75g OGTT*
- If 2h PPG < 130 with one risk factor proceed (III) to 75g OGTT* between 24-28 weeks

Risk factors

- Maternal age > 35 years
- Maternal BMI > 25kg/m2 (generally maternal weight at booking > 65 kg)
- Previous obstetric history suggestive of GDM (birth weight > 3.5kg, late abortion, IUD, recurrent PIH)
- Maternal candidiasis / recurrent UTI
- Polycystic ovary syndrome
- First degree relative with T2DM
- Current pregnancy with fetal macrosomia or polyhydramniosis

Management during pregnancy

- Reinforce education (including complications and management, medical nutrition therapy and exercise)
- Examine eyes at 1st pre-natal visit and each trimester
- Refer all women with GDM for specialist care

Post Partum management

- Encourage breast feeding
- Two months after delivery check 2hr PPG or if possible OGTT
- Advice on future high risk of diabetes and start preventive life style measures even if non-diabetic
- Advice check for DM annually
- Re-enforce the need for pre-pregnancy counseling
- Any form of reliable contraception can be advised (IIb) (including hormonal contraception)

* Abnormal OGTT FPG > 85 mg/dl; 2h PPG>130 mg/dl When 2hBG >160mg/dl – most likely to require insulin (III)

Standard Care (Grade Y)

- Arrange 7 point blood sugar series (BSS) (office-based or home-based self monitoring) and review frequently (target: pre-meal < 90 mg/dl and 2h postmeal <120 mg/dl) (IIb)
- Aim at good glycaemic control by regular review of BSS and adjust insulin therapy appropriately; for those requiring insulin review every 2 weeks
- Manage insulin therapy (address the type of insulin preferably given) by self-injection and through careful and intensive self-monitoring and dose adjustment.
- Expect a rise in insulin requirements as pregnancy proceeds (Iv)
- Monitor weight gain and blood pressure and advice/treat accordingly
- Start aspirin 75 mg daily in nephropathy and chronic hypertension from 13 weeks of gestation (III)
- Coordinate with obstetrician regarding fetal growth and well being
- Recommend delivery by 38 weeks for those on insulin and by 40 weeks for those on nutrition therapy alone(III)

Labour and delivery

- Use IV insulin during labour
- Stop insulin post partum and review requirements
- Provide appropriate care and facilities for the newborn. (Iv)

- Offer specialist ophthalmological review
- Offer personal dietetic support and fitness training
- Self-monitoring of capillary blood glucose during pregnancy would be performed more frequently
- Continuous glucose monitoring would be a further possibility
- HbA1c will be performed at each clinical contact
- Use of continuous subcutaneous insulin infusion may be considered where appropriate (IIb)

21. Non Alcoholic Fatty Liver Disease

- Routinely Consider referring for hepatic ultrasonography for screening of NAFLD. ALT, AST may be normal in the presence of NAFLD. (IIb)
- Recommend Lifestyle measures (diet and increasing physical activity) (IIa)
- Some weight reduction is usually required (IIa)
- Metabolic risk factors should be identified and treated, including optimal glycaemic and lipid control. Use of "statins" in patients with NAFLD is safe and frequent ALT monitoring is not required. (IIb)
- All diabetics with NAFLD should preferably receive Metformin if there is no contraindication (IIa)
- Refer obese who do not respond to attempted lifestyle measures for medical therapy or surgery (III)
- The role of pharmacotherapy is currently investigational and is not recommended for routine clinical practice

- Routinely screen for NAFLD in those with metabolic risk factors using hepatic Ultrasonography and liver function tests (IIb)
- In a patient with otherwise unexplained ALT elevation, NAFLD is highly likely to be the cause if hepatic imaging is compatible with fatty liver and metabolic risk factors are present.(IIb)

Fatty liver can be defined by the presence of at least 2 of 3 abnormal findings on abdominal ultrasonography

- diffusely increased echogenecity (bright) liver
- Liver echogenecity greater than kidney with vascular blurring
- Deep attenuation of ultrasound signal

Metabolic risk factors

- Type 2 DM
- Central obesity - waist >90cm for males >80cm for females
- Dyslipidaemia
- Metabolic syndrome

- Exclude liver diseases (HBV, HCV, autoimmune, Wilson's disease, haemachromatosis and alpha 1 antitrypsin deficiency) hepatic malignancies, infections, biliary tract diseases and drugs (tamoxifen, oestrogens, diltiazem, amiodarone, Valproate, methotrexate, steroids) should be excluded before ascribing abnormal liver tests to NAFLD (III)
- Minimal assessment
  - Biochemical: liver functions, lipids, FPG, PPG (in non diabetics), blood count
  - Anti-HCV, HBsAg, anti-nuclear antibody (ANA)

Once NAFLD is established, optional tests include (III)

- Abdominal CT, if properly conducted ultrasound is not informative
- Liver biopsy is usually not required for diagnosis of NAFLD. However, it should be considered in cases where there is diagnostic uncertainty, in patients at risk of advanced hepatic fibrosis(in the absence of clinical or imaging evidence of cirrhosis), in those subjected to laparoscopy for another purpose.
- Insulin sensitivity: In those with normal FBG, 75G OGTT may be performed
- Prothrombin time

Appendix

Appendix 1. Metabolic Syndrome: Diagnostic criteria*

- Central obesity Waist circumference >85 cm men, >80 cm women

With 2 of the following

- BP>130/85 mmHg
- TG>150mg/dl
- HDL<40 for men, <50 for women
- IFG>5.6mmol/l (100 mg/dl)/IGT/DM

** IDF Criteria 2005*

Appendix 2 Sample Diet

1800 calorie diet

Tea	2 tablespoon (tbs) non fat milk
B'fast	chickpea 1 cup / cowpea 1 cup / green gram 1 cup / bread 2 slices Curry / polsambal 1 tbs
Mid morning	Fruit 1 serving
Lunch	Rice 2 cups Vegetables 6 tbs Green leaves ½ cup Fish or chicken 1 piece Fruit 1 serving
Mid afternoon	Milk non fat
Dinner	Rice 1 cup Vegetable 3 tbs Dhal 3 tbs Fruit 1 serving

1400 calorie diet

Tea	2 tablespoon non fat milk
B'fast	Bread 2 slices / chickpea 1 cup Curry / polsambal 1 tbs
Mid morning	Fruit 1 serving
Lunch	Rice 1 & 1/2 cup Vegetables 6 tbs Green leaves ½ cup Fish or chicken 1 piece Fruit 1 serving
Mid afternoon	Milk non fat

Dinner	Rice ½ cup Vegetable 3 tbs Dhal 3 tbs Fruit 1 serving

Note: One serving of fruit equals 1 small banana or ¼ piece of papaya or 1 small apple or half cup juice. 1 piece pine apple, or ¼ melon

Appendix 3 Common insulin injection sites