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News

TRIGGER-PCI stopped early

The TRIGGER-PCI trial, comparing prasugrel 10 mg and clopidogrel 75 mg in patients with high platelet reactivity on clopidogrel after receiving a drug-eluting stent, has been stopped early because of a low rate of primary cardiovascular events (myocardial infarctions and cardiovascular deaths).

This was said to be likely due to the studied population - low-risk, stable coronary artery disease (CAD) patients after successful, uncomplicated percutaneous coronary intervention (PCI).

The sponsors of the study (Daiichi Sankyo and Eli Lilly) along with the study's steering Committee and primary investigator, Dr Franz-Josef Neumann (Heart Centre, Bad Krozingen, Germany) determined after a blinded review of study data that there is a very high probability that the number of primary end points would be insufficient for clinically relevant statistical analyses.Prasugrel is currently approved only for use in acute coronary syndromes. This was the only study underway looking at its use in stable CAD patients.

A similar lower than expected event rate was seen in the GRAVITAS trial, which showed no difference in events with high dose and normal dose clopidogrel in a similar patient population to that in TRIGGER PCI.

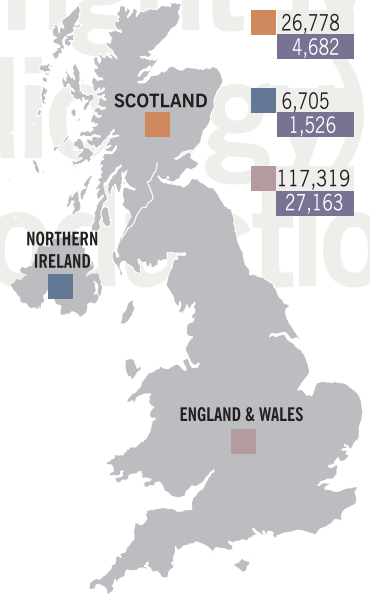
Acute coronary syndrome costs billions per year

New figures for 2009-10 show that direct healthcare expenditure and economic losses due to acute coronary syndromes (ACS) in the UK amount to £3.6 billion annually, while the burden of ACS to society is valued at up to £9.8 billion.

The figures announced recently by HEART UK were published in a report *The burden of acute coronary syndromes in the United Kingdom*, authored by Charles River Associates and commissioned by AstraZeneca (available from www.crai.co.uk/publications).

According to the report, hospitalisations due to ACS in the UK during a 12-month period from 2009-10 were 150,802, with 65% due to myocardial infarction (MI) and 35% due to unstable angina (UA). There were also 33,000 deaths from ACS in the same period (**figure 1**). The direct costs and economic costs due to lost productivity are shown in **table 1**. Looking at the burden of the disease on society, the report estimates 327,522 disability adjusted life years (DALYs) were lost in 2009. Assuming a willingness to pay around £30,000 per DALY to reduce this burden, the authors calculate the societal cost of ACS for the UK as £9.8 billion.

Figure 1. Map showing the number of hospitalisations and deaths due to acute coronary syndrome in England, Wales, Scotland and Northern Ireland in 2009–10



Source: Hospital admissions data and mortality statistics in the different regions.

Note: Number of hospital admissions for England, Wales and Northern Ireland are factual based on hospital discharge records for 2009-10 obtained from regional databases; hospitalisations in Scotland are based on 2008-09 admissions. Mortality is based on regional mortality statistics by cause of death for 2009; for Northern Ireland, data from 2008 were used.

Table 1. Direct and indirect costs associated with acute coronary syndrome in the UK in 2009-10 (in £ millions)

Cost category	Unstable angina	Myocardial infarction
Direct costs		
Hospitalisation costs	25.3	348.7
Physician costs	5.4	24.1
Pharmaceutical costs	94.7	
Economic costs – lost value to British economy		
Productivity losses (morbidity)	8.1	1,851.4
Productivity losses (mortality)	0	1,228.3

At a parliamentary reception to launch the report, HEART UK, together with the British Association of Cardiovascular Prevention and Rehabilitation and AntiCoagulation Europe, identified how using existing post-event services optimally could not only improve the experience and outcomes for patients, but could also save money which could contribute to the £20 billion efficiency savings that must be delivered between 2011 and 2014.

They called for access to cardiac rehabilitation services to be broadened, discharge information to be improved, adherence to medication to be maximised, and psychological health problems in patients suffering a cardiac event to be addressed.

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More suggestion of harm with rosiglitazone

Publication of a new meta-analysis of observational studies provides further evidence that the glitazone, rosiglitazone (Avandia®, GlaxoSmithKline), increases cardiovascular events compared with pioglitazone. Rosiglitazone was taken off the market in Europe last year, but remains available in the US.

The latest analysis, published online in the *BMJ* on March 17th 2011, was conducted by a UK group from the University of East Anglia, Norwich. They examined 16 observational studies involving 810,000 patients taking either rosiglitazone or pioglitazone. Results showed that compared with pioglitazone, use of rosiglitazone was associated with a statistically significant increased risk of myocardial infarction, heart failure, and death.

An accompanying editorial suggests that both rosiglitazone and pioglitazone have too many side effects to justify extensive use.

GSK issued a statement in response to the new meta-analysis noting that many of the observational studies included had also been considered by the US Food and Drug Administration, which concluded that, because they were largely dissimilar they should not be pooled into a single meta-analytic estimate. The company adds that definitive conclusions about differences between rosiglitazone and pioglitazone are hard to make in the absence of long-term head to head trials, and it says that it "stands behind the safety and efficacy of Avandia® when used appropriately".

EU to investigate pioglitazone bladder cancer link

The European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) has also announced it has begun a review of the benefit-risk balance of medications for diabetes containing pioglitazone (Actos®, Takeda) to further explore the signal of a possible increased risk of bladder cancer with the drug. A similar investigation is underway in the US.

Metformin best first-line drug for type 2 diabetes

A new review of oral hypoglycaemic agents supports the choice of metformin as first-line therapy but also finds that the long-term benefits and harms of diabetes medications remain unclear.

For the review, published online in the *Annals of Internal Medicine* on March 14th 2011, the authors reviewed 140 randomised clinical trials and 26 observational studies of oral hypoglycaemic agents. Most of the medications reduced HbA_{1c} levels by approximately 1%, but metformin was more effective than the new DPP-4 inhibitors.

All of the drugs also were associated with weight gain, with the exception of metformin, which was consistently associated with weight reduction or neutrality. Sulphonylureas were associated with a fourfold increased risk for hypoglycaemia versus metformin alone. Glitazones increased the risk for congestive heart failure versus sulphonylureas and the risk for bone fractures relative to metformin. The main side effect of metformin was gastrointestinal-tract effects, particularly diarrhoea.

There was limited difference among various two-drug combinations in impact on HbA_{1c} levels, but the combination of metformin with sulphonylureas was associated with a particularly high risk of hypoglycaemia.

Increased potassium intake cuts stroke

Higher dietary consumption of potassium is associated with lower rates of stroke and could also reduce the risk of coronary heart disease, a new meta-analysis suggests.

"Potassium intake may be increased by well-described dietary changes, mainly an increase in fruit and vegetable consumption, as recommended by all guidelines to prevent vascular diseases," the authors conclude.

The research, published in the March 8th 2011 issue of the *Journal of the American College of Cardiology*, included 11 studies on the association between habitual dietary potassium intake and incidence of vascular events, including 247,510 participants with follow-up of five to 19 years. Results showed a 1.64 g (42 mmol) per day higher potassium intake was associated with a significant 21% lower risk of stroke, with a trend toward lower risk of CHD and total cardiovascular disease. In all of the populations studied in the present meta-analysis, potassium intake was far lower than the recommended intake of 100 mmol or more per day.

The researchers note that the magnitude of risk reduction with increasing potassium intake by 1.64 g per day is similar to that which would result from lowering dietary sodium consumption by 5 g (85 mmol) per day and would translate into a reduction of 1,155,000 stroke deaths per year on a worldwide scale.

Mortality signal still showing at five years in ACCORD

Five-year results of the ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial of intensive glucose lowering in patients with diabetes at high risk of cardiovascular disease continue to show signs of increased mortality in the intensive group. The latest results, published in the March 3rd 2011 issue of the *New England Journal of Medicine*, are consistent with the main results reported at 3.5 years follow-up. Although there is a definite reduction in myocardial infarction with intensive glucose lowering, a mortality increase is still apparent.

The authors note that other trials looking at intensive treatment have not shown such a mortality increase, but because of the ACCORD results, they do not recommend aiming for glucose levels in the normal range in patients with diabetes. They advise a HBA_{1c} level of "below 7%" as reasonable.

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No benefit from lowering blood pressure in acute stroke

Lowering blood pressure in the acute phase of stroke is of no benefit and may be harmful, according to results from SCAST (the Scandinavian Candesartan Acute Stroke Trial).

The trial, published online on February 11th 2011 in *The Lancet*, showed no improvement on vascular events or functional outcomes at six months with the angiotensin receptor blocker and there was actually a trend toward worse outcomes in the candesartan group.

The authors explain that elevated blood pressure is common in the setting of acute stroke and is associated with poor short- and long-term outcomes. The trial randomised 2,029 patients with acute stroke (either ischaemic or haemorrhagic) and systolic blood pressure above 140 mmHg to receive candesartan or placebo for seven days.

After seven days, blood pressure was significantly lower in the active treatment group, but at six months, the rates of the composite vascular end point in the two groups were not significantly different. The functional outcome results were also less favourable for patients treated with candesartan than for those on placebo.

In an accompanying commentary, Dr Graeme Hankey (Royal Perth Hospital, Australia) says that the results of SCAST, when added to the results of 10 previous trials of blood pressure lowering in acute stroke, increase the reliability of the evidence and suggest that pharmacologically lowering blood pressure does not have a beneficial effect. "Clinicians should therefore not be prescribing blood-pressure-lowering drugs within the first week of acute stroke in routine practice," he adds.

Central obesity no worse than other types for cardiovascular risk

The long held view that central obesity, where fat is deposited mainly around the abdomen, is more harmful in terms of cardiovascular risk than other types of obesity has been challenged by a new study led by British researchers.

The study, published online in *The Lancet* on March 11th, 2011, was conducted by the Emerging Risk Factors Collaboration led by Dr John Danesh, (University of Cambridge). They analysed individual data from 221,934 participants from 17 countries in 58 prospective studies to produce reliable estimates of associations of body mass index (BMI), waist circumference, and waist-to-hip ratio with first-onset cardiovascular-disease outcomes. They found that in people with a BMI of 20 kg/m^2 or higher, the risks of cardiovascular disease were similar based on measurements of BMI, waist circumference, or waist-to-hip ratio.

Is obesity an independent risk factor?

The Emerging Risk Factors Collaboration also found that if other risk factors are considered – such as diabetes, cholesterol, and blood pressure, family history, age, and gender – BMI (or any other measure of obesity) does not add much extra to risk prediction scores. But they add that: "The main finding of this study does not, of course, diminish the importance of adiposity as a major modifiable determinant of cardiovascular disease."

But a new analysis of WOSCOPS (West of Scotland Coronary Prevention Study) suggests that obesity is an independent risk factor for coronary heart disease death. In a paper, published online on February 14th 2011, in *Heart*, the authors of the Scottish study report that the risk of fatal coronary heart disease (CHD) events was increased in men with a BMI over 30 kg/m^2 after adjusting for other risk factors. "Our analysis suggests that white men with an increased BMI may have an increased risk of fatal CHD events beyond that mediated by classical risk factors," they say. Non-fatal events, however, were not increased.

Interventional tool aims to simplify aortic valve replacement

An interventional tool providing greater speed and safety in minimally invasive aortic valve replacements (HeartNavigator, Philips) is now commercially available in Europe. The system is designed to help increase the objectivity of procedure planning

The technology merges preoperatively acquired three-dimensional CT scans with live X-ray views. During the procedure it automatically aligns and overlays these scans onto live X-ray fluoroscopy images, allowing clinicians to see the progress of the guidewire, catheter and valve placement in relation to detailed anatomical structures.

"Through the development of transcatheter valves and sophisticated interventional tools…we are now able to have a major positive impact on people's quality of life by offering heart valve replacement therapy to a group of patients for whom the risks associated with open heart surgery are too high," commented Dr JJ Koolen, Head of the Department of Cardiology, Catharina Hospital, Eindhoven, The Netherlands.

"Replacing a valve in a beating heart is a very challenging procedure. By combining detailed 3D CT images with the live 2D X-ray imaging, we get a much better understanding of the patient's anatomy, helping us to achieve better valve placement and improved clinical outcome," he added.

An image-guided valve replacement operation at the Catharina Hospital

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Could use of generic ARBs save the NHS millions?

Substituting generic angiotensin receptor blocker (ARB), losartan, for branded ARBs could save the NHS £200 million per year without any clear decrease in clinical benefits, a new study suggests.

The systematic review and meta-and cost-utility analysis, published online on February 2nd 2011 in the *International Journal of Clinical Practice*, was conducted by a team led by Dr Anthony Grosso (University College London). They conclude that they could find no case to support the prescribing of branded candesartan over generic losartan in the treatment of hypertension or heart failure.

But in an accompanying editorial, Drs Bertram Pitt and Stevo Julius (University of Michigan School of Medicine, Ann Arbor, US) argue that candesartan is more effective in lowering blood pressure than losartan. They say "it would be tragic… if we traded a short-term potential saving in healthcare costs for a real increase in long-term costs and cardiovascular risk".

Dr Grosso *et al* report that the UK NHS currently spends more than £250 million per year on ARBs for the treatment of hypertension and heart failure, with candesartan dominating the market. As losartan is now available generically, they compared the two drugs in the treatment of hypertension and chronic heart failure.

They say that although candesartan reduces blood pressure slightly more than losartan, this is of "questionable clinical significance". And in heart failure, they recommend that if a patient on candesartan is not on a maximal target dose, they should change to losartan.

However, Drs Pitt and Julius retort that the difference in blood pressure-lowering ability between the two agents may have important long-term cardiovascular consequences. And in heart failure, they say that: "Even if the difference between the effectiveness of losartan and candesartan results in only a few percentage points difference in hospitalisations, given the cost of a single hospitalisation for heart failure this could negate all of the potential savings from switching…and in fact result in a substantial increase in healthcare costs that could be far greater than the postulated savings proposed by Grosso *et al*".

Blood pressure readings more accurate with new device

A new wrist-mounted device allows more accurate measurement of blood pressure, according to research published recently in the *Journal of the American College of Cardiology*.

The sensor (A-PULSE CASP®, HealthSTATS) was used by clinicians to non-invasively record patients' central aortic systolic pressure (CASP). The measurements were 99% accurate, compared to the pressure measured by inserting a catheter directly into the aorta during a cardiac catheter procedure.

The new technology uses a sensor on the wrist to record the pulse wave and then, using computerised mathematical modelling of the pulse wave, scientists are able to accurately read the pressure close to the heart. Patients who have tested the new device found it easier and more comfortable, as it can be worn like a watch.

Lead author Professor Bryan Williams, University of Leicester, said: "it is not going to replace what we do overnight but it is a big advance. Further work will define whether such measurements are preferred for everybody or whether there is a more defined role in selective cases to better decide who needs treatment and who doesn't and whether the treatment is working optimally".

The research was funded by the Department of Health's National Institute for Health Research (NIHR). The NIHR has invested £3.4 million to establish a Biomedical Research Unit at Glenfield Hospital, Leicester, dedicated to translational research in cardiovascular research, with a further £2.2 million Capital funding from the Department of Health. Professor Williams added: "The support of the NIHR has been invaluable in backing us to take this project from an idea to the bedside". The University worked closely with the Singapore-based medical device company HealthSTATS International to develop the device.

The new wrist-mounted device

Cardiovascular disease gender gap highlighted

Complacency over cardiovascular disease (CVD) in women was the focus of the European Society of Cardiology's (ESC) recent 'Women@Heart' contest, which called on its 53 member nations to submit ideas for public awareness campaigns.

The Latvian Society of Cardiology won with its proposal for a campaign, 'It's a Red Alert', targeting both medical professionals and the general public with activities timed around International Women's Day and Mother's Day.

Material from the winning campaigns will be available for re-use by other national societies.

Professor Marco Stramba-Badiale, former chair of the ESC's 'Cardiovascular Diseases in Women' task force, said: "The belief that somehow women are protected from cardiovascular disease is completely wrong.... statistics from the World Health Organisation in 2008 actually show that 55% of female deaths in the EU are due to heart attack, stroke and other conditions compared to just 43% of males".

'Stranded Heart' by Diane Maclean, Fellow of the Royal Society of British Sculptors (FRBS), has been donated to the University of Leicester in support of its fundraising campaign for a Cardiovascular Research Centre at Glenfield Hospital. The university needs a further £4m to reach its target. To support the CRC Appeal see: www.le.ac.uk/crcappeal