

Hyperlipidaemia

[Disclaimer](#)

See also:

- [Familial Hypercholesterolaemia](#)
- [Statin Intolerance](#)

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Red Flags

- High triglycerides > 10 mmol/L
- Cholesterol > 8 mmol/L
- Acute pancreatitis
- [Familial Hypercholesterolaemia](#)

Background – About Hyperlipidaemia (raised plasma levels)

- Elevated cholesterol and/or triglycerides may be a significant risk factor for cardiovascular disease and are often asymptomatic.
- They may be the result of inherited risk or lifestyle factors.
- Elevated triglycerides may indicate diabetes or alcoholic cirrhosis.
- Elevated cholesterol may indicate nephrotic syndrome, hypothyroidism, or primary biliary cirrhosis.

Assessment

Practice Point

Consider absolute cardiovascular disease (CVD) risk

It is important to consider [absolute cardiovascular disease \(CVD\) risk](#) assessment when interpreting lipid levels and deciding management.

1. Arrange **fasting cholesterol test** for:
 - patients aged 45 to 75 years
 - Aboriginal and Torres Strait Islander patients aged 35 to 75 years
 - when investigating familial premature cardiovascular disease
 - family cascade screening in [familial dyslipidaemia](#)

Fasting cholesterol test

- *Non-fasting levels are acceptable for total cholesterol, HDL or non-HDL cholesterol, however there is some controversy and fasting samples may be required to accurately determine LDL, glucose, and triglyceride levels. It is therefore advised to arrange a fasting test first line to prevent duplication of cost if practical.*
- *Do not test when suffering an acute intercurrent illness or when pregnant.*
- *Measure fasting lipids on at least 2 occasions before considering treatment.*

2. Compare to **reference ranges**.

Reference lipid values in adult Australians	
Total cholesterol (TC)	< 5.5 mmol/L
Non-HDL Cholesterol	< 4.0 mmol/L
LDL Cholesterol (LDL)	< 3.0 mmol/L
HDL Cholesterol (HDL)	> 1.0 mmol/L (men) > 1.2 mmol/L (women)
Triglycerides	< 2.0 mmol/L

3. Assess hypercholesterolaemia

- Consider the presence of [familial hypercholesterolaemia \(FH\)](#) and review for a **family history of premature cardiovascular disease**. Use the Dutch Lipid Clinic Network Score (DLCNS) to **clinically diagnose FH**.

- **Family history of premature cardiovascular disease**

Defined as premature coronary heart disease (CHD), transient ischemic attack (TIA), or ischaemic stroke in a first degree relative:

- Father or brother aged < 55 years
- Mother or sister aged < 65 years

- **Clinical diagnosis of familial hypercholesterolaemia (FH)**

Access the [DLCNS Online Calculator](#) or [DLCNS printable form](#). The diagnosis is based on the total score:

- Definite FH > 8
- Probable FH 6 to 8
- Possible FH 3 to 5
- Unlikely FH < 3

Cardiovascular risk calculators are not appropriate for patients with suspected or confirmed FH, as they are considered to be at high risk.

In cases of known FH, check all first degree family members (parents, siblings, and children).

- Exclude **secondary causes of hypercholesterolaemia** by checking history and testing TSH, creatinine, LFTs (ALT/AST), fasting blood glucose or HbA1c, and urine dipstick for protein.

Secondary causes of hypercholesterolaemia

- Hypothyroidism
- Nephrotic syndrome and chronic kidney disease (CKD)
- Cholestatic biliary disease
- Diabetes
- Anorexia nervosa
- Hypopituitarism
- Medications – thiazide diuretics, corticosteroids, oral contraceptives, ciclosporin, atypical antipsychotics, anticonvulsants

4. Assess hypertriglyceridaemia:

- Exclude **secondary causes of hypertriglyceridaemia** by checking history and testing HbA1c and creatinine.

Secondary causes of hypertriglyceridaemia

- Diabetes
 - Obesity
 - Alcohol excess
 - Chronic kidney disease (CKD)
 - Pregnancy
 - Gout
 - Hypopituitarism
 - Medications – beta blockers, corticosteroids, oral contraceptives, atypical antipsychotics, ciclosporin, HIV or antiretroviral drugs, retinoids
- Unexplained cases are presumed to represent primary hyperlipidaemia due to gene/environmental interactions.

5. Evaluate the patient's risk of CVD to determine appropriate management:

- **High-risk groups** need management, no matter their calculated CV risk assessment.
 - Diabetes and aged > 60 years
 - Diabetes with microalbuminuria (> 20 micrograms/min or urine albumin:creatinine ratio > 2.5 mg/mmol males, > 3.5 mg/mmol females)
 - Moderate or severe chronic kidney disease (proteinuria or estimated glomerular filtration rate < 45 mL/min/1.73 m²)
 - Known [familial hypercholesterolaemia](#)
 - Systolic blood pressure ≥ 180 mmHg or diastolic ≥ 110 mmHg
 - Serum total cholesterol > 7.5 mmol/L
- Conduct a **cardiovascular (CV) risk assessment** for patients:
 - without pre-existing CVD, aged 45 to 74 years.
 - of Aboriginal and Torres Strait Islander origin, aged ≥ 35 years.

Assess **cardiovascular risk** using:

- [Cardiovascular risk calculator](#)
- [Cardiovascular risk charts](#)

If using a [CV risk calculator](#) as an estimate, enter age 74, regardless of actual age. Age is the predominant determinant of calculated absolute cardiovascular risk, so no additional weighting for age is undertaken beyond 75 years.

Once treatment is started, then the accuracy is reduced.

Risk calculators do not take into account factors such as obesity, family history, socioeconomic status, novel risk factors, mental illness and other ethnic groups. Large ethnic groups exist within Melbourne with an increased risk of vascular disease e.g., other Pacific Islander people and patients from the Indian subcontinent and Fijian Indians.

Lifetime CVD risk

Clinical judgement is necessary when assessing overall CV risk and considerations for early treatment should be given to 'lifetime CVD risk' in younger patients,

particularly those with a family history of premature CVD or familial hypercholesterolaemia.

- Consider **other patient groups**.

- Patients aged > 75 years – there is limited evidence for the treatment of patients aged > 80 years

Patients aged > 75 years

Use clinical judgement to determine risk. Consider:

- Co-morbidities
- Polypharmacy
- Risks and benefits
- Life expectancy

If using a [CV risk calculator](#) as an estimate, enter age as 74 years, regardless of actual age.

- Pregnant women – review postpartum to confirm hyperlipidaemia.
- Children – treatment is via diet and management of underlying metabolic disorders, except in FH where medication should be considered from age 8 to 10 years.⁵
- Patients with HIV – highly active antiretroviral treatment (HAART) causes an increase of LDL-C and TG, and predominance of small, dense LDL particles. This doubles CVD risk.
- Mental illness – antipsychotics can cause elevated lipid levels.
- Chronic kidney disease (CKD) – lipid abnormalities in cholesterol increases with declining GFR.

2. If the patient has a high CVD risk or strong family history of premature atherothrombotic disease, consider plasma **lipoprotein(a) (Lp(a))**. Although not recommended for routine screening, it is an important, independent predictor of cardiovascular disease.

Lipoprotein(a) (Lp(a))

Lp(a) is an independent predictor of cardiovascular disease.

It is not recommended for routine screening (not Medicare rebatable).

Indications for screening:

- Premature cardiovascular disease
- Early onset aortic sclerosis
- Familial hypercholesterolaemia
- Family history of:
 - premature cardiovascular disease
 - elevated lipoprotein(a)
 - aortic sclerosis
- Recurrent cardiovascular disease despite statin treatment
- Persistent elevated LDL despite statin treatment

If **results** indicate elevated levels, seek advice from a [lipid disorders specialist](#).

Lipoprotein(a) results

Lp(a) is reported in several different ways, as mass (mg/dL, grams/L, or mg/L) or as particle numbers (nmol/L):

- Normal level: Lp(a) < 30 mg/dL (< 75 nmol/L or 0.3 grams/L)
- Lp(a) > 30 mg/dL (> 75 nmol/L or 0.75 grams/L) are associated with a 2 to 3-fold increased risk of cardiovascular events independent of conventional risk markers.
- Lp(a) > 50 mg/dL (> 125 nmol/L) are associated with a markedly increased risk.

In terms of risk:

- Desirable: < 14 mg/dL (< 35 nmol/L)
- Borderline risk: 14 to 30 mg/dL (35 to 75 nmol/L)

- Moderately high risk: 31 to 50 mg/dL (75 to 125 nmol/L)
- Very high risk: > 50 mg/dL (> 125 nmol/L)

Management

1. If the plasma triglyceride is > 5 mmol/L, **manage as hypertriglyceridaemia**.
 - Assess and treat diabetes
 - Exclude triglyceride-elevating medications
 - Advise avoidance of alcohol
 - Urgently review diet – consider clear fluid diet or nil by mouth.
 - Prescribe omega-3 fatty acids at least 2 to 3 g daily.
 - Encourage [weight loss](#)
 - If triglycerides remain > 2.3 and HDL is low (< 1 mmol/L), start fenofibrate, 145 mg per day (48 mg per day in renal impairment)
 - Refer to or seek management advice from [cardiology](#) or [endocrinology](#) specialists if unresponsive to medical management.
 - This group is at risk of acute pancreatitis. If pancreatitis is suspected clinically, manage as an emergency and send to the [Emergency Department](#). Plasmapheresis may be considered.
2. Consider and manage [Familial Hypercholesterolaemia](#) if:
 - untreated total (or more specifically, non-HDL) cholesterol > 7.5 mmol/L, or
 - LDL cholesterol > 6.5 mmol/L.
3. If the patient does not fit into these categories treat as primary or secondary prevention as below. Advise **lifestyle modification** as first-line management in all patients.
 - [Smoking cessation](#)
 - **Diet as appropriate for cardiovascular health**
 - [DASH](#) and Mediterranean-style diets are consistent with these principles but portion size and overall energy content (including sweet drinks and alcohol) require consideration.
 - Advise patient to:
 - avoid saturated and trans-fats, and
 - increase [omega 3 consumption](#) – oily fish and plant sources such as walnuts, flaxseed, chia seeds, canola, and soybean oils. (More evidence is needed to confirm the place of supplementation in the prevention of chronic heart disease).
 - Reduce dietary salt
 - Reduce sugar intake
 - limit alcohol intake if elevated triglycerides.
 - Fish oil supplements may assist in decreasing triglycerides but do not alter total cholesterol or LDL.
 - Consider giving patient a [Heart Foundation – Heart Healthy Tips](#) flyer.
 - Increase physical exercise to achieve weight loss and decreased waist measurement. Intensive intervention and support may be required in obesity.

Primary prevention

- High risk (over 15% in 5 years) – start medication in conjunction with lifestyle interventions
- Moderate (10 to 15% in 5 years) and low risk (< 10% in 5 years) – monitor as below

Optimal lipid values in primary prevention for high-risk subjects	
Total cholesterol (TC)	< 4.0 mmol/L
Non-HDL Cholesterol	< 2.5 mmol/L
LDL Cholesterol (LDL)	< 2.5 mmol/L
HDL Cholesterol (HDL)	> 1.0 mmol/L
Triglycerides	< 2.0 mmol/L

Secondary prevention

- All groups require lipid-lowering medication, as below. Measure lipids every 3 months until controlled, then measure every 12 months.
- Optimal lipid values for patients with known cardiovascular, cerebrovascular, peripheral vascular disease

Optimal lipid values in secondary prevention	
Total cholesterol (TC)	< 4.0 mmol/L
Non-HDL Cholesterol	< 2.5 mmol/L
LDL Cholesterol (LDL)	< 1.8 mmol/L*
HDL Cholesterol (HDL)	> 1.0 mmol/L
TC:HDL	< 4.0 mmol/L
Triglycerides	< 2.0 mmol/L

* In patients with progressive CVD despite risk factor control, consider lower LDL-C target, as suggested by:

- IMPROVE-IT: < 1.4 mmol/L
- FOURIER: < 0.7 mmol/L
- EAS: < 1.4 mmol/L

4. Chose appropriate **medications:**

Refer to the **PBS guidelines** prior to prescribing.

PBS guidelines

- Although the Australian PBS guidelines specifically identify Aboriginal and Torres Strait Islander patients as being at very high risk, Maori, other Pacific peoples, patients from the Indian subcontinent, and Fijian Indians are also at high risk.
- See PBS – [A-Z Medicine Listing](#)

➤ **Predominant high LDL**

- Statins are first-line and shown to reduce CV events.
 - In primary prevention, use a statin up to 40 mg. May require higher doses in [Familial Hypercholesterolaemia](#).

- In secondary prevention, use simvastatin or atorvastatin in doses up to 80 mg first-line or rosuvastatin in doses up to 40 mg daily to achieve target levels.
 - Simvastatin in doses up to 40 mg. Do not use 80 mg due to excess myopathy.
 - Atorvastatin in doses up to 80 mg.
 - Rosuvastatin in doses up to 40 mg daily. 5 mg is a suggested starting dose for Asian patients.
- Halve the maximum doses for Asian patients.
- Post CVA or TIA, atorvastatin 80 mg is recommended independent of pre-treatment cholesterol level.
- Check **statin tolerability and compliance**.

Statin tolerability and compliance

- An Australian study found that only 40% of people continued to take their statin at 12 months, with about half stopping before 3 months.
- Statin intolerance has been markedly over diagnosed, especially myalgia. Most people can tolerate some dose of statin when re-challenged. See [Statin Intolerance](#) pathway or [PBS SAMS guide](#).
- The risk of myopathy is increased in patients:
 - taking gemfibrozil or nicotinic acid in addition to a statin – use Fenofibrate
 - taking Simvastatin or atorvastatin with grapefruit juice, macrolide antibiotics such as erythromycin, fusidic acid, calcium channel blockers, cyclosporine, digoxin, and amiodarone – metabolised via the CYP 450 3A4 pathway and can accumulate.
- If LDL cholesterol levels are not adequately reduced with maximally tolerated doses of statin or, if intolerant to statin therapy, consider:

Ezetimibe

- May be used
 - in combination with the highest tolerated dose of statin, available as:
 - Vytorin in combination with simvastatin, or
 - Atozet co packaged with atorvastatin.
 - alone or in combination with a fibric acid derivative (gemfibrozil or fenofibrate) or a resin if no statin is tolerated.
 - fibric acid derivative (gemfibrozil or fenofibrate) or
 - resin.
- Can be prescribed under PBS Authority in eligible patients:
 - Coronary heart disease
 - Diabetes mellitus
 - Peripheral vascular disease
 - Heterozygous or homozygous familial hypercholesterolaemia
 - Symptomatic cerebrovascular disease
 - Family history of coronary heart disease
 - Hypertension
 - Homozygous sitosterolemia
 - Where a statin:
 - is contraindicated.
 - must be discontinued or reduced.

See the [PBS Guidelines for Authority to Prescribe Ezetimibe](#) as single or combination therapy.

Bile acid binding resin or nicotinic acid:

- Colesevelam, Colestid, or [Cholestyramine](#) are considered third- and fourth-line therapies added to the highest dose of statin tolerated.
- For full prescribing details see the Approved Product Information.

Niacin (nicotinic acid)

- Niacin is considered third- and fourth-line therapy added to the highest dose of statin tolerated.
- Available over the counter (OTC)
- For full prescribing details see the Approved Product Information.

Proprotein convertase subtilisin/kexin type 9 (PCSK9 inhibitors)

- Two are currently available on private script:
 - alirocumab (Praluent), indicated for heterozygous FH
 - evolocumab (Repatha), indicated for both heterozygous and homozygous FH
- Evolocumab (Repatha) can be prescribed under [PBS Authority](#) indicated for both heterozygous and homozygous FH.

Novel agents

- Anacetrapib has recently been shown to be effective, but it is yet to be approved for clinical use.
- Bempedoic acid is undergoing clinical trials.

➤ **High triglycerides or low HDL**

- First-line treatment is dietary and lifestyle modification – these are more effective than drug therapy:
 - Weight reduction
 - Decrease alcohol intake
 - Improve diabetes control
 - Reduce dietary sugars
 - Increase exercise to increase muscle mass.
 - High dose fish oil (at least 3 gm twice daily) can assist non-pharmacological management.
- If **fasting triglycerides > 5 mmol/L** on 2 occasions, refer to a [lipid disorders specialist](#)
 - With high triglycerides, LDL is unable to be measured and is often low.
 - Fibric acid derivatives e.g., fenofibrate are first line as statins may be less useful.
 - This group is at risk of acute pancreatitis if the triglycerides are > 10 mmol/L.
- Consider **medications to reduce CV risk.**
 - Use statins first if combined dyslipidaemia if triglycerides < 5 mmol/L.
 - If triglycerides remain > 2.3 mmol/L and HDL is low (< 1 mmol/L), consider adding in a fibrate e.g., [fenofibrate](#) or [gemfibrozil](#).
- Anti-ANGPTL3 is undergoing clinical trials.

➤ **Familial hypercholesterolaemia**

- Maximally tolerated dose of statins
- [Ezetimibe](#)

- **Repatha – PCSK9 inhibitor injection**

Repatha – PCSK9 inhibitor injection is an [antibody](#) that targets a specific protein, called PCSK9.

- *PCSK9 promotes the breakdown of receptors on the liver that remove LDL cholesterol from the blood.*
 - *By blocking PCSK9's ability to work, more receptors are available to remove LDL cholesterol from the blood and, as a result, lower LDL cholesterol levels.*
 - *See the [PBS authority to prescribe Repatha](#).*
- *If patient is pregnant with heterozygous FH and established coronary heart disease, or with homozygous FH, consider bile acid sequestrants and [lipid disorders specialist referral](#) for lipoprotein apheresis.*
 - *Consider aspirin for secondary prevention*
 - *See [Familial Hypercholesterolaemia](#).*

Before starting a statin in a female patient of childbearing age, give **contraception advice** and **pre-pregnancy counselling**, and review annually.

- **contraception advice**, and
 - *Statin are contraindicated in pregnancy, so effective contraception is essential.*
 - *Long-acting reversible contraceptives (LARCs) are particularly useful.*
 - *Combined oral contraceptives can increase TG levels. Risk may exceed benefit for some women with hyperlipidaemia, especially if they have multiple cardiovascular risk factors.*
- **pre-pregnancy counselling.**
 - *Discontinue statins and other systemically absorbed lipid regulating drugs 3 months prior to conception, and during pregnancy and lactation.*
 - *Bile acid sequestrants are the only safe agents to control hypercholesterolaemia in pregnancy and lactation – colesevelam is more tolerable than older resins.*

5. **Monitor response** to intervention and therapy according to clinical context and risk:

- *Lipid response to diet and most medications is established within 3 to 4 weeks.*
- *HDL levels and the lipid response to fibrates are established more slowly (2 to 4 months).*
- *Side-effects and laboratory abnormalities are most likely within the first 8 to 10 weeks of treatment.*
- *Monitor for **statin tolerability and compliance**.*
- *Monitor control of other modifiable risk factors and observe for emergence or recurrence of complex co-morbidities or symptomatic CVD. Consider referral a [lipid disorders specialist](#).*

High risk (over 15% within 5 years)

- *Repeat cardiovascular (CV) risk assessment according to context or need.*
- *Measure lipids every 3 months until controlled, then measure every 12 months.*
- *Consider [blood pressure treatment](#).*

Moderate risk (10 to 15% within 5 years)

- *3 to 6 months lifestyle interventions. If risk is not adequately reduced, commence medication.*

- Consider blood pressure treatment and lipid lowering therapy. See [Hypertension](#) pathway.
- Repeat CV risk assessment every 6 to 12 months.
- Measure lipids every 3 months until controlled, then repeat fasting lipids every 2 years.

Low risk (< 10% within 5 years)

- 3 to 6 months lifestyle interventions. If risk is not adequately reduced, commence medication.
- Consider blood pressure treatment and lipid lowering therapy. See [Hypertension](#) pathway.
- Repeat CV risk assessment every 2 years.
- Repeat fasting lipids every 5 years.

6. Consider [lipid disorders specialist referral](#) if:
 - LDL > 3.5 mmol/L in patients on treatment with high-risk cardiovascular disease e.g., prior acute coronary syndrome.
 - Difficult to control LDL > 3.3.mmol/L in patients with coronary heart disease and with familial hypercholesterolaemia.
7. Consider [urgent or routine endocrinology](#) review if complex co-morbidities e.g., insulin resistance, diabetes, PCOS, NAFLD, and secondary dyslipidaemias such as renal, liver, and inflammatory disorders.

Referral

- If pancreatitis is suspected in a patient with fasting triglycerides > 5 mmol/L, refer to the [Emergency Department](#).
- Refer for [lipid disorders specialist referral](#) if:
 - **fasting triglycerides > 5 mmol/L** unresponsive to medical management
 - With high triglycerides, LDL is unable to be measured and is often low.
 - Fibric acid derivatives e.g., fenofibrate are first line as statins may be less useful.
 - This group is at risk of acute pancreatitis if the triglycerides are > 10 mmol/L.
 - LDL > 3.5 mmol/L in patients on treatment with high-risk cardiovascular disease e.g., prior acute coronary syndrome.
 - difficult to control LDL > 3.3.mmol/L in patients with coronary heart disease and with familial hypercholesterolaemia.
- Consider [urgent or routine endocrinology review](#) if complex co-morbidities e.g., insulin resistance, diabetes, PCOS, NAFLD, and secondary dyslipidaemias such as renal, liver, and inflammatory disorders.

Information

For health professionals

Further information

- Australian Family Physician – [Detecting Familial Hypercholesterolaemia in General Practice](#)

- National Heart Foundation of Australia, 2012:
 - [Lipid Management](#)
 - [Reducing Risk in Heart Disease: An Expert Guide to Clinical Practice for Secondary Prevention of Coronary Heart Disease – Summary](#)
- National Vascular Disease Prevention Alliance (NVDPA):
 - [Australian Absolute Cardiovascular Disease Risk Calculator](#)
 - [Australian Absolute Cardiovascular Disease Risk Calculator: Resources](#)
- NPS MedicineWise – [Managing Lipids](#)
- RACGP – [Cholesterol and Other Lipids](#) (The Red Book – Guidelines for preventive activities in general practice)

For patients

- Australian Atherosclerosis Society – [Familial Hypercholesterolemia](#)
- Heart Foundation:
 - [Healthy Eating Tips](#)
 - [Cholesterol](#)
 - [Coronary Heart Disease](#)
 - [Aboriginal and Torres Strait Islander Resources](#)
 - [Resources for Aboriginal Health](#)
- National Vascular Disease Prevention Alliance – [Australian Absolute Cardiovascular Disease Risk Calculator Patient Information](#)
- NPS MedicineWise – [Statins and Cardiovascular Disease: Frequently Asked Questions](#)

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