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Therapeutic brief

Diabetes Triple Check ✓✓✓

This therapeutic brief asks you to consider a Diabetes Triple Check which, in addition to glycaemic control and lifestyle intervention, involves considering the role of antihypertensive drugs, aspirin and lipid lowering drugs in the management of patients with type 2 diabetes.

Think Diabetes, think Diabetes Triple Check

- Check Blood Pressure ✓
- Check Aspirin ✓
- Check Lipids ✓

The number of adults in Australia with diabetes has trebled over the last two decades. Approximately 24 % of those over 75 years are affected so diabetes has special significance for the veteran population.¹

Cardiovascular disease is the leading cause of morbidity and mortality in patients with diabetes.² Evidence confirms that gains can be made in the management of your patient with diabetes by addressing modifiable risk factors such as hypertension, dyslipidaemia and the use of aspirin.

Almost 65% of Australian veterans dispensed medicines for diabetes have also had an ACE inhibitor or Angiotensin II receptor blocker (A₂RB) dispensed, however only 53% were dispensed lipid lowering therapy and 52% antiplatelet agents³ respectively.

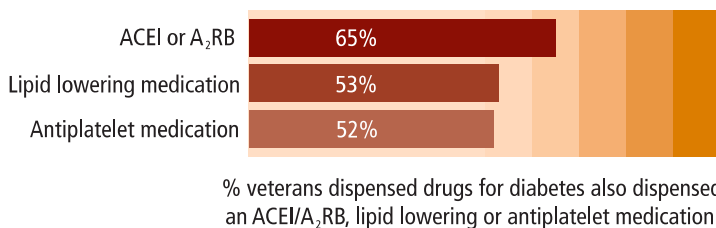


Figure 1. Use of adjunct therapy in Australian veterans with diabetes

A recent study demonstrated that good glycaemic control, dietary and lifestyle interventions and modification of cardiovascular risk factors for people with type 2 diabetes and microalbuminuria reduces the risk of cardiovascular events by about 50%.⁴

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Key Points

- Control of blood pressure in patients with diabetes significantly reduces the risk of micro- and macrovascular disease and associated mortality.
- In patients with diabetes and microalbuminuria, multifactorial intervention can reduce the risk of cardiovascular events by up to 50%.
- For veteran patients with diabetes, ACE inhibitors are advocated as first line therapy because of coexisting conditions.
- Concurrent therapy with more than one drug will often be required to achieve blood pressure targets.
- Using a combination of antihypertensive treatments at low doses can maximise effectiveness and help minimise adverse effects.
- Low dose aspirin is recommended for all patients with diabetes > 50 years unless contraindicated.
- Strong evidence supports the use of lipid lowering therapy in patients with diabetes, in both primary and secondary prevention of cardiovascular events.
- Statins are the drugs of choice for patients with diabetes with elevated total cholesterol or LDL cholesterol.



2 Check Blood Pressure ✓

- For veteran patients with diabetes, ACE inhibitors are often advocated as first line therapy because of coexisting conditions.
- Concurrent therapy with more than one drug will often be required to achieve blood pressure targets^{2,5,6} for most patients with diabetes.⁷
- Using concurrent therapy at low doses, e.g. ACE inhibitor plus a low-dose thiazide diuretic, can maximise effectiveness and help minimise adverse effects.⁶⁻⁸
- Any reduction in blood pressure towards the target is beneficial.

Approximately 70% of patients with diabetes will develop hypertension compared to 20% of patients without diabetes.⁹

Effective treatment of hypertension for people with diabetes reduces cardiovascular risk. Benefits have been established for people with type 2 diabetes *without* hypertension who achieve even lower blood pressure (eg: slowed progression to incipient and overt diabetic nephropathy, reduced progression of diabetic retinopathy and lower incidence of stroke).¹⁰

The target blood pressure for patients with diabetes and no signs of diabetic nephropathy is < 130/80 mmHg.^{6,8,11-13} For patients with diabetic nephropathy with proteinuria > 1 g per day, the target is < 125/75 mmHg.^{6,7,12,14,15}

Both lying and standing blood pressure should be assessed for patients with suspected autonomic neuropathy who are prone to orthostatic hypotension.^{6,15}

Choice of antihypertensive

The benefits of blood pressure control for patients with type 2 diabetes have been shown with ACE inhibitors, low dose thiazide diuretics, beta-blockers, and A2RB.⁶

When selecting an antihypertensive drug, consider effects on coexisting conditions.

ACE inhibitors

For veteran patients with diabetes, ACE inhibitors are often advocated as first line therapy because of coexisting conditions:

- Microalbuminuria or proteinuria^{2,5,7,14}
- Post myocardial infarction^{5,7,16}
- Left ventricular dysfunction^{5,11,16}
- Heart failure.^{5,7,16}

ACE inhibitors reduce progression from microalbuminuria to overt nephropathy, both for patients with and without hypertension.¹⁷

Thiazides

Low-dose thiazide diuretics are an alternative for treatment of hypertension in people with diabetes, particularly in the absence of renal disease.^{2,6,8} Effects on glucose tolerance and plasma lipids are minimal with current recommended low doses.⁵

Beta-blockers

Beta-blockers may be used in patients with type 2 diabetes⁵ with attention to tight glycaemic control and lipid levels. They are an option in people with diabetes, particularly in the presence of coexisting cardiovascular disease such as heart failure, angina or myocardial infarction.⁷

Angiotensin II receptor blockers

An A2RB is an alternative^{2,6,8,17} for patients who experience intolerable cough with ACE inhibitors.

There are limited data to suggest additional benefit from combining an ACE inhibitor with an A2RB; however, large outcomes studies are lacking, and are clearly needed before this approach can be routinely recommended.



Check Aspirin ✓

Low dose aspirin (75-150 mg daily)^{14,15} is recommended for all patients with diabetes and established cardiovascular disease,^{14,15} or patients with diabetes aged 50 years or older, unless there are specific contraindications.¹⁵ Low dose aspirin should be considered for younger patients with diabetes who have a cardiovascular risk, estimated by the New Zealand Cardiovascular Risk Calculator chart, of greater than or equal

to 15% over 5 years unless contraindicated.⁸ The benefits of aspirin therapy must be weighed against the risk of bleeding complications (gastrointestinal bleeds, haemorrhagic stroke).^{8,18}

Although data are limited in patients with diabetes, agents such as clopidogrel may be considered as a substitute in the case of aspirin allergy.^{5,18}

Check Lipids ✓

- Statins are considered first line therapy where there is elevated total cholesterol or LDL cholesterol.^{5,8,16,19}
- Initiate therapy at low doses and gradually increase to achieve target levels.
- Advise patients to immediately report any unexplained muscle pain, tenderness or weakness.⁵
- Guidelines advocate LDL cholesterol as the primary target of therapy.¹⁹ The following target lipid concentrations for patients with diabetes have been recommended:
 - LDL cholesterol < 2.5 mmol/L
 - Total cholesterol < 4.0 mmol/L
 - HDL cholesterol > 1.0 mmol/L
 - Triglycerides < 2.0 mmol/L^{2,14-16,19}
- Any reduction in lipid levels towards the target is beneficial.

Strong evidence supports use of lipid lowering therapy in patients with diabetes, in both primary and secondary prevention of cardiovascular events.²

Choice of lipid lowering drug

Statins

Average effects of statins on cholesterol levels:
 ↓ LDL 20-50%, ↓ TG 5-15%, ↑ HDL 5%.⁵

The likelihood of adverse effects with statins, including serious muscular reactions, is dose-related, increases with age and renal impairment.⁵ Coexisting conditions such as diabetes, hepatic disease, untreated hypothyroidism, surgery and intercurrent illness may also increase risk, as will interactions with grapefruit juice and certain drugs, especially fibrates.^{5,20}

Test liver function and creatine kinase before and at intervals during treatment,⁵ including at least once about four to eight weeks after starting therapy¹⁶, after dose increases and/or when indicated clinically.⁵

Avoid stopping statin if symptoms of an acute coronary syndrome are present (stopping is associated with an increased rate of cardiac events, especially in the first week after stopping).⁵

The prescriber must certify that the patient satisfies criteria set out in the Pharmaceutical Benefits Schedule and the use is in accordance with the registered indications which may differ between agents in this class of medicines.

Fibrates

Fibrates (gemfibrozil, fenofibrate) are effective for hypertriglyceridaemia and low HDL cholesterol (fibrates ↓ LDL 5-15%, ↓ TG 25-40%, ↑ HDL 10 %).^{5,16,19} They are the first choice in marked hypertriglyceridaemia. Choose gemfibrozil if TG is > 4.0 mmol/L, or for mild TG elevation (2 – 4 mmol/L) with low HDL (< 1 mmol/L).¹⁶

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Combinations

Low doses of bile-acid binding resins (cholestyramine, colestipol) can be used with statins^{5,16,19} to increase the lowering of LDL by an additional 5-10%.¹⁹ Caution is required if triglycerides > 3 mmol/L⁵ as resins may exacerbate hypertriglyceridaemia.^{5,16}

Ezetimibe reduces LDL cholesterol by about 18% in short term studies.⁵ When added to a statin, it can increase the LDL lowering effect by up to 20%,^{5,8} but is associated with an increase in adverse effects (myalgia and increased liver enzymes).⁵ There are no long term outcome studies on the efficacy and tolerability of ezetimibe.

For resistant cases, treatment with both a statin and fibrate may be required. This combination is well known to increase the risk of rhabdomyolysis and should only be undertaken with specialist guidance.^{5,16,19}

Omega-3 fatty acids are effective in lowering triglycerides. They may be a useful second-line therapy for hypertriglyceridaemia¹⁶ or mixed hyperlipidaemia in combination with statins with close monitoring of glycaemic control.^{5,8,16,19}



For drug information, including precautions, adverse effects, interactions and contraindications, please refer to the Australian Medicines Handbook (AMH) 2005 and approved product information.

A commonly used risk calculator is the New Zealand Risk Calculator at <http://www.health.govt.nz/publication/assessment-and-management-cardiovascular-risk>

What to tell my veteran patient about diabetes and cardiovascular risk

- Emphasise that diabetes increases the risk of complications of the nerves, eyes, kidneys, heart, circulation and brain.
- The risk can be reduced by addressing relevant lifestyle issues and, if necessary, introducing new medications.
- Veterans may be prescribed more than one medication to treat their individual cardiovascular risk.
- Stopping smoking is the single most important risk factor to help prevent cardiovascular disease (the Quitline is available 24 hours for information and support – Phone 137 848).
- Lifestyle interventions (physical activity, maintaining a healthy body weight, healthy eating, staying a non-smoker) are life long.



Think Diabetes, think Diabetes Triple Check

- ▶ Check Blood Pressure ✓
- ▶ Check Aspirin ✓
- ▶ Check Lipids ✓



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