News

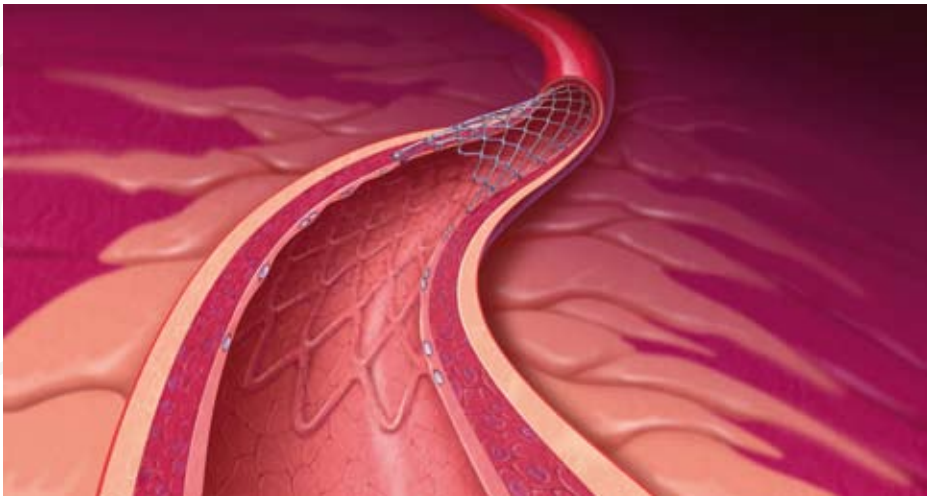
NICE issues new draft guidance on drug-eluting stents

The National Institute for Health and Clinical Excellence (NICE) has recommended that drug-eluting stents can continue to be used in patients who have a higher risk of needing further stents if a conventional bare-metal stent were used instead. It has set a limit for the price differential between drug-eluting and bare-metal stents of £300.

Likely candidates for drug-eluting stents are those in whom the coronary artery is less than 3 mm in diameter, or the segment of the artery to be treated is longer than 15mm.

The new draft guidance on drug-eluting stents, which was issued by NICE on 1st February 2008, is very different from the draft proposals that the agency had put out for comment last year. Those proposals stated that drug-eluting stents "do not represent a cost-effective use of National Health Service resources," after taking into account the risks and benefits of drug-eluting stents as compared with bare-metal stents. The British Cardiovascular Society, the British Cardiovascular Intervention Society (BCIS), and the British Heart Foundation, had all voiced strong objections to the proposals which now seem to have been reversed in the draft guidance.

Andrew Dillon, NICE Chief Executive, said: "This decision to recommend the use of drug-eluting stents for patients was reached by a careful consideration of the evidence, comments received during consultation and further economic modelling. The independent Appraisal Committee took into account the risks and benefits of the different types of stents, and the significant additional costs involved in the use of drug-eluting stents compared to bare-metal stents."



In a statement, BCIS President, Dr Mark de Belder said that several members of his organisation and of the British Cardiovascular Society had worked hard with NICE to achieve the current reversal of the original proposals. He said they had had a "long hard battle" and there was "a fundamental disagreement between the economists and the clinical experts, based mainly on the methodology used in the economic modelling exercise used", but, in the end, the NICE Advisory Committee had paid heed to the clinical experts' advice and alternative economic models to the one they had commissioned.

Dr De Belder noted, however, that the Advisory Committee had rejected the BCIS request that diabetes was added as an independent factor in choosing a drug-eluting stent, which he claims was not based on scientific principles. He also expressed concern about the methodology by which a price differential between bare-metal stents and drug-eluting stents has been reached. But he added that: "The current guidance, in effect, encourages the status quo. Clinicians will, in the vast majority of cases, be able to provide what they believe to be optimal therapy to their patients".

An editorial on this guidance is on pages 63–4

Questions raised on very intensive glucose lowering in type 2 diabetes

The results of two major trials of intensive glucose lowering in patients with type 2 diabetes appear to have reached different conclusions.

The ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial, conducted by the US National Heart, Lung, and Blood Institute (NHLBI), was stopped in February because the group being treated with intensive glucose lowering was showing a higher mortality rate than the group receiving standard treatment. But just days later, the group organising another similar trial, ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation), announced that preliminary results of their study did not confirm the adverse mortality trend with intensive treatment reported from the ACCORD study.

ACCORD suggests harm

In the ACCORD trial, 10,251 patients with type 2 diabetes and at high cardiovascular risk were assigned to intensive therapy (using any available treatments) to get haemoglobin A_{1C} (HbA_{1C}) levels down to 6% or less (the level seen in patients without diabetes) or standard treatment aiming for an HbA_{1C} of 7 to 7.9%. Interim results showed that 257 patients in the intensive treatment group had died, compared with 203 in the standard treatment group. This is a difference of 54 deaths, or three per 1,000 participants each year, over an average of almost four years of treatment.

Although the death rates in both groups were lower than seen in similar populations in other studies, the Data and Safety Monitoring Board recommended that the trial was stopped, and patients in the intensive group will now be treated to the same HbA_{1C} goals as those already in the standard treatment group.

"A thorough review of the data shows that the medical treatment strategy of intensively reducing blood sugar below current clinical guidelines causes harm in these especially high-risk patients with type 2 diabetes," said Dr Elizabeth G Nabel, director, NHLBI.

Extensive analyses by ACCORD researchers have not determined a specific cause for the increased deaths among the intensive treatment group. Based on analyses conducted to date, there is no evidence that any medication or combination of medications is responsible, the researchers said.

They added that the findings should not change therapy for most patients with type 2 diabetes, as few patients with such high cardiovascular risk as those included in ACCORD are treated to glucose levels as low as those tested in this study.

ADVANCE shows no harm

In contrast, the ADVANCE study, has not shown any harm in its intensive treatment arm. In this trial, 11,140 high-risk patients with type 2 diabetes, were randomised to intensive (aiming for an HbA_{1C} A1C level below 6.5) versus standard glucose lowering treatment. Patients in the intensive group started treatment with the sulphonylurea drug, gliclazide modified release, and then other drugs could be added.

Chairman of the ADVANCE Data Monitoring and Safety Committee, Professor Rory Collins from the University of Oxford, said "The interim results from ADVANCE provide no confirmation of the adverse mortality trend reported from the ACCORD study". He also noted that the ADVANCE interim results were based on more than twice as much data and similar levels of glucose control as in ACCORD.

ADVANCE principal investigator, Professor Stephen MacMahon (The George Institute for International Health in Sydney, Australia), stated that "Due to the unexpected report from the ACCORD trial, we felt it was in the public interest for us to ask our Data Monitoring and Safety Committee to make a statement as to whether the available data from ADVANCE provide any support for the suggestion that intensive blood glucose lowering may increase mortality".

The ADVANCE investigators said the results are 99% complete, "so we are confident that the interim findings communicated here are a reliable guide to the final results". Definitive results will be presented later this year.

Cardiovascular mortality patterns in Europe

A new study has highlighted a changing pattern of cardiovascular mortality within Europe, and shows that while cardiovascular mortality rates are decreasing in general, Eastern and Middle European countries have the highest mortality.

The study, conducted by a group led by Dr Jacqueline Müller-Nordhorn (Charité University Medical Centre, Berlin, Germany), was published online on 5th February 2008 in the *European Heart Journal*.

Using data from the European and national statistics offices, the authors calculated age-standardised mortality rates for ischaemic heart disease and cerebrovascular disease.

They found a clear north-east to south-west gradient in mortality from cardiovascular disease. For cerebrovascular disease, however, the pattern is less clear, with the lowest mortality in the centre of Western Europe including France, northern Italy and Spain, and higher mortality rates seen in Central and Eastern Europe and some countries further south such as Greece, Portugal, and certain regions in Southern Spain and Italy.

They note that mortality from both cardiovacsular and cerebrovascular disease has been decreasing in most West European countries over the last decades. In contrast, in most Central and East European countries, cardiovascular mortality increased during the 1970s and 1980s and started to decline in the early to mid-1990s, but is still considerably higher than in Western Europe. "Although most Central and East European countries appear to have reached their peak in cardiovascular mortality, the majority of them can clearly still be classified as high-risk countries," the researchers write.

They add that analysis of regional variation in cardiovascular mortality is important for the classification of countries into high- and low-risk countries and the recommendations provided by current guidelines. "For example, it may be more appropriate and practical to generally classify West European countries as low-risk countries and Central and East European countries as high-risk countries. Otherwise, there may be an overestimation of current cardiovascular risk in certain populations leading to unnecessary therapies and costs", they say.

In brief

New editorial board member

We welcome general practitioner and diabetologist, Dr Neil Munro (left) to the *BJC* editorial board. Dr Munro has been a general practitioner in Surrey since 1984. He is also an Associate Specialist in Diabetes at the Chelsea and Westminster Hospital, London, and has worked in specialist hospital-based diabetes clinics since 1985. In addition, he has provided diabetes services for the practice for over two decades. He was research officer for the St Vincent's Declaration Primary Care Diabetes Group in 1999 and Chairman of Primary Care Diabetes Europe (PCDE) from 2000–2005. His appointment underlines the BJC's increasing commitment to cardiometabolic medicine.

ACUITY indication approved for bivalirudin

The antithrombin, bivalirudin has received European approval for the expanded indication of use in patients with acute coronary syndromes, specifically patients with unstable angina or non-ST segment elevation myocardial infarction (NSTEMI) planned for urgent or early intervention, when used with aspirin and clopidogrel. The approval is based on results from the ACUITY (Acute Catheterisation and Urgent Intervention Triage strategy) trial in which bivalirudin resulted in similar rates of ischaemic clinical outcomes and less major bleeding compared to standard therapy of heparin plus a GP IIb/IIIa blocker.

Losartan to candesartan switch cost-effective and efficacious

Switching from losartan to candesartan achieves significant reductions in blood pressure over two years and is also cost-effective according to a recent study (*Int J Clin Prac* 2008; 1–8). Carried out at a primary care practice in Hertfordshire, 98% (92 out of 94) patients were still taking candesartan two years after a switch from losartan with systolic and diastolic blood pressures being 7.0 and 2.0 mmHg lower, respectively. Candesartan is 21–23% lower in price than losartan.

New website for Fabry disease

A new website about Fabry disease has been launched to highlight this rare condition, characterised by significant damage to the heart as waste products, which are not discharged, build up in the tissue over years. The website was launched on February 29th, which was designated European Rare Disease Day. It can be found at www.focusonfabry.com.

Statins reduce atrial fibrillation?

A new meta-analysis has suggested that statins may reduce atrial fibrillation (AF). In the study, (*J Am Coll Cardiol* 2008; **51**:828–35), statin use was associated with a decreased risk of incidence or recurrence of atrial fibrillation in patients with a history of the condition, those undergoing cardiac surgery, or those who had had an acute coronary syndrome. The authors, led by Dr Laurent Fauchier (Centre Hôspitalier Universitaire Trousseau, Tours, France), call for large-scale randomised clinical trials to look at whether statins would be appropriate treatment for the management of AF.

Watching important football matches increases cardiovascular events

Watching an exciting football match more than doubled the risk of an acute cardiovascular event in a German study. The study (*N Engl J Med* 2008;**358**:475–83) assessed cardiovascular emergencies in the greater Munich area during the World Cup held in Germany in 2006. It found that on days that the German team was playing, cardiac emergencies were increased by 2.66 times compared with control periods in 2003 and 2005, which were chosen to try to exclude other triggers for stresses. Unsurprisingly, there was more of an effect in men who had a 3.26 times greater risk of an event than in the control period, whereas for women the risk was increased by 1.82 times. The intensity of the reaction depended on how exciting the match was, with a documented increase in cardiac events after a penalty shoot-out. The authors say these results lend support to the "trigger" hypothesis, whereby a stressful event provokes additional cardiovascular events.

Antihypertensives within same class can have different tolerability

Certain antihypertensives within the same class are better tolerated by patients than others, a new study suggests. The study, published in the November/December issue of *Pharmacy In Practice*, was based on a retrospective audit at a general practice in North Tyneside. The author, Wasim Baqir, a pharmacist based at the practice, found that among the three angiotensin-converting enzyme (ACE) inhibitors studied, lisinopril (with a discontinuation rate due to adverse effects of 9.1%) was considerably better tolerated than either perindopril (16.4%) or ramipril (20.0%). Calcium blockers were the most commonly prescribed class of drug to patients newly diagnosed with hypertension, and when comparing the two most widely-used drugs within this class, it was found that adverse effects resulted in discontinuation in 25.4% of patients taking amlodipine compared with 11.1% of those taking lercanidipine, the main factor accounting for the difference being less ankle oedema with lercanidipine.