trial, the risk of cardiovascular events was reduced by 50% in a large subset of patients with DM by lowering diastolic BP by 10 mm Hg (from 90 mm Hg to 80 mm Hg) (*Lancet* 1998; 351:1755–1762).

Meeting the target: Non-pharmacologic approaches, such as modest weight loss (even 4–5 kg leads to substantial improvement), restricting salt intake, avoiding excess alcohol, and exercising regularly can produce important benefits.

Most older patients with DM will need medication to reach the target BP, and the majority of these will require several drugs to do so. More than 60% of patients required two or more medications and 30% required three or more to reach BP target levels in the **UKPDS** trial. Thiazide diuretics, ACEIs, ARBs and beta-blockers all show evidence of benefit in patients with DM who have concomitant hypertension. Which to start first? Experts disagree, and we think it's moot, given that most patients won't be controlled with monotherapy (*Ann Int Med* 2003; 138:587–602).

Check points for blood pressure management in persons with DM

- ✔ Aim for BP <130/80 mm Hg.
- ✔ Consider non-pharmacologic approaches.
- ✔ Thiazides, ACEIs, ARBs and β-blockers all have been shown to provide benefit.
- ✔ Multi-drug therapy may be needed (e.g. diuretic with an ACEI or ARB).
- ✔ Keep it simple (e.g. combination tablets, once daily dosing).
- ✔ Tailor therapy to patient's daily routine.
- ✔ Consider BP self-measurement.

Cholesterol-lowering agents have an important role in reducing morbidity and mortality in DM. The Canadian Diabetes Association 2003 guideline (http://www.diabetes.ca/cpg2003/) recommends that the goals of treatment for adults with DM are:

- ✔ LDL <2.5 mmol/L.
- ✔ Total/HDL ratio <4.
- ✔ Total triglycerides <2 mmol/L.

More recently, some experts are suggesting that those with DM at sufficiently high risk of vascular events (e.g. over the age of 50, secondary prevention) will benefit from lipid-lowering therapy *regardless* of the initial cholesterol levels.

Evidence: The Heart Protection study (*Lancet* 2003; 361:2005–2016) looked at the effects of statin therapy in persons with DM or occlusive vascular disease on preventing major coronary events, strokes and revascularizations over a five-year treatment period. There were highly significant reductions of about a quarter overall in both groups. The study also found that there was a 27% reduction in adverse events among those with DM whose pretreatment LDL was *below* 3.0 mmol/L.

Meeting the targets: Non-pharmacologic strategies such as a low fat/high fibre diet and exercise should be encouraged in all patients with DM. Most, however, will need medication to reach the recommended lipid levels.

Which drug to choose? The statins remain the best agents to lower LDL cholesterol. They are believed to have other protective effects that target atherosclerosis, as well as lowering the risk of MI and stroke in patients with or without DM. Fibrates are effective in lowering triglycerides (see table upper-right).

Complications of statin therapy? Up to 10% of patients will experience myalgias. Myositis can occur in about 0.5% and rhabdomyolysis in less than 0.1%. The risk of these complications is potentiated when patients are being treated concomitantly with macrolides (e.g. erythromycin), some antifungals, niacin, fibrates and grapefruit juice. Careful history-taking is important.

Up to 3% of patients will develop elevated transaminase levels within the first three months of statin therapy. Do serum levels at baseline and at three months after initiating therapy. Stop the drug if levels are more than two or three times the upper limit.

Effects of Lipid-lowering Drugs

	LDL	HDL	TGs
Statins	▼▼▼	▲	▼
Fibrates	▼	▲	▼▼
Nicotinic Acid	▼	▲▲	▼▼
Resins	▼▼	⊙	⊙
Cholesterol absorption inhibitors	▼▼	⊙	⊙

▼ decreases ▲ increases ⊙ does not change

TGs: triglycerides;
Resins: bile acid sequestrants (i.e. cholestyramine)

The Bottom Line

A Use ACEIs in patients with DM who have no contraindications:

- ✔ As part of a multi-level hypertension regimen in combination with a diuretic.
- ✔ In patients with microalbuminuria to prevent progression of nephropathy.
- ✔ To reduce the risk of MI, stroke and death.

B Target BP <130/80 to reduce the risk of vascular complications of DM. BP control may be at least as important as tight glycemic control in DM.

C Tight cholesterol/lipid control will reduce cardiovascular risks in DM. In your patients with DM over the age of 50 years, consider starting a statin, even if the cholesterol is normal.

Article

Peer-reviewed

informed

Institute for Clinical Evaluative Sciences (ICES), G1 06, 2075 Bayview Avenue, Toronto, ON M4N 3M5
Phone: (416) 480-4055, Extension 5168 Internet: http://www.ices.on.ca E-mail: informed@ices.on.ca