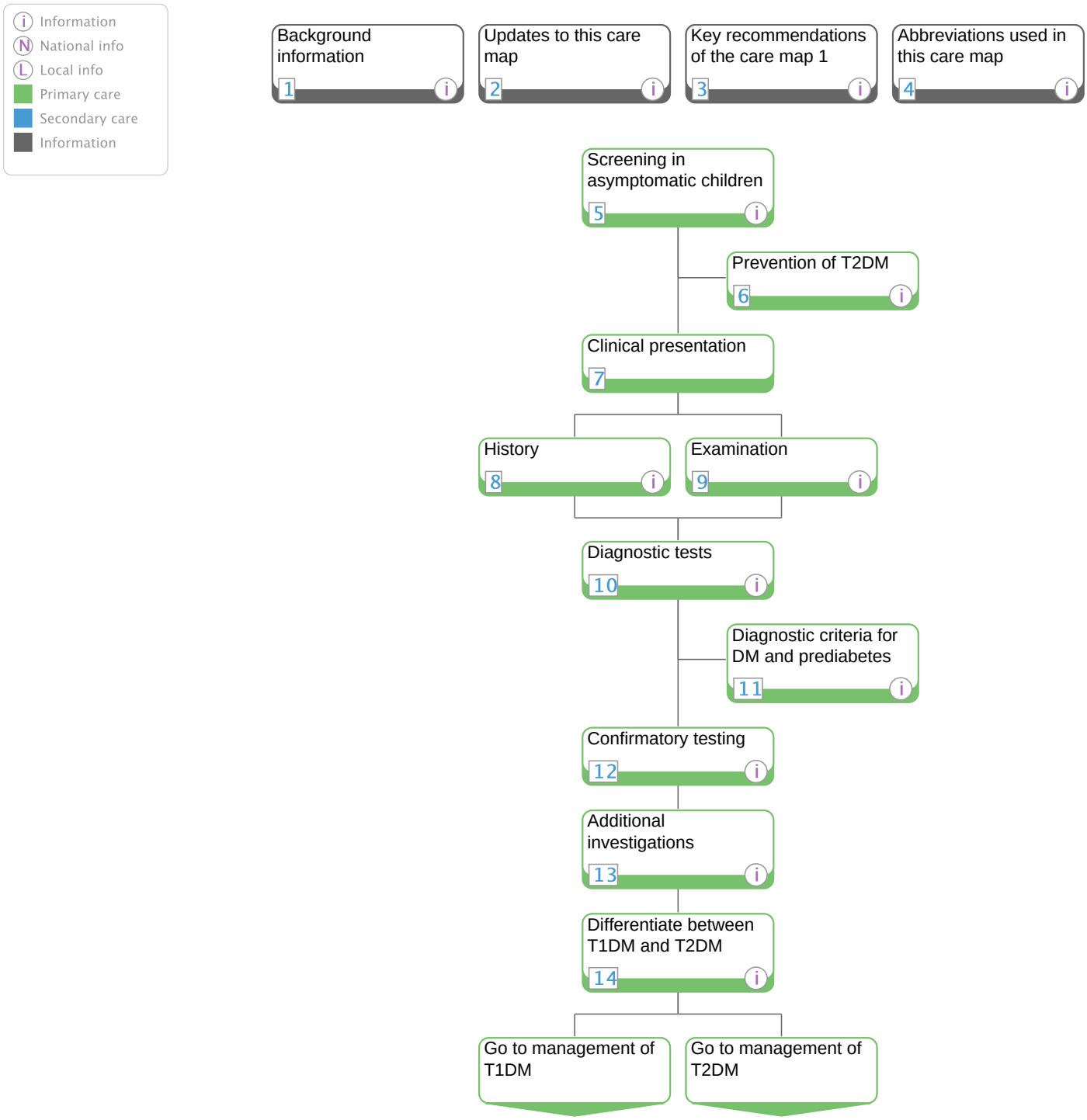
DM in children and adolescents - investigations

Paediatrics > Endocrinology > Diabetes mellitus (DM) in children and adolescents



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DM in children and adolescents - investigations

1 Background information

Quick info:

The purpose of this guideline is to define the appropriate diagnosis and management of both T1DM and T2DM in children and adolescents. The objective is to improve the appropriateness of investigation, prescribing, and referral of patients presenting to provider organisations in Qatar. It is intended that the guideline will be used primarily by generalist physicians in all healthcare settings.

Scope

Aspects of care covered in this guideline include the following:

- Assessment and management of T1DM and T2DM in children and adolescents, including:
  - Diabetes screening.
  - Lifestyle management of confirmed T1DM and T2DM.
  - Pharmacological therapy for T1DM and T2DM.
  - Glycaemic targets and glucose monitoring.
  - Hypoglycaemia prevention and management.
  - Complications and comorbidity screening and management.

Aspects of care not covered in this guideline include the following:

- Neonatal DM.
- Maturity-onset diabetes of the young.
- Detailed management of diabetic complications.

Classification

The general categories of DM are classified as follows [1,2]:

- T1DM arises as the result of beta-cell insufficiency or destruction, usually leading to absolute insulin deficiency.
- T2DM arises as the result of progressive loss of insulin secretion on the background of insulin resistance.
- Specific types of diabetes due to other causes, including:
  - Monogenic diabetes syndromes, e.g.:
    - Neonatal diabetes.
    - MODY.
  - Secondary diabetes, including:
    - Diseases of the exocrine pancreas.
    - Drug- or chemical-induced diabetes.
    - Endocrinopathies.

Childhood T1DM is defined by the presence of one or more of the following autoimmune markers [1]:

- Islet cell autoantibodies.
- Insulin autoantibodies.
- GAD65 antibodies.
- Antibodies to tyrosine phosphatases IA-2 and IA-2β.
- Antibodies to ZnT8.

Childhood T2DM is typically seen in children who [3]:

- Are overweight or obese.
- Have a strong family history of T2DM.
- At diagnosis, have substantial residual insulin secretory capacity (reflected by normal or elevated insulin and C-peptide concentrations).
- Demonstrate insulin resistance (including clinical evidence of PCOS or acanthosis nigricans).
- Lack evidence for diabetic autoimmunity (i.e. are negative for autoantibodies typically associated with T1DM.

Pre-diabetes [4]:

- Is a term used to refer to individuals with an IFG and/or IGT.
- Indicates a high risk for the future development of T2DM and cardiovascular disease.

References:

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Please see the care map's Provenance.

2 Updates to this care map

Quick info:

Date of publication: 19-Mar-2017

Please see the care map's Provenance for additional information on references, contributors, and the editorial process.

3 Key recommendations of the care map 1

Quick info:

The key recommendations of this care map are as follows:

Diagnosis (see the *'Diagnostic criteria for DM'* care point on the *'Investigations'* page):

- Distinguishing between T1DM and T2DM in the paediatric and adolescent population is not consistently easy to define [3].
- T2DM remains a diagnosis of exclusion in adolescents [5].
- Exclude T1DM by assessing immune markers and monogenic diabetes through a careful family history and genetic testing [5].
- American Diabetes Association criteria for the diagnosis of T2DM requires one of the following [1]:
  - FBS: ≥7.0 mmol/L (126 mg/dL).
  - OGTT: ≥11.1 mmol/L (200 mg/dL) at 2-hours post-glucose.
  - RBS: ≥11.1 mmol/L (200 mg/dL) and the patient has classic symptoms of hyperglycaemia.
  - HBA_{1C}: ≥6.5%.
- In the absence of unequivocal hyperglycaemia, the diagnosis of diabetes should be confirmed by repeat testing [1][**L2**].

References:

Please see the care map's Provenance.

4 Abbreviations used in this care map

Quick info:

The abbreviations used in this care map are as follows:

ACE

Angiotensin-converting enzyme

ACR

Albumin-creatinine ratio

ASCVD

Atherosclerotic cardiovascular disease

BG

Blood glucose

BMI

Body mass index

BP

Blood pressure

CSII

Continuous subcutaneous insulin infusion

DBP

Diastolic blood pressure

DKA

Diabetic ketoacidosis

DM

Diabetes mellitus

DSME

Diabetes Self-Management Education

DSMS

Diabetes Self-Management Support

FBS

Fasting blood sugar

GAD65

Glutamic acid decarboxylase

HBA_{1C}

Glycated haemoglobin level

HDL

High density lipoprotein

HHS

Hyperglycaemic hyperosmolar state

IFG

Impaired fasting glucose

IGT

Impaired glucose tolerance

IV

Intravenous route

LDL

Low-density lipoprotein

LDL-C

Low density lipoprotein cholesterol

MODY

Maturity-onset diabetes of the young

MOPH

Ministry of Public Health of Qatar

NAFLD

Non-alcoholic fatty liver disease

NICU

Neonatal intensive care unit

OGTT

Oral glucose tolerance test

PCOS

Polycystic ovary syndrome

PCV

Pneumococcal conjugate vaccine

PPSV23

23-valent pneumococcal polysaccharide vaccine

RBS

Random blood sugar

SBP

Systolic blood pressure

SMBG

Self-monitoring of blood glucose

T1DM

Type 1 diabetes mellitus

T2DM

Type 1 diabetes mellitus

TDD

Total daily dose

ZnT8

Zinc transporter 8

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5 Screening in asymptomatic children

Quick info:

Screening for diabetes and prediabetes should be undertaken in those individuals who are overweight or obese and who have any two of the following risk factors [1]:

- Family history of T2DM in a first- or second-degree relative.
- High-risk ethnicity.
- Signs of insulin resistance or conditions associated with insulin resistance:
  - Acanthosis nigricans.
  - Hypertension.
  - Dyslipidaemia.
  - PCOS.
  - Small-for-gestational age birth weight.
- Maternal history of diabetes or gestational diabetes mellitus during the child's gestation.

Timing of screening test should [1]:

- Start at 10 years of age or at the onset of puberty if puberty starts at a younger age.
- Use either FBS or OGTT as screening tests, as appropriate [**R-GDG**].
- If testing was normal, repeat screening tests every 2 years [**R-GDG**].
- Those with prediabetes should be tested annually.
  - In patients with prediabetes, identify, and if appropriate treat, other ASCVD risk factors.

Evaluation of patients at risk should incorporate a global risk factor assessment for both diabetes and ASCVD [4].

References:

Please see the care map's Provenance.

6 Prevention of T2DM

Quick info:

Approaches can target [6]:

- General population of children, or
- Identification of high-risk individuals:
  - Need to identify those at increased risk and provide the required services.

Intervention can take place at [6]:

- An early stage when BG levels are still normal, or
- At the stage of IGT or IFG.

Prevention of T2DM may include [1,3,6]:

- Weight management.
- Patient education:
  - T2DM and its complications.
  - The role of diet and exercise in preventing diabetes.
- Encouragement of health eating.
- Regular physical activity.

References:

Please see the care map's Provenance.

8 History

Quick info:

Key points to note in the medical history include [1,3][**L2**]:

- Symptoms and duration of hyperglycaemia:
  - Including polyuria, polydipsia, polyphagia, fatigue, blurred vision, and weight loss.
- Symptoms of DKA, including:
  - Abdominal pain, vomiting, drowsiness, tachypnoea, and acetone-smelling breath.
- Pre-natal, birth and post-natal history, including:
  - Maternal gestational diabetes, gestational age at birth, birth weight, NICU admission.
- Family history of autoimmune-mediated disorders, including:
  - T1DM, thyroid disease, coeliac disease, adrenal disease.
- Lifestyle risk factors for DM, including:
  - Eating patterns and habit.
  - Weight history.
  - Physical activity.
- Symptoms of comorbidities associated with obesity including psychosocial problems.
- Social history, including:
  - Family circumstances.
  - School performance.
  - Nurse availability at school.
  - Smoking, alcohol, and/or substance use.
- Medication history:
  - Especially medication that may exacerbate hyperglycaemia, e.g.:
    - Glucocorticoids.
    - Beta-blockers.

References:

Please see the care map's Provenance.

9 Examination

Quick info:

Conduct a general physical examination noting in particular the following [1][**L2**]:

- Height (including standard deviation), weight, and BMI.
- Pubertal development.
- BP, including orthostatic BP, if indicated.
- Head and neck examination, including:
  - Facial dysmorphism.
  - Thyroid or tonsillar enlargement.
- Skin stigmata (e.g. striae, acanthosis nigricans, hyperpigmentation, alopecia, or vitiligo).
- Hepatomegaly.
- Comprehensive foot examination, including [**R-GDG**]:
  - Inspection for skin damage.
  - Palpation of dorsalis pedis and posterior tibialis pulses.
  - Absence or presence of patellar and Achilles tendon reflexes.
  - Determination of proprioception, vibration, and monofilament sensation.

References:

Please see the care map's Provenance.

10 Diagnostic tests

Quick info:

The following investigations are used to test for diabetes [1]:

- FBS.
  - Patients should be fasting for at least 8 hours.
- OGTT:
  - Studies have confirmed that the 2-hour post-glucose value diagnoses more people with diabetes compared with FBS cut points and HBA_{1C}.
  - An anhydrous glucose load of 1.75 g/kg (up to a maximum of 75 g) should be used in children [7].
- RBS.
- HBA_{1C} [1]:
  - In the diagnosis of diabetes in children and adolescents, it is not clear if the same HBA_{1C} cut points as adults should be used.
  - Point-of-care HBA_{1C} assays are not recommended for diagnostic purposes.
  - In haemoglobinopathies and anaemias, an HBA_{1C} assay without interference from abnormal haemoglobins should be used.

References:

Please see the care map's Provenance.

11 Diagnostic criteria for DM and prediabetes

Quick info:

The American Diabetes Association criteria for the diagnosis of diabetes requires one of the following [1]:

- FBS: ≥7.0 mmol/L (126 mg/dL).
- OGTT: ≥11.1 mmol/L (200 mg/dL) at 2 hours post-glucose.
- RBS: ≥11.1 mmol/L (200 mg/dL) – if the patient also has classic symptoms of hyperglycaemia.
- HBA_{1C}: ≥6.5%.

The American Diabetes Association criteria for diagnosis of prediabetes requires one of the following [1]:

- IFG:
  - FBS: 5.6-6.9 mmol/L (100-125 mg/dL).
- IGT:
  - OGTT: 7.8-11.0 mmol/L (140-199 mg/dL) at 2 hours post-glucose.
- HBA_{1C}: 5.7-6.4%.

References:

Please see the care map's Provenance.

12 Confirmatory testing

Quick info:

Confirming the diagnosis:

- A second diagnostic test is usually required to confirm the diagnosis [1][**L2**]:
  - Unless the diagnosis is clear, e.g.:
    - Patient is in hyperglycaemic crisis.
    - Patient has classic symptoms of hyperglycaemia and a RBS ≥11.1 mmol/L (200 mg/dL).
- The same diagnostic test should be repeated using a new blood sample [1][**L2**].

References:

Please see the care map's Provenance.

13 Additional investigations

Quick info:

In patients with symptoms of hyperglycaemia and an elevated plasma glucose of ≥13.9 mmol/L (250 mg/dL) [3]:

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- Test for ketosis with serum (e.g. beta-hydroxybutyrate) or urinary ketones.
- If positive, test for ketoacidosis by performing a venous blood gas.

Further laboratory evaluation [1]:

- Complete blood count.
- Urea, electrolytes and creatinine.
- Spot urinary albumin-creatinine ratio.
- Liver function tests.
- Fasting lipid profile (in children ≥5 years of age), including:
  - Total, LDL and HDL cholesterol and triglycerides.
- Fasting insulin level.
- C-peptide level.
- Thyroid function tests.
- Anti-thyroid antibodies (anti-thyroid peroxidase antibodies).
- Anti-insulin antibodies and anti-islets cell antibodies.
- GAD65 antibodies.
- Coeliac screen:
  - IgG and IgA anti-tissue transglutaminase antibody.
  - Deamidated gliadin antibodies.

Other investigations may be required for evaluation of obese children and adolescents, e.g. [**R-GDG**]:

- Sleep studies for sleep apnoea.
- Hepatic ultrasound for fatty liver disease.

References:

Please see the care map's Provenance.

14 Differentiate between T1DM and T2DM

Quick info:

The American Paediatric Association acknowledges that [3,4]:

- Distinguishing between T1DM and T2DM in the paediatric and adolescent population is not consistently easy to define.
- Clinical judgment plays an important role.

Differentiating between T1DM and T2DM [5]:

- Phenotypic overlap between T1DM and T2DM in children is common.
- T2DM remains a diagnosis of exclusion in adolescents.
- Although T2DM has been reported in preschool children, care must be taken in making this diagnosis in pre-adolescent children.
  - Exclude T1DM by assessing immune markers and monogenic diabetes through a careful family history and genetic testing.

In children and adolescents, the initial classification of diabetes is usually based on clinical features at first presentation and subsequent course [1,6]. Please see the attached table for further information.

References:

Please see the care map's Provenance.

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Diabetes mellitus in children and adolescents

Provenance Certificate

Overview

This guideline document has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The guideline will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

Whilst the MOPH has sponsored the development of the care map, the MOPH has not influenced the specific recommendations made within it.

This care map was approved on **19 Mar 2017**.

For information on changes in the last update, see the information point entitled 'Updates to this care map' on each page of the care map.

Editorial approach

This care map has been developed and issued by the Ministry of Public Health of Qatar (MOPH), through a process which aligns with international best practice in guideline development and localisation. The care map will be reviewed on a regular basis and updated to incorporate comments and feedback from stakeholders across Qatar.

The editorial methodology, used to develop this care map, has involved the following critical steps:

- Extensive literature search for well reputed published evidence relating to the topic.
- Critical appraisal of the literature.
- Development of a draft summary guideline.
- Review of the summary guideline with a Guideline Development Group, comprised of practising physicians and subject matter experts from across provider organisations in Qatar.
- Independent review of the guideline by the Clinical Governance body appointed by the MOPH, from amongst stakeholder organisations across Qatar.

Explicit review of the care map by patient groups was not undertaken.

Whilst the MOPH has sponsored the development of the care map, the MOPH has not influenced the specific recommendations made within it.

Sources of evidence

The professional literature published in the English language has been systematically queried using specially developed, customised, and tested search strings. Search strategies are developed to allow efficient yet comprehensive analysis of relevant publications for a given topic and to maximise retrieval of articles with certain desired characteristics pertinent to a guideline.

For each guideline, all retrieved publications have been individually reviewed by a clinical editor and assessed in terms of quality, utility, and relevance. Preference is given to publications that:

1. Are designed with rigorous scientific methodology.
2. Are published in higher-quality journals (i.e. journals that are read and cited most often within their field).

3. Address an aspect of specific importance to the guideline in question.

Where included, the 'goal length of stay' stated within this guideline is supported by and validated through utilisation analysis of various international health insurance databases. The purpose of database analysis is to confirm the reasonability and clinical appropriateness of the goal, as an achievable benchmark for optimal duration of inpatient admission.

Evidence grading and recommendations

Recommendations made within this guideline are supported by evidence from the medical literature and where possible the most authoritative sources have been used in the development of this guideline. In order to provide insight into the evidence basis for each recommendation, the following evidence hierarchy has been used to grade the level of authoritativeness of the evidence used, where recommendations have been made within this guideline.

Where the recommendations of international guidelines have been adopted, the evidence grading is assigned to the underlying evidence used by the international guideline. Where more than one source has been cited, the evidence grading relates to the highest level of evidence cited:

- **Level 1 (L1):**
  - Meta-analyses.
  - Randomised controlled trials with meta-analysis.
  - Randomised controlled trials.
  - Systematic reviews.

- **Level 2 (L2):**
  - Observational studies, examples include:
    - Cohort studies with statistical adjustment for potential confounders.
    - Cohort studies without adjustment.
    - Case series with historical or literature controls.
    - Uncontrolled case series.
  - Statements in published articles or textbooks.

- **Level 3 (L3):**
  - Expert opinion.
  - Unpublished data, examples include:
    - Large database analyses.
    - Written protocols or outcomes reports from large practices.

In order to give additional insight into the reasoning underlying certain recommendations and the strength of recommendation, the following recommendation grading has been used, where recommendations are made:

- **Recommendation Grade A1 (RGA1):** Evidence demonstrates at least moderate certainty of at least moderate net benefit.
- **Recommendation Grade A2 (RGA2):** Evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care.
- **Recommendation Grade B (RGB):** Evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended.
- **Recommendation Grade C1 (RGC1):** Evidence demonstrates a lack of net benefit; additional research is recommended.
- **Recommendation Grade C2 (RGC2):** Evidence demonstrates potential harm that outweighs benefit; additional research is recommended.
- **Recommendation of the GDG (R-GDG):** Recommended best practice on the basis of the clinical experience of the Guideline Development Group members.

References

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Diabetes mellitus in children and adolescents

Guideline Development Group members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the Clinical Governance Group. The GDG members have reviewed and provided feedback on the draft guideline relating to the topic. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

Guideline Development Group members		
Name	**Title**	**Organisation**
Dr Abeer Abu Abbas	Clinical Operations & Support Manager	Primary Health Care Corp
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Dr Ahmed M. Hussein Babiker	Head of Registration Section & Clinical Pharmacist	Dept of Pharmacy and Drug Control, MOPH[1]
Ms Mona H M M El Gamal	Diabetes Educator	Hamad Medical Corp
Prof Khalid Hussain	Division Chief, Endocrinology Vice Chair for Research, Department of Paediatric Medicine	Sidra Medical & Research Center
Dr Mahmood Ali Zirie	Senior Consultant and Head of Endocrinology	Hamad Medical Corp

Responsibilities of healthcare professionals

This care map has been issued by the MOPH to define how care should be provided in Qatar. It is based upon a comprehensive assessment of the evidence as well as its applicability to the national context of Qatar. Healthcare professionals are expected to take this guidance into account when exercising their clinical judgement in the care of patients presenting to them.

The guidance does not override individual professional responsibility to take decisions which are appropriate to the circumstances of the patient concerned. Such decisions should be made in consultation with the patient, their guardians, or carers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

Acknowledgements

The following individuals are recognised for their contribution to the successful implementation of the National Diabetes Guidelines.

Healthcare Quality Management and Patient Safety Department of the MOPH:

- **Ms Huda Amer Al-Katheeri**, *Acting Director & Project Executive.*
- **Dr Alanoud Saleh Alfehaidi**, *Guideline & Standardisation Specialist.*
- **Dr Ilham Omer Siddig**, *Guideline & Standardisation Specialist.*
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- **Dr Rasmeh Ali Salameh Al Huneiti**, *Research Training & Education Specialist.*
- **Mr Mohammad Jaran**, *Risk Management Coordinator.*

[1] Dr Ahmed Babiker attended the MOPH in his capacity as a Clinical Pharmacist and advisor on the availability of medications in Qatar.

Diabetes mellitus in children and adolescents

Contributors:

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- **Dr Al-Anoud Mohammed Al-Thani**, *Manager, Health Promotion & Non-Communicable Diseases, MOPH and Co-Chair National Diabetes Committee.*
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- **Dr Samya Ahmad Al Abdulla**, *Senior Consultant Family Physician, Executive Director of Operations, Primary Health Care Corporation.*
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Diabetes mellitus in children and adolescents