# NATIONAL CLINICAL GUIDELINES

## THE ASSESSMENT & MANAGEMENT OF DYSLIPIDAEMIA

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المبادئ الإرشادية السريرية لدولة قطر
NATIONAL CLINICAL GUIDELINES FOR QATAR

وزارة الصحـــــة العامـــــة
Ministry of Public Health
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## Version History

| Version | Status | Date | Editor | Description |
|---|---|---|---|---|
| 1.0 | Final | 14th December 2016 | Guidelines Team | Final version for publication. |
| 1.1 | Final | 19th March 2017 | Guidelines Team | Minor amendments and updates to Section 2. |
| 2.0 | Final | 23rd January 2020 | Guidelines Team | Final version for publication. |

## Citation

Suggested citation style:

Ministry of Public Health Qatar. National Clinical Guideline: The Assessment and Management of Dyslipidaemia (2020).

## Abbreviations

The abbreviations used in this guideline are as follows:

| | |
|---|---|
| **ACC/AHA** | American College of Cardiology / American Heart Association |
| **ALT** | Alanine aminotransferase |
| **ASCVD** | Atherosclerotic cardiovascular disease |
| **AST** | Aspartate aminotransferase |
| **Apo** | Apoprotein |
| **ABC** | ATP-binding cassette |
| **FH** | Familial hypercholesterolaemia |
| **HbA1c** | Glycated haemoglobin |
| **HDL-C** | High density lipoprotein cholesterol |
| **LCAT** | Lecithin-cholesterol acyltransferase |
| **LDL-C** | Low density lipoprotein cholesterol |
| **Lp a** | Lipoprotein A |
| **LPL** | Lipoprotein lipase |
| **PCSK9** | Proprotein convertase subtilisin-like/kexin type 9 |
| **PUFA** | Polyunsaturated Fatty Acids |
| **VLDL** | Very low-density lipoprotein |

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## Table of Contents

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# 1 Information about this Guideline

## 1.1 Objective and Purpose of the Guideline

The purpose of this guideline is to define the appropriate management of dyslipidaemia. The objective is to reduce inappropriate investigation, prescribing and referral of patients presenting to provider organisations in Qatar. It is intended that the guideline will be used primarily by physicians in primary care and outpatient settings.

## 1.2 Scope of the Guideline

Aspects of care covered within this guideline include:

- Definitions and classification.
- Assessment, investigation and management of secondary dyslipidaemia and hypertriglyceridaemia.
- Risk assessment in primary prevention of atherosclerotic cardiovascular disease.
- Lifestyle and pharmacological interventions.

Aspects of care not covered within this guideline:

- Specialist management of primary dyslipidaemias.

## 1.3 Editorial Approach

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.

The editorial methodology, used to develop this guideline, 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 healthcare professionals, subject matter experts and patient representatives, from across Qatar.
- Independent review of the guideline by the National Clinical Guidelines & Pathways Committee, appointed by the MOPH, from amongst stakeholder organisations across Qatar.

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

## 1.4 Sources of Evidence

The professional literature 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 member of the Editorial Team 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.
3. Address an aspect of specific importance to the guideline in question.

Further information about the literature search and appraisal process is included in the appendix.

### 1.5 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 A (RGA):** Evidence demonstrates at least moderate certainty of a net benefit from the recommendation.
- **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 C (RGC):** 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.

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## 1.6 Guideline Development Group Members

The following table lists members of the Guideline Development Group (GDG) nominated by their respective organisations and the National Clinical Guidelines & Pathways Committee. The GDG members have reviewed and provided their feedback and approval of the guideline document. 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 Ahmed M. Hussein Babiker | Head of Registration & Pricing Section, Clinical Pharmacist | Dept of Pharmacy and Drug Control, MOPH[1] |
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| Dr Arif Mahmood | Family Physician | Qatar Petroleum |
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[1] Dr Ahmed Babiker attended the MOPH in his capacity as a Clinical Pharmacist and advisor on the availability of medications in Qatar.

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## 1.7 National Clinical Guidelines & Pathways Committee Members

The following table lists members of the National Clinical Guidelines & Pathways Committee (NCGPC), appointed by the MOPH. The NCGPC members have reviewed and provided their feedback and approval of the guideline document. Each member has completed a declaration of conflicts of interest, which has been reviewed and retained by the MOPH.

| National Clinical Guidelines & Pathways Committee (NCGPC) Members | | |
|---|---|---|
| **Name** | **Title** | **Organisation** |
| Ms Huda Amer Al-Katheeri | Chair of the NCGPC,<br>Director- Strategic Planning & Performance Department | Ministry of Public Health |
| Shk Dr Mohammed Hamad J. Al Thani | Co-Chair of NCGPC,<br>Director of Public Health | Ministry of Public Health |
| Prof Anthony Akobeng | Chair Clinical Practice Guidelines Committee | Sidra Medicine |
| Dr Alshaymaa Mohammed A. M. Al-Motawa | Consultant Family Medicine | Qatar Petroleum |
| Dr Basil Bashqawi | Accreditation Coordinator, Dept of Health Professions | Ministry of Public Health |
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| Dr Ghassan Youseph Hommos | Consultant Endocrinology | Al Emadi Hospital |
| Dr Chris Kenny | Executive Director Clinical and Service Development, Office of the Chief Medical Officer | Hamad Medical Corporation |
| Dr Egon Toft | VP and Dean of College of Medicine | College of Medicine, Qatar University |

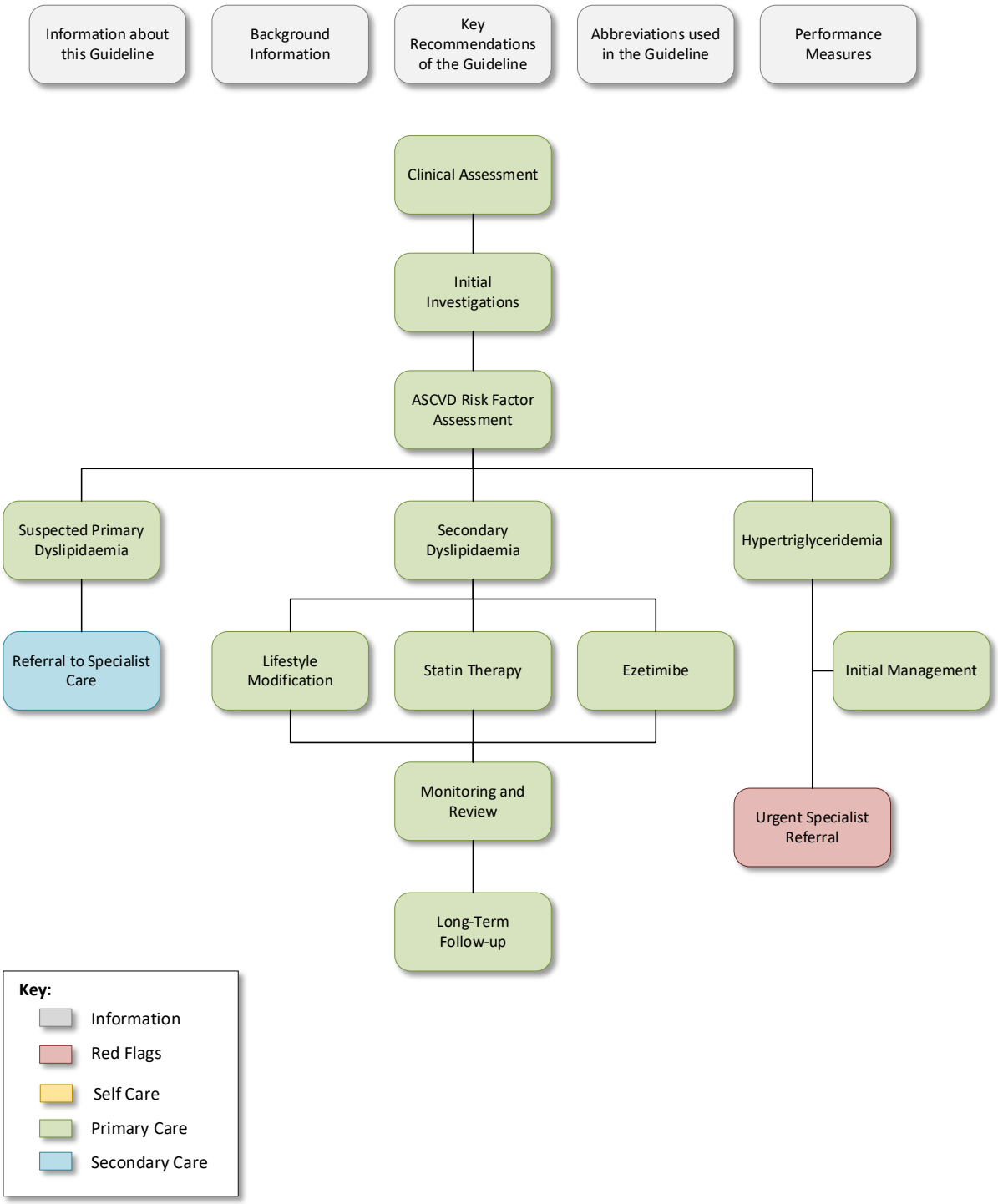
## 1.8 Responsibilities of Healthcare Professionals

This guideline 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 caregivers and should consider the individual risks and benefits of any intervention that is contemplated in the patient's care.

## 2 Dyslipidaemia Management Pathway

Click on a box below to see the relevant page of the Pathway.



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# 3 Key Recommendations of the Guideline

The key recommendations of this guideline are:

**Primary Dyslipidaemias:**

- A primary dyslipidaemia should be considered in adults with raised cholesterol - typically ≥7.5 mmol/L or LDL-C ≥4.9mmol/L, especially in those with a personal or family history of premature coronary artery disease [1–3].
- Refer all patients with a suspected primary dyslipidaemia to a specialist endocrinologist with expertise in dyslipidaemia for further investigation and management [**R-GDG**].

**Assessment of Baseline Lipid Levels:**

- If possible, a 12-hour fasted sample should be performed [4] [**R-GDG**].
- However, a non-fasted sample is also acceptable if fasting is difficult (e.g. diabetic patients on insulin) [1] [**R-GDG**].
- Transaminase levels and creatine kinase should be measured to establish a baseline level prior to initiation of statin therapy [1,3–5].

**Atherosclerotic Cardiovascular Disease (ASCVD) Risk Assessment:**

- The American College of Cardiology / American Heart Association (ACC/AHA) Pooled Cohort Equations should be used to estimate 10-year ASCVD risk in appropriate individuals with and without diabetes [4].
- Available from: http://tools.acc.org/ASCVD-Risk-Estimator/
- NB: The tool can only provide an approximate value of ASCVD risk – interpretation of risk scores should always reflect informed clinical judgement.

**Initiation of Statin Therapy:**

- Unless contraindicated, offer a **moderate intensity statin** in the following patients [4]:
  - Patients aged 40-75 years who have a 10-year risk of ASCVD using the ACC/AHA Pooled cohort equations of ≥7.5%.
  - Patients aged ≥50 years with chronic kidney disease stage 3-5 or those of any age with other manifestations of chronic kidney disease (e.g. albuminuria or polycystic kidney disease) [6].
  - Patients aged 40-75 years with type 2 diabetes mellitus with a 10-year risk of ASCVD using the ACC/AHA Pooled Cohort Equations of <7.5%.
- Unless contraindicated, offer a **high intensity statin** to the following patients [4,5]:
  - Pre-existing ASCVD - for secondary prevention [1,4,5].
  - All patients with an LDL-C level of ≥4.9 mmol/L.
  - Patients aged 40-75 years with type 2 diabetes mellitus who have a 10-year risk of ASCVD using the ACC/AHA Pooled Cohort Equations of ≥7.5%.
  - Adults with type 1 diabetes who:
    - Are older than age 40 years; or
    - Have had diabetes for more than 10 years; or
    - Have established nephropathy; or
    - Have other ASCVD risk factors.
- Statin therapies should be considered in conjunction with lifestyle advice which should continue throughout drug treatment, where pharmacological intervention is indicated (see *Section 8.1*) [1,4,5,7].

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**Treatment Targets for Initiation of Statins:**

- Use the following treatment targets to guide escalation or continuation of statin therapy:
    - If the patient was started on **high-intensity** statin therapy [1,4] [**R-GDG**]:
        - Aim for a reduction in LDL-C of ≥50% from the untreated baseline level; or
        - An absolute level of LDL-C of <1.8 mmol/L (whichever is lower).
    - If the patient was stated on **moderate-intensity** statin therapy [1,4] [**R-GDG**]:
        - Aim for a reduction in LDL-C of 30%-50% from the untreated baseline level; or
        - An absolute level of LDL-C of <2.6 mmol/L (whichever is lower).

**Management of Hypertriglyceridaemia:**

- Extreme triglyceride levels are associated with [5]:
    - Acute pancreatitis.
    - High risk of morbidity and mortality independent of ASCVD.
- Refer for urgent specialist review if the triglyceride concentration is ≥20 mmol/L.
- In patients with a triglyceride concentration of 10-20 mmol/L:
    - Repeat the triglyceride measurement with a fasting test (after an interval of 5 days, but within 2 weeks); and
    - Review for potential underlying causes of the hypertriglyceridaemia; and
    - Seek specialist advice if the triglyceride concentration remains ≥10 mmol/L.
- In patients with a triglyceride concentration of 4.5-9.9 mmol/L:
    - Be aware that the ASCVD risk may be underestimated by risk assessment tools.
    - Statins have been shown to reduce triglycerides in patients with these levels.
    - Seek specialist advice if the non-high-density lipoprotein cholesterol concentration is ≥7.5 mmol/L.
- Statins are the first choice to reduce both total ASCVD risk and moderately elevated triglyceride levels [1].

# 4 Background Information

## 4.1 Definitions and Classification

**Dyslipidaemia** [1,2] :

- Dyslipidaemia is the result of disturbance in lipid metabolism which leads to changes in plasma lipoprotein levels and/or function.
- Dyslipidaemia covers a broad spectrum of lipid abnormalities, including:
    - Elevation of total cholesterol and low-density lipoprotein cholesterol (LDL-C).
    - The atherogenic lipid triad, which consists of:
        - Increased very low-density lipoprotein (VLDL) remnants shown as mildly elevated triglycerides.
        - Increased LDL-C - especially small dense LDL particles.
        - Reduced high density lipoprotein-cholesterol (HDL-C) levels.
    - Dyslipidaemia may be classified by the pattern of elevated lipids or as either primary or secondary according to the underlying cause.

**Fredrickson Classification System**:
The Fredrickson phenotype classification system traditionally classifies dyslipidaemias by the type of lipid and lipoproteins that are elevated [8]. The table below outlines the Fredrickson classification system [8]:

| Phenotype | Elevated Lipoprotein(s) | Elevated Lipids |
|---|---|---|
| I | Chylomicrons | Triglycerides |
| IIa | LDL | Cholesterol |
| IIb | LDL and VLDL | Triglycerides and cholesterol |
| III | VLDL and chylomicron remnants | Triglycerides and cholesterol |
| IV | VLDL | Triglycerides |
| V | Chylomicrons and VLDL | Triglycerides and cholesterol |

***Table 4.1:*** Fredrickson classification system [8].

**Primary Dyslipidaemias** [1–3,9]:

- Primary dyslipidaemias are typically diagnosed when considerable atherosclerosis has already developed at any early age.
- If untreated, they lead to death typically in adolescence or early adulthood due to myocardial ischaemia or aortic stenosis.
- The use of ASCVD risk estimation tools is not recommended in patients with FH who are already at high risk of premature ASCVD.

**Secondary Dyslipidaemia** [1,2]:

- The most common cause of dyslipidaemia.
- Dyslipidaemia is caused by an underlying factor which is not directly related to the genetics of lipid metabolism.
- Causes are listed in *Section 4.2.2* and include:
    - Sedentary lifestyle with diet high in saturated fats, cholesterol and trans fats.
    - Diabetes mellitus.

- Excessive alcohol intake.
- Liver disease.
- Chronic kidney disease.
- Drugs.

**Hypertriglyceridaemia** [1,5,10]:

- Elevated fasting triglycerides >1.7 mmol/L are associated with increased ASCVD risk, especially when HDL-C is low.
- Extreme hypertriglyceride levels are associated with high risk of morbidity and mortality independent of ASCVD risk.
- Triglyceride levels >10 mmol/L are associated with an increased risk of acute pancreatitis:
  - Hypertriglyceridaemia is the cause of 10% of all cases with acute pancreatitis.
  - Patients are at increased risk of acute pancreatitis even when their triglyceride concentration is between 5 and 10 mmol/L.

## 4.2 Aetiology

### 4.2.1 Primary Dyslipidaemias

The table below lists the known primary causes of dyslipidaemia with prevalence or estimates of prevalence where known [2]:

| Primary disorder | Genetic defect/mechanism | Prevalence |
|---|---|---|
| **Primary hypoalphalipoproteinemia (familial or nonfamilial)** | • Unknown, possibly apo A-I, C-III, or A-IV. | • c.5% of the population |
| **Polygenic hypercholesterolaemia** | • Unknown, possibly multiple defects and mechanisms. | • Common |
| **Familial combined hyperlipidaemia** | • Unknown, possibly multiple defects and mechanisms. | • 1/50 to 1/100 |
| **Familial hypertriglyceridaemia** | • Unknown, possibly multiple defects and mechanisms. | • 1/100 |
| **Familial hypercholesterolaemia** | • LDL receptor defect.<br>• Defective LDL clearance. | • Heterozygotes: 1/200 to 1/500<br>• Homozygotes: 1/1 million |
| **Familial defective apoprotein (apo) B-100** | • Apo B (LDL receptor–binding region defect)<br>• Diminished LDL clearance. | • 1/700 |
| **Familial dysbetalipoproteinemia** | • Apo E (usually e2/e2 homozygotes).<br>• Diminished chylomicron and VLDL clearance. | • 1/5000 |
| **Apo C-II deficiency** | • Apo C-II (causing functional LPL deficiency). | • < 1/1 million |
| **Lipoprotein lipase (LPL) deficiency** | • Endothelial LPL defect.<br>• Diminished chylomicron clearance. | • Rare |
| **Familial apo A/apo C-III deficiency/mutations** | • Apo A or apo C-III<br>• Increased HDL catabolism | • Rare |
| **Tangier disease.** | • ATP-binding cassette transporter A1 *(ABCA1)* gene. | • Rare |

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| Primary disorder | Genetic defect/mechanism | Prevalence |
|---|---|---|
| **Familial HDL deficiency** | • *ABCA1* gene | • Rare |
| **Cerebrotendinous xanthomatosis** | • Hepatic mitochondrial 27-hydroxylase defect | • Rare |
| **Sitosterolemia** | • ATP-binding cassette subfamily G members 5 and 8 (*ABCG5* and *ABCG8)* genes | • Rare |
| **Cholesteryl ester storage disease and Wolman disease** | • Lysosomal esterase deficiency | • Rare |
| **Hepatic lipase deficiency** | • Hepatic lipase | • Extremely rare |
| **Familial lecithin-cholesterol acyltransferase (LCAT) deficiency** | • *LCAT* gene | • Extremely rare |
| **Fisheye disease (partial LCAT deficiency)** | • *LCAT* gene | • Extremely rare |
| **Proprotein convertase subtilisin-like/kexin type 9 (PCSK9) gain of function mutations** | • Increased degradation of LDL receptors. | • Unknown |

**Table 4.2.1:** Causes of primary dyslipidaemia [2].

### 4.2.2 Secondary Dyslipidaemias

Causes of secondary dyslipidaemia include the following [1,4,5,10]:

- Hypothyroidism.
- Liver disease.
- Biliary obstruction.
- Nephrotic syndrome.
- Cushing's syndrome.
- Anorexia nervosa.
- Weight gain.
- Obesity.
- Diet high in saturated fat, cholesterol and/or trans fats.
- Pregnancy.
- Excessive alcohol consumption.
- Drugs, including:
    - Androgens.
    - Ciclosporin.
    - Thiazide diuretics.
    - Glucocorticoids.
    - Amiodarone.

Additional conditions which may also cause hypertriglyceridaemia [1,4,5,11,12]:

- Uncontrolled diabetes mellitus or obesity:
    - Hypertriglyceridaemia alone is the more common presentation.
- Chronic renal failure.
- Renal replacement therapy or end stage chronic kidney disease.
- Very low-fat diets.
- Diet high in refined carbohydrates.
- Monoclonal gammopathy.
- Autoimmune disorders, e.g., paraproteinaemia or SLE.

- Lipodystrophies.
- Drugs, including:
    - Retinoic acid derivatives e.g., tretinoin and isotretinoin.
    - Beta-blockers (except carvedilol).
    - Anti-retroviral medications (protease inhibitors).
    - Oestrogens, especially oral.
    - Tamoxifen.
    - Bile acid-binding resins.
    - Psychotropic medications: phenothiazines, second generation antipsychotics.
    - Anabolic steroids.
    - Sirolimus.
    - Raloxifene.

## 4.3 Epidemiology

The incidence and prevalence of primary dyslipidaemias in Qatar is unknown at present. However, in 2013 in Qatar, 12.9% of registered deaths were related to cardiovascular disease [13].

The 2012 Qatar STEPwise survey showed the following prevalence for key ASCVD risk factors in the surveyed population [14]:

- Raised total cholesterol (i.e. ≥5.0 mmol/L or currently taking medication for raised cholesterol):
    - 21.9% of both sexes.
    - 19.1% of men.
    - 24.6% of women.
- Low HDL levels (i.e. <1.03 mmol/L for men; <1.29 mmol/L for women):
    - 49.2% of men.
    - 37.3% of women.
- High LDL-C levels (i.e. ≥3.3 mmol/L):
    - 8.2 % of men.
    - 9.9% of women.
- High fasting triglycerides (i.e. ≥1.7 mmol/L):
    - 16% of men.
    - 15.6% of women.

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# 5 Clinical Assessment

## 5.1 Dyslipidaemia

If a patient is found to have a dyslipidaemia following lipid measurement [5]:

- Consider the possibility of a familial lipid disorder using:
    - Clinical findings.
    - Lipid profile.
    - Family history.
- Exclude possible underlying causes – See *Section 4.2: Aetiology.*
    - The most common underlying causes are [4]:
        - Excessive alcohol intake.
        - Uncontrolled diabetes mellitus.
        - Overt albuminuria.
- Consider referral if [4,5]:
    - A primary dyslipidaemia is suspected.
    - If the triglyceride level warrants specialist review – i.e. levels ≥5 mmol/L.
- Consider lipid-modifying treatment for primary or secondary prevention based on the patient's atherosclerotic cardiovascular disease (ASCVD) 10-year risk, if appropriate (see *Section 8.2*) [4].

Ask patients with raised cholesterol levels about [1,3]:

- Their personal or family history of premature ASCVD.
- Other ASCVD risk factors, e.g.:
    - Smoking status.
    - Alcohol consumption.
    - Hypertension.
    - Diabetes.

Clinical assessment should include measurement of [5]:

- Blood pressure.
- Body mass index, or other measures of obesity e.g. waist and neck circumference.

Examine for clinical signs of primary dyslipidaemia, e.g. [1–3]:

- Tendinous xanthomata:
    - Detected as nodularity or thickening of the tendons.
    - Are most commonly found on the extensor tendons on the dorsum of the hand, elbows, knees and the Achilles tendon.
- Corneal arcus.
- Xanthelasma.

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## 5.2 Suspected Primary Dyslipidaemia

A primary dyslipidaemia should be considered in adults with raised cholesterol - typically ≥7.5 mmol/L or LDL-C ≥4.9mmol/L, especially in those with a personal or family history of premature coronary artery disease [1–3].

Consider a clinical diagnosis of homozygous familial hypercholesterolaemia (FH) if the LDL-C is [3]:

- ≥13 mmol/L in adults.
- ≥11 mmol/L in children.

Record at least a three-generation pedigree if possible, including the following information regarding each relative [3]:

- Age of onset of ASCVD, if any.
- Age and cause of death (if deceased).
- Known lipid concentrations.
- Smoking history.

The diagnosis of FH is based on the Simon Broome criteria [3]. The lipid levels used to make the diagnosis should either be taken pre-treatment or be the highest recorded whilst on treatment.

**Definite FH** is diagnosed if the following criteria are met [3]:

- Total cholesterol >6.7 mmol/L; or LDL-C of >4.0 mmol/L in a child aged <16 years; or
- Total cholesterol >7.5 mmol/L; or LDL-C of >4.9 mmol/L in an adult.
- PLUS at least one of the following:
    - Tendon xanthomas in the patient, or in either a first-degree relative (i.e. parent, sibling, child), or in second-degree relative (i.e. grandparent, uncle, aunt).
    - DNA-based evidence of an LDL-receptor mutation, familial defective apoB-100, or a PCSK9 mutation.

**Possible FH** is diagnosed if the following criteria are met [3]:

- Total cholesterol > 6.7 mmol/L; or LDL-C of >4.0 mmol/L in a child aged <16 years; or
- Total cholesterol >7.5 mmol/L; or LDL-C of >4.9 mmol/L in an adult.
- PLUS at least one of the following:
    - Family history of myocardial infarction at:
        - Age <50 years in a second-degree relative; or
        - Age <60 years in a first-degree relative.
    - Family history of raised cholesterols of:
        - >7.5 mmol/L in an adult first- or second-degree relative; or
        - >6.7 mmol/L in a child, brother or sister aged <16 years.

NB: the absence of clinical signs such as tendon xanthomata does not exclude a diagnosis of FH [3,15].

Familial combined hyperlipidaemia is distinguished from FH by [15]:

- The absence of tendon xanthoma.
- The presence of small, dense LDL.
- The presence of other types of dyslipidaemia in the patient's family – types IIa, IIb, and IV
- In children – a lower degree of increase in LDL-C level compared to that observed in FH.

NB: Refer all patients with a suspected primary dyslipidaemia to a specialist endocrinologist with expertise in dyslipidaemia for further investigation and management [**R-GDG**].

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# 6 Investigations

## 6.1 Initial Investigations for Dyslipidaemia

Baseline blood tests, before starting statin therapy and to exclude underlying causes, should include [1,3–5]:

- Lipid profile: i.e. total cholesterol, LDL-C, HDL-C and triglycerides:
  - If possible, a 12 hour fasted sample should be performed [4] [**R-GDG**].
  - However, a non-fasted sample is also acceptable if fasting is difficult (e.g. diabetic patients on insulin) [1] [**R-GDG**].
- HbA1c: If the diabetes status unknown.
- Renal function and eGFR.
- Urine microalbumin level.
- Transaminase levels (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)).
- Thyroid stimulating hormone.
- Creatine kinase – to establish a baseline level prior to initiation of statin therapy.

## 6.2 Further Investigations for Primary Dyslipidaemias

### 6.2.1 Repeat Lipid Profile

If the initial lipid profile was not fasted and the triglyceride level is borderline or high, confirm the diagnosis with a fasting lipid profile concentration [1].

### 6.2.2 Genetic Testing

Genetic testing increases the certainty of the diagnosis and aids diagnosis amongst relatives [3,15]. All patients with a primary dyslipidaemia should be offered referral to an endocrinologist with expertise in primary dyslipidaemias - in order to confirm the diagnosis and initiate cascade testing of relatives [3].

NB: Genetic testing should only be requested by a specialist, if a primary dyslipidaemia is suspected based on personal and family history, clinical examination and/or lipid profile results [**R-GDG**].

### 6.2.3 Baseline ECG

Consider a baseline ECG for adults suspected of having a primary dyslipidaemia [3,15].

### 6.2.4 Specialist Assessment

Specialist investigation of patients with a primary dyslipidaemia includes [3,9]:

- A comprehensive cardiovascular assessment.
- Cardiovascular disease assessment as indicated, e.g.:
  - Doppler echocardiographic of the heart and aorta.
  - CT coronary angiography.
  - Stress testing.

In all patients with a primary dyslipidaemia, screening for ASCVD before starting prescribed physical activity is important. An exercise ECG and echocardiography should therefore be considered [15].

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# 7 Assessing Atherosclerotic Cardiovascular Disease Risk

## 7.1 Atherosclerotic Cardiovascular Disease

Risk of atherosclerotic cardiovascular disease (ASCVD) [1,4,10]:

- Cardiovascular disease represents a group of diseases caused by atherosclerosis including coronary artery disease, ischaemic stroke, and peripheral arterial disease.
- ASCVD risk estimates the likelihood of developing an atherosclerotic CV event over a defined period.
- The American College of Cardiology / American Heart Association (ACC/AHA) guidelines define *clinical* ASCVD as acute coronary syndromes, or a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischaemia attack, or peripheral arterial disease presumed to be of atherosclerotic origin [4].
- Management aims to reduce the overall risk by addressing the modifiable risk factors [5]:
    - Modifiable risk factors for ASCVD include [1,5]:
        - Smoking.
        - Impaired glucose tolerance or diabetes mellitus.
        - Dyslipidaemia.
        - Hypertension.
        - Sedentary lifestyle.
        - Unhealthy dietary habits.
        - Excess alcohol intake.
        - Psychosocial stress.
        - Obesity.
    - Non-modifiable risk factors include [1,5]:
        - Age:
            - Apart from rare inherited disorders, age is the most important determinant of an individual's risk of ASCVD:
            - ASCVD predominantly affects people over the age of 50 years.
        - Gender:
            - Men have a higher prevalence of coronary artery disease until the age of 75 years.
            - Women aged <75 years have a higher incidence of stroke [8].
        - Family history of premature ASCVD.
        - Ethnicity.

Risk estimation tools should not be used for the following groups of patients who are already at high risk [3,5]:

- Primary dyslipidaemia.
- Type 1 diabetes mellitus – ASCVD risk assessment should be based on the patient's age and the duration since diagnosis.
- Chronic kidney disease stages 3-5 (refer also to the *MOPH National Guideline for Chronic Kidney Disease* [16]).
- Patients aged over 75 years.
- Patients with established cardiovascular disease.

NB: For detailed information on ASCVD risk assessment please refer to the *MOPH National Guideline on Atherosclerotic Cardiovascular Disease Risk Assessment and Management* [17].

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## 7.2 Risk Factor Assessment

Assessment of ASCVD risk [3–5,10]:

- Multiple risk factors contribute to an individual's overall risk of an ASCVD event.
- Management aims to reduce this overall risk by addressing the modifiable risk factors.
- Risk assessment should determine the patient's overall risk of a future ASCVD event.
- NB: Risk is not static and should be repeated every 4-6 years from the age of 40, until either treatment has been started or ASCVD has become established.
- ApoB analysis is recommended for risk assessment and can be used as a replacement for LDL-C for initial screening and management especially in patients with hypertriglyceridaemia, diabetes mellitus, or metabolic syndrome [1] **[L1, RGA]**.
- Patients with very high inherited Lp(a) levels >180 mg/dL may have a lifetime risk of ASCVD equal to the one of those with heterozygous familial hypercholesterolaemia. Thus, Lpa measurement is recommended at least once [1] **[L1, RGA]**.

Patients with established ASCVD can be assumed to be high risk and do not require formal risk assessment[5]. An ASCVD risk assessment tool should not be used in patients diagnosed with primary dyslipidaemias [3].

Risk assessment tools [4]:

- The ACC/AHA Pooled Cohort Equations should be used to estimate 10-year ASCVD risk in appropriate individuals with and without diabetes.
- Available from: http://tools.acc.org/ASCVD-Risk-Estimator/
- NB: The tool can only provide an approximate value of ASCVD risk – interpretation of risk scores should always reflect informed clinical judgement.

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# 8 Management of Secondary Dyslipidaemia in Primary Care

All patients with primary dyslipidaemia need aggressive lipid reduction to reduce ASCVD risk. Refer all patients suspected of having a primary dyslipidaemia to a specialist endocrinologist with expertise in dyslipidaemias, for further investigation and management [**R-GDG**].

If diagnosis of a primary dyslipidaemia is not suspected, cardiovascular risk should be managed as for an individual of the same age and gender in the general population [3].

Management of patients at risk of ASCVD involves [4,5]:

- Lifestyle modification.
- Pharmacological management.
    - Prior to starting treatment ensure:
        - A clinical assessment and appropriate investigations have been performed (see *Sections 5 & 6*).
        - Comorbidities and underlying causes of secondary dyslipidaemia have been considered and treated, where present.

## 8.1 Lifestyle Modification

General considerations [1,4,5,7]:

- Discuss positive effects of altering lifestyle habits.
- Offer optimal management of other modifiable ASCVD risk factors.
- Recognise the need for additional support for lifestyle changes such as:
    - Referring patients to exercise programmes.
- Reassess the risk of ASCVD in patients who have tried to modify their lifestyle.
- NB: It may not be appropriate to delay statin treatment until after lifestyle modification has occurred in those patients at higher levels of ASCVD risk.
- Lifestyle advice should continue with drug treatment.
- Advice should also consider the patient's needs, preferences and circumstances.

### 8.1.1 Diet

Provide support for patients to consume a diet associated with the lowest cardiovascular risk, based on the following principles [2,3,5,5,10,18] [**L1**]:

- A fat intake of 30% or less than total energy intake.
- A saturated fat intake of 10% or less of the total energy intake.
- Replace saturated fats with monounsaturated and polyunsaturated fats.
- A cholesterol intake of <300mg per day.
- At least five portions of fruit and vege*tables* per day − legumes other than soy have been shown to decrease total and LDL-C.
- At least two portions of fish per week, including a portion of oily fish – pregnant women should limit their intake of oily fish to two portions a week, and avoid marlin, shark and swordfish.
- Do not routinely recommend omega-3 fatty acid supplements.
- Inform people who wish to consume food products containing stanols and sterols, that they need to be eaten consistently to be effective [10] [**L1, RGA**].
- Individualised nutritional advice should be offered by a healthcare professional with specific expertise in nutrition.

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### 8.1.2 Alcohol Consumption

Alcohol consumption [10]:

- Advise men who drink alcohol, to limit their alcohol intake to 3-4 units a day.
- Advise women who drink alcohol, to limit their alcohol intake to 2-3 units a day.
- Advise the avoidance of binge drinking.

### 8.1.3 Physical Activity

Physical activity [1,3,4] [**L2, RGA**]:

- Screening for ASCVD before starting prescribed physical activity is important.
- Recommend 30 minutes of at least moderate intensity exercise, at least 5 days a week (or the maximum safe capacity for those unable to manage the recommended level):
    - Advise that this can be broken down into 10-minute sessions (or more) and accumulated throughout the day.
    - Suggest activities that can be easily incorporated into daily routine, e.g.:
        - Cycling.
        - Using stairs rather than elevators.
        - Brisk walking.

### 8.1.4 Weight Management

Offer overweight and obese patients support and advice to achieve a healthy weight [3]. Refer also to the *MOPH National Guideline on Obesity* [19], if the patient has a BMI of ≥30 kg/$m^2$.

### 8.1.5 Smoking Cessation

Advise the patient to stop smoking [1,3–5,8] [**L1, RGA**]:

- Offer support, advice, and referral to an intensive support service.
- If the patient does not wish to accept referral, offer appropriate pharmacotherapy.
- Refer to the *MOPH National Guideline on Tobacco cessation* [20].

## 8.2 Consider Statin Therapy

Before a decision is made about starting with statin, the clinician should inform the patient about the risks and benefits of the treatment [1].

Consider the following, particularly for older people (over 75 years) [5]:

- Potential benefits from lifestyle modifications.
- Informed patient preference.
- Comorbidities.
- Polypharmacy.
- General frailty.
- Life expectancy.

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**Before offering statin treatment** [5]:

- Assess if the patient has muscle pain that is either persistent, generalised or unexplained and associated with or without previous lipid-lowering therapy.
- All patients should have a baseline creatine kinase level measurements performed [5] [**R-GDG**]:
    - If creatine kinase levels are >5 times the upper limit of normal, measure levels again kinase after 7 days [5]:
        - Do not commence statin therapy if creatine kinase levels remain >5 times the upper limit of normal.
    - If creatine kinase levels are raised but <5 times the upper limit of normal, a low dose statin should be initiated [5].
- All patients should have baseline liver function tests performed. If transaminase levels are raised but <3 times the upper limit of normal, statin therapy can still be initiated [5].

### 8.2.1 Low, Moderate and High Intensity Statin Therapies

The following statin therapies are classified as either high, moderate or low intensity and are used according the patient's history, or risk, of ASCVD [4] (see subsequent *sections*).

| High Intensity Therapies | | Moderate Intensity Therapies | | Lower Intensity Therapies | |
|---|---|---|---|---|---|
| Atorvastatin | 40-80 mg | Atorvastatin | 10-20 mg | Simvastatin | 10 mg |
| Rosuvastatin | 20-40 mg | Rosuvastatin | 5-10 mg | Pravastatin | 10–20 mg |
| | | Simvastatin | 20-40 mg | | |
| | | Pravastatin | 40-80 mg | | |

**Table 8.2.1:** Low, moderate and high-intensity statin therapies [4].

### 8.2.2 Primary Prevention of ASCVD

For very high-risk and non-FH patients, it is recommended to reduce LDL-C below 1.4 mmol/L or ≥50% from baseline [1].

Unless contraindicated, offer a **moderate intensity statin** in the following patients [4,6]:

- Patients aged 40-75 years who have a 10-year risk of ASCVD using the ACC/AHA Pooled cohort equations of ≥7.5%.
- Patients aged ≥50 years with chronic kidney disease stage 3-5 or those of any age with other manifestations of chronic kidney disease (e.g. albuminuria or polycystic kidney disease). See also the *MOPH National Guideline on Chronic Kidney Disease.*
- Patients aged 40-75 years with type 2 diabetes mellitus with a 10-year risk of ASCVD using the ACC/AHA Pooled Cohort Equations of <7.5%.

Unless contraindicated, offer a **high intensity statin** to the following patients [4,5]:

- All patients with an LDL-C level of ≥4.9 mmol/L.
- Patients aged 40-75 years with type 2 diabetes mellitus who have a 10-year risk of ASCVD using the ACC/AHA Pooled Cohort Equations of ≥7.5%.
- Adults with type 1 diabetes who:
    - Are older than age 40 years; or
    - Have had diabetes for more than 10 years; or
    - Have established nephropathy; or
    - Have other ASCVD risk factors.

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### 8.2.3 Secondary Prevention of ASCVD

For very high-risk, it is recommended to reduce LDL-C to <1.4 mmol/L or ≥50% from baseline [1]. In case of a second vascular event within 2 years, providing the patient is taking the highest tolerated dose, the LDL-C should be reduced to <1 mmol/L [1].

Unless contraindicated, offer a high-intensity statin to all patients with pre-existing ASCVD for secondary prevention [1,4,5]:

- Do not delay statin therapy for lifestyle modification.
- Use a lower dose if any of the following apply [5] [**L1, RGA**]:
    - Potential drug interactions.
    - High risk of adverse effects.
    - Patient preference.

### 8.2.4 Contraindications to Statins

Contraindications for statins include [3,7,12]:

- Patients who are pregnant or breastfeeding.
- Patients with active liver disease.
- Patients with established skeletal myopathy.

## 8.3 Consider Ezetimibe as an Alternative or Combined with Statin

Increasing the statin therapy dose is recommended prior to the initiation of combination therapy [1]. Ezetimibe is a recommended option for hypercholesterolaemia in adults, under the following conditions [21] [**L1, RGA**]:

- In conjunction with initial statin treatment when:
    - Serum total cholesterol or LDL-C levels are not appropriately controlled after titration of the statin treatment; or dosing is limited by intolerance to the statin.
- As monotherapy if there is:
    - A contraindication to initial statin treatment.
    - Intolerance to statin treatment.
- In very high-risk patients who do not achieve the desired levels of LDL despite taking the highest tolerated dose of statins and ezetimibe, adding a PCSK9 inhibitor is recommended [21] **[L1, RGA]**.

Adverse reactions [21]:

- When given as a monotherapy, most commonly include:
    - Abdominal pain.
    - Diarrhoea and/or flatulence.
    - Fatigue.

- When given together with a statin, most commonly include:
    - Increased ALT and/or increased AST.
    - Headache.
    - Myalgia.

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## 8.4 Special Considerations in Patients with Diabetes Mellitus

Type I diabetes mellitus [5]:

- Offer statin treatment for patients with type 1 diabetes mellitus who:
  - Are older than 40 years; or
  - Have had diabetes for more than 10 years; or
  - Have established nephropathy; or
  - Have other ASCVD risk factors.

Type 2 diabetes mellitus [4]:

- Offer statin therapy for all patients over age 40 years, irrespective of cholesterol value or 10-year ASCVD risk [4] [**L1, RGA**].
- Offer **high-intensity statin therapy** for those [4] [**L1, RGA**]:
  - With established ASCVD.
  - With a 10-year risk of ASCVD using the ACC/AHA Pooled cohort equations of ≥7.5%.
  - With persistent proteinuria or CKD with eGFR 30–60 mL/min.
  - Unable to achieve non-HDL cholesterol targets using a moderate-intensity statin therapy.
  - Statin therapy should be considered for patients with type 2 diabetes under age 40 years with any of the following [4,6] [**L2, RGA**]:
    - Persistent albuminuria.
    - Estimated glomerular filtration rate (eGFR) less than 60mL/min.
    - Proliferative retinopathy.
    - Treated high blood pressure.
    - Autonomic neuropathy.

In patients aged over 75 years with diabetes mellitus [4]:

- Evaluate the potential benefit of reducing ASCVD risk.
  - The risk of adverse effects and drug-drug interactions.
  - Consider also patient preferences when deciding whether to initiate, continue, or intensify statin therapy.

Pre-menopausal women who are not using proper contraception methods and who have diabetes mellitus, should not be prescribed statins [1] **[L1, RGC]**.

## 8.5 Monitoring and Review

### 8.5.1 Patients on Statin Therapy

Advise patients being treated with a statin [3,5,12]:

- That interaction with concomitant use of other drugs, certain foods or supplements may alter efficacy of statins.
- The importance of always seeking advice from either patient information leaflet, a pharmacist, or prescriber when consuming or contemplating the use of other drugs or supplements.
- That in the event of drug interactions (as seen with macrolide antibiotics), statin treatment can be restarted after a course of the drug has been completed.
- To seek prompt medical attention if they develop muscle symptoms, e.g., pain, tenderness, or weakness.
- The potential of teratogenicity in women of childbearing age and to stop using statin in the event of possible pregnancy:
  - Statin should be stopped 3 months before women try to conceive and can be restarted once breastfeeding is finished.

Caution is advised when using statins in conjunction with foods or drugs that interfere with cytochrome P450 enzymes, such as [22,23]:

- Grapefruit juice.
- Gemfibrozil.
- Amiodarone.
- Calcium channel blockers.

In patients started on statins for primary or secondary ASCVD prevention, those with CKD, and those with type 1 or type 2 diabetes mellitus [5]:

- Do not routinely offer fibrates for ASCVD prevention [5] [**L1,RGA**]:
  - Only use if the patient is intolerant to statins.
- Do not offer [5]:
  - Nicotinic acid [5] [**L1, RGA**].
  - Bile acid sequestrant [5] [**L1, RGA**].
  - Omega-3 fatty acid compounds [5] [**L1, RGA**]:
    - There is no evidence of benefit in preventing ASCVD.

For patients being treated with statins [4,5]:

- Provide annual medication reviews.
  - Liver function tests:
  - Measure within 3 months of starting treatment, and again at 12 months – there is no need to measure thereafter unless clinically indicated.
- Do not routinely exclude patients with transaminase levels that are raised but are <3 times the upper limit of normal, from statin therapy.
- Do not routinely monitor creatine kinase in asymptomatic patients taking a statin, but compare creatine kinase levels against baseline, if muscle symptoms develop.
- Assess fasting lipids after 4-12 weeks of starting treatment:
  - Discuss adherence and timing of dose.
  - Optimise adherence to diet and lifestyle measures.
  - Follow-up every 4-12 weeks thereafter until target LDL-C reductions are achieved.
  - Thereafter 6-12 monthly review of lipid levels is considered acceptable [**R-GDG**].

### 8.5.2 Treatment Targets

Patients on high-intensity statin therapy [1,4] [**R-GDG**]:

- Aim for a reduction in LDL-C of ≥50% from the untreated baseline level; or
- An absolute level of LDL-C of <1.8 mmol/L (whichever is lower).

Patients on moderate-intensity statin therapy [1,4] [**R-GDG**]:

- Aim for a reduction in LDL-C of 30%-50% from the untreated baseline level; or
- An absolute level of LDL-C of <2.6 mmol/L (whichever is lower).

### 8.5.3 Adverse Effects of Statins

Statins are well tolerated by the majority of patients and statin-related side effects are generally mild and not medically serious [23].

Adverse effects [5,12,23–26]:

- Statins are associated with a dose-dependent increased risk of myopathy.
- Advise patients to seek medical advice if they develop muscle symptoms:
    - Such as pain, tenderness, or weakness.
    - Measure creatine kinase if muscle symptoms occur.
    - Explore other causes of muscle pain/weakness and raised creatine kinase if they have previously tolerated statin therapy for more than 3 months.
- Statins may be associated with a level of hyperglycaemia in some patients:
    - Formal diabetes care may be appropriate in this situation.
    - The risk appears to be primarily in those already at increased risk of developing diabetes.
    - However, the overall benefits of statins strongly outweigh the risks, including developing diabetes.
- Erectile dysfunction is an under-recognised adverse effect.
- Weight gain – although this may be due to a moral hazard effect of unhealthy eating in patients taking statins.

### 8.5.4 Statin Intolerance

If taking high intensity statins causes side effects in patients, the following options should be discussed [5]:

- Stopping the statin and if symptoms have resolved, retry again to determine whether side effects are related to the statin.
- Lowering dosage within the same intensity statin group.
- Switching statins to a lower intensity group.

Other key points [5,27]:

- If a patient is intolerant to a statin, clinicians are encouraged to have the patient try other statins before ruling them all out.
- If a patient is intolerant to high-intensity stain, the goal is to treat with the maximum tolerated dose.
- Inform patients that a reduction in ASCVD risk can be achieved with any statin at any dose.
- Side effects of statin therapy cannot be reversed with coenzyme Q10 or vitamin D.
- In high-risk patients intolerant to three different statins, specialist advice should be sought for other treatment options.

### 8.5.5 Long-Term Follow-Up

At annual review, address [4,5]:

- Medicines adherence.
- Lifestyle modifications.
- ASCVD risk factors.
- Benefits and potential risks of changing to a high-intensity statin if stable on a low- or medium-intensity statin.
- Consider 6-12 monthly fasted lipid profile for LDL-C to inform discussion [**R-GDG**].

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# 9 Management of Hypertriglyceridaemia

Extreme triglyceride levels are associated with [5]:

- Acute pancreatitis.
- High risk of morbidity and mortality independent of ASCVD.

## 9.1 Initial Management

Initial management of patients with hypertriglyceridaemia consists of the following [1,5]:

- In patients with a **triglyceride concentration of 4.5-9.9 mmol/L:**
  - Be aware that the ASCVD risk may be underestimated by risk assessment tools.
  - Optimise the management of other ASCVD risk factors present, including environmental and lifestyle factors.
  - Statins have been shown to reduce triglycerides in patients with these levels.
  - Seek specialist advice if the non-high-density lipoprotein cholesterol concentration is ≥7.5 mmol/L.
- In patients with a **triglyceride concentration of 10-20 mmol/L:**
  - Repeat the triglyceride measurement with a fasting test (after an interval of 5 days, but within 2 weeks); and
  - Review for potential underlying causes of the hypertriglyceridaemia; and
  - Seek specialist advice if the triglyceride concentration remains ≥10 mmol/L.
- Refer for urgent specialist review if the **triglyceride concentration is ≥20 mmol/L.**
- Admit the patient to the hospital if they are symptomatic of acute pancreatitis.

## 9.2 General Management Strategy

The general strategy to manage patients with hypertriglyceridaemia consists of the following [1,3]:

- Consider possible underlying causes of hypertriglyceridaemia.
- Lifestyle interventions including:
  - Reduce excess body weight.
  - Increase physical activity.
  - Reduce dietary carbohydrates.
  - Reduce alcohol intake.
  - Replace saturated fat with mono- or polyunsaturated fat.
- Lipid-lowering therapy.

The use of drugs to lower triglycerides should only be considered in patients [1]:

- With a triglyceride level of ≥2.3 mmol/L; and
- Who cannot lower this by lifestyle measures alone; and
- At a high ASCVD risk.

In high risk patients who are prescribed statins and whose triglyceride level remains between 1.5 mmol/L and 5.6 mmol/L, the addition of n-3 PUFAs is recommended [1].

Statins are the first choice to reduce both total ASCVD risk and moderately elevated triglyceride levels [1]. Other medications that can be used in specialist setting to lower triglyceride levels in selected high-risk patients include [1,3] [**L1, RGA**]:

- Fibrates.
- Nicotinic acid.
- Combination medications.

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## 10 Referral to Specialist Care

Patients with dyslipidaemia should be referred to a specialist endocrinology or lipid clinic if they [1,28,29]:

- Have suspected Primary Dyslipidaemia [**R-GDG**]. (See *Section 5.2*).
- Have triglyceride levels >20 mmol/L due to the risk of pancreatitis. Urgent referral is recommended. (Also see *Section 9.2*)
- Are refractory to pharmacological treatment due to the type and severity of their dyslipidaemia or intolerant to first-line agents.
- Require collaborative management with paediatric, nephrology, neurology, vascular surgery and HIV specialist.
- Require special investigations such as apolipoproteins, enzyme testing, DNA genotyping, or more detailed vascular assessment (Also see *Section 6.2*)

## 11 Key Considerations for Patient Preferences

Patient preferences refer to patient perspectives, beliefs, expectations, and goals for health and life, and to the steps employed by individuals in assessing the potential benefits, harms, costs, and limitations of the management options in relation to one another. Patients may have preferences when it comes to defining their problems, identifying the range of management options and selecting or ranking the outcomes used to compare these options.

It is important for healthcare professionals to develop an understanding of the patient as an individual and the unique way in which each person experiences a condition and its impact on their life.

The following recommendations are therefore made for physicians and other healthcare professionals regarding general principles of patient care in Qatar. All clinicians and health care practitioners involved in patients' care in the State of Qatar should:

- **Respect Patients:** Treat patients with respect, kindness, dignity, courtesy and honesty. Ensure that the environment is conducive to discussion and that the patient's privacy is respected, particularly when discussing sensitive, personal issues. Ask the patient how they wish to be addressed and ensure that their choice is respected and used.

- **Maintain Confidentiality:** Respect the patient's right to confidentiality and avoid disclosing or sharing patients' information without their informed consent. In this context, students and anyone not directly involved in the delivery of care should first be introduced to the patient before starting consultations or meetings, and let the patient decide if they want them to stay.

- **Clarify Third-Party Involvement:** Clarify with the patient at the first point of contact whether and how they like their partner, family members or carers to be involved in key decisions about their care or management and review this regularly. If the patient agrees, share information with their partner, family members or carers.

- **Obtain Informed Consent:** Obtain and document informed consent from patients, in accordance with MOPH policy and guidance.

- **Encourage Shared Decision Making:** Ensure that patients are involved in decision making about their own care, or their dependent's care, and that factors that could impact the patient's participation in their own consultation and care including physical or learning disabilities, sight, speech or hearing impairments and problems with understanding, reading or speaking English are addressed.

- **Disclose Medical Errors:** Disclose errors when they occur and show empathy to patients.

- **Ensure Effective Communication:** Explore ways to improve communication including using pictures, symbols or involving an interpreter or family members. Avoid using medical jargon. Use words the patient will understand and confirm understanding by asking questions.

**Ensure Continuity of Care:** Provide clear and timely sharing of patient information between healthcare professionals especially at the point of any transitions in care.

## 12 Performance Measures

A list of performance measures is given in the table below. Healthcare organisations are encouraged to monitor service performance using the indicator definitions below [30].

| Number | Numerator | Denominator |
|---|---|---|
| DL01 | The number in the denominator who receive a moderate intensity statin therapy. | Total number of patients aged 40-75 years without a diagnosis of diabetes mellitus, or a prior diagnosis of an ASCVD condition, who are assessed to have a 10-year ASCVD risk of ≥7.5%, using the ACC Pooled Cohort Equations |
| DL02 | The number in the denominator who were commenced on a high intensity statin therapy regimen in the last 12 months. | Total number of patients aged 40-75 years with a diagnosis of diabetes mellitus and a baseline 10-year ASCVD risk of ≥7.5%, using the ACC Pooled Cohort Equations. |
| DL03 | The number in the denominator who achieve a reduction of ≥30% in LDL-C from the untreated baseline level, or an absolute reduction of LDL-C to <2.6 mml/L. | Total number of patients aged 40-75 years who have been started on moderate intensity statins in the past 12 months. |

**Table 12.1:** Performance measures [30].

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## Appendix A: Detailed Description of the Literature Search

A systematic search for existing literature on dyslipidaemia was performed in the period 8th December - 19th December 2019.

All existing references were evaluated and where necessary and applicable, the latest version of the specific manuscript was used to update the guideline and replace the older reference. The search for clinical practice guidelines on dyslipidaemia assessment and/or management was performed in the *PubMed* database and websites of relevant organisations and societies including the *European Society of Cardiology*, the *Joint British Societies,* the *Institute for Clinical Systems Improvement*, the *American College of Cardiology*, and the *Scottish Intercollegiate Guideline Network*. The present guideline is primarily based on *UK NICE*, *ESC/EAS*, and *ACA*/*AHA* guidelines and is supplemented with other relevant studies.

Peer-reviewed scientific publications were found in PubMed and via *Google Scholar* Internet search engine. Non-peer reviewed studies were identified in *bioRxiv*. Books were checked on *Amazon* and via *Google* and *Google Scholar* search engines.

The included publications were identified using the terms “dyslipidaemia” and specified with the following terms in combinations:

*guideline, epidemiology, definition, prevalence, risk factors, screening, diagnosis, symptoms, management, investigation, treatment, referral, specialist, pharmacological therapy, statin, monitoring, classification, primary, secondary, risk assessment, cholesterol, LDL, VLDL, HDL, triglyceride, ASCVD, familial hypercholesterolaemia, hypertriglyceridaemia, lifestyle, diet, exercise, smoking, follow-up.*

*Figure A.1* on the next page demonstrates graphically the results of the search and application of exclusion criteria.

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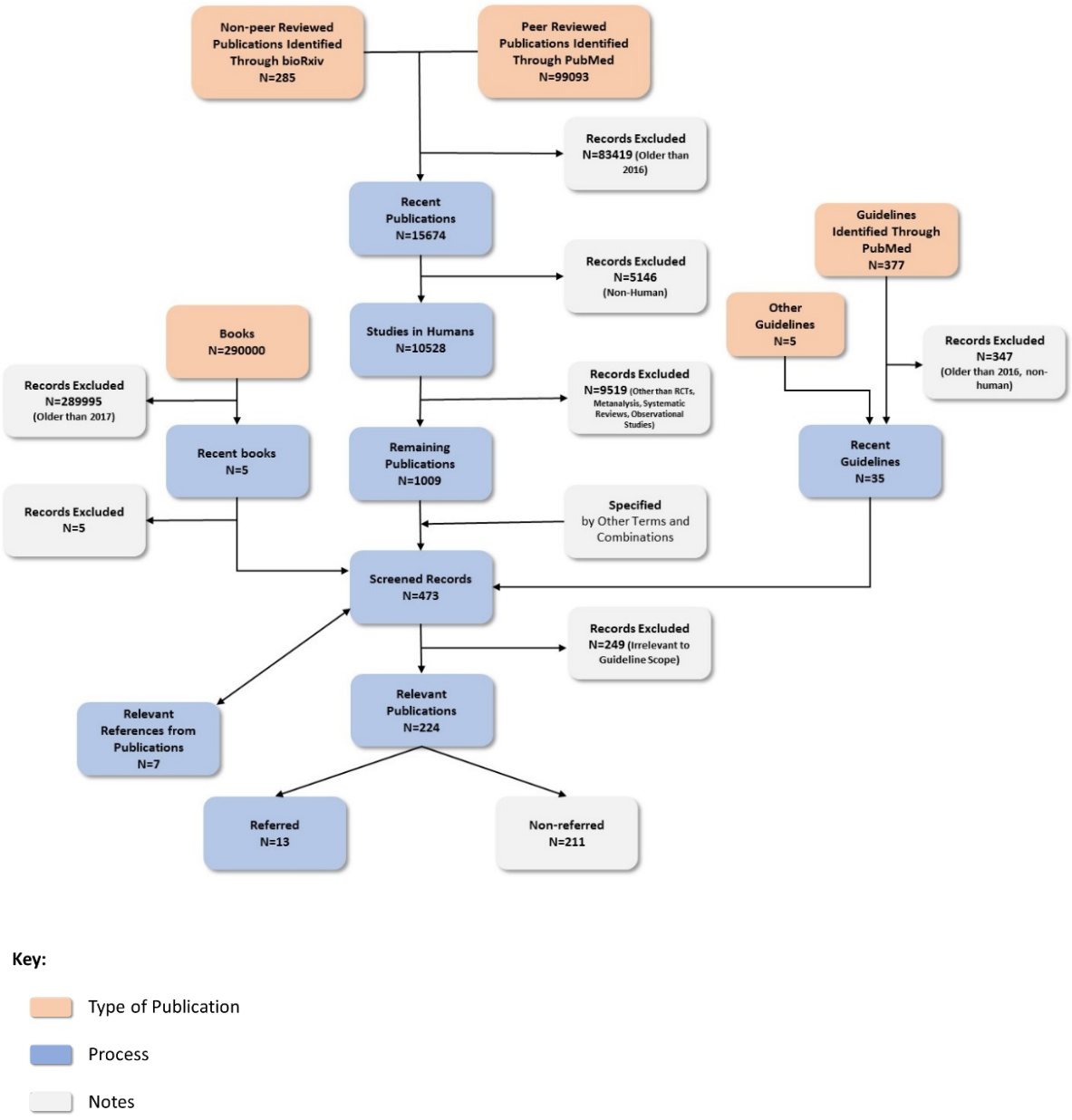


**Fig A.1:** Literature search results and application of exclusion criteria.

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