Statins are one of the most commonly prescribed medicines in Australia, with over 14 million prescriptions dispensed under the Pharmaceutical Benefits Scheme in 2015-16. Statins are primarily used to lower cholesterol and have clear benefits in secondary prevention of heart attacks and strokes. The evidence is less clear in primary prevention and in older people. The prevalence of hyperlipidaemia increases markedly with age; however, in much older people LDL-cholesterol and total cholesterol levels decline. Guidelines recommend not starting lipid-lowering medications in patients with limited life expectancy. In addition, most nursing home residents who use statins at the time of progression to advanced dementia continue use in follow-up. Discontinuation of statins should be considered in frail older residents with limited life expectancy.

Statins
Statins, also known as HMG-CoA reductase inhibitors, include:

- Atorvastatin
- Fluvastatin
- Pravastatin
- Rosuvastatin
- Simvastatin

The LDL-cholesterol lowering effect is best with atorvastatin, rosuvastatin and simvastatin, and lower with fluvastatin and pravastatin. Some statins are available in fixed dose combination products with amlodipine and ezetimibe.

Benefits
Statins reduce the risk of heart attacks (myocardial infarction), stroke, revascularisation procedures and mortality. According to the Australian Medicines Handbook (AMH) statins are the most effective LDL-cholesterol lowering agents, reducing levels by 30 to 50%. Statins prevent approximately 5 major cardiovascular events in 100 patients treated for 5 years, and reduce 5-year cardiovascular mortality by approximately 20 to 30%. This reduction in death is seen in patients taking statins for one to two years.

Long-term statin therapy also protects against strokes in people with known coronary artery disease or other cardiovascular risk factors. Approximately one stroke is prevented for every 100 people taking a statin for 5 years. This benefit can be seen as early as weeks after an acute coronary event.

Adverse effects
Statin-related side effects may more often affect older people, reducing their quality of life. People at end-of-life may be at higher risk for serious side effects from statins.

The most common adverse effect of statins are mild gastrointestinal symptoms such as nausea, vomiting and abdominal pain. Headache, sleep disturbances and dizziness may also occur. Liver enzymes may be increased. Statins appear to reduce or have no effect on cognitive decline.

Statins are also associated with a slightly increased risk of new onset diabetes. When this occurs, most people were likely to develop diabetes anyway. Evidence suggests that treating 255 people with statins for 4 years results in one additional case of diabetes, while possibly preventing 5 major coronary events.

Statins can also cause myalgia, myopathy (with or without creatine kinase elevation) and rhabdomyolysis. Myalgia refers to pain in the muscles. Muscle pain is often seen with statin-based myopathy; however, painless myopathy from statin therapy is also common. Myopathy is a general term for disease of the muscles, and it is characterized by general muscle weakness. Myopathy related to statins is rare and occurs in less than 1 in 1,000 patients. Rhabdomyolysis is the extreme life-threatening form of myopathy, in which the muscle tissue is so inflamed that it begins to break down. The result of this breakdown is a large amount of myoglobin (muscle protein) into the bloodstream, leading to acute renal failure. The incidence of rhabdomyolysis is extremely rare.
Risk factors for statin-related myalgia and myopathy include:

- Age
- Female gender
- Low body weight
- Liver and kidney impairment
- Electrolyte disturbances
- Infection
- Hypothyroidism
- Hypoxia
- Polypharmacy and drug interactions

These muscle-related adverse effects may cause gait disturbances, which can lead to falls in older people.

All these muscle-related side effects appear to be dose-related. To reduce the risk, low doses should be prescribed initially, and then increased according to response.

Deprescribing
Discontinuation or deprescribing is the process of tapering or stopping drugs for the purpose of minimising polypharmacy and improving patient outcomes. Deprescribing has been proposed as a way to reduce polypharmacy in frail older people. When the potential benefit of a therapy is marginal it is reasonable to reconsider ongoing use. Deprescribing is especially relevant for patients with life-limiting illness and in palliative care. The decision to discontinue medicines should weigh the relative benefits and burdens of continuation of therapy. Stopping some medications may be associated with improved quality of life.

The following steps are required in decision making about deprescribing:

1. ascertain all drugs the patient is currently taking and the reasons for each one
2. consider the overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention
3. assess each drug regimen for its eligibility to be discontinued
4. prioritize drug treatments for discontinuation
5. implement and monitor the drug discontinuation regimen

Statin discontinuation
Discontinuation of statins should be considered when:

- Life expectancy is very limited
- Low risk of cardiovascular events
- Adverse side effects experienced
- High-risk for statin-related myopathy
- No recent symptomatic acute coronary events

A recent study suggested that stopping statin treatment at the end-of-life may be safe and is potentially associated with improved quality of life and reduced costs. This study included patients for whom clinicians would not be surprised if they died within the next year. This “surprise” question may be useful in determining the importance of ceasing statins. The findings of this study may provide reassurance to residents or caregivers and their clinicians who are considering stopping statin therapy that doing so may not incur harm in the setting of advanced illness and limited life expectancy. There is little short-term risk of recurrent cardiovascular events for most people when discontinuing statins.

Statins can usually be stopped without the need for tapering the dose. A trial cessation can be implemented to see if adverse effects improve.

Summary
Statins are one of the most commonly prescribed medicines in older people. Most people who have cardiovascular disease will benefit from long-term use of statins to prevent myocardial infarctions and strokes. In some older adults, the burden of the therapy outweighs the benefits due to the high potential for adverse effects. Among people with limited life expectancy, deprescribing of statins should be considered when the risk of harm and pill burden exceed the potential benefits. Quality of life may be improved in those with life-limiting illness.

References