CKM Guidance

Cardiovascular-Kidney-Metabolic Disease

Preventing Adverse Outcomes in Cardiovascular Kidney Metabolic Conditions

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Please make sure to periodically check for updated content.

Instructions:

The guidance is separated into the multiple sections.

Clicking on the yellow highlighted text will take you to the relevant section of the guidance on the guidance web site.

Clicking on a pink highlighted abbreviation will take you to the relevant abbreviation within the abbreviations section of this document.

Clicking on a blue link will open relevant external guidance in a new window for more detailed information.

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Abbreviations

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Definition of dyslipidaemia and familial hypercholesterolaemia

Definition of dyslipidaemia and familial hypercholesterolaemia

- Dyslipidaemia is defined as abnormal levels of circulating lipids, primarily increased LDL cholesterol (LDLc), increased triglycerides (TG) and/or low HDL cholesterol. At present, LDLc is the major treatment target for reducing cardiovascular disease.

- Most cases of significantly raised LDLc (≥ 5 mmol/L) are due to polygenic risk or *secondary causes*. However, **familial hypercholesterolaemia (FH) should be considered if LDLc ≥ 5 mmol/L and no secondary cause evident**, particularly if LDLc > 6.5 mmol/L, xanthomas, or family history of significantly raised LDLc and/or early CVD. If FH suspected, calculate the Dutch Lipid Clinic Network (DLCN) Score. DLCN scores ≥ 6 should be discussed with lipid specialist to proceed with gene testing for FH.

- Secondary causes of high LDLc include:
  - Ketogenic diet
  - Nephrotic syndrome
  - Chronic kidney disease
  - Cholestatic liver disease
  - Type 2 diabetes
  - Hypothyroidism
  - Obesity
  - Anorexia nervosa
  - Post menopause
  - Pregnancy
  - Medications including corticosteroids, antipsychotics, retinoids, protease inhibitors etc.

- Specialist consultation is recommended if FH is confirmed for genetic counselling and cascade testing, particularly if FH is suspected or confirmed in children.
  - FH should be considered in children if LDLc > 3.5 mmol/L
  - FH should be aggressively managed and lipid lowering therapy is recommended from 8 – 10 years of age.

Treatment approach to dyslipidaemia

Treatment approach to dyslipidaemia

- All with dyslipidaemia should have a CKM risk assessment and interventions to optimise healthy living. Specific advice for dyslipidaemia includes:
  - Avoid trans fats and reduce saturated fats and oils (e.g. coconut, lard, butter).
    - Limit processed and deep-fried foods.
    - Unsaturated fats and oils (e.g. canola, rice bran, avocado, olive, plant-based margarines) may be useful alternatives.
  - Increase intake of fruits, vegetables and wholegrain foods which bind excess cholesterol e.g. oats, barley, quinoa, ground flaxseed and chia seeds
  - Specific dietary interventions to reduce TG levels include:

        - Reduced free sugar intake e.g. avoiding sugary drinks and lollies etc.
        - Reduced alcohol intake
        - Eating foods and/or supplements containing omega-3 fats regularly
    - Physical activity and movement can increase HDLc and reduce LDLc and TG
    - Interventions for weight loss if overweight or obese aiming for > 5% total body weight loss

- Lipid lowering therapy is strongly recommended in addition to healthy living interventions aiming for LDLc < 1.4 mmol/L and > 50% reduction in LDLc from baseline if ANY of the below:
    - LDLc ≥ 4.9 mmol/L and/or known familial hypercholesterolaemia
    - CV disease including asymptomatic coronary or carotid disease (includes CT calcium score > 300)
    - Diabetes with any microvascular or macrovascular complication(s)
    - UACR ≥ 30 mg/mmol
    - eGFR < 45 mL/min
    - UACR 3 – 29 mg/mmol AND eGFR 45 – 59 mL/min
    - 5 year CV risk ≥ 10%

- Lipid lowering therapy is recommended in addition to healthy living interventions if 5 year CV risk 5 – 9.9% aiming for target LDLc < 1.8 mmol/L and > 50% reduction in LDLc from baseline.
- Lipid lowering therapy should also be considered if 5 year CV risk 3 – 4.9% and additional risk factors for CVD. Target LDLc is < 1.8 mmol/L.
    - Risk factors to consider lipid lowering therapy include:
        - < 50 years of age
        - Direct family history of CV disease at < 50 years of age
        - Cardiac calcium score 100 - 300
        - Previous gestational diabetes and/or preeclampsia
        - MASLD

Choice of lipid lowering therapy

Choice of lipid lowering therapy

- First line lipid lowering medications are atorvastatin and rosuvastatin.

    - Rosuvastatin is typically preferred if previous CV event but mismatch with special authority criteria
        - Current special authority requires previous failures of atorvastatin or simvastatin to reach LDLc target unless Māori or Pacific ethnicity
        - Maximise rosuvastatin use in Māori and Pacific peoples given funded and their high CV risk
        - Other ethnicities may choose to self-fund rosuvastatin without trialling atorvastatin as cost is currently around $12 per week

- Usual dose range is atorvastatin is 10 – 80 mg daily and rosuvastatin 5 – 40 mg daily
    - Consider starting rosuvastatin 5 mg daily if South East Asian ancestry due to a common genetic polymorphism that increases rosuvastatin levels
    - Maximum dose of rosuvastatin is 10 mg daily if eGFR < 30 mL/min
    - At least 40 mg atorvastatin or 10 mg rosuvastatin daily is typically required to achieve a 50% reduction in LDLc

- Statins have low and potentially no teratogenicity - so statins can be used in women of child-bearing age without fear.
    - Current advice is to stop statins in pregnancy and breastfeeding, but discuss with secondary care if known cardiovascular disease and/or familial hypercholesterolaemia as it may be safest to continue statin.

- Measure non-fasting LDLc at least 3 monthly and titrate statin to reach LDLc target or maximal tolerated dose
    - 90% of LDLc lowering evident within 2 weeks so do not need to wait 3 months before titrating
    - Repeat testing may be barrier to optimising treatment so consider starting statin at or rapidly titrating statin to estimated dose to reach LDLc target

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- Switch atorvastatin to rosuvastatin if LDLc is above target on 80 mg daily or maximal tolerated dose
    - Consider trialling pravastatin if intolerant of low dose atorvastatin and rosuvastatin

- Consider ezetimibe 10 mg daily if LDLc above target despite maximal tolerated dose of statin
    - Ezetimibe no longer requires special authority approval

- Consider evolocumab (Repatha) or inclisiran if LDLc still above target but require SC injection (2-4 weekly or 6 monthly), are not funded and are expensive (particularly evolocumab). They will reduce LDL on average by a further 50% from baseline.

- Measure non-fasting LDLc 6 - 12 monthly once treatment optimised to ensure targets are still met.

Adverse effects of statins

Adverse effects of statins

Statins are typically well tolerated with most adverse effects only minor:

- Many reported adverse effects of statins may be due to the nocebo effect, particularly fatigue, muscle aches and memory loss, particularly as statins protect against and do not cause dementia.
- Serious adverse effects such as rhabdomyolysis and hepatotoxicity are extremely rare with statins other than simvastatin. Doses of simvastatin > 40 mg daily are no longer recommended.
- Only 50% of reported mild adverse effects recur on re-trialling the same statin or a different statin. Mild transient elevation of liver enzymes is common and does not require cessation. Exclude other causes.
- Statin-induced myopathy occurs in < 5% of people and predominantly affects the shoulder and hip girdle rather than generalised muscle pain.
- The benefits of statins almost always outweigh the rare deleterious effects on hyperglycaemia in people with prediabetes or diabetes and should not prevent treatment.

Treatment of persistent hypertriglyceridaemia

Treatment of persistent hypertriglyceridaemia

- Hypertriglyceridaemia is independently associated with increased CV risk but fibrates do not reduce CV events or total mortality in people treated with statins.
- Statins continue to be first line agents to reduce CV risk in hypertriglyceridaemia and healthy living interventions remain important aiming for a TG level < 1.7 mmol/L in secondary prevention and < 5 mmol/L in primary prevention.
    - Avoid trans fats and reduce saturated fats and oils (e.g. coconut, lard, butter).
        - Limit processed and deep-fried foods
        - Unsaturated fats and oils (e.g. canola, rice bran, avocado, olive, plant-based margarines) may be useful alternatives.
    - Increase intake of fruits, vegetables and wholegrain foods which bind excess cholesterol e.g. oats, barley, quinoa, ground flaxseed and chia seeds
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