Kingdom of Saudi Arabia
Ministry of Health
Asst. Deputy Ministry for Preventive Medicine
General Directorate of Noncommunicable Diseases

وزارة الصحة
Ministry of Health

National Reference of Clinical Guidelines

For Care of Diabetic Patients

In Primary Health Care

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National Reference For Diabetes Mellitus Guidelines
In Primary Health Care in Saudi Arabia

These guidelines are updated periodically
comments and suggestions concerning its contents are encouraged and could be sent to

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Preface

بسم الله الرحمن الرحيم

In the Name of Allah, the Most Compassionate, the Most Merciful

There is a growing body of evidence, that diabetes mellitus is one of the most challenging health problems worldwide in the 21st century. For the time being, diabetes mellitus is considered as an epidemic especially in many economically developing and newly industrialized nations around the globe. To add sour to the wound, the diabetes complications such as the related cardiovascular diseases, diabetic neuropathy, amputations, renal failure, and blindness result in disability, reduced life expectancy and huge economic burden both for patients and society as a whole. According to the International Diabetes Federation (IDF), out of the 7 billions total world population for the year 2010, about 6.6% or 285 millions persons have diabetes in the age group 20 – 79 years. By the year 2030, the estimate is about 7.8% or 438 millions patients with diabetes out of the expected 8.4 billions total world population for the age group 20 – 79 years. According to the WHO, almost 80% of diabetes deaths occur in low and middle-income countries and half of diabetes deaths occur before the age of 70 years. It is worth to mention here that healthy diet, regular physical activity, maintaining normal body weight, and avoiding tobacco use can prevent or at least delay the onset of diabetes.

On the other hand, here in the Kingdom of Saudi Arabia (KSA), diabetes became an increasing health burden too. It seems that Saudis have an inherited trait for type 2 diabetes, especially with increased incidence of obesity, consanguinity marriages, and insulin resistance susceptibility. In addition, the sedentary life style changes adopted during the last four decades associated with the oil bonanza, accentuated the situation leading the KSA to become the third country in the world regarding diabetes prevalence for the year 2010 on the IDF list. According to the most recent study in the K.S.A, diabetes prevalence is 14.1% out of the total population for all age groups with 28% prevalence in the age group over 30 years.

These facts urged the Ministry of Health to establish the Diabetes Prevention & Control Program and to adopt a national plan for diabetes prevention and control derived from the Gulf countries' plan in that regard. The plan includes variant goals covering a multiplicity of strategic scopes including

preventive, educational, therapeutic, and research issues. Following on the heels of the directions from the highest rank in the kingdom, the Ministry of Health assembled the National Committee on Diabetes Control & Prevention together with the Guidelines Developing Committee. Invitations were sent to the most authenticated international bodies of health policies mainly the WHO to contribute to the development of Saudi Guidelines for type 2 diabetes and many workshops and meetings were held. The result is this document between your hands which represents the first state-of-the art, evidence-based piece of work as the national guideline for type 2 diabetes in the K.S.A in collaboration with the WHO.

To wrap it up, I would like to extend my greetings and express my sincere gratitude to all those who contributed to the production of this "guidelines" both internationally and locally. My special thanks to the honorable, Dr. Alaa Alwan, the WHO assistant director-general and all the WHO and the EMRO experts who scarified their time and effort to help us. I hope this document will help unify the practice in type 2 diabetes prevention and management. May Allah (SWT) guides us all to the righteous path.

Minister of Health

Abdullah Ben Abdulaziz Alrabiaa

Acknowledgements:

- To the local expert committee, who took the main responsibility to develop this guidelines .....
- To the World Health Organization team who revised this guidelines .....
- To the steering committee who have worked hard to review this guidelines during its development .....
- To the participants in the workshop, managed by the Ministry of Health in collaboration with World Health Organization team, in preparation of this guidelines .....
- To the designers of this guidelines .....

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List of Abbreviations:

ACE	Angiotensin Converting Enzyme
ANC	Antenatal Care
BMI	Body Mass Index
BP	Blood Pressure
CVD	Cardiovascular Disease
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
DN	Diabetic Nephropathy
ECG	Electrocardiogram
GCT	Glucose Challenge Test
GDM	Gestational Diabetes Mellitus
HbA1C	Glycosylated Haemoglobin
HDL	High Density Lipoprotein
IFG	Impaired Fasting Glucose
IHD	Ischaemic Heart Disease
IVF	Intravenous Fluid
LDL	Los Density Lipoprotein
MNT	Medical Nutrition Therapy
NCDs	Non-Communicable Diseases
OGTT	Oral Glucose Tolerance Test
OHA	Oral Hypoglycaemic Agent
PHC	Primary Health Care
SMBG	Self-monitoring of Blood Glucose
TG	Triglycerides
U&E	Urea and electrolytes
WHO	World Health Organization

Methodology:

Introduction:

In the process of improving health services provided by primary health care centres, the undersecretary of the ministry of planning & development established a committee to work on developing evidence based clinical practice guidelines. This aimed at an ultimate goal of improving and standardizing the quality of services delivered by the Ministry of Health in the Kingdom.

In order to prioritize the guidelines that are more important for the guideline development team to begin with two processes were carried out. First, a letter was sent to all primary care centres in the kingdom containing health problems encountered in primary health care in a Likert scale. Physicians were asked to grade the importance of having a guideline for every health problem. Analysis showed that diabetes ranked highest. Second, the statistical analysis of frequency of diseases seen in primary care was reviewed to check for the most commonly encountered problems. Detailed description of the methods used in guideline development is described in the 'MOH Guideline Development Manual'.

1- The development panel of diabetes mellitus guidelines tried to find the most reputable national guidelines.

2- The 6 main guidelines agreed to be used based on their appraisal using the AGREE instrument are:

   a) type 2 diabetes national clinical guideline for management in primary and secondary care (update) 2008.
   b) canadian diabetes association 2008.
   c) clinical practice guidelines for the prevention and management of diabetes in canada.
   d) american diabetes association/standards of medical care in diabetes - 2009.
   e) diabetes care, volume 32, supplement 1, january 2009.
   f) canadian hypertension education program 2009.

3- The guidelines were appraised using AGREE instrument.

4- The guidelines content were analyzed for scope and applicability.

5- The panel Looked at the sources of evidence and the quality of recommendations.

6- Gaps were identified.

7- Other sources of evidences and recommendation to fill the gaps were looked for and references were cited accordingly.

Forming Guideline Recommendation:

The Diabetes Guideline committee agreed on adapting the Strength of Recommendation Taxonomy (SORT). It addresses the quality, quantity, and consistency of evidence and allows rate individual studies or bodies of evidence. The taxonomy is built around the information mastery framework, which emphasizes the use of patient-oriented outcomes that measure changes in morbidity or mortality.

Levels of evidence

Study quality	Diagnosis	Treatment/prevention/ screening	Prognosis
Level 1- good-quality patient-oriented evidence	Validated clinical decision rule SR/meta-analysis of high-quality studies High-quality diagnostic cohort	SR/meta-analysis of RCTs with consistent findings High-quality individual RCT‡ All-or-none study§	SR/meta-analysis of good-quality cohort studies Prospective cohort study with good follow-up
Level 2- limited-quality patient-oriented evidence	Unvalidated clinical decision rule SR/ meta-analysis of lower-quality studies or studies within consistent findings Lower-quality diagnostic cohort study or diagnostic case-control study	SR/meta-analysis of lower-quality clinical trials or of studies with inconsistent findings Lower-quality clinical trial‡ Cohort study Case-control study	SR/meta-analysis of lower-quality clinical trials or of studies with inconsistent findings Lower-quality clinical trial‡ Cohort study Case-control study SR/meta-analysis of lower-quality cohort studies or with inconsistent results Retrospective cohort study or prospective cohort study with poor follow-up Case-control study Case series
Level 3- other evidence	Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), or case series for studies of diagnosis, treatment, prevention, or screening		

Strength of Recommendation Taxonomy (SORT)

Strength of recommendation	Definition
A	Recommendation based on consistent and good-quality patient-oriented evidence*
B	Recommendation based on inconsistent or limited-quality patient-oriented evidence*
C	Recommendation based on consensus, usual practice, opinion, disease-oriented evidence*, or case series for studies of diagnosis, treatment, prevention, or screening.

Ref: American Family Physician 2004; 69:548-56.

Aim:

To develop a national guidelines for type 2 diabetes, which can be used efficiently by both primary and secondary level of care, to manage diabetes type 2 utilizing, the best available evidence, which is adapted to suit our targeted population, culture, system and resources, with main goal towards lowering the incidence of new case, minimize the deleterious impact of its complications.

Scope:

The main scope of this guide lines is towards diabetes type2, diagnosis, classification, screening, prevention, and management for the disease and its complications.
Type 1 diabetes in children and gestational diabetes mellitus is not of the scope of this guideline.

Funding:

There is no funding body behind this Guidelines.
It is supervised by the primary health directorate, Ministry of Health, Saudi Arabia.

Update:

Updates for these guidelines should be performed every 3 years.

Limitations:

In essence, this "guidelines" has been locally adopted from a multiplicity of international sources in the hope that it would fit the local circumstances and constraints in the KSA.

However other countries of the same or different cultures besides the internationally authenticated health bodies are welcomed and encouraged to scrutinize, criticize, use, or modify it accordingly. It worths to mention here that this "guidelines" has been developed in collaboration with the WHO and a variety of the most prestigious and internationally recognized diabetes experts. But, it would be quite a blunder to use this "guidelines" as a text book or a research protocol. The reason is that it is intended only to serve as a practice guide for the sake of enhancing and improving diabetes health care within the KSA.

These limitations maybe divided, into two major categories, current and future ones. The current ones are due to the fact that there is no preceding internationally approved "guidelines" in KSA. It followed that the developing committee has no option but to cite from the best evidence – based currently adopted international guidelines.

There is actually a great body of evidence that this is a common practice even amongst the most developed countries.

This strategy included mainly citing from the NICE in addition to filling the gaps from both the Canadian and ADA guidelines. The lack of Saudi clinical reference texts concerning reliable diabetes-related studies within the KSA beside the differences in clinical approach among health care professionals added to the these barriers too.

Other current limitations comprise no covering for the rare conditions; pharmacological toxicity of the medications; appraisals of individual papers; and service delivery, organization, or medication provision.

As for the future limitations, they may include, but not limited to:

- Qualities of the guidelines based on future practice encounters.
- Characteristics of the health care professionals.
- Incentives.
- Regulations.
- Coordination and cooperation between different health sectors whether public or private.
- Adoption by all health care settings concerned.
- Patient related factors.
- Future plans like the introduction of computerized clinical practice guidelines and integrated clinical pathways.

The major drawback here is that the methodological shortcomings of diagnostic guidelines in DM raise questions regarding the validity of recommendations in these documents that may affect their implementation in practice. Results suggest the need for standardization of guidelines terminology and for higher quality and systematically developed recommendations. This should be based on explicit guideline development and reporting standards in laboratory medicine.
To wrap it up, this "guidelines" is not a life long entity per se and it is recommended to be reviewed and renovated at least every 3 years, in collaboration with the authenticated international diabetes related bodies according to the state - of - the art recommendations.

NB: The Ministry of Health in the KSA disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

References:

1- Canadian Diabetes Association, 2008 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada.
2- Diabetes mellitus in Saudi Arabia Al-Nozha MM, Saudi Med J. 2004 Nov;25(11):1603- 10.
3- Type 2 Diabetes National clinical guideline for management in primary and secondary care (update)2008.

Introduction:

Diabetes is a serious condition with potentially devastating complications. It affects all age groups worldwide[1]. Nowadays statistics showed that there are 280 million people around the world were diagnosed with diabetes; and it is projected to rise further to 420 million by 2030 more than the current populations of the United States, Canada and Australia combined[2-3]. The International Diabetes Federation states that "every ten seconds, two people are diagnosed with diabetes somewhere in this world," [1].
The impact of diabetes is felt in both developed and developing countries. The urban population in developing countries is projected to double between 2000 and 2030. The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people 65 years of age. It is expected that the "diabetes epidemic" will continue even if levels of obesity remain constant.[1]

For this reason, the 61st session of the United Nations General Assembly passed a resolution in 2007 recognizing November 14th as World Diabetes Day, and it encouraged all member states to develop national strategies and policies for the prevention, treatment and care of people with diabetes.[1]

According to the World Health Organization the number of people with diabetes mellitus in Saudi Arabia is 3 million and will increase by year 2030 to 4 million and three hundred thousand. The number of people in Saudi Arabia with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future, is important to allow rational planning and allocation of resources.
The prevalence of DM among age group 30 – 70 year (2004 survey) was 23.7%, with 26.2% being males and 21.5% females ($p<0.00001$). The calculated age-adjusted prevalence for Saudi population for the year 2000 is 21.9%. Diabetes mellitus was more prevalent among Saudis living in urban areas of 25.5% compared to rural Saudis of 19.5% ($p<0.00001$). Despite the readily available access to healthcare facilities in Saudi Arabia, 28% of diabetics were unaware of having DM.[2]

These findings show that the Saudi population can be regarded as a moderate risk population for diabetes mellitus. The present management is unsatisfactory since those who are controlled (HbA1C <7%) are only 20% of diabetic patients. It is suggested that steps must be taken to improve awareness of the disease and to take measures to improve diabetes care.

There is a strong need to develop a National Guideline aiming at improving diabetic care.

Definition, Classification and Diagnosis of Diabetes:

Key Message

- The diagnosis of diabetes can be made on the basis of venous FPG, an OGTT test, or casual glucose if symptomatic.
- The term "prediabetes" is a practical and convenient term for impaired fasting glucose and impaired glucose tolerance, conditions that place individuals at risk of developing diabetes and its complications.

Introduction:

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action or both. The chronic hyperglycemia of diabetes is associated with significant long-term sequelae, particularly damage, dysfunction and failure of various organs – especially the kidneys, eyes, nerves, heart and blood vessels.

Diabetes is classified to type 1 diabetes, type 2 diabetes and gestational diabetes mellitus (GDM), and other specific types as summarized in Table 1.

Table 1 - Classification of diabetes:

Table. 1 Classification of diabetes
Type 1 diabetes* is diabetes that is primarily a result of pancreatic beta cell destruction and is prone to ketoacidosis. This form includes cases due to an auto- immune process and those for which the etiology of beta cell destruction is unknown.
Type 2 diabetes may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance.
Gestational diabetes mellitus refers to glucose intolerance with onset or first recognition during pregnancy.
Other specific types include a wide variety of relatively uncommon conditions, primarily specific genetically defined forms of diabetes or diabetes associated with other diseases or drug use.

* Includes latent autoimmune diabetes in adults (LADA), and includes the small number of people with apparent type 2 diabetes who appear to have immune-mediated loss of pancreatic beta cells.

The diagnostic criteria for diabetes and the plasma glucose thresholds for other diagnostic categories are summarized in Tables 2. These criteria are based on venous samples and laboratory methods.

Table 2 - Criteria for the diagnosis of diabetes:

1. FPG ≥ 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.

OR

2. Symptoms of hyperglycemia and a casual (random) plasma glucose ≥ 200 mg/dl (11.1 mmol/l). Casual (random) is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss.

OR

3. 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.

*In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeated testing.
HbA1c >6.5%

Prediabetes:

- Elevated BG levels below the threshold for diabetes also have clinical consequences. The term "prediabetes" is a practical and convenient term for impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) (Table 3).
- Conditions that place individuals at risk of developing diabetes and its Complications that would benefit from CV risk factor modification.

Table 3 - Criteria for testing for pre-diabetes and diabetes in asymptomatic adult individuals:

1. Testing should be considered in all adults who are overweight (BMI _25 kg/m2*) and have additional risk factors:
   - physical inactivity.
   - first-degree relative with diabetes.
   - women who delivered a baby weighing 9 lb or were diagnosed with GDM.
   - hypertension (140/90 mmHg or on therapy for hypertension).
   - HDL cholesterol level -35 mg/dl (0.90 mmol/l) and/or a triglyceride level -250.
   - mg/dl (2.82 mmol/l).
   - women with polycystic ovarian syndrome (PCOS).
   - IGT or IFG on previous testing.
   - other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans).
   - history of CVD.
2. In the absence of the above criteria, testing for pre-diabetes and diabetes should begin at age 45 years.
3. If results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

Metabolic Syndrome:

- A highly prevalent, multifaceted condition characterized by a distinctive constellation of abnormalities that include abdominal obesity, hypertension, dyslipidemia, insulin resistance and hyperglycemia.
- Individuals with the metabolic syndrome are at significant risk of developing diabetes and

CVD. Evidence now exists to support an aggressive approach to identifying people with the metabolic syndrome and treating not only the hyperglycemia but also the associated CV risk factors, in the hope of significantly reducing CV morbidity and mortality. (Table 4)

Table 4 - Definition of the metabolic syndrome:

	WHO	NCEP ATP III 2004	Explanation
Diagnostic criteria	Diabetes IFG, IGT or insulin resistance plus ≥2 other risk determinants are present	≥ 3 risk determinants are present	Central obesity (using ethnic specific values) plus ≥ 2 other risk determinants are present (if BMI is > 30 kg/m, central obesity can be assumed and WC does not need to be measured).
BG	Diabetes, IFG, IGT or insulin resistance	FPG ≥5. 6 (100mgldl) mmol/L	FBG ≥ 5. 6 mmol/L (or previously diagnosed type 2 diabetes).
BP	≥ 140/90 mm Hg	≥ 130/85 mm Hg	≥ 130/85 mmhg (or receiving treatment for previously diagnosed hypertension).
TG	≥ 1. 7 mmol/L	≥ 1. 7 mmol/L	≥ 1. 7 mmo/L (or receiving treatment)
HDL-C	≥ 0. 9 mmol/L (men) ≥ 1. 0 mmol/L (women	≥ 1. 0 mmol/L (men) ≥ 1. 3 mmol/L (women)	<1. 0 mmol/L (men) <1. 3 mmol/L (women) Or receiving treatment.
Abdominal obesity	Waist-to-hip ratio: ≥ 0. 90 (men) ≥ 0. 85 (women	WC: ≥ 102 cm (men) ≥ 88 cm (women	Europ's/Sub-Saharan Africans/Eastern Mediterranean and Middle East (Arab) population: WC ≥ 94 cm (men). WC ≥ 80 cm (women). SouthAsian/Malaysian/Asian/ Indian/Chinese/Japanese/Ethnic South and Central American populations WC ≥ 90 cm (men). WC ≥ 80 cm (women).
kidney function	Urinary albumin excretion rate >20 pg / min	NA	

BG = blood glucose

BP = blood pressure

FPG = fasting plasma glucose

HDL-C = high-density lipoprotein cholesterol

IFG = impaired fasting glucose

IGT = impaired glucose toleranc

NA=not applicable

NCEP ATP III = National Cholesterol Education program Adult Treatment Panel III

TG = triglycerides

WC = waist circumference

WHO = World Health Organization

Screening for Type 2 Diabetes:

Key Message

- Screening for type 2 diabetes using fasting plasma glucose (FPG) should be performed every 3 years in individuals 40 years of age.
- Testing should be considered in all adults who are overweight (BMI ≥ 25 kg/m2*) and have additional CVS risk factors.
- While the FPG is the recommended screening test, a 2-hour plasma glucose in a 75-g oral glucose tolerance test is indicated when the FPG is 6. 1 to 6. 9 mmol/L (110-125 mg/dl) and suspicion of type 2 diabetes or impaired glucose tolerance is high (e. g. for individuals with risk factors see TABLE 3).

Introduction:

- Tests for hyperglycemia can identify these individuals, many of whom will have or will be at risk for preventable diabetes complications. (5, 6)
- Screening individuals as early as age 40 in family physicians' offices has proved to be useful in detecting unrecognized diabetes. (10).

Clinical Questions:

When & how to screen for type 2 Diabetes?

Recommendation:

1. Screening for diabetes using an FPG should be performed every 3 years in individuals 40 years of age. Level 3. More frequent and/or earlier testing with either an FPG should be considered in people with additional risk factors for diabetes. Level 3

These risk factors include:

- physical inactivity.
- first-degree relative with diabetes.
- women who delivered a baby weighing 4 Kg (9 lb) or were diagnosed with GDM.
- hypertension (140/90 mmHg or on therapy for hypertension).
- HDL cholesterol level 35 mg/dl (0.90 mmol/l) and/or a triglyceride level 250mg/dl (2.82 mmol/l).
- women with polycystic ovarian syndrome (PCOS).
- IGT or IFG on previous testing.
- other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans).
- History of CVD.

Prevention of Diabetes:

Key Message

- Intensive and structured lifestyle modification that results in loss of approximately 5% of initial body weight can reduce the risk of progression from impaired glucose tolerance to type 2 diabetes by almost 60%.
- Progression from prediabetes to type 2 diabetes can also be reduced by pharmacologic therapy with metformin (30% reduction), acarbose (30% reduction) and thiazolidinedione(~60% reduction).

Introduction:

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

- Primary approaches to preventing diabetes in a population include the following:
  1) Programs targeting high-risk individuals in the community.
  2) Programs for the general population, such as those designed to promote physical activity and healthy eating in adults or children.

Recommendations:

1. A structured program of lifestyle modification that includes moderate weight loss, healthy eating and regular physical activity should be implemented to reduce the risk of type 2diabetes in individuals with IGT and IFG. Level 1
2. In individuals with IGT, pharmacologic therapy with metformin or an alpha-glucosidase inhibitor should be considered to reduce the risk of type 2 diabetes. Level 1
3. In individuals with IGT and/or IFG and no known cardiovascular disease, treatment with a thiazolidinedione could be considered to reduce the risk of type 2.

Recommendations:

R1- When setting a target glycated haemoglobin HbA1C:

a) involve the person in decisions about their individual HbA1C target level, which may be above that of 7% set for people with type 2 diabetes in general.

b) encourage the person to maintain their individual target unless the resulting side effects (including hypoglycaemia) or their efforts to achieve this impair their quality of life.

c) offer therapy (lifestyle and medication) to help achieve and maintain the HbA1c target level.

d) inform a person with a higher HbA1c that any reduction in HbA1c towards the agreed targets is advantageous to future health.

e) avoid pursuing highly intensive management to achieve levels less than 7%. *Level 3*

R2- For most individuals with diabetes, A1c should be measured every 3 months, to ensure that glycemic goals are being met or maintained. Testing at least every 6 months may be considered in adults during periods of treatment and lifestyle stability when glycemic targets have been consistently achieved. *Level 3*

R3- For individuals using insulin, SMBG should be recommended as an essential part of diabetes self-management Level 3 (8), for type 2 diabetes and should be undertaken at leas 3 times per day and include both pre- and postprandial measurements in those with type 2 diabetes on once-daily insulin in addition to oral antihyperglycemic agents, testing at least once a day at variable time is recommended. *Level 3*

R4- If HbA1c levels remain above target levels, but pre-meal self-monitoring levels remain well controlled (<126 mg/dl), consider self-monitoring to detect postprandial hyperglycaemia (>153 mg/dl), and manage to below this level if detected.

R5- For individuals treated with oral antihyperglycemic agents or lifestyle alone, the frequency of SMBG should be individualized depending on glycemic control and type of therapy and should include both pre- and postprandial measurements. *Level 3*

R6- In many situations, for all individuals with diabetes, more frequent testing should be undertaken to provide information needed to make behavioral or treatment adjustments required to achieve desired glycemic targets and avoid risk of hypoglycemia. *Level 3*

R7- In order to ensure accuracy of BG meter readings, meter results should be compared with laboratory measurement of simultaneous venous FPG at least annually, and when indicators of glycemic control do not match meter readings. *Level 3*

Self-Management Education:

Key Message

- Self-management education (SME) that incorporates knowledge and skills development, as well as cognitive behavioural interventions, should be implemented for all individuals with diabetes.
- The content of SME programs must be individualized according to the current state of diabetes, treatment recommendations, readiness for change, learning style, ability, resources and motivation.
- SME is a fundamental component of diabetes care and is most effective when ongoing diabetes education and comprehensive healthcare occur together.

Introduction:

- The objectives of diabetes self-management education (SME) are to increase the individual's involvement in, confidence with and motivation for control of their diabetes, its treatment and its effect on their lives.
- SME goes beyond a focus on adherence to guidelines and treatment prescriptions; it incorporates didactic and non-didactic (e.g. active, participatory) education, as well as social, behavioral and psychological interventions.
- The term "SME", rather than "diabetes education", emphasizes the importance of including a variety of client-centered strategies and interventions that address the physical, psychological and social management of living with a chronic illness.

Elements of SME:

- SME, which includes skills training, coping strategies, problem-solving and case management, has been demonstrated to improve the individual's ability to engage in effective self-care, lower glycated hemoglobin (A1C) levels and enhance quality of life.
- The essential components of SME are hypothesized to include (Figure1):
  1. Interventions that include face-to-face delivery.
  2. Education tailored to individual needs and circumstances.
  3. A group setting with others who share the same condition.
  4. Feedback following an intervention.
  5. Psychological emphasis in the intervention.
  6. Involvement of medical providers in providing the intervention.
- Long-term education with scheduled follow-up has also been shown to enhance the effect of education on glycemic control. Education should be offered in a timely and needs-based manner.

- SME program should include a problem-solving component; monitoring of relevant health parameters; healthy eating; physical activity; pharmacotherapy; hypo- and hyperglycemia prevention and management; and prevention and surveillance of complications and comorbid conditions.
- Skill training during SME should include self-monitoring of blood glucose (SMBG), making dietary choices, incorporating an exercise regimen, using medications as recommended and possible medication adjustment. Education for flexible insulin management and dietary freedom has been shown to improve quality of life as well as glycemic control.

Empowerment:

- Empowerment is an essential psychological component of SME, that increases an individual's participation and collaboration in decision making regarding care and education and have been shown to be more effective than a didactic approach in enhancing psychological adjustment to diabetes and potentially preventing psychological distress.
- To implement interventions using an empowerment approach, the educator should engage in the following behaviors:
  - demonstrates acceptance (respect) for the individual's perspectives.
  - explores the affective or emotional aspect of an issue.
  - works in an alliance or partnership with the individual.
  - facilitates active participation of all parties in the education process.

Support Systems:

- Evidence suggests that including family members (parents, spouses, significant others) in educational interventions is beneficial in improving diabetes related knowledge and glycemic control. Interventions that target families' ability to cope with stress or diabetes related conflict are effective.
- Peer programs geared toward developing self-efficacy (i.e.self-confidence in one's ability to carry out a behavior).

Educational Settings:

SME conducted in community gathering places and group education settings has been shown to be effective in improving glycemic control in type 2 diabetes and promoting efficiencies in delivery of diabetes self-management programs.

Methods of Delivery:

- Diabetes self-management is most effective when ongoing diabetes education and comprehensive healthcare occur together.
- Interactive health communications (computer-based information packages combined with either social, decision or behavior-change support) have a largely positive effect on users and support improved behavior and clinical outcomes.

Recommendation:

R1- People with diabetes should be offered timely diabetes education that is tailored to enhance self-care practices and behaviours. *Level 1*

R2 - All people with diabetes who are able should be taught how to self-manage their diabetes, including SMBG. *Level 1*

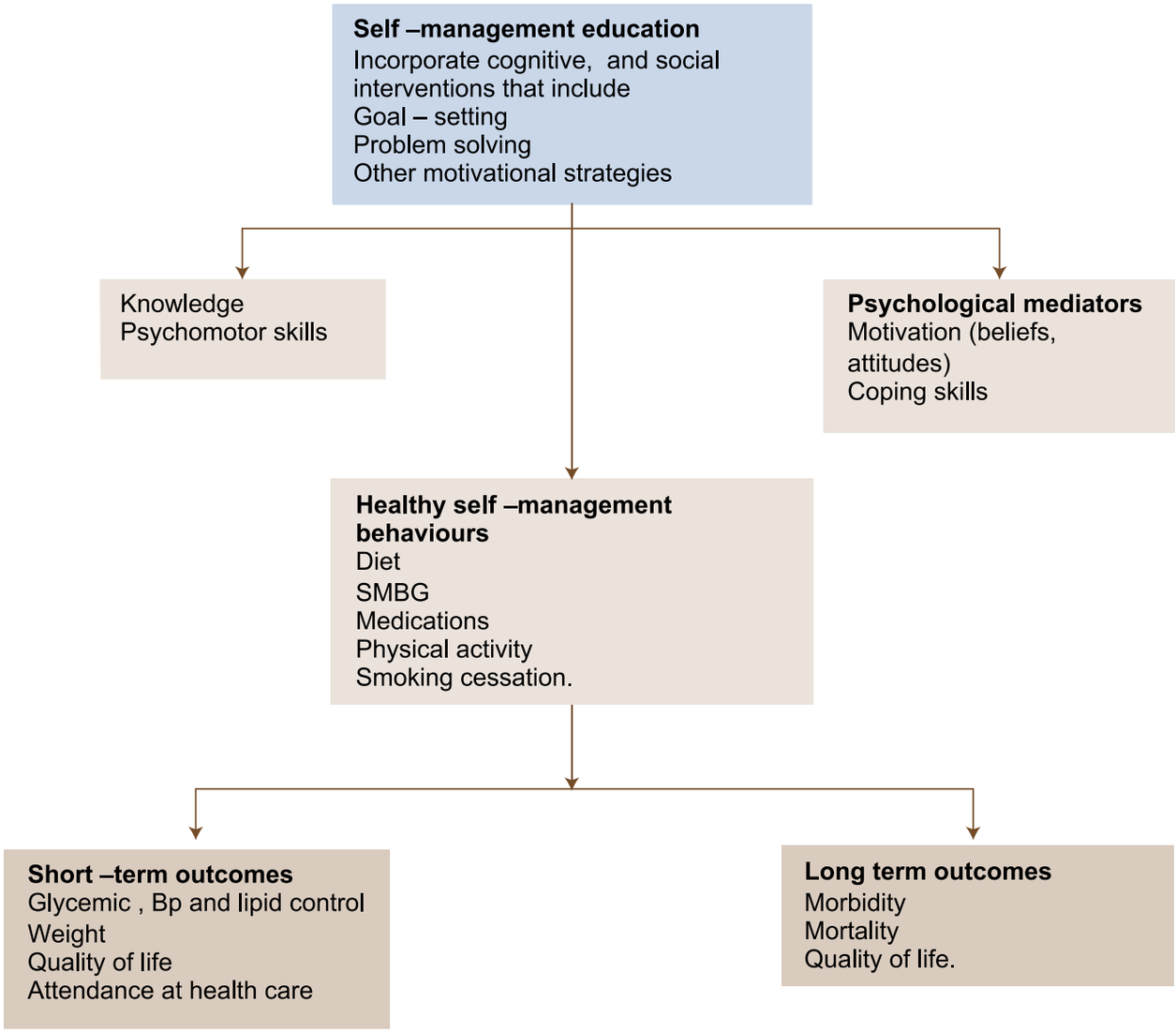
R3 - Self-management education that incorporates cognitive behavioral interventions such as problem-solving, goal setting and self-monitoring of health parameters should be implemented in addition to didactic education programming for all individuals with diabetes. *Level 2*

R4 - Interventions that increase patients' participation and collaboration in healthcare decision-making should be used by providers. *Level 2*

R5 - SME interventions should be offered in small group and/or one-on-one settings, as both are effective for people with type 2 diabetes. *Level 1*

R6 - Interventions that target families' ability to cope with stress or diabetes-related conflict should be consideredin education interventions when indicated. *Level 2*

Figure 1. Process of teaching people to manage their diabetes:



Targets for Glycemic Control:

- *Canadian Diabetes Association Clinical Practice Guidelines Expert Committee.*
- *The initial draft of this chapter was prepared by S. Ali Imran MBBS FRCP (Edin) FRCPC and Stuart A. Ross MB ChB FRCPC FRACP.*

Key Message

- Optimal glycemic control is fundamental to the management of diabetes.
- Both fas ting and postprandial plasma glucose levels correlate with the risk of complications and contribute to the measured glycated hemoglobin value.
- When setting treatment goals and strategies, consideration must be given to individual risk factors such as age, prognosis, presence of diabetes complications or comorbidities, and their risk for and ability to perceive hypoglycemia.

Relationship Between Blood Glucose Levels and Complications of Diabetes:

Optimal glycemic control is fundamental to the management of diabetes. There is compelling evidence that improved glycemic control reduces risks of microvascular complications in both type I and type 2 diabetes (1-4). There is also evidence in patients with type I diabetes that improved glycemic control reduces the risk of' cardiovascular disease (CVD) (5). However, similar benefit of improved glycemic control on macrovascular complications in people with type 2 diabetes has not been demonstrated through randomized controlled trials (4, 6). In epidemiologic analyses, glycated hemoglobin (A1C) levels >7% are associated with a significant increased risk of both microvascular and macrovascular complications, regardless of underlying treatment (3, 7-9). The data from the Diabetes Control and Complications Trial (DCCT) (7) and the United Kingdom Prospective Diabetes Study (UKPDS) (8) demonstrated a continuous relationship between A1C and diabetes complications, with no apparent threshold of benefit. In the DCCT a 10% reduction in A1C (e.g. from 8.0 to 7.2%) was associated with a 40 to 50% lower risk of retinopathy progression, although the absolute reduction in risk was substantially less at lower A1C levels (7). In the subsequent prospective follow-up of the DCC1 cohort over 11 years, the risk of CVD and death from CV causes was reduced by 42 to 57% in the intensive insulin therapy group (5). In the UKPDS, this relationship was directly linear, with each l.0% (absolute) reduction in mean A1C associated with a 37% decline in the risk of microvascular complications, a 14% lower rate of myocardial- infarction (Ml) and fewer deaths from diabetes or any cause (8). Both fasting plasma glucose (FPG) and postprandial PG levels correlate with the risk of complications. The analyses from the DCCT indicated that mean capillary glucose levels (based on both pre- and postprandial measurements) are also directly correlated to

the risk of complications (10). FPG is directly related to CV events, with the increase in risk apparent even at PG levels that are within the normal range for people without diabetes (11). In a meta-analysis of 38 prospective studies, an FPG of >5.5 mmol/L was associated with an increased risk of CV events (12). Postprandial hyperglycemia is a powerful predictor of adverse outcomes. The Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study found the 2-hour postchallenge PG to be a better predictor of CVD and all-cause mortality than FPG (13). This association between CV disease and 2-hour postprandial PG appears to be linear without a threshold (12, 13). In another study, a 2- hour postprandial PG level >7.8 mmol/L was associated with an increase in all-cause mortality (14). The data from the Study to Prevent Non-Insulin Dependent Diabetes Mellitus (STOP-NDDM) also suggest that targeting postprandial PG with acarbose may reduce the risk of CV outcomes (15). There is also a strong association between postprandial hyperglycemia and microvascular complications. In a prospective observational study, postprandial hyperglycemia was found to be a better predictor of diabetic retinopathy than A1C (16). Similarly, in the Kumamoto study, the risk of microvascular complications increased with 2-hour postprandial PG levels >10.0 mmol/L (2). Additionally, the diabetes Intervention Study found that in patients with type 2 diabetes, a 1-hour postprandial PG level ≥ 8.0 mmol/L conferred the lowest risk of MI or death, while levels >10.0 mmol/L were associated with the highest risk (17). Despite the association between PG and CVD, 2 large, randomized, controlled, multicentre trials, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial (5) and the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial (4) have shown that intensive glucose lowering in type 2 diabetes does not reduce major CV events. The ACCORD trial recruited individuals with type 2 diabetes who were between the ages of 40 and 79 years and had CVD, or were between the ages of 55 and 79 years and had evidence of significant atherosclerosis, albuminuria, left ventricular hypertrophy or at least 2 additional risk factors for CVD (obesity, hypertension, dyslipidemia or current status as a smoker). At baseline, mean age was 62.2 years, median duration of diabetes was 10 years and mean A1C was 8.3%. One of the major aims of the trial was to determine whether an intensive PG-lowering approach aimed at achieving A1C levels <6.0% would reduce CV events compared to a more conventional approach, aiming at achieving an A1C between 7.0 and 7.9%. After a mean 3.5 years of follow-up, the intensive treatment aim was halted because of safety concerns. The incidence of death was 11 per 1000 per year in the conventional treatment group (median achieved A1C of 75%) vs. 14 per 1000 per year in the intensive treatment group (median achieved A1C of 6.4%). Furthermore, intensive treatment was also associated with a significantly higher risk of severe hypoglycemia requiring medical assistance (3.1% in the intensive treatment group vs. 1 .4% in the conventional treatment group) and weight gain. At the same time, there was evidence of a non-significant 10% reduction in the primary composite endpoint of nonfatal MI, stroke or CV death. The ADVANCE trial is a similar trial that enrolled individuals with type 2 diabetes who were at least 55 years of age and had a history of' major macrovascular or microvascular disease or at least 1 other risk factor for vascular disease. At baseline, mean age was 66 years, mean duration of diabetes was 8 years and mean A1C was 7.48%. Intensive control with gliclazide (modified release) based therapy (median

achieved A1C of' 6.5%) vs. the conventional treatment (which did not use gliclazide-based treatment) (median achieved A1C of 7.3%) decreased nephropathy by 21% but did not decrease CV events. Similar to the ACCORD study, weight gain and severe hypoglycemia occurred more frequently in the intensive treatment group. The risk of hypoglycemia was 2.7% in the intensive treatment group, compared to 1.5% in the standard group. However, there was no increased risk of death in the intensively controlled group in the ADVANCE trial. These trials suggest that in patients with type 2 diabetes and a CV risk profile similar to the ACCORD population, a strategy to target a normal A1C (i.e. <6.0%) may increase mortality. However, this risk must be balanced against the decrease in the incidence of nephropathy shown in the ADVANCE study, in which a similar population was treated with a strategy to target an A1C <6.5%. Both FPG and postprandial PG values contribute to the A1C value. When the A1C values are higher (>8.5%). the major contribution is from the FPG levels, but as the A1C value approaches the target value of 7.0%, there is a greater contribution from the postprandial PG values (18,19). A recent study by Monnier and colleagues in 130 patients with type 2 diabetes using continuous glucose monitoring demonstrated that a 2-hour postprandial PG of <8.0 mmol/l. correlates best with an A1C of <7.0% (20). In view of this, if A1C targets cannot be achieved with a postprandial target of 5.0 to 10.0 mmol/L, further postprandial PG lowering to 5.0 to 8.0 mmol/L can be considered(20).

Risk of Hypoglycemia:

While epidemiologic data suggest that the lowest risk of complications will occur in those with normoglycemia, the absolute benefit of lowering A1C levels from 7.0 to 6.5% is expected to be small and must be weighed against the risk of hypoglycemia. The hypoglycemia data from the DCCT showed that the risk of' severe hypoglycemia was 3 times higher among participants receiving intensive therapy (1). Similarly,intensive therapy in type 2 diabetes increases the risk of severe hypoglycemia by 2- to -3 fold, particularly among those using insulin (3,4,6).

Glycemic Targets:

The glycemic targets recommended for most patients with type 1 and type 2 diabetes are listed in Table 1. However, clinical judgment is required to determine which people can reasonably and safely achieve these targets. Treatment goals and strategies must be tailored to the patient, with consideration given to individual risk factors (e.g. the patient's age, prognosis, level of glycemic control, duration of diabetes, the presence of diabetes complications or comorbidities, and their risk for and ability to perceive hypoglycemia). To make the guidelines easier to incorporate into clinical practice, a single A1C target is provided, and PG targets have been rounded to whole numbers.

	*A1C** (%)	*FPG or preprandial PG (mmol/L)*	*2-hour post prandial PG (mmol/L)*
Type 1 and type 2 diabetes	7.0	4.0 - 7.0	5.0 - 10.0 (5.0 - 8.0 if A1C targets not being met)

Table 1 - Recommended targets for glycemic control:

- Treatment goals and strategies must be tailored to the individual with diabetes, with consideration given to individual risk factors. Glycemic targets for children 12 years of age and pregnant women differ from these targets. See relevant guidelines for further details. An A1C of 7.0% corresponds to a laboratory value of 0.070. Where possible, Canadian laboratories should standardize their A1C values to Diabetes Control and Complications Trial levels (reference range: 0.040 to 0.060). However as many laboratories continue to use a different reference range, the target A1C value should be adjusted based on the specific reference range used by the laboratory that performed the test. As a useful guide, an A1C target of 7.0% refers to a threshold that is approximately 15% above the upper.

Limit of normal:

A1C = glycated hemoglobin.
FPG = fasting plasma glucose.
PG = plasma glucose.

Recommendations:

1. Glycemic targets must be individualized; however, therapy in most individuals with type 1 or type 2 diabetes should be targeted to achieve an A1C ≥ 7.0% in order to reduce the risk of microvascular {Grade *A*, Level *1A (1-4)*} and, in Individuals with type 1 diabetes, macrovascular complications {Grade *C*, Level *3 (5)*}.

2. A target A1C of ≥ 6.5% may be considered in some patients with type 2 diabetes to further lower the risk of nephropathy {*Grade A Level 1A* (4)}, but this must be balanced against the risk of hypoglycemia {*Grade A Level 1A (4,5)*} and increased mortality in patients who are at significantly elevated risk of cardiovascular disease {Grade *A Level 1A (4)*}.

3. In order to achieve A1C of ≥ 7.0%, people with diabetes should aim for:

   - An FPG or preprandial PG target of 4.0 to 7.0 mmol/L {*Grade* B, *Level 2 (1), for type 1; Grade* B, *Level* 2 (2,3), *for* type 2 *diabetes*}; and
   - A 2-hour postprandial PG target of 5.0 to 10.0 mmol/L {Grade B, *Level* 2 *(1), for* type *1 diabetes; Grade B. Level* 2 (2,3), *for* type 2 *diabetes*}. If A1C targets cannot be achieved with a postprandial target of 5.0 to 10.0 mmol/L, further postprandial BG lowering to 5.0 to 8.0 mmol/L can be considered [*Grade D, Consensus, for* type *1 diabetes; Grade* D, *Level 4 (18,19),* for type 2 diabetes].

Other Relevant Guidelines:

Monitoring Glycemic Control, p. S32.
Hypoglycemia, p. S62.
Type 1 Diabetes in Children and Adolescents, p. S150.
Type 2 Diabetes in Children and Adolescents, p. S162.
Diabetes and Pregnancy, p. S168.
Diabetes in the Elderly, p. S181.

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Monitoring Glycemic Control:

- *Canadian Diabetes Association Clinical Practice Guidelines Expert Committee.*
- *This initial draft of this chapter was prepared by Sharon Brez RN BScN MA(Ed) CDE, Lori Berard RN CDE and Ian Blumer MD FRCPC.*

Key Message

- Glycated hemoglobin (A1C) is a valuable indicator of treatment effectiveness, and should be measured every 3 months when glycemic targets are not being met and when diabetes therapy is being adjusted.
- Awareness of all measures of glycemia, including self- monitoring of blood glucose (SMBG) results and A1C, provide the best information to assess glycemic control.
- The frequency of SMBG should be determined individually, based on the type of diabetes, the treatment prescribed, the need for information about BG levels and the individual's capacity to use the information from testing to modify behaviours or adjust medications.

Glycated Hemoglobin Testing:

The diabetes Control and Complications Trial (DCCT) (1) and the United Kingdom Prospective Diabetes Study (UKPDS) (2) demonstrated that glycated hemoglobin (A1C) and the development of long-term complications are correlated in both type1 and type 2 diabetes, respectively. A1C is a reliable estimate of mean plasma glucose (PG) levels over the previous 3 to 4 months for most individuals (3). In uncommon circumstances where the rate of red blood cell turnover is significantly shortened or extended, or the structure of hemoglobin is altered, A1C may not accurately reflect glycemic status. A1C is a valuable indicator of treatment effectiveness and should be measured every 3 months when glycemic targets are not being met and when diabetes therapy is being adjusted. Testing at 6-month intervals may be considered in situations when glycemic targets are consistently achieved (4).

Currently, A1C is the preferred standard for assessing glycated hemoglobin, and laboratories are encouraged to use assay methods for this test that are standardized to the DCCT reference (4,5). A strong mathematical relationship between mean blood glucose (BG) values and A1C levels has been identified (6). In the future, A1C may be reported as "average blood glucose" in order to assist people to better understand the meaning of the results of this test (7).

Self-Monitoring of Blood Glucose:

Awareness of all measures of glycemia, including self- monitoring of blood glucose (SMBG) results and A1C, provide the best information to assess glycemic control (4). Most people with diabetes can benefit from SMBG (8,9).

Potential benefits, which may include improvement in A1C, avoidance and identification of hypoglycemia and increased lifestyle flexibility, are enhanced when individuals receive self-management education that enables them to adjust their dietary choices, physical activity and medication(s) in response to SMBG values (8,10-14).

Effective education and implementation of strategies that employ patient empowerment and behaviour change theory may be most effective in supporting the incorporation of SMBG into the diabetes management routine (10,15-18).

Frequency of SMBG:

The frequency of SMBG should be determined individually, based on the type of diabetes, the treatment prescribed, the need for information about BG levels and the individual's capacity to use the information from testing to modify behaviours or adjust medication.

For people with type 1 diabetes, SMBG is an essential component of daily diabetes management. In a large cohort study, performance of ≥ 3 self-tests per day was associated with a statistically and clinically significant 1.0% reduction in A1C levels (8). The results of multiple tests each day provide information that is better correlated to A1C than fasting results alone. BG measurements taken after lunch, after supper and at bedtime have demonstrated the highest correlation to A1C (6). More frequent testing is often required to provide the information needed to reduce hypoglycemia risk, adjust treatment and make appropriate lifestyle choices.

The benefits and optimal frequency of SMBG in type 2 diabetes are less clear than for type 1 (8,9,12,19-26). Current evidence is at times contradictory, and methodological and conceptual limitations exist in the literature. SMBG in those who are recently diagnosed, regardless of treatment, has been demonstrated to be of benefit (24). A large cohort study found that for people with type 2 diabetes treated with oral antihyperglycemic agents, testing at least once daily was associated with a 0.6% lower A1C than less frequent monitoring (8).

A more recent randomized controlled trial (RCT) of SMBG with or without instruction on how to use results for diabetes self-management failed to demonstrate improvement in glycemic control (26). However, other adequately powered RCTs, large cohort studies and consensus statements have identified benefits of more frequent testing on glycemic control, especially when this information is used to make appropriate and timely treatment and lifestyle adjustments (8,15,21,22,27,28). Given current uncertainties regarding the benefits of SMBG for individuals with type 2 diabetes not taking insulin, a well designed RCT is needed to adequately answer this important but complex question.

For those with type 2 diabetes using insulin, frequent testing is also an integral component of care. In a large, nonrandomized study of individuals with stable type 2 diabetes using insulin, testing at least 3 times a day was associated with improved glycemic control (28).

In people with type 2 diabetes, timing of testing should take into account the potential for hypoglycemia associated with oral insulin secretagogues, and the fact that postprandial hyperglycemia is associated with increased cardiovascular risk (29). Postprandial PG results are generally better correlated to A1C than tests taken at other times of the day (30,31). In people with very poor glycemic control, however, fasting plasma glucose (FPG) may more strongly reflect overall glycemia (31). Individuals who are intensively managed with multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII), with the goal of near normalization of BG levels, can use information obtained from preprandial and bed time testing, as well as intermittent postprandial and nocturnal tests, to adjust insulin, dietary choices and activity levels. Testing before and after meals is associated with improved glycemic control compared to preprandial testing alone (32). Since nocturnal hypoglycemia may be more frequent in intensively managed individuals, periodic overnight testing at a time corresponding to peak insulin action should be undertaken (1,33-37).

Verification of Accuracy of SMBG Performance and Results:

Variability exists between BG results obtained using self-monitoring devices and laboratory testing of PG. At BG levels >4.2 mmol/L, a difference of <20% between fingertip sampling of capillary BG and simultaneous venous FPG levels is considered acceptable (5). Less variation is recommended for BG readings ≥ 4.2 mmol/L (5). In order to ensure accuracy of meter readings, meter results should be compared with laboratory measurement of PG at least annually and when indicators of glycemic control (10 not match meter readings. In addition, as errors in testing techniques are commonly observed, periodic re-education on correct monitoring technique may improve the accuracy of SMBG results (10,38). In rare situations, therapeutic interventions may interfere with the accuracy of' some BG meter results. For example, icodextrin-containing peritoneal dialysis solutions may cause false high readings in some meters utilizing glucose dehydrogenase methods. To avoid unsafe treatment decisions, care should be taken to select an appropriate meter in these situations.

Alternate Site Testing:

Meters are available that allow SMBG using blood samples from sites other than the fingertip, such as the forearm, palm of the hand or thigh: Accuracy of results over a wide range of BG levels and during periods of rapid change in BG levels is variable across sites. During periods of' rapid change in BG levels (e.g. after meals, after exercise and during hypoglycemia), fingertip testing has been shown to more accurately reflect glycemic status than forearm or thigh testing (39,40). In comparison, blood samples taken from the palm near the base of the thumb (thenar area), demonstrate a closer correlation to fingertip samples at all times of day, and during periods of rapid change in BG levels (41,42).

Ketone Testing:

Ketone testing is recommended for all individuals with type1 diabetes during periods of' acute illness accompanied by elevated BG, when preprandial BG levels remain elevated (>14.0 mmol/L) or when symptoms of diabetic ketoacidosis (DKA) such as nausea, vomiting or abdominal pain are present (4). If' all of' these conditions are present in type 2 diabetes, ketone testing should be considered, as DKA can also occur in these individuals.

During DKA, the equilibrium that is usually present between ketone bodies shifts toward formation of beta hydroxybutyric acid (beta-OHB). As a result, testing methods that measure blood beta-OHB levels may provide more clinically useful information than those that measure urine acetoacetate or acetone levels. Assays that measure acetoacetate through urine testing may not identify the onset and resolution of' ketosis as quickly as those that quantify beta-OHB levels in blood, since acetoacetate or acetone can increase as beta-OHB decreases with effective treatment (4,5). Meters that quantify beta-OHB from capillary sampling may he preferred for self-monitoring of ketones, as they have been associated with earlier detection of ketosis (4,43-45) and may provide information required to prevent progression to DKA. This may be especially useful for individuals with type1 diabetes using CSII, as interruption of' insulin delivery can result in rapid onset of DKA (46).

Continuous Glucose Monitoring Systems:

Continuous glucose monitoring systems (CGMS) measure glucose concentrations in the interstitial fluid. Two types of devices are available - newer systems that display "real time" glucose results directly on the monitoring system, and earlier "non-real time" (i.e. retrospective) devices that do not have this result display capability.

Real-time CGMS has been associated with positive outcomes, including improved A1C (47) and significantly reduced duration of hypoglycemia (48), hyperglycemia (48) and nocturnal hypoglycemia (48) in insulin-treated patients. Real-time CGMS results have been found to be closely correlated to BG values, although some discordance with BG levels during periods of hypoglycemia and significant hyperglycemia have been observed (48,49).

Given the precision of current systems and the lag between changes in BC and interstitial glucose, particularly when BC levels are rapidly fluctuating (such as in the few hours after eating), CGMS readings may not reflect simultaneous BC values (51,52).

As a result, CGMS technologies do not eliminate the need for capillary BC testing. Capillary tests must be performed both for the purposes of calibrating the device and for therapeutic decision-making. With non-real time (i.e. retrospective) CGMS, glucose readings for intermittent time periods (usually 72 hours) are captured, but results are available only for retrospective viewing and analysis when data are downloaded to a computer. Non-real time (i.e. retrospective) CGMS has been associated with detection of unrecognized hypoglycemia in patients with either type I

or type 2 diabetes (52,53), detect ion of unexpected hyperglycemia in women with gestational diabetes mellitus (54), reduction in the duration of hypoglycemia in insulin-treated patients (SS) and less frequent hypoglycemia in a pediatric, insulin-treated population (53).

It is not yet clear if use of non-real time technology reduces Al C values (49, 53, 55, 56). Discrepancies in non-real time CGMS in diabetes accuracy have been identified (46, 57-60), especially durng hypoglycemia (57, 58) and nocturnally (59, 60).

The sacrcity of data (including accuracy data) presently available precludes making definitive recommendations regarding the role of real-time data CGMS in diabetes management. However, given its rapidly increasing use, it is incumbent upon healthcare providers involved in the management of people with diabetes (particularly type I diabetes) to be aware of this technology.

Recommendations:

1. For most individuals with diabetes,A1C should be measured every 3 months to ensure that glycemic goals are being met or maintained. Testing at least every 6 months may be considered in adults during periods of treatment and lifestyle stability when glycemic targets have been consistently achieved *[Grade D, Consensus]*.
2. For individuals using insulin, SMBG should be recommended as an essential part of diabetes self-management *[Grade A, Level I (33), for type I diabetes; Grade C, Level 3 (8), for type 2 diabetes*] and should be undertaken at least 3 times per day *[Grade C, Level 3 (8,28)]* and include both pre- and postprandial measurements *[Grade C, Level 3 (6,28,32)]*. In those with type 2 diabetes on once-daily insulin in addition to oral antihyperglycemic agents, testing at least once a day at variable times is recommended *[Grade D, Consensus]*.
3. For individuals treated with oral antihyperglycemic agents or lifestyle alone, the frequency of SMBG should be individualized depending on glycemic control and type of therapy and should include both pre- and postprandial measurements *[Grade* D, *Consensus*].
4. In many situations, for all individuals with diabetes, more frequent testing should be undertaken to provide information needed to make behavioural or treatment adjustments required to achieve desired glycemic targets and avoid risk of hypoglycemia *[Grade D, Consensus]*.
5. In order to ensure accuracy of BG meter readings, meter results should be compared with laboratory measurement of simultaneous venous FPG at least annually, and when indicators of glycemic control do not match meter readings *[Grade D, Consensus]*.
6. Individuals with type I diabetes should be instructed to perform ketone testing during periods of acute illness accompanied by elevated BG, when preprandial BG levels remain >14.0 mmol/l., or in the presence of symptoms of DKA *[Grade D, Consensus]*. Blood ketone testing methods may be preferred over urine ketone testing, as they have been associated with earlier detection of ketosis and response to treatment *[Grade* B, *Level* 2 (44)*]*.

Other Relevant Guidelines:

Self-Management Education, p. S25.
Targets for Glycemic Control, p. S29.
Physical Activity and Diabetes, p. S37.
Insulin Therapy in Type 1 Diabetes, p. S46.
Hypoglycemia, p. S62.
Hyperglycemic Emergencies in Adults, p. S6.
Type 1 Diabetes in Children and Adolescents, p. S150.
Type 2 Diabetes in Children and Adolescents, p. S162.
Diabetes and Pregnancy, p. S168.

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Pharmacologic Management of Type 2 Diabetes:

Key Message

- If glycemic targets (HbA1c≤ 7) are not achieved within 2 to 3 months of lifestyle management and Metformin, other antihyperglycemic pharmacotherapy should be added.
- Timely adjustments to and/or additions of antihyperglycemic agents should be made to attain target A1C within 6 to 12 months.
- In patients with marked hyperglycemia (A1C ³9. 0%), antihyperglycemic agents should be initiated concomitantly with lifestyle management, and consideration should be given to either initiating combination therapy with 2 agents or initiating insulin.

Introduction:

- Lifestyle modification, including nutritional therapy and physical activity, should continue to be emphasized while pharmacotherapy is being used.
- As type 2 diabetes is characterized by insulin resistance and ongoing decline in beta cell function, glucose levels will likely worsen over time(1) and treatment must be dynamic.

Treatment Regimens:

- The initial use of combinations of sub maximal doses of anti hyperglycemic agents produces more rapid and improved glycemic control and fewer side effects compared to monotherapy at maximal doses (6-9).
- When combining antihyperglycemic agents with or without insulin, classes of agents that have different mechanisms of action should be used. Simultaneous use of agents from different classes but with similar mechanism of action (e. g. sulfonylureas and meglitinides) is currently untested and may be less effective at improving glycemia and is not recommended at this time.
- Symptomatic patients with high blood glucose and A1C levels require agents that lower blood glucose levels quickly(e. g. sulfonylurea).
- The recommendation to use metformin as the initial agent in most patients is based on its effectiveness in lowering blood glucose, its relatively mild side effect profile and its demonstrated benefit in overweight patients(52)
- In patients for whom hypoglycemia is a particular concern, agents associated with less hypoglycemia are preferred.

- A combination of oral antihyperglycemic agents and insulin often effectively controls glucose levels.
- When insulin is added to oral antihyperglycemic agents, a single injection of intermediate-acting (NPH) (6,59) or an extended longacting insulin analogue(insulin glargine or insulin detemir) (19) may be added. This approach may result in better glycemic control with a smaller dose of insulin (60) and may induce less weight gain and less hypoglycemia than that when oral agents are stopped and insulin is used alone (33).
- The addition of bedtime insulin to metformin therapy leads to less weight gain than insulin plus a sulfonylurea or twice daily NPH insulin (16).
- The addition of TZD to insulin in carefully selected patients improves glycemic control and reduces insulin requirements (61). Such combination can result increased weight, fluid retention and, in few patients, CHF.
- As type 2 diabetes progresses, doses of basal insulin (intermediate acting or long acting analogues) will need increasing pre-prandial insulin (short acting or rapid acting analogues) may be required.

Recommendation:

R1- In people with type 2 diabetes, if glycemic targets are not achieved using lifestyle management within 2 to 3 months, antihyperglycemic agents should be initiated. Level 1

R2 - In the presence of hyperglycemia (A1C ≥ 7%), metformin should be initiated concomitantly with lifestyle management, and consideration should be given to initiating combination therapy with 2 agents. (Level 3) ?

R3 - If glycemic targets are not attained when a single antihyperglycemic agent is used initially, another antihyperglycemic agent from a different class should be added. The lag period before adding other agents should be kept to a minimum, taking into account the characteristics of the different agents. Additions of antihyperglycemic agents should be made in order to attain target A1C within 6 to 12 months. (Level 3)

R4 - Pharmacological treatment regimens should be individualized taking into consideration the degree of hyperglycemia and the properties of the antihyperglycemic agents including: effectiveness in lowering blood glucose, durability of glycemic control, side effects, contraindications, risk of hypoglycemia, presence of diabetes complications or co-morbidities, and patient preferences. (Level 3)

R5 - Metformin should be the initial drug used in both overweight patients, and non-overweight patients. Level 1

Metformin:

R6 - Step up metformin therapy gradually over weeks to minimise risk of gastrointestinal side effects. Consider a trial of extended absorption metformin tablets where gastrointestinal Tolerability prevents continuation of metformin therapy. (Level 1)

R7 - Continue with metformin if blood glucose control remains or becomes inadequate, and another oral glucose-lowering medication (usually a sulfonylurea) is added.

R8 - Other classes of antihyperglycemic agents, including insulin, should be added to metformin, or used in combination with each other, if glycemic targets are not met.

R9 - Review the dose of metformin if the serum creatinine exceeds 130 micromol/l or the eGFR is below 45 ml/minute/1.73 m2.

R10 - Stop the metformin if the serum creatinine exceeds 150 micromol/l or the eGFR (Estimated Glomerular Filtration Rate) is Below 30ml/minute/1.73 m2.

R11 - Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45 ml/minute/1.73 m2.

R12 - The benefits of metformin therapy should be discussed with a person with mild to moderate liver dysfunction or cardiac impairment so that:
- due consideration can be given to the cardiovascular-protective effects of the drug.
- an informed decision can be made on whether to continue or stop the metformin.

Insulin Secretagogues:

R 3 - Consider a sulfonylurea (Insulin secretagogues) as an option for first-line glucose lowering-therapy if:
- the person is not overweight.
- the person does not tolerate or is contraindicated.
- a rapid response to therapy is required because of hyperglycaemic symptoms.

R14 - Add a sulfonylurea as second-line therapy when blood glucose control remains, or becomes, inadequate with metformin.

R15 - Continue with a sulfonylurea if blood glucose control remains, or becomes, inadequate and another oral glucose-lowering medication is added.

R16 - When drug concordance is a problem, offer a once daily, long-acting sulfonylurea.

R17- Educate a person being treated with an insulin secretagogue, particularly if renally impaired, about the risk of hypoglycaemia. (Level 1)

R18 - Consider offering a rapid-acting insulin secretagogue to a person with an erratic lifestyle.

Acarbose: (Level 1)

R19 - Consider acarbose as ad on therapy or for a person unable to use other oral glucose-lowering medications.

Thialozidendione:

R20 - Use Thialozidendione as monotherapy, combination therapy with metformin or a sulfonylurea, or as part of triple with metformin and a sulfonylurea, or in combination therapy with insulin. (Level 1)

- as monotherapy in patients (particularly overweight patients) inadequately controlled by diet and exercise for whom metformin is inappropriate because of contraindications or intolerance

- as dual oral therapy in combination with:
  - metformin in patients (particularly overweight patients) with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin
  - a sulfonylurea, only in patients who show intolerance to metformin or for whom metformin is contraindicated, with insufficient glycaemic control despite maximal tolerated dose of monotherapy with a sulfonylurea

- as triple oral therapy in combination with:
  - metformin and a sulfonylurea, in patients (particularly overweight patients) with insufficient glycaemic control despite dual oral therapy

Thialozidendione:

- is also indicated for combination with insulin in Type 2 diabetes with insufficient glycaemic control on insulin for whom metformin is inappropriate because contraindications or intolerance.

Insulin:

R21- When basal insuln is added to antihyperglycemic agents, long acting analogues (insulin detemir or insulin glargine) may be considered instead of NPH to reduce the risk of nocturnal hypoglycemia (Grade A, level 1A (71)). Level

When starting basal insulin therapy:
- continue with metformin and the sulfonylurea (and acarbose, if used)
- review the use of the sulfonylurea if hypoglycaemia occurs.

R22 - When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):
- continue with metformin
- continue the sulfonylurea initially, but review and discontinue if hypoglycaemia occurs.

R23 - Consider combining pioglitazone with insulin therapy for:
- a person who has previously had a marked glucose lowering response to thiazolidinedione therapy.
- a person on high-dose insulin therapy whose blood glucose is inadequately controlled.

Warn the person to discontinue pioglitazone if clinically significant fluid retention develops.

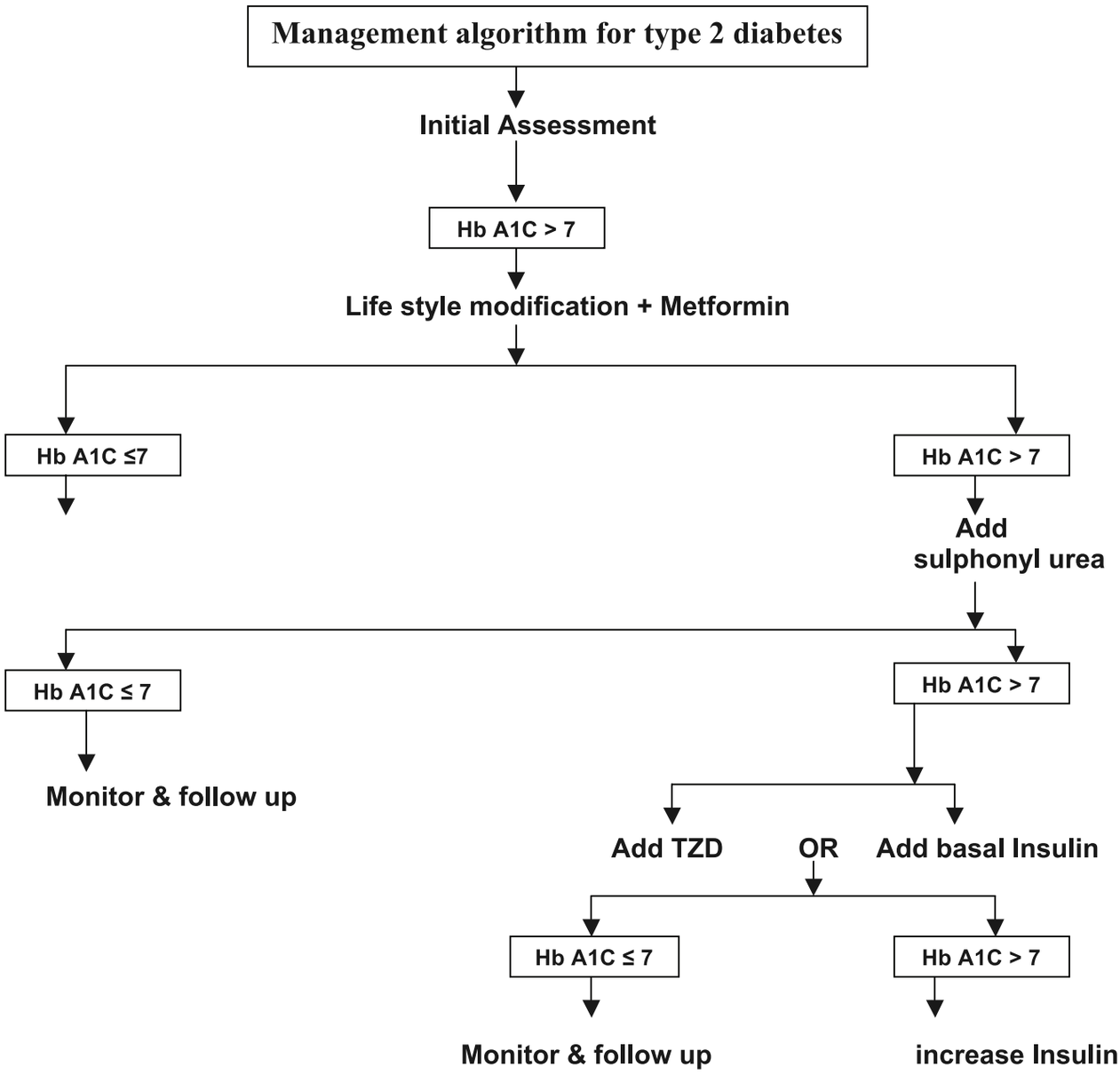
R24 -The following antihyperglycemic agents (listed in alphabetical order), should be considered to lower postprandial blood glucose levels:

a) Alph-glucosidase inhibitor. (Level 2)
b) premixed insulin analogues(i.e. biphasic insulin aspart and insulin lispro/protamine) instead of regular /NPH premixtures. (Level 1)
c) meglitinides (repaglinide, nateglinide) instead of sulfonylureas. (Level 2)
d) rapid-acting insulin analogues(aspart, gluslisine, lispro) instead of short-acting insulin (i.e. regular insulin). (level2)

All individuals with type 2 diabetes currently using or starting therapy with insulin or insulin secretagogues should be counseled about the recognition and prevention of drug-induced hypoglycemia. (Level 3)

Add an agent best suited to the individual based on the advantages / disadvantages listed below and the information in the text.				
Class	Drug (brand name)	Expected decrease in A1C with monotherapy	Hypo-glycemia	Other disadvantages
Alpha-glucosidase inhibitor	Acarbose (Glucobay) (10-12)	↓	Negligible rsik as monotherapy	• Not recommended as initial therapy in people with mild hyperglycemia (A1C≥9. 0%) Often used in combination with other oral antihypergtycemic agents. Weight neutral as monotherapy. • G I (gastrointiestinal) lside effects.
Incretin agent (13-15)	Dpp -4 inhibitor Sitagliptin (lanuvia)	↓ to ↓↓	Negligible risk as monotherapy	• Weight neutral. • Improved postprandial control. • Newer agent with unknown long-term safety.
Insulin (3. 16-22)	Rapid acting analogues Aspart (NovoRapid) Glulisine (Apidra) Lispro (Humakg) Short acting Regular (humulin-R. Novolinge Toronto) Intermediate acting NPH (humulin-N. Novolinge NPH) Long acting basal analogues Detemir (levemir) Glargine (lantus) Premixed Premixed regular-NPH (humulin 30/70; novolin ge 30/70, 40/60, 50/50) Bip hasic insulin aspart (navomix 30) Insulin isprc/lispro prctamin (humalog mix25. mix50)	Depends on regimen, but up to ↓↓↓	Significant risk	• Potentially greates A1C reduction and on maximal dose. • Numerous formulations and delivery systems (including subcutaneous allov for regimen flexibility). • hypoglycemia risk highest with regular and NPH insulin. •When initiating insulin, consider adding bedtime intermediate - acting insulin or long-acting insulin analogue to daytime oral antihyperglycemic agents (although other regimens can be used). • intensive insulin therapy regimen recommended if above fails to attain glycemic targets. • increased risk of weight gain relative to sulfonylueas and metformin.
insulin secretagogues:	Sulfonylureas Gliclazide (diamicron, diamacron MR generic) (22. 24)	↓↓	Minimal moderate risk	• relatively rapid BG lowering response. • All insulin secretagogues reduce glycemia similarly (except nateglinide, which is less effective). • postprandial glycemia is especially reduced by natoglinide and repaglinide. • hypoglycemia and weight gain are especially common with glyburide. • consider using other class (es) of antihyperglycemic agents first in patients at high risk of hypoglycemia (e. g. the elderly, renal/ hepatic failure). • if a sulfonylurea must be used in such individuals, is associated with the lowes incidence of hypoglycemia (32)and glimepinide is associated with less hypo glycemia than glybunide(27). • nateglinide and repaglinide are associated with less hypoglyoemia in the context of missed meals.
	Gimepiride (Amaryl) (25-27)	↓↓	Moderate risk	
	Glyburide (Diabeta, Euglucon, generic) (3)	↓↓	Significant risk	
	Meglitinides Naterglinide (starlix) (28) Repaglinide (gluconam) (29-31)	↓ ↓↓	Mnmal lmodarate risk Mnmal lmodarate risk	

Class	Drug (brand name)	Expected decrease in A1C with monotherapy	Hypo-glycemia	Other disadvantages
Metformin	Glucophage, Glumetza, generic (33, 34)	↓↓	Negligible risk as monotherapy	• Improved cardiovascular outcomes in overweight subjects. • contraindicated if Cr CL/ eGFR <30 mL/min or hepatic failure. • caution if Cr Cl/eGFR < 60 mL/min. • weight neutral as monotherapy, promotes less weight gain when combined with other antihyperglycemic agents including insulin. • GI side effects.
TZDs (35, 45)	Pioglitazone (Actos) Rosiglitazone (Avandia)	↓↓	Negligible risk as monotherapy	• larger duration of glycemic control with monotherapy compared to metformin or glyburide. • mild BP lowering. • between 6 and 12 weeks required to achieve full glycemic effect. • weight gain (waist – to – hip ration not increased) • may induce edema and or heart failure. • avoid in patients with heart failure. • higher rates of heart failure when combined with insulin. • rare occurrence of macular edema. • rare occurrence of fractures in females (44, 46). • suggestion of increased risk of cardiovascular events with rosiglitazone awaits further studies.



NB: TZD =thiazolidinediones (e. g: rosiglitazone, pioglitazone)

Glucose control: insulin therapy

Oral agent combination therapy with insulin

Key Message

- In patients not reaching glycemic target, insulin should be given in combination with oral therapy.
- The introduction of insulin should not be unduly delayed.

Introduction:

- People with Type 2 diabetes with inadequate blood glucose control on oral agents have the pathogenetic problems which caused their diabetes, and still have significantly preserved islet B-cell function.

Clinical Question:

Which oral agents, singly or in combination, should be continued when starting insulin therapy.

Recommendation:

R1 - When starting basal insulin therapy:
1. continue with metformin and the sulfonylurea (and acarbose, if used)
2. review the use of the sulfonylurea if hypoglycaemia occurs. (Level 1)

R2 - When starting pre-mixed insulin therapy (or mealtime plus basal insulin regimens):
1. continue with metformin
2. continue the sulfonylurea initially, but review and discontinue if hypoglycaemia occurs. (Level 1)

R3 - Consider combining pioglitazone with insulin therapy for:
1. a person who has previously had a marked glucose lowering response to thiazolidinedione therapy.
2. a person on high-dose insulin therapy whose blood glucose is inadequately controlled. (Level 1)
3. Warn the person to discontinue pioglitazone if clinically significant fluid retention develops.

Insulin therapy:

Introduction:

Blood glucose control deteriorates inevitably in most people with Type 2 diabetes over a period of years, due to a waning of insulin production. (55)
In these circumstances oral glucose-lowering therapies can no longer maintain blood glucose control to targets and insulin replacement therapy becomes inevitable.
Insulin deficiency is however only relative, not absolute, as there is still considerable endogenous insulin secretion occurring in response to the insulin insensitivity that is also usual in people with Type2 diabetes.

Clinical Question:

Which of the various pharmaceutical types of insulin, and in what combinations, are optimal for the management of Type 2 diabetes?

Recommendations:

R1 - When other measures no longer achieve adequate blood glucose control (to HbA 1c <7 % or other higher level agreed with the individual), discuss the benefits and risks of insulin therapy. (Level 1).

R2 - When starting insulin therapy, use a structured programme employing active insulin dose titration that include:
- Structured education.
- Frequent self monitoring.
- Dietary understanding.
- Management of hypoglycaemia.
- Management of acute changes in plasma glucose control.
- Support from an appropriately and experienced health care professional. (Level 1)

R3 - Initiation of insulin therapy should be from a choice of a number of insulin types and regimens.
1. Preferably begins with human NPH insulin taken at bed time or twice daily according to need.
2. Consider using a long-acting insulin analogue (insulin glargine) for a person who falls into one of the following categories.
   a) Those who require assistance from a carer or health care professional to administer their insulin injections.
   b) Those whose lifestyle is significantly restricted by recurrent hypoglycaemic episodes. (Level 1)
3. Consider twice-daily biphasic human insulin (pre-mix) regimens in particular where HbA1c is elevated above 9.0%. (Level 1)
4. Consider pre-mixed preparations of insulin analogues rather than pre-mixed human insulin preparations when:
   a) Immediate injection before meal is preferred, or
   b) Hypoglycaemia is a problem, or
   c) There are marked post prandial blood glucose excursions. (Level 1)

R4 - Monitor a person using a basal insulin regimen (NPH or a long-acting insulin analogue [insulin glargine]) for the need for mealtime insulin (or a pre-mixed insulin preparation). If blood glucose control remains inadequate (not to agreed target levels without problematic hypoglycaemia), move to a more intensive ,meal time plus basal insulin regimen based on the option of human or analogue insulins.

R5 - Monitor a person using pre-mixed insulin once or twice daily for the need for a further pre-prandial injection or for an eventual change to a meal time plus basal insulin regimen, based on human or analogue insulins, if blood glucose control remains inadequate.

Insulin Delivery Devices:

Recommendations

R1- Offer education to a person who require insulin about using an injection device (usually a pen injector and cartridge or a disposable pen) that they and/or their care giver find easy to use. (Level 1)

R2 - Appropriate local arrangements should be in place for the disposable of sharps. (Level 1)

R3 - If a person has a manual or visual disability and requires insulin, offer a device o adaptation that:
- Takes into account his or her individual needs.
- He or she can use successfully. (Level 1)

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Anti-platelet therapy for people with diabetes:

Key Message

- The first priority in the prevention of macrovascular complications should be reduction of cardiovascular (CV) risk through a comprehensive, multifaceted approach, integrating both lifestyle and pharmacologic measures.
- Low-dose acetylsalicylic acid therapy may be considered in people with stable CVD.
- The decision to prescribe antiplatelet therapy for primary prevention of CV events, however, should be based on individual clinical judgment

Introduction:

- In addition to traditional risk factors for CVD such as smoking, hypertension, hyperglycemia and dyslipidemia, atherosclerosis in people with diabetes can be accelerated by a pro-coagulant state.
- Individuals with diabetes have a variety of alterations in platelet function that can predispose them to increased platelet activation and thrombosis, including increased turnover (1), enhanced aggregation (2) and increased thromboxane synthesis (3). The efficacy of anti-platelet agents in people with diabetes also appears to be reduced, Antiplatelet therapy now has an established role in the management of people at high risk of cardiovascular (CV) events.
- People with Type 2 diabetes are known to have CV risk higher than matched populations after allowance for other CV risk factors, and in some studies as high as those without diabetes who have had a cardiovascular event (CVD).
- The increasing occurrence of Type 2 diabetes in younger people raises the additional question of the use of anti-platelet therapy in those who CV risk may be not be very high.

Clinical Question:

- Does aspirin prevent vascular disease in people with diabetes type 2?

Recommendations:

R1- Offer low-dose aspirin, 75 mg daily, to a person who is 50 years old or over if blood pressure is below 145/90 mmHg.

R2 - Offer low-dose aspirin, 75 mg daily, to a person who is under 50 years old and has significant other cardiovascular risk factors (features of the metabolic syndrome, strong early family history of cardiovascular disease, smoking, hypertension, extant cardiovascular disease, microalbuminuria) if blood pressure is below 145/90 mmHg.

R3 - Clopidogrel (75mg) should be used instead of aspirin only in those with clear aspirin intolerance (except in the context of acute cardiovascular events and procedures).

Identification of Individuals at High Risk of Coronary Events:

Key Message

- Diabetes increases the prevalence of coronary artery disease (CAD) approximately 2- to 3-fold compared to individuals without diabetes.
- People with diabetes develop CAD 10 to 12 years earlier than individuals without diabetes.
- When a person with diabetes has an acute coronary event, the short- and long-term outcomes are considerably worse than for the person without diabetes.
- People with diabetes should be considered to have a high 10-year risk of CAD events if
  - 45 years and male, or 50 years and female.
  - For the younger person (male <45 years or female <50 years) with diabetes, the risk of developing CAD may be assessed from the evaluation of risk factors for CAD (both classical and diabetes related).
- When assessing the need for pharmacologic measures to reduce risk in the younger person with diabetes, it is important to consider his or her high lifetime risk of developing CAD.

Introduction:

- Goals of the screening are to improve life expectancy and quality of life by preventing MI and heart failure through the early detection of coronary artery disease (CAD).
- The majority (65 to 80%) of people with diabetes will die from heart disease (2, 3). Compared to people without diabetes, people with diabetes (especially women) are at higher risk of developing heart disease, and at an earlier age. A high proportion of deaths occur in patients with no prior signs or symptoms of cardiovascular disease (CVD). Furthermore, people with diabetes have a high prevalence of silent myocardial ischemia, and almost one-third of myocardial infarctions (MIs) occur without recognized or typical symptoms (silent MIs) (4).

Clinical Question:

- How we can CHD risk for patients with type 2 diabetes be calculated (1)?

Recommendations:

No.	Recommendations	Grade
R1	Assessment for CAD risk should be performed periodically in people with diabetes and should include • CV history (dyspnea, chest discomfort, past history of a CVD event) • Lifestyle (smoking, sedentary lifestyle, poor eating habits) • Duration of diabetes • Sexual function history • Abdominal obesity • Lipid profile • Blood pressure • Reduced pulses or bruits • Glycemic control • Presence of retinopathy • Estimated glomerular filtration rate and random albumin to creatinine ratio • Periodic electrocardiograms as indicated	Level 3
R2	The following individuals with diabetes should be considered at high risk for CV events: • Men aged ≥45 years, women aged >= 50 years • Men <45 years and women <50 years with one or more of the following: • Macrovascular disease (e. g. silent myocardial infarction or ischemia, evidence of peripheral arterial disease, carotid arterial disease or cerebrovascular disease) • Microvascular disease (especially nephropathy and retinopathy) • Multiple additional risk factors, especially with a family history of premature coronary or cerebrovascular disease in a first-degree relative • Extreme level of a single risk factor (e. g. LDL-C >200 mg/dL, systolic BP >180 mm Hg) • Duration of diabetes >15 years with age >30 years	Level 3
R3	In the following individuals, in addition to CAD risk assessment, a baseline resting ECG should be performed in: • All individuals >40 years of age • All individuals with duration of diabetes >15 years • All individuals (regardless of age) with hypertension, proteinuria, reduced pulses or vascular bruits. A repeated resting ECG should be performed every 2 years in people considered at high risk for CV events	Level 3
R4	Persons with diabetes should undergo investigation for CAD by exercise ECG stress testing as the initial test in the presence of the following: • Typical or atypical cardiac symptoms (e. g. unexplained dyspnea, chest discomfort) • Resting abnormalities on ECG (e. g. Q waves) • Peripheral arterial disease (abnormal ankle-brachial ratio) • Carotid bruits • Transient ischemic attack • Stroke	Level 3
R5	Pharmacologic stress echocardiography or nuclear imaging should be used in individuals with diabetes in whom resting ECG abnormalities preclude the use of exercise ECG stress testing (e. g. LBBB or ST-T abnormalities). In addition, individuals who require stress testing and are unable to exercise should undergo pharmacologic stress echocardiography or nuclear imaging.	Level 3
R6	Individuals with diabetes who demonstrate ischemia at low exercise capacity (<5 metabolic equivalents (METs)) on stress testing should be referred to a cardiac specialist.	Level 3

* Note: Some of the above investigations test (exercise ECG stress testing & pharmacologic stress echocardiography or nuclear imaging) can be achieved by referral to secondary care and feedback can be collected at the primary care.

When to Refer:

1 - Persons with diabetes should undergo investigation for CAD by exercise ECG stress testing as the initial test [Grade D, Consensus] in the presence of the following:

- Typical or atypical cardiac symptoms (e.g. unexplained dyspnea, chest discomfort) [Grade C, Level3].
- Resting abnormalities on ECG (e. g. Q waves) [Grade D, Consensus].
- Peripheral arterial disease (abnormal ankle-brachial ration) [Grade D, Level 4].
- Carotid bruits [Grade D, Consensus].
- Transient ischemic attack [Grade D, Consensus].
- Stroke [Grade D, Consensus].

2 - Pharmacologic stress echocardiography or nuclear imaging shoud be used in individuals with diabetes in whom resting ECG abnormalities preclude the use of exercise ECG stress testing (e. g. LBBB or ST-T abnormalities) [Grade D, Consensus]. In addition, individual who require stress testing and are unable to exercise should undergo pharmacologic stress echocardiography or nuclear imaging [Grade C, Level 3]

3 - Individuals with diabetes who demonstrate ischemia at low exercise capacity (< 5 metabolic equivalents [METs] on stress testing should be referred to a cardiac specialist [Grade D, Consensus].

Treatment of Hypertension:

Key Message

- In the prevention of diabetes-related complications, vascular protection is the first priority, followed by control of hypertension in those whose blood pressure (BP) levels remain above target, then nephroprotection for those with proteinuria.
- People with diabetes and elevated BP should be aggressively treated to achieve a target BP of <130/80 mm Hg to reduce the risk of both micro- and macrovascular complications.
- Most people with diabetes will require more than one BP lowering medications to achieve BP targets.

Introduction:

Most people with diabetes will develop hypertension, People with Type 2 diabetes are at high cardiovascular (CV) risk, high risk of diabetes eye damage, and high risk of renal disease.

These adverse outcomes are known to be reduced by improved blood pressure (BP) control, which can be used to lower the risk of stroke, MI, blindness and renal failure (2).

Some other forms of diabetes microvascular damage, including peripheral nerve damage, are known to be associated with higher BP (3). BP lowering is likely to be highly cost-effective in people with Type 2 diabetes, more than in the general population.

Hypertension is a treatable risk factor. Recent studies suggest that a delay in the recognition and management of hypertension, particularly in high-risk individuals, increases their risk of CV morbidity and mortality (4-6).

Most people with diabetes will require multiple BPlowering medications to achieve BP targets.

Diagnosis based upon the average of two or more properly measured readings at each of two or more visits after an initial screening.

The following classification is used according to:

European society of Hypertension classification of blood pressure:

Category	Systolic		Diastolic
Optimal	<120	And /or	<80
Normal	<130	And /or	<85
High - Normal	130-139	And /or	85-89
Grade 1 (mild hypertension)	140-159	And /or	90-99
Grade 2 (moderate hypertension)	160-179	And /or	100-109
Grade 3 (severe hypertension)	>180	And /or	>110
Isolated Systolic Hypertension (ISH)	>140	And	>90

The category pertains the highest risk blood pressure * ISH = Isolated systolic Hypertension J Hyper tens 2007 25 1105-87.

JNc (American) Classification of Blood Pressure:

Category	Systolic		Diastolic
Optimal	<120	And /or	<80
Normal	<130	And /or	<85
High - Normal	130-139	And /or	85-89
Stage 1 (mild hypertension)	140-150	And /or	90-99
Stage 2 (moderate to severe hypertension)	>160	And /or	100-109
Isolated Systolic Hypertension (ISH)	>140	And /or	100-109

The category pertains the highest risk blood pressure * ISH = Isolated systolic Hypertension Jama 2003 289 2560-72.

The Therapeutic Goals:

- In the prevention of diabetes-related complications, vascular protection is the first priority using comprehensive approach for risk reduction followed by control of hypertension in those whose blood pressure (BP) levels remain above target, then nephroprotection for those with proteinuria.
- People with diabetes and elevated BP should be aggressively treated to achieve a target BP of <130/80 mm Hg to reduce the risk of both micro- and macrovascular complications.

Recommendations:

No.	Recommendations	Grade
R1	Persons with diabetes and hypertension should be treated to attain systolic BP <130 mm Hg *[Grade C, Level 3]* and diastolic BP <80 mm Hg. These target BP levels are the same as the BP treatment thresholds.	*Level 2*
R2	Lifestyle interventions to reduce BP should be considered, including achieving and maintaining a healthy weight and limiting sodium and alcohol intake. Lifestyle recommendations should be initiated concurrently with pharmacological intervention to reduce BP.	*Level 3*
R3	For persons with diabetes and normal urinary albumin excretion and without chronic kidney disease, with BP >= 130/80 mm Hg, despite lifestyle interventions: • Any of the following medications (listed in alphabetical order) is recommended, with special consideration to ACE inhibitors and ARBs given their additional renal benefits. • ACE inhibitor. • ARB . • DHP CCB (dihydropyridonine calcium channel blocker). • Thiazide-like diuretic. • If the above drugs are contraindicated or cannot be tolerated, a cardio-selective beta blocker or non-DHP CCB can be substituted. • Additional antihypertensive drugs should be used if target BP levels are not achieved with standard-dose monotherapy. • Add-on drugs should be chosen from the first-line choices listed above (ACE & ARB combination is not recommended).	*Level 3* *Level 2* *Level 1* *Level 3*
R4	For people with diabetes and albuminuria (persistent albumin to creatinine ratio [ACR] ≥ 2. 0 mg/mmol in men and ≥ 2. 8 mg/mmol in women), an ACE inhibitor or an ARB is recommended as initial therapy. If BP remains ≥ 130/80 mm Hg despite lifestyle interventions and the use of an ACE inhibitor or ARB, additional antihypertensive drugs should be used to obtain target BP.	*Level 2*
R5	For persons with diabetes and a normal urinary albumin excretion rate, with no chronic kidney disease and with isolated systolic hypertension, a long-acting DHP CCB is an alternative initial choice to an ACE inhibitor, an ARB. or a thiazide-like diuretic.	*Level 2*
R6	Alpha-blockers are not recommended as first-line agents for the treatment of hypertension in persons with diabetes.	*Level 1*
R7	A calcium channel blocker should be the first-line blood pressure-lowering therapy for a woman for whom, after an informed discussion, it is agreed there is a possibility of her becoming pregnant (ACE and ARB are absolutecontraindication in pregnancy).	*Level 2*

When to Refer:

Urgent assessment and treatment is required for people with:

1- Accelerated (malignant) hypertension - blood pressure (BP) ≥ 180/110 mmHg with signs of papilloedema and/or retinal hemorrhage.

2- Suspected phaeochromcytoma (possible signs include labile or postural hypotension.

3- Impending cardiovascular complications (e.g. transient ischemic attack, left ventricular failure). Consider referral if:

- The person is suspected to have a secondary causes of hypertension.
- Investigation of suspected secondary causes of hypertension.
- Ambulatory BP monitoring is required in a person with suspected white coat hypertension.
- The person has sever hypertension (greater than 220/120 mmHg), but has no signs of accelerated hypertension.
- Poorly controlled blood pressure (BP) when already on four antihypertensive drugs, for further investigation of the cause and management of hypertension.

4- For hospital initiation of an angiotensin-converting enzyme inhibitor or angiotensin-II receptor antagonist in high-risk groups.

Dyslipidemia:

Key Message

- The beneficial effects of lowering low-density lipoprotein (LDL-C) with statin therapy apply equally well to people with diabetes as to those without.
- The primary target for most people with diabetes is an LDL-C of ²2. 0 mmol/L, which is generally achievable with statin monotherapy.
- The secondary goal is a total cholesterol/high-density lipoprotein cholesterol ratio of <4. 0. This is often more difficult to achieve than the primary LDL-C target, and may require improved glycemic control, intensification of lifestyle changes (weight loss, physical activity, smoking cessation) and, if necessary, pharmacologic interventions.

Introduction:

- Diabetes is associated with a high risk of vascular disease (2- to 4-fold greater than that of individuals without diabetes), with cardiovascular disease (CVD) being the primary cause of death among people with type 1 or type 2 diabetes(1-3).
- Aggressive management of all CV risk factors, including dyslipidemia, is therefore generally necessary (4). The most common lipid pattern in people with type 2diabetes consists of hypertriglyceridemia (hyper-TG), low high-density lipoprotein cholesterol (HDL-C) and normal plasma concentrations of low-density lipoprotein cholesterol (LDL-C).
- Screening should be done by fasting lipid profile (total cholesterol [TC], HDL-C, TG and calculated LDL-C) should be conducted at the time of diagnosis of diabetes, and then every 1 to 3 years, as clinically indicated.

Management of Blood Lipid Levels (Tables)

Table 1. Lipid targets for individuals with diabetes at high risk for CVD

Index	*Target value*
Primary target: LDL-C	<= 2. 0 mmol/L*
Secondary target:TC/HDL-C ratio	<4. 0

Clinical judgement should be used to decide whether additional LDL-C lowering is required for individuals with an on treatment and withLDL-C of 2. 0 to 2. 5 mmol/L
CVD = cardiovascular disease
HDL-C = high-density lipoprotein cholesterol
LDL-C = low-density lipoprotein cholesterol
TC = total cholesterol

Table 2A. First-line therapy to achieve primary lipid target of LDL-C ²2. 0 mmol/L		
*Statins**		
Generic name†	Trade name	Considerations
Atorvastatin	Lipitor	▪ Drugs of choice to lower LDL-C. ▪ At higher doses, modest TG-lowering effects and HDL-C–raising effects
Fluvastatin	Lescol	
Lovastatin	Mevacor and generic	
Pravastatin	Pravachol and generic	
Rosuvastatin	Crestor	
Simvastatin	Zocor and generic	

Prevention of statin-induced myopathy requires attention to factors that increase risk, such as age >80 years (especially women); small body frame and frailty; higher dose of statin; multisystem diseases (e. g. chronic renal insufficiency due to diabetes); multiple medications; hypothyroidism; preoperative periods; alcohol abuse; excessive grapefruit juice consumption; and specific concomitant medications such as fibrates (especially gemfibrozil) (refer to specific statin package inserts for others) Listed in alphabetical order:

HDL-C = high-density lipoprotein cholesterol
LDL-C = low-density lipoprotein cholesterol
TG = triglyceride

Recommendation:

Comments:

The measurement of apoB is not arelevant recommendation for primary care physicians:

No.	Recommendations	Grade
R1	People with type 1 or type 2 diabetes should be encouraged to adopt a healthy lifestyle to lower their risk of CVD. This entails adopting healthy eating habits, achieving and maintaining a healthy weight, engaging in regular physical activity and smoking cessation.	Level 3
R2	Fasting lipid levels (TC, HDL-C, TG and calculated LDLC) should be measured at the time of diagnosis of diabetes and then every 1 to 3 years as clinically indicated. More frequent testing should be performed if treatment for dyslipidemia is initiated.	Level 3
R3	Individuals at high risk of a vascular event should be treatedwith a statin to achieve an LDL-C ≤ 2. 0 mmol/L *[Grade A, Level 1, Level 2]*. Clinical judgement should be used as to whether additional LDL-C loweringis required for those with an on-treatment LDL-C of 2. 0 to 2. 5 mmol/L].	Level 1
R4	The primary target of therapy is LDL-C *[Grade A, Level 1, Level 2]*, the secondary target isTC/HDL-C ratio.	Level 1
R5	If the TC/HDL-C ratio is ≥ 4. 0, consider strategies to achieve a TC/HDL-C ratio <4. 0 *[Grade D, Consensus]*, such as improved glycemic control, intensification of lifestyle modifications (weight loss, physical activity, smoking cessation) and, if necessary, pharmacologic interventions.	Level 3
R6	If serum TG is >10. 0 mmol/L despite best efforts at optimal glycemic control and other lifestyle interventions (e. g. weight loss, restriction of refined carbohydratesand alcohol), a fibrate should be prescribed to reduce the risk of pancreatitis . For those with moderate hyper-TG (4. 5 to 10. 0 mmol/L), either a statin or a fibrate can be attempted as first line therapy, with the addition of a second lipidloweringagent of a different class if target lipid levelsare not achieved after 4 to 6 months on monotherapy.	Level 3
R7	For individuals not at target(s) despite opti mally dosedfirst-line therapy as described above, combination therapy can be considered. Although there are as yet no completedtrials demonstrating clinical outcomes in subjects receiving combination therapy, pharmacologic treatment options include: (listed in alphabetical order): • Statin plus ezetimibe. • Statin plus fibrate. • Statin plus niacin.	

Nephropathy:

Key Message

- Identification of chronic kidney disease (CKD) in diabetes requires screening for proteinuria, as well as an assessment of renal function.
- All individuals with CKD should be considered at high risk for cardiovascular events, and should be treated to reduce these risks.
- The progression of renal damage in diabetes can be slowed through intensive glycemic control and optimization of blood pressure.
- Progression of diabetic nephropathy can be slowed through the use of medications that disrupt the renin-angiotensin-aldosterone system.

Introduction:

- Chronic kidney disease (CKD) is one of the most common and potentially devastating complications of diabetes.
- 50% of people with diabetes have CKD, and CKD associated with diabetes is the leading cause of kidney failure.
- CKD in diabetes can be due to classic diabetic nephropathy or other forms of kidney damage.
- Classic diabetic nephropathy progresses from subclinical disease to the earliest clinically detectable stage characterized by persistent proteinuria (Figure 1).

Table. 1 Stages of classic diabetic nephropathy according to urinary albumin level

Stage of nephropathy	Urine dipstick for protein	Urine ACR mg/mmol	24-urine collection for albumin* (mg/day)
Normal	Negative	<2. 0 (men) <2. 8 (women)	<30
Micro- albumin	Negative	2. 0-20. 0 (men) 2. 8-28. 0(women)	30 – 300
Overt nephropathy (macroalbu- minuria)	positive	>20. 0(men) >28. 0(women)	>300

*Values are for urinary albumin, not total urinary protein, which will be higher than urinary albumin levels. ACR results may be elevated with conditions other than diabetic nephropathy.
ACR = albumin to creatinine ratio.

- The degree of proteinuria is characterized as either microalbuminuria (urinary albumin 30 to 300 mg/day) or overt nephropathy (urinary albumin >300 mg/day) (Table 1).
- Although diabetic nephropathy is common, as many as 50% of people with diabetes and significant renal dysfunction have normal urinary albumin levels with renal disease that is not related to classic diabetic nephropathy.
- For example, hypertensive nephrosclerosis and renovascular disease are common causes of CKD in people with diabetes.

Table 2 lists indicators that favor the presence of renovascular disease. The risk of

- end-stage renal disease in diabetes does not appear to vary significantly whether the kidney disease is related to diabetic nephropathy or alternative renal diagnoses.
- Thus, identification of CKD in diabetes requires screening for proteinuria, as well as an assessment of renal function.
- Regardless of the cause, the stage of kidney disease can be classified based on the level of renal function (Table 3). In the case of diabetes, the kidney damage associated with stage 1 or 2 CKD manifests as persistent albuminuria.

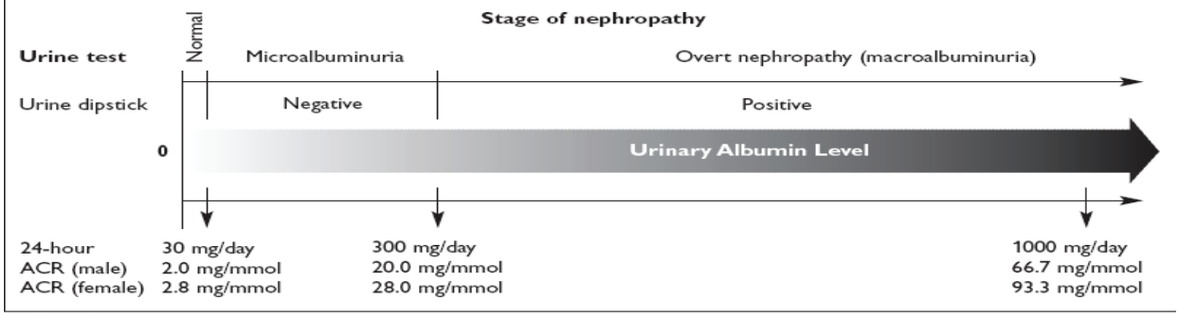
Factors favoring the presence of renovascular disease
○ Severe or refractory hypertension.
○ Low eGFR with normal or near –normal ACR.
○ Low or low –normal serum potassium (especially if patient is on an ACE inhibitor or an ARB).
○ Flank or abdominal bruits.
○ >30% rise in serum creatinine following initiation of an ACE inhibitor or an ARB.
○ Presence of aortic or peripheral arterial disease.
○ "Flash" pulmonary edema .
○ Asymmetric renal size on ultrasound.
○ Advanced hypertensive retinopathy.

ACE = angiotensin-converting enzyme
ACR = albumin to creatinine ratio
ARB = angiotensin II receptor antagonist
eGFR = estimated glomerular filtration rate

Table 2

- It is also important to recognize that people with CKD are among those at highest risk for cardiovascular (CV) morbidity and mortality, and that interventions to lower CV risk remain the most important priority in this population.

Figure 1. Stage of diabetic nephropathy by level of urinary albumin by various test methods



ACR = albumin to creatinine ratio

Clinical questions:

- How often and by what means to detect and confirm the possibility of diabetic renal disease, and the means of monitoring its progression.
- What are the means to reduce or stop such progression, In those with detected renal disease and the point at which to engage specialist renal management.

Recommendations:

R1 - The best possible glycemic control and, if necessary, intensive diabetes management should be instituted in people with type 2 diabetes for the prevention of onset and delay in progression to CKD. *Level 1*

R2 - In adults, screening for CKD in diabetes should be conducted using random urine ACR and a serum creatinine converted into an eGFR.
- Screening should be performed in individuals with type 2 diabetes at diagnosis of diabetes and yearly thereafter.
- Screening should be delayed when causes of transient albuminuria or low eGFR are present. *Level 3*

R3 - Repeat the test if an abnormal albumin: creatinine ratio is obtained (in the absence of proteinuria/UTI) at each of the next two clinic visits but within a maximum of 3–4 months. *Level 1*

R4 - Take the result to be confirming micro albuminuria if a further specimen (out of two more) is also abnormal (>2. 0 mg/mmol for men, >2. 8 mg/mmol for women). *Level 1*

R5 - Suspect renal disease, other than diabetic nephropathy and consider further investigation or referral when the albumin: creatinine ratio (ACR) is raised and any of the following apply: *Level 1*
- there is no significant or progressive retinopathy.
- blood pressure is particularly high or resistant to treatment.
- had a documented normal ACR and develops heavy proteinuria (ACR >100 mg/mmol).
- significant haematuria is present.
- the glomerular filtration rate has worsened rapidly.
- the person is systemically ill.

R6 - Adults with diabetes and persistent albuminuria (ACR >2. 0 mg/mmol in males, >2. 8 mg/mmol in females) should receive an ACE inhibitor or an ARB to delay progression of CKD, even in the absence of hypertension. *Level 1*

R7 - Discuss the significance of a finding of abnormal albumin excretion rate, and its trend overtime, with the individual concerned.

R8 - Have an informed discussion before starting an ACE inhibitor in a woman for whom there is a possibility of pregnancy, assessing the relative risks and benefits of the use of the ACE inhibitor.

R9 - Substitute an angiotensin II-receptor antagonist for an ACE inhibitor for a person with an abnormal albumin: creatinine ratio if an ACE inhibitor is poorly tolerated. *Level 1*

R10 - For a person with an abnormal albumin: creatinine ratio, maintain blood pressure below 130/80mmHg.

R11 - People with diabetes on an ACE inhibitor or an ARB should have their serum creatinine and potassium levels checked within 1 to 2 weeks of initiation or titration of therapy. *Level 1*
Potassium and serum creatinine levels should be checked in people with diabetes receiving an ACE inhibitor or ARB during times of acute illness. *Level 3*

R12 - The use of Thiazide-like diuretics should be considered in individuals with CKD and diabetes for control of sodium and water retention, hypertension or hyperkalemia. *Level 3.* Alternatively, furosemide can be substituted for or added to Thiazide-like diuretics for individuals who fail monotherapy with Thiazide-like diuretics or who have severe sodium and water retention or hyperkalemia. *Level 3*

R13 - Consideration should be given to stopping ACE inhibitor, ARB and/or diuretic therapy during times of acute illness (e. g. febrile illness, diarrhea), especially when intravascular volume contraction is present or suspected. *Level 3*
Women should avoid becoming pregnant when receiving ACE inhibitor or ARB therapy, as the use of medications that has been associated with adverse fetal outcomes.

R14 - A referral to a nephrologist or internist with an expertise in diabetic nephropathy should be considered if there is:
- A chronic, progressive loss of kidney function, if the eGFR is <30 mL/minute.
- If the ACR is persistently >60 mg/mmol.
- Or if the individual is unable to achieve BP targets or remain on renal-protective therapies due to adverse effects, such as hyperkalemia or
- A >30% increase in serum creatinine within 3 months of starting an ACE inhibitor or RRBs

When to Refer:

A referral to a nephrologist or internist with an expertise in diabetic nephropathy should be considered if there is:

- A chronic, progressive loss of kidney function, if the eGFR is <30 mL/minute.
- If the ACR is persistently >60 mg/mmol.
- Or if the individual is unable to achieve BP targets or remain on renal-protective therapies due to adverse effects, such as hyperkalemia or
- A >30% increase in serum creatinine within 3 months of starting an ACE inhibitor or RRBs.
- Conditions appropriate for GP care +/- 'virtual' nephrology support/advice .
  - o isolated microscopic haematuria (after negative urological evaluation where appropriate).
  - o isolated proteinuria with urine protein:creatinine ratio < 100 mg/mmol .
  - o known or suspected polycystic kidney disease with GFR > 60 ml/min/1. 73 m2.
  - o known reflux nephropathy in stage 1-3 without the above.
  - o all other stage 1-2 CKD.
  - o stable stage 3 or 4 CKD with no other indication for referral.

NICE suggest referral criteria for patients with CKD as (2).

- people with CKD in the following groups should normally be referred assessment:
  - o stage 4 and 5 CKD (with or without diabetes).
  - o higher levels of proteinuria (albumin creatine ratio (ACR) 70 mg/mmol or more approximately equivalent to protein creatinine ratio (PCR) 100mg/mmol or more or urinary protein excretion 1g/24 h or more)unless known to be due to diabetes and already appropriately treated.
  - o proteinuria (ACR 30 mg/mmol or more approximately equivalent to PCR 50mg/mmol or more urinary protein excretion 0, 5g/24 h or more) together with haematuria.
  - o rapidly declining estimate of GFR (eGFR) (more than 5ml /min/1. 73m 2 in 1 year, or more than 10 ml/min/1. 73m 2 within 5 year).
  - o hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic dose.
  - o people with or suspected of having rare or genetic causes of CKD suspected renal artery stenosis.

Screening:

- Table 4 l ists indicators that favor the diagnosis of either diabetic or n on diabetic nephropathy.
- In adults, screening is performed by measuring urinary albumin levels and estimating the level of kidney function (Figure 2).

Table 3. Stages of CKD of all types		
Stage	Qualitative / description	GFR (mL/min)
1	Kidney damage, normal GFR	90≥
2	Kidney damage, mildly decreased GFR	60 – 89
3	Moderately decreased GFR	30 – 59
4	Severely decreased GFR	15 – 29
5	End-stage renal disease	15 (or dialysis)<

CKD = chronic kidney disease
eGFR= estimated glomerular filtration rate
GFR = glomerular filtration rate

(Table 3)

Urine testing:

- A urine dipstick test should also be performed, either in the laboratory or at the point of care, as a screen for renal disease other than diabetic nephropathy.
- Twenty-four-hour urine collections are frequently performed incorrectly, are unpopular with patients and are unnecessary in routine diabetes care. However, a 24- hour collection can be useful when there is doubt about the accuracy of an eGFR, when screening for non albumin urinary proteins (e. g. multiple myeloma) or when estimating daily sodium intake in an individual with refractory edema or hypertension. Individuals should be counseled to discard the first morning urine on the day of collection, and then collect all subsequent urine for a 24-hour period, including the first morning urine of the next day.

Table 4	Clinical and laboratory factors favoring the diagnosis of clinical diabetic nephropathy or an alternate renal diagnosis
Favors diabetic nephropathy	Favors alternate renal diagnosis
•Persistent albuminuria •slow progression of disease •Low eGFR associated with overt proteinuria •Presence of other complications of diabetes •Known duration of diabetes >5 years	•Extreme proteinuria (>6 g/day) •Persistent hematuria (microscopic or macroscopic) or active urinary sediment. •Rapidly falling eGFR. •Low eGFR with little or on proteinuria. •Other complications of diabetes not present or relatively not as severe. •Known duration of diabetes≤ 5 years. •Family history of non-diabetic renal disease (e. g. polycystic kidney disease). •Signs or symptoms of systemic disease.

eGFR = estimated glomerular filtration rate.

(Table 4)

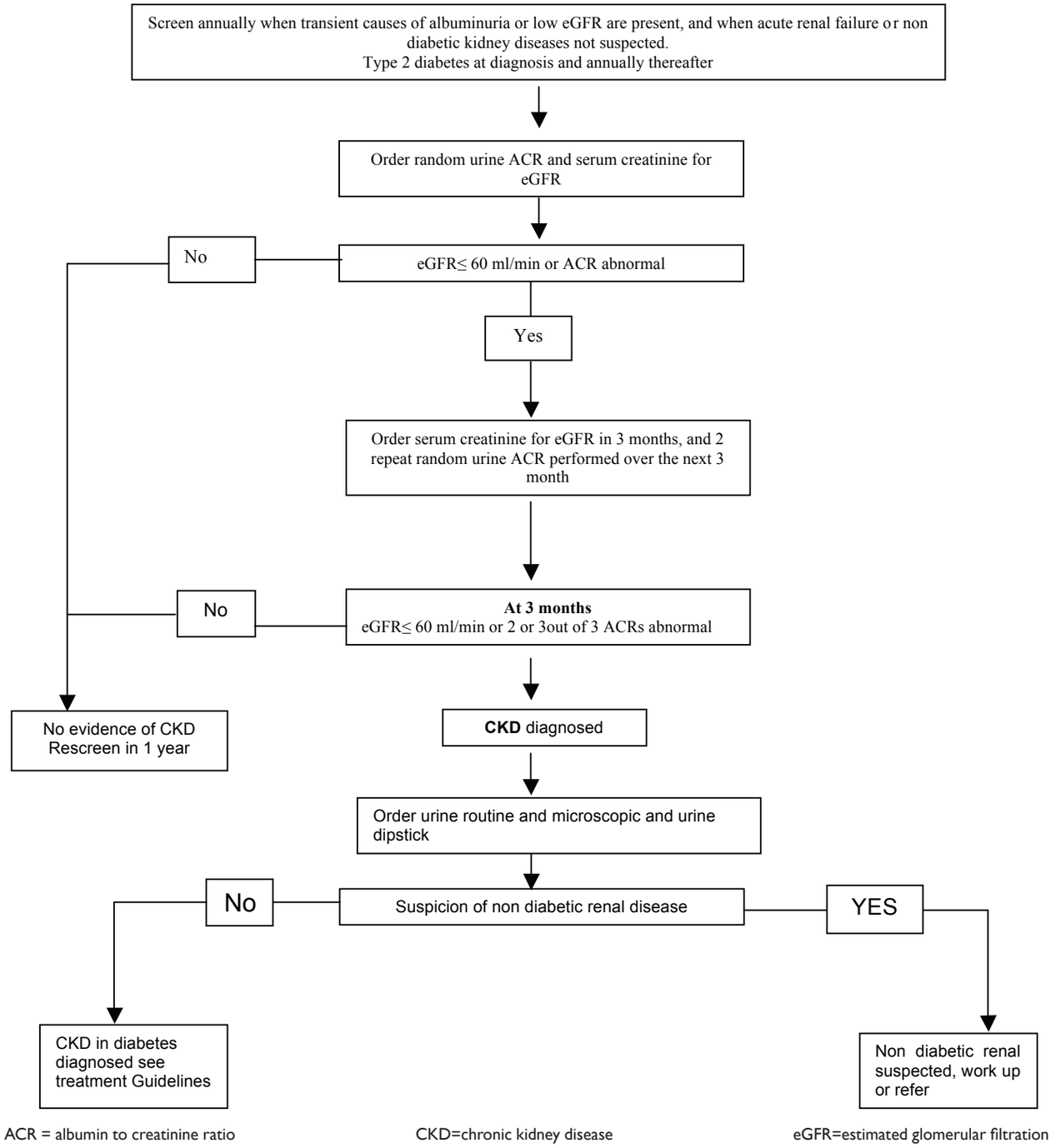

Screen annually when transient causes of albuminuria or low eGFR are present, and when acute renal failure or non diabetic kidney diseases not suspected.
Type 2 diabetes at diagnosis and annually thereafter
Order random urine ACR and serum creatinine for eGFR
No
eGFR≤ 60 ml/min or ACR abnormal
Yes
Order serum creatinine for eGFR in 3 months, and 2 repeat random urine ACR performed over the next 3 month
No
At 3 months
eGFR≤ 60 ml/min or 2 or 3out of 3 ACRs abnormal
No evidence of CKD
Rescreen in 1 year
CKD diagnosed
Order urine routine and microscopic and urine dipstick
No
Suspicion of non diabetic renal disease
YES
CKD in diabetes diagnosed see treatment Guidelines
Non diabetic renal suspected, work up or refer
ACR = albumin to creatinine ratio
CKD=chronic kidney disease
eGFR=estimated glomerular filtration

Figure 2

Retinopathy:

Key Message

- Screening is important for early detection of treatable disease.
- Screening intervals for diabetic retinopathy vary according to the individual's age and type of diabetes.
- Tight glycemic, BP, and lipid control reduces the onset and progression of sight-threatening diabetic retinopathy.
- Laser therapy reduces the risk of significant visual loss.

Introduction:

- Diabetic retinopathy is the most common cause of new cases of legal blindness in people of working age.
- Visual loss is associated with significant morbidity, including increased falls, hip fractures and a 4-fold increase in mortality.
- Diabetic retinopathy is clinically exclusively defined, diagnosed and treated based on the extent of retinal vascular disease.
- Forms of diabetic retinopathy are:
  1- back ground retinopathy.
    - Micro aneurysms.
    - Dot and blot hemorrhages.
    - Flame-shaped hemorrhages - Splinter hemorrhages that occur in the more superficial nerve fiber layer.
    - Retinal edema and hard exudates.
    - Cotton-wool spots.
    - Venous loops, venous beading.

  2 - Macular edema.
  3 - Nonproliferative diabetic retinopathy.
  4 - Proliferative diabetic retinopathy (neovascularisation).

Clinical Questions:

- How should people with developing retinopathy be selected for ophthalmological referral in time for optimal treatment?
- Whether preventative therapy other than good blood glucose, good blood pressure, and good blood lipid control can be useful in people with Type 2 diabetes?

Recommendations:

R1 - Arrange or perform eye screening at, or around, the time of diagnosis In all individuals of type 2 diabetes.
Arrange repeat of structured eye surveillance annually.

R2 - Explain the reasons for and success of eye surveillance systems to the individual and ensure attendance is not reduced by ignorance of need, or fear of outcome.

R3
- Use mydriasis with tropicamide when photographing the retina, after prior informed agreement following discussion of the advantages and disadvantages.
- Discussions should include precautions for driving.

R4 - Use:
- 7-Standard field, stereoscopic-colour fundus photography with interpretation by a trained reader (gold standard).
- Direct ophthalmoscopy or indirect slit-lamp fundoscopy through dilated pupil.
- Digital fundus photography.

R5 - Perform visual acuity testing as a routine part of eye surveillance programmes.

R6 - Repeat structured eye surveillance according to the findings by:
- routine review in 1 year, or
- earlier review, or
- referral to an ophthalmologist.

R7 - Arrange emergency review by an ophthalmologist for:
- sudden loss of vision
- rubeosis iridis
- pre-retinal or vitreous haemorrhage
- retinal detachment.

R8 - Arrange rapid review by an ophthalmologist for new vessel formation.

R9 - Refer to an ophthalmologist in accordance with the National Screening Committee criteria and timelines if any of these features is present:
- referable maculopathy.
- Exudate or retinal thickening within one disc diameter of the centre of the fovea
- Circinate or group of exudates within the macula (the macula is defined here as a circle centred on the fovea, with a diameter the distance between the temporal border of the optic disc and the fovea)
- Any microaneurysm or haemorrhage within one disc diameter of the centre of the fovea, only if associated with deterioration of best visual acuity to 6/12 or worse.
- Referable pre-proliferative retinopathy (if cotton wool spots are present, look carefully for the following features, but cotton wool spots themselves do not define pre-proliferative retinopathy):
  - Any venous beading.
  - Any venous loop or reduplication.
  - Any intraretinal microvascular abnormalities.
  - Multiple deep, round or blot haemorrhages.
  - Any unexplained drop in visual acuity.

When to Refer:

- Arrange emergency review by an ophthalmologist for:
  - Sudden loss of vision.
  - Rubeosis iridis.
  - Pre-retinal or vitreous hemorrhage.
  - Retinal detachment.
- Arrange rapid review by an ophthalmologist for new vessel formation.
- Refer to an ophthalmologist if any of these features is present:

1- Referable maculopathy.

2- Exudates or retinal thickening within one disc diameter of the centre of the fovea.

3- Circinate or group of exudates within the macula (the macula is defined here as a circle centered on the fovea, with a diameter the distance between the temporal border of the optic disc and the fovea).

4- Any micro aneurysm or hemorrhage within one disc diameter of the centre of the fovea, only if associated with deterioration of best visual acuity to 6/12 or worse.

5- Referable pre-proliferative retinopathy (if cotton wool spots are present, look carefully for the following features, but cotton wool spots themselves do not define pre-proliferative retinopathy):

- Any venous beading.
- Any venous loop or reduplication.
- Any intraretinal Microvascular abnormalities.
- Multiple deep, round or blot hemorrhages.
- Any unexplained drop in visual acuity.

Neuropathy:

Key Message

- Exposure to higher levels of glycemia, elevated triglycerides, high body mass index, smoking and hypertension are risk factors for neuropathy.
- In people with Type 2 diabetes, lower blood glucose levels are associated with reduced frequency of neuropathy.

1- Sensorimotor Polyneuropathy

Introduction:

Detectable sensorimotor Polyneuropathy will develop within 10 years of the onset of diabetes in 40 to 50% of people with Type 2 diabetes, especially those with poor glycemic control. Although <50% of these patients have motor or sensory symptoms, the neuropathic pain associated with symptomatic disease is frequently bothersome.

While neuropathy is uncommon in people with type 1 diabetes within the first 5 years after onset of diabetes, people with Type 2 diabetes may have neuropathy at the time of diagnosis.

Foot ulceration, which depends on the degree of foot insensitivity, and amputation are important and costly sequelae of diabetic neuropathy.

Both somatic and autonomic neuropathy may occur, and may require referral to a specialist experienced in managing neuropathic pain.

Mononeuropathy, particularly carpal tunnel syndrome, is common in people with diabetes.

Clinical Question:

When should specific drug therapy be started, which medications should be used?

What order should they be tried for treatment of neuropathy?

Screening for Peripheral Neuropathy:

Screening for neuropathy can be performed rapidly and reliably using the 10-g Semmes-Weinstein monofilament or 128-Hz tuning fork.

Other screening maneuvers can include assessment of pinprick sensation and reflexes.

In individuals with significant early progressive symptoms of neuropathy or in whom a clinical suspicion of non-diabetic neuropathy exists, referral for additional neurologic evaluation is indicated.

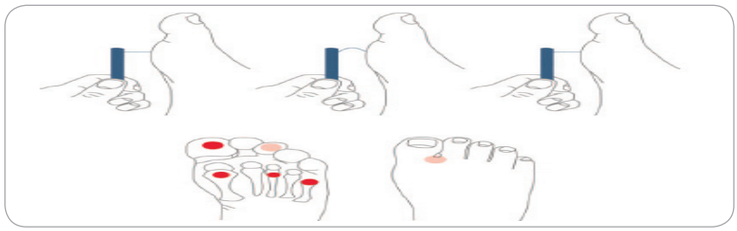
Rapid Screening for Diabetic Neuropathy:

These methods are designed to screen for the presence or absence of diabetic neuropathy, as opposed to screening for specific sites on the feet that are at risk of ulceration (multisite testing). If neuropathy is identified by either of these methods, other sites may be tested to identify high-risk areas for ulceration.

Monofilament:

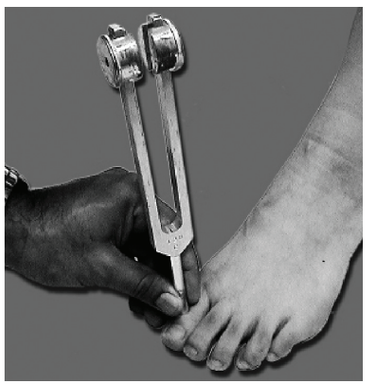
1. Show the 10-g Semmes-Weinstein monofilament to the patient.
2. Touch it first to the patient's forehead or sternum so that the sensation is understood.
3. Instruct the patient to say "yes" every time the monofilament stimulus is perceived.
4. With the patient's eyes closed, apply the monofilament to the dorsum of the great toe proximal to the nail bed as shown in the illustration below. Use a smooth motion - touch the skin; bend the filament for a full second, then lift from the skin.
5. Perform this stimulus 4 times per foot in an arrhythmic manner so the patient does not anticipate when the stimulus is to be applied.
6. Add up all correct stimuli for a score out of 8. A score of 7 or 8 correct responses likely rules out the presence of neuropathy.

Rapid Screening for Diabetic Neuropathy Using the 10-g Semmes-Weinstein Monofilament



Rapid Screening for Diabetic Neuropathy Using the 128-Hz Vibration Tuning Fork (The "On-Off" Method):

1. Strike the tuning fork against the palm of your hand hard enough that it will vibrate for approximately 40 seconds.
2. Apply the base of the tuning fork to the patient's forehead or sternum and ensure that the vibration sensation (not just the touch sensation) is understood.
3. With the patient's eyes closed, apply the tuning fork to the bony prominence situated at the dorsum of the first toe just proximal to the nail bed. Ask if the vibration sensation is perceived.
4. is stopped, and then dampen the tuning fork with your other hand.
5. One point is assigned for each vibration sensation perceived (vibration "on"). Another point is assigned if the correct timing of dampening of the vibration is perceived (vibration "off ").



Rapid Screening for Diabetic Neuropathy Using the 128-Hz Vibration Tuning Fork

6. Repeat this procedure again on the same foot, then twice on the other foot in an arrhythmic manner so the patient does not anticipate when the stimulus is to be applied.
7. Add up all correct stimuli for a score out of 8. A score of 7 or 8 correct responses likely rules out the presence of neuropathy.

Recommendations:

R1 - Screen regularly for peripheral neuropathy by use of monofilament as shown above.

R2 - Make a formal enquiry annually about the development of neuropathic symptoms.
- Discuss the cause and prognosis (including possible medium-term remission) of troublesome neuropathic symptoms, if present (bearing in mind alternative diagnoses).
- Agree appropriate therapeutic options and review understanding at each clinical contact. *(Level 1)*

R3 - Be alert to the psychological consequences of chronic painful diabetic neuropathy and offer psychological support according to the needs of the individual. *(Level 1)*

R4 - People with diabetes should be treated with intensified glycemic control to prevent the onset and progression of neuropathy. *(Level 2)*

R5 - Use a tricyclic drug to treat neuropathic discomfort (start with low doses, titrated as tolerated) if standard analgesic measures have not worked, timing the medication to be taken before the time of day when the symptoms are troublesome; advise that this is a trial of therapy. *(Level 1)*

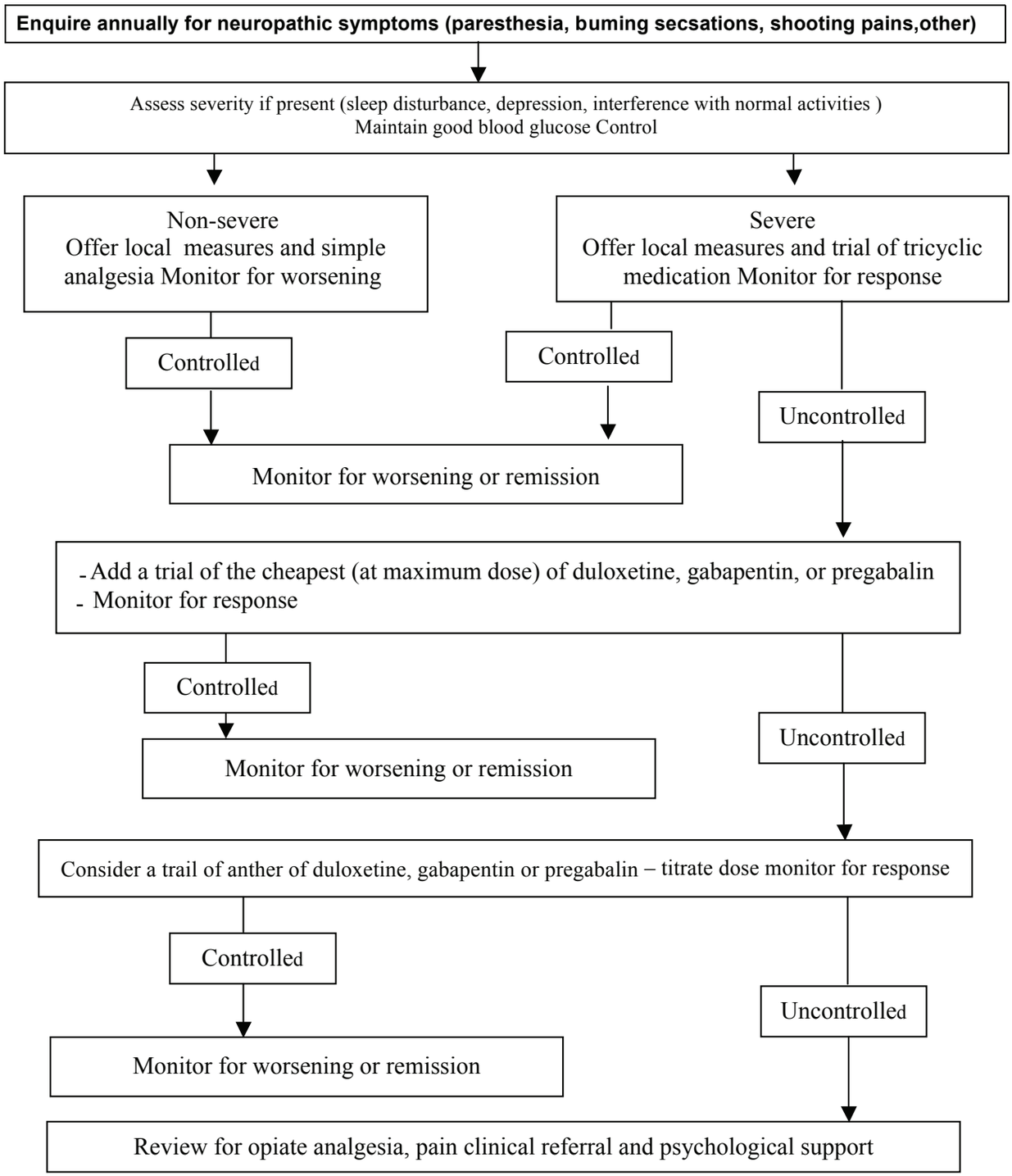
R6 - Offer a trial of duloxetine, gabapentin or pregabalin if a trial of tricyclic drug does not provide effective pain relief. The choice of drug should be determined by current drug prices. Trials of these therapies should be stopped if the maximally tolerated drug dose is ineffective. If side effects limit effective dose titration; try another one of the drugs. *(Level 1)*

R7 - Consider a trial of opiate analgesia if severe chronic pain persists despite trials of other measures. If there is inadequate relief of the pain associated with diabetic neuropathic symptoms, seek the assistance of the local chronic pain management service following a discussion with the person concerned. *(Level 1)*

R8 - If drug management of diabetic neuropathic pain has been successful, consider reducing the dose and stopping therapy following discussion and agreement with the individual. *(Level 1)*

R9 - If neuropathic symptoms cannot be controlled adequately, it may be helpful to further discuss:
- the reason for the problem.
- the likelihood of remission in the medium term.
- the role of improved blood glucose control. *(Level 1)*

Type 2 diabetes:



When to Refer:

- Patients should be referred to a specialist in pain management following a discussion with the person concerned:
  - if there is doubt about the diagnosis of neuropathic pain, or,
  - if there has been an inadequate response to treatment of neuropathic pain, or,
  - if other treatments are thought to be required that are not directly available in primary care.

2- Autonomic Neuropathy

Introduction:

There are many manifestations of autonomic neuropathy as a complication of long-term hyperglycaemia. These include gastroparesis, diarrhoea, faecal incontinence, erectile dysfunction, bladder disturbance, orthostatic hypotension, gustatory and other sweating disorders, dry feet, and unexplained ankle oedema.

A - Gastroparesis:

It is more common in type 1 than in Type 2 diabetes.
This can be one of the more devastating complications of autonomic neuropathy.
While it can present as bloating, nausea and fullness on eating, severe intermittent hypoglycaemia can be a major problem for people on glucose-lowering therapy, while vomiting may be intermittent and sudden or occasionally severe and protracted.

Clinical Questions:

In whom should gastroparesis be suspected?
What medications might help, and what other measures might be taken?

Recommendations:

R1 - Consider the diagnosis of gastroparesis in an adult with erratic blood glucose control or unexplained gastric bloating or vomiting, taking into consideration possible alternative diagnoses. *(Level 1)*

R2 - Consider a trial of metoclopramide, domperidone, or erythromycin for an adult with gastroparesis. *(Level 1)*

R3 - If gastroparesis is suspected consider referral to specialist services if:
- the differential diagnosis is in doubt, or
- persistent or severe vomiting occurs. *(Level 1)*

When to Refer:

- consider referral to specialist services if:
  - the differential diagnosis is in doubt, or
  - persistent or severe vomiting occurs. *(Level1)*

B - Erectile Dysfunction:

Key Message

- Erectile dysfunction (ED) affects approximately 34 to 45% of men with diabetes, has been demonstrated to negatively impact quality of life among those affected across all age strata, and may be the earliest sign of cardiovascular disease.
- All adult men with diabetes should be regularly screened for ED with a sexual function history.
- The current mainstays of therapy are phosphor diesterase type 5 inhibitors. They have been reported to have a major impact on erectile function and quality of life, and should be offered as first-line therapy to men with diabetes wishing treatment for ED.

Introduction:

Erectile Dysfunction in men with diabetes is common, and to a greater extent than in the matched general population.
There have been dramatic changes in the approach to male erectile dysfunction in recent years, stimulated by the advent of the phosphodiesterase type 5 (PDE-5) inhibitors.
This review deals only with care that would routinely be provided within diabetes services, and not with that normally provided by other specialist services.

Clinical Question:

What is the effectiveness and relative effectiveness of the PDE-5 inhibitor drugs in people with Type 2 diabetes?

Recommendations:

R1 - Review the issue of erectile dysfunction with men annually. *(Level 1)*
R2 - Provide assessment and education for men with erectile dysfunction to address contributory factors and treatment options. *(Level1)*
R3 - Offer a phosphodiesterase-5 inhibitor (choosing the drug with the lowest acquisition cost), in the absence of contraindications, if erectile dysfunction is a problem. *(Level 1)*
R4 - Following discussion, refer to a service offering other medical, surgical, or psychological management of erectile dysfunction if phosphodiesterase-5 inhibitors have been unsuccessful or are contraindicated. *(Level 3)*
R5 - Men with diabetes and ED who do not respond to PDE5 therapy should be investigated for hypogonadism. *(Level 3)*
R6 - Men with diabetes and ejaculatory dysfunction who wish fertility should be referred to a healthcare professional experienced in the treatment of ejaculatory dysfunction. *(Level 3)*

When to Refer:

- Referral to a specialist in ED should be considered for whom the use of PDE5 inhibitors is contraindicated. *(Level 3)*
- Following discussion, refer to a service offering other medical, surgical, or psychological management of erectile dysfunction if phosphodiesterase-5 inhibitors have been unsuccessful.
- Men with diabetes and ejaculatory dysfunction who wish fertility should be referred to a healthcare professional experienced in the treatment of ejaculatory dysfunction. *(Level 3)*

Other aspects of autonomic neuropathy:

Clinical Introduction:

Other aspects of autonomic neuropathy, including diarrhea, faecal incontinence, bladder disturbance, orthostatic hypotension, gustatory and other sweating disorders, dry feet, and unexplained ankle oedema, can offer diagnostic and management problems, which on occasion can be very disabling.

Alternatively symptoms may be vague and may present insidiously without realisation that they are diabetes-related, while nerve damage can be also be found in asymptomatic people. A mixed presentation is common, may be exacerbated by other drug therapy (e. g. tricyclic drugs), and may give troublesome hypoglycaemia. People with advanced autonomic neuropathy may also have advanced retinopathy, nephropathy, and somatic neuropathy.

Recommendations:

R1 - Consider the possibility of contributory sympathetic nervous system damage for a person who loses the warning signs of hypoglycaemia. *(Level 1)*

R2 - Consider the possibility of autonomic neuropathy affecting the gut in an adult with unexplained diarrhea, particularly at night. *(Level 1)*

R3 - When using tricyclic drugs and antihypertensive medications in people with autonomic neuropathy, be aware of the increased likelihood of side e ffects such as orthostatic hypotension. *(Level 1)*

R4 - Investigate a person with unexplained bladder-emptying problems for the possibility of autonomic neuropathy affecting the bladder. *(Level 1)*

R5 - Include in the management of autonomic neuropathy symptoms the specific interventions indicated by the manifestations (for example, for abnormal sweating or nocturnal diarrhea). *(Level 1)*

Diabetes in the Elderly:

Introduction:

- Definition of an elderly age is an age continuum starting after 60 and is characterized by a slow, progressive frailty that continues until the end of life.
- Lifestyle interventions are effective in prevention of diabetes in elderly people at high risk for the development of the disease as well as Acarbose and TZD, but metformin is not.
- The same glycemic targets apply to otherwise healthy elderly as to younger people with diabetes.
- In people with multiple comorbidities, a high level of functional dependency and limited life expectancy, the goal should be less strict, and clinicians should try to avoid symptoms of hyperglycemia and prevent hypoglycemia.
- Nutrition education programs can improve metabolic control in ambulatory older people with diabetes.
- Physical training programs can be successfully implemented in older people with diabetes, although comorbid conditions may prevent aerobic physical training in many patients, and increased activity levels may be difficult to sustain.
- The initial therapy in lean elderly people should involve agents that stimulate insulin secretion.
- The Initial therapy in obese older people with diabetes should involve agents that improve insulin resistance.
- Alpha-glucosidase inhibitors are modestly effective in older people with diabetes, but a substantial percentage of individuals cannot tolerate them because of gastrointestinal side effects.
- Thiazolidinediones are effective agents, but are associated with an increased incidence of edema and congestive heart failure (CHF) in older people and should be used with caution in individuals with cardiovascular disease (CVD).
- Sulfonylureas should be used with caution because the risk of hypoglycemia increases exponentially with age and appears to be higher with glyburide.

Gliclazide and glimepiride are preferred over glyburide in the elderly because they are associated with a lower frequency of hypoglycemic and CV events.

- A long-acting formulation of gliclazide resulted in equivalent glycemic control and the same frequency of hypoglycemic events as regular gliclazide in the elderly, and appears to result in a lower frequency of hypoglycemic events than glimepiride.
- Meglitinides (repaglinide and nateglinide) are associated with a lower frequency of hypoglycemia in the elderly compared to glyburide, and would be preferred in individuals with irregular eating habits.
- Insulin regimens in the elderly should be individualized and selected to promote patient safety.

- In elderly people, the use of premixed insulin's as an alternative to mixing insulin's and prefilled insulin pens as an alternative to conventional syringes minimizes dose errors and may improve glycemic control.
- Rapid-acting insulin analogue mixtures can be used and be administered after meals, although recent data suggest that the kinetics of regular and rapid-acting insulin are similar in the elderly.
- Multiple daily injections (MDI) may be associated with greater improvements in glycemic control, health status and mood than twice-daily injections of long acting insulin.
- In older people with poorly controlled Type 2 diabetes requiring insulin, both continuous subcutaneous insulin infusion (CSII) and MDI can result in excellent glycemic control, with good safety and patient satisfaction.

Prevention and Treatment of Complications

Hypertension:

- Treatment of isolated systolic hypertension or combined systolic and diastolic hypertension in elderly people with diabetes is associated with a significant reduction in CV morbidity and mortality and may also preserve renal function.
- Several different classes of antihypertensive agents have been shown to be effective in reducing the risk of CV events and end-stage renal disease, including thiazide-like diuretics, long-acting calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists.
- Any of these agents is a reasonable first choice although the calcium channel blocker amlodipine may be associated with an increased risk of CHF.
- Cardio selective beta blockers and alpha-adrenergic blockers are less likely to reduce CV risk than the above agents.
- ACE inhibitors may be particularly valuable for people with diabetes and other CV risk factor.

Dyslipidemia:

- The treatment of hypercholesterolemia with statins for both primary and secondary prevention of CV events has been shown to significantly reduce CV morbidity and mortality in older people with diabetes

Erectile dysfunction:

- Type 5 phosphodiesterase inhibitors appear to be effective for the treatment of erectile dysfunction in carefully selected elderly people with diabetes.

Recommendations:

R1	In elderly individuals with impaired glucose tolerance, a structured program of lifestyle modification that includes moderate weight loss and regular physical activity should be considered to reduce the risk of Type 2 diabetes.	[Grade A Level 1A(2)]
R2	Otherwise healthy elderly people with diabetes should be treated to achieve the same glycemic, blood pressure and lipid targets as younger people with diabetes. In people with multiple comorbidities, a high level of functional dependency or limited life expectancy, the goals should be less strict.	[Grade D consensus]
R3	Elderly people with diabetes living in the community should be referred for interdisciplinary interventions involving education and support.	Grade C Level 3
R4	Aerobic exercise and/or resistance training may benefit elderly people with Type 2 diabetes and should be recommended for those individuals in whom it is not contraindicated.	Grade B Level 2
R5	In elderly people with Type 2 diabetes, sulfonylurea›s should be used with caution because the risk of hypoglycemia increases exponentially with age. In general, initial doses of sulfonylurea›s in the elderly should be half those used for younger people, and doses should be increased more slowly. Gliclazide and gliclazide MR [Grade B Level 2] and glimepiride [Grade C Level 3 (49)] are the preferred sulfonylurea›s, as they are associated with a reduced frequency of hypoglycemic events. Meglitinides (repaglinide and nateglinide) should be considered in patients with irregular eating habits[Grade D consensus].	[Grade D consensus] Level 4
R6	In elderly people, the use of premixed insulin and prefilled insulin pens as alternatives to mixing insulin should be considered to reduce dose errors, and to potentially improve glycemic control.	[Grade B, Level 2]

Management of Obesity in Diabetes:

Key Message

- An estimated 80 to 90% of persons with Type 2 diabetes are overweight or obese.
- A modest weight loss of 5 to 10% of initial body weight can substantially improve insulin sensitivity and glycemic, blood pressure and lipid control.
- A comprehensive healthy lifestyle intervention program should be implemented in overweight and obese people with diabetes to achieve and maintain a healthy body weight. The addition of a pharmacologic agent should be considered for appropriate overweight or obese adults who are unable to attain clinically important weight loss with lifestyle modification.
- Adults with severe obesity may be considered for bariatric surgery when other interventions fail to result in achieving weight goals.

Introduction:

- Weight loss has been shown to improve glycemic control by increasing insulin sensitivity and glucose uptake, and diminishing hepatic glucose output (2, 3).
- The risk of death from all causes, cardiovascular disease (CVD) and some forms of cancer increases with excessive body fat(4). This relationship between increasing body fat accumulation and adverse health outcomes exists throughout the range of overweight and obese men and women in all age groups, including those ³75 years of age (5).

Assessment of Body Weight:

The initial assessment of people with diabetes should include height and weight measurements, calculation of BMI (kg/m2) (see Table1), and waist circumference (WC) to assess the degree of abdominal fat (Table 2)(6) . Metabolic comorbidities, such as hypertension, dyslipidemia and CVD, should also be assessed since they are highly correlated with increasing BMI (7, 8). Excessive upper body fat, or abdominal obesity, is a strong independent predictor of metabolic comorbidities (9, 10).

Cutoff values for WC vary among expert guidelines. The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines and Health Canada identify WC values ³102 cm (40 inches) in men and ³88 cm (35 inches) in women as being associated with substantially increased abdominal fat accumulation and health risks (Table 2). The International Diabetes Federation (13) has proposed population-specific WC cutoff values that are associated with increased risk of complications and are lower than the NCEP-ATP III guidelines (Table 3) (13).

Table 1. Canadian Guidelines for Body Weight Classification in Adults using BMI (6)		
Classification	*BMI* category (kg/m2)*	*Risk of developing health problems*
Underweight	<18. 5	Increased
Normal weight	18. 5–24. 9	Least
Overweight	25. 0–29. 9	Increased
Obese Class I Class II Class III	≥30. 0 30. 0–34. 9 35. 0–39. 9 ≥40. 0	 High Very high Extremely high

** BMI values are age and gender independent, and may not be correct for all ethnic populations BMI = body mass index.*

Table 2. WC and risk of developing health problems (6)	
WC cutoff points†*	*Risk of developing health problems*
Men ³102 cm (40 inches)	Increased
Women ³88 cm (35 inches)	Increased

**WC cutoffs may be lower in some populations (e. g. older individuals, Asian population , especially in the presence of the metabolic syndrome (such as hyper triglyceridemia).*
† Increased WC can also be a marker for increased risk, even in persons with normal weight WC = waist circumference.

Treatment of Obesity:

- The goals of therapy for overweight and obese people with diabetes are:
  1 - to reduce body fat.
  2 - attain and maintain healthy or lower body weight for the long term.
  3 - prevent weight regain.
- The optimal rate of weight loss is 1 to 2 kg/month. A negative energy balance of 500 kcal/day is typically required to achieve a weight loss of 0. 45 kg/week. (20).

Lifestyle interventions:

- Lifestyle intervention is recommended for weight loss in order to improve health status and quality of life. In people with diabetes who are overweight or obese, achieving a healthy weight through an active lifestyle promotes a general sense of well-being and cardiovascular (CV) fitness, along with other benefits, such as reducing CVD, morbidity, mortality and other complications attributable to obesity. (22)
- Lifestyle interventions that combine dietary modification, increased and regular physical activity and behavior therapy are the most effective. (23-25)
- All weight-loss diets must be well balanced and nutritionally adequate to ensure optimal health. In general, a carbohydrate intake of at least 100 g/day is required to spare protein breakdown and muscle wasting, and to avoid large shifts in fluid balance and ketosis.
- High-fiber foods that take longer to eat and digest are associated with greater satiety.

- Adequate protein intake is required to maintain lean body mass and other essential physiological processes.
- Reduced intake of saturated fat and energy-dense foods should be emphasized to achieve the required daily energy deficit to promote weight loss.
- Very low-calorie diets with <900 kcal/day are not recommended, except under medical supervision.
- People with diabetes should be counseled by a dietitian on appropriate serving sizes and on how to select meals, preferably nutrient-rich meals (i.e. containing whole grains and legumes), which are associated with greater satiety and lower caloric intake (28).

Behavioral therapy:

- Members of the healthcare team should consider using a structured approach to providing advice and feedback on physical activity, healthy eating habits and weight loss (31-34).

Pharmacotherapy:

- Pharmacotherapy for overweight people with diabetes not only improves glycemic control, but also results in a significant reduction in the doses of antihyperglycemic agents (26).
- Pharmacotherapy can be considered for people with BMI ³30. 0 kg/m2 with no obesity related comorbidities or risk factors, or BMI 27.0 kg/m2with obesity-related comorbidities or risk factors (20). Antiobesity drug therapy may be considered as an adjunct to nutrition therapy, physical activity and behavior modification to achieve a target weight loss of 5 to 10% of initial body weight and for weight maintenance (20, 35).
- Pharmacotherapy is an acceptable adjunct in the short- and long-term management of obesity when lifestyle measures fail to achieve the desired weight loss after an adequate trial of 3 to 6 months(20, 35).
- Drug therapy leads to even greater weight loss when coupled with lifestyle intervention and behavior modification therapy.
- Two medications, orlistat and sibutramine, have been shown to be effective in obese people with Type 2 diabetes, improving glycemic and metabolic control, and resulting in favourable changes in lipid levels, BP profile and fat distribution (26, 36, 37).
- When pharmacotherapy is being considered in the treatment of the obese or overweight person with Type 2 diabetes, the choice of drug should be based on the individual's CV risk profile, dietary habits and concomitant disease(s).
- In obese people with impaired glucose tolerance (IGT), orlistat also improves glucose tolerance and reduces the progression to Type 2 diabetes (38). Orlistat should be avoided in patients with inflammatory or other chronic bowel disease.
- People with irregular eating habits, such as those who "snack "frequently, may be better suited to sibutramine therapy because of its long-acting satiety-enhancing properties. Sibutramine should be avoided in patients with ischemic heart disease, congestive heart failure or other major cardiac disease.

- Combining orlistat and sibutramine therapy is not advocated for clinical use.
- Other available antiobesity drugs, such as diethylpropion and phentermine, are sympathomimetic noradrenergic appetite suppressants that are approved only for short-term use of a few weeks. They are not recommended because of modest efficacy and frequent adverse side effects.

Clinical Question:

1 - What type of intervention is to be used in obese diabetic patients?
2 - Is there is a rule of oral anti obesity medication in treat of obese diabetic patient?

Recommendations:

No.	Recommendations	Evidence level
R1	A comprehensive healthy lifestyle intervention program (including a hypocaloric, nutritionally balanced diet, regular physical activity or exercise, and behavioural modification techniques) for overweight and obese people with, or at risk for diabetes, should be implemented to achieve and maintain a healthy body weight. Members of the healthcare team should consider using a structured approach to providing advice and feedback on physical activity, healthy eating habits and weight loss.	Level 3 Level 2
R2	In overweight or obese adults with Type 2 diabetes, a pharmacologic agent such as orlistat or sibutramine should be considered as an adjunct to lifestyle modifications to facilitate weight loss and improve glycemic control.	Level 1 Level 2
R3	Adults with class III obesity (BMI ³40. 0 kg/m2) or class II obesity (BMI 35. 0 to 39. 9 kg/m2) with other comorbidities may be considered for bariatric surgery when other lifestyle interventions are inadequate in achieving weight goals.	Level 2

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Management of Diabetic Emergencies:

Key Message

- It is important to prevent, recognize and treat hypoglycemic episodes secondary to the use of insulin or insulin secretagogues.
- The goals of treatment for hypoglycemia are:
  1- to detect and treat a low blood glucose (BG) level promptly by using an intervention that provides the fastest rise in BG to a safe level.
  2- to eliminate the risk of injury.
  3- to relieve symptoms quickly.
- It is important to avoid overtreatment, since this can result in rebound hyperglycemia and weight gain.

Introduction:

Hypoglycemia is defined by:

1) The development of autonomic or neuroglycopenic symptoms (Table 1).
2) A low plasma glucose (PG) level [<4.0 mmol/L (<70mg/dl) for patients treated with insulin or an insulin secretagogue)].
3) Symptoms responding to the administration of carbohydrate.

The severity of hypoglycemia is defined by clinical manifestations (Table 2).

Table 1. Symptoms of hypoglycemia

Neurogenic (autonomic)	*Neuroglycopenic*
Trembling	Difficulty concentrating
Palpitations	Confusion
Sweating	Weakness
Anxiety	Drowsiness
Hunger	Vision changes
Nausea	Difficulty speaking
Tingling	Headache
	Dizziness

Table 2. Severity of hypoglycemia

Mild: Autonomic symptoms are present. The individual is able to self-treat.
Moderate: Autonomic and neuroglycopenic symptoms are present. The individual is able to self-treat.
Severe: Individual requires assistance of another person. Unconsciousness may occur. PG is typically <2. 8 mmol/L (50mg/dl).
PG = plasma glucose

Complications of Severe Hypoglycemia:

- Short-term risks of hypoglycemia include the dangerous situations that can arise while an individual is hypoglycemic, whether at home or work (e. g. driving, operating machinery).
- In addition, prolonged coma is sometimes associated with transient neurological symptoms such as paresis, convulsions and encephalopathy.
- The potential long-term complications of severe hypoglycemia are mild intellectual impairment and permanent neurologic sequelae such as hemiparesis and pontine dysfunction. The latter are rare and have been reported only in case studies.
- There is a link between frequent severe hypoglycemia (5 episodes since diagnosis) and a decrease in intellectual performance.

Recommendations:

R1	Mild to moderate hypoglycemia should be treated by the oral ingestion of 15 g of carbohydrate, preferably as glucose or sucrose tablets or solution. These are preferable to orange juice and glucose gels [Grade B, Level 2 (15)]. Patients should be encouraged to wait 15 minutes, retest BG and retreat with another 15 g of carbohydrate if the BG level remains <4. 0 mmol/L 70mg/dl).	[Grade D, Consensus]
R2	Severe hypoglycemia in a conscious person should be treated by the oral ingestion of 20 g of carbohydrate, preferably as glucose tablets or equivalent. Patients should be encouraged to wait 15 minutes, retest BG and retreat with another 15 g of glucose if the BG level remains <4. 0 mmol/L 70mg/dl). Patients taking an alpha-glucosidase inhibitor (acarbose) must use glucose (dextrose) tablets or, if unavailable, milk or honey to treat hypoglycemia.	Level 4
R3	Severe hypoglycemia in an unconscious individual >5 years of age, in the home situation, should be treated with 1 mg of glucagons subcutaneously or intramuscularly. Caregivers or support persons should call for emergency services and the episode should be discussed with the diabetes healthcare team as soon as possible.	Level 3
R4	For individuals at risk of severe hypoglycemia, support persons should be taught how to administer glucagon by injection].	Level 3
R5	To treat severe hypoglycemia with unconsciousness, when intravenous access is available, glucose 10 to 25 g (20 to 50 cc of D50W) should be given over 1 to 3minutes.	Level 3
R6	To prevent repeated hypoglycemia, once the hypoglycemia has been reversed, the person should have the usual meal or snack that is due at that time of the day. If a meal is >1 hour away, a snack (including 15 g of carbohydrate and a protein source) should be consumed.	Level 3

Hyperglycemic Emergencies in Adults:

Key Message

- Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) should be suspected in ill patients with diabetes.
- If either DKA or HHS is diagnosed, precipitating factors must be sought and treated.
- DKA and HHS are medical emergencies that require treatment and monitoring for multiple metabolic abnormalities and vigilance for complications.
- Ketoacidosis requires insulin administration (0. 1U/kg/hour) for resolution; bicarbonate therapy should be considered only for extreme acidosis (pH 7. 0).

Introduction:

- Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are diabetes emergencies with overlapping features.
- With insulin deficiency, hyperglycemia causes urinary losses of water and electrolytes (sodium, potassium, chloride) and the resultant extracellular fluid volume (ECFV) depletion. Potassium is shifted out of cells, and ketoacidosis occurs as a result of high catecholamine levels suppressing insulin release.
- In DKA, ketoacidosis is prominent, while in HHS the main features are ECFV depletion and hyperosmolarity.
- Risk factors for DKA include new diagnosis of diabetes mellitus, insulin omission, infection, myocardial infarction, abdominal crisis, trauma and possibly treatment with insulin infusion pumps.
- Risk factors for HHS include cardiac surgery, and use of certain drugs, including diuretics, glucocorticoids, lithium and atypical antipsychotics.
- HHS is much less common than DKA.
- The clinical presentation of DKA includes symptoms of hyperglycemia, Kussmaul respiration, acetone-odoured breath, ECFV contraction, nausea, vomiting and abdominal pain. There may be a decreased level of consciousness.
- The clinical presentation of HHS includes, decreased level of consciousness, a variety of neurological presentations, including seizures and a stroke-like state.

Diagnosis:

To make the diagnosis and determine the severity of DKA or HHS, the following should be assessed:

- plasma levels of electrolytes (and anion gap), glucose, creatinine, osmolality, blood gases, serum and urine ketones, fluid balance.

- Level of consciousness, precipitating factors and complications (5). There are no definitive criteria for the diagnosis of DKA.
- Typically, the arterial pH is 7. 3, serum bicarbonate is 15 mmol/L, and the anion gap is >12 mmol/L with positive serum and/or urine ketones (5-7). Plasma glucose is usually 14. 0 mmol/L, but can be lower (8).

Management:

Objectives of management include restoration of normal ECFV and tissue perfusion; resolution of ketoacidosis; correction of electrolyte imbalances and hyperglycemia; and the diagnosis and treatment of coexistent illness.

The issues that must be addressed in the patient presenting with DKA or HHS are outlined in Table 1.

A summary of fluid therapy is outlined in Table 2.

A management algorithm and formulas for calculating key measurements are provided in Figure 1.

Patients with DKA and HHS are best managed in an intensive care unit (ICU) or step-down setting (5-7) with specialist care (9, 10).

Volume status (including fluid intake and output), vital signs, neurologic status, plasma concentrations of electrolytes, anion gap, osmolality and glucose need to be monitored closely, initially as often as every 2 hours (5-7). Precipitating factors must be diagnosed and treated (5-7).

Table 1: Priorities* to be addressed in the management of patients presenting with hyperglycemic emergencies

Metabolic	*Precipitating cause of DKA/HHS*	*Other complications of DKA/HHS*
•ECFV contraction •Potassium deficit and abnormal concentration •Metabolic acidosis •Hyperosmolality (water deficit leading to increased corrected sodium concentration plus hyperglycemia)	•New diagnosis of diabetes •Insulin omission •Infection •Myocardial infarction •Drugs	•Hyper/hypokalemia ECFV overexpansion •Cerebral edema •Hypoglycemia •Pulmonary emboli •Aspiration •Hypocalcemia (if phosphate used) •Stroke •Acute renal failure •Deep vein thrombosis

*Severity of issue will dictate priority of action:
DKA = diabetic ketoacidosis.
ECFV = extracellular fluid volume.
HHS = hyperosmolar hyperglycemic state.

Summary of fluid therapy for DKA and HHS in adult

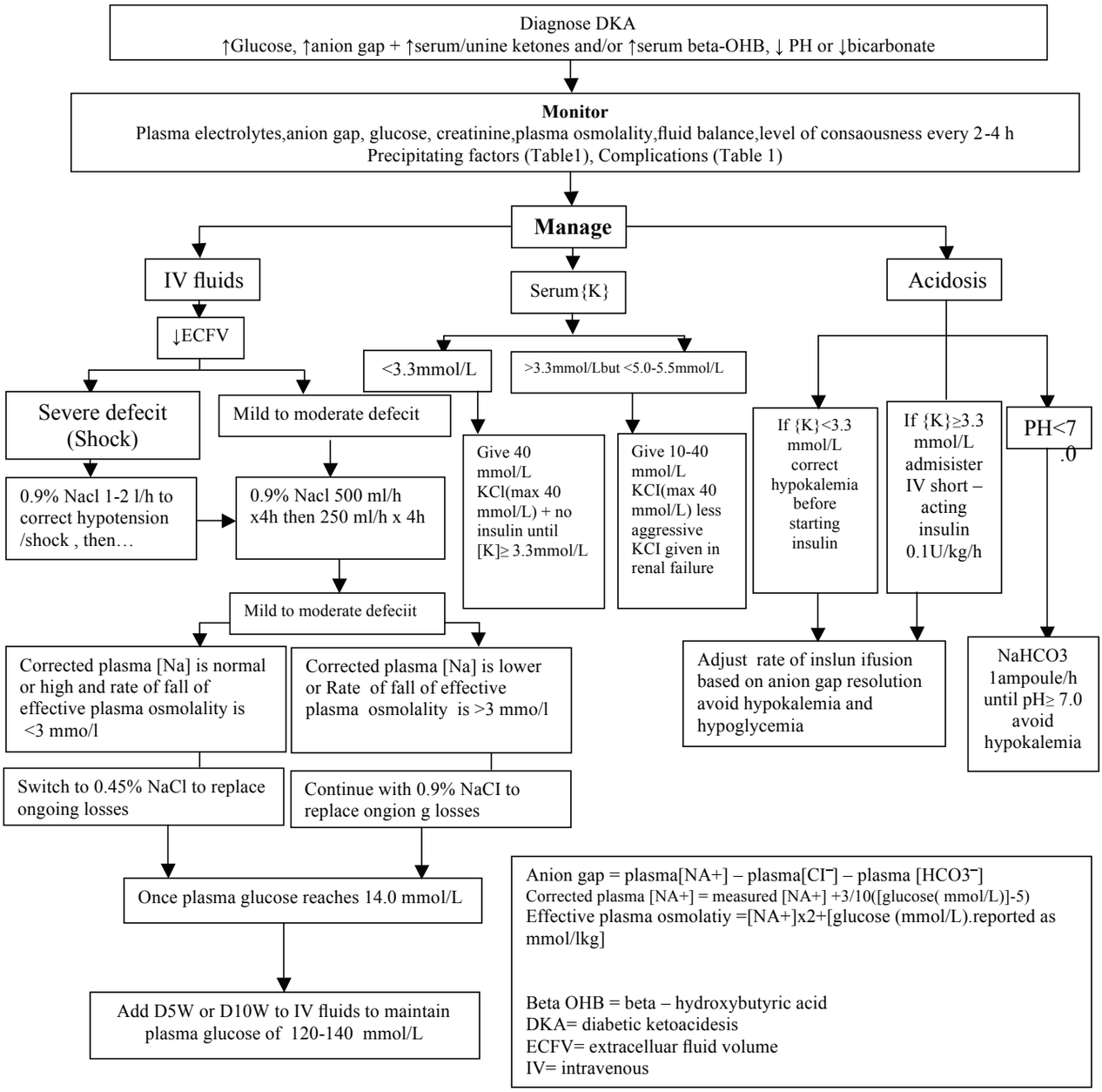
1. Administer IV normal saline initially. If the patient is in shock, give 1 to 2 L/hour initially to correct shock; otherwise, give 500 mL/hour for 4 hours, then 250 mL/hour for 4 hours.
2. Add potassium immediately if patient is normo- or hypokalemic. Otherwise, if initially hyperkalemic, only add potassium once serum potassium falls to <5 to 5. 5 mmol/L and patient is diuresing.
3. Once plasma glucose reaches 14. 0 mmol/L, add glucose to maintain plasma glucose at 12. 0 to 14. 0 mmol/L.
4. After hypotension has been corrected, switch normal saline to half-normal saline (with potassium chloride). However, if plasma osmolality is falling more rapidly than 3 mmol/kg/hour and/or the corrected plasma sodium is reduced, maintains IV fluids at higher osmolality (i. e. may need to maintain on normal saline).

DKA = diabetic ketoacidosis.
HHS = hyperosmolar hyperglycemic state.
IV = intravenous.

Recommendations:

R1	In patients with DKA, a protocol incorporating the principles illustrated in Figure 1 should be followed. For HHS, a similar protocol can be used; however, in this case, the plasma glucose level is used to titer the insulin dose.	Level 3
R2	In individuals with DKA, IV 0. 9% sodium chloride should be administered initially at 500 mL/hour for 4 hours, then 250 mL/hour for 4 hours with consideration of a higher initial rate (1–2 L/hour) in the presence of shock. For persons with a HHS, IV fluid administration should be individualized based on the patient's need.	Level 2
R3	In patients with DKA, IV short-acting insulin should be administered at an initial dose of 0. 1 U/kg/hour). The insulin infusion rate should be maintained until the resolution of ketosis as measured by the normalization of the plasma anion gap]. Once the plasma glucose concentration reaches 14. 0 mmol/L, IV dextrose should be started to avoid hypoglycemia.	Level 2

Figure 1.Management Of DKA in adults



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Influenza and Pneumococcal Immunization:

Key Messages

- Studies in high-risk individuals, which included people with diabetes, have shown that influenza vaccination can reduce hospitalizations by approximately 40%.
- As people with diabetes are at least as susceptible to pneumococcal infection as other people with chronic diseases, the use of the pneumococcal vaccine is encouraged.

Introduction:

People with diabetes, especially those with renal and cardiac complications, are at high risk for morbidity and mortality from influenza and Pneumococcal disease (1).

Influenza Immunization in Adults:

The majority of studies on influenza immunization rely on observational reports of increased death rates in people with diabetes during influenza epidemics (6-9).
A retrospective case-control study demonstrated the effectiveness of influenza vaccination in reducing rates of hospitalization by 79% of people with diabetes for influenza, pneumonia or diabetes-related events during 2 influenza epidemics that had been immunized against influenza during the period immediately preceding the epidemic in Leicestershire, England, United Kingdom (10). The study detected a Another nested case-control study in the Netherlands demonstrated that vaccination was associated with a 56% reduction in any complication, a 54% reduction in hospitalizations and a 58% reduction in deaths in people with Type 2 diabetes (11).

Pneumococcal Immunization in Adults:

There is widespread acceptance that people with diabetes are at least as susceptible to Pneumococcal infection as other people with chronic diseases (1), and therefore the use of the Pneumococcal vaccine is encouraged in this population.A one-time revaccination is recommended for individuals >65 years of age if the original vaccine was administered when they were <65 years of age and >5 years earlier.

Clinical Question:

Did diabetic patient benefit from influenza & Pneumococcal vaccinations?

Recommendations:

R1	People with diabetes should receive an annual influenza vaccine to reduce the risk of complications associated with influenza epidemics.	Level 3
R2	People with diabetes should be considered for vaccination against Pneumococcal.	Level 3

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Psychological Aspects of Diabetes:

Introduction:

Significant behavioural demands and challenging psychosocial factors affect nearly all aspects of diabetes management and subsequent diabetes control (1, 2). Psychological issues related to the diagnosis and/or self-care demands may present anywhere on a continuum from impairment in quality of life to clinically significant depressive and/or anxiety disorders.

Adjustment Problems:

Both adults and children face challenges associated with adjustment to diabetes. Some children and/or their parents have adjustment problems soon after the diagnosis of diabetes (3, 4). Those who do not solve these problems within the first year of diagnosis are at risk for poor adaptation to diabetes, including regimen adherence problems, poor glycemic control and continued psychosocial difficulties (5, 6). Stress (general and diabetes-specific) (7, 8), inadequate social and family interactions (9, 10), inappropriate beliefs about the nature of diabetes (10), and poor coping skills (11, 12) may have a negative impact on self-care behaviours and glycemic control.

Adults with type 1 and 2 diabetes across many culturesreport significant psychological distress related to the diagnosis of diabetes, with a negative impact on diabetes selfmanagement (13).

The diagnosis of diabetes may precipitate or exacerbate existing psychological disorders (14, 15). As quality of life is adversely affected by the presence of comorbid psychological disorders and health complications (14, 15), the identification of potential psychiatric conditions, such as depression, anxiety and eating disorders, is critical.

Depression:

Depressive symptoms are common in people with diabetes compared with the general population (14, 16, 17), and major depressive disorder is present in approximately 15% of patients with diabetes (18). Depressive disorders in adults and children are associated with poorer self-care behavior (19, 20), poorer glycemic control, health complications, decreased quality of life and psychological well-being (14, 21), increased family problems, and higher healthcare costs (22-25).

Anxiety:

Generalized anxiety disorder appears to be increased in individuals with diabetes compared with the general population (14 vs. 3 to 4%, respectively) (27). As many as 40% of patients have at least some anxiety symptoms (27), and fear of hypoglycemia (28, 29) is not uncommon in those with diabetes. A recent meta-analysis suggested that the presence of clinically significant anxiety disorders among those with type 1 and 2 diabetes is associated with poor glycemic control (28).

Screening:

All individuals with diabetes and their families should be regularly screened for symptoms of psychological and social distress (2, 20). Healthcare professionals should actively explore psychological factors by asking empathetic but frank openended questions about stress, social support, unhealthy selfcare behaviours, health beliefs about risk of complications, treatment efficacy and the degree of interference with normal functioning (37). People with diabetes should be screened for depression and anxiety regularly, either through direct queries (e. g. "During the past month, have you often been bothered by feeling down, depressed, or hopeless?" and "During the past month, have you often been bothered by little interest or pleasure in doing things?") (38), or with a standardized questionnaire (e. g. Beck Depression Inventory [39]).

Interventions:

Preventive psychological interventions should be incorporated into all primary care and self-management education interventions to enhance adaptation to diabetes and reduce stress. Educational and psychological interventions often share a theoretical basis around increasing readiness to change and self-efficacy (41, 42).

Effective interventions for children and adults include psychosocial support, feedback and reinforcement (20, 43-45); coping skills training (46); cognitive-behavioural therapy (CBT) (47); and family behaviour therapy (48). Approaches that increase patient participation in decisionmaking regarding care and education have been shown to be more effective than a "do as I say" approach in enhancing psychological adjustment to diabetes, and potentially preventing psychological distress (49-51).

For those with suboptimal self-care or significant psychological symptoms, focused interventions using CBT or family behaviour therapy need to be considered (43, 52).

These issues should be addressed using psychosocial services within diabetes teams or resources in the community. In pediatric populations, intensive case management with psychoeducation may be required (43, 52). In-home, multisystemic therapy can be used to reduce diabetes-related stress (53), improve glycemic control and reduce inpatient admissions for adolescents with poor glycemic control (2, 54).

Antidepressant medication (55) and CBT have each been shown to be specifically effective in treating depression in adults with diabetes (56). Risk of significant weight gain during extended use of selective serotonin reuptake inhibitor antidepressants may be greater for paroxetine (57); sertraline or fluoxetine may be preferred in this weight-sensitive population.

Recommendations:

1- Individuals with diabetes should be regularly screened for subclinical psychological distress and psychiatric disorders (e.g. depressive and anxiety disorders) by interview or with a standardized questionnaire. *(level 2)*

2- Patients diagnosed with depression or anxiety should be referred to mental health professionals who are either part of the diabetes team or are in the community Level3 Those diagnosed with depression should be offered treatment with CBT Level 2 and/or antidepressant medication. *(Level 1)*

3- Multidisciplinary team members with required expertise should offer CBT-based techniques, such as stress management strategies and coping skills training Level 1 for type 2 diabetes, family behavior therapy Level 2 and case management Level 2 to improve glycemic control and/or psychological outcomes. *(Level 2)* in individuals with suboptimal self-care behaviours, suboptimal glycemic control and/or psychological distress.

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Breaking Bad News:

What is "bad news"?

While this question may seem obvious, it is important to remember that what the physician feels is "bad news" may not match what the patient feels is "bad news" and vice versa. As an example, patient had an episode of facial tingling that lasted several hours. The patient saw her physician, who ordered diagnostic tests. When the tests came back saying the patient had a transient ischemic attack ("mini-stroke"), the physician was concerned about delivering this bad news to the patient. However, when told, the patient responded, "Oh, what a relief…I thought it was MS."

Physicians often tell patients that they have chronic diseases (hypertension, diabetes, high cholesterol, etc.). Those illnesses are so commonplace in the medical field that the physician may forget that these represent "bad news" to some patients. As an example, the diagnosis of diabetes may be devastating to a patient who witnessed a relative with amputations or on dialysis due to its complications. It is important for the physician to remember the patient's perspective when determining what constitutes "bad news. "

What are potential bad news situation in Diabetes?

1 - Diagnosis.
2 - Side effect of medication.
3 - Insulin therapy.
4 - Complication.
5 - Life style modification.
6 - Regular check-up and referral.

Do patients want to know?

Contrary to what many physicians have thought in the past, recent studies have proven that most patients do want to know the truth about their health conditions. Today, most physicians believe that telling patients the truth fosters trust and demonstrates respect. The patient should be told all relevant information regarding the illness, expected outcomes, treatment options, risks and benefits of treatment, and other needed information based on the patient's specific values and needs.

How do I break bad news?

There are many guidelines and protocols for breaking bad news, we are going to demonstrate Robert Buckman's Six Step Protocol for Breaking Bad News:

1. Getting started:

- The physical setting ought to be private, with both physician and patient comfortably seated.
- You should ask the patient who else ought to be present, and let the patient decide (studies show that different patients have widely varying views on what they would want).
- It is helpful to start with a question like, "How are you feeling right now?" to indicate to the patient that this conversation will be a two-way affair.

2. Finding out how much the patient knows

- By asking a question such as, "What have you already been told about your symptom?" you can begin to understand:
  - what the patient has already been told ("I have diabetes, and I need Insulin"),
  - or how much the patient understood about what's been said ("the doctor said something about a sugar in my blood"),
  - the patients level of technical sophistication ("I've got a HBA1C > 12 "), and the patient's emotional state ("I've been so worried I might have diabetes that I haven't slept for a week").

3. Finding out how much the patient wants to know:

- It is useful to ask patients what level of detail you should cover. For instance, you can say, "Some patients want me to cover every medical detail, but other patients want only the big picture-what would you prefer now?" This establishes that there is no right answer, and that different patients have different styles. Also this question establishes that a patient may ask for something different during the next conversation.

4. Sharing the information :

- Decide on the agenda before you sit down with the patient, so that you have the relevant information at hand.
- The topics to consider in planning an agenda are: diagnosis, treatment, and support or coping. However, an appropriate agenda will usually focus on one or two topics.
- Give the information in small chunks, and be sure to stop between each chunk to ask the patient if he or she understands ("I'm going to stop for a minute to see if you have questions").
- Long lectures are overwhelming and confusing.
- Remember to use simple clear language.

5. Responding to the patients feelings:

- If you don't understand the patient's reaction, you will leave a lot of unfinished business, and you will miss an opportunity to be a caring physician.
- Learning to identify and acknowledge a patient's reaction is something that definitely improves with experience, if you're attentive, but you can also simply ask ("Could you tell me a bit about what you are feeling?").

6. Planning and follow-through:

- At this point you need to synthesize the patient›s concerns and the medical issues into a concrete plan that can be carried out in the patient›s system of health care.
- Outline a step-by-step plan, explain it to the patient, and contract about the next step.
- Be explicit about your next contact with the patient («I'll see you in clinic in 2 weeks") or the fact that you won't see the patient ("I'm going to be rotating off service, so you will see Dr. Back in clinic").
- Give the patient a phone number or a way to contact the relevant medical caregiver if something arises before the next planned contact

When to Refer:

- Patients diagofesed with depression anxiety or eating disorders should be referred to mental health professionals who are either part of the diabetes teamor are in the community [Grade D Consensus].
- Following discussion refer to a service offering CBT- based techniques such as stress management strategies and coping skills training [Grade A, Level 1 A for type 2 diabetes (42) Grade B, Level 2 family behavior therapy [Grade B Level 2 (48, 53)] and case management [Grade B , Level 2 (43, 53)] to improve glycemic control and / or psychological outcomes (Level 2).

The ABCDE Memonic for Breaking Bad News:

Check list:

Advance preparation	Arrange for adequate time in a private, comfortable location.
	privacy and no interruptions (turn pager off or to silent mode).
	Review relevant clinical information. provide at least basic information about prognosis and treatment options.
	Mentally rehearse how you will deliver the news, identify words or phrases to use and avoid.
	Prepare yourself emotionally.
Build a therapeutic environment/relationship	Determine what and how much the patient wants to know.
	Have family or support persons present. at the patient's discretion.
	Introduce yourself to everyone.
	Warn the patient that bad news is coming.
	Use touch when appropriate. Be sensitive to cultural differences and personal preference.
	Schedule follow-up appointments.
Communicate well	Ask what the patient or family already knows: what the patient has already been told (*"I have diabetes, and I need Insulin"*), or how much the patient understood about what's been said (*"the doctor said something about a sugar in my blood"*), the patients level of technical sophistication (*"I've got a HBA1C > 12"*), and the patient's emotional state (*"I've been so worried I might have diabetes that I haven't slept for a week"*). Find out the patient's expectations before you give the information.
	Be frank but compassionate; avoid euphemisms and medical jargon.
	Allow for silence and tears; proceed at the patient›s pace.
	Have the patient describe his or her understanding of the news; repeat this information at subsequent visits.
	Allow time to answer questions; write things down and provide written information.
Deal with patient and family reactions	Assess and respond to the patient and the family›s emotional reaction; repeat at each visit.
	Be empathetic.
	Do not argue with or criticize colleagues.
Encourage and validate emotions	Explore what the news means to the patient
	Offer realistic hope according to the patient's goals.
	Use interdisciplinary resources.
	Take care of your own needs; be attuned to the needs of involved house staff and office or hospital personnel.

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Appendices

Appendix 1
Diabetic Clinic Forms

Personal Data:

Patient Name:				Rec. No.	Nationality:
Address:					
Gender:		M	F	Educational Level:	Marital status:
Tel. No.	Occupation:				

Problems:

No.	Description	Date	Comment
1	Smoking addiction		
2	Retinopathy: BDR		
	Preproliferative		
	Laser surgery		
	Impaired vision		
	Blind		
3	Macrovascular: Hypertension		
	CAD		
	MI		
	PTCA		
	CABG		
	Peripheral vase dz.		
	CVA		
	TIA		
	CHF		
4	Nephropathy: Microalb		
	Macroalb		
	Nephropathy		
	ESRD		
5	Hyperlipidemia: Cholesterol		
	HDL		
	LDL		
	TG		
6	Depression		
	Anxiety		
	Stress disorder		
7	Obesity		

Diabetes Mellitus Follow up Sheet:

Patient Name:	File No.	Date of visit:
Gender:	M F	Date of Birth:	Height:

Patient's Goal of the visit		
History & Physical Examination (including risk factors, exercise and diet history)		
Assessment of Hyper / hypoglycemia (review signs, symptoms and treatment)		
High Risk Behaviors Smoking		
Psychosocial Adjustment Screen for depression		
Blood Pressure every visit : Goal: <130/80 mmHg	Weight / BMI every visit: Goal: BMI ≥18. 5 ≤25	
A1C every 3 – 6 months Goal: <7. 0%	(SMBG)Mean FBS Goal<130mg/dl	(SMBG)Mean 2hpp Goal<180mg/d l
Foot Exam: High Risk Yes No [N = Normal,A = Abnormal]		
Left feet		Right feet
	Sensory	
	Vascular	
	Skin	
Diabetes Education Nutrition, exercise Counseling		
List Current Medication, OTC Aspirin		
Comments, plan (e. g. : assessment of complications, follow-up, adherence to plan, referrals, etc.)		

Diabetes Mellitus Flow Sheet:

Patient Name:						File No.
Gender:		M		F	Date of Birth:	Height:

Examination / Test	Result	Result	Result	Result	Result	Result	Result	Result
A1C ≤ 7% (3-6 months)								
Blood Pressure ≤ 130 / 80 mmHg & Weight – Goal Blood Pressure								
Weight								
BMI								
GFR:								
Urine albumin / Microalbumia (annual)								
Lipid (annual): Cholesterol								
Trig: <150								
HDL: [M<40 & F<50]								
LDL: <100								
Serum creatinie to estimate Glomerular Filtration Rate								
Flu Vaccine								
Retinal Exam (annual) Right								
Left								
Dental every 6 months Evaluate teeth and gums, refer to dentist								

Initial Assessment: Assessment includes appraisal of cardiovascular risks and end-organ damage. A detailed assessment needs to be made at first diagnosis.

HISTORY:

Specific Symptoms:

Glycosuria	☐ Yes	☐ No
Polyuria	☐ Yes	☐ No
Polydipsia	☐ Yes	☐ No
Polyphagia	☐ Yes	☐ No
Weight loss	☐ Yes	☐ No
Nocturia	☐ Yes	☐ No
Hyperglycemia	☐ Yes	☐ No
Malaise / fatigue	☐ Yes	☐ No
Altered vision	☐ Yes	☐ No

Risk factors for Complications including:

Personal or family history of cardiovascular disease	☐ Yes	☐ No
Smoking	☐ Yes	☐ No
Hypertension	☐ Yes	☐ No
Dyslipidemia	☐ Yes	☐ No

Lifestyle issues:

Smoking	☐ Yes	☐ No
Alcohol	☐ Yes	☐ No
Occupation	☐ Yes	☐ No
Eating & activity habits	☐ Yes	☐ No

Predisposition to Diabetes:

Age over 40	☐ Yes	☐ No
Family History	☐ Yes	☐ No
Over weight	☐ Yes	☐ No
Physical inactivity	☐ Yes	☐ No
Hypertension	☐ Yes	☐ No
Medication causing hyperglycemia	☐ Yes	☐ No
Personal or family history of haemochromatosis	☐ Yes	☐ No
Autoimmune disease (personal and /or family history of other autoimmune disease (e. g. hypo or hyperthyroidism	☐ Yes	☐ No

General symptom review:

Cardiovascular symptoms	☐ Yes	☐ No
Neurological symptoms	☐ Yes	☐ No
Bladder and sexual function	☐ Yes	☐ No
Foot and toe problems	☐ Yes	☐ No
Recurrent infections (especially urinary and skin)	☐ Yes	☐ No

Examination:

Weight / waist	BMI:
	Waist/hip:
Cardiovuscular system:	BP laying:
	BP standing:
	Peripheral neck, abdominal vessels:
Eyes:	Visual acuity (with correction)
	Retinopathy
Feet:	Sensation and circulation
	Skin condition
	Pressure areas
	Interdigital problems
	Abnormal bone architecture
Peripheral nerves:	Tendon reflexes
	Sensation: touch (e. g. 10g monofilament)
	Vibration (e. g. 128 hz running fork)
Urinalysis:	Albumin
	Ketones
	Nitrates and / Leucocytes

INVESTIGATIONS:		
Baseline:	Renal Function:	Bun:
		Creatinine:
		Microalbuminuria:
	Lipids:	LDL:
		HDL:
		Triglycerids:
		Cholesterol:
	Hba1C:	
	FBS:	
Other:	ECG every 2 years, if >50 years and at least one other vascular risk factor	
	Thyroid function tests if there is family history or clinical suspicion	
	Micro-urine if high risk group (woman, neuropathy, vaginal pessary)	

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Appendix 11
Experts' Opinion of Diabetes in Ramadan and Hajj

Fasting Guidelines to Diabetes Patients:

Surah Al-Baqarah: 183-184

*you who believe observing As-Saum (the fasting) is prescribed for you as it was prescribed for those before you, that you may become Al-Mutaqun (the pious)*Observing Saum (fast) for a fixed number of days, but if any of you is ill or on a journey, the same number (should be made up) from other days. And as for those who can fast with difficulty, (e.g. an old man), they have a choice either to fast or to feed a Miskin (poor person) for every day. But whoever does good of his own accord, it is better for you if only you Know.*

Guidelines to Determine which Diabetes Patients can Fast:

Each patient wishing to fast must be assessed as an individual. However, there are few guidelines that may assist the physician to make the decision.

Forbid fasting in:

- All brittle type 1 diabetes patients.
- Poorly controlled type 1 or type 2 diabetes patients.
- Diabetic patients known to be incompliant in terms of following advice on diet drug regimens and daily activity.
- Diabetic patients with serious complications such as unstable angina or uncontrolled hypertension.
- Patients with a history of diabetic ketoacidosis.
- Pregnant diabetic patients.
- Diabetic patients with inter-current infections.
- Elderly patients with any degree of alertness problems.
- Two or more episodes of hypoglycaemia and/or hyperglycemias during Ramadan.

Allow fasting in:

- Patients who do not have the previous criteria.
- Type II DM patients treated with biguanides or sulphonylurea, who are stable and do not have any complicating progressive co morbid pathology.
- Patient who accept medical advisement.
- Some Type I DM patients with proper self-monitoring and close professional supervision.
- In all cases patients must be made aware of the risks involved in fasting even if under medical supervision.

Pre-Ramadan preparation for Diabetes Patients who Want to Fast:

General Considerations:

- Individualization. Perhaps the most crucial issue is the realization that care must be highly individualized and that the management plan will differ for each specific patient.
- People with diabetes wishing to fast should be assessed before the month of Ramadan to check their physical health, diabetes control and suitability for fasting.
- It is important to find out if they have fasted before, and how well they coped with it.
- Hypoglycemia should be anticipated when good controlled diabetics are going to fast.
- Patients should be informed that giving blood or measuring blood glucose does not break the fast.
- Educate the patient about warning symptoms of dehydration, hypoglycaemia and hyperglycemias.
- Educate the patient about breaking fast as soon as any complication or new harmful condition occurs.
- All patients should understand that they must always and immediately end their fast if hypoglycemia (blood glucose of 60 mg/dl [3.3 mmol/l] or less) occurs.
- Checking urine for acetone (type 1 patients) is important.
- Measuring daily weights and informing physicians of weight reduction (dehydration, low food intake, and polyuria) or eight increase (excessive calorie intake) above two kilograms.
- Further attention on fasting during the summer season and geographical areas with longer fasting hours.

Recommendation and Treatment Options for Diabetes Patients:

During Fasting:

- All patients who intend to fast should be given an educational advice (program) in regards to coping up with diabetes during fasting in term of modifying the regimen, dietary considerations, and the importance of monitoring.
- Medications regimen during Ramadan need to be modified in timing and possibly dose, and should be tailored for each individual patient.
- It is very important not to stop taking insulin during Ramadan.
- Patients should be advised and forbidden from skipping meals, and taking medication irregularly.
- Adjustment of the diet protocol for Ramadan fasting.
- Home blood glucose monitoring should be performed, especially for patients on Insulin just before the sunset meal and two hours afterwards. It should also be performed before the pre-dawn meal to adjust the insulin dose and prevent any hypoglycaemia and postprandial hyperglycaemia

General Dietary Guidelines:

- Adjustment of the diet protocol for Ramadan fasting.
- Limit the amount of sweet foods taken at sunset meal.
- Include fruits, vegetables, and yoghurt with sunset and Dawn meals.
- Choose sugar-free drinks or water to quench the thirst.
- It is recommended that fluid intake be increased during non-fasting hours.
- It is recommended that the predawn meal be taken as late as possible just before sunrise and the start of the daily fast, not at midnight.
- Limit fried foods.
- Abstain from high calorie and highly refined foods prepared during Ramadan.

Physical Activity General Guidelines:

- Continue the usual physical activity especially during non-fasting periods.
- Engorgement of continued appropriate physical activity.
- If Tarawaih prayer (multiple prayers after the sunset meal) is performed, then it should be considered a part of the daily exercise program.
- Where possible, recommend rest during the day to help avoid low blood glucose levels.

Treatment Recommendation and Guidelines:

Drug Regimens for Type2 DM. Patients on Oral Medications:

- Medications regimen during Ramadan need to be modified and tailored for each individual patient.
- It has been suggested to use short acting oral hypoglycemic agents be used rather than long acting drugs that may increase the risk of hypoglycemia.
- Patients on Metformin alone should be able to fast safely.
- Patients treated with once-daily agent such as glipizide, glimepiride, glibenclamide or gliclazide with breakfast it should be taken with the sunset meal instead.
- Patients treated with Sulfonylureas twice a day, e.g glibenclamide or gliclazide, it is recommended to use the full morning dose before the sunset meal, and reduce the evening dose by 25 – 50% and take it before dawn meal.
- Chlorpropamide or Glimepiride would be safe providing there is some dose reduction to allow for their long-acting nature.
- Glitazones (Rosiglitazone and Pioglitazone) taken with or without food at the same time each day dosage should not be affected.

Drug Regimens for Type 1 and Insulin Requiring DM. Patients:

- Insulin regimen during Ramadan needs to be modified and tailored for each individual patient.
- Strongly recommend avoiding premixed insulin during fasting if possible, and to avoid hypoglycaemia it may be necessary to change this for the duration of the fast.
- If patients remain on premixed insulin, the morning and evening doses should be reversed. Larger dose should be taken before the sunset meals, the second dose should be reduced by about 50% and taken before Dawn meals. Further adjustment of doses according to the results of home blood glucose monitoring is essential.
- Use of a short-acting insulin before the pre-dawn and sunset meals with an intermediate or long-acting insulin administered before the evening meal secures good control and is considered safe.
- Patients on conventional twice daily insulin regimens should take their usual morning dose before sunset meals, and their usual evening dose before dawn. However, the latter needs to be adjusted so that the fast-acting component remains the same and the intermediate acting insulin is cut by 50% or omitted.
- Three-dose insulin regimen: two doses before meals (sunset and Dawn) of short-acting insulin and one dose in the late evening of intermediate-acting insulin.

- Consider a lower dose of long-acting insulin (eg Isophane or Glargine) to avoid higher risk of hypos mid-day/mid-fast.
- Insulin prandial analogues (Lispro and Novo-Rapid) are useful for fasting because they allow people to inject during or just after their break of fast meal, and give a lower risk of hypoglycaemia during the night.
- Patients on Continuous subcutaneus insulin infusion are advised to reduce their basal infusion rates whilst increasing bolus doses to cover morning and evening meals.

Post-Ramadan Supervision of Fasting Diabetes Patients:

- After the month of Ramadan ends, the patients' therapeutic regimen should be changed back to its previous schedule.
- Patients should also be required to receive education about the general impacts o fasting on their physiology.

Diabetes & Pilgrimage:

Diabetic Patients who Intend to Perform Hajj are Advised to:

- Planning ahead for a trip.
- A pre-travel office visit to the physician.
- Wear or carry some form of medical identification or medical report.
- Preferably travel with a relative or a friend that have enough information about the patient and his treatment who can help in case it is needed.
- Use a comfortable shoes and daily inspections of the feet and keep feet clean, dry.
- Diabetic pilgrims should not walk barefoot on hot surfaces or sharp objects.
- Use an umbrella; or stay in the shade as far as possible and avoid overcrowded places as possible.
- Drink a lot of water to avoid dehydration.
- Adhere to their normal diet and treatment at appropriate times.
- Avoid foods that are prepared in unhygienic conditions, to prevent food poisoning.
- Insistence on taking mid-morning snacks is also important when exercise is expected to be more strenuous, as during the days of travel between Mecca–Medina–Mount Arafat.
- Obtain all required immunizations ahead of time.
- Take enough supply of syringes, insulin, needles and testing equipments or any other medications.
- Proper Storage of insulin and other medications avoiding extremes in temperature like freezing and direct sunlight.
- All patients should carry emergency supplies, such as glucagon injection kits or glucose tablets and a snack pack containing fastacting carbohydrates to use in case of hypoglycemia.
- Before performing tawaf or Saiy it is advised that they should check BS and take a small snake and enough amount of fluids.
- It may be necessary to advise the well-controlled diabetic patient to slightly reduce the morning dose of oral hypoglycemic agent or insulin as he/she is likely to be exercising the equivalent of 2 hours or more, which is contrary to most peoples' routine.

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Appendix III

Diabetic Medical Nutritional Therapy

Medical Nutrition Therapy in the Management of Type 2 Diabetes:

Introduction:

a) Definition of Medical Nutrition Therapy (MNT):

MNT service is defined as "nutritional diagnostic, therapy, and counseling services for the purpose of diabetes management which are provided by a dietitian or diabetic health educator (1).

Medical Nutrition Therapy Provider:

Because of the complexity of nutrition issues, it is recommended that a dietitian who is knowledgeable and skilled in implementing nutrition therapy into diabetes management and education be the team member who provides nutritional assessment and advice. However, since the access to dietitian is difficult due to non availability at the level of primary care and the delayed long appointments waiting list at either diabetes & hypertension centers or hospitals, it is essential that all team members, specially treating doctors and nurses (trained), are knowledgeable about nutrition therapy and are supportive of the person with diabetes.

b) Importance of MNT:

Medical nutrition therapy (MNT) is important in preventing diabetes, managing existing diabetes, and preventing, or at least slowing, the rate of development of diabetes complications. It is, therefore, important at all levels of diabetes prevention. MNT is also an integral component of diabetes self-management education (or training).

Medical nutrition therapy (MNT) is a part of team work effort to manage diabetic patients. MNT provides the diabetic patient with the knowledge, skills and motivation to successfully implement healthy life style modification in their daily lives.

The goals of lifestyle interventions in those with established type 2 diabetes are to reduce premature cardiovascular and all cause mortality and reduce morbidity due to diabetes complications. Some intermediate aims to enable these goals to be achieved are improved glycemic, lipid, and blood pressure control, and weight reduction or weight control.

The major lifestyle interventions are altering the diet (both in terms of nutritional composition and total energy content), increasing exercise and standardization of weight.

Achieving nutrition-related goals requires a coordinated team effort that includes the active involvement of the person with diabetes.

Nutrition counseling for the diabetic patient is a long process that needs time and space throughout the management plan. It is advisable to book separate sessions for dietary counseling for maximum benefit.

c) Aims of in type 2 DM patient:

1. Achieving and maintaining metabolic control:
   a. Glycemic control (normal blood glucose or as close to normal as safely possible)
   b. Serum lipid profile that reduces risk for cardiovascular disease.
   c. Blood pressure level that reduces risk for cardiovascular disease and nephropathy.
2. Improving health through modified nutrition and lifestyle habits.
3. Addressing the needs of people at risk for and with diabetes through individualized therapy.
4. Reducing the prevalence of obesity.
5. Preventing or managing diabetes complications.
6. Increasing physical activity.

Table 1: American Diabetes Association Therapeutic Goals*

Glycemic control A1C Preprandial plasma glucose Peak postprandial plasma glucose	Therapeutic goal: <7.0% 90–130 mg/dl (5.0–7.2 mmol/l) <180 mg/dl (<10.0 mmol/l)
Lipids LDL cholesterol Triglycerides HDL cholesterol	Therapeutic goal: <100 mg/dl (<2.6 mmol/l) <150 mg/dl (<1.7 mmol/l) >40 mg/dl (>1.1 mmol/l) for men >50 mg/dl (>1.4 mmol/l) for women
Blood pressure	Therapeutic goal: <130/80 mm Hg

**Source: American Diabetes Association, 2006*

d) Effectiveness of MNT:

Evidence-based research strongly suggests that MNT is provided by a registered dietitian who is experienced in the management of diabetes is clinically effective. Nutrition intervention has the largest statistically significant effect on metabolic control and weight loss. The UK Prospective Diabetes Study that included 2595 newly diagnosed patients with type 2 diabetes, who received intensive MNT, found that HbA1c decreased 1.9% in 3 months. Franz et al. conducted a randomized controlled trial in 179 persons with type 2 diabetes, comparing the usual nutrition care (consists of one visit) with a more intensive nutrition therapy (consists of at least 3 visits). The study that lasted for 6 months found that HbA_{1c} dropped by 0.7% with basic nutrition care, and 0.9% with nutrition practice guideline care. HbA_{1c} was unchanged in the comparison group with no nutrition intervention. A retrospective chart review by Christensen et al found that HbA_{1c} levels decreased 1.6% after referral to a registered dietitian in 102 patients (15 type 1 and 85 type 2 diabetic patients with duration of diabetes > 6 months). (Pastors, 2006).

However, MNT should be considered as an individualized type of therapy, along with physical activity. Despite the fact that the effective promotion of healthy eating and physical activity is challenging in our society, it is now well documented that MNT does make a difference.

Table 2: Effectiveness of Medical Nutrition Therapy:

Glycemic control	■ 1 – 2 % decrease in HbA_1C ■ 50 – 100 mg/dl decrease in fasting plasma glucose
Lipids	■ 10 – 13 % decrease in total cholesterol (24 – 32 mg/dl) ■ 12 – 16 % decrease in LDL cholesterol (18 – 25 mg/dl) ■ 8 % decrease in TG (15 – 17 mg/dl) ■ Exercise increase HDL cholesterol by 4.6 %
Hypertension	■ 5 mmHg decrease in systolic blood pressure ■ 2 mmHg decrease in diastolic blood pressure in hypertensive patients

Adapted and modified from Marion J, Diane R, Arlene M. Implementing Group & Individual Medical Nutrition Therapy for Diabetes. American Diabetic Association; 2002.

Obesity and Weight Management:

- About 80% of people with type 2 diabetes are overweight. Indeed, most cases might be prevented or delayed by early and effective weight management.
- Weight management improves all aspects of diabetes control, including blood glucose, blood lipids and hypertension.
- In adults Overweight is defined as a body mass index of 25.0-29.9 kg/ m^2 while obesity is defined as BMI ≥ 30.0 kg/ m^2.
- For adults, a BMI of 25.0-34.9 kg/ m^2, and a waist circumference ≥ 102cm in men and ≥ 88cm in women is a sign of excess abdominal fat, which is associated with an increased risk of metabolic complications.
- Many symptoms experienced by overweight people with diabetes may be related more to excess body weight than poor glycemic control.
- Weight management is best achieved by gradual rather than quick weight loss.
- Weight management in obesity should focus on adopting a healthy lifestyle through food choices and regular physical activity.
- Reducing energy intake by restricting dietary fat is considered a better nutritional strategy than a general restriction of energy, and may also reduce the risk of heart disease and some forms of cancer.
- Very low-carbohydrate diets (restricting total carbohydrate to <130 g/day) are not recommended in the treatment of overweight/obesity. The long-term effects of these diets are unknown and although such diets produce short-term weight loss, maintenance of weight loss is similar to that from low-fat diets and impact on CVD risk profile is uncertain.
- A gradual weight loss of 0.25 -1.0 kg/week should be advised with an achievable, time limited target such as 7 kg over 3 months.
- Weight loss of 5-10% of initial body weight should be sufficient to result in significant improvement in glycemic control and other co-morbidities.
- If weight loss is not possible, preventing of further weight gain should be attempted.
- 60 min of physical activity daily and ≤ 30% energy from fat including a variety of food such as whole fruits and vegetables and appropriately refined whole grain products are recommended for long-term weight management.

Nutrition Recommendation for Controlling Diabetes Complications:

1. CVD (cardiovascular disease)

CVD is the major cause of morbidity and mortality for individuals with diabetes. Hypertension and dyslipidemia are clear risk factors for CVD, and they often coexist with type 2 diabetes.

Studies have shown the efficacy of controlling individual cardiovascular risk factors (e.g. HTN) in preventing or slowing CVD in diabetic patients. (ADA, 2009)

Recommendations:

- Target A1C is as close to normal as possible without significant hypoglycemia. (B)
- For patients with diabetes at risk for CVD, diets high in fruits, vegetables, whole grains, and nuts may reduce the risk. (C)
- For patients with diabetes and symptomatic heart failure, dietary sodium intake of <2,000 mg/day may reduce symptoms. (C)

2. HTN (Hypertension)

Hypertension affects the majority of diabetic patients, with prevalence depending on type of diabetes, age, obesity, and ethnicity.

Blood pressure should be measured at every routine diabetes visit. Patients found to have a systolic blood pressure of > 130 mmHg or a diastolic blood pressure of >80 mmHg should have blood pressure confirmed on a separate day. Repeat systolic blood pressure of >130 mmHg or diastolic blood pressure of >80 mmHg confirms a diagnosis of hypertension. (ADA, 2009)

Recommendations:

- Patients with diabetes should be treated to a systolic blood pressure ≤ 130 mmHg.
- Patients with diabetes should be treated to a diastolic blood pressure ≤ 80 mmHg.
- In normotensive and hypertensive individuals with asymptomatic CVD and diabetic patients, a reduced sodium intake (e.g. 2000 mg/day) with a diet high in fruits, vegetables, and low-fat dairy products lowers blood pressure. (A)
- In most individuals, a modest (5 – 10% of body weight) amount of weight loss beneficially affects blood pressure. (C)

3. Nephropathy:

Diabetic nephropathy occurs in 20–40% of patients with diabetes and is the single leading cause of end-stage renal disease (ESRD). Persistent albuminuria in the range of 30–299 mg/24 h (microalbuminuria) has been shown to be a marker for development of nephropathy in type 2 diabetes. Persons with diabetes are more prone to kidney disease than the general population. Nutritional recommendations in people with diabetes and renal disease depend on the degree of nephropathy, in addition to treatments such as dialysis and transplantation. Protein intake should be limited to no more than requirements (0.86 g/kg/d for adults) to manage diabetic nephropathy at all stages of the diabetic nephropathy disease.

Studies in patients with varying stages of nephropathy have shown that protein restriction helps slow the progression of albuminuria, GFR decline, and occurrence of ESRD. Protein restriction should be considered particularly in patients whose nephropathy seems to be progressing despite optimal glucose and blood pressure control. Restricting protein intake to less than requirements has no additional benefit on the progression of renal disease and may result in inadequate intake of essential amino acids. Restriction of sodium, potassium and phosphorus intakes should be considered on an individual basis according to the results of laboratory tests. (ADA, 2009).

Recommendations:

- Reduction of protein intake to 0.8 – 1.0 g/kg body weight/day in individuals with diabetes and earlier stages of CKD and to 0.8g/ kg body weigh t/ day in the later stages of CKD may improve measures of renal function (urine albumin excretion rate, GFR) and is recommended (B).
- For children, protein intake should be limited to the recommended nutrient intake (RNI) for age and gender.
- Sodium, potassium and phosphorus restriction should be individualized. When ACE inhibitors ARBs or diuretic are used monitor serum creatinine and potassium levels for the development of acute kidney disease and hyperkalemia (E).

4. Retinopathy:

Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes, with prevalence strongly related to the duration of diabetes. Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years. Glaucoma, cataracts, and other disorders of the eye occur earlier and more frequently in people with diabetes.

In addition to duration of diabetes, other factors that increase the risk of, or are associated with, retinopathy include chronic hyperglycemia, the presence of nephropathy, and hypertension. Intensive diabetes management with the goal of achieving near normoglycemia has been shown in large prospective randomized studies to prevent and/or delay the onset and progression of diabetic retinopathy. Lowering blood pressure has been shown to decrease the progression of retinopathy. (ADA, 2009).

Recommendations:

- To reduce the risk or slow the progression of retinopathy,optimize glycemic control. (A)
- To reduce the risk or slow the progression of retinopathy, optimize blood pressure control. (A)

Nutrition Recommendations for the Management of Diabetes:

A. Macronutrients:

The optimal mix of macronutrients for people with diabetes has not been defined. Research does not support any ideal percentage of energy from macronutrients for persons with diabetes. Macronutrient intake should be individualized and is primarily based on the individual's willingness and ability to make food and eating changes. The Dietary Reference Intakes recommendations suggesting that adults should consume 45%–60% of total energy from carbohydrate, 20%–35% from fat and 10%–35% from protein to minimize the risk of chronic diseases can be used as a starting point. (ADA, 2009, 2).

1. Carbohydrates:

The recommended dietary allowance for digestible carbohydrate is 130 g/day and is based on providing adequate glucose as the required fuel for the central nervous system without reliance on glucose production from ingested protein or fat. Foods containing carbohydrate (e.g., fruits, vegetables, whole grains, legumes, low-fat milk) should be included in a healthy diet. Postprandial glucose response depends on the amount of carbohydrate ingested and available insulin. Therefore, to achieve glycemic control, carbohydrate should be monitored by carbohydrate counting, exchanges or experience-based estimation. Increased use of low GI foods such as legumes, barley, and pasta may help improve blood glucose control and allow carbohydrate intake to be increased without raising serum triglycerides. However, the role of the GI in diabetes therapy is controversial.

In newly diagnosed type 2 diabetics, there is evidence that nutrition education based on the GI is associated with higher carbohydrate, lower fat and higher fiber intakes – as well as better blood glucose and lipid control – compared to those educated using traditional dietary advice. (ADA, 2009).

Recommendations:

- Carbohydrates should provide 50–60% of daily energy requirements.
- The amount and source of carbohydrate in meal planning should be considered.
- Including low GI foods may be helpful in optimizing blood glucose control.

DM: Carbohydrate Intake Consistency:

In persons on either MNT alone, glucose-lowering medications or fixed insulin doses, meal and snack carbohydrate intake should be kept consistent on a day-to-day basis. Consistency in carbohydrate intake results in improved glycemic control.

DM: Carbohydrate Intake and Insulin Dose Adjustment:

In persons with type 1 or type 2 diabetes who adjust their mealtime insulin doses or who are on insulin pump therapy, insulin doses should be adjusted to match carbohydrate intake (insulin-to-carbohydrate ratio). This can be accomplished by comprehensive nutrition education and counseling on interpretation of blood glucose patterns, nutrition-related medication management and collaboration with the healthcare team. Adjusting insulin dose based on planned carbohydrate intake improves glycemic control and quality of life without any adverse effects.

Research clearly shows that sugars are an acceptable part of a healthy diet for those with diabetes, particularly sugars obtained from fruits, vegetables and dairy products. Up to 10% of total daily energy requirements may consist of added sugars, such as table sugar and sugar-sweetened products, without impairing glycemic control in people with type1 or type 2 diabetes. Avoidance of foods containing simple sugars is not necessary. Intake of added fructose, sucrose or high-fructose corn syrup in excess of 10% of energy should be avoided, since evidence suggests that this may increase serum triglycerides and/or LDL cholesterol in susceptible individuals. (ADA, 2009).

Recommendations:

- Naturally occurring and added sugars should be included as part of the daily carbohydrate allowance and as part of a healthy eating plan.
- Most people with diabetes can include added sugars up to 10% of daily energy requirements without deleterious effects on blood glucose or lipid control.

2. Fiber:

Soluble fiber intake of 5–10 g/d from oats, barley, legumes or such as psyllium, pectin and guar, can reduce serum cholesterol by 5–10%. However, whether soluble fiber content alone is a reliable indicator of the food's metabolic effects is still questionable. Research indicates that the insoluble fiber content of whole foods is more closely related to their GI than the soluble fiber content. Data from epidemiological studies suggest that insoluble fibers from cereals may reduce the risk for coronary heart disease and type 2 diabetes by up to 30% for each 10 g increment in intake. (ADA, 2009).

Recommendations:

- Total dietary fiber intake of at least 25–35 g/d from a variety of sources.
- Including more foods and food combinations that combine cereal fiber with low GI may be helpful in optimizing health outcomes for people with diabetes or at risk for diabetes.

Protein:

A number of small, short-term studies in persons with diabetes have shown that glucose produced from ingested protein does not increase circulating glucose levels, however, it does produce acute insulin responses. People with diabetes have similar protein requirements to those of the general population – about 0.86 g/kg per day. Although protein plays a role in stimulating insulin secretion, excessive (>30%) intake should be avoided due to its role in the pathogenesis of diabetic nephropathy. (2, 6, 4)

Recommendations:

- Protein intake should be at least 0.86 g/kg/day.
- Protein should not be used to treat acute or prevent nighttime hypoglycemia (A).
- High-protein diets are not recommended for weight loss (E).

3. Fats:

Several studies indicate that diets high in fat can impair glucose tolerance and promote obesity, dyslipidemia and atherosclerotic heart disease. However, metabolic abnormalities are reversed or improved by reducing saturated fat intake. Current recommendations on fat intake for the general population apply equally to people with diabetes: reduce saturated fats to 10% or less of total energy intake and cholesterol intake to 300 mg/d or less. Adults who have normal lipid levels and maintain a reasonable weight are recommended to have a daily fat intake of 30% of energy requirements, comprised of 10% saturated fat and 10% polyunsaturated fat, with the remainder coming from monounsaturated fat. Research suggests monounsaturated fat (such as canola, olive and peanut oils) may have beneficial effects on triglycerides and glycemic control in some individuals with diabetes, however, care must be taken to avoid weight gain. Omega-3 fatty acids, found in fish such as salmon, may reduce serum triglycerides without impairing glycemic control. Ingesting trans-fatty acids that are commonly found in many manufactured foods should be limited. (7, 3).

Recommendations:

- Total fat should be limited to 30% of daily energy requirements.
- Saturated and polyunsaturated fats should each provide 10% of daily energy requirements.
- Monounsaturated fats should be used where possible.
- Use of processed foods containing saturated fats and trans-fatty acids should be limited.
- Fish rich in omega-3 fatty acids should be recommended at least once weekly.

4. Sweeteners:

Moderate use of nutritive (sucrose, fructose, the sugar alcohols [xylitol, mannitol, sorbitol, isomalt, lactitol and maltitol] and aspartame) and non-nutritive sweeteners (acesulfame potassium, sucralose, cyclamate and saccharin) can be part of a well-balanced diet for people with diabetes.

The energy and/or carbohydrate content of nutritive sweeteners needs to be included in the meal plan, whereas non-nutritive sweeteners do not affect blood glucose levels and provide little or no energy. Sugar alcohols raise blood glucose only minimally and contribute a small amount of energy to the diet. Sugar alcohols are absorbed and metabolized at different rates in the small intestine and can cause flatulence and diarrhea in some individuals. It should be noted though that during pregnancy and lactation, saccharin and cyclamate is not recommended. Acesulfame potassium, aspartame and sucralose are acceptable in moderation. Individuals with diabetes should receive individualized counselling on how to include the use of foods containing sweeteners. These foods are often not low in energy due to the fat content of the product. Individuals should therefore be advised on how to evaluate food labels for total fat and sweetener content and on how to substitute these products for other food choices within the meal plan. Blood glucose and lipid levels should be monitored on a regular basis and assess their response to routine sweetener use. (ADA, 2009).

Recommendations:

- Individuals with diabetes should be educated on the appropriate use of nutritive and non-nutritive sweeteners.
- The impact of nutritive sweeteners on the individual's blood glucose levels and lipid profiles should be assessed on a regular basis.

B. Micronutrients:

Uncontrolled diabetes is often associated with micronutrient deficiencies *(Mooradian AD)*. Individuals with diabetes should be aware of the importance of acquiring daily vitamin and mineral requirements from natural food sources and a balanced diet.

- There is no clear evidence of benefit from vitamin or mineral supplementation in people with diabetes (compared with the general population) Who do not have underlying deficiencies. (A)
- Routine supplementation with antioxidants, such as vitamins E and C and carotene, is not advised because of lack of evidence of efficacy and concern related to long-term safety. (A)
- Benefit from chromium supplementation in individuals with diabetes or obesity has not been clearly demonstrated and therefore can not be recommended. (E)

Physical Activity and Diabetes:

- Increased physical activity by individuals with type 2 diabetes can lead to improved glycemia, decreased insulin resistance, and a reduction in cardiovascular risk factors, independent of change in body weight.
- At least 150 min/week of moderate-intensity aerobic physical activity, distributed over at least 3 days and with no more than 2 consecutive days without physical activity is recommended *(Diabetes Care, 2004)*.

- Resistance training is also effective in improving glycemia
- In the absence of proliferative retinopathy, people with type 2 diabetes can be encouraged to perform resistance exercise three times a week *(Diabetes Care, 2004)*.
- The RD should instruct individuals on insulin or insulin secretagogues on the safety guidelines to prevent hypoglycemia (frequent blood glucose monitoring and possible adjustment in insulin dose or carbohydrate intake). Research indicates that the incidence of hypoglycemia during exercise may depend on baseline glucose levels.

Diabetes Mellitus (DM): Monitor & Evaluate Diabetes:

Monitoring and Evaluation:

The RD should monitor and evaluate food intake, medication, metabolic control (glycemia, lipids, and blood pressure), anthropometric measurements and physical activity. Research reports sustained improvements in A1C at 12 months and longer with long-term follow-up encounters with an RD.

Evaluation of Glycemic Control:

The RD should primarily use blood glucose monitoring results in evaluating the achievement of goals and effectiveness of MNT. Glucose monitoring results can be used to determine whether adjustments in foods and meals will be sufficient to achieve blood glucose goals or if medication additions or

- adjustments needed to be combined with MNT.

General Principles for Type 2 Diabetes:

- Individuals with prediabetes or diabetes should receive individualized MNT, preferably administered by a registered dietitian knowledgeable about the components of diabetes MNT (B).
- Nutrition counseling should be tailored to the personal needs of the individual with prediabetes or diabetes and his or her willingness and ability to make changes (E).
- Modest weight loss in overweight and obese insulin-resistant individuals has been shown to improve insulin resistance and is therefore recommended for all such individuals who have or are at risk for diabetes (A).
- In the short-term (up to 1 year), either low-carbohydrate or low-fat, energy-restricted diets may be effective for weight loss (A).
- Patients receiving low-carbohydrate diets should undergo monitoring of lipid profiles, renal function, and protein intake (in patients with nephropathy), and have adjustment of hypoglycemic therapy as needed (E).

- Physical activity and behavior modification aid in weight loss and are most helpful in maintaining weight loss (B).
- Primary prevention for individuals at high risk of developing type 2 diabetes should include structured programs targeting lifestyle changes, with dietary strategies of decreasing energy and dietary fat intakes. Goals should include moderate weight loss (7% body weight), regular physical activity (150 minutes/week) (A), dietary fiber intake of 14 g/1000 kcal, and whole grains comprising half of total grain intake (B).
- Intake of low-glycemic index foods that are rich in fiber and other vital nutrients should be encouraged (E), both for the general population and for those with diabetes.
- Secondary prevention, or controlling diabetes, should include a healthy dietary pattern emphasizing carbohydrate from fruits, vegetables, whole grains, legumes, and low-fat milk (B).
- A key strategy for achieving glycemic control is to monitor carbohydrate by counting, exchanges, or experienced-based estimation (A). Use of glycemic index and load may be modestly beneficial vs considering only total carbohydrate (B).
- Sucrose-containing foods should be limited but can be substituted for other carbohydrates or covered with insulin or other glucose-lowering medications (A). Glucose alcohols and nonnutritive sweeteners are safe within daily US Food and Drug Administration intake levels (A).
- Saturated fat should be limited to less than 7% of total energy (A), and trans fat should be minimized (E). In individuals with diabetes, dietary cholesterol should not exceed 200 mg/day (E).
- At least 2 servings of fish per week (except for commercially fried fish) are recommended for n-3 polyunsaturated fatty acids (B).
- Protein should not be used to treat acute or prevent nighttime hypoglycemia (A).
- High-protein diets are not recommended for weight loss (E).
- Food frequency: 3 meals or 3 smaller meals with snacks is based on individual preference and on drug regimen.
- When insulin is required, consistency in timing of meals and CHO content is important (5).

Behavioral outcomes:

Patients with diabetes should be able to:

- Eat meals / snacks at appropriate times.
- Choose food and amount per food plan.
- Accurately use nutrition facts on food labels.
- Participate in physical activity per exercise prescription.
- Appropriately follow prescribed medication regimen.
- Make nutritional changes based on home blood glucose monitoring.

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وزارة الصحة
Ministry of Health

Appendix IV
Diabetic Foot

A CLINICAL PRACTICE GUIDELINE FOR DIABETIC FOOT DISORDERS

(2010 revision)

Table of Contents

I. Introduction:

Diabetes mellitus is emerging as a major public health problem in Saudi Arabia in parallel with the worldwide diabetes pandemic, which is having a particular impact upon the Middle East and the third world. This pandemic has accompanied the adoption of a modern lifestyle and the abandonment of a traditional lifestyle, with a resultant increase in rates of obesity and other chronic non-communicable diseases.

The indigenous Saudi population seems to have a special genetic predisposition to develop type 2 diabetes which is further amplified by a rise in obesity rates, a high rate of consanguinity and the presence of other variables of the insulin resistance syndrome. Diabetes is well studied in Saudi Arabia; however, there seems to be little research in the area of education and health care delivery. This is of paramount importance to offset the perceived impact on health care delivery services, to lessen chronic diabetes complications, and to reduce the expected morbidity and mortality from diabetes.

Foot complications are one of the most serious and costly complications of diabetes mellitus. Amputation of (part of) a lower extremity is usually preceded by a foot ulcer. A strategy which includes prevention, patient and staff education, multi-disciplinary treatment of foot ulcers and close monitoring can reduce amputation rates by 49-85%. Therefore, several countries and organizations, such as the World Health Organization and the International Diabetes Federation, have set goals to reduce the rate of amputations by up to 50%.

Preliminary data from the Western part of Saudi Arabia suggests that the overall prevalence of neuropathy in diabetic patient is 82%, which is one of the highest in the world. 62 Among those with neuropathy, 57% were asymptomatic, implying subclinical disease, and symptomatic disease is related to old age, longer duration of diabetes, poor diabetes control, type 2 diabetes and smoking. On the other hand, a study by Fonseca et al found relatively common abnormalities in tests of autonomic nerve dysfunction in a group of patents who had a relatively short duration of diabetes, implying a longer duration of subclinical diabetes in Saudi Arabs. The same group confirmed their earlier finding by documenting prolonged cardiac systolic time, a surrogate.

In a study by Akbar and Qari (2000) in which looked exclusively into diabetic foot lesions in Saudi diabetics, but involved a small number of patients, found that the problem is mainly seen in males, and that 23.5% ended with major amputations.

In these brief clinical practice guidelines principles of prevention and treatment will be described, based upon the document entitled “International Consensus on the Diabetic Foot” and “American Diabetes Association”. Depending upon local circumstances these principles have to be translated for local use, taking into account socio-economics, accessibility to healthcare.

II. Diabetic foot Screening and Risk Categorization:

1. The Pathway to Foot Ulceration

The lifetime risk of a person with diabetes developing a foot ulcer may be as high as 25%, whereas the annual incidence of foot ulcers is 2% (6-10). Up to 50% of older patients with type 2 diabetes have one or more risk factors for foot ulceration (6-9). A number of component causes, most importantly peripheral neuropathy, interact to complete the causal pathway to foot ulceration (4,6-8). A list of the principal contributory factors that might result in foot ulcer development is provided in Table 1. The most common triad of causes that interact and ultimately result in ulceration has been identified as neuropathy, deformity, and trauma (8). As identification of those patients at risk of foot problems is the first step in preventing such complications. This report will focus on key components of the foot exam.

2. Components of The Foot Exam:

a. History:

While history is a pivotal component of risk assessment, a patient cannot be fully assessed for risk factors for foot ulceration based on history alone; a careful foot exam remains the key component of this process. Key components of the history include previous foot ulceration or amputation. Other important assessments in the history (Table 2) include neuropathic or peripheral vascular symptoms (10-11), impaired vision, or renal replacement therapy. Lastly, tobacco use should be recorded, since cigarette smoking is a risk factor not only for vascular disease but also for neuropathy.

b. General inspection:

A careful inspection of the feet in a well-lit room should always be carried out after the patient has removed shoes and socks. Because inappropriate footwear and foot deformities are common contributory factors in the development of foot ulceration (4, 8), the shoes should be inspected and the question "Are these shoes appropriate for these feet?" should be asked.

Table 1: *Risk factors for foot ulcers*	Table 2: *Essential features of history*	Table 3: *Key components of the diabetic foot exam*
■ Previous amputation ■ Past foot ulcer history ■ Peripheral neuropathy ■ Foot deformity ■ Peripheral vascular disease ■ Visual impairment ■ Diabetic nephropathy (especially patients on dialysis) ■ Poor glycemic control ■ Cigarette smoking	Past history ■ ulceration ■ amputation ■ Charcot joint ■ vascular surgery ■ angioplasty ■ cigarette smoking Neuropathic symptoms ■ positive (e.g., burning or shooting pain, electrical or sharp sensations, etc.) ■ negative (e.g., numbness, feet feel(dead) Vascular symptoms ■ claudication ■ rest pain ■ nonhealing ulcer Other diabetes complications ■ renal (dialysis, transplant) ■ retinal (visual impairment)	Inspection Dermatologic ■ skin status: color, thickness, dryness, cracking ■ sweating ■ infection: check between toes forbfungal infection ■ ulceration ■ calluses/blistering: hemorrhage into callus? Musculoskeletal ■ deformity, e.g., claw toes, prominent metatarsal heads, Charcot joint (Fig. 1) ■ muscle wasting (guttering between metatarsals) Neurological assessment 10-g monofilament 1 of the following 4 ■ vibration using 128-Hz tuning fork ■ pinprick sensation ■ ankle reflexes ■ VPT Vascular assessment ■ foot pulses ■ ABI, if indicated

Examples of inappropriate shoes include those that are excessively worn or are too small for the person's feet (too narrow, too short, toe box too low), resulting in rubbing, erythema, blister, or callus. Features that should be assessed during foot inspection are outlined in Table 3.

c. Dermatological Assessment

The dermatological assessment should initially include a global inspection, including interdigitally, for the presence of ulceration or areas of abnormal erythema. The presence of callus (particularly with hemorrhage), nail dystrophy, or paronychia should be recorded (12), with any of these findings prompting referral to a specialist or specialty clinic. Focal or global skin temperature differences between one foot and the other may be predictive of either vascular disease or ulceration and could also prompt referral for specialty foot care (13 –16).

d. Musculoskeletal Assessment:

The musculoskeletal assessment should include evaluation for any gross deformity (17). Rigid deformities are defined as any contractures that cannot easily be manually reduced and are most frequently found in the digits. Common forefoot deformities that are known to increase plantar pressures and are associated with skin breakdown include metatarsal phalangeal joint hyperextension with interphalangeal flexion (claw toe) or distal phalangeal extension (hammer toe) (18–20). (Examples of these deformities are shown in Fig. 1.) An important and often overlooked or misdiagnosed condition is Charcot arthropathy. This occurs in the neuropathic foot and most often affects the midfoot. This may present as a unilateral red, hot, swollen, flat foot with profound deformity (21–23). A patient with suspected Charcot arthropathy should be immediately referred to a specialist for further assessment and care.

e. Neurological Assessment:

Peripheral neuropathy is the most common component cause in the pathway to diabetic foot ulceration (4,7,8,10). The clinical exam recommended, however, is designed to identify loss of protective sensation (LOPS) rather than early neuropathy. The diagnosis and management of the latter were covered in a 2004 ADA technical review (10). The clinical examination to identify LOPS is simple and requires no expensive equipment. Five simple clinical tests (Table 3), each with evidence from well-conducted prospective clinical cohort studies, are considered useful in the diagnosis of LOPS in the diabetic foot (4–10). The task force agrees that any of the five tests listed could be used by clinicians to identify LOPS, although ideally two of these should be regularly performed during the screening exam–normally the 10-g monofilament and one other test. One or more abnormal tests would suggest LOPS, while at least two normal tests (and no abnormal test) would rule out LOPS. The last test listed, vibration assessment using a biothesiometer or similar instrument, is widely used in the U.S.; however, identification of the patient with LOPS can easily be carried out without this or other expensive equipment.

- 10-g Monofilaments.

Monofilaments, sometimes known as Semmes-Weinstein monofilaments, were originally used to diagnose sensory loss in leprosy (24). Many prospective studies have confirmed that loss of pressure sensation using the 10-g monofilament is highly predictive of subsequent ulceration (6,24,25). Screening for sensory loss with the 10-g monofilament is in widespread use across the world, and its efficacy in this regard has been confirmed in a number of trials, including the recent Seattle Diabetic Foot Study (7,24,26,27).

Nylon monofilaments are constructed to buckle when a 10-g force is applied; loss of the ability to detect this pressure at one or more anatomic sites on the plantar surface of the foot has been associated with loss of large-fiber nerve function.

It is recommended that four sites (1st, 3rd, and 5th metatarsal heads and plantar surface of distal hallux) be tested on each foot. The technique for testing pressure perception with the 10-g monofilament is illustrated in Fig. 2; patients should close their eyes while being tested.

Caution is necessary when selecting the brand of monofilament to use, as many commercially available monofilaments have been shown to be inaccurate. Single-use disposable monofilaments or those shown to be accurate by the Booth and Young (23) study are recommended.

The sensation of pressure using the buckling 10-g monofilament should first be demonstrated to the patient on a proximal site (e.g., upper arm).

The sites of the foot may then be examined by asking the patient to respond "yes" or "no" when asked whether the monofilament is being applied to the particular site; the patient should recognize the perception of pressure as well as identify the correct site. Areas of callus should always be avoided when testing for pressure perception.

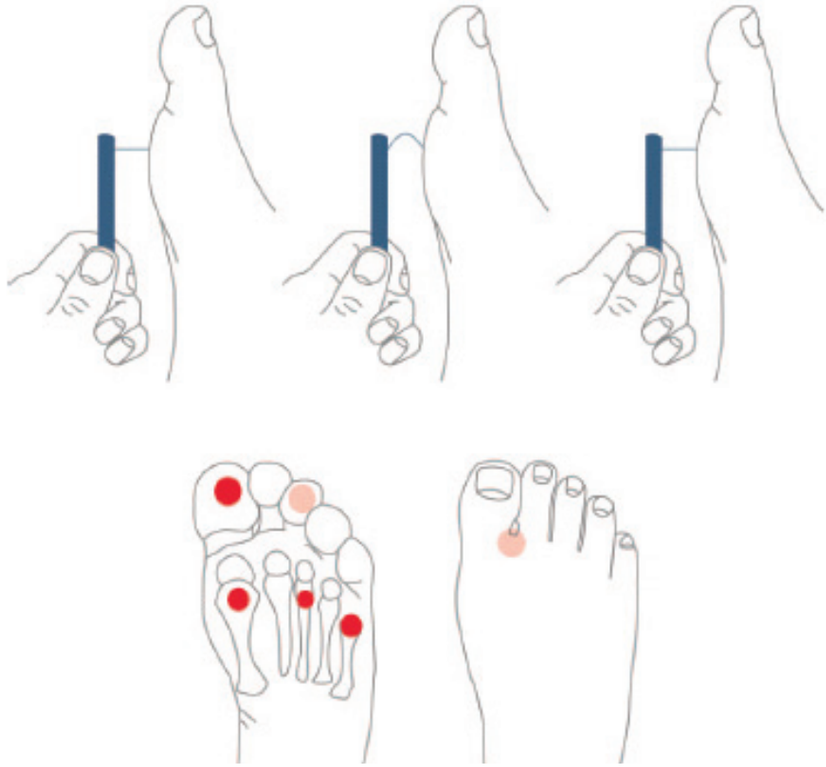

Figure 2 - Upper panel: *For performance of the 10-g monofilament test, the device is placed perpendicular to the skin, with pressure applied until the monofilament buckles. It should be held in place for 1 s and then released.*

Lower panel: *The monofilament test should be performed at the highlighted sites while the patient's eyes are closed.*

- 128-Hz Tuning Forks:

The tuning fork is widely used in clinical practice and provides an easy and inexpensive test of vibratory sensation. Vibratory sensation should be tested over the tip of the great toe bilaterally. An abnormal response can be defined as when the patient loses vibratory sensation and the examiner still perceives it while holding the fork on the tip of the toe (6,7).

- Pinprick Sensation:

Similarly, the inability of a subject to perceive pinprick sensation has been associated with an increased risk of ulceration (7). A disposable pin should be applied just proximal to the toenail on the dorsal surface of the hallux, with just enough pressure to deform the skin. Inability to perceive pinprick over either hallux would be regarded as an abnormal test result.

Ankle Reflexes:

Absence of ankle reflexes has also been associated with increased risk of foot ulceration (7). Ankle reflexes can be tested with the patient either kneeling or resting on a couch/table. The Achilles tendon should be stretched until the ankle is in a neutral position before striking it with the tendon hammer. If a response is initially absent, the patient can be asked to hook fingers together and pull, with the ankle reflexes then retested with reinforcement. Total absence of ankle reflex either at rest or upon reinforcement is regarded as an abnormal result.

Vibration Perception Threshold Testing:

The biothesiometer (or neurothesiometer) is a simple handheld device that gives semi-quantitative assessment of vibration perception threshold (VPT). As for vibration using the 128-Hz tuning fork, vibration perception using the biothesiometer is also tested over the pulp of the hallux. With the patient lying supine, the stylus of the instrument is placed over the dorsal hallux and the amplitude is increased until the patient can detect the vibration; the resulting number is known as the VPT. This process should initially be demonstrated on a proximal site, and then the mean of three readings is taken over each hallux. A VPT 25 V is regarded as abnormal and has been shown to be strongly predictive of subsequent foot ulceration (18, 25).

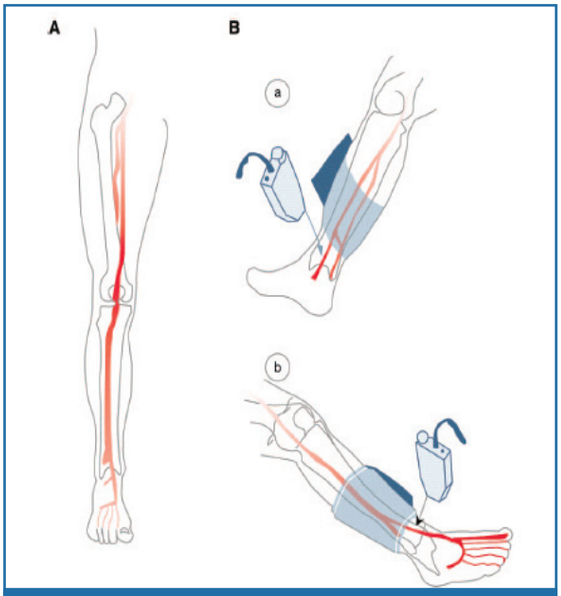

Figure 3: *Lower-extremity circulation and the ABI test. A: Anterior view, right lower limb, normal arterial anatomy. B: ABI. Place blood pressure cuff above pulse. Place Doppler probe over arterial pulse; a: posterior tibial artery, b: dorsalis pedis artery. ABI calculation: Divide ankle systolic blood pressure by brachial artery systolic blood pressure. (ABI _0.9 is normal.) Adapted from Khan et al., JAMA 295:536 –546, 2006.*

f. Vascular Assessment:

Peripheral arterial disease (PAD) is a component cause in approximately one-third of foot ulcers and is often a significant risk factor associated with recurrent wounds (8,28). Therefore, the assessment of PAD is important in defining overall lower extremity risk status. Vascular examination should include palpation of the posterior tibial and dorsal is pedis pulses (13,29), which should be characterized as either "present" or "absent" (29). Diabetic patients with signs or symptoms of vascular disease (Table 2) or absent pulses on screening foot examination should undergo ankle brachial pressure index (ABI) pressure testing and be considered for a possible referral to a vascular specialist. The ABI is a simple and easily reproducible method of diagnosing vascular insufficiency in the lower limbs. Blood pressure at the ankle (dorsal is pedis or posterior tibial arteries) is measured using a standard Doppler ultrasonic probe.

This technique is outlined in Fig. 3. The ABI is obtained by dividing the ankle systolic pressure by the higher of the two brachial systolic pressures (11). An ABI 0.9 is normal, 0.8 is associated with claudication, and 0.4 is commonly associated with ischemic rest pain and tissue necrosis.

The ADA Consensus Panel on PAD recommended measurement of ABI in diabetic patients over 50 years of age and consideration of ABI measurement in younger patients with multiple PAD risk factors, repeating normal tests every 5 years (11). ABI may therefore be part of the annual comprehensive foot exam in these patient subgroups. ABI measurements may be misleading in diabetes because the presence of medial calcinosis renders the arteries incompressible and results in falsely elevated or supra-systolic ankle pressures. In the presence of incompressible calf or ankle arteries (ABI 1.3), measurements of digital arterial systolic pressure (toe pressure) or transcutaneous oxygen tension may be performed.

3. Risk Classification and Referral/follow-up:

Once the patient has been thoroughly assessed as described above, he or she should be assigned to a foot risk category (Table 4). These categories are designed to direct referral and subsequent therapy by the specialty clinician or team (20,23) and frequency of follow-up by the generalist or specialist. Increased category is associated with an increased risk for ulceration, hospitalization, and amputation (20). Patients in risk category 0 generally do not need referral and should receive general foot care education and undergo comprehensive foot examination annually.

Patients in foot risk category 1 may be managed by a generalist or specialist every 3–6 months. Consideration should be given to an initial specialist referral to assess the need for specialized treatment and follow-up. Those in categories 2 and 3 should be referred to a foot care specialist or specialty clinic and seen every 1–3 months.

Table 4: Risk classification based on the comprehensive foot examination:

Risk category	Definitions	Treatment recommendations	Suggested follow-up
0	No LOPS, no PAD, no deformity	▪ Patient education including advice on appropriate footwear.	Annually (by generalist and/or specialist)
1	LOPS ± deformity	▪ Consider prescriptive or accommodative footwear. ▪ Consider prophylactic surgery if deformity is not able to be safely accommodated in shoes. Continue patient education.	Every 3-6 months (by generalist or specialist)
2	PAD ± LOPS	▪ Consider prescriptive or accommodative footwear. ▪ Consider vascular consultation for combined follow-up	Every 2-3 months (by specialist)
3	History of ulcer or amputation	▪ Same as category 1. ▪ Consider vascular consultation for combined follow-up if PAD present.	Every 1-2 months (by specialist)

4. Conclusion:

It cannot be overstated that the complications of the diabetic foot are common, complex, and costly, mandating aggressive and proactive preventative assessments by generalists and specialists. All patients with diabetes must have their feet evaluated at least at yearly intervals for the presence of the predisposing factors for ulceration and amputation (neuropathy, vascular disease, and deformities). This report summarizes a simple protocol for doing so. If abnormalities are present, more frequent evaluation of the diabetic foot is recommended depending on risk category, as described above and in Table 4. It is through systematic examination and risk assessment, patient education, and timely referral that we may further reduce the unnecessarily high prevalence of lower-extremity morbidity in this population.

III. Specific Guidelines for Diabetic Foot Management:

1. Diagnosing and Treating the Infected Diabetic Foot

Based upon: The International Consensus on Diagnosing and Treating the Infected Diabetic.

Introduction:

Based upon the International Consensus on Diagnosing and Treating the Infected Diabetic Foot and prepared by the IWGDF working group on diagnosing and treating the infected diabetic foot in 2003.

The Working G roup recognizes that the availability of diagnostic procedures and antimicrobial agents will vary greatly in different clinical sites and in different countries.

While the basic principles of treating diabetic foot infections are the same in all situations, they have provided guidance that must be adapted to local circumstances.

Pathophysiology:

1. Foot infections in persons with diabetes usually begin with a break in the skin, especially a neuropathic ulceration.
2. This allows colonizing skin flora to invade the skin and subcutaneous tissues.

Diagnosis:

1. Diagnose wound infections clinically (recognizing that the inflammatory response may be mitigated by diabetic complications), by the presence of purulent secretions or local evidence of inflammation, or occasionally systemic toxicity.
2. Laboratory tests, including cultures, may suggest but do not establish the presence of infection, with the exception of reliably obtained deep bone cultures in suspected osteomyelitis.

Classification:

1. Assess the severity of the infection by examining the wound, limb, and the overall status of the patient, to determine the appropriate approach to treatment.
2. Classifying infections by their severity helps determine the site, type and urgency of treatment.

Microbiology:

1. Cultures

A. Obtaining proper specimens for culture is usually advisable, to help select an appropriate antibiotic regimen. Cultures may not be necessary in previously untreated, mild infections.

B. Take wound cultures by obtaining tissue (by curettage or biopsy) of the debrided wound base or by aspirating pus, rather than by swabbing. If swabs are the only option, take them from the ulcer base after debridement, and process quickly.

C. Consider obtaining blood cultures from systemically toxic patients and consider bone cultures from patients with osteomyelitis

2. Etiologic agents

A. Aerobic gram-positive cocci (especially staphylococci) are usually the initial, often the only, and almost always the most frequently isolated pathogens in soft tissue and bone infections.

B. Gram-negative and anaerobic bacteria are commonly isolated, but usually as part of a polymicrobial, chronic or necrotic infection.

Non-antimicrobial Treatment:

1. Consult a diabetic foot care team or specialist, where available.
2. Correct any metabolic derangements, optimize wound care, and assess vascular status.
3. Hospitalize patients: with a severe infection, needing multiple or complex diagnostic or surgical procedures; having critical foot ischemia; needing intravenous therapy; or unlikely to comply with therapy.

In case of severe infection, consult appropriate specialists promptly for any necessary invasive diagnostic or surgical procedures.

Antimicrobial Therapy:

1. General principles

A. Prescribe for all clinically infected wounds immediately, but not for uninfected wounds.

B. Select the narrowest spectrum therapy possible for mild or moderate infections.

C. Choose initial therapy based on the commonest pathogens and known local antibiotic sensitivity data.

D. Adjust (broaden or constrain) empiric therapy based on the culture results and clinical response to the initial regimen.

2. Specific choices (see below)

A. Cover staphylococci and streptococci in almost all cases.

B. Broaden the spectrum if necessary based on the clinical picture, or previous culture or current Gram-stained smear results.

C. Topical therapy for mild superficial infections has not been adequately studied; oral therapy is effective for most mild to moderate infections; parenteral therapy (at least initially) is advisable for severe infections.

D. Choose agents that have demonstrated efficacy in treating complicated skin and soft tissue infections. These include semisynthetic-penicillins, cephalosporins, penicillin-lactamase inhibitors, clindamycin, fluoroquinolones, carbapenems, and oxazolidinones.

E. Treat soft tissue infections for 1-2 weeks if mild infections, and about 2-4 weeks for most that are moderate and severe. When the clinical evidence of infection has resolved antibiotic therapy can be stopped.

Appendix:

Suggested systemic antibiotic regimens for treating diabetic foot infections:

Severity of Infection	Usual Pathogen(s)	Potential Regimens
Non-severe (oral for entire course)		
No complicating features	⬭ GPC	⬭ S-S pen; 1 G Ceph
Recent antibiotic therapy	⬭ GPC +/- GNR	⬭ FQ, ß-L-ase
Drug allergies		⬭ Clindamycin; FQ; T/S
Severe (intravenous until stable, then switch to oral equivalent		
No complicating features	⬭ GPC2 +/- GNR	⬭ ß-L-ase; $^{2}/_{3}$ G Ceph
Recent antibiotic/necrosis	⬭ GPC + GNR/anaerobes	⬭ ¾ G Ceph; FQ + Clindamycin
Life-threatening (prolonged intravenous)		
MRSA unlikely	⬭ GPC + GNR + anaerobes	⬭ Carbapenem; Clindamycin Aminoglycoside
MRSA likely		⬭ Glycopeptide or linezolid + ¾ G Ceph or FQ + metronidazole

1. Given at usual recommended doses for serious infections; modify for azotemia, etc.; based upon theoretical considerations and available clinical trials.

2. A high local prevalence of methicillin-resistance among staphylococci may require using vancomycin or other appropriate anti-staphylococcal agents active against these organisms:

GPC = gram-positive cocci.
GNR = gram-negative rod.
S-S pen = semi-synthetic (anti-staphylococcal) penicillin (e.g., flucloxacillin, oxacillin).
1 G Ceph = first generation cephalosporins (e.g., cephalexin, cefazolin).
FQ = fluoroquinolones (e.g., ciprofloxacin, levofloxacin).
ß-L-ase = lactam- ß lactamase- ß inhibitor (e.g., amoxicillin/clavulanate, piperacillin/tazobactam)
T/S = trimethoprim/sulfamethoxazole.
2/3/4 G Ceph = 2nd/3rd/4th generation cephalosporins (e.g., cefoxitin, ceftazidime, cefepime).
Carbapenem: e.g., imipenem/cilastatin, meropenem, ertapenem.
Aminoglycoside: e.g., gentamicin, tobramycin, amikacin.
Glycopeptide: e.g., vancomycin, teicoplanin.

2. Wound and Wound Bed Management (30):

Based upon: The consensus report: The effectiveness of interventions to enhance the healing of chronic ulcers of the foot in diabetes - an evidence based guideline.

- The Principles of Care of a Chronic Diabetic Foot Ulcer are:
  a. Treatment of any associated infection.
  b. Revascularization if possible and feasible.
  c. Off-loading in order to minimize trauma to the ulcer site.
  d. Management of the wound and wound bed in order to promote healing.

- The Most Important Principles of Wound and Wound Bed Management are the Most Simple:
  a. Regular inspection.
  b. Cleansing.
  c. Removal of surface debris.
  d. Protection of the regenerating tissue from the environment.

The International Working Group on the Diabetic Foot has recently conducted a systematic review of the evidence available to support the use of any particular approach which may enhance wound healing. The review searched for published controlled trials or cohort studies in which the response to the intervention being tested was compared with a control group. The results of this search are included in the current guidelines.

- Wound Management of Diabetic Foot Ulcers Can be Addressed with a Set of Simple Interventions:
  a. The wound should be cleaned regularly with clean water or saline.
  b. Exudate should be controlled in order to maintain a moist wound environment; usually a sterile, inert protective dressing is sufficient.
  c. In addition to regular debridement with a scalpel, other agents may be used to attempt to clean the wound bed. The best evidence supports the use of Hydrogels (although contraindication should be considered, such as infection, excessive exudate or critical limb ischemia), but other debriding agents may also be effective.
  d. Plantar neuropathic ulcers which do not heal readily with appropriate off-loading can be considered (provided the arterial blood supply is adequate) for management by excision of the whole ulcer bed and (if indicated to reduce abnormal pressure loading) of underlying bone. However, there are currently insufficient data regarding the long term outcome of these bony resections, such as re-ulceration and the development of transfer ulcers.
  e. Negative pressure therapy, by using vacuum devices, may hasten healing of postoperative wounds but the effectiveness and cost-effectiveness of the approach remains to be established in chronic diabetic foot ulcers.

- There are currently no data to indicate that the use of the other treatments (including silver-containing dressings or other antiseptic products) enhances ulcer healing, although
  a. There is limited evidence that systemic (as opposed to topical) hyperbaric oxygen therapy (HBO) may reduce ulcer area, but further (especially blinded) studies are required, as well as studies of cost-effectiveness;
  b. Various early studies of the effectiveness of the supernatant of platelet suspensions have suggested benefit but there are no recent data;
  c. There are a limited number of reports suggesting that bioengineered skin products might hasten wound healing, but further evidence to justify their routine use is required, including evidence of cost-effectiveness;
  d. Evidence justifying the use of platelet-derived growth factor (PDGF, becaplermin) remains to be confirmed.

3. Footwear and Off-loading

Based upon: The consensus report: Footwear and off-loading for the diabetic foot-an evidence based guideline.

- Prevention of ulceration;

a. Callus removal:

- Regular callus removal should be performed in people with diabetes and neuropathy by a skilled health care provider.

b. Footwear:

- Patients with an at-risk diabetic foot should be urged not to walk barefoot but to wear protective footwear both at home and outside.
- Although no evidence exists, it is often apparent clinically that even extra-depth footwear may not accommodate a foot with significant deformity. In such cases, custom footwear is recommended.
- Therapeutic shoes can be used for preventing plantar ulceration in the at-risk diabetic foot.
- To achieve maximal reduction of peak plantar pressures in footwear prescription, custom molded insoles should be incorporated in the therapeutic footwear as long as sufficient space exists (see, for example, 'Extra-depth shoe' in Appendix).

c. Surgical offloading:

- Given the paucity of data, no definitive statement can be made about the effectiveness and safety of preventive surgery.
- Achilles tendon lengthening can be considered in selected patients but this procedure carries the risk of heel ulceration. More information, including high quality studies, is needed before the procedure can be recommended for widespread use.
- There are few high quality studies on metatarsophalangeal (MTP) joint arthroplasty and metatarsal head (MTH) resection. These approaches cannot be recommended for widespread use before further evidence is available.
- One should also be aware of the disadvantages of applying surgical techniques for the prevention of plantar ulcers in the diabetic foot which can include post-operative wound infection, induction of acute neuro-osteoarthropathy (Charcot) and development of ulcers at other sites (transfer ulcers).

- Treatment of Ulceration:

a. Offloading:

The total contact cast (TCC - see Appendix) is the preferred treatment for noninfected, neuropathic diabetic plantar forefoot ulcers in patients with no signs of critical limb ischemia. Adverse effects of TCC include: immobilisation of the ankle, reduced activity level, difficulty with sleeping or driving a car, and pressure ulcers due to poor casting technique.
If casting is not available, then removable walkers with an appropriate interface should be considered. Preferably, these walkers should be made irremovable as this 'forced adherence' increases healing rates.
The use of half-shoes or cast shoes for neuropathic plantar ulcer treatment is recommended if TCC or below knee removable walkers are contra-indicated or cannot be tolerated by the patient.

b. Footwear:

- Conventional or standard therapeutic shoes should not be chosen for treatment of plantar foot ulcers as, usually, there are many devices available that are more effective.
- Non-plantar ulcers and post-surgical wounds also need relief of mechanical stress. Depending on the location of the ulcer, various modalities can be considered, including shoe modifications, temporary footwear, and toe spacers.

c. Surgical offloading:

- More studies are needed to better define the role of surgical off-loading compared to conservative treatment and one should be aware of the disadvantages of applying surgical techniques for the treatment of plantar ulcers in the diabetic foot (see above).

d. Other offloading interventions:

- If other forms of biomechanical relief are not available, felted foam in combination with appropriate footwear can be used to provide accommodative off-loading at an ulcer site. It should not be used as a single treatment method.

4. Treatment for Diabetic Foot Osteomyelitis

Based upon: The management of diabetic foot osteomyelitis - a progress report on diagnosing and a consensus on treating osteomyelitis.

The principle of treatment is to administer antibiotics while providing a local environment in which they can work. This typically involves the removal of dead soft tissue and accessible dead bone during the wound care process. These interventions may be undertaken by any appropriately trained healthcare provider.

- Surgical procedures for removing necrotic and infected bone range from simple outpatient debridement to major amputation.
  a. Urgent surgery is indicated for necrotising fasciitis, deep soft tissue abscess or gangrene accompanying osteomyelitis. All systemically unwell patients should be evaluated with these possible diagnoses in mind.
  b. Non-urgent surgery may be necessary if there is significant compromise of the soft tissue envelope, loss of mechanical function or integrity of the foot, when the degree of bone involvement is likely to threaten life or limb, or where patient or provider wish to avoid prolonged antibiotic therapy.
  c. Otherwise, surgical debridement of infected bone appears not to be necessary in some cases of diabetic foot osteomyelitis, though one cannot predict with certainty which patients will fail medical therapy.

- Antibiotic regimens should be as targeted and narrow spectrum as possible. Bone culture and sensitivity results, if obtained, can assist in achieving this goal.
  a. No specific agent has been shown to be most effective for osteomyelitis. Empiric regimens must include anti-staphylococcal coverage, with activity against methicillin-resistant strains (MRSA) according to local prevalence data.
  b. Achieving adequate levels of antibiotics in the infected bone can be accomplished with intravenous therapy or highly bioavailable oral antibiotics. There are no data to indicate the superiority or inferiority of any particular route of delivery of systemic antibiotic for treating osteomyelitis. Available data are insufficient to assess the efficacy of locally administered antibiotics.
  c. There are also no data to inform decisions on duration of antibiotic therapy. The scheme produced by the Infectious Diseases Society of America, which assesses the extent of residual soft tissue infection, bone infection and dead bone, and adjusts duration accordingly, appears to be useful.

- Adjunctive Treatments
  a. Limb ischaemia considered critical or compromising of wound healing should be corrected through revascularization procedures.
  b. There is no evidence to support the use of hyperbaric oxygen G-CSF or larval therapy in the treatment of diabetic foot osteomyelitis.

IV. Addendum (30):

Evidence Table 1: Wound bed preparation by sharp debridement and the use of larvae

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Saap 2002 (1)	Cohort study Study quality: 5/8	143 evaluable subjects with neuropathic superficial diabetic foot ulcers followed for 12 weeks in a parent RCT	Assessment of the extent of debridement, on Day 0 using a debridement index	Closure of ulcer	A wound with a debridement index of 3-6 was 2.4 times more likely to heal than one with index of 0-2 (p=0.03).	2+	This was a sub-analysis of a study of the effectiveness of another intervention, (Apligraf) Veves, et al (2001) (72)
Sherman 2003 (14)	Cohort study Study quality: 3/8	18 subjects with 20 chronic, non-healing ulcers divided into three groups: 6 conventional therapy, 6 debridement therapy with larvae, 8 conventional therapy followed by larval debridement therapy. Followed for 14 weeks total	Debridement therapy with larvae	Decrease in extent of necrotic tissue at	2 weeks: Decrease in necrotic tissue (4.1 vs 0 cm2) (p = 0.02) Larvae: complete debridement at 4 weeks versus 33% at 5 weeks (p = 0.001)	2-	Complex study. Comparison between groups difficult because of the use of different times to outcome.
Armstrong 2005 (15)	Case control study Study quality 1/7	30 people (mean age 72 years; 26M) with diabetes and peripheral arterial disease and confined to either bed or wheelchair, who had had foot ulcers treated with larvae, compared with 30 age and sex matched controls who had not	History of wound debridement with larvae	Healing; Time to healing; major amputations Antibiotic use (antibiotic-free days)	Trend to difference in ulcer healing (p=0.07); Shorter time to healing (I:18.5 vs C: 22.4 days, p=0.04); Fewer major amputations (I: 10% versus C: 33%, p=0.03) and more antibiotic-free days: (I: 127 vs C: 82, p=0.0001)	2-	High percentage male. Unusual population. Cases and follow-ups selected by those in whom 6 month follow-up data were available. Not clear if controls matched for criteria other than age and sex

Evidence Table 2: Wound bed preparation using antiseptics, applications and dressing products

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Apelqvist 1996 (16)	RCT Quality 3/9	41 patients with diabetes, >40years old, with toe/ankle pressure >30mm/80 mmHg, respectively, and with exudating, cavity wounds with an area of 1-25 cm2 Intervention group 22 Control group 19 Lost to follow-up 5	Iodosorb daily initially and then less often for 12 weeks or until the wound was less exudative versus saline-moistened gauze	Healing and decrease in area >50%	Healing in intervention group 5/17 versus 2/18 (NS)	1-	Primarily a health economic analysis, with limited results presented on clinical outcomes Per protocol analysis; 5 said to be lost to follow-up but results given on only 35
Apelqvist 1990 (17)	RCT Quality 3/9	44 patients with necrotic ulcers. Intervention group 22, Control group 22 Followed for 5 weeks Lost to follow-up: 2	Adhesive zinc oxide tape versus hydrocolloid	Necrotic ulcer area reduction greater than 50%	Outcome achieved in 14/21 in the intervention group vs 6/21 controls (P<0.025)	1-	Uncertain numbers of withdrawals
Donaghue 1998 (18)	RCT Quality 5/9	Patients with non-ischaemic foot ulcers, area >1cm2 : Intervention group 50, Control group 25 Followed for 8 weeks Lost to follow-up: 14	Collagen-alginate wound dressing vs saline moistened gauze	Ulcer healing, reduction in ulcer area	48% of the intervention group healed versus 36 % controls (NS); Mean reduction in ulcer area: 81 % vs. 61 % in controls (NS)	1+	Open label study
Lalau 2002 (19)	RCT Quality 4/9	77 with both chronic and acute wounds, area >1cm^2 Intervention group 39, Control group 38	Calcium alginate vs vaseline gauze	>75% wound granulation plus decrease in ulcer area by >40%	Combined endpoint achieved in 42.8% intervention group versus 28.5% in controls (NS)	1-	Included acute wounds Study duration reduced from 6 weeks to 4 weeks because of high drop-out rate Mean ulcer area at recruitment was very high at 8 cm^2

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
							High % with type I diabetes suggests selected population
Jensen 1998 (20)	RCT Quality 3/9	Patients with non-ischaemic foot ulcers; area >1cm^2 Intervention group 14, Control group17 Followed for 20 weeks Lost to follow-up: 0	Hydrogel dressing vs. saline moistened gauze	Ulcer healing	85 % in the intervention group vs 46 % in controls ($p<0.05$)	1-	Open label study
Cangialosi 1982 (21)	Prospective cohort series Quality 1/8	28 diabetics with 37 lower extremity ulcers Intervention group 14, Control group 14 Drop out: unknown. Follow-up: unknown	Hydrogel and sterile gauze	Ulcer healing	Healing said to be "about 33% more rapid in hydrogel group"	2-	No statistical analysis Duration of follow-up and number lost to follow-up not stated Stated results vague
Capasso 2003 (22)	Cohort retros pective Quality 2/8	50 patients (28 with diabetes) with arterial disease and foot ulcers Intervention group 25, Control group 25 Follow-up 7 weeks.	Amorphous hydrogel vs wet or dry sterile gauze	Cost; Wound healing; Time to healing	No differences observed in wound healing Time to heal: p=0.02 in favour of hydrogel	2-	Complex series of primarily health economic studies No raw data presented on either wound healing or time to healing

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Piaggesi 2001 (23)	RCT Quality 3/9	20 patients with foot ulcers >1cm deep Intervention group10, Control group10 Followed for 8 weeks	Hydrofibre carboxymethyl cellulose dressing vs saline moistened gauze	Days to healing	127 (46 SD) days in the intervention group versus 234 (61) controls ($p < 0.001$)	1-	
Blackman 1994 (24)	RCT Quality 4/9	18 patients with diabetes and Wagner grade 1 or 2 ulcers. Intervention group 7 (mean age 51 years; 6M)	Semi-permeable membrane dressing applied for two months vs wet-to-dry saline gauze; late cross-over for 5/7 control group	Healing by two months Change in ulcer area over two months (intervention vs control);	Intervention group 3/11 healed versus 0/7 (no statistical analysis	1-	Further reduction in area in the cross-over group

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
		Control group 11 (59 years; 11M)			Intervention: reduction in area 35±16% baseline at two months vs 105±28%, p=0.03		
Muthukum-arasamy 1991 (25)	Cohort Quality 4/8	100 patients with type 2 diabetes and Wagner grade 1 or 2 foot ulcers Intervention group 50 (27M) Control group 50 (27M)	Topical phenytoin versus saline 35 days versus an occlusive dry dressing	Decrease in ulcer area, and complete healing	Intervention group % decrease in area was 88% of baseline versus 50% (p<0.005) 20/50 healed in the Intervention group versus 12/50	2-	No statistical analysis given for the numbers which healed
Pai 2001 (26)	RCT Study Quality 5/9	70 patients with type 2 diabetes and Wagner grade 1 or 2 ulcers Intervention group: 36 (mean age 56 years, ulcer area 11.9 cm2; 25M) Control group: 34 (60 years, 11.9cm2; 22M) Drop-outs: 13	Topical phenytoin powder for 6 weeks versus talc/silicone dioxide	% decrease in cross-sectional area	Intervention group 73.5% reduction inarea versus 73.5% (NS)	1+	

Evidence Table 3: Resection of the chronic wound

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Piaggesi 1998 (27)	RCT Study quality: 5/9	Patients with plantar diabetic forefoot ulcers Intervention group 21 Control group : 20 Followed for at least 6 months None lost to follow up	Ulcer excision with removal of bone and closure of wound vs conservative treatment	Healing, and time to healing	21/22 ulcers treated with surgery healed compared with 19/24 controls (NS) Time to healing (days) shorter in the intervention group (46 vs 128 days) (p <0.001)	1+	Also recorded incidence of secondary infection per ulcer (not per patient): 3/24 intervention group versus 1/22 (p= 0.72)
Armstrong 2005 (28)	Retrospective cohort study Quality 3/8	40 patients with a chronic ulcer under 5th metatarsal head Intervention group 22, Control group 18 Followed for 6 months	5th MT head resection vs medical treatment only	Time of ulcer healing	5.8 (2.9) weeks in cases vs 8.7 (4.3) in controls (p <0.05)	2-	
Armstrong 2003 (29)	Cohort study Quality 2/8	Uninfected, non-ischaemic ulcers under the interphalanageal joint of the hallux or the 1st metatars-ophalangeal joint Intervention group 21, Control group 20 Followed for 6 months	1st MTP joint arthroplasty, and resection head of 1st metatarsal versus non-surgical management	Time to ulcer healing and ulcer recurrence	24.2 days in the intervention group vs 67.1 in controls (p=0.0001) Ulcer recurrence in intervention group 4.8% versus 35% controls (p=0.02)	2-	
Tan 1996 (30)	Cohort study Quality 3/8	112 patients hospitalized with 164 diabetic foot infections 77 patients had surgery within 3 days 87 had no surgery within 3 days	Surgery within 3 days of hospital admission vs no surgery within 3 days	Amputation and resolution of infection	Those operated early had 77 episodes of infection and 10 major amputations versus 87 infection episodes and 35 major amputations in the non-surgical group (p<0.01)	2-	Description of outcomes and lesion types is incomplete. The incidence of amputation in the control group was high.

Evidence Table 4: Hyperbaric oxygen therapy - both topical and systemic

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Leslie 1998 (31)	RCT Study quality 6/9	28 with diabetic foot ulcers (16 hispanic, 7 black, 7 white) Intervention group 12, Control group 16	Topical HBO versus standard care	Change in cross-sectional area at day 7 and 14	Day 7: Area reduced to 67.1% in the intervention group versus 69.6% controls (NS) Day 14: 45.6% versus 35.6% (NS)	1+	
Heng 2000 (32)	RCT Study quality 3/9	Intervention group 13, Controls 13 (plus an additional 14 controls who were not randomised) Follow for 4 weeks Lost to follow-up: not clear	Topical HBO vs standard care	Ulcer healing	90 % healing in the intervention group versus 28% controls	1-	Partial randomisation: the control group was larger because of lack of treatment spaces Complicated data presentation. No statistical analysis presented. Not all patients had diabetes
Faglia 1996 (33)	RCT Study quality 5/9	68 diabetic patients with ulcers Wagner grade 2-4 Intervention group 35, Control group 33	Systemic HBO (2.5 ATA, 90 minutes daily) continued until healing or amputation vs standard care	Amputation	30 % fewer major amputations in Wagner grade 4 patients ($p<0.016$)	1+	Randomization process unclear. Not blinded. Time to healing not reported. High frequency of vascular surgery after randomization. Mean age in the Intervention group 61.7 years vs 65.6 years in the control group.

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Kessler 2003 (34)	RCT Study quality 6/9	28 patients with neuropathic ulcers Wagner grade 1-3 and Duration >3 months Intervention group 15, Control group 13 Followed for 4 weeks Lost to follow-up:1	HBOT (2,5 ATA, 90 minutes twice daily 5 days a week for 2 weeks) vs standard care	Reduction in ulcer area at 2 weeks and at 4 weeks	Wound area reduction: 2 weeks: 42% in the intervention group versus 21% (p=0.037. and 62% at 2 4 weeks: 62% versus 55% (NS)	1+	1 patient excluded from evaluation due to barotraumatic otitis
Doctor 1992 (35)	RCT Study quality 3/9	30 patients: 23 with gangrene and 5 neuropathic ulcers Intervention group 15, Control group 15	Systemic HBO (3 ATA, 45 minutes, 4 sessions - mean 34 treatments) vs standard care	Amputation	Major amputation: 2 in the intervention group versus 7 controls (p<0.05)	1-	Wound size and depth are not reported No differences in number of healed ulcers Less positive bacterial cultures in HBOT group
Abidia 2003 (36)	RCT Study quality 9/9	18 patients with diabetic ulcers area 1-10 cm^2 and duration >6 weeks Intervention group 9,Control group 9 Lost to follow-up: 2	Systemic HBO (2,4 ATA, 90 minutes, 30 sessions) vs hyperbaric air (2,4 ATA, 90 minutes, 30 sessions)	Healing; Reduction in ulcer area Number healed at 12 months	Median area reduction 100% in the intervention group versus 52% controls (p=0.02) Healed at 12 months 5/8 in the intervention group versus 1/8 controls (p=0.026)	1++	

Evidence Table 5: Reduction of tissue oedema

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
McCallon 2000 (38)	RCT Quality 4/9	Non-healing ulcers of duration >1 month Intervention group 5, Control group 5 Followed until healing Lost to follow-up: 0	NPT therapy versus saline moistened gauze	Time to ulcer healing	22.8 days in the intervention group versus 42.8 days controls (NS)	1-	Small numbers
Eginton 2003 (39)	RCT Quality 4/9	10 patients with non ischaemic foot ulcers Followed for 4 weeks Lost to follow-up: 4	Cross-over design Randomly allocated to start with either NPT therapy for 2 weeks or with saline moistened gauze for 2 weeks	Reduction in ulcer volume	59% reduction with NPT therapy compared with 0.1 % for saline moistened gauze ($p<0.05$)	1-	Small numbers and with 40% drop out rate
Armstrong 2005 (40)	RCT Quality 5/9	162 patients with residual wounds of mean duration 1.5 months after foot surgery Intervention group 77, Control group 85 Followed for 16 weeks Lost to follow-up: 38	NPT therapy versus standard dressings	Healing (but including those unhealed and rendered suitable for surgical closure)	56% in the intervention group versus 39% controls ($p=0.04$)	1+	This study was of wounds after diabetic foot amputation, rather than chronic foot ulcers. It was also marred by a high rate of drop-out. The strength of the observation is weakened by the definition of healing used
Armstrong 2000 (41)	RCT Quality 6/9	115 patients with postoperative infected diabetic neuropathic foot ulcers Intervention group 52, Control group 45 Followed for 12 weeks Lost to follow-up: 18	Pneumatic foot compression device versus placebo non-functioning device	Wound healing	39/52 healed in the intervention group versus 23/45 ($p<0.02$) Odds ratio 2.9 (1.2 - 6.8)	1+	In addition there was a difference in the intervention group between those who were and were not adherent

Evidence Table 6: Application of products designed to correct aspects of wound biochemistry and cell biology associated with impaired wound healing

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Di Mauro 1991 (47)	RCT Study quality 3/9	20 patients (6 with ischaemic, 4 with neuropathic, and 9 with neuro-ischaemic ulcers Followed until healing Lost to follow-up: 0	Lyophilised collagen vs hyaluronic acid medicated gauze	Time to healing	32 days in the intervention group vs 49 days controls ($p<0.001$)	1-	One ulcer was a wrist ulcer
Krupski 1991 (48)	RCT Study quality 8/9	18 non-healing ulcers of both leg and foot (14 had diabetes) Followed for 12 weeks Lost to follow-up: Nil	Autologous platelet factor versus saline	Healing and reduction in area	24% healed in the intervention group versus 33% controls; 4.3 cm^2 reduction in area per week in intervention group versus 1.9 cm^2 controls (NS)	1++	Both diabetic and non-diabetic patients Outcomes were for wounds and per patient
Steed 1992 (49)	RCT Study quality 6/9	13 subjects with neuropathic diabetic foot ulcers Intervention group 7 Control group 6 Followed for 20 weeks	Platelet derived wound healing formula (CT-102) vs normal saline	Proportion of healing and area reduction	5/7 healed in the intervention group vs 1/6 control ($p<0.05$) Reduction in ulcer area 6.2mm^2/day in the intervention group vs 1.8 mm^2/day controls ($p < 0.05$)	1+	Definition of healing unclear (3 subjects still needed dressings in one treatment arm)
Margolis 2001 (50)	Retrospec-tive cohort Study quality 5/8	20347 patients with neuropathic ulcers identified from the database of the CHS healthcare system Followed for 20 weeks	Platelet Factor given to 6252 within 12 weeks	Proportion healed	50% healed in intervention group vs 41% in controls RR:1.38 (1.33-1.42)	2+	Retrospective analysis of treatment given in practice: Inconsistent dose and duration of treatment. Selected population
Feng 1999 (51)	Cohort Study quality 2/8	78 cases with diabetes and ulcers of the leg, foot (and elsewhere); 62 on the foot. Mean ulcer area 10.7 cm2; mean ulcer duration 8.9 days	EGF or Platelet derived wound healing fluid or saline control administered daily	Wound closure index at 6 weeks % healed at 2, 4, 6 and 8 weeks	Closure index higher in both the EGF and PDWHF groups when compared with placebo ($p<0.01$) % healed higher in EGF and PDWHF groups ($p<0.01$)	2-	Incomplete reporting of results. Mean duration of the ulcers was short at 8.9 days.

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Driver 2006 (52)	RCT Study quality 7/9	72 (out of 129 screened) people with diabetes (type 1 or 2) and uninfected ulcers (UT 1A) of more than 4 weeks duration Intervention: mean age 56 years; 32 M; mean ulcer area 3.2 cm^2 Control: 58 years; 27 M; mean ulcer area 4.0 cm^2	Platelet autogel for 12 weeks versus placebo gel, with 11 weeks follow-up	Proportion healed (confirmed at 1 week) and time to healing	Healing in 13/16 in the Intervention group versus 8/19 in Controls. Time to healing significantly shorter in the Intervention group (p=0.018)	1+	Very high exclusion rate necessitated per protocol analysis. High percentage of heel ulcers
Niezgoda 2005 (53)	RCT Study quality 3/9	98 with diabetic foot ulcers Intervention group 37 Control group 36 Followed for 12 weeks Lost to follow up: 25 patients (25%)	Acellular wound care product versus becaplermin (PDGF)	Healing at 12 weeks, time to healing	49% healed in the intervention group versus 28% controls (NS) Time to healing 67 days in the intervention group versus 73 days controls (NS)	1-	Unexplained high drop out rate
Steed 1995 (54)	RCT Study quality 2/9	118 subjects with diabetic foot ulcers Intervention group 61, Control group 57 Followed for 20 weeks Lost to follow-up: 3	Recombinant Platelet derived growth factor versus placebo gel	Proportion of patients healed at 20 weeks	29 (48%) of 61 PDGF vs 14 (25%) of 57 patients randomized to the placebo group (p = 0.01)	1-	Details of treatment in the two arms unclear Although only 3 were lost to follow-up total withdrawals were high, with only 86/118 completing the study
Wieman 1998 (55)	RCT Study quality 6/9	Uninfected non-ischaemic ulcers present for 8 weeks or more Intervention groups: (30 mcg/g) 132 (100 mcg/g) 123 Placebo gel 127 Followed up to 20 weeks Lost to follow-up: 73/382	Dose ranging becaplermin gel applied daily versus placebo gel	Proportion healed at 20 weeks, time to healing, reduction in ulcer area	100 mcg/g associated with 50% versus 35% placebo (p=0.007) Time to healing 100mcg/g 86 days versus 127 placebo (p=0.013) No differences between 30 mcg/g & placebo	1+	Details of randomization not specified, nor the blinding of the assessor

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Robson 2005 (56)	RCT Study quality 4/9	146 Neuropathic plantar foot ulcers, duration >4 weeks Intervention group 74 Control group 72 Lost to follow up: 3	0.01% becaplermin (PDGF) vs an adaptive dressing	Healing at 20 weeks, time to healing	Healing in 42% in the intervention group vs 35% controls (NS) Time to healing NS (no data reported)	1-	Only 146 enrolled of target of 340
Richard 1995 (57)	RCT Study quality 6/9	17 patients with diabetic foot ulcers Intervention group 9 Control group 8 Followed for 12 weeks	Fibroblast growth factor (bFGF) vs placebo vehicle	Ulcer healing and reduction in ulcer area	5 healed in the intervention group vs 3 controls (NS) 47.2% had reduction in area in intevrention group 35.8% controls (NS)	1+	Small sample size
Tsang 2003 (58)	RCT Study quality 7/9	61 patients with neuropathic diabetic foot ulcers Intervention groups 0.02% 21 0.04% 21 Control group 19 Followed for 12 weeks	Dose ranging study of epidermal growth factor (EGF) 0.02% versus EGF 0.04% versus placebo	Proportion of healing	12 /21 receiving 0.02% EGF healed, compared with 20/21 0.04% EGF, and 8/19 controls (p=0.0003) at 12 wks for 0.04% gel	1+	Small sample size
Afshari 2005 (59)	RCT Study quality 4/9	0 patients, including 25% with a leg ulcer Intervention group 30, Control group 20 Followed for 4 weeks Lost to follow-up: 0	Topical epidermal growth factor vs placebo	Proportion healed by 4 weeks; >70% reduction in ulcer area	No difference in proportion of ulcers healed. 70% reduction in area in 50% of the intervention group versus 15 % in controls (p=0.05)	1-	Reduction in ulcer area adopted as an endpoint retrospectively after no difference found in primary end point

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Veves 2002 (60)	RCT Study quality 2/9	276 diabetic foot ulcers Intervention group 138 Control group 138 Followed for 12 weeks Lost to follow-up: 27%	Hydrofibre (cellulose/ collagen dressing) versus saline moistened gauze	Healing by 12 weeks	No significant difference in healing (37.0% vs 28.3% p>0.05)	1-	High drop-out rate Suboptimal off-loading strategy
Tom 2005 (61)	RCT Study quality 7/9	24 subjects with neuropathic diabetic foot ulcers Intervention group 13 Control group 11 Followed for 16 weeks Lost to follow-up: 2	Solution of topical Tretinoin (retinoin A-) versus placebo saline solution applied for 4 weeks	Proportion healed by 16 weeks Reduction in ulcer area and depth	6/13 healed in the intervention group vs 1/11 controls (p = 0.03) Reduction in area (p<0.02), and depth (p<0.01) greater in intervention group	1+	Details of the analysis are not clear

Evidence Table 7: Stem cell therapy (including G-CSF)

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Gough 1997 (62)	RCT Study quality 9/9	Patients with foot ulcers complicated by soft tissue infection Intervention group 20 Control group 20 Followed for 7 days Lost to follow-up: 0	G-CSF administered sc daily for 7 days vs saline injections sc	Ulcer healing	4 healed in the intervention group versus 0 controls (p=0,09)	1++	This was primary a study of the eradication of infection and not powered for ulcer healing. Short duration of intervention
De Lalla 2001 (63)	RCT Study quality 4/9	Patients all with osteomyelitis. Intervention group 20 Control group 20 Followed for 6 months Lost to follow-up: 4	G-CSF sc and conventional treatment vs conventional treatment alone	Cure, improvement of infection, failure, amputation	No significant differences were reported	1-	All drop outs were in the intervention group. The use of composite endpoints makes interpretation difficult
Yonem 2001 (64)	RCT Study quality 3/9	Patients with ulcers Wagner grade 2 complicated by soft tissue infection (inflammation >2cm) Intervention group 15 Control group 15 Lost to follow-up: Nil	G-CSF given sc vs standard treatment for 10 days	Duration of hospital admission, time to infection resolution and proportion of amputation	Duration of hospital admission 26.9 days in the intervention group vs 28.3 controls (NS). Amputation 13.3% in the intervention group vs 20% controls (NS) Time to resolution 23.6 days in the intervention group vs 22.3 controls (NS)	1-	No data regarding healing rate No information given on blinding

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Kastenbauer 2003 (65)	RCT Study quality 7/9	Patient with foot ulcers complicated by cellulitis Intervention group 20 Control group 17 Followed for 10 days Lost to follow-up: 0	G-CSF sc daily for 10 days vs saline sc	Ulcer volume reduction	Reduction in ulcer volume in 59 % in the intervention group vs 35 % controls (NS)	1+	Primary endpoint was eradication of infection (study not powered for volume reduction)
Huang 2005 (66)	RCT Study quality 4/9	Patients with ischaemic ulcers Intervention group 14 Control group 14 Followed for 3 months Lost to follow-up: 0	IM administration of autologous monocytes following G-CSF sc for 5 days vs iv administration of prostaglandin E2	Ulcer healing	14/18 healed in the Intervention group versus 7/18 controls (p=0.016)	1-	The primary endpoint was improvement of limb ischemia Ulcers were analysed instead of patients

Evidence Table 8: Bioengineered skin and skin grafts

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Gentzkow 1996 (68)	RCT Study quality 6/9	Patients with non-ischaemic plantar foot ulcers Intervention groups: 12,14,11 Control group 13 Followed for 12 weeks Lost to follow-up: 0	Group 1: application of 1 piece of dermal fibroblast culture weekly, Group 2: 2 pieces every 2 weeks Group 3: 1 piece every 2 weeks Controls: saline-moistened gauze	Proportion with ulcer healing	Group 1: 50% Group 2: 21% Group 3: 18% Controls: 8% (Group 1 vs controls, p< 0.05)	1+	The percentage of controls healing at 12 weeks was very low
Naughton 1997 (69)	RCT Study quality 3/9	281 Patients with non-ischaemic plantar neuropathic ulcers of duration >2 weeks and area >1cm2 Intervention group 139 Control group 142 Followed for 12 weeks Lost to follow-up: 46 (17.4%)	Dermal fibroblast culture weekly for 8 weeks vs standard care	Healing at 12 weeks	38.5% healed in the intervention group versus 31.7% controls (NS)	1-	Per protocol analysis. The data were also re-analyzed on the basis of perceived metabolic inactivity of some batches of dermal fibroblast culture Short ulcer duration before study
Marston 2003 (70)	RCT Study quality 5/9	245 patients with non-ischaemic plantar neuropathic ulcers of duration >2 weeks and area >1 cm2 Intervention group 130 Control group 115 Lost to follow-up : 46 (19%)	Dermal fibroblast culture weekly for up to 8 treatments versus conventional therapy	Healing at 12 weeks, time to healing	30% healed in the intervention group versus 18% controls (p=0.023) RR = 1.6 Time to healing: p=0.04 in favour of the intervention group	1+	Ninety percent of patients were male, suggesting selection bias No raw data on time to healing Short ulcer duration before study

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Veves 2001 (72)	RCT Study quality 5/9	277 patients with non-ischaemic plantar neuropathic ulcers of duration >2 weeks and area >1cm2 Intervention group 112	Tissue engineered sheet of fibroblast / keratocyte co-culture once a week for 12 weeks vs saline moistened gauze	Numbers healed at 12 weeks, days to healing	56% healed in the intervention group vs 38% controls (p=0.004) OR = 2.14 (95% CI 2.3-3.74)	1+	Suboptimal offloading strategy Open study (difficult to blind)
		Control group 96 69 were excluded and ITT analysis performed on remaining 208 44 withdrawals (21%)			Median time to healing 65 days in the intervention group vs 90 controls (p=0.003)		Large number of exclusions and withdrawals
Bayram 2005 (73)	RCT Study quality 0/9	40 patients with Wagner grade 2 and 3 foot ulcers Intervention group 20 Control group 20 Followed for 1 year Lost to follow-up: unknown	Keratinocyte loaded microcarrier vs microcarrier placebo	Ulcer healing, reduction of ulcer area and wound condition	Reduction in ulcer area: 92% in the intervention group vs 32 % controls Wound condition: Intervention group 5.86 versus 2.85 controls (p<0.001)	1-	Ulcer healing: no data given Missing data make interpretation difficult
Puttirutvong 2004 (74)	RCT Study quality 3/9	80 patients with infected ulcers of both legs and feet Intervention group 36 Control group 44	Meshed skin graft vs split thickness graft	Time to healing	19.8 days in the intervention group versus 20.4 days controls (NS)	1-	Inconsistency between patient numbers in the abstract and the text

Evidence Table 9: Electrical, electromagnetic, lasers, and ultrasound

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Baker 1997 (75)	RCT Study quality 3/9	80 people with 114 chronic ulcers randomized to one of four groups: three with different amounts of stimulation and one control	Electrical stimulation for four weeks and then follow-up for an unspecified period	Ulcer healing Compliance with treatment	No difference between Intervention and Control groups	1-	Post hoc analysis with stratification by compliance, and combination of one of the treatment groups into the controls suggested a statistically significant difference of uncertain meaning
Peters 2001 (76)	RCT Study quality 9/9	40 people with uninfected ulcers (UT Grade 1A-2A) and TcpO2 >30mmHg Intervention: 21 (mean age 54 years; 19M) Controls: 20 (59.4 years; 16M) Lost to follow-up: 5	Electrical stimulation	Healing Time to healing	Intervention: 13/21 (65%) healed versus 7/20 (35%); p=0058 No difference in time to healing	1++	The difference between groups was significant when adjusted post hoc for compliance
Ennis 2005 (77)	RCT Quality 6/9	133 neuropathic DFU (Wagner 1), duration >30 days Follow-up 12 weeks. Lost to follow up: 24 (+ 12 study violations) leaving only 97 then a further 42 had study violation (leaving only 55 assessed)	Ultrasound versus sham therapy	Ulcer healing	Analysis of 133 patients: no data (p=0.69) Per protocol: 1 41% vs 14% in controls (p=0.04)	1+	Data only given on the 55 patients who did not violate the protocol or drop out in some way. Number of patients randomized to each arm not given.

Reference	Study design	Study population and characteristics	Intervention and control conditions	Outcome category	Results primary outcome + statistic	Level of evidence SIGN	Comments on weaknesses
Alvarez 2003 (78)	RCT Quality 5/9	20 patients with neuropathic DFU Intervention group 10 Control group 10 12 weeks follow-up Lost to follow-up: 0	Non-contact thermal wound care system versus saline dressing	Ulcer healing	Intervention group 70% healing vs 40% in controls at 12 weeks (p=0.069).	1+	Interim analysis
Szor 2002 (79)	RCT Quality 4/9	56 subjects of whom 37 completed the study: Intervention group 19 Control group 18	Magnetic stimulation: magnets implanted into insoles held on by stockinette for 12 hours (overnight), for a total of 8 weeks	Wound healing	None reported	1-	Sample required was 70. Insufficient evaluable patients for results to be analyzed
Chiglashvili 2004 (80)	Cohort Study quality 1/8	46 people with diabetes Intervention group 28 Control group 18 Lost to follow up: 0	Complex intervention involving the administration of antioxidant and immunomo-dulatory agents, combined with laser therapy	Time to elimination of debris and fibrin Time to wound healing	12.6 2,1 days vs 16,3 2,6 days and wound healing duration 27,3 2.8 vs 36,4 3,9 days (vs control)	2-	No clear description of the patient groups, the intervention or trial design. No statistical analysis

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وزارة الصحة
Ministry of Health

Foot Assessment File

FULL ASSESSMENT SHEET

Assessor: ..... Date of Assessment: ..... /...../.....
Name: ..... Age: ..... Sex: .....
Address: ..... Phone No.: .....

Type of Diabetes: Type I ☐
Type II ☐
OTHERS ☐ Specify .....
Duration of Diabetes: . .....

Associated diabetes complications:

Neuropathy ☐
Nephropathy ☐
Retinopathy ☐
Vasculopathy ☐
Others ☐ Specify .....

Associated Diseases:

1. .....
2. .....
3. .....
4. .....
5. Current Treatment

Oral Agents: 1. .....
2. .....
3. .....

Insulin:

Insulin	AM	Noon	PM	BT
R				
NPH				
Mixed				
Novo				
Lantus				

FOOT ASSESSMENT

History of Foot Complications:

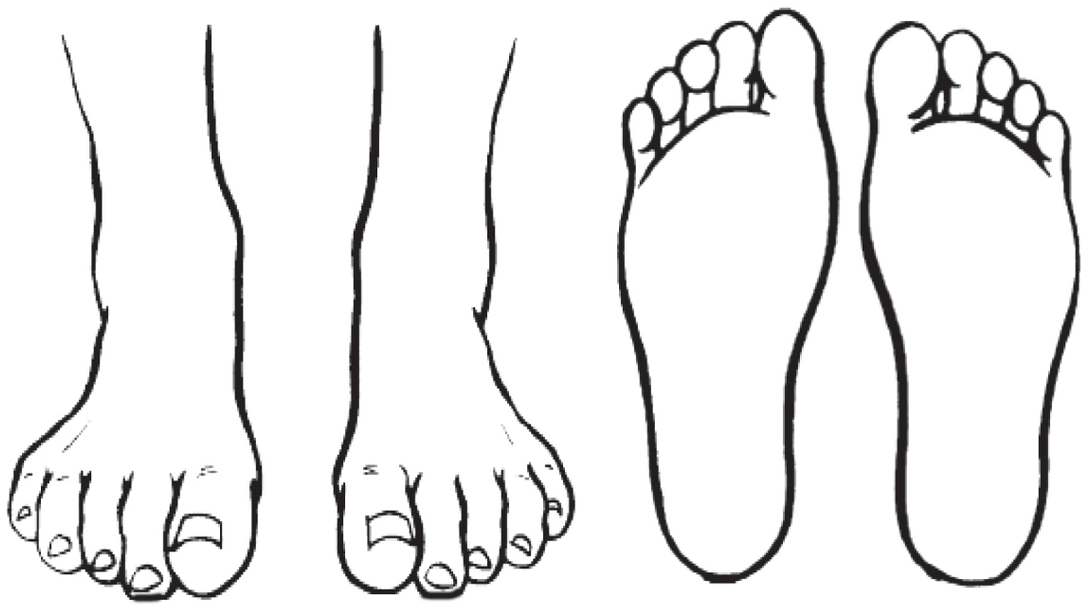
☐ Amputation ..... Date ..... ☐ Ulceration ..... Date .....

☐ Osteomylitis ..... Date ..... ☐ Charcot foot ..... Date .....

☐ Ingrowing nail ..... Date ..... ☐ Infection ..... Date .....

Current complain: . .....

. .....



Cause of Ulcer: ☐ Trauma ☐ Heat/Burn ☐ Sharp ☐ Footwear

☐ Under callus (Pressure) ☐ Not known

TEXAS CLASSIFICATION

Stage	Grade 0	Grade I	Grade II	Grade III
A	Pre or post ulcerative lesion completely epithelialized	Superficial wound, not involving tendon, capsule or bone	Wound penetrating to tendon or capsule	Wound penetrating to bone or joint
B	Infection	Infection	Infection	Infection
C	Ischemia	Ischemia	Ischemia	Ischemia
D	Infection and Ischemia	Infection and Ischemia	Infection and Ischemia	Infection and Ischemia

Grade ..... Stage .....

Wound Bed:

☐ Epithelialising ..... ☐ Granulating ..... ☐ Slough / Granulating .....
☐ Slough ..... ☐ Necrotic ..... ☐ Gangrene .....

Exudate Amount:

☐ None ..... ☐ Light ..... ☐ Moderate ..... ☐ Heavy .....

Infected: ☐ Yes ☐ No
☐ Superficial ..... ☐ Cellulitis ..... ☐ Osteomylitis .....

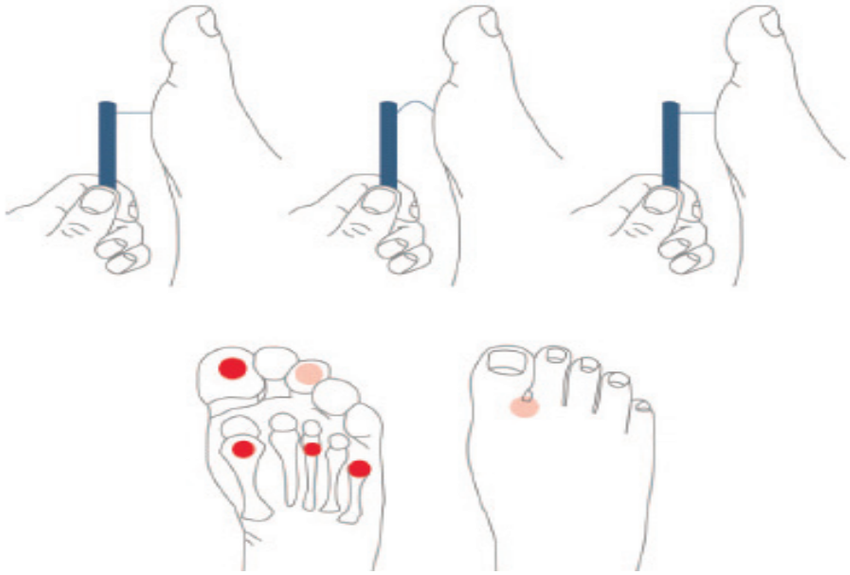
Odour: ☐ Yes ☐ No

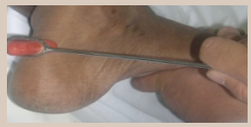
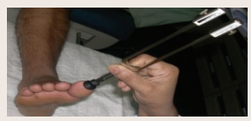
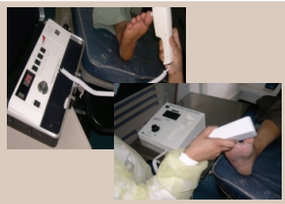
DERMATOLOGICAL EXAMINATION

- Quality of the skin: ☐ Fragile ☐ Shiny ☐ Dry
- Fissures (heels) / Callus: ☐ Rt. foot ☐ Lt. foot
- Nail: ☐ Normal ☐ Abnormal

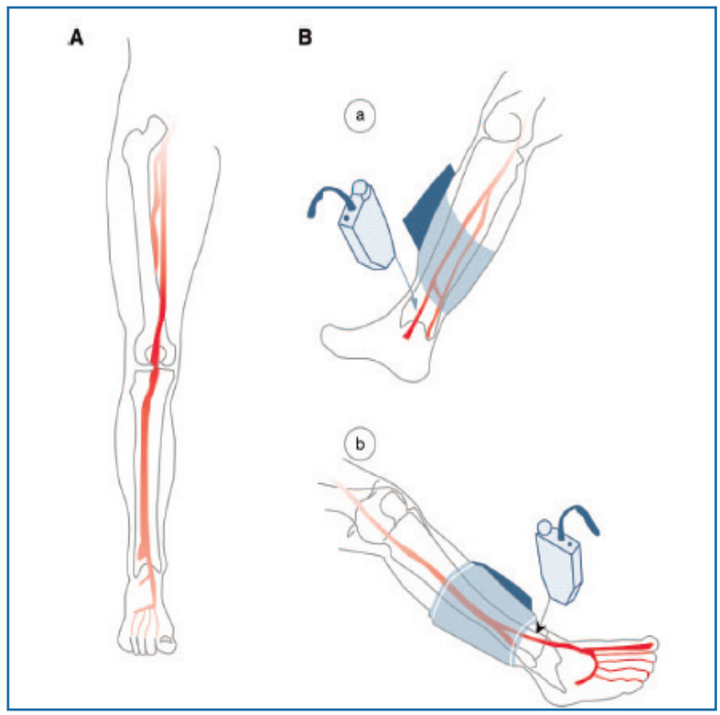
- Hair growth: Abnormal ☐ Normal ☐
- Tinea pedis: Site .....

NEUROPATHIC ASSESSMENT



Neuro-tip Discrimination	Hallux – Dorsal surface Proximal to the toe nail	
Temperature Discrimination	Hallux – Dorsal surface Proximal to the toe nail	
Reflexes	Achilles tendon	
128 kHz Tuning Fork	Pulp of Hallux	
Vibration Perception Threshold	Hallux Plantar	
Mono-filament (10g)	Hallux Plantar	
	MPJ 1 Plantar	
	MPJ 3 Plantar	
	MPJ 5 Plantar	

VASCULAR ASSESSMENT



Pedal Pulses Palpation:	DP Yes / No R ☐ L ☐	PT Yes / No R ☐ L ☐	
Ankle Brachail Pressure Index	Brachial Artery	..... mmhg	..... mmhg
	Post. Tibial Artery	..... mmhg	..... mmhg
	Dorsalis Pedis Artery	..... mmhg	..... mmhg
	ABPI	..... mmhg	..... mmhg

Toe Pressure:

Rt.	Lt.
Big toe	Big toe .....
2nd toe	2nd toe .....
3rd toe	3rd toe .....
4th toe	4th toe .....
5th toe	5th toe .....

BIOMECHANICAL ASSESSMENT

MUSCULOSKELETAL EXAMINATION

- Biomechanical abnormalities:
  - Pronated / Supinated Foot: Rt. ☐ Lt. ☐ -ROM ankle(R/L):DF(0-20)°/PF(0- 45)
  - Equinus / Drop foot: Rt. ☐ Lt. ☐ -ROM bigtoe(R/L):DF(0-70)°/PF(40- 70)°
  - Tendo Achilles contracture: Rt. ☐ Lt. ☐

- Structural deformities:
  - Hammertoes/Claw toes/ Overlapping toes: Rt. ☐ Lt. ☐ B/L ☐
  - Hallux valgus/limitus/rigidus: Rt. ☐ Lt. ☐ B/L ☐
  - Pes cavus / planus: Rt. ☐ Lt. ☐ B/L ☐
  - Drop Foot : Rt. ☐ Lt. ☐ B/L ☐
  - Charcot deformities: Rt. ☐ Lt. ☐ B/L ☐
  - Limited Joint Mobility: (Prier Sign: positive ☐ negative ☐)
  - Intrinsic atrophy Rt. ☐ Lt. ☐ B/L ☐
  - Amputation:
    - Complete foot Rt. ☐ Lt. ☐ B/L ☐
    - Chopart's joint line Rt. ☐ Lt. ☐ B/L ☐
    - Lisfranc's joint line Rt. ☐ Lt. ☐ B/L ☐