MINISTRY OF HEALTH
SINGAPORE

Lipids

MOH Clinical Practice Guidelines 2/2016

Chapter of Family Medicine Physicians Academy of Medicine, Singapore

Chapter of Endocrinologists Chapter of General Physicians College of Physicians, Singapore

College of Family Physicians, Singapore

Singapore Cardiac Society

Endocrine & Metabolic Society of Singapore

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Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1^{++}	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1^{+}	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1^{++} and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Lipids

MOH Clinical Practice Guidelines 2/2016

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care.

Contents

Foreword

It has been 10 years since the last edition of the clinical practice guideline for lipids. In that time, numerous studies have been published that have confirmed the benefits of statin therapy for the prevention of cardiovascular disease. In particular, the role of high intensity statins for individuals at the highest risk of coronary artery disease, and the roles of non-statin lipid lowering therapies has been clarified through a number of randomised controlled trials.

The committee has worked hard to come up with a guideline that is as simple as possible, taking into account several recent changes in the guidelines published by organisations in other countries. I hope these guidelines will assist all doctors, particularly primary care physicians, to provide the most appropriate treatment to their patients.

ASSOCIATE PROFESSOR BENJAMIN ONG
DIRECTOR OF MEDICAL SERVICES

Commonly used abbreviations

The following is a list of abbreviations commonly used in this set of guidelines (arranged in alphabetical order), and a description of what they represent:

- ALT Alanine transaminase
- ApoA1 Apolipoprotein A1
- ApoB Apolipoprotein B
- AST Aspartate transaminase
- BNP B-type natriuretic peptide
- CAD Coronary artery disease
- DHA Docosahexaenoic acid
- eGFR Estimated glomerular filtration route
- EPA Eicosapentaenoic acide
- HDL High density lipoprotein
- HMG-CoA 3-hydroxy-3-methyl-glutaryl-CoA
- IDL Intermediate density lipoprotein
- LDL Low density lipoprotein
- Lp(a) Lipoprotein(a)
- NT-proBNP N-terminal prohormone of brain natriuretic peptide
- TC Total cholesterol
- TG Triglyceride
- VLDL Very low density lipoprotein
- FH Familial Hypercholesterolemia

List of recommendations

Details of recommendations can be found on the indicated pages.

Key recommendations are highlighted in blue.

Measurement of lipids

	Recommendation	Grade, Level of Evidence	CPG page no.
1	Clinicians should routinely screen men and women aged 40 years and older for lipid disorders.	Grade B, Level 2^{++}	19
2	Clinicians can routinely screen younger adults (men and women aged 18 and older) for lipid disorders if they have other risk factors for CAD.	GPP	19
3	For individuals with screening results within the LDL cholesterol target levels (see Table 7 page 34) and have low TG levels, screening should be repeated at 3 yearly intervals unless they are at very high or high risk of CAD, in which case screening should be repeated annually.	GPP	20
4	A lipid profile should include TC, TG, LDL cholesterol and HDL cholesterol. These should be obtained after 10 to 12 hours of fasting, which is required for the measurement of TG.	Grade D, Level 4	21
5	Routine ApoB and ApoA1 determination is not recommended.	Grade D, Level 4	17
6	Lp(a) determination is not recommended for routine cardiovascular disease screening. However, further to a global cardiovascular risk assessment, Lp(a) measurements may be useful in individuals with strong family history of premature cardiovascular disease.	Grade C, Level 2^{+}	18
7	Physicians and patients may wish to defer lipid tests for at least 2 weeks after a febrile illness as blood lipids may be abnormal after an acute illness such as an infection.	GPP	20

	Recommendation	Grade, Level of Evidence	CPG page no.
8	Patients who suffer myocardial infarction may have depressed cholesterol levels that do not require treatment. These patients should have their blood lipids repeated 3 months after a myocardial infarction.	Grade D, Level 3	20

Risk Assessment

	Recommendation*	Grade, Level of Evidence	CPG page no.
9	The recommended LDL cholesterol target level for the very high risk group is <2.1mmol/L (80mg/dL). The 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults recommended high intensity statin therapy, e.g. atorvastatin 40-80 mg or its equivalent in patients with clinical atherosclerotic cardiovascular disease based on evidence from randomised controlled trials using fixed-dose statin therapy. The physician may consider increasing statin therapy to these doses, if tolerated, even after the LDL cholesterol goal is achieved on a lower dose of statin, especially if the patient is not on other lipid lowering therapy (e.g. ezetimibe).	Grade B, Level 1^{++}	34
10	The recommended LDL cholesterol target level for the high risk group is <2.6mmol/L (100mg/dL). The 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults recommended moderate intensity statin therapy, e.g. simvastatin 20-40 mg or its equivalent in patients with diabetes mellitus without established chronic CAD or chronic kidney disease based on evidence from randomised controlled trials using fixed-dose statin therapy. The physician may consider increasing statin therapy to these doses, if tolerated, even after the LDL cholesterol goal is achieved on a lower dose of statin, especially if the patient is not on other lipid lowering therapy (e.g. ezetimibe).	Grade B, Level 1^{++}	35

	Recommendation*	Grade, Level of Evidence	CPG page no.
11	The recommended LDL cholesterol target level for the intermediate risk group is <3.4mmol/L (130mg/dL), with an LDL cholesterol level of <2.6mmol/L (100mg/dL) being an option if the physician feels that the benefits of more intensive therapy outweigh the risks.	Grade B, Level 1^{++}	35
12	The recommended LDL cholesterol target level for the low risk group is <4.1mmol/L (160mg/dL), with an LDL cholesterol level of <3.4mmol/L (130mg/dL) being an option if the physician feels that the benefits of more intensive therapy outweigh the risks.	Grade B, Level 1^{++}	36
13	In patients with 2 consecutive values of LDL cholesterol levels less than 1.03mmol/L (40mg/dL), decreasing the statin dose may be considered.	GPP	37
14	Individuals with very high levels of TG, e.g. >4.5mmol/L (400mg/dL) or especially >10mmol/L (900mg/dL), have an increased risk of acute pancreatitis and should be treated. In these patients, the first priority is to reduce the TG level to prevent acute pancreatitis.	Grade C, Level 2^{+}	36
15	Fibrates (but not gemfibrozil) can be considered as add-on therapy to statins in very high or high risk patients when TG is between 2.3mmol/L (200mg/dL) and 4.5mmol/L (400mg/dL), in the presence of low HDL cholesterol (<1.0mmol/L or 40mg/dL in males, <1.3mmol/L or <50mg/dL in females).	Grade B, Level 1^{++}	36

* Special considerations apply to children, pregnant women, elderly and patients with renal disease, liver disease and familial hypercholesterolemia.

Lifestyle changes

	Recommendation	Grade, Level of Evidence	CPG page no.
16	Patients who smoke should be advised to stop smoking immediately.	Grade B, Level 2^{++}	38
17	If body mass index is above 23 kg/m^2, weight reduction through diet modification and exercise is recommended.	Grade A, Level 1^{+}	38
18	Persons with dyslipidemia should undertake 150 to 300 minutes per week (~30-60 minutes per day) of moderate intensity aerobic activity spread out over 5 to 7 days per week.	Grade A, Level 1^{+}	39
19	For good overall health, individuals who do not currently drink should not start. For individuals who do drink, a maximum of two standard drink per day for women and three per day for men is recommended.	Grade C, Level 2^{+}	42
20	A diet rich in wholegrain foods, vegetables, fruit, legumes, nuts, fish and unsaturated oils and low in saturated and trans fat, refined grains and cholesterol should be encouraged.	Grade A, Level 1^{+}	39
21	Dietary fibre intake should be 25-30 grams per day by increasing consumption of whole-grains, fruit and vegetables and reducing consumption of processed grains and sugar.	Grade C, Level 2^{+}	40
22	Saturated fat intake should be reduced to <7% of total calories and polyunsaturated fat intake should be around 10% of total calories. A total fat intake of 25-35% total calories will be most compatible with these targets.	GPP	40
23	Saturated fat should be replaced with mono and polyunsaturated fats to lower TC and LDL cholesterol (without lowering HDL cholesterol) and lower risk of CAD.	Grade A, Level 1^{+}	39

	Recommendation	Grade, Level of Evidence	CPG page no.
24	Trans fat intake should be limited to <1% of total energy or <2 grams per day.	Grade A, Level 1^{+}	39
25	Cholesterol intakes should be reduced to less than 300mg per day as this reduces serum LDL cholesterol levels.	Grade A, Level 1^{++}	40
26	For patients with high TG levels, simple sugars (mono and disaccharides) should be limited to <10% of total calories.	Grade C, Level 2^{+}	40

Drug therapy

	Recommendation	Grade, Level of Evidence	CPG page no.
27	Statins are the first line drug for both hypercholesterolemia (elevated LDL cholesterol) and mixed hyperlipidemia when pharmacotherapy is indicated, except when TG > 4.5mmol/L (400mg/dL).	Grade A, Level 1++	43
28	Since patients are at increased risk for acute pancreatitis when TG is >4.5mmol/L (400mg/dL) and the risk is greater with higher TG level, fibrates are the first line drug to reduce the risk of pancreatitis when TG > 4.5mmol/L (400mg/dL). Niacin and high intakes of omega 3 fish oils can also be considered for treatment of severe hypertriglyceridemia.	Grade D, Level 3	43
29	If LDL cholesterol remains elevated with fibrate therapy, a statin can be added.	Grade D, Level 4	43

	Recommendation	Grade, Level of Evidence	CPG page no.
	Statins		
30	In patients with pre-diabetes / impaired fasting glucose / impaired glucose tolerance, closer monitoring of glycemic control is recommended upon initiation of statin therapy.	GPP	46
31	Due to risk of myopathy and rhabdomyolysis, high dosages of statins should be prescribed with caution, especially in elderly patients, in those with impaired renal function and when a statin is combined with a fibrate or niacin.	Grade D, Level 4	46
32	When using simvastatin, the highest dose should be 40mg. However, in patients who have been taking 80mg for more than 12 months without any evidence of myopathy or other side effects, it is acceptable to continue the dose.	Grade D, Level 4	46
33	When using statins, monitor creatinine kinase in patients with muscle symptoms (e.g. pain, tenderness, cramping, weakness).	Grade D, Level 4	47
34	When using statins, monitor ALT and AST in patient developing symptoms suggestive of hepatotoxicity (e.g. fatigue, weakness, loss of appetite, jaundice).	Grade D, Level 4	47
35	When using statins, patients should be advised to report promptly to their doctors if they develop any of the above liver or muscle symptoms.	Grade D, Level 4	47
36	Elevation in the levels of serum transaminases above 3 times the upper limit of the normal range is an indication to stop statins. The drugs can be reintroduced at a lower dose when liver function has returned to normal.	Grade D, Level 4	48
37	Elevation of serum creatine kinase greater than 5 to 10 times the upper limit of the normal range, when associated with muscle pain is an indication to stop statins. Patients who are troubled by muscle pain, even in the absence of a raised serum creatine kinase, may benefit from either: (i) stopping the statin therapy or (ii) reducing the dosage.	Grade D, Level 4	48

	Recommendation	Grade, Level of Evidence	CPG page no.
	Ezetimibe		
38	Ezetimibe can be used as an add-on drug in association with statins when the therapeutic target is not achieved at the maximum tolerated statin dose, or as an alternative to statins in patients who are intolerant of statins or with contraindications to statins.	Grade A, Level 1^{++}	49
	Fibrates		
39	Addition of fenofibrate to a statin may benefit certain patients with Type 2 diabetes with both high TG and low HDL cholesterol dyslipidemic pattern, particularly those with microvascular complications.	Grade C, Level 2^{+}	49
	Niacin		
40	When a patient's LDL cholesterol remains above target despite being on the maximum tolerated dose of statin, or in cases of severe hypertriglyceridemia (TG ≥4.5mmol/L or 400mg/dL) when statin therapy is not indicated as first line therapy, niacin can be considered.	Grade A, Level 1^{+}	50
	Omega 3 fish oils		
41	In severe hypertriglyceridemia (e.g. TG >10mmol/L [900mg/dL]), where fibrates alone may not adequately lower the markedly elevated TG levels, omega 3 fish oils should be added in dosages of 3 to 12 gm per day, which contains 1-4 gm of EPA and DHA.	Grade A, Level 1^{+}	50
	Combination therapies		
42	The decision to combine a statin and another lipid lowering agent must be individualised and should be initiated only when it is strongly indicated. When statin therapy fails to achieve LDL target on the maximum tolerated dose, consideration should be given to use other therapies such as ezetimibe or resin as an add-on drug to achieve the LDL target level for the patient.	Grade D, Level 4	51

	Recommendation	Grade, Level of Evidence	CPG page no.
43	Fibrates can be considered as add-on therapy to a statin in very high or high risk patients when TG is between 2.3mmol/L (200mg/dL) and 4.5mmol/L (400mg/dL), in the presence of low HDL cholesterol (<1.0mmol/L or 40mg/dL in males, <1.3mmol/L or <50mg/dL in females).	Grade C, Level 2^{+}	51
44	When a fibrate is combined with a statin, fenofibrate is recommended. Gemfibrozil should not be given because it significantly increases the level of most statins and this may increase the risk of complications.	Grade D, Level 3	51
45	When combination therapy is used, (i) patients should be advised to promptly report to their doctors if they have muscle pain, tenderness or weakness, (ii) physicians should consider doing serum creatine kinase in patients who complain of muscle pain.	Grade, Level 4	51
	Cost-effectiveness of lipid therapy		
46	Generic formulations cost less than non-generic drugs and can be considered if they meet prescribed standards.	Grade D, Level 4	52
	Referral of patients to specialist		
47	Patients who remain outside the LDL cholesterol target values or with TG levels persistently >4.5mmol/L (400mg/dL) despite dietary changes and maximum tolerated drug therapy should be referred to lipid specialists.	GPP	52
	Children		
48	Routine screening for dyslipidemia is not recommended in children. However, screening can be carried out from the age of 2 years in children who have a first degree relative diagnosed with familial hypercholesterolemia, as this gives the opportunity to teach good eating habits.	GPP	53

Special considerations

	Recommendation	Grade, Level of Evidence	CPG page no.
49	Dietary management and physical activity is the mainstay of treatment for dyslipidemia in children.	Grade D, Level 4	53
50	Drug therapy should be considered only in children aged 8 years and older with severe familial hypercholesterolemia whose LDL cholesterol target cannot be achieved with diet and exercise. The serum LDL cholesterol target for children 8-10 years should be <4.0mmol/L (~160mg/dL), and for those older than 10 years <3.4mmol/L (~130mg/dL). Consider lower treatment targets in those with particular adverse family history of CAD or with other major cardiovascular risk factors.	Grade D, Level 4	54
51	If drug therapy is required, a statin is the drug of choice for use in children with dyslipidemia.	Grade A, Level 1^+	54
52	Resins can be added on to statin therapy in children if LDL cholesterol targets are not achieved.	Grade B, Level 1^+	54
53	Children are more vulnerable and may be less likely to report symptoms or side effects accurately. Hence, creatine kinase and transaminases should be measured before initiation of statins or after changes in the regime, and monitored 4 monthly thereafter.	GPP	54
	Pregnancy		
54	During pregnancy, treatment is indicated only in patients with severe hypertriglyceridemia (e.g. TG >10mmol/L [900mg/dL]). The only drug recommended is omega 3 fish oils after dietary therapy.	GPP	55
55	Statins are contraindicated in women who are pregnant, likely to be pregnant, or who are still breastfeeding.	Grade D, Level 4	55

	Recommendation	Grade, Level of Evidence	CPG page no.
	Elderly		
56	In the elderly (age>75 years), the decision to start treatment should take into account the potential risk-reduction associated with treatment, risk of adverse effects, drug-drug interactions, and patient preferences.	Grade D, Level 4	55
57	In very high risk elderly patients (>75 years), physicians may wish to consider less intensive targets (e.g. 2.6 mmol/L or 100mg/dL). When used, lipid lowering medications in the elderly (age>75 years) should be started at the lowest dose and then titrated to achieve optimal LDL cholesterol levels, in order to avoid statin-associated side effects.	GPP	56
58	For patients on treatment with a statin and LDL cholesterol < 2.1mmol/L or 80mg/dL when they turn >75 years of age, there is no need to reduce therapy, if the treatment is well tolerated without any adverse effects.	GPP	56
	Renal disease		
59	The starting dose of statins in chronic kidney disease should be low. During therapy, serum creatine kinase and renal function should both be carefully monitored.	GPP	56
60	Fibrates can be used in patients with chronic kidney disease in stage 1 to 3 but the dosages should be reduced, with appropriate monitoring for side effects, especially myopathy. When creatinine clearance is less than 30 ml/min (stage 4 or 5), fibrates are contraindicated.	GPP	57
	Liver disease		
61	Screen liver function (especially transaminases) on 2 consecutive occasions in patients with dyslipidemia and chronic liver disease.	Grade D, Level 4	57

	Recommendation	Grade, Level of Evidence	CPG page no.
62	In patients with dyslipidemia and chronic liver disease, if the level of the two transaminases (ALT and AST) is elevated but < 1.5 times the upper limit of the normal range, statins can be given but the starting dose should be low. Careful monitoring of the serum transaminases and creatine kinase after commencement is recommended.	Grade D, Level 4	57
63	In patients with dyslipidemia and chronic liver disease, if the level of the two transaminases (ALT and AST) is between 1.5 to 3 times the upper limit of the normal range, statins can still be given but with caution and the starting dose should be low. Careful monitoring of the serum transaminases and creatine kinase after commencement is recommended.	Grade D, Level 4	57
64	Fibrates can be given in patients whose transaminase levels are elevated < 3 times the upper limit of the normal range, but at a lower starting dosage. Careful monitoring of the serum transaminases and creatine kinase after commencement is recommended.	GPP	58
	Familial hypercholesterolemia		
65	Screening of all first degree relatives of diagnosed familial hypercholesterolemia patients is recommended.	GPP	58
66	Due to the high risk of CAD, a more aggressive treatment target of LDL cholesterol of 2.1mmol/L (<80mg/dL) is needed for familial hypercholesterolemia patients.	GPP	58

Quality indicators for lipid management

	Recommendation	Grade, Level of Evidence	CPG page no.
67	Process indicators and recommended frequency are found in Table 14.	GPP	61

1 Introduction

Cardiovascular disease, especially coronary artery disease (CAD) is a very important health problem in Singapore today. CAD is second only to cancer as a leading cause of mortality in this country. Dyslipidemia is one of the most important modifiable risk factors for CAD. Many studies have demonstrated the efficacy of treating dyslipidemia, in the prevention of CAD.

1.1 Objectives & scope of guidelines

The main aim of these guidelines is to assist physicians and other healthcare professionals in clinical decision making by providing well-balanced information on the management of patients with dyslipidemia, without restricting the physician's individual clinical judgement.

1.2 Target group

These guidelines are developed for all health care professionals, in particular, primary care physicians, who are involved in the care of patients with dyslipidemia.

1.3 Guidelines development

The workgroup, comprising cardiologists, endocrinologists, lipid specialists, public health specialists and family physicians, was appointed by MOH to develop these guidelines.

1.4 What's new in the revised guidelines

This revision of the guideline incorporates data from several recent randomised controlled trials that have been published since 2006. In doing so, the committee has tried to simplify the recommendations, wherever possible. The key revisions are in the following Chapters.

1. The chapter on risk assessment (page 25) has been revised to:

    a. Do away with the previous approach of counting risk factors as part of the algorithm for risk stratification. In its place is a 2 step process that stratifies patients into one of 4 levels of risk of CAD (very high risk, high risk, intermediate risk and low risk).
    b. Include clear guidelines for the diagnosis of familial hypercholesterolemia and recognise that patients with familial hypercholesterolemia are at very high risk of CAD and therefore, should be treated aggressively.
    c. Introduce chronic kidney disease as one of the risk factors to consider when stratifying patients by risk of future CAD.
    d. Recognise that patients with diabetes mellitus may not necessarily experience the same risk as patients with established CAD. As such, patients with diabetes can be stratified into 2 levels of risk (very high or high risk) based on the presence or absence of chronic kidney disease.
    e. Retain treat to target levels of low density lipoprotein (LDL) cholesterol based on the risk of CAD in individual patients. However, there is also the option for physicians to increase the dose of statins to those used in randomised controlled trials, even when the LDL cholesterol targets have been achieved.

2. The Chapter on lifestyle changes (page 38) has been extensively revised to focus on areas which are supported by the strongest evidence, including some food based dietary recommendations (in addition to macronutrients) to help physicians support the dietary changes necessary for patients.

3. The Chapter on drug therapy (page 43) has been revised to:

    a. Emphasise that statins remain the primary lipid lowering drugs used to reduce CAD risk, and identifies the dosage range of statins used in randomised clinical trials in various patient groups to guide the choice of statin and the dose.
    b. Clarify the role of other lipid lowering therapies including fibrates, niacin and ezetimibe and this clinical practice guideline identifies situations where these drugs may be beneficial based on recent clinical trials.
    c. Provide information on over the counter preparations for lipid lowering which has the most clearly documented effects on blood lipids given that patients often consume such products. These are omega 3 fish oils, red yeast rice, and plant sterols and stanols (in the chapter on lifestyle change).

4. The Chapter on special considerations (page 53) has been revised to:

    a. Provide recommendations on how to diagnose familial hypercholesterolemia; and greater clarity on drug therapy for children with familial hypercholesterolemia
    b. Make special recommendations for the elderly to recognize the limited data supporting the use of high intensity statins in patients age >75 years and the need to consider the presence of other co-morbidities, multiple medications and altered pharmacokinetics and pharmacodynamics of drugs in these individuals. The decision to start a statin should also take into account the life expectancy and the quality of life of these patients.

1.5 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or if new evidence appears that requires substantive changes to the recommendations. This clinical practice guideline (CPG) refers to the CPG for "Screening for cardiovascular disease and risk factors" (MOH CPG 1/2011). As such, revision of this CPG could be undertaken in the event of a revision to MOH CPG 1/2011.

2 Lipids and apolipoproteins in coronary artery disease

2.1 Lipids in coronary artery disease

Blood lipid levels are important risk factors for CAD. Recently, the Emerging Risk Factors Collaboration has carried out a large meta-analysis to provide reliable estimates of the risk of vascular disease associated with various lipid and apolipoprotein measures.[1] Although these studies have been conducted mostly in European and North American populations, data from the Asia Pacific Cohort Studies Collaboration have shown that the risk of CAD associated with dyslipidemia in populations in Asia, are similar to those observed in populations of European ancestry. [2, 3]

The relationship between CAD and total cholesterol levels is continuous and curvilinear. Most of the cholesterol in the blood is carried on LDL particles, and LDL cholesterol is a well-established risk factor for CAD. However, other lipoproteins including very low density lipoprotein (VLDL), intermediate density lipoproteins (IDL) and lipoprotein remnants are also atherogenic; and non-high density lipoprotein (non-HDL) cholesterol has been used as a surrogate measure of these atherogenic particles.[4]

Elevated levels of HDL cholesterol are associated with reduced risk of CAD.[5] Therefore, low HDL cholesterol is an important independent risk factor for CAD.

Several studies suggest that elevated blood triglyceride (TG) levels are associated with CAD.[6, 7] However, the associations between TGs are significantly attenuated after adjustment for other blood lipid levels.[1]

In these guidelines, total cholesterol (TC), LDL cholesterol, HDL cholesterol and TG are used for risk stratification (Chapter 5) and for making decisions on treatment (Chapter 7).

2.2 Apolipoproteins A1 and B

Each of the atherogenic lipoprotein particles, i.e. VLDL, IDL, LDL and lipoprotein(a) (Lp(a)) contains one molecule each of apolipoprotein B (ApoB). Therefore, serum concentration of ApoB reflects the total number of these particles.

Prospective studies have found ApoB to be a better estimate of the risk of vascular events than LDL cholesterol. Risk is highest in individuals with ApoB levels higher than 1.2g/L and TG levels higher than 1.5mmol/L (134mg/dL). This profile is often associated with the presence of smaller, denser LDL particles, which are more atherogenic and prevalent in patients with the metabolic syndrome and Type 2 diabetes. Apolipoprotein A1 (ApoA1) is associated with HDL particles. There is no requirement for a fasting specimen for apolipoprotein measurement.

In the INTERHEART study, the population attributable risk of raised ApoB/ApoA1 ratio was 49.2%, compared to 35.7% for smoking, 17.9% for hypertension and 9.9% for diabetes.[8]

Although the levels of ApoB and ApoA1 improves the prediction of CAD when combined with the currently measured lipid profile, the improvement is marginal.[9] There are technical issues of reliability and comparability of ApoB and ApoA1 assays. At this time, they should not be routinely measured for use in global risk assessment.[10]

D Routine ApoB and ApoA1 determination is not recommended.[10]

Grade D, Level 4

Lp(a) is an LDL particle in which ApoB is attached to the apolipoprotein (a) protein. Apolipoprotein (a) has structural homology to plasminogen, and competitive binding can impair fibrinolysis. Lp(a) has been identified as an independent risk factor for CAD.11 However, there are no available therapies targeting Lp(a) that have been shown to reduce CAD risk or mortality.[12]

C Lp(a) determination is not recommended for routine cardiovascular disease screening. However, further to a global cardiovascular risk assessment, Lp(a) measurements may be useful in individuals with strong family history of premature cardiovascular disease.[11]

Grade C, Level 2+

Lp(a) is an LDL particle in which ApoB is attached to the apolipoprotein (a) protein. Apolipoprotein (a) has structural homology to plasminogen, and competitive binding can impair fibrinolysis. Lp(a) has been identified as an independent risk factor for CAD.11 However, there are no available therapies targeting Lp(a) that have been shown to reduce CAD risk or mortality.[12]

3 Measurement of lipids

3.1 Screening for dyslipidemia

The committee recommends that screening for dyslipidemia be carried out in accordance with MOH CPG 1/2011 "Screening for cardiovascular disease and risk factors". These recommendations are as follows:

KEY RECOMMENDATION

B Clinicians should routinely screen men and women aged 40 years and older for lipid disorders.[13]

Grade B, Level 2^{++}

KEY RECOMMENDATION

GPP Clinicians can routinely screen younger adults (men and women aged 18 and older) for lipid disorders if they have other risk factors for CAD.[14]

GPP

Risk factors for CAD include:[14]

1. Diabetes mellitus.[15]
2. Multiple CAD risk factors (e.g. tobacco use, hypertension, impaired fasting glycaemia or impaired glucose tolerance[16]).
3. A family history of cardiovascular disease before age 50 years in male relatives or before age 60 years in female relatives.
4. A family history suggestive of familial hyperlipidemia.

KEY RECOMMENDATION

GPP For individuals with screening results within the LDL cholesterol target levels (see Table 7 page 34) and have low TG levels, screening should be repeated at 3 yearly intervals unless they are at very high or high risk of CAD, in which case screening should be repeated annually.

GPP

It should be noted that blood lipids may be abnormal after an acute illness such as an infection. Hence, tests might not be accurate for at least 2 weeks after a febrile illness.

GPP Physicians and patients may wish to defer lipid tests for at least 2 weeks after a febrile illness as blood lipids may be abnormal after an acute illness such as an infection.

GPP

For patients suffering from acute myocardial infarction, the cholesterol level may be depressed between 24 hours to about 3 months after the infarction.[17-20]

D Patients who suffer myocardial infarction may have depressed cholesterol levels that do not require treatment. These patients should have their blood lipids repeated 3 months after a myocardial infarction.[17-20]

Grade D, Level 3

3.2 Lipid Measurements

KEY RECOMMENDATION

D A lipid profile should include TC, TG, LDL cholesterol and HDL cholesterol. These should be obtained after 10 to 12 hours of fasting, which is required for the measurement of TG. [21]

Grade D, Level 4

LDL cholesterol is usually calculated using the Friedewald formula[22] which is as follows:

LDL cholesterol (mmol/L) = TC - (HDL cholesterol + TG/2.2)

This formula cannot be used if the TG is ≥4.5mmol/L (400mg/dL). Direct measurement of LDL cholesterol is now available in some laboratories in Singapore.

4 Classifications of dyslipidemia

Dyslipidemia can be classified as hypercholesterolemia, mixed (combined) dyslipidemia, hypertriglyceridemia, and severe hypertriglyceridemia. The classification as illustrated in Table 1 may be helpful in deciding on the most appropriate therapy to be used (see Table 10 in Chapter 7 on drug therapy, page 44).

Table 1 Classification of dyslipidemia

Types of Dyslipidemia	Increased Concentration	
	Lipoprotein	Serum Lipid
Hypercholesterolemia	LDL	TC & LDL cholesterol*
Mixed (Combined) Dyslipidemia	LDL & VLDL	TC, LDL cholesterol* & TG (1.7-4.5mmol/L [150-399mg/dL])
Hypertriglyceridemia	VLDL	TG (1.7-4.5mmol/L [150-399mg/dL])
Severe Hypertriglyceridemia	Chylomicrons	TG (≥4.5mmol/L [400mg/dL])

** LDL cholesterol (mmol/L) = TC - (HDL cholesterol + TG/2.2)*

Hypercholesterolemia, mixed (combined) dyslipidemia and hypertriglyceridemia are the 3 commonest dyslipidemias. The HDL cholesterol level is usually inversely related to the TG level and is therefore frequently low in both mixed (combined) dyslipidemia and hypertriglyceridemia. In severe hypertriglyceridemia, the TG levels are extremely high, e.g. ≥4.5mmol/L (400mg/dL) but especially if >10mmol/L (900mg/dL), due to the presence of chylomicrons. The main complication in patients with this form of hyperlipidemia is acute pancreatitis.

Secondary dyslipidemia may occur in the various conditions listed in Table 2. These conditions should be excluded in any patient presenting with dyslipidemia.

Table 2 Common causes of secondary dyslipidemia

Disorder	Lipid abnormalities
Diabetes mellitus[23]	↑ TG and ↓ HDL cholesterol
Chronic kidney disease[24]	↑ TG
Nephrotic syndrome[25]	↑ TC
Hypothyroidism[26]	↑ TC
Alcohol abuse[27]	↑ TG
Cholestasis[27]	↑ TC
Pregnancy[28]	↑ TG
Drugs[29] e.g. diuretics, beta-blockers, oral contraceptives, corticosteroids, retinoids, anabolic steroids, progestins related to testosterone	↑ TG and / or TC, ↓ HDL cholesterol

Although there is limited utility for clinical decision making, dyslipidemia can also be classified at a population level to describe the burden of dyslipidemia in the population based on the serum lipids levels in Table 3. However, it is important to note that in making decisions for treatment of individual patients, the primary consideration should be a person's risk of developing future coronary events and the appropriate LDL cholesterol target levels associated with that level of risk.

Table 3 Classification of total, LDL and HDL cholesterol and triglyceride levels

Measurement in mmol/L (mg/dL)	Classification
Total Cholesterol	
< 5.2 (200)	Desirable
5.2- 6.1 (200-239)	Borderline high
≥ 6.2 (240)	High
LDL Cholesterol	
< 2.6 (100)	Optimal
2.6-3.3 (100-129)	Desirable
3.4- 4.0 (130-159)	Borderline high
4.1- 4.8 (160-189)	High
≥ 4.9 (190)	Very high
HDL Cholesterol	
< 1.0 (40)	Low
1.0-1.5 (40-59)	Desirable
≥ 1.6 (60)	Optimal
Triglyceride	
< 1.7 (150)	Optimal
1.7-2.2 (150-199)	Desirable
2.3- 4.4 (200-399)	High
≥ 4.5 (400)	Very high

5 Risk assessment

5.1 Assessment of risk status

A basic principle in the prevention of CAD is that the intensity of risk reduction therapy should be adjusted to a person's risk of developing future coronary events. As such, the first step to be taken is the assessment of the individual's risk status and assigning individuals to one of four risk categories. These are:

1. Very high risk
2. High risk
3. Intermediate risk
4. Low risk

5.2 Risk factors considered in assessing risk status

The following risk factors are considered in the assessment of risk status

1. Age
2. Gender
3. Ethnicity
4. Smoking
5. Blood pressure
6. Diabetes mellitus
7. Chronic kidney disease
8. The presence of CAD, atherosclerotic cerebrovascular disease or peripheral arterial disease

For recommendations regarding the use of C-reactive protein, homocysteine, fibrinogen and natriuretic peptides (B-type natriuretic peptide [BNP] and N-terminal prohormone of brain natriuretic peptide [NT-proBNP]) for the assessment of risk status, readers are referred to MOH CPG 1/2011 "Screening for cardiovascular disease and risk factors".

5.3 Assessing the risk status for an individual

The **following 2 steps** are taken for risk stratification (see Figure 1, page 28).

Step 1
Identify individuals who will automatically fall into the very high or high risk groups (Table 4). For such individuals estimation of the 10-Year CAD Risk Score is not necessary.

Table 4 Individuals at very high and high risk of developing future coronary events

Risk Level	Clinical Presentation of Individuals
Very high risk	(1) Individuals with established CAD, atherosclerotic cerebrovascular disease, aortic aneurysm or peripheral artery disease (2) Individuals with diabetes mellitus with chronic kidney disease (3) Individuals with familial hypercholesterolemia which should be suspected in patients with low density lipoprotein cholesterol (LDL cholesterol) >4.9mmol/L (190mg/dL) with diagnosis based on criteria presented on page 59).
High risk	(1) Individuals with moderate to severe chronic kidney disease (estimated glomerular filtration rate [eGFR] <60ml/min/1.73 m^2) (2) Individuals with diabetes mellitus without established CAD, atherosclerotic cerebrovascular disease, aortic aneurysm or peripheral artery disease or chronic kidney disease.

Step 2

For all other individuals, estimate the **10-Year CAD Risk Score** using **Tables 5 (for men) or Table 6 (for women)** (pages 29-32). **The 10-year CAD risk** refers to the risk of having **myocardial infarction** or **coronary death** in the next 10 years. Based on this risk score, the risk status of the individual is classified as follows:

1. >20% - high risk
2. 10 to 20% - intermediate risk
3. <10% - low risk.

Tables 5 and 6 show the 10-Year CAD Risk Score for Chinese, Malay and Indian males and females in Singapore*.

Since there are insufficient data for other ethnic minorities, the 10-Year CAD Risk Score (as shown in tables 5 and 6) for the lowest risk group (i.e. Chinese) applies for these individuals.

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* These risk scores are derived from the Framingham-based NCEP ATP III 10-Year Risk Score Tables[4] and are no longer used in the American Heart Association/American college of Cardiology guideline on the treatment of blood cholesterol. However, the risk scores were retained in these guidelines because these risk functions have been re-calibrated based on epidemiological data derived within each of the three ethnic groups in Singapore. The modification was carried out as part of collaboration between investigators at the Singapore Ministry of Health, Singapore General Hospital, National University of Singapore and Prof. Ralph B D'Agostino from the Framingham Heart Study, USA. As such, these risk functions provide the most precise estimate of absolute cardiovascular disease risk for the Singapore population that is currently available. Future guidelines may consider new predictive functions as data becomes available for the Singapore population. The use of 10 year risk was retained in these guidelines as opposed to lifetime risk because most randomised controlled trials addressed the short term impact of statin therapy, and the impact of long term treatment in individuals with low risk in the short term, but elevated lifetime risk, is unclear.

Figure 1 Risk Stratification

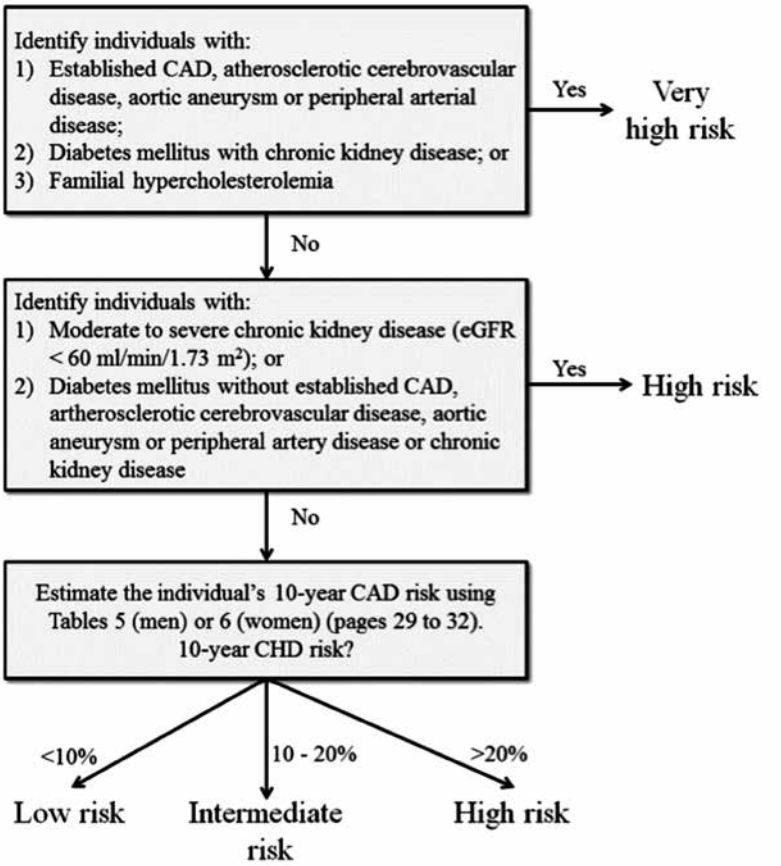

Table 5-1 Estimation of 10-Year Coronary Artery Disease Risk for Men

Age	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

1. Estimate the individual's 10-year CAD risk by allocating points based on his age, total and HDL cholesterol levels, smoking status and systolic blood pressure (BP).

2. Check the total points against Table 5-2 to estimate that individual's 10-year CAD risk.

Total Cholesterol mmol/L (mg/dL)	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
< 4.1 (160)	0	0	0	0	0
4.1-5.1 (160-199)	4	3	2	1	0
5.2-6.1 (200-239)	7	5	3	1	0
6.2-7.2 (240-279)	9	6	4	2	1
≥ 7.3 (280)	11	8	5	3	1

Smoker	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
No	0	0	0	0	0
Yes	8	5	3	1	0

HDL Cholesterol mmol/L (mg/dL)	Points
≥ 1.6 (60)	-1
1.3-1.5 (50-59)	0
1.0-1.2 (40-49)	1
< 1.0 (40)	2

Systolic BP (mmHg)	Points	
	If untreated	If treated
< 120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥ 160	2	3

Table 5-2 Estimation of 10-Year Coronary Artery Disease Risk for Men

Total Points	10-Year Risk (%)		
	Chinese	Malay	Indian
-1	< 1	< 1	1
0	< 1	< 1	1
1	< 1	1	1
2	1	1	1
3	1	1	2
4	1	1	2
5	1	1	3
6	1	2	3
7	2	2	4
8	2	3	5
9	3	4	7
10	4	5	9
11	5	6	11
12	6	8	14
13	8	11	18
14	11	13	> 20
15	13	17	> 20
16	17	> 20	> 20
≥ 17	> 20	> 20	> 20

Table 6-1 Estimation of 10-Year Coronary Artery Disease Risk for Women

Age	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

1. Estimate the individual's 10-year CAD risk by allocating points based on her age, total and HDL cholesterol levels, smoking status and systolic blood pressure (BP).

2. Check the total points against Table 6-2 to estimate that individual's 10-year CAD risk.

Total Cholesterol mmol/L (mg/dL)	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
< 4.1 (160)	0	0	0	0	0
4.1-5.1 (160-199)	4	3	2	1	1
5.2-6.1 (200-239)	8	6	4	2	1
6.2-7.2 (240-279)	11	8	5	3	2
≥ 7.3 (280)	13	10	7	4	2

Smoker	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
No	0	0	0	0	0
Yes	9	7	4	2	1

HDL Cholesterol mmol/L (mg/dL)	Points
≥ 1.6 (60)	-1
1.3-1.5 (50-59)	0
1.0-1.2 (40-49)	1
< 1.0 (40)	2

Systolic BP (mmHg)	Points	
	If untreated	If treated
< 120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥ 160	4	6

Table 6-2 Estimation of 10-Year Coronary Artery Disease Risk for Women

Total Points	10-Year Risk (%)		
	Chinese	Malay	Indian
5	< 1	< 1	1
6	< 1	< 1	1
7	< 1	1	1
8	< 1	1	1
9	1	1	2
10	1	1	2
11	1	2	3
12	1	2	3
13	1	3	4
14	2	4	6
15	3	5	7
16	3	6	10
17	4	8	12
18	5	10	16
19	7	13	20
20	9	16	> 20
21	12	20	> 20
22	15	> 20	> 20
23	19	> 20	> 20
≥ 24	> 20	> 20	> 20

5.4 Target lipid levels

In 2013, the American College of Cardiology and the American Heart Association released a guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults in which treatment initiation and statin dose was driven primarily by risk status and not by LDL cholesterol level.[30] This recommendation is based on randomised controlled trials of lipid lowering for the prevention of CAD which used fixed doses of statins, as opposed to treating patients to a specific target as many other guidelines recommended. However, this view is not universally accepted by physicians, even those within the United States, at this time.

While it was noted that randomised controlled trials used fixed doses of statins, physicians in Singapore involved in treating patients at risk of CAD with lipid lowering therapy were of the view that there was sufficient evidence for a causal link between LDL cholesterol and the risk of CAD, such that a strategy to treat patients to achieve target lipid levels (i.e. treat to target strategy) remains relevant today. This is supported by the findings of the IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT trial) which showed that additional LDL cholesterol lowering provided by adding Ezetimibe (a non-statin lipid lowering agent) to a statin resulted in further reduction in cardiovascular events.[31] It is also believed that there are patients with relatively low risk but high LDL cholesterol who would, nevertheless, benefit from statin therapy despite the lack of definitive evidence from randomised clinical trials. For these reasons, the recommendations for a treat to target strategy is retained in this edition of the clinical practice guideline.

However, where randomised controlled trials have clearly shown a benefit of fixed dose statin therapy, ie. in those at very high and high risk, we have highlighted the dose of statin used in randomised controlled trials so that that physicians can consider increasing the dose of statins to those used in randomised clinical trials. This is particularly relevant if the patient is not on other lipid lowering therapy (e.g. ezetimibe). However, the physician and the patient must balance the benefits against the cost and potential side effects of high doses of medication.

Table 7 shows the recommended LDL cholesterol target levels in the four risk group categories. It is important to note that the higher the risk category, the lower will be the target LDL cholesterol level. It should be noted that the advantage of this approach with respect to patient outcomes has yet to be addressed in clinical trials.

Table 7 LDL cholesterol target levels in the four risk group categories

Risk group category	LDL cholesterol target level
Very high risk group	< 2.1 mmol/L (80 mg/dL)
High risk group	< 2.6 mmol/L (100 mg/dL)
Intermediate risk group	< 3.4 mmol/L (130 mg/dL)
Low risk group	< 4.1 mmol/L (160 mg/dL)

KEY RECOMMENDATION

Very high risk group

B The recommended LDL cholesterol target level for the very high risk group is <2.1mmol/L (80mg/dL).[32-41]

Grade B, Level 1++

The 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults recommended high intensity statin therapy, e.g. atorvastatin 40-80 mg or its equivalent in patients with clinical atherosclerotic cardiovascular disease based on evidence from randomised controlled trials using fixed-dose statin therapy.[30] The physician may consider increasing the statin therapy to these doses, if tolerated, even after the LDL cholesterol goal is achieved on a lower dose of statin, especially if the patient is not on other lipid lowering therapy (e.g. ezetimibe).

KEY RECOMMENDATION

High risk group

B The recommended LDL cholesterol target level for the high risk group is <2.6mmol/L (100mg/dL).[37-39, 41-44]

Grade B, Level 1^{++}

The 2013 American College of Cardiology/American Heart Association guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults recommended moderate intensity statin therapy, e.g. simvastatin 20-40mg or its equivalent, in patients with diabetes mellitus without established chronic CAD or chronic kidney disease based on evidence from randomised controlled trials using fixed-dose statin therapy.[30] The physician may consider increasing the statin therapy to these doses, if tolerated, even after the LDL cholesterol goal is achieved on a lower dose of statin, especially if the patient is not on other lipid lowering therapy (e.g. ezetimibe).

KEY RECOMMENDATION

Intermediate risk group

B The recommended LDL cholesterol target level for the intermediate risk group is <3.4mmol/L (130mg/dL), with an LDL cholesterol level of <2.6mmol/L (100mg/dL) being an option if the physician feels that the benefits of more intensive therapy outweigh the risks.[39, 44, 46, 47]

Grade B, Level 1^{++}

KEY RECOMMENDATION

Low risk group

B The recommended LDL cholesterol target level for the low risk group is <4.1mmol/L (160mg/dL), with an LDL cholesterol level of <3.4mmol/L (130mg/dL) being an option if the physician feels that the benefits of more intensive therapy outweigh the risks.[39, 44, 46, 47]

Grade B, Level 1^{++}

KEY RECOMMENDATION

C Individuals with very high levels of TG, e.g. >4.5mmol/L (400mg/dL) or especially >10mmol/L (900mg/dL), have an increased risk of acute pancreatitis and should be treated to reduce the risk of pancreatitis. In these patients, the first priority is to reduce the TG level to prevent acute pancreatitis.[48]

Grade C, Level 2^{+}

KEY RECOMMENDATION

B Fibrates (but not gemfibrozil) can be considered as add-on therapy to statins in very high or high risk patients when TG is between 2.3mmol/L (200mg/dL) and 4.5mmol/L (400mg/dL), in the presence of low HDL cholesterol (<1.0mmol/L or 40mg/dL in males, <1.3mmol/L or <50mg/dL in females). [49-51]

Grade B, Level 1^{++}

GPP In patients with 2 consecutive values of LDL cholesterol levels less than 1.03mmol/L (40mg/dL), decreasing the statin dose may be considered.

GPP

Special considerations apply to children, pregnant women, elderly and patients with renal disease, liver disease and familial hypercholesterolemia (Page 53).

6 Lifestyle changes

Appropriate lifestyle changes are an integral part of dyslipidemia management. Lifestyle interventions can reduce risk of cardiovascular disease[52]

6.1 Tobacco smoking

KEY RECOMMENDATION

B Patients who smoke should be advised to stop smoking immediately.[53]

Grade D, Level 4

Smoking cessation has clear benefits on overall cardiovascular disease risk[54] and on HDL cholesterol.[55]

6.2 Weight reduction

KEY RECOMMENDATION

A If body mass index is above 23 kg/m^2, weight reduction through diet modification and exercise is recommended.[56]

Grade A, Level 1$^+$

Weight reduction reduces fasting TG and increases HDL cholesterol, with some effect on lowering of TC and LDL cholesterol.[56]

6.3 Exercise

KEY RECOMMENDATION

A Persons with dyslipidemia should undertake 150 to 300 minutes per week (~30 to 60 minutes per day) of moderate intensity aerobic activity spread out over 5 to 7 days per week.[57-59]

Grade A, Level 1+

Regular aerobic activity increases HDL cholesterol and reduces TG.[57-59]

6.4 Diet

KEY RECOMMENDATION

A A diet rich in wholegrain foods, vegetables, fruit, legumes, nuts, fish and unsaturated oils and low in saturated and trans fat, refined grains and cholesterol should be encouraged.[60]

Grade A, Level 1+

This may achieve an LDL cholesterol reduction of up to 15%.[60]

A Saturated fat should be replaced with mono and polyunsaturated fats to lower TC and LDL cholesterol (without lowering HDL cholesterol)[61] and lower risk of CAD.[62]

Grade A, Level 1+

A Trans fat intake should be limited to < 1% of total energy or < 2 grams per day.[63]

Grade A, Level 1+

Consumption of trans fat increases LDL cholesterol and reduces HDL cholesterol.[63]

GPP Saturated fat intake should be reduced to <7% of total calories and polyunsaturated fat intake should be around 10% of total calories. A total fat intake of 25-35% total calories will be most compatible with these targets.

GPP

A Cholesterol intake should be reduced to less than 300mg per day as this reduces serum LDL cholesterol levels.[64]

Grade A, Level 1++

Eggs, prawns and shrimp are relatively high in cholesterol (one egg contains approximately 200mg cholesterol and one prawn contains approximately 30 mg cholesterol).

C Dietary fibre intake should be 25-30 grams per day by increasing consumption of whole-grains, fruit and vegetables and reducing consumption of processed grains and sugar. [65, 66]

Grade C, Level 2+

C For patients with high TG levels, simple sugars (mono and disaccharides) should be limited to <10% of total calories. [66]

Grade C, Level 2+

Table 8 below outlines foods to consume to achieve these nutrient recommendations.

Table 8 Examples of dietary measures for patients

Food	Suggested Change
Grains	Choose wholegrains instead of refined grains (e.g. brown rice, oats, wholegrain noodles and breads)
Fruit	At least two servings* per day
Vegetables	At least two servings† per day
Meat, Fish and alternatives	Choose oily fish (such as mackerel, pomfret, scad) twice per week Choose lentils, chickpeas, beans, tofu and nuts, and fish in place of red meat Choose white meat such as chicken instead of red meat. If you do consume red meat (mutton, beef, pork) choose lean cuts of meat. Eat eggs (egg yolk) and shrimp/prawn in moderation
Dairy foods	Choose reduced or low fat dairy products
Butter and oils	Choose canola, olive, peanut, corn, safflower, sunflower, mustard and soybean oil Limit intake of butter, ghee, palm and coconut oil
Sweets and sweetened drinks	Limit intake of sweets, cakes, soft drinks, and sweetened teas, sports, and juice drinks
Cooking procedures	Limit intake of deep fried foods and dishes cooked with coconut cream/milk

**One serve of fruit is equivalent to a small apple / orange / medium banana or wedge of papaya or pineapple equal to 130g*
†One serve of vegetables is equivalent to ¾ of a mug (100g) cooked vegetables

6.5 Alcohol Consumption

Alcohol intake raises HDL cholesterol concentrations even at light-to-moderate levels of intake (12.5-30 g).[67] However, heavy alcohol consumption (>60 gram per day) can increase fasting TG concentrations. [67]

C For good overall health, individuals who do not currently drink should not start. For individuals who do drink, a maximum of two standard drink per day for women and three per day for men is recommended. [67]

Grade C, Level 2+

A standard drink is 10g of alcohol which is the equivalent of 2/3 can of 220ml beer, one small 100ml glass of wine or 1 nip (30ml) of spirits.

6.6 Plant Sterols and Stanols

Plant sterols/stanol esters are similar in structure to cholesterol and are thought to inhibit cholesterol absorption. They can be found in fortified fat-containing foods such as margarines and milk. Regular daily consumption of 2g of plant sterols/stanol esters per day may reduce LDL cholesterol up to 10% for plant sterols and up to 18% for plant stanol esters. However, fat-soluble vitamin levels may be affected, and long term safety data is not available.

7 Drug therapy

7.1 Choice of drugs

In considering the choice of drugs for dyslipidemia, there are 3 important principles.

KEY RECOMMENDATION

A Statins are the first line drug for both hypercholesterolemia (elevated LDL cholesterol) and mixed hyperlipidemia when pharmacotherapy is indicated, except when TG > 4.5mmol/L (400mg/dL). [38, 68]

Grade A, Level 1++

KEY RECOMMENDATION

D Since patients are at increased risk for acute pancreatitis when TG is >4.5mmol/L (400mg/dL) and the risk is greater with higher TG level, fibrates are the first line drug to reduce the risk of pancreatitis when TG > 4.5mmol/L (400mg/dL). Niacin and high intakes of omega 3 fish oils can also be considered for treatment of severe hypertriglyceridemia.[48]

Grade D, Level 3

D If LDL cholesterol remains elevated with fibrate therapy, a statin can be added.[21]

Grade D, Level 4

7.2 Drugs used to treat dyslipidemia

Table 9 shows the important contemporary drugs and their effects on lipid levels, and Table 10 shows the recommended drugs for the different dyslipidemias.

Table 9 Percentage change with the various drugs

Drug	LDL cholesterol	HDL cholesterol	TG
Statins	↓ 18-55%	↑ 5-15%	↓ 7-30%
Resins	↓ 15-30%	↑ 3-5%	– / ↑
Fibrates	↓ 5-25%	↑ 10-20%	↓ 20-50%
Niacin	↓ 5-25%	↑ 15-35%	↓ 20-50%
Ezetimibe	↓ 18%	↑ 1%	↓ 8%
Omega 3 fish oils	↑ 5-10%	↑ 1-3%	↓ 15-50%

Table 10 Drugs that can be used for different dyslipidemias

Dyslipidemia	Drugs of Choice
Hypercholesterolemia	Statin, adding ezetimibe if lipids still not at target
Mixed Dyslipidemia	Statin, adding ezetimibe, then fibrate or niacin if lipids still not at target
Hypertriglyceridemia (>4.5mmol/L or 400mg/dL)	Fibrate, adding omega 3 fish oils or niacin if triglyceride >4.5mmol/L (400mg/dL)
Severe hypertriglyceridemia (>10mmol/L or 900mg/dL)	Fibrate and omega 3 fish oils, adding niacin if triglyceride >4.5mmol/L (400mg/dL)

7.2.1 Statins

Statins are very effective in lowering both TC and LDL cholesterol. Recent mega-trials have shown that statins are beneficial for both secondary as well as primary prevention of CAD.[38, 40, 45, 68-76]

The approximate equipotency of the different statins is as follows: 10 mg atorvastatin = 5 mg rosuvastatin = 20 mg simvastatin = 40 mg lovastatin / pravastatin = 80 mg fluvastatin.[77, 78]

The range of daily dosages used in clinical trials examining cardiovascular outcomes in very high risk and high risk patients are outlined in Table 11. High intensity statin therapy is defined as the ability to lower LDL cholesterol by more than 50%. This is a property of the specific statin at the dose indicated and not the statin per se. Dosages below these ranges have not been used in clinical trials examining cardiovascular outcomes. Increasing the dose of medication to these levels, in pateints at very high and high risk, may be considered by the physician even if the LDL cholesterol target is achieved. However, the physician and the patient must balance the benefits against the cost and potential side effects of high doses of medication.

Decreasing the statin dose may be considered when 2 consecutive values of LDL cholesterol levels are <1.0mmol/L (40mg/dL).

Table 11 Daily dosages of statins used in clinical trials in very high and high risk patients[30]

High-Intensity Statin Therapy (in very high risk patients)	Moderate-Intensity Statin Therapy (in high risk patients)
Daily dose lowers LDL cholesterol on average, by approximately ≥ 50%	Daily dose lowers LDL cholesterol on average, by approximately 30% to <50%
Atorvastatin 40 – 80 mg Rosuvastatin 20 – 40 mg*	Atorvastatin 10 – 20 mg Rosuvastatin 5 – 10 mg Simvastatin 20 – 40 mg Pravastatin 40 – 80 mg Lovastatin 40 mg Fluvastatin 80mg

*In rare cases where rosuvastatin at doses higher than 20 mg is indicated, initiation of therapy should be under close specialist supervision.[79] Among the Chinese, a higher incidence of myopathy has been noted at lower statin doses (simvastatin 40mg daily) in studies such as Heart Protection Study 2-Treatment of HDL to Reduce the Incidence of Vascular Events (HPS THRIVE). [80]

The incidence of side effects is low, consisting mainly of a rise in the liver enzymes (especially the transaminases – ALT and AST) and myopathy. The recent finding that the incidence of diabetes may increase with statins should not discourage initiating treatment with statins, as

the absolute risk reduction in the risk of cardiovascular disease in high risk patients outweighs the possible adverse effects of a small increase in the incidence of diabetes.[81]

GPP In patients with pre-diabetes / impaired fasting glucose / impaired glucose tolerance, closer monitoring of glycemic control is recommended upon initiation of statin therapy.

GPP

Some patients may choose supplements such as red yeast rice over statin therapy. It is important to note that red yeast rice contains varying amounts of compounds, including monacolins, that have 3-hydroxy-3-methyl-glutaryl-CoA (HMG CoA) reductase inhibitor activity (monacolin K is the active ingredient in lovastatin), and has been found to lower TC and LDL cholesterol. Monacolin content and cholesterol-lowering efficacy varies substantially across different commercial preparations. Side effects are similar to that of statins. Long term safety data is not available.

Myopathy and rhabdomyolysis

High dosages of statins are more likely to result in myopathy and rhabdomyolysis. Although considerably rarer, rhabdomyolysis is a much more serious complication.[41]

D Due to risk of myopathy and rhabdomyolysis, high dosages of statins should be prescribed with caution, especially in elderly patients, in those with impaired renal function and when a statin is combined with a fibrate or niacin. [34, 79, 82, 83]

Grade D, Level 4

D When using simvastatin, the highest dose should be 40mg. However, in patients who have been taking 80mg for more than 12 months without any evidence of myopathy or other side effects, it is acceptable to continue the dose. [34, 79, 82, 83]

Grade D, Level 4

Some statins including atorvastatin, simvastatin and lovastatin are metabolised by the cytochrome P450 isoform 3A4. Drugs such as erythromycin, clarithromycin, azole antifungal agents and cyclosporine that are also metabolised by the same enzyme pathway may elevate the serum level of these statins when administered concomitantly and therefore may increase the risk of toxicity. Other statins such as pravastatin are not affected as they are metabolised by other pathways.[84]

Monitoring for side effects of statins

Baseline measurements of serum aspartate/alanine transaminase and creatine kinase are recommended to establish patient's baseline prior to starting statin therapy. Routine repeat measurement of these are not needed for patients who are well and asymptomatic. Monitoring of creatinine kinase is necessary in patients with muscle symptoms (e.g. pain, tenderness, cramping, weakness).

D When using statins, monitor creatinine kinase in patients with muscle symptoms (e.g. pain, tenderness, cramping, weakness).[79,85,86]

Grade D, Level 4

D When using statins, monitor ALT and AST in patients developing symptoms suggestive of hepatotoxicity (e.g. fatigue, weakness, loss of appetite, jaundice).[79, 85, 86]

Grade D, Level 4

D When using statins, patients should be advised to report promptly to their doctors if they develop any of the above liver or muscle symptoms.[79, 85, 86]

Grade D, Level 4

Indications for stopping statins

D Elevation in the levels of serum transaminases above 3 times the upper limit of the normal range is an indication to stop statins. The drugs can be reintroduced at a lower dose when liver function has returned to normal.[87]

Grade D, Level 4

D Elevation of serum creatine kinase greater than 5 to 10 times the upper limit of the normal range, when associated with muscle pain is an indication to stop statins. Patients who are troubled by muscle pain, even in the absence of a raised serum creatine kinase, may benefit from either: (i) stopping the statin therapy or (ii) reducing the dosage. [86]

Grade D, Level 4

Some patients who experience muscle symptoms without elevations of creatine kinase may experience a reduction in symptoms when switched to an alternative statin.

7.2.2 Ezetimibe

Ezetimibe is a class of lipid lowering agents that selectively inhibits the intestinal absorption of cholesterol and related plant sterols. When added to a statin (e.g. simvastatin), 10 mg of ezetimibe will produce a further 18% lowering of the LDL cholesterol. This effect is similar to doubling the dose of the statin three times(e.g. increasing 10 mg simvastatin to 80 mg).[88] Ezetimibe is also available as a combination tablet consisting of ezetimibe and simvastatin.[89] The combination of simvastatin and ezetimibe has been shown to reduce cardiovascular events in patients with chronic kidney disease, compared to placebo. In patients with established coronary artery disease, ezetimibe, when added to a statin, produces further lowering of LDL cholesterol and cardiovascular events.[31]

A Ezetimibe can be used as an add-on drug in association with statins when the therapeutic target is not achieved at the maximum tolerated statin dose, or as an alternative to statins in patients who are intolerant of statins or with contraindications to statins.[31]

Grade A, Level 1^{++}

7.2.3 Resins (Bile acid sequestrants)

Resins (e.g. cholestyramine) are effective in lowering TC and LDL cholesterol. However, they are infrequently used because of side effects.[21, 90]

7.2.4 Fibrates

Commonly available fibrates in Singapore include fenofibrate and gemfibrozil. Of these two, gemfibrozil shows greater propensity to interact with statins when used together.[91,92] See section on use of combination therapy with statins.

C Addition of fenofibrate to a statin may benefit certain patients with Type 2 diabetes with both high TG and low HDL cholesterol dyslipidemic pattern, particularly those with microvascular complications.[49,50]

Grade C, Level 2^{+}

The side effects of fibrates include: (i) elevation of liver enzymes (transaminases) (ii) myopathy and (iii) gallstones.

7.2.5 Niacin

Niacin lowers LDL cholesterol and TG effectively and can elevate HDL cholesterol. The main side effect is flushing. Newer formulations of extended release niacin can be better tolerated.[93]

A When a patient's LDL cholesterol remains above target despite being on the maximum tolerated dose of statin, or in cases of severe hypertriglyceridemia (TG ≥4.5mmol/L or 400mg/dL) when statin therapy is not indicated as first line therapy, niacin can be considered.[93]

Grade A, Level 1+

In contrast, in patients with atherosclerotic cardiovascular disease and low levels of LDL cholesterol levels <2.1mmol/L (~80mg/dL), the HPS2-THRIVE and AIM-HIGH studies showed no incremental clinical benefit from addition of niacin to other LDL cholesterol lowering therapy (statin or statin-ezetimibe combination).[79, 94]

7.2.6 Omega 3 fish oils

A In severe hypertriglyceridemia (e.g. TG >10mmol/L [900mg/dL]), where fibrates alone may not adequately lower the markedly elevated TG levels, omega 3 fish oils should be added in dosages of 3 to 12 gm per day, which contains 1-4 gm of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[95]

Grade A, Level 1+

Omega 3 fish oils can lower TC (due to lowering of TG) but has no effect on LDL cholesterol and cardiovascular mortality[96-98]. Thus, they should not be used as a substitute for statins.

7.3 Use of combination therapy with statins

D The decision to combine a statin and another lipid lowering agent must be individualised and should be initiated only when it is strongly indicated. [99, 100] When statin therapy fails to achieve LDL target on the maximum tolerated dose, consideration should be given to use other therapies such as ezetimibe or resin as an add-on drug to achieve the LDL target level for the patient.

Grade D, Level 4

C Fibrates can be considered as add-on therapy to a statin in very high or high risk patients when TG is between 2.3mmol/L (200mg/dL) and 4.5mmol/L (400mg/dL), in the presence of low HDL cholesterol (<1.0mmol/L or 40mg/dL in males, <1.3mmol/L or <50mg/dL in females).[49,50]

Grade C, Level 2+

D When a fibrate is combined with a statin, fenofibrate is recommended. Gemfibrozil should not be given because it significantly increases the level of most statins and this may increase the risk of complications.[91,92]

Grade D, Level 3

D When combination therapy is used, (i) patients should be advised to promptly report to their doctors if they have muscle pain, tenderness or weakness, (ii) physicians should consider doing serum creatine kinase in patients who complain of muscle pain.[79, 85, 101]

Grade D, Level 4

7.4 Cost-effectiveness of lipid therapy

One of the factors influencing the choice of lipid modifying drugs is cost and cost-effectiveness. Recent studies have shown that statins and fibrates are cost effective when used for both secondary as well as primary prevention.[38, 48, 68-74, 102-104] Importantly, most of these studies had been done in the countries at a time when generic drugs were not available. Today, with the wide availability of generic drugs, statin and fibrate therapy have become even more cost-effective.[103, 104]

D Generic formulations cost less than non-generic drugs and can be considered if they meet prescribed standards. [70, 103-105]

Grade D, Level 4

7.5 Referral of patients to specialist

GPP Patients who remain outside the LDL cholesterol target values or with TG levels persistently >4.5mmol/L (400mg/dL) despite dietary changes and maximum tolerated drug therapy should be referred to lipid specialists.

GPP

8 Special considerations

8.1 Children

GPP Routine screening for dyslipidemia is not recommended in children. However, screening can be carried out from the age of 2 years in children who have a first degree relative diagnosed with familial hypercholesterolemia, as this gives the opportunity to teach good eating habits.

GPP

D Dietary management and physical activity is the mainstay of treatment for dyslipidemia in children.[106]

Grade D, Level 4

KEY RECOMMENDATION

D Drug therapy should be considered only in children aged 8 years and older with severe familial hypercholesterolemia whose LDL cholesterol target cannot be achieved with diet and exercise. The serum LDL cholesterol target for children 8-10 years should be <4.0mmol/L (~160mg/dL), and for those older than 10 years <3.4mmol/L (~130mg/dL).[107] Consider lower treatment targets in those with particular adverse family history of CAD or with other major cardiovascular risk factors.

Grade D, Level 4

A If drug therapy is required, a statin is the drug of choice for use in children with dyslipidemia.[108-110]

Grade A, Level 1+

B Resins can be added on to statin therapy in children if LDL cholesterol targets are not achieved.[111-113]

Grade B, Level 1+

GPP Children are more vulnerable and may be less likely to report symptoms or side effects accurately. Hence, creatine kinase and transaminases should be measured before initiation of statins or after changes in the regime, and monitored 4 monthly thereafter.

GPP

8.2 Pregnancy

GPP During pregnancy, treatment is indicated only in patients with severe hypertriglyceridemia (e.g. TG >10mmol/L [900mg/dL]). The only drug recommended is omega 3 fish oils after dietary therapy.

GPP

KEY RECOMMENDATION

D Statins are contraindicated in women who are pregnant, likely to be pregnant, or who are still breastfeeding.[79, 114]

Grade D, Level 4

8.3 Elderly

The elderly (age >75 years) often have co-morbidities, take multiple medications, and have altered pharmacokinetics and pharmocodynamics. In very high risk elderly patients (>75 years), more intensive therapy (achieving LDL cholesterol in the range of 2.1mmol/L (80mg/dL)) has not shown benefit over less intensive therapy. Treatment for such patients should be individualised and special precautions need to be taken when instituting pharmacotherapy for hyperlipidemia in elderly patients.

KEY RECOMMENDATION

D In the elderly (age >75 years), the decision to start treatment should take into account the potential risk-reduction associated with treatment, risk of adverse effects, drug-drug interactions, and patient preferences.[30]

Grade D, Level 4

GPP In very high risk elderly patients (>75 years), physicians may wish to consider less intensive targets (e.g. 2.6 mmol/L or 100mg/dL). When used, lipid lowering medications in the elderly (age >75 years) should be started at the lowest dose and then titrated to achieve optimal LDL cholesterol levels, in order to avoid statin-associated side effects. [28]

GPP

KEY RECOMMENDATION

GPP For patients on treatment with a statin and LDL cholesterol <2.1mmol/L or 80mg/dL when they turn >75 years of age, there is no need to reduce therapy, if the treatment is well tolerated without any adverse effects.

GPP

8.4 Renal disease

GPP The starting dose of statins in chronic kidney disease should be low. During therapy, serum creatine kinase and renal function should both be carefully monitored.

GPP

In patients with end stage chronic kidney disease on dialysis, statins did not significantly improve cardiovascular outcomes.[35, 115-117] In a sub-group analysis of the 4D study, atorvastatin treatment was associated with a statistically significant reduction in cardiovascular disease outcomes in those with LDL cholesterol >145mg/dL (~3.7mmol/L).[118] However, this was not a pre-specified sub-group analysis and the clinical interpretation of these data must be made with caution. The decision whether to start or continue statin therapy in these patients must balance the benefits against the cost and potential side effects of statins in this group of patients.

GPP Fibrates can be used in patients with chronic kidney disease in stage 1 to 3 but the dosages should be reduced, with appropriate monitoring for side effects, especially myopathy. When creatinine clearance is less than 30 ml/min (stage 4 or 5), fibrates are contraindicated.

GPP

8.5 Liver disease

D Screen liver function (especially transaminases) on 2 consecutive occasions in patients with dyslipidemia and chronic liver disease.

Grade D, Level 4

D In patients with dyslipidemia and chronic liver disease, if the level of the two transaminases (ALT and AST) is elevated but < 1.5 times the upper limit of the normal range, statins can be given but the starting dose should be low.[119] Careful monitoring of the serum transaminases and creatine kinase after commencement is recommended.

Grade D, Level 4

D In patients with dyslipidemia and chronic liver disease, if the level of the two transaminases (ALT and AST) is between 1.5 to 3 times the upper limit of the normal range, statins can still be given but with caution and the starting dose should be low.[119] Careful monitoring of the serum transaminases and creatine kinase after commencement is recommended.

Grade D, Level 4

GPP Fibrates can be given in patients whose transaminase levels are elevated < 3 times the upper limit of the normal range, but at a lower starting dosage. Careful monitoring of the serum transaminases and creatine kinase after commencement is recommended.

GPP

8.6 Familial hypercholesterolemia

Familial hypercholesterolemia (FH) is a group of inherited genetic defects resulting in severely elevated serum cholesterol concentrations. In the heterozygous FH, cholesterol levels rise to about two times the normal levels due to a defect in LDL clearance. Affected individuals have a much higher risk (about 20-fold) of premature CAD if untreated. The prevalence of FH is 1 in 300 to 500 in many populations, making FH among the most common of serious genetic disorders.

Clinical diagnosis of FH can be made by applying any one of several validated sets of criteria, including the Simon Broome Trust diagnostic criteria provided in Table 12. For patients with definite FH, primary care physicians can initiate therapy based on the guidelines or refer patients to a specialist to initiate and stabilise the patient on therapy. For patients with possible FH, primary care physicians may want to refer patient to specialists to make a recommendation on the need for therapy and to initiate therapy if required.

GPP Screening of all first degree relatives of diagnosed familial hypercholesterolemia patients is recommended.

GPP

GPP Due to the high risk of CAD, a more aggressive treatment target of LDL cholesterol of 2.1mmol/L (<80mg/dL) is needed for familial hypercholesterolemia patients.

GPP

This target may not be achievable despite the use of the maximum tolerated dose of lipid lowering therapy in patients with FH, which may include the use of combination therapy with multiple lipid lowering drugs. However, pharmacotherapy remains beneficial in spite of the failure to achieve the LDL cholesterol target in such patients.

Table 12 Simon Broome Trust Diagnostic criteria for Familial hypercholesterolemia

Diagnosis	Criteria
Definite Familial hypercholesterolemia	- TC above 7.5mmol/L (~290mg/dL) or LDL cholesterol above 4.9mmol/L (~190mg/dL) in an adult. - TC above 6.7mmol/L (~260mg/dL) or LDL cholesterol above 4mmol/L (~160mg/dL) in a child aged under 16 years. **PLUS** - Tendon xanthomas in patient or a first degree relative (parent, sibling, child), or in a second degree relative (grandparent, uncle, aunt). **OR** - DNA-based evidence of an LDL receptor mutation, familial defective apoB-100, or a PCSK9 mutation.
Possible Familial hypercholesterolemia	- TC above 7.5mmol/L (~290mg/dL) or LDL cholesterol above 4.9mmol/L (~190mg/dL) in an adult. - TC above 6.7mmol/L (~260mg/dL) or LDL cholesterol above 4mmol/L (~160mg/dL) in a child aged under 16 years. **PLUS** - Family history of myocardial infarction (MI): Before 50 years in a second degree relative or below age 60 in a first degree relative. **OR** - Family history of raised TC: Above 7.5mmol/L (~290 mg/dL) in adult first or second degree relative or above 6.7mmol/L (~260mg/dL) in a child or sibling aged under 16 years.

Source: Identification and Management of Familial Hypercholesterolaemia (FH) [120]

9 Quality indicators for lipid management

The following clinical quality indicators for recommended LDL cholesterol target levels (Table 13) and process indicators for review frequency (Table 14) are proposed for lipid management. However, measurement of attainment of these target levels should exclude those age >75 years.

Table 13 LDL cholesterol target levels

Risk group category	Recommended LDL cholesterol target levels
Very high	The recommended LDL cholesterol target level for the very high risk group is <2.1mmol/L (80mg/dL)
High risk	The recommended LDL cholesterol target level for the high risk group is <2.6mmol/L (100mg/dL)
Intermediate risk	The recommended LDL cholesterol target level for the intermediate risk group is <3.4mmol/L (130mg/dL), with an LDL cholesterol level of <2.6mmol/L (100mg/dL) being an option if the physician feels that the benefits of more intensive therapy outweigh the risks.
Low risk	The recommended LDL cholesterol target level for the low risk group is <4.1mmol/L (160mg/dL), with an LDL cholesterol level of <3.4mmol/L (130mg/dL) being an option if the physician feels that the benefits of more intensive therapy outweigh the risks.

GPP Table 14 Process indicators and recommended frequency

Performance parameter	Recommended review frequency
All patients who are on stable lipid modifying drug therapy with LDL cholesterol target levels achieved.	Lipid measurement at least every 12 months
Patients who are not on lipid modifying drug therapy (with LDL cholesterol target levels achieved as stated above):	
(1) Very high risk and high risk	Lipid measurement every 12 months
(2) Intermediate risk and low risk	Lipid measurement every 3 years

GPP

In the management of an individual patient, good clinical judgment, which takes into account other factors that may influence overall morbidity or mortality risk, should be exercised in every situation. As such, aiming for 100% attainment of these targets is inappropriate. Furthermore, measurements of attainment of these targets should exclude those age > 75 years.

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning – Verificable Self-Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: http://sma.org.sg/publications/index.aspx?ID=26 (*the link will only be available once the March 2017 issue of the SMJ becomes available*). The answers will be published in the SMJ May 2017 online issue and at the MOH webpage for these guidelines after the period for submitting the answers is over.

Instruction: Choose True or False for each statement.

	True	False
1. With regards to lipids in coronary artery disease		
A. Elevated levels of HDL are associated with increased risk of CAD.	☐	☐
B. ApoB and ApoA1 assays should be routinely measured for use in global risk assessment.	☐	☐
C. Further to a global cardiovascular risk assessment, lipoprotein(a) measurements may be useful in individuals with a strong family history of premature cardiovascular disease.	☐	☐
D. The association between blood TG and CAD is attenuated after adjustment for other lipids.	☐	☐
2. With regards to screening for dyslipidaemia,		
A. It is strongly recommended that clinicians routinely screen all adults (men and women aged 18 years and older) for lipid disorders.	☐	☐
B. Blood lipids may be abnormal after an acute illness such as an infection. As such, physicians and patients may wish to defer tests for at least 2 weeks after a febrile illness.	☐	☐
C. Screening is recommended for men and women aged 18 and older in the presence of multiple CAD risk factors (e.g., tobacco use, hypertension).	☐	☐
D. Patients who suffer myocardial infarction and have low LDL cholesterol levels that do not require treatment during this period should have their blood lipids repeated 3 months after a myocardial infarction.	☐	☐

	True	False
3. The following risk factors are considered in the assessment of risk status:		
A. Gender.	☐	☐
B. Alcohol consumption.	☐	☐
C. Presence of chronic kidney disease.	☐	☐
D. Occupation.	☐	☐
4. With regards to target lipid levels		
A. The higher the risk category, the lower will be the target LDL cholesterol level.	☐	☐
B. The recommended LDL cholesterol target level for the Very High Risk Group is <2.1mmol/L (80mg/dL).	☐	☐
C. In individuals with very high levels of TG, e.g. >4.5mmol/L (400mg/dL) or especially >10mmol/L (900mg/dL), the first priority is to reduce the LDL cholesterol level to prevent acute hepatitis.	☐	☐
D. The recommended LDL cholesterol target level for a diabetic patient with chronic kidney disease is <3.4mmol/L (130mg/dL).	☐	☐
5. With regards to management of dyslipidaemias:		
A. Statins are safe and not contraindicated in pregnancy or breastfeeding.	☐	☐
B. When a fibrate is combined with a statin, fenofibrate is recommended. Gemfibrozil should not be given because it significantly increases the blood level of most statins and this may increase the risk of complications.	☐	☐
C. Saturated fat should be replaced with mono and polyunsaturated fats to lower total and LDL cholesterol (without lowering HDL cholesterol) and lower risk of CAD.	☐	☐
D. Omega 3 fish oils can lower LDL cholesterol and cardiovascular mortality.	☐	☐

Workgroup members

The members of the workgroup, who were appointed in their personal professional capacity, are:

Chairman

A/Prof Tai E Shyong
Senior Consultant,
Department of Endocrinology
University Medicine Cluster
National University Health System
National University Hospital

Members (in alphabetical order)

Prof Chia Boon Lock (Advisor)
Emeritus Professor
National University of Singapore
Emeritus Consultant
National University Heart Centre

Dr Amber Carla Bastian
Manager
Centre of Excellence (Nutrition)
Health Promotion Board

A/Prof Terrance Chua Siang Jin
Medical Director
National Heart Centre

Dr Sally Ho Chih Wei
Program Director
(Family Medicine, SingHealth Residency)
Assistant Director (Education)
SingHealth Polyclinics

Mdm Koh Teck Siew
Principal
Yishun Junior College

Dr Low Lip Ping
Low Cardiology Clinic
Mount Elizabeth Medical Centre

Dr Jeannie Tey
Deputy Director (Non-Communicable Diseases)
Epidemiology & Disease Control Division,
Ministry of Health

A/Prof Poh Kian Keong
Associate Professor
National University of Singapore
Senior Consultant
National University Heart Centre

Members (in alphabetical order)

Dr Tan Chee Eng
Tan Chee Eng Diabetes
Lipid & Endocrine Practice
Gleneagles Medical Centre

Dr Peter Ting
The Harley Street Heart and Cancer Centre

Dr Tham Tat Yean
CEO and Family Physician
Frontier Healthcare Group
Assoc Prog Director
NUHS Family Medicine Residency
Adj Asst Professor
NUS Yong Loo Lin School of Medicine

Dr Sue-Anne Toh Ee Shiow
Senior Consultant,
Department of Endocrinology
University Medicine Cluster
National University Health System
National University Hospital
Clinical Director, NUHS Regional Health System Planning and Development

A/Prof Rob M. van Dam
Associate Professor
Saw Swee Hock School of Public Health
National University Health System

Subsidiary editors:

Ms Elaine Teo
Deputy Director (Health Technology Assessment/ Utilisation Management Review)
Clinical Quality, Performance and Technology Division
Ministry of Health

Dr Pwee Keng Ho
Consultant (Health Technology Assessment)
Clinical Quality, Performance and Technology Division
Ministry of Health

Mr Muhammad Farid
Manager (Health Technology Assessment)
Clinical Quality, Performance and Technology Division
Ministry of Health

Secretariat team:

Ms Chin Mien Chew
Senior Manager (Health Technology Assessment)
Clinical Quality, Performance and Technology Division
Ministry of Health

Ms Suriana Taib
Manager (Health Technology Assessment)
Clinical Quality, Performance and Technology Division
Ministry of Health

Dr Edwin Chan Shih-Yen
Head, Epidemiology
Singapore Clinical Research Institute
Assoc Professor, Duke-NUS Graduate Medical School, Singapore
Director, Singapore Branch, Australasian Cochrane Centre;
Consultant Biostatistician
Clinical Quality, Performance and Technology Division
Ministry of Health

These organisations have commented on and endorsed the guidelines (in alphabetical order):
Chapter of Family Medicine Physicians, Academy of Medicine, Singapore
Chapter of Endocrinologists, College of Physicians, Singapore
Chapter of General Physicians, College of Physicians, Singapore
College of Family Physicians, Singapore
Endocrine & Metabolic Society of Singapore
Singapore Cardiac Society

Ministry of Health, Singapore

College of Medicine Building
16 College Road
Singapore 169854

Tel (65) 6325 9220
Fax (65) 6224 1677

www.moh.gov.sg

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