FEDERAL MINISTRY OF
HEALTH

NATIONAL GUIDELINES

ON THE PREVENTION, CONTROL AND MANAGEMENT OF DIABETES MELLITUS

Preface

Diabetes is a common clinical condition in Nigeria. It is a major non-communicable disease that affects the highly productive segment of the nation's populace. Currently, it is being managed at primary, secondary and tertiary health centres, in both private and public health facilities across the country. Diabetes is caused by a relative or absolute lack of insulin, a hormone that regulates glucose utilization in the body.

According to the World Health Organization, 347 million people worldwide have diabetes and out of the 1.5 million deaths that resulted from diabetes in 2012, more than 80% occurred in low- and middle-income countries, including Nigeria. An estimated 5 million adult Nigerians are living with diabetes and less than 50% of them are diagnosed of their condition. Furthermore, diabetes is a chronic illness that requires continuing medical care and patient self-management education for optimal management outcomes and to reduce the risk of complications.

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The Federal Ministry of Health (FMOH) recognizes that this chronic illness, which is assuming epidemic proportions in Nigeria requires management and control, based on a national guideline. This has informed the decision of the Federal Ministry of Health to develop a guideline that will ensure standardized medical care and patient self-management education to prevent acute complications and reduce the risk of long-term debility from the disease.

It is our earnest desire therefore, that this document will form the foundation for improving the standard of care for persons living with diabetes in all our healthcare facilities across the country.

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Acknowledgments

We are very delighted that the national guideline for the prevention and management of diabetes in Nigeria has become a reality, despite the challenges that slowed down the process. Our sincere gratitude goes to all stakeholders, who committed time and other resources towards the development of this document.

The leadership role of the Head, Department of Public Health; the coordination of the process by the hardworking staff of the Non-Communicable Diseases Division, and the contributions of other officers from the Federal Ministry of Health, especially, Departments of Family Health and Hospital Services are acknowledged with thanks. So also, are those of the National Primary Health Care Development Agency, FCT Primary Health Care Board, Health & Human Services Secretariat of the FCT, the Academia, and Diabetes Association of Nigeria (DAN).

Special note of thanks goes to Health Strategy and Delivery Foundation (HSDF), who made significant financial and human resource contributions towards the development and finalization of the guideline. We also appreciate Cochrane Nigeria for the great work on the grading of evidence for this document.

Finally, profound gratitude goes to World Diabetes Foundation (WDF), who catalyzed the development of the guideline and supported the finalization and printing as part of the activities approved for the Diabetes Awareness and Care project under the grant, WDF17-1474.

We believe that the selfless dedication displayed in the development of this document would also be demonstrated in its use for effective management and control of Diabetes Mellitus in Nigeria.

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Foreword

Diabetes is increasingly becoming an epidemic especially among adolescents and young adults. The incidence and prevalence of the disease especially Type II is increasing worldwide. The risk for developing diabetes (Type II) globally is rising; it is further accentuated by civilization and globalization, resulting in overweight/obesity, and the proliferation of industries producing unhealthy diets, including those with unhealthy fats and high sugar content. The current global burden of Diabetes Mellitus (DM) is estimated to be 366 million. A projection for the year 2030 is put at 500 million people, and 80% of this increase is expected to occur in developing countries, including Nigeria if nothing urgent is done.

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Fortunately, Type II DM can be prevented and controlled by avoiding risky behaviours and unhealthy lifestyle habits. The modifiable shared risk factors for diabetes include tobacco use, harmful use of alcohol, and unhealthy nutrition (such as excessive consumption of red meat, saturated fat, refined sugars in foods and drinks, inadequate consumption of fiber rich diet, vegetables and fruits), and physical inactivity.

Concerned about the enormous challenges caused by diabetes in Nigeria, the Federal Ministry of Health, in collaboration with stakeholders developed the National guideline for the prevention, control and management of diabetes in Nigeria. This was to inform evidence-based interventions with regards to the prevention and management of the disease in Nigeria, such that standards are prescribed, quality of life and disease outcomes are improved.

Furthermore, the publication of this guideline shows the Nigerian government's continuous commitment to reduce the burden of diabetes in Nigeria, as it is essential that affected individuals receive appropriate clinical interventions in all healthcare facilities nationwide. This national guideline will ensure standardized medical care and patient self-management education to prevent acute complications, delay the on-set of complications and reduce the risk of long-term complications among diabetic patients.

I therefore encourage all healthcare practitioners and facilities to take advantage of this opportunity to improve their standard of care for diabetic patients; thereby enhancing the management and control of diabetes in Nigeria. In addition, this publication contributes to the government's efforts in bringing hope and succor to those affected by this disease.

Dr E. Osagie Ehanire MD, FWACS

Honourable Minister
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Abbreviations & Acronyms

ACEi	Angiotensin Converting Enzyme inhibitor
ADA	American Diabetes Association
AER	Albumin Excretion Rate
AGREE	Appraisal of Guidelines for Research & Evaluation
A2RB	Angiotensin II Receptor Blocker
BP	Blood Pressure
CCB	Calcium Channel Blocker
CHEW	Community Health Extension Worker
DAN	Diabetes Association of Nigeria
DASH	Dietary Approach to Stop Hypertension
DKA	Diabetic Keto-Acidosis
DM	Diabetes Mellitus
DPP-4	Dipeptidyl Peptidase – 4
EML	Essential Medicines List
FMoH	Federal Ministry of Health
FBS	Fasting Blood Sugar
FPG	Fasting Plasma Glucose
GCS	Glasgow Coma Scale
GDM	Gestational Diabetes Mellitus
GoN	Government of Nigeria
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
GLD	Glucose Lowering Drugs
GLP	Glucagon like Peptide
HbA1C	Glycated Haemoglobin
HDL	High Density Lipoprotein
HHS	Hyperglycaemic Hyperosmolar State
HIV	Human Immuno-Deficiency Virus
IDF	International Diabetes Federation
ISH	International Society of Hypertension

ISO	International Standards Organization
JCHEW	Junior Community Health Extension Worker
LCHW	Lay Community Health Worker
LDL	Low Density Lipoprotein
NCDs	Non-Communicable Diseases
NGC	National Guideline Clearinghouse
NICE	National Institute for Health and Care Excellence
OGTT	Oral Glucose Tolerance Test
PA	Physical Activity
PIPOH	Population, Intervention, Professional, Outcomes/outcome measurement and Health settings
PLWHA	People Living with HIV/AIDS
RCT	Randomized Controlled Trial
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
WDF	World Diabetes Foundation
WHO	World Health Organization

List of Tables

List of Figures

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Table of Contents

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Introduction

Diabetes is a common clinical condition in Nigeria, being managed at primary, secondary, and tertiary health centres in both private and public sectors. It is the most common endocrine disorder encountered in clinical practice. Presently, management and prevention strategies have been carried out at different centres using various local guidelines. The Federal Ministry of Health (FMoH) recognizes that this chronic illness which is assuming epidemic proportions in Nigeria, requires management and control, based on national guidelines. This guideline will ensure standardized medical care and patient self-management education to prevent acute complications, and to reduce the risk of long-term complications.

The prevalence of diabetes is increasing worldwide. The global burden of diabetes mellitus (DM) is estimated to be 425 million among adults (20 to 79 years) in 2017.[1] A projection for the year 2045 is put at 629 million with the largest increase expected to take place in regions where economies are moving from low- to middle- income status.[1] The World Health Organization has described the situation of non-communicable diseases as "epidemic'. Consequently, many countries (developed and developing), have identified DM as one of the major public health problems.

The prevalence of DM in Nigeria is increasing with current WHO estimates of 4.3%.[2] Local studies carried out by researchers have figures ranging from 3 – 10%.[3,4,5,6]

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This is a 2011 estimate. It is too old for a 2020 document. The 2017 Diabetes Atlas estimates 425 million. The reference is International Diabetes Federation. IDF Diabetes Atlas, 8th edn. Brussels, Belgium:International Diabetes Federation, 2017. Available@ http://www.diabetesatlas

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You can add a 6th reference here with that from the 2018 Systematic review and meta analysis which is a stronger paper. Uloko AE, Musa BM, Ramalan MA, Gezawa ID, Puepet FH, Uloko AT, et al. Prevalence and risk factors for diabetes mellitus in Nigeria: a systematic review and meta-analysis. Diabetes Ther. 2018;9(3):1307–1316. doi: 10.1007/s13300-018-0441-1.

Rationale for guidance

This minimum standard of care is intended to equip patients, clinicians, researchers, and other health care professionals with the components of diabetes care, treatment goals, and tools for adequate patient management. It provides goals and targets that are suitable for most patients. However, individual preferences, co-morbidities, and other patient-specific factors may require modification of goals and targets occasionally. These standards are not intended to preclude more extensive evaluation and management of the patient by other specialists as required.

Methodology

The recommendations in this document were adapted from high quality diabetes prevention, care and treatment guidelines. The tools and processes used to produce this guideline were guided by the ADAPTE guideline development methodology.[5]

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Guideline development core team

The Federal Ministry of Health led the guideline development process and formed a core team to coordinate the guideline development process. This core group was mandated to:

- Develop the scope and purpose of the guidelines.
- Develop the health questions to be addressed.
- Identify and appraise the quality of existing Diabetes Mellitus guidelines, using the AGREE II checklist and scoring system.
- Select the guidelines that will be used for the adaptation process.
- Extract recommendations from selected guidelines.
- Develop the zero draft of the guidelines.

The core team was made up of representatives from the Non-Communicable Diseases (NCDs) Division of the Public Health Department of the Federal Ministry of Health, Health Strategy & Delivery Foundation, Healthcare Leadership Academy and the Nigerian office of the World Health Organization.

Developing the scope, purpose and questions

The core team used the PIPOH checklist to define the scope, purpose and health questions to be addressed by the guideline. PIPOH is an acronym for **P**atient population (including disease characteristics), **I**nterventions, **P**rofessionals, **O**utcomes and outcomes measures and **H**ealth care setting and context.[67]

Each member of the team completed the PIPOH checklist and then discussions were held to build consensus on the items that would be included through simple majority votes. Disagreements that had a bearing on implementation or costs of the guideline recommendations were carried over for further discussions in subsequent phases of the guideline development.

Box 1: Determining the scope, purpose and health questions using the PIPOH checklist

- **Patient population (including disease characteristics):** The core team decided that recommendations should cover type 1 diabetes and type 2 diabetes in children, adolescents and young adults, gestational diabetes in pregnant women and pre-diabetes in adults. Other types of diabetes mellitus were excluded due to paucity of data to elucidate their burden in the country. Recommendations for complications of DM, management of DM related emergencies and co-morbidities such as hypertension, dyslipidemia and HIV will also be included.
- **Interventions**: These will cover prevention measures at individual, community and policy levels, screening to identify individuals at risk of DM, diagnosis in resource-constrained settings, structured diabetes education, lifestyle modification and pharmacological treatments. Early identification of complications of DM, as well as management of DM-related emergencies at primary care levels were also included.
- **Professionals**: Guideline recommendations will target health professionals such as primary care non-specialist/GP doctors, nurses, community health extension workers, junior community health extension workers and community volunteers. Individuals, organizations and stakeholder groups who were identified to have potential vested interests in the development, implementation, monitoring and evaluation of this guideline are FMoH, State Ministry of Health (SMoH), public health practitioners and implementing partners. The primary end-users of the recommendations were identified to be the patients and their caregivers.
- **Outcomes and outcome measures**: The recommendations will aim to primarily prevent or delay the onset of DM among high-risk individuals and improve survival among people with DM. Health system level outcomes of importance were cost of care, improvement in quality of care, achieving task-shifting of some aspects of DM care and treatment from doctors and nurses to lower cadre health professionals (CHEWs/JCHEWs) and lay health workers. The guideline also aims to define standards for quality of care to address variations in treatment across the various health facilities in the country. In a broader context, public health outcomes that will be addressed by the guideline recommendations include morbidity, mortality, incidence and prevalence of DM.
- **Health care setting and context**: The recommendations will primarily target communities for preventive interventions and primary health care settings for screening, diagnosis and treatment. These will also be tailored to address the resource constraints related to equipment, infrastructure, health workers, etc. in most primary health care settings.

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Search for existing guidelines

The core team searched National Guideline Clearinghouse (NGC) and websites of National Institute for Health and Care Excellence (NICE), International Diabetes Federation (IDF), World Diabetes Foundation (WDF), and American Diabetes Association (ADA). Guidelines produced by the Diabetes Association of Nigeria (DAN) were sought through communication with experts due to the absence of a website.

Search term used was 'diabetes mellitus' or 'hyperglycaemia.'

Table 1: Search Process and Results (May/June 2018)

Database searched	Filters used	Search yield	Relevant to DM	Included for appraisal
NGC	Date limit: 2015 to 2018	133	17 guidelines	10
NICE	Date limit: 2015-2018 Document type: Guidance Guidance category: Clinical guideline, NICE guideline, public health guideline, quality standards.	90	6 guidelines 3 quality standards	6
IDF	No filters applied during electronic search, but manual screening was done to apply date limit from 2015 to 2018 and to make clear distinction between job-aids and practice guidelines.	20	4 guidelines	4
WDF	No filters were applied during electronic search. But manual screening was done to apply date limit from 2015 to 2018 and to make clear distinction between job-aids and practice guidelines.	36	7 guidelines	0
ADA	No filters applied.	1	1 guideline	1

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Eight duplicates were identified from the NGC, NICE, IDF and WDF websites.

Only guidelines that addressed the pre-determined PIPOH scope/questions and which were published between 2015 and 2018 were included.

Appraisal of eligible guidelines

Two members of the core team applied the AGREE II tool to appraise the quality of eligible guidelines.[87] AGREE II consists of 23 items grouped in six domains: scope and purpose; stakeholder involvement; rigour of development; clarity of presentation; applicability; and editorial independence. Items are rated on a 7-point Likert scale ranging from '1 = strongly disagree' to '7 = strongly agree.'

All the AGREE II domains were used to rate the overall quality of the guideline as minimum quality (domain score ≥ 50%) or high quality (domain score ≥ 70%). All six domains were selected because they address the rigour needed to identify and interpret the risk of bias and quality of evidence for the recommendation in the guidelines.

In cases where the method and processes of all guidelines developed by an organization were identical (e.g. NICE), the guidelines were not appraised separately but rather they were appraised as a single guideline.

The two assessors then compared their individual scores for each item. When their scoring on each domain differed by more than three points, differences were resolved through discussion. If an agreement could not be reached, a third assessor helped to resolve the disagreement. The AGREE inter-rater agreement spreadsheet and AGREE score calculation spreadsheet were used to guide the scoring and consensus building between the two assessors.

The Kappa statistic for the inter-rater agreement was also calculated using stata version 13.

Selecting guidelines to be used for adaptation

Only guidelines that scored 70% and above were selected for adaptation.

Developing guideline recommendations

Recommendations in the selected guidelines that addressed the health questions were extracted by members of the core team using an extraction template. Discussions were held to decide if the recommendations would be included in the guidelines based on the following considerations:

- Implementation considerations to determine if the extracted recommendations would fit into the patient needs, professional standards as well as the organizational, health system, economic, political, social/cultural context in Nigeria.
- Resource considerations to determine if the available resources (equipment, infrastructure and human resources) at community, primary, secondary and tertiary health care levels would be adequate to enable application of the extracted guideline recommendation.
- Costs to determine if the recommendations will be affordable by the public and health care decision makers.
- Equity to determine if the coverage and access to the health intervention in the recommendation can be achieved. The Nigerian Essential Medicines List (EML) of 2016,[98] was searched to determine the equitable availability of drugs in extracted recommendations.

Extracted recommendations that included drugs that were not in the EML 2016 were mentioned but not included as final recommendations in the guideline. This also applied to recommendations that were deemed to be too costly or not feasible for implementation within the available resources and contextual factors at play in the Nigerian health system.

In cases, where a health question was not included in a guideline, a rapid electronic search for a systematic review, primary study or policy statement that addressed the recommendation was conducted.

Determining the level of evidence and grading of recommendations

The core team engaged with experts with strong technical expertise in the use of GRADE (Grading of Recommendations, Assessment, Development and Evaluation)[109] methodology to determine the strength of each recommendation and the quality of the evidence.

External expert review and consensus building

An inclusive participatory process was used in the guideline development process to ensure that the diverse scenarios of clinical and public health practice across the country, technical expertise of health care providers, and lived experiences of persons living with diabetes were adequately considered in the recommendations.

The zero-draft was reviewed by experts who are either endocrinologists or specialists with strong technical knowledge of diabetes mellitus, health care providers working in primary health care settings, persons living with diabetes who are members of DAN, diabetes educators or guideline development experts as well as policy experts from the Federal Ministry of Health's Non-Communicable Diseases (NCDs) division.

The initial review was done remotely through electronic forms and templates to allow experts review the guideline recommendations for technical accuracy, consistency and feasibility in the local context. The quality of evidence and risk of bias associated with each recommendation was also reviewed by guideline development experts. The input from the experts was used to build the first draft of the guideline.

This was followed by a two-day meeting to review the first draft. The experts reviewed the background information and recommendations to ensure that all guideline recommendations will ensure comprehensive prevention and management of the types of diabetes mellitus within the outlined scope. This review also ensured that recommendations were in line with current evidence, practice approaches and scenarios in the country, and could be applied given the resource constraints in the Nigerian health system. A consensus on the recommendations was reached by simple majority votes. The input from this meeting was collated to build the second draft of the guidelines.

A four-day meeting was held to review and finalize the second draft in line with the agreed scope and purpose as well as the overall vision and targets of the Federal Ministry of Health.

Scope and purpose

The aim of this document is to provide evidence-informed recommendations on the prevention, care and treatment of diabetes mellitus that are feasible in resource-constrained settings and the different levels of care in the Nigerian health system. This guideline will also set the quality standards to inform trainings and clinical practice on diabetes care and treatment in Nigeria.

The scope of this guideline will cover the following areas:

- Prevention of type 2 diabetes through community and policy level interventions.
- Screening to identify individuals at high risk for developing type 2 diabetes.
- Prevention or delay of onset of type 2 diabetes in individuals at high risk of developing type 2 diabetes.

- Lifestyle modification for managing type 1 and type 2 diabetes mellitus in children, adolescents and adults.
- Drugs for treating type 1 and type 2 diabetes mellitus in children, adolescents and adults.
- Screening to identify pregnant women with gestational diabetes mellitus.
- Lifestyle modification and drug treatment for managing diabetes in pregnancy.
- Prevention and early identification of DM complications.
- Management of DM-related emergencies at primary and secondary health care levels in resource-constrained settings.
- Addressing risk factors and managing co-morbidities such as hypertension and HIV.

Health questions

Table 2: Guideline questions

Prevention	1. What community and policy level measures can be taken to prevent T2DM among the general population? 2. What recommended intervention(s) can prevent or delay the onset of T2DM among individuals with high risk of developing T2DM? 3. What are the recommended measures for preventing progression to T2DM among individuals with pre-diabetes or impaired glucose tolerance?
Screening	1. What are the recommended tools for risk assessment for T2DM?
Diagnosis	1. What are the recommendations for diagnosis of DM at primary care level in resource-constrained settings?
Diabetes education persons with DM	1. What is the evidence for including diabetes education in routine diabetes care and treatment? 2. What should be the recommended scope for diabetes education? 3. How should diabetes education be delivered in resource-constrained settings?
Lifestyle modification	1. What are the recommended targets for lifestyle changes in treatment of DM?
Drug treatment	1. What drugs are recommended for treating T1DM in children? 2. What drugs are recommended for treating T2DM in children? 3. What drugs are recommended for treating T1DM in adults? 4. What drugs are recommended for treating T2DM in adults? 5. What add-on drugs are recommended for managing T1DM, and under what circumstances should they be used?

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	6. Which hierarchical order should be considered in the choice of first-line, second-line regimens for T2DM? 7. Should insulin be considered as a first or second-line drug in the treatment of T2DM? If yes, under what circumstances should it be considered as either? 8. Is there a preferred combination for triple therapy for T2DM? If yes, what combination?
DM-related emergencies	1. What are the recommended life-saving measures that can be taken at primary health care level to manage DM related emergencies? (disaggregate by each type of complication). 2. What are the recommendations for management of DM emergencies at secondary level?
DM complications	1. What are the recommended measures for preventing DM related complications? 2. What are the recommendations for early identification of DM related complications?
Co-morbidities	1. What are the recommendations for the management of other cardiovascular risk factors? 2. What are the recommended drug combinations for the treatment of high blood pressure in DM? 3. What are the recommendations for managing DM in HIV positive individuals?
DM & pregnancy	1. What are the recommended tools for screening for gestational diabetes mellitus (GDM)? 2. How can GDM be diagnosed? How can you determine if a woman had overt diabetes prior to pregnancy? 3. What are the recommended measures for preventing the onset of GDM in pregnant women with high risk? 4. What are the recommended measures for managing GDM? 5. What are the recommendations for management of DM in women who were diabetic prior to pregnancy?
Health professionals and settings	1. What are the recommended roles of different cadres of health workers in the prevention, care, treatment and management of DM? 2. What are the recommended roles of different health care settings in the prevention, care, treatment and management of DM?

Target audience

The guideline recommendations will target the following groups of health professionals:

- Primary care/general practice doctors.

- Non-physician health workers such as nurses, community health extension workers (CHEWs), junior community health extension workers (JCHEWs).
- Lay community health workers (LCHW).

The emphasis of recommendations in this section is on how non-physician and lay community health workers can work with skilled health workers to optimize diabetes prevention, care and treatment in resource-constrained, under-served and hard-to-reach settings.

Role of the different cadres of health workers

Primary Care/General Practice doctors

Primary care or general practice doctors are responsible for

- Confirmation of diagnosis.
- Clinical evaluation.
- Follow-up of persons with diabetes.
- Identification of the circumstances necessary for drug treatment.
- Prescription of drugs and determination of the line of management.
- Working with other members of the care team to provide structured diabetes education and support for self-care.

Role of Nurses, CHEWs/JCHEWs

- To provide culturally- appropriate and structured diabetes education.
- To convey diabetes self-management information and healthcare provider recommendations accurately to persons living with diabetes.
- To identify and refer high-risk individuals to physicians.
- To identify and overcome cultural barriers to self-care or behavior change.
- To participate in the evaluation of program, unit, or agency using clinical practice guidelines.
- To support persons with diabetes, prevent complications associated with DM and to identify them early when they do occur.

Lay Community Health Workers (LCHW)

A lay health worker (LHW) is defined as a health worker who performs functions related to health care delivery and is trained in some way in the context of an intervention, but who has not received a formal professional or paraprofessional certificate or tertiary education

degree. Other terms for lay health workers include 'community health workers' (CHWs) and 'village health workers' (VHWs). They are also regarded as lay health workers.[11~~10~~]

Training and empowering LCHWs to deliver current, accurate, and evidence-based information is very important to support persons living with diabetes in self-management, behavioral change and problem-solving skills. This support to patients optimizes the available health care services to improve health outcomes in people affected by diabetes and their communities. Lay community health workers should be trained by a skilled health worker who understands evidence-based guidelines for diabetes education.

Lay community health workers should play the following roles:

- Implement diabetes community awareness and prevention programmes.
- Provide diabetes prevention messages and information to community members.
- Support persons living with diabetes to gain access to diabetes support system in their communities.
- Work with the health provider team to apply basic concepts of behavior change to support persons living with diabetes in effective self-management.
- Build community coalitions to meet the needs of persons living with diabetes in the community.

Recommendations for integrating LCHWs into diabetes prevention, care and management

1. Lay community health workers should work under the supervision of a licensed skilled health care provider (e.g. doctors, nurses, CHEWs).
2. Lay community health workers should be trained and mentored on core diabetes prevention, care and management knowledge, skills and competencies.
3. Lay community health workers should be integrated as part of a multi-level diabetes education and support team.
4. Lay community health workers serve as a link between persons living with diabetes (or at risk of diabetes) and other healthcare providers and the health care system.
5. Other health professionals should support the role of CHWs in the primary prevention of diabetes.
6. Lay community health workers should be involved in community activities for advocacy and mobilization.

Role of the different health care settings

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This guideline also recommends a multi-level approach in diabetes prevention, care and treatment with a focus on community and primary health care settings.

A. **At community level**, the following aspects of diabetes prevention, care and treatment are recommended:

   1. Community-based health promotion.
   2. Screening to identify individuals at risk of developing DM using risk assessment tools. This can be done during outreaches, mobile health services and community engagement.
   3. Support to individuals identified to be at high risk of developing DM to prevent or delay onset of DM.
   4. Support to persons living with diabetes to achieve self-management and lifestyle changes.
   5. Support to persons living with diabetes to prevent and identify complications/ emergencies.

B. **At primary health care level**, in addition to community level activities, the following aspects of diabetes prevention, care and treatment are recommended:

   1. Diagnosis of DM using point-of care devices, diagnostic algorithms and risk assessment tools.
   2. Basic clinical management of non-complicated DM such as:
      a. Patient evaluation
      b. Structured diabetes education
      c. Drug treatment
      d. Support for lifestyle changes
      e. Prevention and early recognition of DM complications
      f. Early recognition of other co-morbidities
   3. Basic life-saving measures in management of DM-related emergencies.
   4. Referral of complicated DM cases and emergencies.

C. **At secondary and tertiary health care level**, in addition to A and B above, there will be comprehensive management of DM complications and emergencies.

Recommendations in this guideline aim to achieve the following health system outcomes:

- Reduced cost of care.
- Improved quality of care.
- Task-shifting of some aspects of DM care and treatment from doctors and nurses to lower cadre health professionals (CHEWs/JCHEWs) and lay health workers.
- Well defined standards for quality of care.
- Reduced variations in treatment across the various health facilities across the country.
- Reduced DM-related morbidity and mortality.
- Reduced incidence and prevalence of DM.

Target population

The recommendations in this guideline are targeted at meeting the needs of persons with diabetes, their caregivers and communities. It aims to achieve the following health outcomes among individuals:

- Primarily prevent or delay onset of DM among high-risk individuals.
- Improve survival among people with DM.

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1. Classification and Diagnosis of Diabetes Mellitus

1.1. Classification of diabetes mellitus

Depending on the aetiology (cause) and patho-physiology (abnormal course) of the disease, diabetes mellitus can be classified into[1,2]:

- Type 1 diabetes mellitus (T1DM)
- Type 2 diabetes mellitus (T2DM)
- Gestational diabetes mellitus (GDM)
- Other types of diabetes mellitus

Paradigm shift in classifying DM

The traditional belief that Type 1 DM occurs only in children and Type 2 DM occurs only in adults is no longer accurate. Extensive clinical research suggests that it occurs in both age groups.

Extensive clinical research has also shown that Type 1 DM may be idiopathic but rare with no known cause among Africans and is strongly inherited.

1.1.1. Type 1 DM

Type 1 DM is caused by autoimmune destruction of β-cells with consequent absolute insulin deficiency. Extensive studies show that the persistent presence of two or more auto-antibodies is a strong marker for developing hyperglycaemia. However, the rate of progression to T1DM depends on the age at which the autoantibodies were first detected, the number, specificity and titer of autoantibodies.

Type 1 DM has three distinct stages that can be used to inform clinical decision making.[3,4]

Stage 1 is characterized by autoimmunity, normal blood sugar levels, diagnosed by presence of multiple autoantibodies but no impaired glucose tolerance or impaired fasting glucose.

Stage 2 is characterized by autoimmunity, impaired glucose tolerance and no symptoms, and can be diagnosed by the presence of multiple autoantibodies with impaired glucose tolerance or impaired fasting glucose. Fasting plasma glucose of 100-125 mg/dL (5.6-6.9 mmol/L) or 2-hour plasma glucose of 140-199 mg/dL (7.8-11.0 mmol/L) is suggestive of this stage.

Stage 3 is characterized by onset of increased blood sugar levels (hyperglycaemia) and presence of clinical symptoms and can be diagnosed using standard criteria of DM diagnosis.

1.1.2. Type 2 DM

Type 2 DM is due to insulin resistance with a progressive loss of or impaired β-cell insulin secretion. This could be due to metabolic stress and other genetic or environmental factors.[3]

The condition also manifests as a continuum from normal to impaired glucose tolerance to overt diabetes.[3]

1.1.3. Gestational diabetes mellitus

Gestational diabetes mellitus is high blood sugar levels (hyperglycaemia) that manifest for the first time in pregnancy usually during the second or third trimester. A distinction between overt or pre-existing diabetes can be made if screening for pre-existing diabetes is done during the first trimester of pregnancy.[5,6]

1.1.4. Other types of diabetes mellitus

These include:

- Monogenic diabetes syndromes (neonatal diabetes, maturity-onset diabetes of the young).[7]
- Diseases of the pancreas (pancreatitis).[8]
- Drug or chemical-induced diabetes due to the use of steroids or anti-retroviral treatment or organ transplantation.[9]

1.2. Diagnosis of diabetes mellitus

1.2.1. Diagnosis of diabetes mellitus in adults

Diagnosis of diabetes mellitus in adults can be made based on either[10,11,12]:

- Fasting blood glucose
- 75-g oral glucose tolerance test (OGTT)
- Random blood glucose
- HbA1C

Special diagnostic consideration for adults at primary health care level in resource-constrained settings

Random blood sugar of more than 200mg/dl or 11.1 mmol/L in individuals with symptoms like frequent thirst, increased frequency of urination and increased appetite).

BOX 1: RECOMMENDATIONS FOR DIAGNOSIS OF DIABETES MELLITUS IN ADULTS[10,11,12,13]

Diagnosis of diabetes mellitus should be made on any of the following:

Fasting plasma glucose: Blood glucose after eight hours of no food/calorie intake of more than 126mg/dL or 7 mmol/L (Expert Consensus Opinion).

OR

75-g oral glucose tolerance test (OGTT): Blood glucose after two hours following a glucose load of 75g of anhydrous glucose dissolved in water of more than 200mg/dL or 11.1 mmol/L (Expert Consensus Opinion).

OR

Random blood sugar of more than 200mg/dl or 11.1 mmol/L in individuals with symptoms suggestive of hyperglycaemia or DM (increased thirst, increased frequency of urination and increased appetite) (Expert Consensus Opinion).

OR

HbA1C of more than 6.5% (48mmol/mol) (Expert Consensus Opinion).

In absence of symptoms of hyperglycaemia, diagnosis requires two abnormal test results on two separate days or from two different test samples.

Pre-diabetes will give the following blood sugar ranges:

Fasting blood glucose: 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L).

2-h blood glucose during 75-g OGTT: 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (Expert Consensus Opinion).

Procedure for OGTT in adults

Procedure for OGTT in adults using 75-g glucose

Person should be fasting for at least eight hours (overnight). Note the time of last meal taken the previous night before commencing test.

Person is advised not to consume any food, drink or smoke for the duration of the test.

In the fasting state, draw 5ml of venous blood into a fluoride tube.

Then a glucose solution consisting of 75g~~m~~ glucose powder in 200 to 300ml of water is administered and should be drunk by the person within five minutes.

At one and two hours after the glucose load, draw 5ml of venous blood.

1.2.2. Diagnosis of diabetes mellitus in children and adolescents

Diabetes mellitus in children can manifest through symptoms that are common to other diseases. These presentations can be misleading. Therefore, the recommendation is that children who present with these symptoms should be tested for diabetes mellitus.[14]

Table 3: Common presentations of DM in children and adolescents

Symptoms of diabetes in children		Other diseases with similar symptoms
Most common symptoms	Weight loss, bedwetting (urinating while sleeping in a child that has achieved nighttime continence), polyuria (frequent urination during the day and night), excessive thirst and tiredness.	Tiredness and weight loss are common with malnutrition and malaria.
Less common symptoms	Excessive hunger, blurred vision, mood changes, infections and abdominal pain.	Abdominal pain is common in gastro-intestinal and surgical problems.
Severe symptoms	Frequent vomiting, dehydration, decreased consciousness, rapid and deep breathing.	Vomiting and dehydration are common in gastro-enteritis. Rapid and deep breathing is common in pneumonia or bronchitis.

BOX 2: RECOMMENDATIONS FOR DIAGNOSIS OF DIABETES MELLITUS IN CHILDREN[14]

Diagnosis of diabetes mellitus should be made on any of the following in addition to the presence of overt symptoms**:**

Fasting plasma glucose: ≥7 mmol/L or ≥ 126 mg/dL (Expert consensus opinion).

OR

Random blood sugar: ≥11.1 mmol/L or 200 mg/dL (Expert consensus opinion).

OR

2-hour OGTT: ≥11.1 mmol/L or 200 mg/dl (normal glucose tolerance).

2-hour OGTT: ≥7.8 — <11.1 mmol/L or ≥140 – <199.8 mg/dL (Impaired glucose tolerance)

(Expert consensus opinion).

Procedure for OGTT in children

Procedure for OGTT in children

- Ensure that the child has had an adequate diet (minimum of 150 g/day of carbohydrate) for at least five days before the test.
- Child should be fasting overnight (allow four hours in infants) not less than eight hours and not more than 10 hours. Note the time of last meal taken the previous night before commencing the test.
- Child can consume water during this period, but consumption of sweet drinks is not allowed.
- Physical exercise is not allowed during this period.
- Use capillary blood and glucometer to measure blood sugar before administering the glucose load OR draw 1ml of venous blood into a fluoride tube before administering the glucose load and send to the lab.
- Then a glucose solution consisting of 1.75g glucose powder per kg body weight (maximum 75g) diluted in 200mls of water is administered and should be drunk by the child within five minutes.
- At one and two hours after the glucose load, repeat blood sugar test using capillary blood and glucometer or draw 1ml of venous blood and send to the lab.

1.2.3. Diagnosis of gestational diabetes mellitus

Screen all pregnant women at their first appointment (booking) to enable early detection of GDM and rule-out pre-existing diabetes or overt diabetes mellitus before pregnancy. Repeat GDM screening test for all undiagnosed pregnant women at 24-28 weeks using OGTT.[5,6] Fasting Blood Glucose, two hours Post Prandial Blood Glucose assay or a Random Blood Glucose. Test women with GDM for persistent diabetes at 4–12 weeks postpartum, using OGTT.

BOX 3: RECOMMENDATIONS FOR DIAGNOSIS OF GESTATIONAL DIABETES MELLITUS[5,6]

- Screen all pregnant women at their first appointment (booking) to enable early detection of GDM [FPG value ≥ 5.1 mmol/L (92 mg/dL) OR 2hPPG ≥ 8.5 mmol/L (153 mg/dL)] and to rule-out pre-existing diabetes or overt diabetes before pregnancy that is FPG value ≥ 7.0 mmol/L (126 mg/dL) OR RPG ≥ 11.1 mmol/L (200 mg/dL) (*Expert consensus opinion*).
- Perform GDM screening test for all undiagnosed pregnant women at 24-28 weeks using Oral Glucose Tolerance Test (OGTT), Fasting Blood Glucose, two hours Post Prandial Blood Glucose assay or a Random Blood Glucose (*Expert consensus opinion*).
- Test women with gestational diabetes mellitus for persistent diabetes at 4–12 weeks postpartum, using the oral glucose tolerance test and clinically appropriate non pregnancy values (*Expert consensus opinion*).

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Table 4: Diagnostic algorithm for GDM[7]

Diagnostic Algorithm for GDM		
1. GDM Screening at booking using fasting or random blood glucose test		
Overt/pre-existing DM prior to pregnancy	**GDM**	**Normal**
FPG value ≥ 7.0 mmol/L (126 mg/dL) RPG ≥ 11.1 mmol/L (200 mg/dL)	FPG > 5.1 - 6.9 mmol/L (92-125mg/dL).	FPG < 5.1mmol/L (92mg/dL)
2. GDM screening at 24-28 weeks using OGTT		
Fasting Plasma Glucose (FPG)	**1-hour after glucose load**	**2-hour after glucose load**
5.1 -6.9 mmol/L (92-125mg/dL)	> 10mmol/L (180mg/dL)	> 8.5 mmol/L (153mg/dL)

1.3. Considerations about recommendations on diagnosis of DM

1.3.1. Implementation considerations for the diagnosis of DM

Oral glucose tolerance test (OGTT) should only be performed by trained and skilled health workers. HbA1C result is affected by conditions that are characterized by rapid red blood cell turnover like anaemia. The results are also affected by haemoglobinopathies. HbA1C should also be conducted using a method that is standardized to the DCCT (Diabetes Control and Complications Trial) aligned assay and certified by NGSP (National Glycohemoglobin Standardization Program) and is thus not recommended for community-based screening.

1.3.2. Harms/benefits of recommendations on diagnosis of DM

No harm is associated with early detection of DM, while late diagnosis is associated with more complications.

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2. Preventing Diabetes Mellitus

2.1. General preventive measures for non-communicable diseases (NCDs)

Health promotion and lifestyle management are recommended for modifying both behavioral and metabolic risk factors for non-communicable diseases.[1] Health promotion for preventing non-communicable diseases include community, social, policy and environmental interventions that will enable individuals make healthy lifestyle choices.[2] The holistic approach embodied in the recommendations in this guideline, are therefore, in line with the WHO Global NCD Action Plan 2013-2020[3] and the Nigerian multi-sectoral action plan for NCD prevention and control.[4]

2.1.1. General measures for preventing NCDs in adults and adolescents

Adults (pregnant women inclusive) and adolescents can take lifestyle measures to reduce their modifiable risk factors for NCDs.[2] Their surrounding policy, social, physical and economic environments should also support these healthy lifestyle choices.[2]

Lifestyle measures for preventing NCDs focus on diet, physical activity, smoking and alcohol intake.[3,5] The lifestyle change targets are shown in the table 5 below.

Table 5: Lifestyle change targets for preventing NCDs

Healthy eating	Physical activity	Smoking and alcohol
• Reduce saturated fatty acid intake to less than 7-10% of total energy intake. • Increase dietary fibre (minimum of 20g daily intake). • Intake of at least six servings of fruits and vegetables a day. • Reduce intake of free sugars to less than 5-10% of total energy intake.	• 150 minutes of moderate-intensity aerobic physical activity a week; OR • 75 minutes of vigorous-intensity aerobic physical activity a week. • Muscle strength training and balance exercise in older adults above 64 years.	• Quit smoking or never smoke at all. • Avoid exposure to passive smoking. • Reduce alcohol intake.

• Reduce sodium/salt intake to not more than 2g/day.		

Physical activity intensity refers to the effort required to perform an activity. It depends largely on a person's fitness or experience in doing physical activity. Moderate-intensity activities can be described as those that increase the heart rate with little or no rapid breathing while vigorous-intensity activities increase the heart rate substantially and cause significant rapid breathing. The table below provides examples of moderate- and vigorous-intensity exercises.

Table 6: Moderate and vigorous intensity exercises[5]

Moderate-intensity physical activity	Vigorous-intensity physical activity
Brisk walking	Running
Dancing	Walking/climbing up a hill
Gardening	Fast cycling
Housework or domestic chores	Aerobics
Traditional hunting and gathering	Fast swimming
Active involvement with games and sports with children/walking domestic animals	Competitive sports and football
General building tasks (e.g. roofing, thatching, painting)	Heavy shoveling and digging
Carrying or moving loads less than 20kg	Carrying or moving loads more than 20kg

2.1.2. General measures for preventing NCDs in children

Breastfeeding is associated with the prevention of childhood obesity and it reduces the risk of developing obesity and its associated NCDs later in life.[5,6,7] For the first six months of life, exclusive breast-feeding is recommended for adequate nutrition and child survival.[8] Breast milk provides all the essential nutrients, enzymes and antibodies that children need to grow well in the first six months of life and beyond.[7] After six months, continued breast feeding and complementary feeding with nutritious food groups (semi-solids and soft foods) help to meet the energy and nutritional demands of infants and promotes healthy eating patterns in the long run.[9]

Promoting physical activity through both structured and unstructured play time is also critical and essential for preventing childhood obesity and its associated NCDs in later life.[10]

2.1.3. Community, social, economic, environmental and policy interventions for preventing NCDs

2.1.3.1. Whole-of-community health promotion activities

Community members and their leaders can initiate, implement and sustain interventions that help individuals within the communities to eat healthy diets and increase physical activity.[5] Examples of communities include schools, workplaces, residential areas, health professional groups, etc. The box below provides examples of whole-of-community health promotion activities.

Whole-of-community health promotion interventions

Educational programs on healthy diet, physical activity, tobacco use cessation and reduced alcohol intake

- Information, education and communication.
- Mass media public awareness/social marketing campaigns.
- SMS based mobile applications (SMS based) for education and risk assessment and management.

Healthy feeding/eating programs

- Healthy infant and young children feeding programs.
- School based feeding programs.
- Removal of vending machines from schools and communities.
- Garden to kitchen cooking programs in schools.

Targeted community-based activities

- School based physical activity programs.
- Community physical activity programs like marathons, swimming, dancing etc.

Workplace interventions

- Discounted vouchers for sports/gym facilities.
- Active spaces or gyms in the workplace.
- Periodic workplace recreational

2.1.3.2. Environmental and policy health promotion interventions

These interventions are adapted from the *Nigerian Multi-Sectoral Action Plan (MSAP) for the prevention and control of NCDs*. Examples of these interventions are shown in the box below.

Environmental and policy health promotion interventions from the Nigerian MSAP[1]

- Create active spaces and opportunities for physical activity.
- Effective implementation, prioritization and enforcement of the National Tobacco Control Act, 2015.
- Enactment and implementation of a National alcohol control law (act).
- Develop a regulation on reformulation of industrially produced foods to reduce salt content and replace trans-fats and saturated fats with unsaturated fats.

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- Develop and implement a policy on marketing sweetened foods and non-alcoholic beverages to children.

BOX 4: RECOMMENDATIONS FOR PREVENTION OF T2 DM

Individual level [11,12,13]

- Individual behaviour for preventing diabetes should focus on healthy eating/diet, increased physical activity, reduced smoking habits and alcohol intake.

  (Moderate–high certainty evidence, strong recommendation).

- Individual level behaviour change interventions are enhanced and sustained through behavioural counselling/therapy.

- Devices such as pedometers or mobile phone applications should be used to support and monitor behaviour change (Moderate certainty evidence, strong recommendation).

Community Level [14,15]

- Whole-of-community preventive measures are important for engaging communities to support community members to achieve behaviour changes that will prevent DM.

- Community rail- trails, pedometers and school-health education programmes are the most cost-effective population wide interventions (Moderate certainty evidence, weak recommendation).

Policy Level[16,17]

- Environmental and policy approaches for promoting healthy eating, physical activity and alcohol/drinking habits include:

  - Town/city planning to promote active recreation and physical activity
    fiscal policies to reduce the consumption of calorie-dense foods, alcohol and tobacco to prevent diabetes (Low certainty eviden_ce, strong recommendation).

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2.2. Prevention of T2DM among high-risk individuals

Individuals at high risk for developing T2DM can be identified through risk assessment using a web-based or paper-based validated questionnaire/tool and/or blood glucose tests.

BOX 5: RECOMMENDATIONS FOR PREVENTION/DELAY OF ONSET OF T2DM/GDM IN HIGH RISK INDIVIDUALS[12,13,14,15]

Combined diet and physical activity are recommended for preventing onset of T2DM and GDM among individuals with high risk.
(Moderate certainty evidence, strong recommendation)

Combined diet and physical activity can be enhanced and sustained through behavioural counselling/therapy.

Web-based and mobile apps can be used to deliver combined diet and physical activity programs.

(Low certainty evidence, weak recommendation)

There are two categories of high-risk individuals:

- Category 1: Individuals that have a high-risk score using a validated risk assessment questionnaire **BUT** have fasting plasma glucose levels of less than 5.5mmol/L or 99mg/dL.
- Category 2: Individuals that have a high-risk score using a validated risk assessment questionnaire **AND** have fasting plasma glucose levels between 5.6mmol/L (99mg/dL) and 6.9 mmol/L. These second category is considered pre-diabetes.

Intensive lifestyle management is essential for delaying progression to T2DM among individuals with high risk.[18]

2.2.1. Combined diet and physical activity for preventing or delaying onset of T2DM or GDM among individuals with high risk

All individuals with high risk for developing T2DM should be counselled on combining diet and physical activity.[18] Combining diet and physical activity is effective in reducing blood glucose to normal thresholds and also reduces other cardiovascular disease risk factors (weight, blood pressure, and lipid levels).[19]

Combined diet and physical activity can be enhanced and sustained through behavioural counselling/therapy.[19,20] Support from family members also helps to initiate and sustain behavior change regarding diet and physical activity.[19,20] In addition, technology such as web-

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based and mobile applications can be used to provide counselling and support, as well as monitor behaviour change.[21,22]

2.2.2. Metformin for preventing or delaying onset of Type 2 DM among individuals with pre-diabetes

Commented [OO32]: pre-diabetes has not been defined earlier

Metformin has demonstrated long-term effectiveness and safety prevention in clinical trials for preventing or delaying onset of T2DM in individuals with pre-diabetes.[23] Metformin is recommended for individuals with pre-diabetes especially those who have BMI ≥35 kg/m^2, those aged 60 years, and women with prior gestational diabetes mellitus.[24,25,26,27] Metformin is also recommended when intensive lifestyle modifications is not feasible, i.e. when it is not achieving the desired blood glucose control among persons with pre-diabetes.[11]

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An initial low dose of about 500mg daily should be the starting dose. This can be increased gradually as tolerated. Modified release metformin can be used if the standard metformin is not well tolerated.[18]

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Persons with pre-diabetes placed on metformin should be monitored using three-monthly fasting blood glucose for about 6-12 months. If no improvement in blood sugar is observed, metformin should be stopped.[18]

2.3. Considerations about recommendations for prevention

2.3.1. Implementation considerations

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Combined diet and physical activity programs can be delivered as group or individual sessions to support individuals in setting goals for weight loss, diet, exercise and address barriers that impede behaviour change. Group programmes are more cost-effective[13] and should be considered in resource-constrained settings.

These programmes may include structured dietary and physical activity interventions. Due to low internet penetration and coverage in Nigeria, SMS based mobile applications can be used to deliver content for these programmes. The local languages should also be considered when developing content and mode of delivery for these programmes.

BEST PRACTICE STATEMENT ON PREVENTION OF DIABETES

Monitor persons with pre-diabetes using metformin for 6-12 months and stop if there is no improvement in blood sugar levels[18].

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In rural settings with limited access to internet and smart phones, use basic phones to send text messages. Customized diabetes education messages should be translated to local languages and circulated as posters, fliers, etc. Non-electronic tools can also be used for behavioural change communication (BCC).

Diaries for recording physical activity duration, intensity and dietary intake can be considered when web-based or mobile applications are not readily available.

BOX 6: RECOMMENDATIONS FOR PREVENTING ONSET OF T2DM AMONG PERSONS WITH PRE-DIABETES[24,25,26,27]

Intensive lifestyle modification should be used to prevent onset of DM.
(High certainty evidence, strong recommendation)

Metformin* should only be used when intensive lifestyle modification is not feasible among pre-diabetes individuals with BMI ≥35 kg/m2, those aged 60 years, and women with prior GDM
(Moderate certainty evidence, strong recommendation)

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2.3.2. Harms/benefits of recommendations on prevention

There is no harm associated with lifestyle changes for preventing diabetes mellitus and other NCDs. Metformin use may be associated with vitamin B12 deficiency and peripheral neuropathy.

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3. Screening for Diabetes Mellitus in Adults

3.1 Rationale for screening

About half of the people with Type 2 Diabetes Mellitus (T2DM) are not aware that they have the condition and may develop complications before they are diagnosed or even treated.[1] Screening for T2DM helps people to understand their risk of developing the disease and then take measures to prevent or delay progression to diabetes.[2] A two-stage screening for T2DM facilitates early diagnosis, prevention and initiation of treatment.[2] It also provides an opportunity to identify and manage other cardiovascular risk factors.[2]

The first stage involves the use of a validated risk assessment questionnaire to elucidate known risk factors for developing T2DM and calculates a risk score that categorizes a person to either have a high, moderate or low risk for developing T2DM. An example of a risk assessment questionnaire is the FINDRISC (Finnish Diabetes Risk Score), which is an eight-item questionnaire that provides a measure of the probability of developing T2DM over the following 10 years. This assessment tool has been validated in Nigeria.[3] The second stage of the screening will depend on the diabetes risk score elucidated in the first stage. Individuals with moderate to very high-risk scores should proceed to do a diagnostic blood glucose test.

If the diabetes risk score is moderate to high, but the result of the diagnostic blood glucose test is normal, the diagnostic blood glucose test should be repeated every year. The person should also be advised on lifestyle management for preventing onset of T2DM. Other identified cardiovascular risk factors should also be actively managed.

Screening should be provider-initiated within health facilities. Community screening programs should only be carried out when there is a strong referral system.

3.2. FINDRISC tool

The Finnish Diabetes Risk Score (FINDRISC) questionnaire is a user-friendly and affordable two-page tool that is suitable to predict future risk of diabetes development and detect non-symptomatic ~~type 2 diabetes mellitus~~ (T2DM) in most populations. Its performance and effectiveness have been evaluated in Nigeria.

BOX 7: RECOMMENDATIONS FOR SCREENING FOR T2DM[4]

- Screening should be provider-initiated whenever a person visits a health facility.
- Community based intensified case finding or large-scale community screening programs are not recommended unless there is a clear referral pathway.
- Screening should be done using a locally validated screening tool such as the FINDRISC score.

  (Low certainty evidence, strong recommendation).
- Individuals identified as high- risk should proceed to a diagnostic test.
  If the result of the diagnostic test is normal, the diagnostic test should be repeated every year.

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3.3. Consideration about recommendations on screening

3.3.1. Implementation considerations

The FINDRISC questionnaire can be used either as a paper-based form or an electronic form.

- Risk-based screening for prediabetes and/or type 2 diabetes should be considered in children and adolescents after the onset of puberty or ≥10 years of age, whichever occurs earlier, who are overweight (BMI >85th percentile) or obese (BMI >95th percentile) and who have one or more additional risk factors for diabetes.

3.3.2. Harms/benefits of recommendations on risk assessment and screening

There is no risk or harm associated with the use of FINDRISC questionnaire as a risk assessment tool.

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Finnish Diabetes Association

TYPE 2 DIABETES RISK ASSESSMENT FORM

Circle the right alternative and add up your points.

1. Age

0 p. Under 45 years
2 p. 45–54 years
3 p. 55–64 years
4 p. Over 64 years

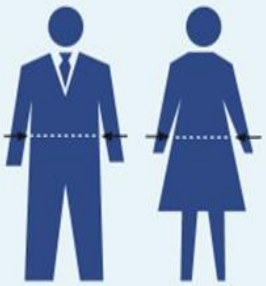
2. Body-mass index

(See reverse of form)

0 p. Lower than 25 kg/m²
1 p. 25–30 kg/m²
3 p. Higher than 30 kg/m²

3. Waist circumference measured below the ribs (usually at the level of the navel)

	MEN	WOMEN
0 p.	Less than 94 cm	Less than 80 cm
3 p.	94–102 cm	80–88 cm
4 p.	More than 102 cm	More than 88 cm



4. Do you usually have daily at least 30 minutes of physical activity at work and/or during leisure time (including normal daily activity)?

0 p. Yes
2 p. No

5. How often do you eat vegetables, fruit or berries?

0 p. Every day
1 p. Not every day

6. Have you ever taken medication for high blood pressure on regular basis?

0 p. No
2 p. Yes

7. Have you ever been found to have high blood glucose (eg in a health examination, during an illness, during pregnancy)?

0 p. No
5 p. Yes

8. Have any of the members of your immediate family or other relatives been diagnosed with diabetes (type 1 or type 2)?

0 p. No
3 p. Yes: grandparent, aunt, uncle or first cousin (but no own parent, brother, sister or child)
5 p. Yes: parent, brother, sister or own child

Total Risk Score

☐ **The risk of developing type 2 diabetes within 10 years is**

Lower than 7	**Low:** estimated 1 in 100 will develop disease
7–11	**Slightly elevated:** estimated 1 in 25 will develop disease
12–14	**Moderate:** estimated 1 in 6 will develop disease
15–20	**High:** estimated 1 in 3 will develop disease
Higher than 20	**Very high:** estimated 1 in 2 will develop disease

Please turn over

Test designed by Professor Jaakko Tuomilehto, Department of Public Health, University of Helsinki, and Jaana Lindström, MFS, National Public Health Institute.

Finnish Diabetes Association

WHAT CAN YOU DO TO LOWER YOUR RISK OF DEVELOPING TYPE 2 DIABETES?

You can't do anything about your age or your genetic predisposition. On the other hand, the rest of the factors predisposing to diabetes, such as overweightness, abdominal obesity, sedentary lifestyle, eating habits and smoking, are up to you. Your lifestyle choices can completely prevent type 2 diabetes or at least delay its onset until a much greater age.

If there is diabetes in your family, you should be careful not to put on weight over the years. Growth of the waistline, in particular, increases the risk of diabetes, whereas regular moderate physical activity will lower the risk. You should also pay attention to your diet: take care to eat plenty of fibre-rich cereal products and vegetables every day. Omit excess hard fats from your diet and favour soft vegetable fats.

Early stages of type 2 diabetes seldom cause any symptoms. If you scored 12–14 points in the Risk Test, you would be well advised to seriously consider your physical activity and eating habits and pay attention to your weight, to prevent yourself from developing diabetes. Please contact a public-health nurse or your own doctor for further guidance and tests.

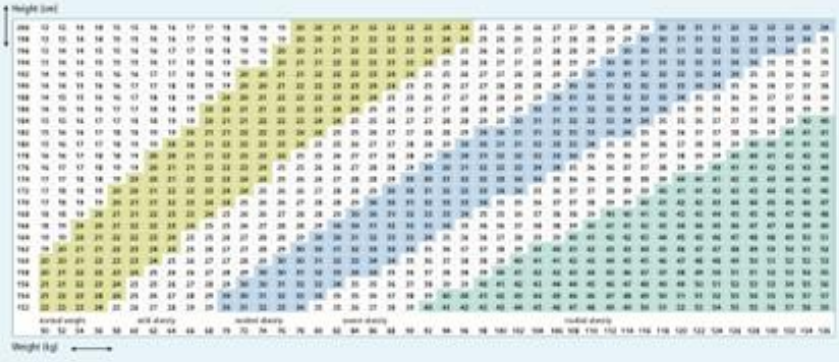
If you scored 15 points or more in the Risk Test, you should have your blood glucose measured (both fasting value and value after a dose of glucose or a meal) to determine if you have diabetes without symptoms.

BODY-MASS INDEX

The body-mass index is used to assess whether a person is normal weight or not. The index is calculated by dividing body weight (kg) by the square of body height (m). For example, if your height is 165 cm and your weight 70 kg, your body-mass index will be 70/(1.65 x 1.65), or 25.7.

If your body-mass index is 25–30, you will benefit from losing weight; at least you should take care that your weight doesn't increase beyond this. If your body-mass index is higher than 30, the adverse health effects of obesity will start to show, and it will be essential to lose weight.

BODY-MASS INDEX CHART



4. Diabetes Education for Adults and Caregivers of Children and Adolescents

4.1 Rationale for diabetes education and support

Structured diabetes education is effective in supporting persons diagnosed with diabetes to achieve self-care, adopt lifestyle changes, adhere to medications, monitor blood glucose, meet targeted glucose control targets, prevent complications and emergencies and improve treatment outcomes.[1,2]

Diabetes education should also be aimed at supporting family members and care givers in developing attitudes, beliefs, knowledge and skills for home care and support for self-management.

BOX 8: RECOMMENDATIONS FOR DIABETES EDUCATION.[3,4,6,7]

- A structured diabetes education program is recommended as part of comprehensive diabetes care and treatment.

  Diabetes education should be offered immediately after diagnosis. (Very low to low certainty evidence, strong recommendation)

- Diabetes education must cover prevention, changes, medication adherence and self-care including footcare education. (Evidence not Graded)

- Diabetes education should be delivered in a mode, intensity, frequency and duration that is suitable to the patient needs and health care settings.[4] (Evidence not Graded)

4.2 Timing of diabetes education and support

Structured diabetes education should be offered at the following four critical timepoints[8]:

BEST PRACTICE STATEMENT ON DIABETES EDUCATION

- Diabetes education must be delivered by a health worker trained on diabetes education according to national standards.[5]

1. **At diagnosis:** All adults or children with diabetes should be offered an effective structured education programme immediately after diagnosis has been made. If a person is unable to participate in a structured education programme, an alternative form of diabetes education that is equally effective should be provided.
2. ~~**Every year**~~**Annually:** to assess nutritional, emotional and educational needs of the person with diabetes every year.

3. When there is a change in factors that affect self-management and may also cause complications. Such factors include: change in health condition, living conditions or emotional needs.
4. When there is a change or transition in care and treatment.

4.3 Content of structured diabetes education

Structured diabetes education should cover the following areas: nutrition advice and skills to estimate the nutritional content (especially carbohydrates) of locally available foods, physical activity, weight control, how to take medications including how to inject the right dose of insulin for persons on insulin, blood glucose monitoring and strategies to achieve the targeted blood glucose level and diabetes footcare.[8]

Children, adolescents and young people with diabetes and their parents/caregivers (for patients aged less than 19 years) should receive culturally sensitive and developmentally appropriate individualized diabetes self-management education and support according to national standards at diagnosis and routinely thereafter. Persons with diabetes including children, adolescents and young persons should be offered information and education to promote mental wellbeing.

4.4. Considerations about recommendations on diabetes education

4.4.1. Implementation considerations

Intensity, duration and mode of delivery of diabetes education

The effectiveness of diabetes education depends on the duration, intensity, mode of delivery and person delivering the education.[9] Duration, intensity and mode of delivery of structured diabetes education must be appropriate, feasible for the implementation context and settings, and suitable to the patient's needs.

Inter-personal (group/one-on-one), electronic/digital platforms (videos and mobile apps) and printed forms (brochures and booklets) can be used to deliver diabetes education.[10,11,12,13]

Key Contents of Comprehensive Structured Diabetes Education[14,15]

- Nutrition advice and skills to estimate the nutritional content (especially carbohydrates) of locally available foods.
- Appropriate intensity and duration of physical activity.
- How to take medications as prescribed including how to inject the right dose of insulin.
- Blood glucose monitoring and strategies to achieve the targeted blood glucose level.
- How to avoid emergencies such as hypoglycaemia and how to maintain awareness of hypoglycaemia.
- Monitoring and self-management of cardiovascular risk factors complications.
- Prevention of complications like diabetic foot ulcers.
- Early identification of complications.
- Access to support group and networks.

4.4.2. Harms/benefits of recommendations on diabetes education

Diabetes education is associated with better treatment outcomes. It is associated with improved knowledge and self-care behaviour.[13]

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5. Lifestyle Management for Adults

Lifestyle management is necessary to achieve blood glucose control target and reduce associated cardiovascular risk factors. Strict blood glucose control is vital for preventing or delaying onset of complications,[3] but this may not be easily achievable without lifestyle changes.

Lifestyle changes focus on diet, physical activity, alcohol and tobacco intake, and are usually targeted at weight loss or control, and strict blood glucose control.[4,5,6,7]

BOX 9: RECOMMENDATIONS FOR LIFESTYLE CHANGES IN DM MANAGEMENT [1,2]

- Lifestyle changes are an essential add-on to drug treatment in diabetes management.
- Lifestyle changes should begin as soon as a diagnosis is made to achieve targeted blood glucose control.
- Lifestyle changes focus on diet, physical activity, alcohol & tobacco intake.

(Moderate certainty evidence, strong recommendation)

5.1. Nutritional recommendations

Reducing or controlling caloric intake, as well as improving nutritional content of foods consumed to healthier options is imperative to achieve strict blood glucose control and reduce cardiovascular risk.

General nutritional recommendations associated with reduced cardiovascular risk are:

- Avoiding processed foods high in free sugars.
- Increased consumption of high fiber foods.
- Increased consumption of fruits and vegetables.
- Higher intake of nuts, berries and unsweetened yogurt.
- Avoiding saturated fats and replacing cooking fats with monounsaturated or polyunsaturated fats.

Weight loss targets for lifestyle changes in overweight or obese persons with DM

- Reduce weight by 5 to 10% over a period of 12 months
- BMI should be monitored at each encounter with a health worker or diabetes educator

Evidence supports the use of Dietary Approaches to Stop Hypertension (DASH)[8] and Mediterranean dietary plans for reducing cardiovascular risk factors. Locally available foods

that are similar or fit into food types in either the DASH or Mediterranean diet are, therefore, recommended.

The quantity and frequency of diets are also important in achieving targeted metabolic goals for keeping blood glucose and blood lipid levels within normal thresholds. Health care providers and diabetes educators should evaluate their patients for the presence of eating disorders, disrupted eating patterns and circumstances that could disrupt eating patterns. The treatment regimen and meal plan of people with diabetes who present with symptoms of eating disorders or disrupted eating patterns should be reviewed. There are dietary considerations that are specific to either T1DM or T2DM.

BOX 10: RECOMMENDED CALORIC TARGETS FOR LIFESTYLE CHANGE [1,2]

- Reduce daily caloric intake by 500 to 600 calories in obese and overweight persons with DM.
- Follow a low-calorie diet (800 to 1200 calories per day) under the supervision of a health worker or diabetes educator.

(Moderate certainty evidence, strong

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5.1.1. Special dietary considerations for adult T1DM[9-20]

In a person with T1DM, the following nutritional advice should be considered and discussed by health workers or diabetes educators:

- Carbohydrate counting where carbohydrate content of food as well as fat and protein gram estimation is known, is important.
- Low glycaemic index diet for blood glucose control is not recommended.
- A food plan that enables the person to make optimal choices using different locally available variety of foods and which fits into evidence-based dietary plans like DASH or Mediterranean diet.

BEST PRACTICE STATEMENT ON DIET FOR PERSONS WITH T1DM

Health care providers and diabetes educators should work with their patients to develop individualized meal plans that suit the patient's taste, budget, culture, family situation and which can be made from cheap, locally available foods.

Fad diets (such as ketogenic, banting or atkins diet etc.) that are not evidence-based should be avoided. Caution should also be applied in consuming foods that are labeled to be suitable for diabetes. The content of such foods should be reviewed in line with dietary recommendations from a diabetes educator or health care provider.

- The insulin dose changes that are appropriate when taking different quantities of these foods.
- Choice of snacks with emphasis on the content, timing and quantity of snacks that will be consumed between meals.
- The different alcohol content of drinks and their effects on blood sugar and calorie intake.
- The benefits of healthy eating (consuming appropriate amount of fats, fruits and vegetables) in managing blood glucose and in reducing cardiovascular risk factors.
- Unique features of the person like obesity, eating disorders, other co-morbidities like hypertension, renal disease and cultural/religious requirements.

5.1.2. Special dietary considerations for T2DM

Persons with T2DM should be advised on:

- Diets that are rich in high-fiber and low-glycemic index foods that can be sourced locally.
- Consumption of three to five daily portions of vegetables and/or fruits, fish, grains and monounsaturated fats.
- Avoiding sugar, sweets and sweetened beverages.
- Use of individualized diet plans that promote caloric restriction but differ in type of protein, carbohydrate, and fat content.
- Review of the medication plans to identify potential treatment-related effects (signs of increased or reduced sugar levels) associated with consuming different diets or caloric quantity.

5.2. Physical activity

Commented [OO39]: This section is not referenced

Physical activity in persons with DM should be structured and regular to achieve best glycaemia and cardiovascular results.

General physical activity recommendations for persons with DM include:

- Moderate-intensity physical activity of 150min/week (see section 2.1 for descriptions of moderate and vigorous intensity) not more than 48 hours apart.
- Avoid prolonged sedentary time.
- Breaking up prolonged sedentary time periodically helps in reducing lower glucose levels after mealtimes.

BOX 11: RECOMMENDATIONS FOR PHYSICAL ACTIVITY FOR PERSONS WITH DM[1,2]

Moderate-intensity physical activity of 150min/week, not more than 48 hours apart.

(Moderate certainty evidence, strong recommendation)

Commented [OO40]: Ensure this reference is accurate incase table of content numbering is revised

There are special considerations for physical activity in T1DM and T2DM.

5.2.1. Special physical activity considerations for T1DM

Glycaemic response to exercise in individuals with T1DM varies by person. ~~Each individual with type 1 diabetes has different glycemic response to exercise.~~ These differences should be considered when recommending the type, intensity and duration of exercise for a person with T1DM~~type 1 DM~~.

Physical activity may cause hypoglycaemia if the dose of insulin or carbohydrate consumption is not altered. It may be necessary to consume additional carbohydrates if pre-exercise glucose levels are less than 100 mg/dL (5.6 mmol/L), depending on whether insulin doses can be lowered during the workout (such as with an insulin pump or reduced pre-exercise insulin dosage), the timing of the exercise (morning/evening), and the intensity and duration of the activity. In some patients, exercise increases insulin sensitivity and may cause hypoglycaemia to persist for several hours after exercise.

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- Emphasize that physical activity helps in reducing cardiovascular risk in medium and long term.

- Advice on the adequate intensity, duration and frequency of physical activity, and the effects on blood glucose level and nutritional needs.
- Emphasize the effect of exercise in reducing blood glucose level when insulin is adequate and the risk of worsening hyperglycaemia and ketonaemia when insulin levels are low.
- Advice on appropriate adjustments of insulin dosage and nutritional intake during and after exercise.

Steps for counseling on cessation of tobacco use[21]

The five steps are:

1. Reinforce message that tobacco increases cardiovascular risk.
2. Advise to quit in a clear, strong and personalized manner.
3. Provide information on health hazards of tobacco and give leaflet to the patient if available.
4. Assist in preparing a quitting plan.
5. At follow up visit, congratulate success and reinforce messages. If patient has relapsed, consider more intensive follow-up and support

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- Advice on how alcohol affects exercise and vice versa.

5.2.2. Special physical activity considerations for T2DM

- People with T2DM who are not physically active should increase their physical activity.
- Such persons should start with brisk walking for at least 150 minutes per week, at intervals of no longer than 48 hours.
- Vigorous intensity exercise of at least 90 minutes a week may be needed for overweight and obese people with T2DM to achieve weight loss and to avoid regaining weight.

5.3. Smoking and alcohol

- Avoid smoking for individuals who have never smoked.
- Quit smoking for individuals who smoke.
- Avoid excess alcohol intake.
- Alcohol affects blood sugar levels and should be continued moderately in people who are unable to quit or who drink customarily and should not exceed 1 to 2 units per day.

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- Alcohol should be avoided when taking low-calorie diets.

5.4. Considerations about recommendations on lifestyle management

5.4.1. Implementation considerations

Mobile and internet applications can support lifestyle changes and goals.

Locally available foods can be used to ensure adherence to dietary recommendations. Physical activity can also be achieved through home-based activities.

5.4.2. Harms/benefits of recommendations on lifestyle management

There is no risk associated with lifestyle management interventions.

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6. Blood Sugar Control Targets in Adults

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6.1. Recommended blood sugar targets

Persons with diabetes should aim to achieve the following blood glucose targets:

BOX 12: RECOMMENDATIONS FOR BLOOD SUGAR TARGETS AND MONITORING IN RESOURCE-CONSTRAINED SETTINGS[7]

A fasting capillary blood glucose <6 mmol/L (roughly 110 mg/dL) and postprandial blood glucose <10 mmol/L (180 mg/dL) in most measurements may predict an HbA1c <7% (53 mmol/mol).

This does not replace HbA1c.

Best Practice Statement

HbA1c

HbA1c is effective in monitoring long term blood glucose control.[1] An HbA1c target of 48 mmol/mol - 53 mmol/mol (6.5% - 7%) is recommended to reduce the risk of vascular complications when a person has access to HbA1C and can afford it.[2,3,4,5,6]

- HbA1c of 64 mmol/mol (8%) may be appropriate for patients with a history of severehypoglycaemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes.[1]

Fasting blood sugar targets

Fasting blood sugar in self-monitoring should be:

- 5-7 mmol/L when waking up in the morning,
- 4-7 mmol/L before meals and other times of the day in persons with T1DM,
- 5-9 mmol/L after meals in persons with T1DM.

6.2. Self-monitoring of blood glucose

Self-monitoring of blood glucose using a glucometer that meets current ISO standards is essential in achieving strict blood glucose targets. It helps the individual to tailor diets and physical activity to the observed blood glucose level, predict periods of hypogylcaemia and take the needed measures to avoid emergencies.

Self-monitoring is only useful for long term blood glucose control if it is used to inform clinical decisions and self-management plans.[7] Educating persons with diabetes on how to interpret results is very important.[8]

The finger tips are the recommended sites for self-monitoring. Use of other sites are not recommended for conventional routine self-monitoring.

In resource-constrained settings where HbA1c is not readily available, achieving targeted fasting blood glucose levels daily can be useful as an insight into HbA1c.[7]

6.2.1. Special considerations for self-blood glucose monitoring for persons on insulin, pregnancy and breastfeeding

- Advice the patient on routine self-monitoring of blood glucose for at least four times a day (before meals and before bed) in persons on insulin.[9,10] On some occasions, when blood glucose levels are suspected to be low, it can be monitored prior to exercise or after meals.
- Advice the patient to test more often and when affordable; if the desired target for blood glucose control is not achieved, if there is increase in frequency of hypoglycaemia, when unwell or during periods of increased physical activity, pregnancy or breastfeeding.
- Persons with T2DM using insulin or sulfonylurea (SU) should monitor blood glucose before driving or exercise.

6.3. Considerations about recommendations on diagnosis of DM

6.3.1. Implementation considerations

HbA1c is not readily available in primary health care settings in Nigeria, and it is very expensive. It should be used only when it is accessible, available and affordable.

6.3.2. Harms/benefits of recommendations for blood sugar control targets

Very tight blood sugar control targets may lead to repeated episodes ofhypoglycaemia and weight gain. On the other hand, intensive control has been shown to prevent or slow down the progression of diabetes related complications. There is need to balance the risks and benefits in children, the elderly, those who have experienced repeated episodes ofhypoglycaemia as well as those with severe cardiovascular complications.

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7. Drug Treatments for Diabetes

Individualized care should be considered when initiating drug treatment for persons living with diabetes.[1] This involves tailoring the medication to meet the patient's needs/ preferences and entails taking the following into consideration:

- Efficacy of the drugs
- Risk of low blood sugar
- Blood sugar levels at the time of diagnosis
- Body weight
- Side effect(s)
- Cost of medication
- Patient's income
- Patient's activities and preferences

Glucose Lowering Drugs for Diabetes in the 2016 Essential Medicines list

Insulin injections		
Mixed insulin	Biphasic isophane insulin	30% soluble, 70% isophane, 100 units/ml
Short-acting /bolus	Insulin, soluble (short acting)	100 units/ml in 10-ml vial
Long-acting/basal	Insulin, glargine	100 units in 10-ml vial
Oral anti-diabetic medications (tablets)		
Second generation sulphonylurea	Glibenclamide	5mg
	Gliclazide	80mg
	Glimepyride	1mg, 2mg, 3mg, 4mg
Biguanides	Meformin (hydrochloride)	500mg
DPP-4 inhibitors	Vidagliptin	50mg

In view of resource constraints and equity, only drugs in the 2016 Essential Medicines List[2] will be recommended in this guideline (see box above). Clinical inertia, that is, failure to initiate or intensify treatment promptly in individuals when needed to avoid raised blood sugar levels and subsequent complications, should be avoided in the treatment of T2DM.

Intensifying drug treatment by using combinations, changing drug types when necessary, or adjusting dosages when blood glucose targets are not met within 3-6 months, is very important for improving treatment outcomes and avoiding complications.

7.1. Drugs for Type 1 Diabetes Mellitus

Insulin is recommended for T1DM. Metformin should however be considered as an add-on to insulin therapy, in adult patients with TIDM who are overweight or obese or in circumstances where the person wants to reduce daily insulin requirement and improve blood glucose control.[3,4]

BOX 13: RECOMMENDATIONS FOR DRUG TREATMENT OF ADULTS WITH TD1M IN RESOURCE-CONSTRAINED SETTINGS

Insulin regimens recommended at primary care level in resource-constrained settings

Insulin determir and rapid-insulin analogues are not in the current (2016) Nigerian Essential Medicines List

Based on this,

- a basal-bolus regimen made up of rapid-acting soluble human insulin and insulin-glargine should be used with strict self-blood glucose monitoring to avoid hypoglycaemia.
- use a twice-daily human or analogue mixed insulin regimen when a multiple daily injection basal–bolus insulin regimen is not possible or a twice-daily mixed insulin regimen is preferred.

(Moderate certainty evidence, strong recommendation)

Insulin regimens

- Multiple daily injection basal-bolus insulin regimens/prandial and basal insulin should be offered as the insulin injection regimen of choice for adults.
- Guidance should be provided to the person on how to use multiple daily injection basal-bolus insulin regimens.
- Newly diagnosed patients with type 1 diabetes should not be offered non-basal-bolus insulin regimens (that is, twice-daily mixed, basal only or bolus only).
- Twice-daily insulin determir should be offered as basal insulin therapy for adults with type 1 DM.
- Continue to use an existing insulin regimen that has achieved agreed blood glucose control targets.
- Use once-daily insulin glargine or insulin detemir if twice-daily basal insulin injection is not acceptable to the person, or once-daily insulin glargine if insulin detemir is not tolerated.

- Rapid-acting insulin analogues injected before meals should be offered instead of rapid-acting soluble human insulin to reduce the risk ofhypoglycaemia for mealtime insulin replacement for adults with type 1 diabetes.
- Routine use of rapid-acting insulin analogues after meals is not advised for adults.
- If a multiple daily injection basal–bolus insulin regimen is not possible and a twice-daily mixed insulin regimen is preferred, a twice-daily human mixed insulin regimen for adults should be offered.
- If hypoglycaemia that considerably affects the quality of life occurs frequently in an adult using a twice-daily human mixed insulin regimen, twice-daily analogue mixed insulin regimen should be considered.

BOX 14: RECOMMENDATIONS FOR DRUG TREATMENT OF CHILDREN WITH TD1M

The treatment for type 1 diabetes in children is insulin.

• Twice-daily insulin using both short-acting and intermediate-acting insulin. (If these insulins are not always available, pre-mixed insulin can be used as an alternative regimen).
• Basal bolus regimen (the preferred option) - with short acting insulin given with main meals (usually three times per day) and intermediate-acting insulin given once or twice daily (evening, or morning and evening).

(High certainty evidence, strong recommendation)

7.2. Drugs for Type 2 diabetes mellitus

7.2.1. Initial/first-line treatment

Drugs are the first-line of treatment to be given to a person that has been newly diagnosed with T2DM. The choice of initial or first-line treatment should depend on the effectiveness of the drug, presence of other diseases, weight, blood sugar level of the newly diagnosed person, kidney function and drug safety.[5]

Initial treatment may involve the use of one drug (monotherapy), a combination of drugs (combination therapy), or even insulin.

BOX 15: RECOMMENDATIONS FOR FIRST-LINE DRUG TREATMENT OF TYPE 2 DIABETES IN ADULTS

Metformin is the preferred choice for initial monotherapy.
Dosage should be titrated from 500 to 2000 mg per day with or after meals.
Initial combination therapy is recommended when there is marked cardiovascular risk factor or high blood sugar levels between 11 -15 mmol/l.
A combination of metformin and another glucose lowering drug is recommended.

(High certainty evidence, strong recommendation)

Monotherapy

The choice of drug for initial first-line treatment with one drug in primary care settings should depend on making quick clinical decisions based on efficacy, safety, preference, patient compliance and cost-effectiveness.[1] Clinical decisions on efficacy should be made quickly with minimal clinical and laboratory evaluations. This is because the equipment and expertise for extensive clinical evaluation that will inform drug efficacy and safety for the person with T2DM may not be available at primary care level.

Monotherapy is not recommended when blood glucose at diagnosis is up to 16.7mmol/L or the person clearly shows symptoms like frequent urination and frequent thirst.

Metformin is the recommended initial or first-line drug for monotherapy when there is no clear contraindication.[6,7] This treatment must be accompanied by lifestyle changes. The use of metformin is associated with better blood sugar control, reduced cardiovascular risk and safety among persons with some reduction in kidney function (estimated glomerular filtration rate as low as 30ml/min/1.73m^2). Metformin is also effective in overweight and obese persons.[3,4]

BOX 16: RECOMMENDATIONS FOR FIRST-LINE DRUG TREATMENT OF TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS[3,4]

Metformin is the first-line drug for treating T2DM in adolescents and young people.

Basal insulin can be used as first-line if blood glucose level is as high as 13.9mmol/L and there is marked symptoms such as frequent urination (bedwetting), weight loss, frequent thirst and dehydration.

Basal insulin can also be used when metformin fails to achieve the targeted blood glucose levels.

(High certainty evidence, strong recommendation)

Metformin should not be used when there is marked vomiting and dehydration. It is also important to note that the use of metformin is associated with vitamin B12 deficiency, so long-term use of metformin should be accompanied with vitamin B12 supplementation and monitoring.[8] When metformin plus lifestyle change is unable to achieve blood glucose control targets, then dual therapy should be considered.

Initial combination therapy

Initial combination therapy has been shown to achieve better reduction in fasting blood sugar compared to monotherapy.[9] Initial combination therapy should be considered when there is narrowing of the arteries because of plaque build-up (atherosclerosis) or hypertension and therefore the need to reduce cardiovascular risk is a priority.

Due to the efficacy and safety of metformin, initial combination therapy comprising metformin and any other drug in the essential medicines list can be used.

For patients with narrowing of the arteries, hypertension or cardiovascular disease, using another drug for which there is clear evidence of efficacy in reducing cardiovascular risk factor such as SGLT-2 inhibitors (e.g. empagliflozin) and GLP-1(e.g. Liraglutide) should be considered.[5,6]

BOX 17: RECOMMENDATIONS FOR INITIAL INSULIN[10]

Insulin only or in combination with other glucose- lowering drugs in the essential medicines list can be considered as first-line treatment in the following conditions:

- Very high blood glucose level above 16mmol/l
- Acute weight loss
- Dehydration
- Acute illness or
- Presence of ketones

(Very low certainty evidence, strong recommendation)

When metformin is poorly tolerated, other drugs in the essential medicines list can be used to replace metformin in the combination.

Initial insulin

Insulin only or in combination with other glucose-lowering drugs in the essential medicines list can be considered in the following conditions:

- Very high blood glucose level above 16mmol/L
- Acute weight loss
- Dehydration
- Acute illness or
- Presence of ketones

Basal (long acting) insulin is preferable to achieve a target fasting blood sugar levels between 3.9 – 7.2 mmol/L.

Dual therapy

When metformin plus lifestyle change is unable to achieve blood glucose control targets within three-six months, then dual therapy should be considered.[5]

BOX 18: RECOMMENDATIONS FOR DUAL/TRIPLE THERAPY[11,12]

The preferred combination for dual therapy is metformin + sulfonylurea. Consider person's age, body weight, the presence of complications and duration of disease.

(Low certainty evidence, strong recommendation)

When triple therapy becomes imperative, the recommended and most feasible combination is Metformin + sulfonylurea + vidagliptin (DPP-4 inhibitor).
Basal insulin can also be added if dual or triple therapy does not yield the blood glucose targets.

(Moderate certainty evidence, strong recommendation)

The choice of drugs for dual therapy is similar to initial combination therapy. The preferred combination to metformin is a sulfonylurea that is on the essential medicines list.

The choice of second line drugs for dual therapy should be informed by the following:[5,13]

- **A**ge: lower blood glucose targets should be set for younger people.
- **B**ody weight: drugs that help in weight loss should be considered in overweight or obese persons.
- **C**omplications: People with chronic kidney disease, cardiovascular disease or who are likely to have very low blood sugar levels should use drugs that help in reducing these complications.
- **D**uration: People who have had the condition for a longer period and are yet to achieve the blood sugar targets are likely to experience complications. These patients require combinations that will achieve targeted blood sugar levels quickly.

Triple therapy

When dual therapy is unable to achieve blood glucose control targets within three-six months, then triple therapy should be considered.[5]

The third drug of choice will depend on the patient's health status, weight loss goals, cardiovascular risk factors as well as the efficacy and safety of the drug.

The third drug can be another oral glucose lowering drug in the essential medicines list or basal insulin.

It is advisable to try a combination of three oral glucose lowering drugs and then assess the patient after three months before adding insulin.

Based on the Essential Medicines List,[2] the triple therapy combination of oral glucose lowering drugs that is readily available in Nigeria is:

Metformin + sulfonylurea + vidagliptin (DPP-4 inhibitor).

Note that DPP-4 inhibitors raise concerns about major adverse cardiovascular outcomes. However cardiovascular safety studies show that apart from saxagliptin, other DPP-4 inhibitors do not seem to have any effect on major adverse cardiovascular outcomes and risk for heart failure.[14,15] Saxagliptin is associated with an increased risk for hospitalization for heart failure particularly in patients with chronic kidney disease or pre-existing heart failure.[16]

Algorithm for treating Adults with T2DM[5]

At diagnosis, there are four critical blood sugar levels to consider in order to determine the choice of drugs. These critical blood sugar levels are at HbA1c (corresponding blood sugar levels in mmol/l or mg/dl):

1. Less than 9% (11.7mmol/L or 210mg/dL).
2. Greater or equal to 9% (11.7mmol/L or 210mg/dL).
3. Greater than or equal to 10% (13.3mmol/L or 239.4 mg/dL).
4. Greater than or equal to 12% (16.7mmol/L or 300mg/dL) plus symptoms.

Note this algorithm is adapted from the ADA 2018 Standards for Diabetes care.[5] A conversion table[17] was used to approximate the average blood glucose level for a period of two-three months which corresponded to the HbA1c level.

Treatment Algorithm Chart

Random blood sugar at diagnosis is greater than 11.1mmol/l (199.8mg/dl) but less than 11.7mmol/l .

Random blood sugar at diagnosis is greater than 11.7mmol/l (210mg/dl)

Random blood sugar at diagnosis is greater than 13.3mmol/l (239.4 mg/dl)

Random blood sugar at diagnosis is greater than 16.7mmol/l (300mg/dl)

Consider Monotherapy: Lifestyle management + Metformin (If there is no contraindication)

Monitor glucose for 3-6 months.

Is the target blood glucose level achieved?

Yes, continue treatment

No

Consider Initial combination therapy/Dual therapy: Lifestyle management + metformin + Sulfonylurea in EML

If there is cardiovascular disease; add a second oral glucose lowering drug that reduces adverse cardiovascular events

Monitor glucose for 3-6 months.

Is the target blood glucose level achieved?

Yes, continue treatment

No

Consider triple therapy: Lifestyle management + metformin + Sulfonylurea in EML + DDP-4 (vidagliptin)

No improvement after close monitoring

Consider initial insulin/triple therapy: Lifestyle management + metformin + Sulfonylurea in EML + basal insulin

7.3. Considerations about recommendations on drug treatments for diabetes

7.3.1. Implementation considerations

A stepped care approach is necessary for optimizing blood glucose levels using drugs that are available, accessible and affordable.

Primary care physicians should initiate therapy and refer to specialists when triple therapy may be required.

For children and adolescents, having a flexible insulin regimen is preferred.

The offerings in the Essential Drug List and coverage by the NHIS should be considered in choosing the medications for patients. However, this should not be allowed to limit the choice of therapy.

7.3.2. Harms/benefits of recommendations for drug treatments for Diabetes

The various diabetes medications may cause hypoglycaemia (low blood sugar) with devastating consequences. Some medications have adverse cardiovascular or neurologic effects. These should be explained to patients, appropriate risk stratification done, and treatments instituted to mitigate them. Good blood glucose control with drugs has the benefit of preventing or slowing down the onset of complications.

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8. Managing Cardiovascular Risk Factors

8.1. Lifestyle management[1,2]

Cardiovascular risk factors in persons with diabetes mellitus can be managed through lifestyle management to achieve the following goals:

- Weight loss in obese and overweight persons
- Lower blood pressure
- Lower blood lipid levels
- Improved metabolic and vascular health
- Prevention of adverse cardiovascular events like stroke.

Lifestyle management for lowering cardiovascular risk factors in persons with diabetes is specifically focused on:[2,3]

- Caloric restriction
- Reducing sodium intake to 2,300 mg/day
- Increasing consumption of fruits and vegetables (8–10 servings per day) and low-fat dairy products (2–3 servings per day)
- Reducing alcohol intake to no more than 2 servings per day in men and no more than 1 serving per day in women
- Increasing physical activity levels (see section 2.1).

The DASH (Dietary Approaches to Stop Hypertension) diet is particularly helpful as dietary support for managing cardiovascular risk factors in persons with diabetes.[1]

BEST PRACTICE STATEMENT

Blood Pressure should be measured at every routine visit and at home.

All hypertensive patients with diabetes should monitor their blood pressure at home.

Lifestyle changes are important to reduce cardiovascular risk factors.

Drugs should be used when other cardiovascular risk factors like hypertension and high blood cholesterol levels are identified.

Drug treatment for managing cardiovascular risk factors such as hypertension and dyslipidaemia is discussed in section 11.

8.2. Aspirin for managing cardiovascular risk factors

Low-dose aspirin is useful for both primary and secondary prevention of atherosclerotic cardiovascular diseases in certain circumstances.

It is no longer recommended to use aspirin (ASA) for primary prevention among adults with DM who have increased CV risk but have no previous history of vascular disease and have an increased risk of bleeding.[4]

Aspirin has been shown to be effective in reducing adverse cardiovascular events among persons with diabetes who have had a previous cardiovascular event like myocardial infarction or stroke (secondary prevention).[5]

Aspirin is recommended for primary prevention in adults with diabetes who are aged 50 years or older and have at least one additional major risk factor (family history of premature atherosclerotic cardiovascular disease, hypertension, dyslipidemia, smoking, or chronic kidney disease/ albuminuria) who are not at increased risk of bleeding (e.g., older age, anemia, renal disease).

BOX 20: RECOMMENDATIONS FOR THE USE OF ASPIRIN FOR SECONDARY PREVENTION OF CARDIOVASCULAR RISK FACTORS IN PERSONS WITH DIABETES[6]

Use aspirin (75–162mg/day) as a secondary prevention strategy in those with diabetes and a history of atherosclerotic cardiovascular disease.

(High certainty evidence, strong recommendation)

8.3. Considerations about recommendations for managing cardiovascular risk factors

8.3.1. Implementation considerations

Low dose aspirin is widely available, as captured in the essential medicines list and covered by the National Health insurance scheme. Patients with diabetes (especially T2DM) patients should have a risk assessment done, taking into consideration bleeding risk, age, baseline CVD risk as well as patient's preferences about taking ASA and then availed the opportunity of its appropriate use.

8.3.1. Harms/benefits of recommendations for managing cardiovascular risk factor

The use of aspirin is of substantial benefit in reducing risk for cardiovascular events such as non-fatal myocardial infarction and stroke in adult persons with diabetes with prior cardiovascular disease. Aspirin use increases the risk of gastrointestinal bleeding and

haemorrhagic stroke. The overall benefits should be weighed against the harms for individual patients.

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Early Identification of Complications

9.1. Common diabetes-related complications

Complications of diabetes are mainly due to damage of small blood vessels in the eye, kidney and foot as well as damage to large blood vessels in the heart and lower limbs. These complications occur when blood glucose control is very poor and there are prolonged high blood sugar levels (hyperglycaemia).

The most common complications that result from damage of small blood vessels include [1]:

- Progressive damage to the retina (retinopathy).
- Progressive loss of kidney function (nephropathy).
- Damage to peripheral nerves (peripheral neuropathy).
- Foot ulcers or blisters due to damage to the blood vessels of the foot.

BOX 21: RECOMMENDATIONS ON MEASURES FOR PREVENTING DM-RELATED COMPLICATIONS AT PRIMARY CARE LEVEL

Generally, primary health care workers can work with persons with diabetes to prevent all complications by:

- Ensuring the person with diabetes achieves and sustains the targets for blood sugar control to reduce or slow disease progression.
- Ensuring that blood pressure and blood lipid levels are within normal limits to reduce or slow the disease progression.

(Evidence not graded)

Damage to large blood vessels was discussed in the previous section 8 on managing cardiovascular risk factors.

9.2. Identifying diabetes-related complications at primary care[2]

Diabetes-related complications require specialist care and advanced medical evaluations for monitoring and management. They cannot be managed at primary care level given the lack of specialist care and equipment for definitive diagnosis and management.

See Box 17 for recommendations on measures that primary healthcare workers can take to prevent complications in persons with diabetes.

9.2.1. Identifying diabetic retinopathy at primary Care

A health worker at primary care should do the following to prevent and identify early signs of diabetic retinopathy [2,3]:

BOX 22: RECOMMENDATIONS FOR SCREENING FOR DIABETIC RETINOPATHY AT PRIMARY CARE[3]

- Ask questions about difficulties with vision.
- Conduct visual acuity using a simple visual acuity chart.
- Refer for comprehensive eye examination.

(Evidence not graded)

- Ask the person with diabetes about their sight and any problems they are experiencing with vision. Ask for common symptoms of retinopathy such as:
  - Seeing spots or floaters
  - Blurred vision
  - Having a dark or empty spot in the centre of vision
  - Difficulty seeing well at night
- Conduct visual acuity measurements using simple and easy to use visual acuity charts to determine how much central vision is affected.
- Counsel and refer the person for comprehensive eye examination to screen for retinopathy.

BEST PRACTICE STATEMENT ON FREQUENCY OF SCREENING FOR DIABETIC RETINOPATHY

- Persons with T1DM should have an initial dilated and comprehensive eye examination within five years of the onset of diabetes.
- Persons with T2DM should have an initial dilated and comprehensive eye examination at the time of diagnosis.
- If blood sugar is well controlled and previous comprehensive eye examinations do not show any sign of retinopathy, then follow-up eye examinations should be done every one–two years.
- If previous comprehensive eye examinations showed signs of retinopathy, then follow-up eye examinations should be repeated at least annually. If retinopathy is progressing or sight-threatening, the examinations will be required more frequently.

9.2.2. Identifying diabetic nephropathy at primary care

A health worker at primary care should do the following to prevent and identify early signs of diabetic nephropathy:[3]

- Estimate albumin excretion rate (AER)
  - Use microalbumin/creatinine urine reagent strips (dipsticks) for urinalysis in a random spot urine sample. Timed or 24-hour collections are very cumbersome and do not yield any advantage in terms of accuracy.
  - Albumin excretion rate is estimated by the albumin-creatinine ratio (urine albumin per gram of urine creatinine in the same sample of urine).
  - A reading of 30microgram per gram of creatinine in a sample in two or three measurements taken four- six weeks apart shows persistent albuminuria.

BOX 23: RECOMMENDATIONS FOR SCREENING FOR DIABETIC NEPHROPATHY[3]

- Assess urinary albumin or albumin-to-creatinine ratio at least once a year.
- Estimate glomerular filtration rate in patients who have had T1DM for up to five years, in all patients with T2DM and in all patients with comorbid hypertension.

(Evidence not graded)

- Estimate glomerular filtration rate (eGFR) by measuring serum creatinine.
  - Serum creatinine can be converted to eGFR using validated calculators such as MDRD (Modification of Diet in Renal Disease) or CKDEpi (Chronic Kidney Disease Epidemiology Collaboration) in people with T2DM.
  - Glomerular Filtration Rate (eGFR) of <60 mL/min/1.73m^2 shows evidence of diabetic nephropathy.
  - Diabetic nephropathy is divided into the following stages:
    - Stage 3A when eGFR is 59-45 mL/min/1.73m^2
    - Stage 3B when eGFR is 44-30 mL/min/1.73m^2
    - Stage 4 when eGFR is 29-15 mL/min/1.73m^2
    - Stage 5 when eGFR is <15 mL/min/1.73m^2

- Refer persons with diabetes who show persistent albuminuria or abnormal glomerular filtration rate for specialist care.

9.2.3. Identifying diabetic peripheral neuropathy (DPN) at primary care[4,5,6]

A health worker at primary care should do the following to prevent and identify early signs of diabetic neuropathy:

- Ask simple questions about the presence of abnormal sensation and the type of abnormal sensation in the feet. These abnormal sensations vary based on the class of sensory fibres affected.
    - Unpleasant or painful burning and tingling sensations show that small fibres are involved.
    - Numbness and loss of protective sensations (not being aware of pain) show that large fibres are involved. Loss of protective sensation is a serious risk factor for diabetic foot ulcers.
- Conduct the following simple tests to find out if there is small and large-fiber function and protective sensation:
    - Pin prick and temperature sensation tests to evaluate small fiber function.
    - Vibration perception and 10-g monofilament to evaluate large fiber function.
    - 10-g monofilament to evaluate loss of protective sensation.

BOX 24: RECOMMENDATIONS FOR IDENTIFYING DIABETIC PERIPHERAL NEUROPATHY AND FOOT PROBLEMS[3,7]

- Screen for DPN within five years of diagnosis of T1DM and immediately after diagnosis of T2DM.
- After the initial screening, screen annually, regardless of the results.
- Conduct full sensory and foot examination annually.
- Inspect foot at every visit to the health facility.

(Low certainty evidence, strong recommendation)

9.2.4. Diabetic foot care[8,9]

Health workers in primary health care facilities should work with persons with diabetes to prevent diabetic foot ulcers.

This can be achieved by:

- Complete foot examination. This entails:
  - Foot inspection with shoes and socks removed in a well-lit room.
  - Checking for the presence of calluses, nail abnormalities, and foot abnormalities.
  - Taking foot temperature.
  - Checking for pulses in the lower legs and feet.
- Educating the person on foot care as part of self-management. The person with diabetes should be taught to do the following:
  - Check foot every day for red spots, cuts, blisters and swellings.
  - Wear comfortable shoes.
  - Wash feet every day and dry them carefully, particularly between the toes.
  - Trim toenails carefully and file the edges with an emery board to avoid cuts while trimming the nails.
  - Avoid putting feet in hot or cold water.
  - Put feet up when sitting and do not cross legs for long periods of time.
  - Avoid smoking.
- Referring persons that show loss of sensation or foot abnormalities for specialist care.

9.2.5. Autonomic neuropathy

Another serious complication of DM is autonomic neuropathy. This is due to damage to the nerves that control body functions and that are involuntary such as blood pressure, bladder function, temperature control, digestion and sexual function.[10,11] The health workers should

ask for common symptoms of autonomic neuropathy that can be elucidated at primary care level such as:

- Not being aware of when blood sugar levels become very low (hypoglycaemia unawareness)
- Rapid heartbeats even when at rest (resting tachycardia)
- Low blood pressure on standing (orthostatic hypotension)
- Constipation
- Diarrhea
- Not being able to control the urge to go to defecate (fecal incontinence)
- Erectile dysfunction
- Urgency to urinate, frequent urination and sometimes retention of urine (neurogenic bladder)
- Sudomotor dysfunction with either increased or decreased sweating

9.3. Considerations about recommendations on early identification of complications

9.3.1. Implementation considerations

Primary care practitioners should recognize the thresholds for referring patients with any diabetes-related complication to the appropriate specialist. An initial link should be established with the relevant experts and care planned collaboratively. At primary health care centres where tests may not be available, a checklist of symptoms should be used for assessment and patients referred accordingly.

9.3.2. Harms/benefits of recommendations for early identification of complications

The assessment for early diabetic complications is done with instruments that lead to minimal harm or no harm at all. The psychological distress associated with the diagnosis of any

complication of diabetes should be borne in mind. The benefits of early diagnosis far outweigh the risks of non- or delayed diagnosis.

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10. Managing Emergencies in Primary Care Settings

10.1. Hypoglycaemia

Hypoglycaemia, also known as low blood sugar levels of less than 4mmol/L can pose an emergency in persons with diabetes.[1] It could be mild, moderate or severe. It is a life-threatening condition when it occurs in severe forms and warrants urgent management.

Although most persons with DM know when their blood glucose is getting very low, some persons who have had DM for a very long time are not aware of this and as such are more likely to experience the serious forms of hypoglycaemia.[2]

Persons on insulin and/or sulfonylureas (glibenclamide, glyburide, gliclazide, glimepiride, glipizide and tolbutamide) are more prone to having very low blood sugars less than 4mmol/L (72mg/dL).[3]

Primary health care workers should work with persons with diabetes to help them recognize when their blood sugar level is getting lower than 4mmol/L (72mg/dL) by telling them to watch out for the following basic symptoms:

- Sweating
- Dizziness or tiredness
- Blurred vision
- Confusion
- Increased heart rate
- Convulsion
- Loss of consciousness
- Coma

The following algorithm shows the management of very low blood sugar levels at primary health care centres and at higher levels of care.

10.2. Diabetic keto-acidosis

Diabetic keto-acidosis (DKA) is a serious complication that occurs most commonly due to infections but also following non-adherence to insulin treatment plans[5] or unrecognized symptoms of new-onset T1DM. People with T1DM are particularly at risk for DKA.

BOX 24: RECOMMENDATIONS FOR MANAGING DKA AT PRIMARY CARE LEVEL

DKA cannot be treated at primary care, as it requires specialist management.

(Evidence not graded)

High blood glucose, if not treated for a long time can lead to the build-up of harmful ketones in the blood.

Managing DKA requires emergency treatment in hospital by a specialist care team.[6] However, DKA can be prevented at home and at primary health care to avoid emergency situations.

BEST PRACTICE STATEMENT ON PREVENTING DKA AT PRIMARY CARE LEVEL

DKA can be prevented from occurring at primary health care by:

- Looking out for symptoms of hyperglycaemia and dehydration
- Monitor blood glucose and ketone levels at home
- Adjust insulin dosage during sick days and when blood sugar is still very high
- Adjust insulin dosage with food consumption quantity and pattern to achieve best results
- Refer patients as soon as warning signs are recognized

Preventing DKA at home and at primary care

Primary health care workers should be able to provide education on the warning symptoms and signs of DKA in all age groups.

These warning signs are:

- Experience of frequent thirst, frequent urination and frequent appetite up to 20 days at a stretch
- Blood glucose levels ≥13.32mmol/L (240mg/dL)
- Periods of illness
- Ketones in urine using dipsticks
- Signs of dehydration like dry lips and mouth

Diabetic keto-acidosis can be prevented by observing sick day rules by adjusting insulin during periods of illness, frequent glucose monitoring and checking urine ketone levels using a dipstick test at home.

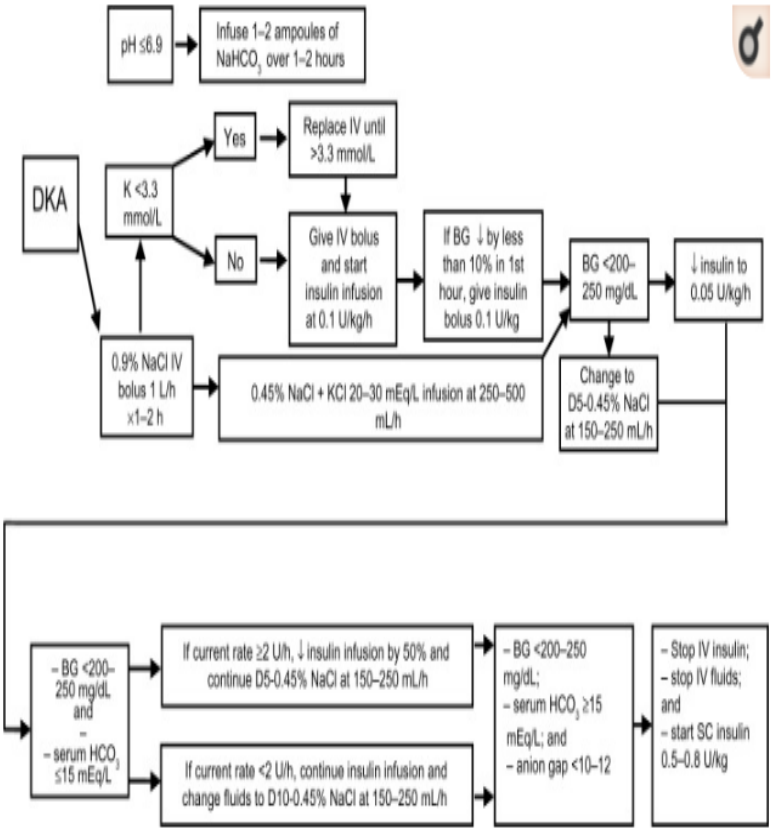
Refer person with diabetes with high ketones and very high blood sugar levels and symptoms of high blood sugar for secondary care.

Treating DKA in adults

- Evaluate person presenting DKA to determine the blood sugar level, dehydration, ketones, potassium loss, blood pH.
- Replace fluids.
- Give insulin intravenously.
- Maintain serum potassium levels between 4 and 5 mEq per L (4 and 5 mmol per L).
- Recommend bicarbonate replacement in persons with a pH lower than 6.9 using 100mEq of sodium bicarbonate in 400 mL of sterile water with 20 mEq of potassium chloride at a rate of 200 mL per hour for two hours.

Follow the treatment algorithm below.

WORKFLOW OF MANAGEMENT OF ADULT DKA[7]



10.3. Hyperglycaemic hyperosmolar state

The hyperglycaemic hyperosmolar state (HHS) is associated with significant morbidity and higher mortality than DKA and must be diagnosed promptly and managed intensively by a specialist team.[6]

At primary health care, the following signs can be used to recognized HHS:

- Blood sugar level of 600 milligrams per deciliter (mg/dL) or 33.3 millimoles per liter (mmol/L) or higher.
- Excessive thirst
- Dry mouth
- Increased urination
- Warm, dry skin
- Fever
- Drowsiness, confusion
- Hallucinations
- Vision loss
- Convulsions
- Coma

Hyperglycaemic hyperosmolar state cannot be managed at primary health care but it can be prevented.

BEST PRACTICE STATEMENT FOR PREVENTING HHS AT HOME OR PRIMARY CARE

- Recognize the symptoms of high blood sugar like increased thirst, increased urinating, dry mouth and skin or fever.
- Monitor your blood sugar level and be alert when it is above 13 mmol/L. This is because HHS may occur when it increases up to 30mmol/L.
- Drink plenty of water when sick.
- Adhere to medications as well as dietary and physical activity plans.

Clinical Evaluation

As soon as HHS is diagnosed, assess for the severity by measuring the following:

- Serum electrolyte, urea and creatinine
    - plasma osmolality greater than 350 mOsmol/kg (Normal range 280-300)
    - sodium above 160 mmol/L (Normal range 135-145)
    - venous/arterial pH below 7.1 (Normal range 7.35-7.45)
    - hypokalaemia (less than 3.5 mmol/L) or hyperkalaemia (greater than 6 mmol/L) (Normal range 3.5-5.0)
    - serum creatinine >200 µmol/L (Normal range 60-110)
- Systolic blood pressure below 90 mmHg
- Pulse over 100 or below 60 bpm
- Urine output less than 0.5 ml/kg/hr
- Temperature below normal
- Level of consciousness below 12 using the Glasgow Coma Scale (GCS)

Check for other adverse cardiovascular events such as myocardial infarction or stroke.

Treatment goals

The goals of treatment of HHS are to treat the underlying cause and to gradually and safely:

- normalise plasma osmolality
- replace fluid and electrolyte losses
- normalise blood glucose

Other goals include prevention of:

- arterial or venous thrombosis
- other potential complications e.g. cerebral oedema/central pontine myelinolysis
- foot ulceration

Treatment procedure

A. Hour 1: Immediate management upon diagnosis: 0 to 60 minutes

- Commence IV 0.9% sodium chloride – one liter to run over one hour.
- Consider more rapid replacement if SBP below 90 mmHg.
- Caution in the elderly where too rapid rehydration may precipitate heart failure but at the same time insufficient rehydration may fail to reverse acute kidney injury.
- Only commence insulin infusion (0.05 units/kg/hr) IF there are ketones in urine (2+ or more).

Conduct full evaluation

B. 60 minutes to 6 hours

Commented [DM44]: Prof: Shouldn't this be 2?

- Using 0.9% sodium chloride, aim to give a further 0.5 – 1 L/hr depending on clinical assessment of dehydration / risk of precipitating heart failure and fluid balance (target is to achieve positive fluid balance of 2-3 L by 6 hours).
- Measure glucose, urea and electrolytes hourly and calculate osmolality (2Na+ glucose + urea).
- If plasma Na+ increasing but osmolality declining at appropriate rate, continue 0.9% sodium chloride.
- If plasma Na+ increasing AND osmolality increasing (or declining at less than 3 mOsmol/kg/hr) check fluid balance.
- If positive balance inadequate increase rate of infusion of 0.9% sodium chloride.
- If osmolality increasing and fluid balance adequate, consider switching to 0.45% sodium chloride at same rate.
- If osmolality falling at rate exceeding 8 mOsmol/kg/hr consider reducing infusion rate of IV fluids and/or insulin (if already commenced).
- If blood glucose falling less than 5 mmol/L per hour check fluid balance.
- If positive balance inadequate, increase rate of infusion of 0.9% sodium chloride.
- If positive fluid balance adequate, commence low dose IV insulin (0.05 units/kg/hr) or if already running, increase rate to 0.1 units/kg/hr.

- To maintain potassium in the normal range:
    - Hypokalaemia (less than 3.5 mmol/L) and hyperkalaemia (greater than 6 mmol/L) are life-threatening conditions and warrant senior review.
    - Potassium replacement in infusion solution if potassium levels are very low.
    - Treat for high potassium levels.
- Avoidance of hypoglycaemia
    - Aim to keep blood glucose 10-15 mmol/L in first 24 hours.
    - If blood glucose falls below 14 mmol/L commence 5% or 10% glucose at 125 ml/hr AND CONTINUE 0.9% sodium chloride solution.
- Monitor vital signs and chart Early Warning Score (EWS).
- Maintain accurate fluid balance chart (minimum urine output 0.5 ml/kg/hr).
- Repeat clinical evaluation.

C. 6 to 12 hours

The aim within this period is to:

- Ensure that clinical and biochemical parameters are improving.
- Continue charting blood glucose hourly, sodium and calculated osmolality 2 hourly.
- Continue IV fluid replacement to achieve positive balance of 3-6 litres by 12 hours.
- Maintain an accurate fluid balance chart.
- Assess for complications of treatment e.g. fluid overload, cerebral oedema, extra pontine myelinolysis (e.g. deteriorating conscious level).
- Continue treatment of any underlying precipitant.
- Call for help if patient is not improving.
- Avoid hypoglycaemia.
- Aim to keep blood glucose 10-15 mmol/L in first 24 hours.

- If blood glucose falls below 14 mmol/L commence 5% or 10% glucose at 125 ml/hr AND CONTINUE 0.9% sodium chloride solution.
- Ensure referral has been made to diabetes team.

D. 12 to 24 hours

- Ensure continuing improvement of clinical and biochemical parameters.
- Continue charting blood glucose hourly. Frequency for measurement of sodium and calculated osmolality can be reduced (4 hourly) if improvement is maintained (if not continue 2 hourly).
- Do not expect biochemistry to have normalised by 24 hours (sodium and osmolality are likely to be raised).
- Take appropriate action (as outlined in time 60 minutes to 6 hours) as outlined above depending on results.
- Continue IV fluid replacement to achieve remaining replacement of estimated fluid losses within next 12 hours – this will be dependent on factors such as initial degree of dehydration/body weight etc. and MOST IMPORTANTLY the response to treatment so far.
- Therefore, continue maintaining accurate fluid balance chart, plotting osmolality and making appropriate adjustments to fluid replacement rates.
- Continue IV insulin with or without 5 or 10% glucose solution to maintain blood glucose 10-15 mmol/L.
- Adjust insulin infusion rate hourly by 1 unit/hour increments or decrements to achieve desired blood glucose.
- Assess for complications of treatment e.g. fluid overload, cerebral oedema, extra pontine myelinolysis (e.g. deteriorating conscious level).
- Continue treatment of any underlying precipitant. If patient is not improving seek senior advice.

E. 24 hours to Day 3

- Ensure that clinical and biochemical parameters are improving or have normalized.
- Continue IV fluids until eating and drinking normally.
- Vary dosage of insulin if not eating and drinking and convert to appropriate subcutaneous regime when biochemically stable.
- Encourage early movement.
- Assess for signs of fluid overload or cerebral oedema.
- Review the patient.

F. After care at primary care level

- Most patients should go home on subcutaneous insulin (the regime being determined by their circumstances).
- For patients with previously undiagnosed diabetes or well controlled on oral agents, switching from insulin to the appropriate oral hypoglycaemic agent should be considered after a period of stability (weeks or months).
- Ensure patient has appropriate diabetes education prior to discharge and arrange follow-up by diabetes team.

10.4. Considerations about recommendations on managing emergencies in primary care settings

10.4.1. Implementation considerations

The management of diabetic emergencies should be left for specialists. However, primary care practitioners should identify these emergencies and offer appropriate initial emergency care before referring for specialist care.

10.4.2. Harms/benefits of recommendations for management of emergencies in primary care settings

The risk of increased morbidity and mortality is high with missed or delayed diagnosis. Low blood sugar and electrolyte disorders may result from use of inappropriate fluids. However,

outcomes are better with prompt initial management and aggressive institution of appropriate therapy supervised by a diabetes specialist.

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11. Managing Comorbidities

11.1. High blood pressure

Both diabetes and high blood pressure are serious cardiovascular risk factors on their own. The presence of high blood pressure (HBP) in a person with diabetes, therefore, constitutes a very serious cardiovascular risk which must be managed adequately to reduce the risk.[1,2,3] Management of these co-morbidities involves both lifestyle modification and drug treatment.

Target blood pressure in persons with Type 2 diabetes mellitus

While the evidence from epidemiological studies and randomized controlled trials (RCTs) shows that it is possible to achieve intensive blood pressure control with a systolic blood pressure <140mmHg and a diastolic blood pressure <80mmHg,[4] the experience of clinicians is that this may be difficult to achieve in some instances.[5,6] Individual blood pressure targets, therefore, need to be set following an informed discussion between the patient and provider after weighing the risks and benefits of therapy.

BOX 25: RECOMMENDATIONS FOR BLOOD PRESSURE TARGETS IN PERSONS WITH T2DM[7]

Target blood pressure in persons with diabetes should be:

- <140/80mmHg where there is no sign of kidney, eye, or cerebrovascular damage.
- < 130/80mmHg where there is evidence of kidney (including microalbuminuria), eye, or cerebrovascular damage.

(Expert consensus opinion)

Recommended frequency of blood pressure measurement

BEST PRACTICE STATEMENT ON FREQUENCY OF BP MEASUREMENT

- For adults with DM but no history of hypertension or kidney disease, measure BP annually.
- For adults with DM with known hypertension, measure every:
  - 1 month if blood pressure is higher than 150/90 mmHg.
  - 2 months if blood pressure is higher than 140/80 mmHg.
  - 2 months if blood pressure is higher than 130/80 mmHg and there is kidney (including microalbuminuria), eye or cerebrovascular damage.

Provide lifestyle advice, if blood pressure is confirmed as being consistently above 140/80 mmHg (or above 130/80 mmHg if there is kidney, eye or cerebrovascular damage), and add

medications if lifestyle advice does not reduce blood pressure to below 140/80 mmHg (below 130/80 mmHg if there is kidney, eye or cerebrovascular damage).

For adults with DM with known hypertension who have consistently maintained their blood pressure target, measure BP every four-six months, and at these visits, assess for side effects of treatment including risks from an unnecessarily low blood pressure.

Recommended management[8]

Provide lifestyle advice to persons with DM at every visit even where there is no history of hypertension.

For adults with DM already on antihypertensive drug treatment when diabetes is diagnosed, review blood pressure control and medications used and make changes **only** if there is poor control or if the current drug treatment is not appropriate because of microvascular complications or metabolic problems. Where the person is already on antihypertensive therapy, and there is kidney, eye or cerebrovascular damage, intensify treatment until the blood pressure is consistently below 140/80mmHg or 130/80mmHg.[9]

BOX 26: RECOMMENDATIONS FOR DRUG COMBINATIONS FOR FIRST-LINE TREATMENT OF HIGH BLOOD PRESSURE IN DM

Depending on the blood pressure at diagnosis or presence of proteins in urine, the first-line antihypertensive drug treatment should be a combination that contains Angiotensin Converting Enzyme inhibitor (ACEi) plus either a thiazide-diuretic (long acting versions have been shown to reduce cardiovascular events) or a generic calcium-channel blocker (CCB).

(High certainty evidence, strong recommendation)

Note: *There is no ACEi in the 2016 EML, therefore, the recommended first-line drug is either a thiazide diuretic or a calcium blocker if there is no protein in urine.*

First-line antihypertensive drug treatment

The number and combination of drugs that will be used as first-line depend on:

- Blood pressure at diagnosis (between 140/90mmHg and 160/100mmHg or above 160/100mmHg).

- The presence of proteins (albumin) in urine.

(See Box 25)

For persons intolerant of ACE inhibitors (where this intolerance does not include hyperkalaemia or renal dysfunction), substitute with an angiotensin II-receptor antagonist (A2RB) – however, **do not** combine an ACE-inhibitor with an A2RB to treat hypertension.[9,10,11]

Second-line antihypertensive drug treatment

Where blood pressure does not meet the set target with first-line therapy, add whichever drug that was not a part of the initial combination (calcium channel blocker or diuretic).

BOX 27: RECOMMENDATIONS FOR FIRST-LINE TREATMENT IN WOMEN PLANNING PREGNANCY

A calcium-channel blocker should be the first-line antihypertensive drug treatment for a woman, where it is agreed that there is possibility of her becoming pregnant – this decision should be made following an informed discussion with the woman – avoid ACE inhibitors or A2RB in women who are planning a pregnancy as these drugs cause fetal damage.

(Very low certainty evidence, strong recommendation)

Third-line antihypertensive drug treatment

Where the blood pressure does not meet the set target despite the addition of both a calcium-channel blocker and a diuretic, an additional antihypertensive should be introduced (see Box 29 for recommendations for third-line drug treatment).

BOX 28: RECOMMENDATIONS FOR DRUG COMBINATIONS FOR SECOND-LINE TREATMENT OF HIGH BLOOD PRESSURE IN DM

Where blood pressure does not meet the set target with first-line therapy, add whichever drug that was not a part of the initial combination (CCB or diuretic).

(High certainty evidence, strong recommendation)

If there is albumin in the urine or signs of kidney disease, ACEi or ARB should be used as first-line and included in the combinations.

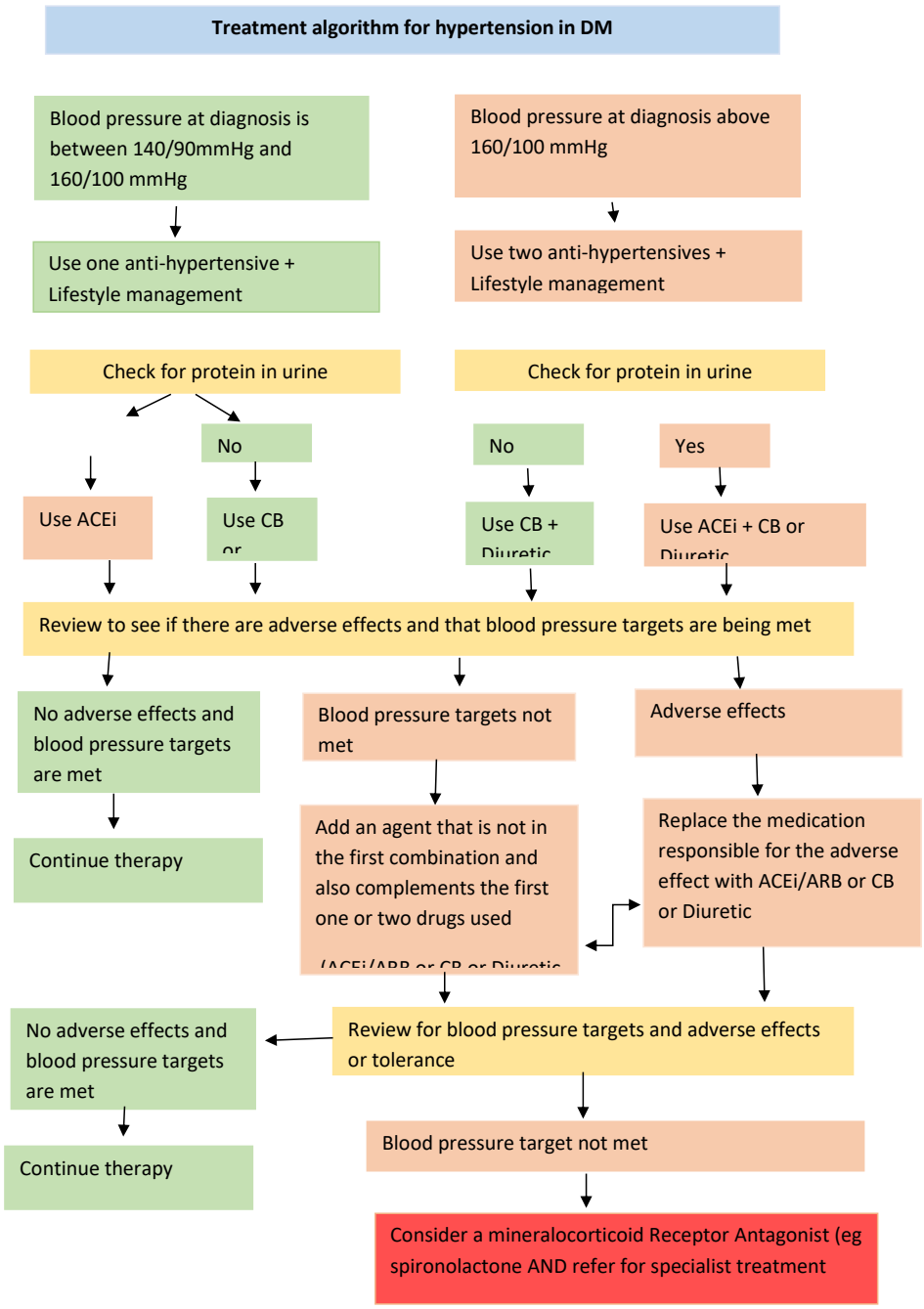
We maintain this recommendation despite the absence of ACEi or ARB in the EML because they are the only class of anti-hypertensives that show protective effects in the kidneys in persons with T2DM.

BOX 29: RECOMMENDATIONS FOR DRUG COMBINATIONS FOR THIRD-LINE TREATMENT OF HIGH BLOOD PRESSURE IN DM

Add an alpha-blocker, a beta-blocker or a *potassium-sparing diuretic or a mineralocorticoid receptor antagonist (*where the person is on either an ACE inhibitor or A2RB, potassium-sparing diuretics should be added with caution and serum potassium carefully monitored – additionally, spironolactone should **not** be administered to a pregnant woman as it causes fetal damage).

For patients on any one of the following: ACE inhibitors, A2RBs, thiazide diuretics, or potassium-sparing diuretics, renal function (serum creatinine and estimated glomerular filtration rate) and serum potassium should be checked at least annually.

(Moderate certainty evidence, strong recommendation)


Treatment algorithm for hypertension in DM
Blood pressure at diagnosis is between 140/90mmHg and 160/100 mmHg
Use one anti-hypertensive + Lifestyle management
Blood pressure at diagnosis above 160/100 mmHg
Use two anti-hypertensives + Lifestyle management
Check for protein in urine
No
Use ACEi
Use CB
Check for protein in urine
No
Yes
Use CB +
Use ACEi + CB or
Review to see if there are adverse effects and that blood pressure targets are being met
No adverse effects and blood pressure targets are met
Continue therapy
Blood pressure targets not met
Add an agent that is not in the first combination and also complements the first one or two drugs used
Adverse effects
Replace the medication responsible for the adverse effect with ACEi/ARB or CB or Diuretic
No adverse effects and blood pressure targets are met
Continue therapy
Review for blood pressure targets and adverse effects or tolerance
Blood pressure target not met
Consider a mineralocorticoid Receptor Antagonist (eg spironolactone AND refer for specialist treatment

11.2. Dyslipidaemias

Persons with T2DM have a higher prevalence of dyslipidaemia, which is a well-recognised cardiovascular risk factor. Various lipid patterns may be seen in patients with diabetes, however the most commonly observed is an elevated triglyceride level often with a low level of HDL cholesterol.[12] Of the lipid abnormalities, a high level of LDL (low-density lipoprotein) cholesterol is of concern and statins remain the preferred treatment option for LDL cholesterol reduction and cardio-protection.

Multiple clinical trials have shown that statins have beneficial effects on cardiovascular disease outcomes in persons with or without pre-existing coronary heart disease, and subgroup analyses show that this holds true for persons with diabetes on statins.[13] In addition, there is evidence of benefit from very low-dose statins even when these are not taken daily – for example, in patients who are unable to tolerate higher, more frequent doses due to side effects. While there is limited trial data on the effectiveness of statin therapy in persons with type 1 diabetes mellitus, the current recommendations are that similar approaches should be adopted for lipid lowering in persons with type 1 and type 2 diabetes mellitus.

There is much evidence from randomised controlled trials[14-17] to support the use of statins in persons with diabetes between the ages of 40 and 75 years in the primary prevention (where they do not have pre-existing atherosclerotic cardiovascular disease) or secondary prevention of atherosclerotic cardiovascular disease; and this recommendation remains the same for those aged >75 years due to the higher cardiovascular risk conferred by age. Commencement of lipid-lowering therapy in persons with diabetes <40 years should be made after consideration of the presence of additional cardiovascular risk factors and an informed discussion with the patient, carefully weighing the risks and benefits of therapy.

Recommendations for lipid monitoring

Where resources permit, it is advised that a lipid profile (serum total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) is performed:

- At the time of diabetes diagnosis or at the initial medical review.
- Within one-three month period post commencement of statins, or following a change in statin dose or type, in order to gauge the individual's response.

- At least once every five years in <40 years old patients with diabetes who are not on lipid lowering medication.

LDL cholesterol ≥100mg/dL is considered a risk factor for atherosclerotic cardiovascular disease, and in individuals who are known to have pre-existing cardiovascular disease, a target LDL < 70mg/dL is recommended.

There is currently no consensus on a threshold for triglycerides, though levels >500mg/dL are considered to increase the risk of pancreatitis.

Statins are required to achieve targeted blood lipid levels in persons with diabetes as follows:

- LDL cholesterol of <70mg/dL (1.8mmol/L) in persons that have/had a cardiovascular disease.
- LDL cholesterol of <70mg/dL (1.8mmol/L) in persons with a high risk of having a cardiovascular disease based on the WHO/ISH cardiovascular risk calculator.
- LDL cholesterol of <100mg/dL (2.6 mmol/L) in persons that do not have a cardiovascular disease and do not have high risk of having a cardiovascular disease based on the WHO/ISH cardiovascular risk calculator.
- Triglyceride level of >500 to 1000 mg/dL (5.7-11.4 mmol/L) that have persisted in people with lifestyle management and good blood sugar control.

Recommendations for lipid-lowering therapy

Lifestyle modification advice should be given to all persons living with diabetes, with specific advice to:

- Lose weight, where the person is overweight or obese.
- Increase physical activity.
- Reduce the consumption of trans fat, saturated fat, and cholesterol.
- Increase the consumption of dietary n-3 fatty acids, plant sterols/stanols, and viscous fibre.

Where the individual already has atherosclerotic cardiovascular disease, high-intensity statin treatment is required in addition to lifestyle modification for secondary prevention of further cardiovascular events. (See Box 29 for recommended therapy)

BOX 30: RECOMMENDATIONS FOR MANAGING DYSLIPIDEMIAS IN PERSONS WITH DM

Where the individual already has atherosclerotic cardiovascular disease, high-intensity statin treatment is required in addition to lifestyle modification for secondary prevention of further cardiovascular events.

High-intensity statin therapy with either Atorvastatin 40mg-80mg daily or Rosuvastatin 20mg to 40mg daily has been shown to reduce LDL cholesterol by ³ 50%.

(High certainty evidence, weak recommendation)

In patients with atherosclerotic cardiovascular disease in whom the serum LDL cholesterol remains ≥70mg/dL despite high intensity statin therapy (at maximal dosage) and lifestyle modifications, Ezetimibe may be added to the regime following an assessment of the patient's risk, and after careful consideration of the patient's preferences and the side effect profile of the medications.

(High certainty evidence, weak recommendation)

- Where the patient is not known to have atherosclerotic cardiovascular disease, but is ≥ 40 years, moderate-intensity statins should be initiated for primary prevention. There are several statins available within this category, and the choice of statin should depend on what is affordable, available and accessible within the community, and tolerated by the patient.

  A few options are presented in Table 7.

- It is advised that statins are continued lifelong following initiation, provided they are tolerated by the patient.

- Statins are potentially teratogenic and must be avoided in pregnancy.

Table 7: Moderate-intensity statins

Atorvastatin10–20mg od
Rosuvastatin 5–10mg od
Simvastatin 20–40mg od
Pravastatin 40–80mg od
Lovastatin 40mg od

od – once daily dosing

- Combination therapy of statins with fibrates or niacin to improve lipid profiles is not recommended as there is trial evidence to suggest that they carry a higher risk of side effects including an increased risk of rhabdomyolysis and myositis with the fibrate/statin combination, and increased risks of stroke with the statin/niacin combination. Moreover, they do not provide an overall cardiovascular benefit above that attributable to statins alone.

- Where fasting triglyceride levels are ≥ 500mg/dL, the patient should be investigated for secondary causes of hypertriglyceridaemia and advised to avoid alcohol due to the increased risk of acute pancreatitis.

- Improved glycaemic control combined with intense lifestyle measures (as listed above) is recommended for improving the lipid profile of patients with elevated triglyceride and low HDL levels. Where the patient has poor glycaemic control and markedly elevated triglycerides (≥ 500mg/dL), insulin may be considered.

BOX 31: RECOMMENDATIONS FOR MANAGING DM IN HIV+ INDIVIDUALS

Recommendations for blood glucose targets and lifestyle management for managing DM in PLHIV is the same as in HIV- persons.
However due to drug interaction between glucose lowering drugs and anti-retroviral drugs, there are special considerations for treating diabetes in PLHIV.

(Low certainty evidence, strong recommendation)

There are no statins in the 2016 Essential Medicines List. Therefore, choice of statin depends on the cost and efficacy of the drug.

11.3. HIV

Depending on age, lifestyle, environmental and genetic factors, risk for developing NCDs exist among people living with HIV/AIDS (PLWHA).

Some anti-retroviral drugs like protease inhibitors (PIs) increase insulin resistance and use of first-generation ART agents, such as stavudine and indinavir have been found to be strongly associated with developing DM. Efavirenz has also been found to increase glucose levels.[18]

Recommendations for blood glucose targets and lifestyle management for managing DM in PLHIV is the same as in non-HIV persons.

However due to drug interaction between glucose lowering drugs and anti-retroviral drugs, there are special considerations for treating diabetes in PLHIV.

Table 8: Oral diabetes medications with special considerations in HIV

Class	Mechanism	Special Considerations in HIV
Biguanides (Metformin)	Decrease hepatic glucose production. Improve insulin sensitivity.	Dolutegravir increases metformin concentrations.
Sulfonylureas (glibenclamide, glimepiride, glyburide, glicazide, glipizide)	Stimulate insulin release from the pancreatic β cells. Reduce glucose output from the liver. Increase insulin sensitivity.	
Thiazolidinediones (rosiglitazone, pioglitazone)	Lower blood glucose by improving target cell response to insulin.	When used with CYP2C8 inhibitors (many PIs),

Class	Mechanism	Special Considerations in HIV
	Do not increase pancreatic insulin secretion.	rosiglitazone/pioglitazone levels may increase. Monitor carefully.
GLP-1 Analogues (liraglutide, exenatide, exenatide LAR)	Increase glucose-dependent insulin secretion. Decrease inappropriate glucagon secretion. Increase β-cell growth/replication. Slow gastric emptying.	
DPP-IV inhibitors (sitagliptin, saxagliptin, vildagliptin, linagliptin)	Increase insulin synthesis and release from pancreatic β cells. Decrease glucagon secretion from pancreatic α cells. Decreased glucagon secretion results in decreased hepatic glucose production.	Gliptins have molecular targets on immune cells; however, no evidence that gliptin use changes CD4 or HIV RNA. Saxagliptin interacts with strong CYP3A4/5 inhibitors (eg, ritonavir); reduce saxagliptin dose when used with CYP3A4/5 inhibitors.
Gliflozins (dapagliflozin, canagliflozin)	Reduce reabsorption of filtered glucose from the tubular lumen and lower	If UGT enzyme inducers (eg, ritonavir) are co-administered with canagliflozin, consider increasing the dose to 300 mg

Class	Mechanism	Special Considerations in HIV
	the renal threshold for glucose. Increase urinary excretion of glucose.	
Meglitinides	Stimulate insulin release from pancreatic β-cells	When used with CYP3A4/CYP2C8 inhibitors (many PIs), Repaglinide/nateglinide levels may increase. Monitor carefully. EFV and ETR may increase nateglinide

11.4. Considerations about recommendations for managing comorbidities

11.4.1. Implementation considerations

Some of the medications with proven efficacy for treating diabetes comorbidities are not in the Essential Medicines List. Practitioners should be aware of this and advise their patients appropriately. Adverse drug reactions should be monitored closely, reported and medications changed as appropriate. Where facilities for monitoring are not available, patients should be referred to the next level of care.

11.4.2. Harms/benefits of recommendations for managing co-morbidities

ACE inhibitors and ARBs for BP control as well as statins for lipids treatment have substantial benefits in reducing the risk of cardiovascular diseases. Antiretroviral drugs have also been shown not only to improve outcomes in HIV infected patients but also to prolong life. However, the risk of low blood pressure, high potassium levels and impaired kidney function associated with the use of ACE inhibitors or ARBs should be weighed against the benefits. Patients on

statins should be warned of the risk of muscle inflammation and breakdown and those on ARTs of the risk of worsening blood sugar control. The risk of increased incidence of adverse events from drug-drug interactions should be discussed with the patients. All the medications should be avoided in pregnancy.

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12. Managing Diabetes in Children and Adolescents

12.1. Blood glucose targets and monitoring in children

Blood glucose levels should be monitored regularly in children (at least two times a day for those on a twice daily insulin regimen, or a minimum of four times a day for those on multiple daily dose insulin regimen) to ensure optimal blood glucose control in children.

Self-monitoring of blood glucose (SMBG) is an important part of managing and achieving blood glucose control in children and adolescents. The optimal blood glucose targets are:

- Before meals: 4-7 mmol/L (70-126 mg/dL)
- After meals: 5-10 mmol/L (90-180 m/dL)
- At bedtime: 4,4-7.8 mmol/L (80–140 mg/dL)
- At 3am: 5-8 mmol/L (90-144 mg/dL)[1]

12.2. Treatment of diabetes in children

Treatment of diabetes in children entails both lifestyle management and drug treatment. Individualized nutrition management is highly recommended for children and adolescents. Comprehensive nutrition education at the time of diagnosis is important, followed by annual reviews by the dietician or nutritionist.

Lifestyle Management

Diet & Carbohydrate counting

Carbohydrate (CHO) counting is a diet strategy that emphasizes the role of carbohydrates as the primary nutrient that increases blood glucose after meals. It involves flexible meal plans that help in achieving blood glucose control.[2,3]

There are three levels of CHO counting: (Use level 1 only when levels 2 and 3 are not feasible. Flexibility and individualized insulin use are highly recommended).

- **Level 1 - Consistent CHO intake**

This involves consistent carbohydrate intake of pre-specified quantities of food. This is appropriate for those using twice-daily insulin.

- **Level 2 - Pattern management principles**

An intermediate step in which patients maintain a consistent carbohydrate intake, use a consistent baseline insulin dose, and frequently monitor blood glucose level. They learn to recognize patterns of blood glucose response to carbohydrate intake modified by insulin and exercise. With this understanding, and team support, they adjust their insulin dose for food and exercise to achieve blood glucose goals.

- **Level 3 - Insulin to carbohydrate ratios (ICR)**

Appropriate when using basal bolus (multiple daily injections). The ICR (amount of carbohydrates in grams covered by 1 Unit of insulin) is calculated, individualized according to age, sex, pubertal status, duration of diagnosis, and activity. This lets patients adjust their prandial (mealtime) insulin dose according to carbohydrate consumption.

Methods of quantifying carbohydrate include:

- Gram increments of carbohydrate
- 10 – 12 g carbohydrate portions
- 15 g carbohydrate exchanges

The "500-rule" used as a first estimate for ICR at diagnosis, which is then adjusted according to the individual response of the child. Divide 500 by the Total Daily Dose (Total Daily Dose is the sum in units of all insulin injections on a normal day). Fine-tuning of insulin dosage is guided by blood glucose monitoring. Regular review is necessary as children grow and new foods are introduced.

Physical activity

Physical activity is very important for maintaining optimal blood glucose levels in children. It is difficult to make recommendations on the specific intensity and duration of physical activity among children. Efforts to reduce periods of physical inactivity in children are important. A minimum of 60 minutes of moderate to vigorous level of physical activity per day is recommended (and strength training on at least three days/week).[4] Insulin dosages should also be adjusted during periods of moderate to vigorous physical activity due to increased insulin sensitivity during exercise, which could lead to hypoglycaemia.

Children and adolescents who engage in competitive sports require an essential support and education management therapy to prevent dehydration and hypoglycaemia during and after exercise maintaining a pre-exercise blood glucose level of 90–250 mg/dL (5–13 mmol/L) and having access to carbohydrate before exercise.[5]

Blood glucose should be checked frequently before, during and after moderate to vigorous exercise to detecthypoglycaemia or hyperglycaemia.

Insulin treatment

The treatment for type 1 diabetes in children is insulin. Other forms of diabetes may also require the use of insulin.

The aim of using insulin is to attempt to achieve the natural physiological insulin levels after meals and during fasting periods. Having low levels of insulin can lead to high blood sugar levels which heighten the occurrence of complications and affects normal growth and development of the child.

The two most commonly used insulin regimens are:

- Twice-daily insulin using both short-acting and intermediate-acting insulin. (If these forms of insulin are not always available, pre-mixed insulin can be used as an alternative regimen).
- Basal bolus regimen (the preferred option) - with short acting insulin given with main meals (usually three times per day) and intermediate-acting insulin given once or twice daily (evening, or morning and evening)[6] or basal analogue like Determir or Lantus once a day evening or morning.

Pre-mixed insulins limit the opportunities to adjust insulin dosage with varying amount of food and physical activity.

Insulin should be administered using appropriate needles/syringes or pens when available and should be injected subcutaneously on the various available injection sites on the body in a rotation routine.

Education on the pharmacokinetics (onset, peak and duration) of the types of insulin available and used in the country even if not on the essential drug list is important.

Use of glucose-lowering drugs

Apart from insulin, other glucose lowering drugs are usually used in adolescents and young people with T2DM.

Metformin is the first-line drug for treating T2DM in adolescents and young people[7,8] (See Box 16, Chapter 7).

Basal insulin used as first-line if blood glucose level is as high as 13.9mmol/L on diagnosis and there are marked symptoms such as frequent urination (bedwetting), weight loss, frequent thirst and dehydration. Basal insulin can also be used when metformin fails to achieve the targeted blood glucose levels. Glucagon-like Peptide 1 receptor agonist though used by the pediatric age group is not yet recommended in children.

Sick day rules

Parents and caregivers of children with diabetes who are ill are advised as follows:

- Consult the doctor about management of the diabetes and the cause of the illness.
- Insulin should not stop but dosages may have to be adjusted during periods of illness.
- Avoid sugar-laden medications.
- Measure blood glucose more frequently.
- Give fluids more frequently.
- Ensure children have their vaccinations as scheduled to prevent periods of avoidable ill health.

12.3. Management of diabetic emergencies in children

Treating DKA in children and young persons

Some children may not have typical signs and symptoms of DKA, and vigilance needs to be applied to recognize DKA in children; it can resemble other common diseases like severe malaria, pneumonia, gastroenteritis with electrolyte imbalance.

Some children with T1DM may not have been previously diagnosed and may present for the first time in a health facility with DKA. Check the blood glucose of any very ill child or adolescent.

Recognition of DKA in children and young persons

Children with no previous diagnosis of DM

Capillary blood glucose should be measured if a child or young person without a previous diagnosis of DM presents with the following symptoms:

- Increased thirst
- Increased urination
- Recent unexplained weight loss
- Excessive tiredness
- Nausea or vomiting
- Abdominal pain
- Hyperventilation
- Dehydration
- Reduced level of consciousness

If blood glucose levels of more than 11 mmol/L are recorded in a child or young person without known diabetes, and the symptoms and signs mentioned above are present, suspect DKA and refer the child or young person to a health facility with expertise and facilities for emergency care.[8] Start correction of dehydration with oral rehydration therapy (ORT) if the child can tolerate orally and continue with transfer.

Children and young persons with previous diagnosis of DM

Children and young persons with a prior diagnosis of DM who are taking insulin for diabetes may still develop DKA with normal blood glucose levels.

Suspect DKA even if the blood glucose is normal and the child or young person with a known history of diabetes shows any of the following symptoms:

- Nausea or vomiting
- Abdominal pain
- Hyperventilation
- Dehydration
- Reduced level of consciousness

BEST PRACTICE STATEMENT

Measure the blood ketones in a child or young person with known DM that shows any of these symptoms:

- Nausea or vomiting
- Abdominal pain
- Hyperventilation
- Dehydration, or
- Reduced level of consciousness

If the levels are elevated, refer to a health facility with expertise and capacity to manage DKA in a child or young person.

Diagnosis of DKA in children and young persons

When DKA is suspected in a child or young person, measure:

- Capillary blood glucose
- Urine ketones
- Blood pH

If capillary blood sugar is high, there are ketones in the urine and blood pH is lower than 7.0, a definitive diagnosis of DKA is made.

Educate caregivers and family members about the conditions and appropriate care the child or young person will need.

Specialist Care for DKA in children and young persons

After making a diagnosis of DKA, check for:

- Level of consciousness
- Vital signs (heart rate, blood pressure, temperature, respiratory rate [look for Kussmaul breathing])
- Signs of dehydration
- Measure blood electrolytes, urea and creatinine
- Check the temperature and blood pressure to rule out septic shock

- Provide adequate nursing and close monitoring.

If unconscious, review with an anesthetist if available and consider inserting a nasogastric tube to reduce risk of aspiration.

Table 9: Recommendations for managing DKA in children and young persons[9,10]

Child or young person is alert and not vomiting or nauseated and not dehydrated.	Child or young person is not alert or vomiting or nauseated or dehydrated.
Treat DKA with oral fluids first and only after initial bolus correction commence subcutaneous insulin given at frequency of 1-2 hours. Ensure that the child or young person is recovering by monitoring for resolution of ketonaemia and acidosis.	Treat DKA with initial intravenous fluids replacement for an hour. Commence intravenous insulin given as a continuous infusion only after commencing intravenous fluid replacement for dehydration.
Do not give an intravenous fluid bolus to children and young people with mild or moderate DKA (indicated by a blood glucose > 250mg/dL, blood pH of 7.2-7.3 and bicarbonate 15-18). Give oral fluid replacement. Commence intravenous fluid bolus or pass in a nasogastric tube to a child or young person with severe DKA that is in stupors or unconscious (indicated by a blood pH below 7.1). Do not give more than one intravenous fluid bolus of 10 ml/kg 0.9% sodium chloride for 1-2 hours to a child or young person with severe DKA (indicated by a blood glucose > 250mg/dL, blood pH below 7.and bicarbonate < 10mmol/L.) without discussion with a specialist.	
When and how to give insulin	
Start an intravenous insulin infusion only after 1–2 hours of beginning intravenous fluid therapy in children and young people with DKA.	
When treating DKA with intravenous insulin in children and young people, use a soluble insulin infusion at a dosage between 0.05 and 0.1 units/kg/hour. Do not give bolus doses of intravenous insulin. When expertise to give and monitor insulin infusion is not available give subcutaneous soluble insulin every hour at a dosage between 0.05 and 0.1 units/kg/hour and refer or discuss with a specialist.	

- Calculate their total fluid requirement for the first 48 hours by adding the estimated fluid deficit to the fluid maintenance requirement.
- When calculating the fluid requirement for children and young people with DKA, assume:
    - A 5% fluid deficit in mild to moderate DKA (indicated by a blood bicarbonate of 15-18 mmol/L or blood pH of 7.1 or above).
    - A 10% fluid deficit in severe DKA (indicated by a blood bicarbonate of less than 10mmol/L, or blood pH below 7.1).
- Calculate the maintenance fluid requirement for children and young people with DKA using the following 'reduced volume' rules:
    - If they weigh less than 10 kg, give 2 ml/kg/hour.
    - If they weigh between 10 and 40 kg, give 1 ml/kg/hour.
    - If they weigh more than 40 kg, give a fixed volume of 40 ml/hour.
- Aim to replace the fluid deficit evenly over the first 48 hours in children and young people with DKA, because faster rehydration is associated with an increased risk of cerebral oedema.
- Use 0.9% sodium chloride without added glucose for both rehydration and maintenance fluid in children and young people with DKA until the plasma glucose concentration is below 14 mmol/L.
- Ensure that all fluids (except any initial bolus) administered to children and young people with DKA contain 40 mmol/L potassium chloride, unless they have renal failure.
- If more than 20 ml/kg of fluid has been given by intravenous bolus to a child or young person with DKA, subtract any additional bolus volumes from the total fluid calculation for the 48-hour period.
- Do not give intravenous sodium bicarbonate to children and young people with DKA.

- Change fluids to 0.9% sodium chloride with 5% glucose and 40 mmol/L potassium chloride once the plasma glucose concentration falls below 14 mmol/L in children and young people with DKA.
- If during treatment for DKA a child or young person's plasma glucose falls below 6 mmol/L, increase the glucose concentration of the intravenous fluid infusion, and if there is persisting ketosis, continue to give insulin at a dosage of least 0.05 units/kg/hour.
- If the blood ketone level is not falling within 6–8 hours in a child or young person with DKA, think about increasing the insulin dosage to 0.1 units/kg/hour or greater.
- Think about stopping intravenous fluid therapy for DKA in a child or young person if ketosis is resolving, they are alert, and they can take oral fluids without nausea or vomiting.
- Do not change from intravenous insulin to subcutaneous insulin in a child or young person with DKA until ketosis is resolving, they are alert, and they can take oral fluids without nausea or vomiting.
- Start subcutaneous insulin in a child or young person with DKA at least 30 minutes before stopping intravenous insulin.

Monitoring

Monitor and record the following at least hourly in children and young people with DKA:

- Capillary blood glucose.
- Vital signs (heart rate, blood pressure, temperature, respiratory rate [look for Kussmaul breathing]).
- Fluid balance, with fluid input and output charts.
- Level of consciousness (using the modified Glasgow coma scale).
- Monitor and record the level of consciousness (using the modified Glasgow coma scale) and the heart rate (to detect bradycardia) every 30 minutes.

At two hours after starting treatment, and then at least every four hours, carry out and record the results of the following blood tests in children and young people with DKA:

- Glucose (laboratory measurement)
- Blood pH and pCO2
- Plasma sodium, potassium, bicarbonate and urea
- Blood or urine ketones

A doctor involved in the care of the child or young person with DKA should review them face-to-face at diagnosis and then at least every two hours, and more frequently if:

- They are aged under two years.
- They have severe DKA (indicated by a bicarbonate less than 10mmol/L or blood pH below 7.1).
- There are any other reasons for special concern.

At each face-to-face review of children and young people with DKA, assess the following:

- Clinical status, including vital signs and neurological status
- Results of blood investigations
- Cumulative fluid balance record

Provide update on progress to the caregivers and family members of the child or young person.

Watch out for complications like cerebral oedema and very low potassium.

Cerebral oedema

Immediately assess children and young people with DKA for suspected cerebral oedema if they have any of these early manifestations:

- Headache
- Agitation or irritability

- Unexpected fall in heart rate
- Increased blood pressure

If cerebral oedema is suspected in a child or young person with DKA, treat immediately with the most readily available form of mannitol (20%, 0.5–1 g/kg over 10–15 minutes) or hypertonic sodium chloride (2.7% or 3%, 2.5–5 ml/kg over 10–15 minutes).

Immediately treat for cerebral oedema using the most readily available form of mannitol (20%, 0.5–1g/kg over 10–15 minutes) or hypertonic sodium chloride (2.7% or 3%, 2.5–5 ml/kg over 10–15 minutes) if a child or young person with DKA develops any of these signs:

- Deterioration in level of consciousness
- Abnormalities of breathing pattern, for example respiratory pauses
- Oculomotor palsies
- Pupillary inequality or dilatation

After starting treatment for cerebral oedema with mannitol or hypertonic sodium chloride in a child or young person with DKA, immediately seek specialist advice on further management, including which care setting would be best.

Low potassium levels

If a child or young person with DKA develops hypokalaemia (potassium below 3 mmol/L):

- Think about suspending the insulin infusion.
- Discuss hypokalaemia management urgently with a paediatric critical care specialist.
- Refer to a higher center of care.

Avoiding future episodes of DKA in children and young persons

Provide education to caregivers and family members of children and young persons on how to avoid DKA in future by adhering to treatment recommendations.

Treatment of hypoglycaemia

Mild hypoglycaemia occurs when the patient can recognise hypoglycaemia and is able to self-treat without assistance of others. Blood glucose level is ≤ 3.9 mmol/L or ≤ 70mg/dL.

Severe hypoglycaemia is when the patient either loses consciousness or has a seizure associated with low blood glucose or is unable to help him/herself.[11,12,13,14,15]

Managing mild or moderate hypoglycaemia

STEP 1

- Give fast acting glucose immediately. Examples are:
  - Half cup/glass of a sweet drink
  - 2 cubes of sugar or 3-4 teaspoons of sugar or honey
  - 6 large or 12 small jellybeans if available

BOX 32: RECOMMENDATIONS FOR MANAGING HYPOGLYCAEMIA IN CHILDREN

Mild hypoglycaemia can be managed at home or primary care using fast acting sugar drinks and foods.

Severe hypoglycaemia requires specialist care with glucose drip and close monitoring.

STEP 2

If hypoglycaemia is caused by a missed meal or snack (but insulin has been taken as usual), follow with a meal or snack including an appropriate amount of carbohydrates. Where blood glucose testing equipment is available, re-test blood glucose 10-15 minutes after treatment, to confirm the blood glucose level is within normal limits (> 100 mg/dL, 5.6 mmol/L).

If the blood glucose level remains low or symptoms persist, repeat Step 1.

Managing severe hypoglycaemia with loss of consciousness or convulsions

Give intravenous glucose carefully and slowly over several minutes, using 10% or 25% glucose/dextrose solution (or 50% if these are unavailable).

Total dose over several minutes is 0.2-0.5 gm/kg of glucose/dextrose (2-5 ml/ kg of 10% glucose, 1-1.5 ml/kg of 25-30% glucose).

12.4. Transitioning to adulthood

Most young people are lost to follow as they transition from childhood to adolescence and then adulthood. Adequate psychosocial care and support should be put in place to guide the caregivers and family members of children and adolescents with diabetes on this transition period to ensure retention in care and optimal treatment outcomes.

12.5. Considerations about recommendations for managing diabetes in children and adolescents

12.5.1. Implementation considerations

Management of diabetes and especially diabetes complications in children and adolescents should be individualized and done by specialists leading a multidisciplinary team. However, primary care providers should recognise the symptoms and signs (which may be similar to common childhood acute conditions), give appropriate initial care and refer timeously to a centre with paediatric endocrinologists or paediatrician. While the care of children is undertaken by parents, adolescents should be involved in their care early enough for optimal outcomes. The overall focus should be on meeting treatment goals, prevention of acute complications, reduction of diabetes related organ specific complications, participation in

normal age-appropriate activities and ensuring normal physical and psychological development for age.

12.5.2. Harms/benefits of recommendations for managing diabetes in children

The risk of catastrophichypoglycaemia especially with insulin use is very high in children. The benefits of goal directed therapy linked to optimal blood glucose control and prevention of diabetes related complications warrants the use of glucose lowering agents. These should all be communicated to parents and children.

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13. Managing Diabetes in Pregnancy

13.1. Preconception counselling

Diabetes in pregnancy poses a risk to both the mother and the child in the womb if blood glucose levels are high for a long period of time.[1,2]

High blood sugar levels within the first 10 weeks of conception are associated with fetal abnormalities.[3,4]

High blood sugar during pregnancy is also associated with onset of diabetic retinopathy or rapid progression of existing diabetic retinopathy.[6]

BOX 33: RECOMMENDATIONS FOR PRE-CONCEPTION COUNSELLING[5]

Pre-conception counseling should be integrated into routine diabetes care for all women of childbearing age.

Family planning should be discussed and offered to women who do not intend to get pregnant.

(Moderate certainty evidence, strong recommendation)

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All women of childbearing age with diabetes should be counseled about the importance of tight glycemic control prior to conception, the risk of fetal abnormalities in unplanned pregnancies and use of effective contraception to avoid unplanned pregnancies.[5,7]

Women with diabetes who wish to become pregnant should monitor their blood glucose regularly and make adequate lifestyle changes and adjustments in drug regimens to achieve the adequate blood glucose targets prior to pregnancy.[8]

13.2. Blood glucose targets in pregnancy

Blood glucose targets in pregnancy are lower and tighter than that in non-pregnancy. This is required to balance the effects of increased uptake of glucose by the fetus and insulin resistance caused by placental hormones.[9,10]

Fasting blood sugar target in pregnancy is 5.3 mmol/L (95 mg/dL)

Women with T1DM usually have insulin sensitivity during the first trimester and insulin resistance during the second and third trimesters making it imperative to adjust insulin dosages as pregnancy progresses.[8,11]

Pregnancy also increases the risk of DKA in women with DM because pregnancy is a ketogenic state.

Lifestyle changes and strict adherence to recommended drugs are important to maintain blood sugar targets within tight optimal limits.[8]

The targeted blood glucose levels for both GDM and pregnant women with pre-existing DM are:

- Fasting blood sugar of 5.3 mmol/L (95 mg/dL)
- One-hour postprandial of 7.8mmol/L (140 mg/dL)
- Two-hour postprandial 6.7 mmol/L (120 mg/dL)

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13.3. Management of diabetes in pregnancy

Treatment of gestational diabetes mellitus

Lifestyle management is essential for managing GDM and may be sufficient in reversing blood glucose level to normal thresholds.[8,12]

Insulin is the preferred drug for gestational diabetes mellitus as it does not cross the placenta.

Metformin and glyburide may be used but they both cross the placenta. Glyburide is associated with neonatal hypoglycaemia and macrosomia while metformin is safer in this regard but has been shown to slightly increase the risk of prematurity.[13,14,15]

BOX 34: RECOMMENDATIONS FOR MANAGING GESTATIONAL DIABETES MELLITUS[16]

Lifestyle management is the first line for pregnant women with fasting glucose levels of 5.3mMol/L and below.

(High certainty evidence, strong recommendation)

If lifestyle management fails, then insulin or metformin should be commenced~~nsidered~~.

(High certainty evidence, strong recommendation)

Insulin is first line for fasting glucose levels above 5.3mmol/l

Specialist care is needed to use insulin

(High Certainty Evidence, ??? Recommendation

Treatment of pre-existing diabetes

T1DM

It is important to adjust insulin doses to match the rapidly changing requirements during pregnancy. Frequent blood glucose monitoring is important to recognize when the need for insulin changes.[8]

Daily insulin needs might reduce during the first trimester due to insulin sensitivity and increase in episodes of low blood sugar levels.

Biweekly or weekly increase in insulin dose because of the rapidly increasing insulin resistance is recommended. The recommended regimen is a smaller proportion of daily doses as basal insulin (<50%) and a greater proportion as bolus insulin (>50%).

BOX 35: RECOMMENDATIONS FOR MANAGEMENT OF PREGNANT WOMEN WITH PRE-EXISTING DIABETES MELLITUS[17]

Insulin is the drug of choice for managing both T1DM & T2DM.
Adjust insulin dosages to respond to the changing insulin demands throughout the course of the pregnancy in T1DM.
This adjustments in insulin doses require specialist care.
(Evidence not graded)

Low dose aspirin 60–150 mg/day (usual dose 81 mg/day) should be given from the end of the first trimester up to 34 weeks to reduce the risk of pre-eclampsia.

(High certainty evidence, strong recommendation)

Calcium blockers or alpha-methyl dopa should be used to control blood pressure in women with DM who also have chronic hypertension.

(High certainty evidence, strong recommendation)

The insulin demands at third trimester may reduce and insulin doses will need to be changed accordingly.

T2DM

Oral glucose lowering drugs are not enough to achieve blood glucose targets because of the marked insulin resistance in pregnancy.[8]

Insulin is required for T2DM during pregnancy.

T2DM is also more likely to be associated with other comorbidities during pregnancy.

13.4. Managing or preventing comorbidities during pregnancy

Women with T2DM are more likely to gain weight during pregnancy. Women who are overweight or obese should ensure that they keep weight gain during pregnancy within 6 - 10kg.[18] This can be achieved through lifestyle management and metformin.

Women with DM also have an increased risk for pre-eclampsia.[19] This risk can be minimized by using low dose aspirin (81mg) immediately after the first trimester until 34 weeks.[17] It is discontinued before the baby is born to avoid coagulopathies, clotting disorders, and excessive bleeding.

Women with both DM and pre-existing hypertension should maintain blood pressure within 120/80mmHg and 160/105mmHg to prevent impaired fetal growth and reduce adverse cardiovascular events in the mother.[20,21] Drugs that are linked to fetal abnormalities such as ACE inhibitors and ARBs should not be used prior to pregnancy, during pregnancy or breastfeeding. Calcium channel blockers and centrally acting anti-hypertensives (like alpha-methyl dopa) are safe for use during pregnancy and breastfeeding.

13.5. Management of diabetes after delivery

Women with diabetes should be encouraged and supported to breastfeed exclusively for six months due to the immediate and long-term nutritional and metabolic benefits breastfeeding confers on both the mother and the baby.[22,23]

As soon as the baby and placenta are delivered, insulin resistance reverses to insulin sensitivity and then normal insulin regulation returns gradually within one-two weeks.[8] This makes it important to establish meal planning and drug regimens that can help to prevent hypoglycaemia during breastfeeding and sleep deprivation.

13.6. Considerations about recommendations for managing diabetes in pregnancy

13.6.1. Implementation considerations for managing diabetes in pregnancy

Pre-pregnancy counseling should be undertaken for all ~~established diabetic~~ women of child-bearing age and especially for women with diabetes. Diabetes in pregnancy should be managed by a multi-professional team that includes an endocrinologist, maternal-foetal medicine specialist, dietitian, and diabetes educator where these are all available. Self-monitoring of

blood glucose should be encouraged for glycemic control. Insulin is the preferred glucose lowering agent-it is in the EML and covered by the NHIS.

13.6.2. Harms/benefits of recommendations for managing diabetes in pregnancy

The risk of hypoglycaemia in pregnancy is high with insulin use. However, as other agents are not licensed for now, insulin is the only choice. It has significant benefits leading to optimal maternal and foetal outcomes.

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Advocacy

One of the objectives of this guideline is to ensure that diabetes care is rendered to everyone based on recommended standards of care that are evidence-based. Advocacy is essential in many areas in achieving this including:

- Persons with diabetes should not suffer any form of discrimination whether at work, school or within social groups. Communicating the provisions of this guideline with diabetes care related organizations, schools, policy makers, lawmakers, labour organizations, the prisons and remand homes is essential.
- Diabetes medications should be available, affordable and accessible. In this regard, the EML's update should include medications not currently listed.
- Engagement of the NHIS to ensure coverage of diabetes care especially in relation to diabetes-related organ complications.
- Different cadres of health workers in the health system need to be engaged constructively to ensure a buy-in into the task shifting and sharing policy as it affects diabetes care at the different levels.

Monitoring and evaluation

The monitoring and evaluation plan for this guideline (see appendix) is linked to key outcome measures expected to be driven by its full implementation. The key indicators have been disaggregated for gender, age, facility type and location and specific responsible agencies named.

Planning for update

It is expected that as new evidence emerges, this guideline will be updated. However, it is recommended that the current guideline be updated annually or as often as necessary. In this regard, updates of the EML will warrant an update of recommendations herein.

Implications for practice

- Task-shifting of diabetes prevention and community awareness to lay community health workers.

- Task-shifting of diabetes education to nurses and CHEWs/JCHEWs who have been trained on diabetes education.
- Task-shifting necessitates the need to update the curriculum for pre-service and in-service training for nurses, CHEWs and JCHEWs.
- Diagnosis of DM in primary care health facilities using glucometers and risk assessment tools.
- Management of uncomplicated diabetes at primary health care level.
- Management of hypoglycaemia in persons who are alert at primary care level.
- Active prevention of DKA and HHS at primary care level.

Implications for update of 2016 Essential Medicines List

- Need to include additional glucose lowering drugs with proven effectiveness in reducing cardiovascular risk factors.
- Need to include ACEIs ARBs because of their renal protectiveness.
- Need to include statins for reducing cardiovascular risk factors.

Implications for future research

- Understanding of the pathway for β-cell destruction in T1DM or dysfunction in T2DM among Nigerians.
- The effectiveness of structured diet and physical activity programs in preventing onset of T2DM or GDM among individuals with high risk.
- Determining the feasibility and effectiveness of different modes of delivering structured diabetes education in the Nigerian health system.

Quality standards

This guideline is essentially an adaptation of the ADA and NICE guidelines for diabetes care. The ADAPTE framework for adapting clinical practice guidelines has been followed and has informed the entire methodology. In this regard, the scope has been carefully defined in line with the task shifting and sharing policy of the country, extensive stakeholder consultation has

been done (has included patient groups, policy makers, academics, specialists etc.), recommendations have been graded and presented in clear and readable format, and where necessary, the implications of implementing the recommendations have been highlighted taking into consideration resource constraints etc. The benefits and harms of all considered/recommended interventions have been highlighted.

Appendices

PIPOH checklist

1. Patient population (including disease characteristics)					Final decision
1.1. Type of diabetes mellitus	**Include**	**Exclude**	**Did not vote**	**Details/Rationale**	
Type 1 Diabetes mellitus	6	2	0	**Reasons for exclusion** Type 1 is more of a genetic etiology and has different management and treatment options. Since resources are limited, it may not be feasible to develop separate guidelines for each type of DM.	Include but have dedicated recommendations for Type 1 DM
Type 2 Diabetes mellitus	8	0	0	Evidence shows that Type 2DM is the most prevalent form of DM globally and even in Nigeria.	Include
Gestational Diabetes	8	0	0	There is presently no quality standard to screen and identify GDM among pregnant women in Nigeria.	Include
Pre-diabetes/Impaired glucose tolerance	8	0	0	Screening to identify pre-diabetes/impaired glucose tolerance is important for prevention.	Include
Other types of diabetes mellitus	0	8	0	There is a paucity of data to understand the burden and aetiology of other types of DM in Nigeria.	Exclude other types of DM
1.2. Complication of diabetes mellitus					
Diabetes eye disease	8	0	0		

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Diabetic nephropathy	8	0	0	Each of the complications need specialized care and the specialist in these areas may have different guidelines for their practice in managing each of these complications.	Include but recommendations should be limited to early identification and prevention of complications and referrals.
Diabetic neuropathy	8	0	0		
Diabetic foot disease	8	0	0		
1.3. Management of emergencies in DM				These are the most common causes of DM related mortality and the recommendations should be lifesaving. The following questions were raised: Is there availability of equipment and other facilities to manage the complications at primary health care? At what point can these emergencies be managed at primary health level before they are referred?	Include but emphasize recommendations for life-saving measures that can be taken at primary care level including home management.
Diabetic ketoacidosis (DKA)	8	0	0		
Hyperosmolar Hyperglycaemic state (HHS)	8	0	0		
Normo-osmolar Non-ketotic Hyperglycaemic state (NNHS)	8	0	0		
Lactic acidosis	8	0	0		
Hypoglycaemia	8	0	0		
1.4. Management of other comorbidities in DM patients					
Hypertension	8	0	0	DM is a risk factor for adverse cardiovascular event on its own. It is important to include other cardiovascular risk factors that may further put a person living with diabetes at risk of cardiovascular events (such	Include but limit recommendations to identification and management of other
Cardiovascular diseases (M1/Strokes)	8	0	0		

Dyslipidemia	8	0	0	as myocardial infarction and stroke dyslipidemia) that increase cardiovascular risk factors will be included.	cardiovascular risk factors using cardiovascular risk assessment tools. Also include management of common morbidities like hypertension and dyslipidemia.
Obesity	1	7	0	It is more of a risk factor and should not be treated as a disease on its own in our settings. It will be included in preventive section.	Exclude
Other comorbidities like HIV, TB, Sickle cell	4	3	1	There may be possible drug interactions in managing these co-morbidities in a diabetic person.	Include only HIV & TB
1.5. Sex					
Male	7	0	1	The guideline will focus on both sexes and if there are any sex differences in the recommendations from existing guidelines, this will be noted when adapting recommendations.	Include both male and female
Female	7	0	1		
1.6. Age					
0-9 years (children)	7	0	1	Type 1 DM treatment and management for children should be considered here. Prevention is a serious global health consideration for childhood obesity.	Include

				Primary prevention for T2DM is important for this age group in the general population.	
10- 24 years (Adolescents and young people)	7	0	1	Prevention & treatment of both type 1 & 2 DM is relevant to these age groups.	Include
25 – 64 years (Adults)	7	0	1		
65 + (Elderly)	0	7	1		Exclude care and treatment for elderly
Diabetes in Pregnancy	7	0	1	Managing diabetes in pregnancy is challenging and there is need for recommendations to manage it.	Include
1.7. Cultural and religious context					
Fasting for Christians and Muslims	0	7	1	Cultural and religious considerations are numerous and may be beyond the scope of this guideline.	Exclude
Others					
2. Interventions					
2.1. Prevention					
Individual preventive measures	7	0	1	Frame recommendations for in a way that it emphasizes the distinction between policy recommendations for prevention and individual counselling recommendations	
Community preventive measures	7	0	1		
Environmental preventive measures	7	0	1		
Health promotion at policy level	7	0	1	Policy recommendations are being considered in the multi-sectoral strategy for NCD prevention.	

2.2. Screening					
Risk assessment tool	7	0	1	Due to resource constraints, questionnaire-based screening tools will be prioritized over use of capillary blood and glucometer.	Include
Random Capillary blood sugar test	7	0	1		Exclude as a screening method but include as a diagnostic method in resource constrained settings.
2.3. Diagnosis					
HbA1C	7	0	1	All these methods will be considered in the guideline but priority will be given to random blood sugar as a diagnostic test in resource constrained settings.	Include all but emphasize random blood sugar
Fasting Blood Sugar	7	0	1		
Random Blood Sugar	7	0	1		
OGTT	7	0	1		
2.4. Treatment					
Diabetic education	7	0	1	Diabetes education is now an integral part of diabetes care and treatment and should be considered in this guideline. Diabetes education via nurses has been piloted at the University of Abuja Teaching hospital.	Include
Lifestyle changes (weight loss, physical activity and diet)	7	0	1	Lifestyle change is important for care and treatment.	Include
Pharmacological treatment (drugs/insulin)	7	0	1	Need to ensure that current recommendations for treatment are captured.	Include

Targets for glucose control and monitoring	7	0	1	This needs a dedicated chapter to ensure that the blood sugar control targets for each type of diabetes are adequately considered.	Incude
3. Professionals/Patients: Targeted users					
3.1. Health workers					
Doctors (specialists)	0	7	1	Each specialty should have dedicated guidelines	Exclude
Doctors (General)	7	0	1	Make a clear distinction on what each of these cadres will do (roles and responsibility) in terms of diabetes care and treatment. Simple and plain language should be used throughout the document.	Include
Nurses	7	0	1		
Community Health Extension workers	7	0	1		
Lay health workers (Community Resource Persons)	7	0	1		
3.2. Stakeholders					
Federal Ministry of Health	7	0	1		Consider policy implications such as National Council on Health meeting for stepping down guideline to the states
State Ministry of Health	7	0	1		
Public health practitioners	7	0	1		
Implementing partners	7	0	1		
3.3. End-users					
Patients	7	0	1		Include

Caregivers	7	0	1	Recommendations are targeted at care and treatment of patients and support for self-care by caregivers.	
4. Outcome- purpose of guideline For selecting evidence recommendations For measuring implementation					
4.1. Patient outcomes					
Prevent onset of DM in high risk individuals	7	0	1	Recommendations for prevention will be aimed at preventing onset of DM among high risk individuals. Only evidence-informed interventions that are effective in producing this outcome will be recommended.	Include
Achieving blood glucose target	7	0	1	Interventions that are effective for achieving blood glucose targets will be recommended.	Include
Improving survival	7	0	1	Intervention that are effective for improving survival will also be recommended.	Include
Quality of life	7	0	1	Interventions that also improve quality of life will be recommended.	Include
Treatment adherence	6	1	1	Adherence should be considered in terms of regimens (first line). Adherence should be emphasized in counselling and diabetic education.	Include
4.2. Health system outcomes					

Cost of care	7	0	1	The cost of the interventions will be considered to ensure that recommendations will be affordable, available, feasible and accessible. Equity should also be considered. Refer to the essential medicines list.	Include
Improvement in quality of care (appropriateness, optimized use, access, efficiency, safety, continuity, timeliness)	7	0	1	The overall aim of guideline recommendation is to improve quality of care, optimize efficient use of available resources for care, improve coverage and access at primary care level and avoid loss to follow up as clients go through the cascade of care and treatment.	Include
Task-shifting/task-sharing	7	0	1	The National task-shifting policy does not include NCDs. This guideline considers involvement of lay community health workers in diabetes prevention and community support for self-care.	Include
Uniformity in practice	7	0	1	The guideline aims to achieve uniform quality standards for diabetes care and treatment across all levels of care and health facilities in the country. Need to develop quality standards and job aids from the guideline.	Include
4.3. Public health outcomes					
Morbidity	7	0	1	Need to measure the burden of diabetes mellitus using population-based surveys.	Include in M & E section
Mortality	7	0	1		
Incidence	7	0	1		

Prevalence	7	0	1	The global burden of disease that is currently used to determine the burden and risk factors for NCDs is heavily modelled.	
5. Healthcare setting					
5.1. Health facility					
Primary health care	8	0	0	Based on the current strategic direction for NCD care and management championed by WHO-PEN, there is need to prioritize and address quality gaps at the primary care level. Primary health care is aimed at reaching people in their communities and is usually the primary entry into the Nigerian Health System.	Include
Secondary health care	4	4	0	Secondary health facilities are useful for managing complications	
Tertiary health care	0	8	0	Management of complications require specialized care which in turn have their own specialized guidelines The Nigerian tertiary health care level is highly specialized and each specialty have their own practice guidelines.	Exclude
5.2. Within health facility					
In-patient	8	0	0	Interventions that can be provided at in-patient or out-patient or even intensive care will be included and clearly stated.	Include all
Out-patient	8	0	0		
Intensive	8	0	0		

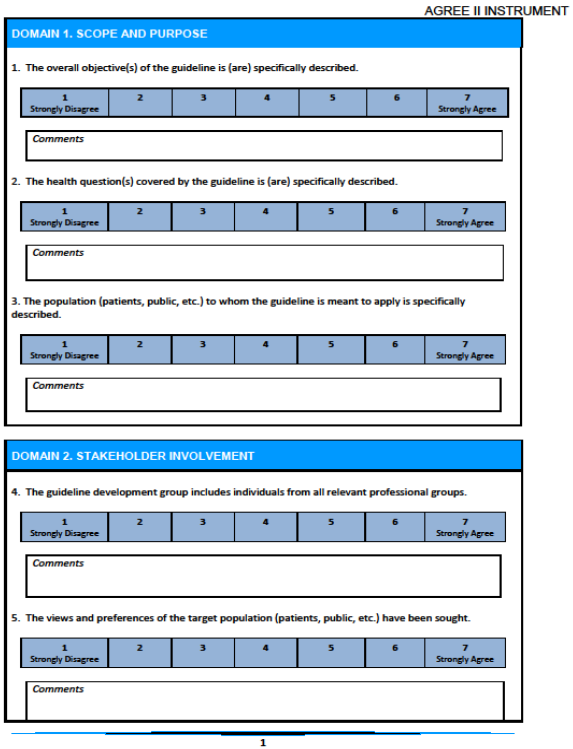
				We envisage that emergencies like DKA & HHS will require intensive and in-patient care.	
5.3. Community					
Home care	8	0		Home care is important for prevention and self-monitoring.	Include
Rehabilitative facility (hospice, aged)	0	8		There is paucity of information on the utilization rate of rehabilitative facilities in Nigeria.	Exclude
5.4. Context					
National context	7	0	1	There may be state-specific contexts that may affect guideline implementation. However, they cannot all be considered at this stage of development. During state-level step-down activities, they will be considered.	Include
State- specific context	0	7	1		Exclude
Local context (tribal, religion etc)	0	7	1		Exclude

Guideline search and retrieval

Database searched	**Filters used**	**Search yield**	**Relevant to DM**	**Included for appraisal**
National Guideline Clearinghouse	Date limit: 2015 to 2018	133	17 guidelines	10

NICE	Date limit: last 3 years (2015-2018) Document type: Guidance Guidance category: Clinical guideline, NICE guideline, public health guideline, quality standards	90	6 guidelines 3 quality standards	6
IDF	No filters applied during electronic search But manual screening was done to apply date limit from 2015 to 2018 and to make clear distinction between job-aids and practice guidelines	20	4 guidelines	4
WDF	No filters were applied during electronic search But manual screening was done to apply date limit from 2015 to 2018 and to make clear distinction between job-aids and practice guidelines	36	7 guidelines	0
ADA	No filters applied	1	1 guideline	1

Guideline assessment checklist



AGREE II INSTRUMENT

DOMAIN 1. SCOPE AND PURPOSE

1. The overall objective(s) of the guideline is (are) specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

2. The health question(s) covered by the guideline is (are) specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 2. STAKEHOLDER INVOLVEMENT

4. The guideline development group includes individuals from all relevant professional groups.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

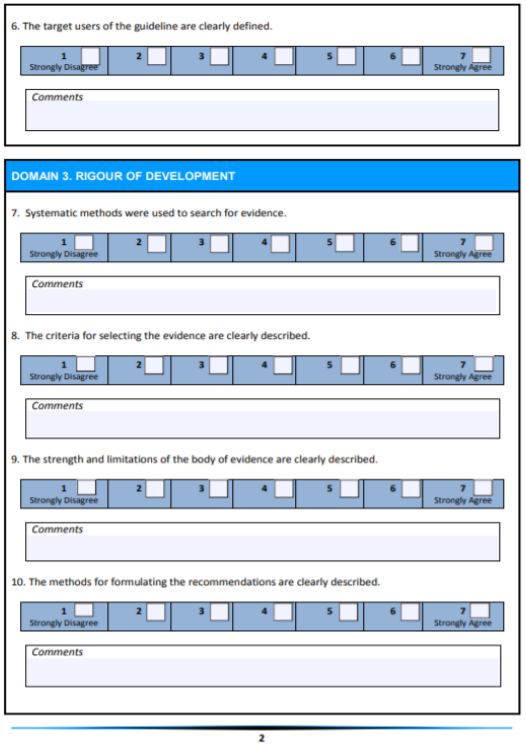
Comments

5. The views and preferences of the target population (patients, public, etc.) have been sought.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

1



6. The target users of the guideline are clearly defined.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 3. RIGOUR OF DEVELOPMENT

7. Systematic methods were used to search for evidence.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

8. The criteria for selecting the evidence are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

9. The strength and limitations of the body of evidence are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

10. The methods for formulating the recommendations are clearly described.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

2

11. The health benefits, side effects, and risks have been considered in formulating the recommendations.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

12. There is an explicit link between the recommendations and the supporting evidence.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

13. The guideline has been externally reviewed by experts prior to its publication.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

14. A procedure for updating the guideline is provided.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 4. CLARITY OF PRESENTATION

15. The recommendations are specific and unambiguous.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

16. The different options for management of the condition or health issue are clearly presented.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

17. Key recommendations are easily identifiable.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 5. APPLICABILITY

18. The guideline describes facilitators and barriers to its application.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

19. The guideline provides advice and/or tools on how the recommendations can be put into practice.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

20. The potential resource implications of applying the recommendations have been considered.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

21. The guideline presents monitoring and/or auditing criteria.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

DOMAIN 6. EDITORIAL INDEPENDENCE

22. The views of the funding body have not influenced the content of the guideline.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

23. Competing interests of guideline development group members have been recorded and addressed.

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Comments

OVERALL GUIDELINE ASSESSMENT

For each question, please choose the response which best characterizes the guideline assessed:

1. Rate the overall quality of this guideline.

1 Lowest possible quality	2	3	4	5	6	7 Highest possible quality

2. I would recommend this guideline for use.

YES	
YES, With modifications	
NO	

NOTES

Guideline appraisal inter-rater spreadsheet and scoring sheet

		Guidelines																	
AGREE II Checklist		Combined diet and physical activity promotion programs for prevention of diabetes Community Preventive Services Task Force recommendation		IWGDF guidance on the prevention of foot ulcers in at-risk patients with diabetes		Gestational diabetes mellitus evidence-based nutrition practice guideline		Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes		Final recommendation statement healthful diet and physical activity for cardiovascular disease prevention in adults without known risk factor		Healthy lifestyles		Hypertension evidence-based nutrition practice guideline		IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care Recommendations		IDF-Diabetes_Eye_Health	
Section	Item	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1
Scope and Purpose	1	7	7	7	7	7	7	6	6	7	7	7	7	7	7	7	7	6	7
Scope and Purpose	2	7	6	6	6	2	5	1	5	1	4	7	5	4	5	7	7	1	7
Scope and Purpose	3	7	5	5	5	7	7	5	5	7	7	7	7	7	6	6	7	7	7
Stakeholder Involvement	4	5	6	7	5	6	5	4	7	7	7	7	5	7	6	5	5	1	5
Stakeholder Involvement	5	3	6	6	4	7	3	4	3	7	3	7	3	7	4	4	4	1	5
Stakeholder Involvement	6	7	6	6	6	7	5	6	6	7	6	7	6	7	7	7	7	7	7
Rigour of Development	7	7	7	5	6	7	6	7	7	7	7	7	6	7	7	4	4	1	4
Rigour of Development	8	7	6	5	6	7	6	7	5	7	6	7	6	7	7	4	4	1	4
Rigour of Development	9	7	5	5	4	5	4	6	3	7	4	7	6	7	4	4	3	1	4
Rigour of Development	10	7	4	7	6	6	6	6	7	7	7	7	6	7	6	6	6	1	4
Rigour of Development	11	7	4	7	6	7	6	6	7	7	6	7	5	7	6	6	7	4	7
Rigour of Development	12	7	7	7	6	7	6	7	6	7	6	7	6	7	5	5	4	1	4
Rigour of Development	13	7	6	3	2	7	6	7	7	7	4	7	7	7	6	7	5	1	4
Rigour of Development	14	7	4	3	3	7	3	1	3	2	5	3	3	7	4	6	3	1	4
Clarity of Presentation	15	7	6	5	6	7	6	6	6	7	7	7	6	7	6	7	7	5	7
Clarity of Presentation	16	7	4	6	3	7	4	6	5	7	3	7	4	7	3	7	7	5	7
Clarity of Presentation	17	7	7	6	6	7	6	7	6	7	7	7	6	7	7	7	7	4	7
Applicability	18	7	6	5	3	7	3	2	3	5	3	7	3	7	3	6	4	3	5
Applicability	19	7	5	4	3	7	7	6	6	6	6	7	7	7	7	6	7	4	7
Applicability	20	6	6	3	1	4	4	4	6	5	3	7	3	7	7	6	4	2	6
Applicability	21	4	3	5	2	2	3	1	3	3	3	3	4	3	3	4	5	1	4
Editorial Independence	22	7	6	7	6	7	6	2	6	7	6	3	6	7	6	5	4	4	4
Editorial Independence	23	7	7	7	5	7	7	4	7	7	7	7	7	7	6	5	5	3	1
Overall Assessment	OA1	7	6	4	5	6	6	5	5	7	6	6	6	6	6	6	6	3	6
Overall Assessment	OA2	Yes	Yes with modifications	Yes with modifications	Yes with modifications	Yes	Yes with modifications	Yes	Yes	Yes	Yes with modifications	Yes	Yes with modifications	Yes	Yes	Yes	Yes	No	Yes

		Guideline															
AGREE II Checklist		IDF-GDM-model-of-care-2015		IDF-Pocketbook-2nd-edition-low-resource-Mgt of DM in adolescents and children		NICE guidelines		Diabetes type 1 and type 2 evidence-based nutrition practice guideline.		Oral pharmacologic treatment of type 2 diabetes mellitus a clinical		Screening for DM		Standards of care for Diabetes Mellitus		VADoD clinical practice guideline for the management of type 2 diabetes mellitus in primary care	
Section	Item	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1	Appraiser 2	Appraiser 1
Scope and Purpose	1	6	7	5	7	6	6	7	7	7	6	7	6	7	7	6	6
Scope and Purpose	2	1	6	2	7	4	6	5	6	5	5	5	6	7	6	2	5
Scope and Purpose	3	6	6	7	7	7	7	7	6	6	5	7	7	7	6	7	7
Stakeholder Involvement	4	1	5	2	6	5	7	7	6	6	4	7	5	7	6	5	7
Stakeholder Involvement	5	1	5	2	2	5		7	5	7	2	7	5	7	3	5	6
Stakeholder Involvement	6	4	4	2	7	7		7	4	7	6	6	6	7	7	7	6
Rigour of Development	7	1	2	1	4	7		7	7	7	7	7	6	7	7	7	7
Rigour of Development	8	1	2	1	4	7		7	7	7	6	7	6	7	6	7	6
Rigour of Development	9	1	1	1	4	7		7	5	5	5	7	4	7	6	6	5
Rigour of Development	10	1	3	1	5	7		7	6	7	6	7	6	7	7	7	6
Rigour of Development	11	3	4	1	5	6		7	6	7	6	6	6	7	6	7	7
Rigour of Development	12	3	3	1	4	7		7	7	7	6	7	5	7	7	7	6
Rigour of Development	13	1	2	1	7	7		7	7	7	5	7	7	7	5	7	6
Rigour of Development	14	1	2	1	6	7		7	3	3	3	7	3	7	7	3	3
Clarity of Presentation	15	6	7	1	7	4		7	6	6	3	7	6	7	6	6	6
Clarity of Presentation	16	6	7	6	7	7		7	3	7	3	7	4	7	7	6	3
Clarity of Presentation	17	6	7	6	7	5		7	7	5	7	7	6	7	7	7	6
Applicability	18	4	5	5	4	5		7	4	5	3	6	3	7	4	7	3
Applicability	19	5	6	6	6	7		7	6	3	1	7	6	7	5	5	4
Applicability	20	2	4	4	4	6		5	1	5	3	4	1	7	6	3	3
Applicability	21	1	5	1	4	6		4	1	2	3	2	3	7	6	2	2
Editorial Independence	22	1	2	4	1	7		7	7	5	3	6	3	7	6	6	4
Editorial Independence	23	1	1	1	4	3		7	7	5	6	7	6	7	7	7	4
Overall Assessment	OA1	4	5	2	6	6		6	6	6	5	5	5	7	6	6	5
Overall Assessment	OA2	Yes	Yes with modifications	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes with modifications	Yes	Yes with modifications	Yes	Yes	Yes	Yes with modifications

Summary of evidence for the recommendations

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
Prevention	1. What individual, community and policy level measures can be taken to prevent T2DM among the general population?	1	Individual behaviour for preventing diabetes focus on healthy eating/diet, increased physical activity, smoking habits and alcohol intake. Individual level behaviour change interventions are enhanced and sustained through behavioural counselling/therapy. Devices such as pedometers or mobile phone applications should be used to support and monitor behaviour change.	Kottke T, Wilkinson J, Baechler C, Danner C, Erickson K, O'Connor P, Sanford M, Straub R. Healthy lifestyles. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2016 Jan. 58 p. [152 references]	Bertholet N, Daeppen JB, Wietlisbach V, Fleming M, Burnand B. Reduction of alcohol consumption by brief alcohol intervention in primary care: systematic review and meta-analysis. Arch Intern Med. 2005 May 9;165(9):986-95. PubMed Bravata DM, Smith-Spangler C, Sundaram V, Gienger AL, Lin N, Lewis R, Stave CD, Olkin I, Sirard JR. Using pedometers to increase physical activity and improve health: a systematic review. JAMA. 2007 Nov 21;298(19):2296-304. [51 references] PubMed Patnode et al., 2015; U.S. Preventive Services Task Force (USPSTF), 2015; U.S. Department of Health and Human Services, 2008.	Systematic review	Use of pedometers (Moderate certainty evidence); Brief behavioral intervention for individuals who screen positive on a validated tool for risky/hazardous drinking (Moderate); Community program to elderly individuals who have insufficient levels of physical activity (High certainty evidence); Self-monitoring (food journals, mobile applications, tracking websites, advanced meal planning) for obese and overweight patients (High

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
							certainty evidence).
		2	Whole of community preventive measures are important for engaging communities to support community members to achieve behaviour changes that will prevent DM.		1)Laine J, Kuvaja-Köllner V, Pietilä E, Koivuneva M, Valtonen H, et al. (2014) Cost-Effectiveness of Population-Level Physical Activity Interventions: A Systematic Review. Am J Health Promot 29: 71–80. doi: 10.4278/ajhp.131210-LIT-622 [PubMed] 2)McGill R, Anwar E, Orton L, Bromley H, Lloyd-Williams F, et al. (2015) Are interventions to promote healthy eating equally effective for all? Systematic review of socioeconomic inequalities in impact. BMC Public Health 15: 1–15. [PMC free article] [PubMed]	Systematic review	Community rail-trails ,pedometers and school-health education programmes most cost-effective population wide interventions (Moderate certainty evidence)
		3	Environmental and policy approaches for promoting healthy eating, physical activity and alcohol/drinking habits include : • Town/city planning to promote active recreation and physical activity. • Fiscal policies to reduce the consumption of calorie-dense foods, alcohol and tobacco to prevent diabetes.	Fiscal policies for diet and the prevention of noncommunicable diseases-2016	1)Powel LM, Chriqui JF, Khan T, Wada R, Chaloupka FJ. Assessing the potential effectiveness of food and beverage taxes and subsidies for improving public health: a systematic review of prices, demand and body weight outcomes. Obes Rev. 2013; 14(2):110–28. 2)Andreyeva T, Long MW, Brownell KD. The impact of food prices on consumption: a systematic review of research on the price elasticity of demand for food. Am J Public Health, 2010; 100(2):216–22. doi: 10.2105/AJPH.2008.151415	Systematic review	Low certainty evidence
	2. What recommended	4	Combined diet and physical activity is more effective	NICE guideline: Type 2 diabetes: prevention in people at high risk	Balk, E. M., Earley, A., Raman, G., Avendano, E. A., Pittas, A. G.,	Systematic review	

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Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
	intervention can prevent or delay onset of T2DM among individual with high risk of developing T2DM?		than diet or physical activity only. Structured group or individual counselling is essential to achieve dietary, physical activity and weight loss targets. Mobile apps can be used to deliver combined diet and physical activity programs.	Combined diet and physical activity promotion programs for prevention of diabetes: Community Preventive Services Task Force recommendation statement.	& Remington, P. L. (2015). Combined Diet and Physical Activity Promotion Programs to Prevent Type 2 Diabetes Among People at Increased Risk: A Systematic Review for the Community Preventive Services Task Force. Annals of Internal Medicine, 163(6), 437–451. http://doi.org/10.7326/M15-0452		Combined diet and physical activity is more effective than diet or physical activity only (Moderate certainty evidence) Structured group or individual counselling is essential to achieve dietary, physical activity and weight loss targets (Moderate certainty evidence) Mobile apps can be used to deliver combined diet and physical activity programs (Low certainty evidence)
	3. What are the recommended measures for preventing progression to T2DM among individuals with pre-diabetes or impaired glucose tolerance?	5	Intensive lifestyle modification should be used to prevent onset of DM. Metformin should only be used when intensive lifestyle modification is not feasible among pre-diabetic individuals with BMI >=35	American Diabetes Association standards of medical care-2018		Randomized controlled trials	Intensive lifestyle modification should be used to prevent onset of DM (High certainty evidence).

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			kg/m2, those aged 60 years, and women with prior GDM				Metformin should only be used when intensive lifestyle modification is not feasible among pre-diabetic individuals with BMI >=35 kg/m2, those aged 60 years, and women with prior GDM (Moderate certainty evidence)
Screening	1. What are the recommended tools for risk assessment for T2DM?	6	Recommendations for screening for T2DM. Screening should be provider-initiated whenever a person visits a health facility. Community based intensified case finding or large-scale community screening programs are not recommended unless there is a clear referral pathway. Screening should be done using a locally validated screening tool such as the FINDRISC score. Individuals identified as high risk should proceed to a diagnostic test. If the result of the diagnostic test is normal, the diagnostic test should be repeated every year.	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care	Noble, D., Mathur, R., Dent, T., Meads, C., & Greenhalgh, T. (2011). Risk models and scores for type 2 diabetes: systematic review. The BMJ, 343, d7163. http://doi.org/10.1136/bmj.d7163	Systematic review	Low certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
Diagnosis	1. What are the recommendations for diagnosis of DM at primary care level in resource constrained settings?	7	Fasting plasma glucose: Plasma glucose after 8 hours of no food/calorie intake of more than 126mg/dl or 7 mmol/L	American Diabetes Association standards of medical care-2018		Expert review	Not graded
		8	75-g oral glucose tolerance test (OGTT): Plasma glucose after two hours following a glucose load of 75g of glucose dissolved				Not graded
		9	HbA1C criteria				
		10	**Recommendation for PHC level:** Random blood sugar of more than 200mg/dl or 11.1 mmol/L in high risk individuals with symptoms suggestive of hyperglycaemia or DM (increased thirst, increased frequency of urination and increased appetite)				Not graded
Diabetes education for persons with DM	1. What is the evidence for including diabetes education in routine diabetes care and treatment?	11	A structured Diabetes Education program is recommended as part of comprehensive diabetes care and treatment. Diabetes education should be offered immediately after diagnosis or within 6-12 months of diagnosis or any time it is feasible following diagnosis.	NICE: Type 1 diabetes in adults: diagnosis and management NICE: Type 2 diabetes in adults: diagnosis and management American Diabetes Association standards of medical care-2018	Butcher MK, Vanderwood KK, Hall TO, Gohdes D, Helgerson SD, Harwell TS. Capacity of diabetes education programs to provide both diabetes self-management education and to implement diabetes prevention services. JPublicHealth Manag Pract 2011;17:242–247		Very low to low certainty evidence
	2. What should be the recommended scope for diabetes education?	12	Diabetes education must cover prevention, changes, medication adherence and self-care. Diabetes education must be delivered by a health worker trained on Diabetes Education according to national standards				Not graded

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
	3. How should diabetes education be delivered in resource constrained settings?	13	Diabetes education should be delivered in a mode, intensity, frequency and duration that is suitable to the patient needs and health care settings				Not graded
Lifestyle modification	1. What are the recommended targets for lifestyle changes in treatment of DM?	14	Lifestyle changes are an essential add-on to drug treatment in Diabetes management Lifestyle changes should begin as soon as a diagnosis is made to achieve strict blood glucose control. Lifestyle changes focus on diet, physical activity, alcohol & tobacco intake. Reduce daily caloric intake by 500 to 600 calories in obese and overweight persons with DM. Follow a low-calorie diet (800 to 1200 calories per day) under the supervision of a health worker or diabetes educator Moderate (150 mins/week) or vigorous (90 mins/week) physical activity Smoking cessation	NICE: Type 1 diabetes in adults: diagnosis and management NICE: Type 2 diabetes in adults: diagnosis and management American Diabetes Association standards of medical care-2018			Moderate certainty evidence
Drug treatment	1. What drugs are the recommended for treating T1DM in children?	15	The treatment for type 1 diabetes in children is insulin. • Twice-daily insulin using both short-acting and intermediate-acting insulin. (If these insulins are not always available, pre-mixed insulin can be used as an alternative regimen).	Pocketbook for management of diabetes in childhood and adolescence in under-resourced countries. American Diabetes Association standards of medical care-2018			High certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			• Basal bolus regimen (the preferred option) - with short acting insulin given with main meals (usually three times per day) and intermediate-acting insulin given once or twice daily (evening, or morning and evening).				
	2. What drugs are the recommended for treating T1DM in adults?	16	• A basal-bolus regimen made up of insulin-glargine and rapid-acting soluble human or animal insulin should be used with strict self-blood glucose monitoring to avoid hypoglycaemia • Use a twice-daily human mixed insulin regimen when a multiple daily injection basal–bolus insulin regimen is not possible or a twice-daily mixed insulin regimen is preferred.		Guidelines on second- and third-line medicines and type of insulin for the control of blood glucose in non-pregnant adults with diabetes mellitus.		Moderate certainty evidence
	3. What drugs are recommended for treating T2DM in children	17	Metformin is the first-line drug for treating T2DM in adolescents and young people. Basal insulin can be used as first-line if blood glucose level is as high as 13.9mmol/L and there is marked symptoms such as frequent urination (bedwetting), weight loss, frequent thirst and dehydration. Basal insulin can also be used when metformin fails to achieve the targeted blood glucose levels.	Pocketbook for management of diabetes in childhood and adolescence in under-resourced countries. American Diabetes Association standards of medical care-2018			High certainty evidence

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	4. What drugs are recommended for treating T2DM in adults?	18	Metformin is the preferred choice to for initial monotherapy. Dosage should be titrated from 500 to 2000 mg per day with or after meals. Initial combination therapy is recommended when there is marked cardiovascular risk factor or high blood sugar levels between 11 -15 mmol/l A combination of metformin and another glucose lowering drug except (Glibenclamide and glyburide) is recommended.	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care. American Diabetes Association standards of medical care-2018			High certainty evidence
	5. What add-on drug (s) is recommended for managing T2DM? and under what circumstances should it be used?	19	Basal insulin can also be added if dual or triple therapy does not yield the blood glucose targets	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care. American Diabetes Association standards of medical care-2018. NICE: Type 2 diabetes in adults: diagnosis and management			Moderate certainty evidence
	6. Which a hierarchical order should be considered in the choice of first-line, second-line regimens for T2DM?	20	The preferred combination for dual therapy is metformin + another sulfonylurea (except Glibenclamide/glyburide) Consider person's age, body weight, presence of complications and duration of disease. When triple therapy becomes imperative, the recommended and most feasible combination is Metformin + another sulfonylurea + vidagliptin (DPP-4 inhibitor). Basal insulin can also be added if dual or triple	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care. American Diabetes Association standards of medical care-2018. NICE: Type 2 diabetes in adults: diagnosis and management	Metformin and second- or third generation sulphonylurea combination therapy for adults with type 2 diabetes mellitus (Cochrane Review)		Metformin + sulfonylurea (low certainty) Metformin + another sulfonylurea + vidagliptin (DPP-4 inhibitor). (Moderate certainty evidence)

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			therapy does not yield the blood glucose targets				
	8. Should insulin be considered as a first- or second-line drug in T2DM? If yes, under which circumstances should it be considered as either a first or second-line drug?	21	Insulin only or combination with other glucose lowering drugs in the essential medicines list can be considered as firstline in the following conditions: • Very high blood glucose level above 16mmol/l • Acute weight loss • Dehydration • Acute illness or • Presence of ketones	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care. American Diabetes Association standards of medical care-2018. NICE: Type 2 diabetes in adults: diagnosis and management	Roglic G, Norris SL. Medicines for Treatment Intensification in Type 2 Diabetes and Type of Insulin in Type 1 and Type 2 Diabetes in Low-Resource Settings: Synopsis of the World Health Organization Guidelines on Second- and Third-Line Medicines and Type of Insulin for the Control of Blood Glucose Levels in Nonpregnant Adults With Diabetes Mellitus. Ann Intern Med. 2018;169:394–397. doi: 10.7326/M18-1149		Very low certainty evidence
	8. Is there a preferred combination for triple therapy for T2DM? If yes, which?	22	When triple therapy becomes imperative, the recommended and most feasible combination is Metformin + another sulfonylurea + vidagliptin (DPP-4 inhibitor).	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care.	Kothny W, Foley J, Kozlovski P, Shao Q, Gallwitz B, Lukashevich V. Improved glycaemic control with vildagliptin added to insulin, with or without metformin, in patients with type 2 diabetes mellitus. Diabetes Obes Metab. 2013 Mar;15(3):252-7.		Moderate certainty evidence
DM related emergencies	1. What are the recommended life-saving measures that can be taken at primary health care level to manage DM related emergencies? (disaggregate by each type of emergency)	23	Management of mild and moderate forms of hypoglycaemia is feasible at primary health care setting by giving fast acting sugars or carbohydrate	American Diabetes Association standards of medical care-2018			Not graded
		24	Management of DKA and HHS is not very feasible at primary health care setting.				Not graded
	2. What are the recommended management of DM	25	Management of severe forms of hypoglycaemia with loss of consciousness	NICE: Type 1 diabetes in adults: diagnosis and management NICE: Type 2 diabetes in adults: diagnosis and management			

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	emergencies at secondary level?	26	Management of DKA and HHS is not feasible at primary health care setting				Not graded
DM complications	1. What are the recommended measures for preventing DM related complications (disaggregate by each type of complication)?	27	Generally, primary health care workers can work with persons with diabetes to prevent all complications by: o Ensuring the person with diabetes achieves and sustains the targets for blood sugar control to reduce or slow disease progression; o Ensuring that blood pressure and blood lipid levels are within normal limits to also reduce or slow the disease progression.	NICE: Type 1 diabetes in adults: diagnosis and management NICE: Type 2 diabetes in adults: diagnosis and management			Not graded
	2. What are the recommendations for early identification of DM related complications?	28	**Diabetic retinopathy at primary care** Ask questions about difficulties with vision. Conduct visual acuity using a simple visual acuity chart Refer for comprehensive eye examination	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care.			Not graded
		29	**Diabetic nephropathy** Assess urinary albumin or albumin–to–creatinine ratio at least once a year. Estimate glomerular filtration rate in patients with T1DM with duration of 5years and in all patients with T2DM, and in all patients with comorbid hypertension.	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care.			Not graded
		30	**Diabetic Peripheral Neuropathy and foot problems**	IDF Clinical Practice Recommendations for Managing Type 2 Diabetes in Primary Care. IWGDF guidance on the prevention			Low certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			Screen for DPN within 5 years of diagnosis of T1DM and immediately after diagnosis of T2DM Then screen annually after the initial screening, regardless of the results. Conduct full sensory and foot examination annually. Inspect foot at every visit to the health facility.	of foot ulcers in at-risk patients with diabetes.			
Comorbidities	1. What are recommendations for the management of other CV risk factors?	31	Cardiovascular risk factors can be assessed in resource constrained settings (with no specialist physician or doctor and no laboratory facility for lipid profile) using the WHO/ISH (World Health Organization/International Society of hypertension) risk prediction chart.	American Diabetes Association standards of medical care-2018			Not graded
		32	Blood Pressure should be measured at every routine visit and at home. All hypertensive patients with diabetes should monitor their blood pressure at home. Lifestyle changes are important to reduce cardiovascular risk factors. Drugs should be used when other cardiovascular risk factors like hypertension and high blood cholesterol levels are identified.	American Diabetes Association standards of medical care-2018			Low certainty evidence Low certainty evidence
		33	Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy for persons with diabetes who are >=50	American Diabetes Association standards of medical care-2018	Baigent C, Blackwell L, Collins R, et al.; Antithrombotic Trialists' (ATT) Collaboration. Aspirin in	Systematic review	Low certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			years with at least one additional major risk factor (family history of premature atherosclerotic cardiovascular disease, hypertension, dyslipidemia, smoking, or albuminuria) and are not at increased risk of bleeding.		the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009;373:1849–1860		
		34	Use aspirin (75–162mg/day) as a secondary prevention strategy in those with diabetes and a history of atherosclerotic cardiovascular disease.	American Diabetes Association standards of medical care-2018	Peters SAE, Huxley RR,Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775,385 individuals and 12,539 strokes. Lancet 2014;383: 1973–1980	Systematic review	High certainty evidence
	2. What are the recommended drug combinations for treatment of high blood pressure in DM?	35	Depending on the blood pressure at diagnosis or presence of proteins in urine, the first-line antihypertensive drug treatment should be an or a combination that contains Angiotensin Converting Enzyme inhibitor(ACEi) plus either a thiazide-diuretic (long acting versions have been shown to reduce cardiovascular events) or a generic calcium-channel blocker.	American Diabetes Association standards of medical care-2018	Cardiovascular and renal outcomes of renin-angiotensin system blockade in adult patients with diabetes mellitus: a systematic review with network meta-analyses. PLoS Med 13(6): e1002064 Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease: a network meta-analysis. Lancet 20015 385(9982): 2047-56	Systematic review	High certainty evidence
		36	A calcium-channel blocker should be the first-line antihypertensive drug treatment for a woman, where it is agreed that there is possibility of her becoming pregnant – this decision should be made	American Diabetes Association standards of medical care-2018	BulloM, Tschumi S, Bucher BS, BianchettiMG, Simonetti GD. Pregnancy outcome following exposure to angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists: a systematic		Very low certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			following an informed discussion with the woman – avoid ACE inhibitors or A2RB in women who are planning a pregnancy as these drugs cause foetal damage.		review. Hypertension 2012;60:444–450		
		37	Add whichever drug of the calcium-channel blocker or diuretic that was not a part of the initial combination	American Diabetes Association standards of medical care-2018	Yusuf S, Teo KK, Pogue J, et al.; ONTARGET Investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. NEngl JMed 2008;358:1547–1559 Fried LF, Emanuele N, Zhang JH, et al.; VANEPHRON-D Investigators. Combined angiotensin inhibition for the treatment of diabetic nephropathy. N Engl J Med 2013;369:1892–1903 Makani H, Bangalore S, Desouza KA, Shah A, Messerli FH. Efficacy and safety of dual blockade of the renin-angiotensin system: meta-analysis of randomised trials. BMJ 2013;346:f360		High certainty evidence
		38	Add an alpha-blocker, a beta-blocker or a *potassium-sparing diuretic or a mineralocorticoid receptor antagonist (*where the person is on either an ACE inhibitor or A2RB, potassium-sparing diuretics should be added with caution and serum potassium carefully	American Diabetes Association standards of medical care-2018	Bakris GL, Agarwal R, Chan JC, et al.; Mineralocorticoid Receptor Antagonist Tolerability Study–Diabetic Nephropathy (ARTS-DN) Study Group. Effect of finerenone on albuminuria in patients with diabetic nephropathy: a randomized clinical trial. JAMA 2015;314:884–894	Randomised controlled trials	Moderate certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			monitored – additionally, spironolactone should not be administered to a pregnant woman as it causes fetal damage). ` For patients on any one of an ACE inhibitor, A2RB, thiazide diuretic, or potassium-sparing diuretic, renal function (serum creatinine and estimated glomerular filtration rate) and serum potassium should be checked at least annually.		Williams B, MacDonald TM, Morant S, et al.; British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment care for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet 2015;386:2059–2068 Filippatos G, Anker SD, B¨ohm M, et al. A randomized controlled study of finerenone vs. eplerenone in patients with worsening chronic heart failure and diabetes mellitus and/or chronic kidney disease. Eur Heart J 2016;37:2105–2114 Bomback AS, Klemmer PJ. Mineralocorticoid receptor blockade in chronic kidney disease. Blood Purif 2012;33:119–124		
	3. What are the recommendations for managing dyslipidemias?	39	Where the individual already has atherosclerotic cardiovascular disease, high-intensity statin treatment is required in addition to lifestyle modification for secondary prevention of further cardiovascular events. High-intensity statin therapy with either Atorvastatin	American Diabetes Association standards of medical care-2018	Mihaylova B, Emberson J, Blackwell L, et al.; Cholesterol Treatment Trialists' (CTT) Collaborators. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet 2012;380:581–590	Randomised controlled trials	High certainty evidence

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			40mg-80mg daily or Rosuvastatin 20mg to 40mg daily has been shown to reduce LDL cholesterol by [3] 50%.		Baigent C, Keech A, Kearney PM, et al.; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet 2005;366:1267–1278		
		40	In patients with atherosclerotic cardiovascular disease in whom the serum LDL cholesterol remains [3] 70mg/dl despite high intensity statin therapy (at maximal dosage) and lifestyle modifications, Ezetimibe may be added to the regime following an assessment of the patient's risk, and after careful consideration of the patient's preferences and the side effect profile of the medications.	American Diabetes Association standards of medical care-2018	Cannon CP, Blazing MA, Giugliano RP, et al.; IMPROVE-IT Investigators. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med 2015;372:2387–2397	Randomized controlled trial	High certainty evidence
	4. What are the recommendations for managing DM in HIV+ individuals?	41	Recommendations for blood glucose targets and lifestyle management for managing DM in PLHIV is the same as in HIV- persons. However due to drug interaction between glucose lowering drugs and anti-retroviral drugs, there are special considerations for the treating Diabetes in PLHIV.	Monroe AK, Glesby MJ, Brown TT. Diagnosing and managing diabetes in HIV-infected patients: current concepts. Clin Infect Dis. 2015 Feb 1;60(3):453-62. doi: 10.1093/cid/ciu779. Epub 2014 Oct 13.			Low certainty

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
	5. What are the recommendations for managing DM & TB co-morbidity?						
DM & Pregnancy	1. What are the recommended tools for screening for GDM?	42	Screen all pregnant women at their first appointment (booking) to rule-out pre-existing diabetes or overt diabetes before pregnancy that is FPG value ≥ 7.0 mmol/L (126 mg/dl) OR RPG ≥ 11.1 mmol/L (200 mg/dl)	IDF Model of Care for GDM-2015. American Diabetes Association standards of medical care-2018	International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiler JL, Lowe LP, McIntyre HD, Oats JJ, Omori Y, Schmidt MI. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010 Mar;33(3):676-82.	Consensus panel	Not graded
		42	Perform GDM screening test at 24-28 weeks using Oral Glucose Tolerance Test (OGTT). OGTT should be administered appropriately by a health worker and the lab testing should be done by a lab technician.				Not graded
	2. How can GDM be diagnosed? How can you determine if a woman had overt diabetes prior to pregnancy?	44	Test women with gestational diabetes mellitus for persistent diabetes at 4–12 weeks postpartum, using the oral glucose tolerance test and clinically appropriate non pregnancy				Not graded
	3. What are the recommended measures for preventing onset of GDM in pregnant women with high risk?	45	Combined diet and physical activity is more effective than diet or physical activity only Structured group or individual counselling is essential to achieve dietary, physical activity and weight loss targets Mobile apps can be used to	IDF Model of Care for GDM-2015. American Diabetes Association standards of medical care-2018			Combined diet and physical activity is more effective than diet or physical activity only (Moderate certainty evidence) Structured group or individual counselling is

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
			deliver combined diet and physical activity programs				essential to achieve dietary, physical activity and weight loss targets (Moderate certainty evidence) Mobile apps can be used to deliver combined diet and physical activity programs (Low certainty evidence)
	4. What are the recommended measures for managing GDM?	46	Lifestyle management is the first line	IDF Model of Care for GDM-2015. American Diabetes Association standards of medical care-2018	Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403	Randomized controlled trial	High certainty evidence
		47	If lifestyle management fails, then insulin or metformin should be considered.	IDF Model of Care for GDM-2015. American Diabetes Association standards of medical care-2018			High certainty evidence
	5. What are the recommendations for management of DM in women who were diabetic prior to pregnancy?	48	Pre-conception counseling should be integrated into routine diabetes care for all women of childbearing age. Family planning should be discussed and offered to women who do not intend to get pregnant.	IDF Model of Care for GDM-2015. American Diabetes Association standards of medical care-2018	Charron-Prochownik D, Sereika SM, Becker D, White NH, Schmitt P, Powell AB 3rd, Diaz AM, Jones J, Herman WH, Fischl AF, McEwen L, DiNardo M, Guo F, Downs J. Long-term effects of the booster-enhanced READY-Girls preconception counseling program on intentions and behaviors for family planning in teens with diabetes. Diabetes Care. 2013 Dec;36(12):3870-4.	Randomized controlled trial	Moderate quality evidence
		49	Insulin is the drug of choice for managing both T1DM & T2DM	IDF Model of Care for GDM-2015. American Diabetes Association standards of medical care-2018		Expert consensus	Insulin is the drug of choice for managing

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			Adjust insulin dosages to respond to the changing insulin demands throughout the course of the pregnancy in T1DM These adjustments in insulin doses require specialist care. Low dose aspirin 60–150 mg/day (usual dose 81 mg/day) should be given from the end of the 1st trimester up to delivery to reduce the risk of pre-eclampsia. Calcium blockers or alpha-methyl dopa should be used to control blood pressure in women with DM who also have chronic hypertension.		Henderson JT, Whitlock EP, O'Connor E, Senger CA, Thompson JH, Rowland MG. Low-dose aspirin for prevention of morbidity and mortality from preeclampsia: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2014 May 20;160(10):695-703.		both T1DM & T2DM Adjust insulin dosages to respond to the changing insulin demands throughout the course of the pregnancy in T1DM This adjustment in insulin doses require specialist care. (Not graded) Low dose aspirin 60–150 mg/day (usual dose 81 mg/day) should be given from the end of the 1st trimester up to delivery to reduce the risk of pre-eclampsia (High certainty evidence) Calcium blockers or alpha-methyl dopa should be used to control blood pressure in women with DM who also have chronic hypertension (High certainty evidence)

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
	1. What are the recommended role of different cadres of health workers in prevention, care, treatment and management of DM?	50	**Doctors:** Primary care or general practice doctors are responsible for: • Confirmation of diagnosis. • Clinical evaluation • Clinical follow up of persons with diabetes • To identify the circumstances necessary for drug treatment • To prescribe drugs and determine the line of management • Work with other members of the care team to provide structured diabetes education and support for self-care			Expert consensus	Not graded
		51	**Nurses/CHEWs/JCHEWs:** • To provide culturally – appropriate structured diabetes education. • To convey diabetes self-management information and healthcare provider recommendations accurately to the person with diabetes. • To identify and refer high-risk individuals to physicians. • To identify and overcome cultural barriers to self-care or behavior change. • Participate in the evaluation of program, unit, or agency using clinical practice guidelines. • To support diabetic persons to prevent complications associated with DM and to identify			Expert consensus	Not graded

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			them early when they do occur.				
Health professionals and settings		52	**Lay Community Health Workers:** LCHWs should play the following roles • Implement diabetes community awareness and prevention program • Provide diabetes prevention messages and information to community members • Support persons with diabetes to gain access to diabetes' support system in their communities • Work with the health provider team to apply basic concepts of behavior change to support person with diabetes with effective self-management. • Build community coalitions to meet the needs of people affected by diabetes in the community.	Halimatou Alaofè, Ibitola Asaolu, Jennifer Ehiri, Hayley Moretz, Chisom Asuzu, Mobolanle Balogun, Olayinka Abosede, John Ehiri. Community Health Workers in Diabetes Prevention and Management in Developing Countries. Annals of Global Health, Volume 83, Issues 3–4, 2017, Pages 661-675, ISSN 2214-9996, https://doi.org/10.1016/j.aogh.2017.10.009.			Low certainty evidence
	2. What are the recommended roles of different health care settings of health prevention, care, treatment and management of DM?	53	**At community level**, the following aspects of diabetes prevention, care and treatment are recommended: 1. Community based health promotion. 2. Screening to identify individuals at risk of developing DM, using risk assessment tools. This can be done during outreaches, mobile health services and community engagement. 3. Support to individuals			Expert consensus	Not graded

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			identified to be at high risk for developing DM to prevent or delay onset of DM. 4. Support to persons with diabetes to achieve self-management and lifestyle changes. 5. Support to persons with diabetes to prevent and identify complications/ emergencies.				
		54	**At primary health care level**, in addition to community level activities the following aspects of diabetes prevention, care and treatment are recommended: 1. Diagnosis of DM using point-of care devices, diagnostic algorithms and risk assessment tools. 2. Basic clinical management of non-complicated DM such as: a. Patient evaluation. b. Structured diabetes education. c. Drug treatment. d. Support for lifestyle changes. e. Prevention and early recognition of DM complications. f. Early recognition of other comorbidities. 3. Basic life saving measures in management of DM related emergencies. 4. Referral of complicated DM cases and emergencies.			Expert consensus	Not graded

Scope	Health Questions	Recommendation Number	Recommendations	Guideline source of recommendation	Source of evidence for recommendation	Hierarchy/type of evidence	Quality of Evidence
		55	**At secondary and tertiary health care level**, in addition to the type of care provided at community and primary care level, comprehensive management of DM complications and emergencies.			Expert consensus	Not graded

Types of glucose lowering drugs

CLASS	Examples	Essential Medicines List
Insulins	Regular	Yes
	Lispro	No
	Aspart	No
	Glulsine	No
	Glargine	Yes
	Detemir	No
	Pre-mixed	Yes
Biguanides	Metformin	Yes
Sulphonylureas	Glibenclamide	Yes
	Glyburide	No
	Glipizide	No
	Gliclazide	Yes
	Glimepiride	Yes
α-glucosidase inhibitors	Acarbose	No

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	Miglitol Voglibose	No No
Meglitinides ('Glinides')	Repaglinide Nateglinide	No No
Thiazolidinediones	Pioglitazone Rosiglitazone	No No
DPP4 inhibitors ('Gliptins')	Sitagliptin Vildagliptin Saxagliptin Linagliptin Alogliptin	No Yes No No No
GLP-1 agonists	Exenatide Exenatide extended release Liraglutide	No No No
SGLT2 inhibitor	Gliflozins	No

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	Canagliflozin Dapagliflozin Empagliflozin	No No NO