Optimising the care of patients with type 2 diabetes and cardiovascular disease:

Translating evidence-based medicine into practice

This report is from a conference that took place on 29 November 2006 at The Magic Circle, London.

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Introduction

Optimising the care of people with type 2 diabetes and cardiovascular disease by translating evidence-based medicine into practice was the focus of this meeting. The conference speakers reviewed recent landmark clinical trials, the management of service users in primary care and the likely implications of practice-based commissioning.

s many as 80% of people with type 2 diabetes may die of cardiovascular disease (CVD),' said Martin Hadley-Brown, a GP in Norfolk, and Chairman of the Primary Care Diabetes Society. 'Having type 2 diabetes may shorten life expectancy by up to 10 years, depending on age of diagnosis, as well as diminishing the individual's quality of life.

'All our patients with type 2 diabetes are at very high risk of CVD. Therefore, when considering treatments such as statins to reduce the risk of CVD, people with type 2 diabetes are considered in the same high risk category as those who have already had a cardiovascular event. People with metabolic syndrome or pre-diabetes are also considered in this high risk category. In addition, most people with type 2 diabetes have at least one other risk factor for CVD, such as smoking status, weight, hypertension or a sedentary lifestyle.'

He suggested that during the annual review of a person with diabetes it is important during history-taking to look for signs of, for example, angina and breathlessness. The patient should be asked about his or her exercise tolerance in order to detect silent ischaemia. The clinician should check for raised blood pressure, poor or absent pulses and for signs of ischaemia in the foot. He also recommended checking for microalbuminuria, as it is an indicator of increased cardiovascular risk in people with type 2 diabetes.

Discuss complications early

People with diabetes often have fears about what may happen to them based on the negative experiences of others (such as those who have had an amputation). This fear may prevent them from confronting their own condition and from taking effective steps to delay the worsening of the condition. Dr Hadley-Brown also recommended discussing both the serious complications and possible preventative measures as early as possible post-diagnosis. He also



Martin Hadley-Brown

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commented that lifestyle advice remains important, even if people are already receiving pharmacotherapy.

Negotiate with patients

'We must explain to and negotiate with our patients, as treating diabetes is something that can only be achieved by the clinician and the patient working together,' said Dr Hadley-Brown. 'This can be facilitated through structured education sessions, consultations, diabetes liaison nurses and access to dietitians.

'Once an individual is diagnosed with type 2 diabetes, they have the condition for life,' stressed Dr Hadley-Brown. 'Systematic follow-up and review, practice registers and recalling patients for annual review are important tools in management. The therapeutic momentum should be maintained: that is, increase doses or alter therapies to meet ideal targets rather than waiting for things to go wrong,' he continued. 'That means being proactive rather than reactive and continuing education for both the healthcare professionals and the patients. In the future, appropriate commissioning will be crucial to providing the right management for patients.'

Dr Hadley-Brown believes that the Quality and Outcomes Framework (QOF) has been the major driver of improved standards of care in general practice in the UK. The targets can be debated but 'are not far off the mark'. While National Service Frameworks and NICE guidance have not been implemented everywhere, the financial incentives attached to the QOF have forced everyone to try to achieve the goals. 'It can make care mechanistic,' he said, 'but it is better to have the boxes ticked rather than completely ignored.'

Landmark studies

'What is a landmark study?' asked Miles Fisher, Consultant Physician from Glasgow, at the start of his talk on evidence-based medicine in people with diabetes at high risk of CVD. He suggested that such a study: 'Answers a clinically important question, is scientifically and statistically well designed, provides clear cut results, is presented in a major journal, is widely discussed by the medical community and changes clinical practice. The 4S study is, therefore, a good example of a landmark study, as it meets all these criteria (Scandinavian Simvastatin Survival Study Investigators, 1994).' He then moved on to discuss more recent landmark studies.

The hypothesis of the Anglo–Scandinavian Cardiac Outcomes Trial (ASCOT; Dahlof et al, 2005) was that blood pressure lowering with newer agents (amlodipine and perindopril) confers benefits over older agents (atenolol and bendroflumethiazide). There were 19257 participants with hypertension and three other risk factors included in the study, who had a median follow-up time of 5.5 years. Blood pressure was slightly lower with the newer agents and there was an insignificant reduction in non-fatal myocardial infarction (MI; including silent MI), and death from coronary heart disease. There was a significant reduction in all-cause mortality (P= 0.025).

Approximately 27 % (n = 5145) of people in the ASCOT had diabetes. According to Dr Fisher, 'the implications for people with diabetes from the ASCOT study are that beta-blockers are no longer recommended as first- or second-line therapy. In addition, angiotensin converting enzyme (ACE) inhibitors should be recommended first line, with amlodipine or a diuretic second line.'

The Treating to New Targets (TNT) study (LaRosa et al, 2005) tested the hypothesis that more intensive lowering of cholesterol with atorvastatin 80 mg versus 10 mg would further reduce cardiovascular events. Over 10 000 people with a history of CVD were recruited and a 22% reduction in major

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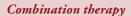
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Mike Mead

cardiovascular events was found in those receiving the higher dose (*P*<0.001). There was a 25 % reduction in major cardiovascular events among the 1501 people with diabetes involved in the trial. Dr Fisher reasoned that the implications for people with diabetes of the TNT study are that medium to high doses of statins should be used to achieve a total cholesterol of less than 4 mmol/l.

The PROspective pioglitAzone Clinical Trial In macroVascular Events (PROactive; Dormandy et al, 2005) hypothesised that 45 mg pioglitazone would reduce total mortality and macrovascular morbidity in type 2 diabetes when added to existing therapy. People with type 2 diabetes and existing CVD (n = 5238) were recruited and followedup for, on average, 3 years. There was a significant 16% risk reduction in the incidence of the combined secondary endpoints of death, MI and stroke (P=0.027). Dr Fisher suggested that as a result of the PROactive study, pioglitazone should be used in the majority of people with type 2 diabetes and CVD.



Treatment of hypertension often requires combination therapy to achieve targets, said Mike Mead, a GP from Leicester. 'If two drugs are not controlling the blood pressure, use three or four,'

he commented. 'There is no reason why patients in this situation should be referred for specialist care as they can be treated by a GP.

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'What is diabetes?' he then posed. 'To some extent it is an artificial concept. If a person has a fasting blood glucose level of 6.6 mmol/l, do you advise them that they do not have diabetes and plan to see them in a year's time?' There is a continuum over the years from impaired fasting glucose to impaired glucose tolerance and diabetes.

'Sugar is part of the cardiovascular risk spectrum,' said Dr Mead, 'and rather than defining people as having diabetes or not, we should be considering their overall cardiovascular risk.'

Practical drug therapy

The drugs used in preventing CVD can be summarised by the mnemonic MASA (Metformin, Aspirin, Statin, and ACE inhibitor or Angiotensin receptor blocker).

The UK Prospective Diabetes Study (UKPDS) showed that metformin reduced the incidence of MI by 38% (UKPDS Group, 1998). It should not be restricted to obese people only and renal function must be assessed prior to its use.

'Most people with type 2 diabetes should be on aspirin, although the evidence of its benefit is not comprehensive,' said Dr Mead. Every person with type 2 diabetes over the age of 40 should receive a statin, as supported by data from the 4S study, the Heart Protection Study (HPS) Collaborative Group and the Collaborative Atorvastatin Diabetes Study (CARDS; The Scandinavian Simvastatin Survival Study Investigators, 1994; HPS Collaborative Group, 2002; Colhoun et al, 2004; respectively). ACE inhibitors or angiotensin receptor blockers should also be given. 'You need a pretty good reason for a person with type 2 diabetes to not be on these agents,' said Dr Mead.

Beta-blockers are now being used further down the line as a result of the ASCOT (Dahlof et al, 2005). They are, however, useful in people with high sympathetic drive, angina and post-MI.

About 20–30% of cholesterol is transported as HDL. HDL reverses cholesterol transport and takes cholesterol from the periphery, including plaques, back to the liver where it is excreted in bile. A low HDL is one of the biggest risks for CVD. People with type 2 diabetes often have a low



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and dysfunctional HDL. HDL levels can be raised by exercise, reducing smoking and by drinking alcohol moderately (2–3 units per day). The glitazones can also raise HDL and, as there is a lack of drugs that can cause this action, this is a particularly valuable event. Fibrates have also been shown to provide an increase in HDL.

'In summary, we should be using combination therapy across the board, for lipids, for hypertension and for diabetes,' said Dr Mead. 'By the time someone is diagnosed with diabetes, 50% of β -cell function has been lost and they are probably already 10 years along the continuum.'

Practice-based commissioning

'Practice-based commissioning is being introduced to achieve the best possible health outcomes and health care and will be a partnership between primary care trusts, general practice and local government,' said Colin Kenny, a GP from Dromore, County Down. He linked practice-based commissioning with other reforms such as patient choice and payment by results.

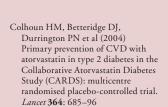
Commissioning is a process that determines how the healthcare budget is used. As a minimum, it involves an assessment of need, production of a specification to meet this

need, procuring services to deliver the specification and proactive monitoring. There are financial incentives for taking part, including an enhanced service payment, use of savings to reinvest in services and the ability to expand in-house provision. The general practice is also given more autonomy and power and, through collective enterprise, more clout to redesign services.

The perceived benefits of practice-based commissioning include a greater variety of services from a greater number of providers. Front-line doctors and nurses will have more involvement in commissioning decisions and service users will receive treatment closer to home. Dr Kenny suggested that this system is quite similar to the GP fund holding policy of the previous government.

People with diabetes want accessibility, expertise, continuity of care and well-planned services. With that in mind, when commissioning services, the things that specialist care does well should also be considered: detailed expertise, depth of experience, familiarity with rareties, the ability to perform and interpret research, access to specialist teams, teaching and leadership. However, 'specialist care services are expensive and it should be possible through practicebased commissioning

to find cheaper ways of delivering the services,' said Dr Kenny. He concluded by recommending the recently published *Diabetes Commissioning Toolkit* as a way of planning commissioning (DoH, 2006).



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