



Coronary Heart Disease Case Study

History

1998: First HTA research in the area of CHD published. Review of the effectiveness of different treatments for chronic stable angina concludes that healthcare purchasers and providers should consider local information, such as cost structures and available patterns of care, when allocating resources. (*Health Technol Assess* 1998; 2:10)

1999: Review of the evidence around the clinical and cost-effectiveness of statins suggests support for the use of statins over a wide range of CHD risks, covering both primary and secondary prevention. (*Health Technol Assess* 1999; 3:19)

2000: The Government's National Service Framework for Coronary Heart Disease (NSF CHD) is published, setting out a strategy to modernise CHD services over ten years.

2000: HTA study (*Health Technol Assess* 2000; 4:29) finds that a case finding strategy to identify inherited hypercholesterolaemia would be cost-effective, as would screening all 16-year-olds.

2001: HTA programme commissions the Birmingham Rehabilitation Uptake Maximisation Study (*Health Technol Assess* 2007; 11.35), a clinical trial to compare home-based and hospital-based cardiac rehabilitation programmes.

2004: Review of the long-term effects of treatments for obesity concludes that the drugs orlistat, sibutramine and metformin appear beneficial for the treatment of adults with obesity, as do exercise and behaviour therapy when added to diet. (*Health Technol Assess* 2004; 8:21)

2004: HTA review of the provision, uptake and cost of cardiac rehabilitation programmes in the UK finds provision and uptake is well below the goal set out in the NSF, and that the many interventions aimed at improving patient uptake needed to be properly evaluated. (*Health Technol Assess* 2004; 8:41)

2005: HTA clinical trial (*Health Technol Assess* 2005; 9:40) of different systems of screening for atrial fibrillation (AF) in people aged 65 and over finds that a national programme of opportunistic screening is likely to lead to significantly more cases of AF being identified annually.

2005: HTA research (*Health Technol Assess* 2005; 9:17) targets uncertainty around angioplasty compared with thrombolysis and finds evidence to suggest an advantage of immediate angioplasty over hospital thrombolysis.

2005: HTA study of LVADs as a bridge to transplantation, recovery and as long term chronic support finds that while LVADs appear to be effective as a bridge to transplant, they are not cost-effective. (*Health Technol Assess* 2005; 9:45)

2005: HTA research (*Health Technol Assess* 2005; 9:27) clarifies area of most uncertainty around management of angina: the use of glycoprotein IIb/IIIa antagonists (GPAs) in all patients as part of initial medical management is more cost-effective than selected or no use.

2005: The NSF CHD publishes a new chapter (chapter eight) setting out quality requirements for the development of arrhythmia and sudden cardiac death services.



2006: HTA research investigates the effectiveness and cost-effectiveness of screening for heart disease using Computer tomography (CT), concluding that CT imaging can detect risk factors indicative of CHD in many people, but would miss many of the most dangerous signs of arterial disease. (*Health Technol Assess* 2006; 10:39)

2006: HTA review (*Health Technol Assess* 2006; 10:27) of the evidence around the effectiveness and cost-effectiveness of ICD therapy in different patient groups uses international trial data to calculate the cost-effectiveness of ICDs in a UK context.

2007: HTA clinical trial compares different types of exercise programme for helping people at risk of cardiovascular disease to improve their levels of physical activity. Researchers conclude that, on cost-effectiveness grounds, referral for advice supported by written materials may be the most appropriate method to initiate action in the first instance. (*Health Technol Assess* 2007; 11:10)

2008+ Key HTA research is ongoing in important CHD areas, including drugs for preventing CHD (project ref. 06/10/01 and 07/19/01), methods to promote smoking cessation (project ref. 06/09/01 which has just published its finds this year *Health Technol Assess* 2008; 12:2 and 06/32/01), and research into the best tests for diagnosing heart attack and heart failure (project ref. 06/302/19 and 05/06/01).

Background

Coronary heart disease (CHD) is the most common form of cardiovascular disease where the blood vessels that lead to the heart become narrowed or blocked, resulting in angina (chest pain due to decreased blood flow to the heart) and heart attack.

CHD is a major public health issue in the UK. It is a significant cause of illness and death, accounting for more than 110,000 deaths every year. More than 1.2 million people suffer from angina and 275,000 people have a heart attack annually. Research by the British Heart Foundation suggests that the UK spends more of its healthcare budget on heart disease (around £16 billion) than any other country in the EU. Treating patients with chest pain caused by angina is thought to cost the NHS at least £700 million a year.

Heart disease can be asymptomatic until the first event, which may be a fatal heart attack. Half of all heart attacks occur in people who have had no prior warning of coronary disease, and almost half will die from the first attack. Risk factors for heart disease include age, blood pressure, smoking, cholesterol and diabetes, but not all high-risk people develop heart disease, and many low-risk people do. Indeed, depending on which cut-off is used to define high risk, most heart attacks occur in low-risk people, because the number of people at low risk is much greater than the number at high risk. Therefore research into better ways of identifying those at risk, preventive measures to help reduce risk, and the best treatments for those diagnosed with CHD is important.

There are also conditions affecting the heart's muscle tissue or the electrical activity of the heart, cardiac arrhythmia, causing it to beat less effectively, too quickly, too slowly, irregularly, or a combination of these. Some arrhythmias are life-threatening and can cause cardiac arrest and sudden death. They affect more than 700,000 people in England and are consistently in the top ten reasons for hospital admission, putting significant strain on resources.



Policy

In 1999 the Government set a target of reducing the death rate from CHD and stroke and related diseases in people under 75 by at least 40 per cent by 2010, which has since been amended to include a commitment to a reduction in the health inequalities between the areas with the worst health and deprivation indicators and the population as a whole. The National Service Framework for Coronary Heart Disease (NSF CHD), published in March 2000, set out a strategy to modernise CHD services over 10 years. It details 12 standards for improved prevention, diagnosis, treatment and rehabilitation, and goals to secure fair access to high quality services. They mainly cover: reducing heart disease in the population; preventing CHD in high-risk patients in primary care; treating heart attack and other acute coronary syndromes; investigating and treating stable angina; revascularisation; managing heart failure and cardiac rehabilitation.

The NSF CHD states that GPs and primary care teams should develop a register of CHD patients, through which they can review medication, offer advice on diet and lifestyle, and maintain the necessary contact with patients most at risk of suffering renewed heart problems. Those above a certain level of risk should be prescribed statins (drugs that reduce the levels of cholesterol in the blood).

The NSF CHD is evidenced-based and was devised by a wide group of stakeholders taking into account evidence of effectiveness and cost-effectiveness of interventions to prevent and treat CHD, and in 2005 an additional chapter was added covering the development of services for arrhythmias and sudden cardiac death. The HTA programme has added significantly to the evidence base in this area, informing service delivery and helping efforts to achieve all of the 12 standards outlined in the NSF.

HTA research has also played a key role informing NICE guidance in the area of CHD. Over 40 per cent of the programme's CHD portfolio comprises of research commissioned to inform NICE. This includes over 19 projects in areas ranging from smoking cessation and obesity prevention to treatments for arrhythmias and the effectiveness of drugs such as aspirin and clopidogrel and the wider role of statins. HTA research has informed key NICE guidance, including advice about how stents should be used in operations for coronary artery disease (*Health Technol Assess* 2000; 4:23, *Health Technol Assess* 2004; 8:35, *Health Technol Assess* 2007; 11:46, guidance ref. TA71), which patients should receive ICDs for the treatment of arrhythmias (*Health Technol Assess* 2000; 4:26, *Health Technol Assess* 2005; 9:36 and guidance ref. TA95) when dual chamber pacemakers should and should not be used to treat symptomatic bradycardia (*Health Technol Assess* 2005; 9:43, guidance ref. TA88), and the initiation of statin therapy in adults with clinical evidence of cardiovascular disease and adults considered to be at risk of CVD (*Health Technol Assess* 2007; 11:14, guidance ref. TA94). HTA research has also informed NICE guidance on cardiac resynchronization therapy (*Health Technol Assess* 2007; 11:47, guidance ref. TA120), and informed NICE's guideline on the management of atrial fibrillation in 2006 (*Health Technol Assess* 2005; 9:40, guideline ref. CG36).

Contrast with the US

Much of the research base for CHD depends on studies carried out in the US, making it difficult to generalise results to the UK, particularly in relation to cost-effectiveness. The HTA research portfolio in CHD draws upon the international database of research, to investigate treatments and tests in the UK context. One area of research has examined the clinical and cost-effectiveness of immediate angioplasty in myocardial infarction compared with thrombolysis. Thrombolysis is still the main treatment for heart attack in the UK but immediate angioplasty is developing rapidly,



mainly in urban centres. It is however much more common in the USA. An HTA study (*Health Technol Assess* 2005; 9:17) reviewed the existing research evidence in a UK context and found evidence to suggest that there is an advantage of immediate angioplasty over hospital thrombolysis. Another area includes research (*Health Technol Assess* 2006; 10:27) into the use of implantable cardioverter defibrillators for arrhythmias, for which guidance has relied heavily upon trials in the US.

Adding to the evidence base

HTA research into CHD covers prevention and screening, diagnosis, treatment and rehabilitation across several different types of heart disease, including myocardial infarction (MI), heart failure and angina. By February 2008, the programme had invested over £6.5 million in a portfolio of 53 projects, 36 of which have been published in its journal series, and more than 17 of which are ongoing. Over 40 per cent of the CHD portfolio comprises projects commissioned by the HTA programme to inform the work of NICE. There are also nine clinical trials involving up to 20,000 patients, and 25 evidence syntheses.

Prevention and screening research

In the area of prevention the HTA programme has commissioned key reviews of the existing evidence around the role of statins for preventing CHD, as well as the effectiveness of other drugs such as aspirin. It has also investigated the best ways to promote lifestyle changes such as smoking cessation and tackling obesity to help prevent CHD.

Statins and drug treatments

A 1999 review (*Health Technol Assess* 1999; 3:19) investigated the effectiveness and cost-effectiveness of statins for the prevention of CHD, compared with other treatments. The reviewers found that the evidence lent support to the use of statins over a wide range of CHD risks covering both primary and secondary prevention. Statins were concluded to be less cost-effective than other treatments, such as aspirin, antihypertensives and mediterranean diet, but the researchers said that they might be cost-effective in secondary prevention because they achieve effects additional to those of other treatments. The researchers also concluded however, that other, more cost-effective treatments were insufficiently used in the UK and that greater efforts were required to ensure that they were used optimally.

Research currently under way (project ref. 06/10/01) is assessing aspirin for the primary prevention of cardiovascular disease. Currently, aspirin is commonly used to treat those at high risk of cardiovascular disease. It can have serious side effects including gastrointestinal bleeding, but the benefits of the drug in preventing blood clots outweigh the risks. This research is evaluating the evidence for using aspirin to treat those who are at lower risk of cardiovascular disease to see whether the benefits also outweigh the risks for these groups. The findings of the research are due to be published in 2008.

Another drug treatment for heart disease, clopidogrel, is being assessed by HTA researchers (project ref. 07/19/01) for its benefits over a shorter period. Current NICE guidance recommends treatment with clopidogrel in combination with aspirin for up to one year after the most recent acute episode of angina in patients with moderate to high risk of heart attack or death, but there are uncertainties concerning the optimal duration of the drug. The guidance recommends that a study is needed to compare the effect of stopping treatment with clopidogrel within a few months



of the acute event with a strategy of continued long-term treatment. The HTA research aims to assess the potential value and feasibility of conducting a clinical trial to investigate fully.

Lifestyle factors

The HTA programme has commissioned important research to investigate the effectiveness of interventions that promote lifestyle changes to help prevent CHD. A 2004 review (*Health Technol Assess* 2004; 8:21) of the long-term effects of treatments for obesity concluded that the drugs orlistat, sibutramine and metformin appear beneficial for the treatment of adults with obesity, as do exercise and behaviour therapy when added to diet. The researchers also found evidence to suggest that low fat diet and exercise in those at risk of obesity-related illness such as CHD are of comparable cost to drug treatments. However more clinical trials in primary care in high risk populations are needed to investigate fully.

Following this an HTA clinical trial which published in 2007 (*Health Technol Assess* 2007; 11:10) compared different types of exercise programme for helping people at risk of cardiovascular disease to improve their levels of physical activity. Researchers used a large local exercise referral scheme in London as the setting for the trial, with patients receiving either a leisure centre-based exercise programme, an instructor-led walking programme, or provision of advice only. Following up after 10 weeks and six months the researchers found that all three groups had increased their levels of activity, and blood pressure and cholesterol levels were reduced, but there was no significant difference between groups. The researchers concluded that, on cost-effectiveness grounds, referral for advice, supported by written materials that include details of locally available facilities, might be the most appropriate method to initiate action in the first instance.

An HTA study (*Health Technol Assess* 2002; 6:8) on promoting physical activity in South Asian Muslim women for prevention of a range of diseases including CHD explored the literature, surveyed areas with large South Asian populations, carried out case studies and evaluated a pilot intervention programme. The researchers concluded that there are some exercise on prescription schemes in which special provision is made for South Asian Muslim women, but in many schemes no such provision is made. The study highlighted some of the barriers to exercise and the general issues in existing exercise schemes, informing the development of future services.

Current HTA research is also aiming to expand the evidence base around treatments to help with smoking cessation. A review of the evidence about a new strategy for smoking cessation (*Health Technol Assess* 2008; 12:2), was recently delivered to NICE's Centre for Public Health Excellence. The study looked at the 'cut down to quit' approach to smoking cessation using nicotine replacement therapy. Researchers assessed the evidence for the approach, as well as whether there are any associated harms and whether it provides good value for money. NICE is set to issue its smoking cessation guideline to the NHS in 2008. A second review (project ref. 06/32/01) is investigating the effectiveness of different relapse prevention strategies provided by NHS Stop Smoking Services to help those who have quit smoking from restarting. It is hoped the research will help determine priorities for future research in this field, the value of such treatment approaches to the NHS and whether or not they should be part of NHS Stop Smoking Services.

Screening

There is currently no screening programme for CHD in the UK although opportunistic risk factor assessment and subsequent management is currently carried out. Research into screening for CHD by the HTA programme comprises three main studies; screening for hypercholesterolaemia, screening for atrial fibrillation, and the effectiveness of computed tomography (CT) imaging in



screening for CHD. All of these studies have helped to inform the discussions of the UK National Screening Committee (NSC), which has supported the development of the Vascular Risk Management Programme. An HTA study (*Health Technol Assess* 2000; 4:29) published in 2000 reviewed the evidence around screening for familial hypercholesterolaemia (FH). Most people with the condition are undiagnosed or only diagnosed after their first coronary event, but early detection and treatment can reduce illness and death. The research team evaluated whether screening was appropriate, assessing different types of screening system. From a modelling exercise they concluded that a case-finding strategy to identify hypercholesterolaemia in families of known FH patients would be cost-effective, as would screening all 16-year-olds and patients admitted to hospital with premature MI. However they suggest that further studies, particularly primary research, are needed to fully evaluate the effectiveness of different screening strategies. This research helped to inform the current NSC policy not to screen.

A 2005 clinical trial (*Health Technol Assess* 2005; 9:40) commissioned by the HTA programme investigated different systems of screening for atrial fibrillation (AF) in people aged 65 and over (see atrial fibrillation section). The report helped to inform discussions of the NSC in November 2005.

A 2006 review (*Health Technol Assess* 2006;10:39) investigated the effectiveness and cost-effectiveness of screening for heart disease using CT, informing the discussions of the NSC. CT is a form of x-ray which produces pictures of slices of the body and allows the coronary arteries to be examined. The researchers concluded that CT imaging can detect risk factors indicative of CHD in many people (including those who would be at low risk when assessed by traditional risk factors). However it would miss many of the most dangerous signs of arterial disease, while in some cases identifying abnormalities that would not lead to a heart attack. The team concluded that there was insufficient evidence to suggest that screening using CT imaging would be cost-effective, and that most of the NSC criteria were not met or only partially met.

Diagnostics research

Key HTA studies to evaluate the effectiveness of different diagnostic tests for identifying CHD are under way. One study (project ref. 06/15/01) aims to establish whether CT imaging may provide a clinically and cost-effective alternative to angiography in the investigation of coronary artery disease. The review aims to examine whether CT imaging can be as effective as angiography even if only in some patients, whether it would be cost-effective, and if so how much of the current angiography workload could be replaced by CT.

A second HTA study (project ref. 05/40/04) is investigating the effectiveness and cost-effectiveness of bio markers (blood tests that measure specific substances) for helping to decide which patients are in more urgent need of surgery for their angina, to help inform clinical decisions, while a major new clinical trial (project ref. 06/302/19) has been commissioned to investigate a new blood test for helping to diagnose or rule out heart attacks. The RATPAC trial, the largest of its kind, aims to find out whether using a point-of-care cardiac marker panel (a test that can be used by a doctor or nurse at a patient's bedside) can more quickly and accurately confirm or rule out a heart attack in selected low risk patients. Researchers will compare a group of patients who receive the point-of-care blood test with a group of patients who receive standard, currently available tests, across six NHS hospitals. This research is due to report its findings in 2010.

Research into different types of heart disease



Much of the HTA programme's CHD research portfolio is focused on three different types of heart disease: myocardial infarction (MI), angina and heart failure.

Myocardial infarction

The HTA programme has funded a number of studies in the area of myocardial infarction (MI), most notably looking at cardiac rehabilitation, although the best treatments for MI have also been studied as part of the HTA research portfolio in this area. One key area of research has targeted the uncertainty around angioplasty compared with thrombolysis. Thrombolysis (clot dissolving drugs that help to restore blood supply in the coronary arteries to the affected part of the heart) is still the main treatment for heart attack in the UK although immediate angioplasty (primary angioplasty) is developing rapidly in mainly urban centres. It is however much more common in the USA. A 2005 HTA study (*Health Technol Assess* 2005; 9:17) reviewed the existing research evidence around the clinical and cost-effectiveness of immediate angioplasty for acute MI, using thrombolysis as the main comparator. The research team identified several good quality reviews as well as a trial which suggested that there is an advantage of immediate angioplasty over hospital thrombolysis. There was also evidence to suggest that angioplasty could be more cost effective than thrombolysis. The Department of Health and British Cardiovascular Society are collaborating on a feasibility study to test the extent to which primary angioplasty can be rolled out across England as the main treatment for heart attack (the National Infarct Angioplasty Project).

Cardiac rehabilitation

Cardiac rehabilitation has historically been focused on the survivors of MI (as opposed to those who have had coronary revascularisation or who have heart failure) and provides one of the main health inducing interventions, along with secondary prevention. The evidence suggests that when people are offered comprehensive and tailored help with lifestyle modification, involving education and psychological input as well as exercise training, cardiac rehabilitation can make a substantial difference, perhaps reducing mortality by as much as 20-25 per cent over three years. The NSF CHD states that prior to leaving hospital, all heart patients should be invited to participate in a multidisciplinary programme of secondary prevention and cardiac rehabilitation.

HTA research commissioned in 2001 (*Health Technol Assess* 2004; 8:41) reviewed the provision, uptake and cost of cardiac rehabilitation programmes in the UK, assessing the effectiveness and cost-effectiveness of interventions to improve uptake and adherence. The researchers found that nearly 146,000 patients discharged from hospital with a primary diagnosis of acute MI, unstable angina or following revascularisation were potentially eligible for cardiac rehabilitation. In England in 2000, 45-67 per cent of these patients were referred, with 27-41 per cent attending outpatient cardiac care, with average costs to the health service of around £490 per patient. They concluded that provision and uptake was well below the goal set out in the NSF CHD (85 per cent of patients), and that the many interventions aimed at improving patient uptake needed to be properly evaluated. In 2001 the HTA programme commissioned the Birmingham Rehabilitation Uptake Maximisation Study (*Health Technol Assess* 2007; 11:35), a clinical trial that compared home-based and hospital-based cardiac rehabilitation programmes. The study included a high proportion of people from groups where take up was particularly low, including the elderly, ethnic groups and women. They received either a home-based programme of rehabilitation using the Heart Manual, or a centre-based rehabilitation programme involving education, relaxation and exercise. The research team concluded that for low to moderate risk patients following MI, a home-based cardiac rehabilitation programme does not produce inferior outcomes compared with centre-based programmes.

Heart Failure



Heart failure is an increasing health problem, affecting over 63,000 people in the UK every year. Concerns about this have resulted in several government policy initiatives and the HTA programme has commissioned a significant number of studies to expand the evidence base around diagnosis and treatment of heart failure, to help inform service provision.

HTA research currently under way (project ref. 05/06/01) is investigating the best way for GPs to diagnose heart failure. The research team is working together with researchers at the University of Queensland in Australia to identify a cost-effective diagnostic strategy for GPs to follow, enabling them to confirm or rule out the condition more easily and accurately. The work includes a review of all the evidence concerning the different signs and symptoms of the condition and the diagnostic tests used to investigate heart failure. Researchers are using the actual data gathered in some of the studies identified to better understand how to interpret test results in different types of patients. Two members of the research team were closely involved in the National Clinical Guideline on heart failure produced by the National Institute for Health and Clinical Excellence (NICE), and it is anticipated that the results of this research will inform the next version of this guideline.

With continued decreases in organ donation in England and Wales transplantation is an option available to few. However, technological advances in recent years have created other options for preventing heart failure, and the HTA programme has played a key role in evaluating the effectiveness of these.

Mechanical circulatory support through left ventricular assist devices (LVADs) has attracted increased interest as an alternative option to transplantation, but more research is needed. A 2005 HTA study (*Health Technol Assess* 2005; 9:45) reviewed the clinical and cost-effectiveness of LVADs as a bridge to transplantation, to recovery and as long term chronic support. The study found that while LVADs appear to be effective as a bridge to transplant, they are not cost-effective, and the primary future of the technology is likely to be in providing long term chronic support, although this needs to be researched further.

In addition to this, a parallel HTA study (*Health Technol Assess* 2006; 10:48) evaluated the provision of a ventricular assist device programme in the UK to help inform the National Specialist Commissioning Advisory Group (NSCAG) now the National Commissioning Group (NCG). The study involved three specialist VAD therapy centres in the UK, supported by NSCAG. Researchers assessed 70 patients with a VAD as a bridge to transplant, measuring survival, transplantation rates and resource use. The researchers concluded that there was insufficient data from either published studies or the current study to construct a fair comparison group for VADs.

HTA research has also assessed the effectiveness of implantable cardioverter defibrillators (ICDs) for preventing heart failure. ICDs, small devices fitted under the skin, prevent sudden cardiac death as a result of irregular heart rhythms (arrhythmia) by restoring normal heart rhythm. HTA research published in 2006 (*Health Technol Assess* 2006; 10:27) reviewed the evidence around the effectiveness and cost-effectiveness of ICD therapy in different patient groups. The study was designed not simply to update an existing systematic review of the research evidence, but also to collect original data relating to the UK, which the researchers used together with international trial data to calculate the cost-effectiveness of ICDs in a UK context. The research team concluded that there is increasing evidence for the survival benefits of ICDs compared with medical management of arrhythmias, but ICDs are not as cost-effective as antiarrhythmic drug treatment. One reason is the high rates of post-implantation hospitalisation. Better patient targeting and efforts to reduce the need for such hospitalisation may improve cost-effectiveness.



This systematic review updates two previous reviews conducted by the HTA programme into the clinical and cost-effectiveness of ICDs. (*Health Technol Assess* 2000; 4:26 and *Health Technol Assess* 2005; 9:36).

Angina

In the UK about 345,000 new patients are diagnosed with angina each year. The HTA programme has commissioned many different studies to help expand the evidence base in this area.

A review of resource allocation for chronic stable angina in 1998 (*Health Technol Assess* 1998; 2:10) concluded that healthcare purchasers and providers should consider local information and cost structures, and that the evidence suggests that blanket decisions to provide only one form of intervention may not be appropriate. The various main forms of treatment should be made available, with patients informed of the options available to them.

This was followed by a 2004 review (*Health Technol Assess* 2004; 8:2) which considered the evidence around the investigation of acute and chronic chest pain in primary care and concluded that in patients in whom an acute coronary syndrome is suspected, emergency referral for further assessment in a specialist setting is justified. Further research in 2005 (*Health Technol Assess* 2005; 9:27) investigated the cost-effectiveness of alternative strategies for the initial medical management of presumed unstable angina. The researchers identified that the area of most clinical uncertainty was around the use of new drugs glycoprotein IIb/IIIa antagonists (GPAs). Through a systematic review and economic model they found that the use of GPAs in all patients as part of initial medical management was more cost-effective than selected or no use.

Atrial Fibrillation

Atrial fibrillation (AF) is the most common arrhythmia, affecting up to 1 per cent of the population, in England, absorbing almost 1 per cent of the entire NHS budget. The HTA programme has published a significant research in this area.

In 2005 the HTA programme published the results of a clinical trial (*Health Technol Assess* 2005; 9:40) which investigated different systems of screening for atrial fibrillation (AF) in people aged 65 and over. The study involved 15,000 people at 50 primary care centres across England. Three different methods of screening were examined over a 12 month period, and the researchers found that a national programme of opportunistic screening, where GPs take a patient's pulse during the course of a normal consultation, is likely to lead to significantly more cases of AF being identified annually, and is likely to be considered a cost-effective measure for early detection by NHS policy makers.

Reducing uncertainty

HTA research has played an important role in efforts to meet the government's target of reducing the death rate from CHD, stroke and related diseases in people under 75 by at least 40 per cent by 2010. It has informed service delivery and efforts to achieve the different standards outlined in the NSF CHD, including reducing heart disease in the population, preventing CHD in high-risk patients in primary care, treating heart attack and other acute coronary syndromes, investigating and treating stable angina, revascularisation, managing heart failure and cardiac rehabilitation.



The programme's research portfolio has added significantly to the evidence base in the areas of prevention and screening, diagnosis and treatment for many different types of heart disease. More than £6 million has been invested in over 50 pieces of key research, such as comparisons of new drug treatments with older drugs and diet; investigations of new methods for screening and diagnosis; research to clarify uncertainty around surgery compared with drug treatment for MI; projects focused on rehabilitation post MI; and investigations of different interventions for heart failure.

The HTA programme has also commissioned research which has informed 17 pieces of NICE guidance in important CHD areas, including the use of coronary stents and ICDs, methods for promoting smoking cessation and preventing obesity, and the effectiveness of drugs such as aspirin and clopidogrel together with advice about the wider role of statins.

The HTA programme's portfolio of CHD research demonstrates its ability to meet the demonstrable need of the NHS for research-based evidence that other funders – both commercial and public sector – have not met.

Ends

Appendix

Project Title and selected key journal papers (Click on the project title of your choice to view further details)

Resource allocation for chronic stable angina: a systematic review of the effectiveness, costs and cost-effectiveness of alternative interventions.

HTA ref: 93/01/02. *Research Type: Secondary Research (e.g. systematic review)* Published

- ▶ Kmietowicz, Z. **Cholesterol screening is not worth while.** BMJ Vol: 316, Page: 725.
- ▶ Sheldon, T; Sharp, F; Boutle, MT. Cholesterol and coronary heart disease: screening and treatment. Effective Healthcare Vol: 4, Issue: 1.

Cost-effectiveness of the "statins".

HTA ref: 96/14/01. *Research Type: Secondary Research (e.g. systematic review)* Published

Cost-effectiveness of screening for hypercholesterolaemia versus case finding for familial hypercholesterolaemia.

HTA ref: 95/29/04. *Research Type: Secondary Research (e.g. systematic review)* Published

- ▶ Marks, D; Wonderling, D; Thorogood, M; Lambert, H; Humphries, SE; Neil, HAW. **Cost-effectiveness analysis of different approaches of screening for familial hypercholesterolaemia.** BMJ 2002; 324: 1303.

Coronary artery stents in the treatment of coronary artery disease.



HTA ref: 99/15/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

The clinical effectiveness and cost-effectiveness of implantable cardioverter defibrillators in people with arrhythmias.

HTA ref: 00/07/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

A systematic literature review, with decision analytic modelling, on the use of intravascular ultrasound imaging in coronary artery disease.

HTA ref: 96/35/01. *Research Type: Secondary Research (e.g. systematic review)* Published

A systematic review of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists in the treatment of unstable angina.

HTA ref: 00/04/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation.

HTA ref: 01/22/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

The clinical effectiveness and cost-effectiveness of bupropion (zyban) and nicotine replacement therapy.

HTA ref: 00/17/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

A systematic review update of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists.

HTA ref: 00/04/02. *Research Type: NICE Technology Assessment Report (TAR)* Published

Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation.

HTA ref: 01/27/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

A policy for the drug treatment of high blood pressure.

HTA ref: 93/05/01. *Research Type: Secondary Research (e.g. systematic review)* Published

A systematic review of the urgent assessment of chest pain in general practice and of the most cost-effective method of investigation of recurrent chest pain.

HTA ref: 97/12/01. *Research Type: Secondary Research (e.g. systematic review)* Published

- ▶ McManus, RJ; Mant, J; Davies, MK; Davies, RC; Deeks, JJ; Oakes, RAL; Hobbs, FDR. A systematic review of the evidence for rapid-access chest pain clinics. *International Journal of Clinical Practice* 2002 Jan-Feb; 56(1): 29-33.



A multi-centre randomised controlled trial of minimally invasive bypass grafting vs angioplasty with stenting for single vessel disease of the left anterior descending coronary artery.

HTA ref: 96/04/06. *Research Type: Primary Research (e.g. trial)* Published

Systematic review of the long-term outcomes of the treatments for obesity and implications for health improvement and the economic consequences for the NHS.

HTA ref: 99/02/02. *Research Type: Secondary/Primary Research* Published

- ▶ Avenell, A.; Brown, T.J.; McGee, M.A.; Campbell, M.K.; Grant, A.M.; Broom, J.; Jung, R.T.; Smith, W.C.S.. What interventions should we add to weight reducing diets in adults with obesity? A systematic review of randomized controlled trials of adding drug therapy, exercise, behaviour therapy or combinations of these interventions. *Journal of Human Nutrition and Dietetics* August 2004 Vol 17 (4) pages 1-24.
- ▶ Aucott, L; Poobalan, A; Smith, WCS; Avenell, A; Jung, R; Broom, J. Effects of Weight loss in overweight/obese individuals and long-term hypertension outcomes. *Hypertension* 2005;45: 1035-41.

Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction.

HTA ref: 02/19/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

Coronary artery stents: a rapid systematic review and economic evaluation.

HTA ref: 02/16/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

Clinical effectiveness and cost-effectiveness of clopidogrel and modified-release dipyridamole in the secondary prevention of occlusive vascular events: a systematic review and economic evaluation.

HTA ref: 02/24/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

Clopidogrel used in combination with aspirin compared with aspirin alone in the treatment of non-ST-segment-elevation acute coronary syndromes: a systematic review and economic evaluation.

HTA ref: 02/24/02. *Research Type: NICE Technology Assessment Report (TAR)* Published

Provision, uptake and cost of cardiac rehabilitation programmes: improving services to under-represented groups.

HTA ref: 99/21/02. *Research Type: Secondary Research (e.g. systematic review)* Published

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Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: systematic review and economic evaluation.

HTA ref: 02/15/01. *Research Type: HTA Technology Assessment Report* Published

Effectiveness and cost-effectiveness of alternative strategies for the initial medical management of presumed unstable angina: a decision model and systematic literature review.

HTA ref: 98/29/04. *Research Type: Secondary Research (e.g. systematic review)* Published

The clinical effectiveness and cost effectiveness of implantable cardioverter defibrillators: arrhythmias.

HTA ref: 03/32/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

Randomised controlled trial and cost effectiveness study of targeted screening versus systematic population screening for atrial fibrillation in the over 65s: the SAFE study.

HTA ref: 96/22/11. *Research Type: Primary Research (e.g. trial)* Published

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The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation.

HTA ref: 03/25/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

The clinical and cost-effectiveness of left ventricular assist devices: a systematic review and economic evaluation.

HTA ref: 01/12/02. *Research Type: Secondary Research (e.g. systematic review)* Published

A review of the evidence on the effects and costs of implantable cardiac defibrillators (ICD) therapy in different patient groups, and modelling of cost-effectiveness and cost-utility for these groups in a UK context.



HTA ref: 99/23/04. *Research Type: Secondary Research (e.g. systematic review)* Published

The effectiveness and cost-effectiveness of computed tomography screening for coronary artery disease: systematic review.

HTA ref: 04/45/01. *Research Type: HTA Technology Assessment Report* Published

Evaluation of the ventricular assist device programme in the UK (EVAD).

HTA ref: 01/19/01. *Research Type: Primary Research (e.g. trial)* Published

EXERT (exercise evaluation randomised trial) - randomised trial comparing leisure centre-based exercise on prescription, home-based walking and usual advice in primary care.

HTA ref: 95/33/01. *Research Type: Primary Research (e.g. trial)* Published

A systematic review and economic evaluation of statins for the prevention of coronary events.

HTA ref: 03/30/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

What is the cost effectiveness of self-monitoring and self-management of anticoagulation treatment compared with clinic based monitoring?

HTA ref: 05/33/01. *Research Type: Secondary Research (e.g. systematic review)* Published

Cardiac resynchronisation (biventricular pacing) for the treatment of heart failure.

HTA ref: 04/21/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

Coronary artery stents for the prevention of ischaemic heart disease.

HTA ref: 04/42/01. *Research Type: NICE Technology Assessment Report (TAR)* Published

Cut down to quit with nicotine replacement therapies (NRT) in smoking cessation: systematic review of effectiveness and economic analysis (update of NICE Guidance 39).

HTA ref: 06/09/01. *Research Type: HTA Technology Assessment Report* Published

The cost-effectiveness of functional cardiac testing in the diagnosis and management of coronary heart disease.

HTA ref: 99/26/04. *Research Type: Primary Research (e.g. trial)* Published

Clinical and cost effectiveness of rimonabant within its licensed indications as an



adjunct to diet and exercise for the treatment of obese and overweight patients.

HTA ref: 07/14/01. *Research Type: NICE Evidence Review Group Report (ERG)*

Varenicline for smoking cessation.

HTA ref: 06/50/01. *Research Type: NICE Evidence Review Group Report (ERG)*

The effect of withdrawal of clopidogrel in patients with ischaemic heart disease.

HTA ref: 07/19/01. *Research Type: HTA Technology Assessment Report*

Ezetimibe for the treatment of hypercholesterolaemia.

HTA ref: 05/22/01. *Research Type: NICE Technology Assessment Report (TAR)*

Curative catheter ablation in atrial fibrillation and typical atrial flutter.

HTA ref: 06/13/01. *Research Type: HTA Technology Assessment Report*

Aspirin in the primary prevention of cardiovascular disease.

HTA ref: 06/10/01. *Research Type: HTA Technology Assessment Report*

The clinical and cost-effectiveness of computed tomography as an alternative to angiography in investigation of coronary artery disease.

HTA ref: 06/15/01. *Research Type: HTA Technology Assessment Report*

Intravenous magnesium compared with sotalol for prevention of atrial fibrillation after coronary artery bypass surgery.

HTA ref: 07/18/01. *Research Type: HTA Technology Assessment Report*

The long term effects of biofeedback treatment for essential hypertension in adults.

HTA ref: 07/04/01. *Research Type: HTA Technology Assessment Report*

Multi-centre randomised controlled trial of the cost-effectiveness of infra-inguinal percutaneous transluminal angioplasty (PTA) versus reconstructive surgery for severe limb ischaemia (BASIL).

HTA ref: 96/05/01. *Research Type: Primary Research (e.g. trial)*

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controlled trial. The Lancet 2005: 366: 1925-34.

Randomised controlled trial of continuous positive airways pressure and non-invasive positive pressure ventilation in the management of patients presenting with acute cardiogenic pulmonary oedema (3CPO).

HTA ref: 01/43/01. *Research Type: Primary Research (e.g. trial)*

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Systematic review and individual patient data meta-analysis of diagnosis of heart failure, with modelling of the implications of different diagnostic strategies in primary care.

HTA ref: 05/06/01. *Research Type: Secondary Research (e.g. systematic review)*

The effectiveness and cost effectiveness of biomarkers for the prioritisation of patients awaiting coronary revascularisation: a systematic review and decision model.

HTA ref: 05/40/04. *Research Type: Secondary Research (e.g. systematic review)*

The RATPAC Trial: Randomised Assessment of Treatment using Panel Assay of Cardiac markers.

HTA ref: 06/302/19. *Research Type: Primary Research (e.g. trial)*

Relapse prevention in NHS stop smoking services: Current practice, potential effectiveness and cost effectiveness.

HTA ref: 06/32/01. *Research Type: Secondary Research (e.g. systematic review)*