Cardiovascular disease risk assessment in primary care: **managing lipids**

The Cardiovascular Disease Risk Assessment and Management for Primary Care consensus statement was released earlier in 2018. This is the third in a series of articles about the statement and provides guidance on the assessment and management of lipids. Key changes include the revised CVD risk thresholds, advice to consider initiation of lipid-lowering medicines at intermediate levels of risk (5–15% 5-year estimated risk), the provision of a new treatment target for patients at high risk and a percentage reduction target for low-density lipoprotein cholesterol (LDL-C) for intermediate risk. Statins continue to be recommended as the first-line lipid-lowering medicine.

KEY PRACTICE POINTS:

- A healthy lifestyle focusing on smoking cessation, a balanced diet, regular physical activity and maintenance of an optimal weight should be encouraged for everyone
- For the majority of people, the estimated five-year CVD risk should be used to inform decisions about the use of lipid-lowering medicines
- Lipid-lowering medicines are recommended regardless of predicted risk in all patients with prior CVD or those with a five-year risk ≥ 15% and for people who have a total cholesterol to HDL-cholesterol (TC/HDL-C) ratio ≥ 8
- The benefits and harms associated with lipid-lowering medicines should be discussed to allow an individualised decision in people with intermediate risk (5–15%)
- Once lipid-lowering treatment is started, a new LDL-C target of ≤ 1.8 mmol/L is recommended for people at high risk and a 40% or greater reduction in LDL-C is recommended for intermediate risk groups
- Statins remain the first-line pharmacological treatment to lower lipids

This is the third in a series of articles updating the cardiovascular guidelines for primary care. For further information on cardiovascular risk assessment and blood pressure management see: "What's new in cardiovascular disease risk assessment and management for primary care clinicians", **www.bpac.org.nz/2018/cvd.aspx** and "Cardiovascular disease risk assessment in primary care: managing blood pressure", **www.bpac.org.nz/2018/bp.aspx**

A full copy of the consensus statement is available from the Ministry of Health website: **https://www.health.govt.nz/publication/cardiovascular-disease-risk-assessment-and-management-primary-care**

For further information on the use of statins to lower CVD risk see: "Prescribing statins to reduce cardiovascular risk", **www.bpac.org.nz/2017/statins.aspx**

Lipid management continues to be based on overall five-year cardiovascular risk

The assessment of an individual's overall five-year CVD risk is the key factor in determining treatment decisions for primary prevention.* Evidence shows that better outcomes can be achieved, especially for primary prevention, by managing overall CVD risk rather than hyperlipidaemia as a single risk factor in isolation.[1]

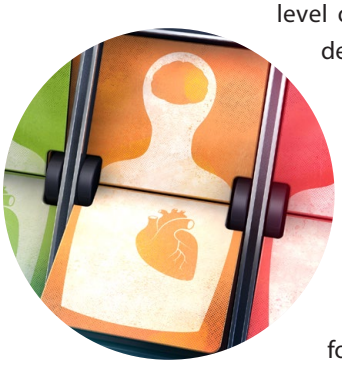
People with very high lipid levels (TC:HDL-C ≥ 8), however, including those with familial hyperlipidaemia, should be treated with lipid-lowering medicines regardless of their estimated CVD risk. Treatment is generally recommended for people with very high triglyceride levels (≥ 11 mmol/L) as the high lipid levels increase not only CVD risk but also the risk of acute pancreatitis.[1] (See: "People with very high triglycerides need special consideration")

An approach to management based on overall CVD risk rather than individual factors means that patients with the highest risk achieve the greatest absolute reduction in cardiovascular risk. Furthermore, the benefits of lipid-lowering treatment have been clearly shown to be directly proportional to an individual's pre-treatment CVD risk.[1, 2] Meta-analyses of randomised controlled trials show that every 1 mmol/L reduction in LDL-C from statin treatment is associated with an approximately 25% reduction in the relative risk of major cardiovascular events over five years.[1–3] However, this benefit is very small for people with an overall five-year risk < 5%.[1]

* The NZ Primary Prevention equations are not yet fully available for clinicians to use in practice, but the recommendations in the 2018 CVD risk assessment Consensus Statement based on categorisations of risk can be applied now. A Canadian interactive online CVD risk calculator now includes the ability to estimate risks and benefits based on the Predict equations. It is available at: **http://chd.bestsciencemedicine.com/calc2.html**

Clear communication about level of risk is needed

The new CVD consensus statement emphasises the importance of clear communication with people about their level of risk. Information should be presented to people in such a way that they can understand what their cardiovascular risk is and that allows them to take part in the decision-making. It should also be recognised that people with a similar estimated level of risk may not all make the same decisions regarding treatment. Factors such as the patient's co-morbidities, life-expectancy and personal preferences are important to consider, as are the benefits and harms of treatment options.[1] The aim is to come to a shared decision about the person's level of risk and formulate an individualised solution.



No change to lipid test requirements

A single non-fasting lipid level that provides a ratio of total cholesterol to high-density lipoprotein cholesterol (TC:HDL-C) ratio should be used when estimating CVD risk.[1, 4, 5] A fasting lipid level is still preferred in some patients, e.g. those with very high triglyceride levels.[6]

The TC:HDL-C ratio is used when calculating overall CVD risk and to guide treatment decisions. Once treatment has been initiated, LDL-C levels are used to inform decisions about the intensity of lipid-lowering medicines.

When to recommend lipid-lowering medicines

Decisions on the pharmacological treatment of lipids should generally be determined by the person's calculated overall level of CVD risk, with some exceptions, e.g. those with a TC:HDL-C ratio ≥ 8 (Table 1).

Medicines are not recommended for people at low risk (< 5%)

Lipid-lowering medicines are generally not recommended for patients with a five-year cardiovascular risk less than 5%; lifestyle interventions should be encouraged.[1]

Discuss the use of medicines for people with a 5–15% five-year risk

The benefit of lipid lowering therapy is likely to outweigh harm for most people in this risk group. The benefits and harms of lipid-lowering medicines should be clearly presented and discussed with all patients with a five-year cardiovascular risk of 5–15% to allow an individualised decision about the initiation of pharmacological treatment.[1]

Lipid-lowering medicines are recommended for patients with existing CVD or a ≥ 15% five-year risk

All patients with known CVD or with a five-year risk ≥ 15% should be prescribed lipid-lowering treatment along with advice on lifestyle interventions.

Lipid-lowering medicines are recommended for patients with TC:HDL-C ratio ≥ 8 regardless of cardiovascular risk

If a patient has a TC:HDL-C ratio of ≥ 8 despite lifestyle interventions, lipid-lowering medicines are recommended, regardless of their calculated cardiovascular risk.[1]

People who have high levels of total and LDL-cholesterol may have a familial hypercholesterolaemia inherited via autosomal dominance. A family history of premature heart disease in a first degree relative and the presence of tendon xanthomas may also support the diagnosis of a familial lipid condition if lipid levels of family members are not available.[1]

Table 1: Five-year CVD risk levels for lipid-lowering interventions in patients aged under 75 years[1, 4, 7]

New CVD risk level (based on NZ Primary Prevention equations)	**Old CVD risk level** (based on Framingham equations)	**Recommendation**
< 5%	< 10%	Lifestyle interventions are recommended for all people. Lipid-lowering medicines are not recommended.
5–15%	10–20%	The benefit of lipid lowering treatment is likely to outweigh adverse effects in most people. Discuss clearly the benefits and harms of initiating lipid-lowering medicines for patients and encourage dietary changes. If lipid-lowering medicines are started, a target reduction in LDL-C of ≥ 40% is recommended.
≥ 15%	≥ 20%	Lipid-lowering medicines are strongly recommended for patients in addition to dietary changes. An LDL-C treatment target of < 1.8mmol/L is recommended.
TC:HDL-C ratio ≥ 8 with any level of cardiovascular risk		Lipid-lowering medicines are recommended
▪ Familial hypercholesterolaemia ▪ Hypertriglyceridaemia		Individualised management is required, lipid-lowering medicines are usually recommended regardless of estimated CVD risk

People with very high triglycerides need special consideration

Patients with very high triglyceride levels (≥ 11 mmol/L) may benefit from lipid-lowering medicines, independent of their estimated CVD risk, as they are at increased risk of acute pancreatitis.[1] Advice on lifestyle interventions and appropriate management of co-morbidities (e.g. diabetes) is strongly recommended and may successfully reduce triglyceride levels.[1] If triglyceride levels remain high in these patients despite lipid-lowering treatment, consider discussion with a specialist.[1]

Managing lipids

Lifestyle interventions remain important for all

The most effective dietary approach to lowering LDL-C while continuing to maintain or improve HDL-C is to substitute saturated fats with mono- and polyunsaturated dietary fats.[1] Following a "heart health" diet and other sustainable lifestyle interventions such as exercise and smoking cessation should be encouraged for all patients. Those with the highest CVD risk have the greatest potential to benefit from lifestyle changes and advice should be tailored to the individual.[1]

Starting pharmacological treatment – statins are preferred

Evidence shows that statins are the most effective choice of cholesterol lowering medicine and therefore remain the recommended first line pharmacological treatment.[5, 8, 9] This also applies to patients requiring lipid-lowering treatment for familial hypercholesterolaemia or high triglycerides.[5, 8]

Statins vary in potency; their approximate equivalence is shown in Table 2. Atorvastatin is the first line choice of statin in New Zealand for most patients (also see **rosuvastatin**).

It is recommended that prior to initiation of a statin, other causes of dyslipidaemia should be considered such as hypothyroidism, renal disease or treatment with corticosteroids.[1]

New targets have been recommended

The Consensus Statement includes new recommendations for target LDL-C levels once lipid-lowering medicines have been initiated.

New LDL-C target for people at high risk

A LDL-C treatment target of 1.8 mmol/L or less is recommended for high risk patients.[1]

Aim for 40 % reduction in LDL-C in people with a 5–15 % five-year risk

Once lipid-lowering treatment has been started for people in this risk group, the aim should be to achieve a reduction of 40% or greater in LDL-C.[1] This is a new addition in the Consensus Statement and is based on a similar recommendation in the National Institute for Health and Care Excellence (NICE) guideline.[1, 8]

Adverse effects of statins

Most people tolerate statins well and serious adverse effects from treatment are rare.[1] If patients report symptoms after the initiation of statin treatment it is recommended that the statin is stopped, and then when symptoms have resolved, the statin re-started and the patient monitored for a return of symptoms.[1] If symptoms recur consider lowering the dose, alternate day dosing or switching to an alternative statin.[10]

It is estimated that:[1]

- Five people out of every 10,000 treated for five years will develop myopathy
- A further 10–20 people out of every 10,000 treated per year will have muscle-related problems, however, only one of these is likely to have elevated creatine kinase levels (see "Monitoring for adverse effects")
- 50–100 new cases of diabetes will occur for every 10,000 people treated for five years, however, harms from this are outweighed by the reduction in CVD risk

Other reported statin-associated symptoms include effects on cognitive function, primarily memory loss and confusion but also effects on sleep and mood, and changes in hepatic and renal function. There is a lack of evidence that these symptoms are actually caused by statins but they are clinically important as they contribute to the way people feel about taking statins and can result in poor adherence and cessation.

Check for medicine interactions – statins can have serious interactions with some other medicines; in particular, be aware of the interaction between simvastatin and potent CYP3A4 inhibitors such as erythromycin, clarithromycin, azole antifungals (e.g. itraconazole, ketaconazole) and ciclosporin, which can result in rhabdomyolysis.

For further information on managing adverse effects of statins see "Prescribing statins to reduce cardiovascular risk" **www.bpac.org.nz/2017/statins.aspx**

For further information on medicine interactions see the New Zealand formulary: **www.nzf.org.nz**

Monitoring after initiation of a statin

Monitoring for response

Once a statin is initiated, re-check a non-fasting lipid level every six to 12 months until the agreed treatment target has been reached and annually after that.[1] Previously the advice was to monitor three to six monthly until stable.[4]

Table 2. Statin potency and approximate equivalence (adapted from[1])

Treatment intensity	% reduction LDL-C	Rosuvastatin	Atorvastatin	Simvastatin*	Pravastatin
Low	30			10 mg	20 mg
Medium	38		10 mg	20 mg	40 mg
Medium	41	5 mg	20 mg	40 mg	80 mg
High	47	10 mg	40 mg	80 mg	
High	55	20 mg	80 mg		
Very High	63	40 mg			

* Doses of simvastatin above 40 mg should be used with caution due an increased risk of myopathy

Monitoring for adverse effects

Liver function tests are not routinely required once a statin has been initiated as the risk of liver toxicity appears low.[1] It is also not necessary to routinely check creatine kinase (CK) unless symptoms of muscle pain, tenderness or weakness develop which could indicate myopathy.[1] The risk of myopathy is dose-related and is increased in older people and those on combination lipid-lowering treatments*.[1] Advice from the new consensus statement regarding interpretation and management of CK testing is as follows:[1]

- For muscle pain without a rise in CK, consider reducing the dose or discontinuing the statin but also consider re-challenging once symptoms subside
- With a CK rise 3–10 times above normal with symptoms, reduce the dose or discontinue the statin and monitor symptoms and CK weekly
- With a CK rise more than 10 times above normal with symptoms, discontinue the statin immediately

* The use of a statin and a fibrate is now often advised against due to this increased risk[8]

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This article is available online at:
www.bpac.org.nz/2018/lipids.aspx