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Rapid review

Coronary artery stents in the treatment of ischaemic heart disease: a rapid and systematic review

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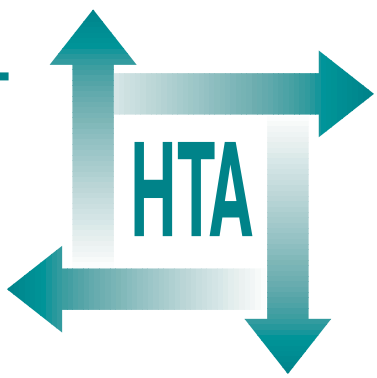
Health Technology Assessment
NHS R&D HTA Programme



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Coronary artery stents in the treatment of ischaemic heart disease: a rapid and systematic review

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Contents

Glossary and list of abbreviations

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context but a glossary is provided for the non-specialist reader. In some cases usage differs in the literature but the term has a constant meaning throughout this review.

Glossary

Abciximab A glycoprotein IIb/IIIa antagonist, used to inhibit blood clotting.

Acute coronary syndrome Severe symptomatic coronary artery disease including unstable angina and non-Q wave myocardial infarction.

Angina Pain in the heart muscle due to lack of blood-borne oxygen, it is usually induced by exercise and relieved by rest.

Angiography Radiographic technique using contrast medium to show outline of coronary artery lumens.

Angioplasty Short for percutaneous transluminal coronary angioplasty (PTCA).

Atherosclerosis A disease of the arteries in which fatty plaques develop on their inner walls leading to reduced blood flow or obstruction.

Bailout stent Stent inserted as an emergency during PTCA because of dissection of the vessel wall.

Braunwald Classification Classification of unstable angina.

Cardiac catheterisation Passing a catheter from femoral artery into coronary arteries for angiography or percutaneous coronary intervention (PCI).

Clopidogrel Drug that inhibits platelet function, now used instead of warfarin during stent placement.

Creatinine kinase A cardiac enzyme, the blood levels of which are raised during myocardial infarction.

ECG Electrocardiogram – maps electrical activity in the heart muscle. ECG findings might include Q waves or ST elevation

Exercise stress test Diagnostic test used to find exercise-induced ECG changes indicating myocardial ischaemia

Elective Non-emergency treatment.

Graft (saphenous vein) Insertion of graft vessel into coronary artery during coronary artery bypass grafting (CABG).

Heterogeneity Variability or differences between studies.

Hypertension High blood pressure.

Invasive treatment Used in this report to refer to PCI or CABG.

Ischaemia Lack of blood flow or oxygen.

Lumen The space within a blood vessel.

MEDLINE A database of medical journal articles.

Meta-analysis Method of combining results from different studies to produce a summary statistic.

Minimally invasive CABG CABG technique using a small thoracotomy only and not always requiring stopping of the heart during the operation.

Myocardium Heart muscle.

Myocardial infarction Death of a segment of heart muscle because of severe ischaemia.

Ostial lesion Lesion of the ostium of coronary artery (which is difficult to stent).

continued

Glossary *contd*

Platelets Blood constituents involved in blood clot formation.

Provisional stenting Stent placement depending on suboptimal result of PTCA.

Q wave An abnormal wave on ECG indicating past myocardial infarction.

Reocclusion Repeat complete blockage of coronary artery.

Restenosis Re-narrowing of coronary artery.

Revascularisation Maintaining or improving coronary artery blood supply.

Silent ischaemia Ischaemia of heart muscle found with exercise stress test where patient has no angina symptoms.

Stent Small prosthesis inserted into coronary artery to keep the lumen open.

Subacute ischaemic heart disease All manifestations of ischaemic heart disease except acute myocardial infarction.

Thrombus Blood clot.

Ticlopidine Drug that inhibits platelet function, now used instead of warfarin during stent placement.

List of abbreviations

AMI	acute myocardial infarction (see myocardial infarction)
BCIS	British Cardiovascular Intervention Society
CABG	coronary artery bypass graft(ing)
CAD	coronary artery disease
CEA	cost-effectiveness analysis*
CI	confidence interval (95%)
CK-MB	creatine kinase
CO	chronic coronary occlusion*
cost/EFS	cost per event-free survivor
CU	cost–utility study*
CVA	cerebrovascular accident (stroke)*
DARE	Database of Abstracts of Reviews of Effectiveness
DEC	Development and Evaluation Committee
DFl	Dutch Guilder
eCABG	emergency CABG*
EFS	event-free survival or survivor
EUROQOL	standardised assessment method for quality of life (used in cost–utility studies)*
IHD	ischaemic heart disease
INR	International Normalised Ratio*
LAD artery	left anterior descending coronary artery
LMW heparins	low molecular weight heparins (used for blood anticoagulation)*
LoS	length of stay*
LVEF	left ventricular ejection fraction (measure of heart performance)*
MACCE	major adverse coronary and cerebrovascular events*
MACE	major adverse coronary events*
MI	myocardial infarction (heart attack)
MLD	minimal lumen diameter of coronary artery
MVD	multi-vessel coronary disease*
N/A	not applicable*
N/C	not clear*
NR	not recorded*
NS	not statistically significant*
NHSEED	NHS Economic Evaluations Database
NICE	National Institute for Clinical Excellence
NSF	National Service Framework
OR	odds ratio
PCI	percutaneous coronary intervention (includes PTCA, atherectomy, excimer laser, rotablator, stents)
PMI	previous myocardial infarction*
PTCA	percutaneous transluminal coronary angioplasty
PYAR	person years at risk
QALY	quality adjusted life-year
QOL	quality of life*
RCT	randomised controlled trial
SA	stable angina*
SD	standard deviation*
SF-36	Short Form 36
SMR	standardised mortality ratio
SVD	single vessel coronary disease*
TIMI flow grade	Thrombolysis In Myocardial Infarction flow grade [0 (poor) – 4 (good)]*
TLR	target lesion revascularisation
TVR	target vessel revascularisation
UA	unstable angina*
YLL	years of life lost

* Used only in tables

Executive summary

Background

Coronary artery stents are prosthetic linings inserted into coronary arteries via a catheter to widen the artery and increase blood flow to ischaemic heart muscle. They are used in the treatment of ischaemic heart disease (IHD).

IHD is a major cause of morbidity and mortality (123,000 deaths per annum) in the UK and a major cost to the NHS. Clinical effects of IHD include subacute manifestations (stable and unstable angina) and acute manifestations (particularly myocardial infarction [MI]). Treatment includes attention to risk factors, drug therapy, percutaneous invasive interventions (PCIs) (including percutaneous transluminal coronary angioplasty [PTCA] and stents) and coronary artery bypass graft surgery (CABG).

In the last decade there has been a steady and significant increase in the rate of PCIs for IHD. In the UK, rates per million population increased from 174 in 1991 to 437 in 1998. Stents are now used in about 70% of PCIs. Data from the rest of Europe suggest there is potential for PCI and stent rates to increase considerably. In the UK there is evidence of under-provision and inequity of access to revascularisation procedures.

Objectives

The following questions were addressed.

1. What are the effects and effectiveness of elective stent insertion versus PTCA in subacute IHD, particularly stable angina and unstable angina?
2. What are the effects and effectiveness of elective stent insertion versus CABG in subacute IHD, particularly stable angina and unstable angina?
3. What are the effects and effectiveness of elective stent insertion versus PTCA in acute MI (AMI)?
4. What are best estimates of UK cost for elective stent insertion, PTCA and CABG in the circumstances of review questions 1 to 3?
5. What are best estimates of cost-effectiveness and cost–utility for elective stent insertion relative to PTCA or CABG in the circumstances of review questions 1 to 3?

Methods

A systematic review addressing the objectives was undertaken.

Data sources

A search was made for RCTs comparing stents (inserted during a PTCA procedure) with PTCA alone or with CABG in any manifestation of IHD. The search strategy covered the period from 1990 to November 1999 and included searches of electronic databases (MEDLINE, EMBASE, BIDS ISI, The Cochrane Library), Internet sites, and handsearches of cardiology conference abstracts and 1999 issues of cardiology journals. Lead researchers and local clinical experts were contacted. Manufacturers' submissions to the National Institute for Clinical Excellence were searched.

The search strategy was expanded to look for relevant economic analyses and information to inform the economic model (including searching MEDLINE, the NHS Economic Evaluation Database and the Database of Abstracts of Reviews of Effectiveness). Searches focused on research that reported costs and quality of life data associated with IHD and interventional cardiology.

Study selection

For the review of clinical effectiveness, inclusion criteria were: (i) RCT design; (ii) study population comprising adults with IHD in native or graft vessels (including patients with subacute IHD or AMI); (iii) procedure involving elective insertion of coronary artery stents; (iv) elective PTCA (including PTCA with provisional stenting) or CABG as comparator; (v) outcomes defined as one or more of: combined event rate (or event-free survival), death, MI, angina, target vessel revascularisation, CABG, repeat PTCA, angiographic outcomes; (vi) trials that had closed and reported results for all or almost all recruited patients.

For the economic evaluation, studies of adults with IHD were included if they were of the following types: studies reporting UK costs; comparative economic evaluation combining both costs and outcomes; economic evaluations reporting costs and outcomes separately for the years 1998 and 1999 (to ensure current practice was included).

Data extraction

For the review of clinical effectiveness, data were extracted into data extraction forms and RCT quality was assessed using standard methods. Decisions relating to data extraction and quality were made by two independent reviewers. Disagreements were resolved by discussion and with the aid of a third party if there was any residual discrepancy. The quality assessment of cost-effectiveness analyses was based on a pre-determined check-list.

Data synthesis

For the review of clinical effectiveness, abstracted data were collated in summary tables. Whenever possible, analysis was on an intention-to-treat basis. Meta-analyses were carried out when adequate data were available.

For the economic evaluation, cost data and health economic assessments were documented and evaluated.

Results

Effects and effectiveness

Thirty-five RCTs which fulfilled the study criteria were found: 25 compared stent with PTCA for subacute IHD; three compared stents with CABG for subacute IHD; seven compared stents with PTCA following AMI. In general, the trials were open to bias, which introduced uncertainty. Despite this, convincing evidence of impact was identified in the following.

1. Elective stent insertion versus PTCA in subacute IHD for:
   - event rates (generally death, MI, repeat PTCA and CABG) – odds ratio (OR), 0.68 (95% confidence interval [CI], 0.59 to 0.78)
   - repeat PTCA – OR, 0.57 (95% CI, 0.48 to 0.69)
2. Elective stent insertion versus PTCA in AMI for:
   - event rates (generally death, MI, repeat PTCA and CABG) – OR, 0.39 (95% CI, 0.28 to 0.54)
   - repeat PTCA – OR, 0.44 (95% CI, 0.26 to 0.74).

There was no clear evidence of impact on deaths, MI or CABG in comparison (1) or (2) above. Although trials were identified, there was insufficient evidence to draw any conclusions on the effectiveness of elective stent insertion versus CABG in subacute IHD.

Costs and economic analyses

The information identified contributes only to conclusions concerning elective stent insertion compared with PTCA in subacute IHD. There was wide variation in the estimates of cost, cost-effectiveness and cost–utility. Cost estimation, particularly for wider costs, was generally poor. It was probably conducted best in the context of the cost-effectiveness studies. These generally showed that cost/event-free survivor for elective stenting was equivalent to or less than that of PTCA. They support the view that higher initial costs of stents are outweighed by savings from reduced requirement for repeat PTCA. The majority of cost–utility studies reported cost/QALY estimations in the range of £20,000–£30,000. Reasons why these estimates should be treated with caution were identified.

The efficiency of the use of stents compared with CABG in subacute IHD or stents compared with PTCA in AMI is unknown.

Conclusions

In subacute IHD (especially stable angina and unstable angina), there is evidence for the effectiveness of elective stents in reducing the need for repeat PTCA. This appears to represent an efficient use of resources. However, this assertion could be made with more confidence if the resource neutrality of stents could be confirmed using more rigorously derived cost data. There is currently insufficient evidence to assess the effectiveness of the extension of stent use to patients with baseline risks or indications different from those of the patients in the trials reviewed (for review question 1).

Recommendations for further evaluation and research

1. For many important stenting applications, research is ongoing and a reassessment of research evidence and health economic evaluations in 1–2 years' time would be valuable.
2. Further research on the use of stents is needed to: acquire better cost data, using explicit micro-costing; investigate the impact of stents on severity of angina and quality of life; evaluate the effectiveness of newer technologies.
3. It is very important to establish clearly the effectiveness and efficiency of stents compared with CABG, and even though there is considerable ongoing research in this area, further targeted research may be valuable.

Chapter 1

Review aims and background

Aims

- To assess the effectiveness of coronary artery stents compared with other established revascularisation procedures (percutaneous transluminal coronary angioplasty [PTCA] alone and coronary artery bypass grafting [CABG]) in the main manifestations of ischaemic heart disease (IHD).
- To assess the costs, cost-effectiveness and cost–utility of the above.

Introduction

A coronary artery stent is a metal tube, coil or mesh that is inserted into a coronary artery, via a catheter inserted in an artery in the groin or arm, in order to widen the coronary artery and improve the blood flow to ischaemic heart muscle.

Interventional cardiologists are increasingly using coronary artery stents to treat IHD.[1] The procedure is carried out in a cardiac catheterisation laboratory. The stents can be inserted as an elective procedure (elective stenting), or after a PTCA with sub-optimal results ('provisional stenting') or where there is an acute closure of the artery after PTCA (emergency or 'bailout' stenting).

Description of health problem

Disease

IHD is caused by an insufficient supply of oxygen to the heart muscle. It can be 'silent' (when the patient has no symptoms) or can cause angina, unstable angina, myocardial infarction (MI) or death.

In this report we distinguish between **acute myocardial infarction** (AMI) and the subacute manifestations of IHD, particularly angina and unstable angina.

Pathology

IHD is generally caused by constriction or blockage of the coronary arteries supplying the heart. This is also known as **coronary artery disease** (CAD). The vast majority of IHD is due to atheroma and its complications. **Atheroma** occurs when there is damage to the linings of arteries leading to the formation of raised patches of fibrous and fatty material, known as **atheromatous plaques**.

Epidemiology

IHD is the major cause of death of men and women in the UK.[2] In 1997 there were 122,780 deaths due to IHD in the UK (22% of all deaths and 25% of deaths in men).[3]

Although deaths from IHD have fallen over by over two-thirds in the last 30 years, UK rates remain higher than in many countries (e.g. the death rate in the UK is over three times that of France, the EU country with the lowest death rate).[4] When measured in terms of years of life lost (YLL), IHD accounts for 15.6% of all years of life lost (1,365,995 YLL per year). The figure is 19.3% for men.[3]

It is estimated that, in Europe, IHD is the leading single cause of disability accounting for 9.7% of total disability adjusted life-years.[5] Given the high incidence of IHD in England and Wales, the figure will be even higher here.

The results of the 1998 Health Survey for England[6] indicate an overall prevalence of IHD of 7.1% in men and 4.6% in women. Prevalence increases markedly with age, reaching 23.4% in men and 18.4% in women aged over 75 years. The point prevalence of angina is estimated to be 3.2% for men and 2.5% for women; 5.3% of men and 3.9% of women reported ever having had angina. Overall 4.2% of men and 1.8% of women reported having had a heart attack (0.6% of men and 0.3% of women reported having it within the last 12 months).[6]

The Fourth General Practice Morbidity Survey (1991–1992)[7] gives the prevalence and incidence rates per 10,000 person years at risk (PYAR) for AMI and angina pectoris[8] (*Table 1*). Comparison of the Fourth Survey with the Third General Practice Morbidity Survey (1981) suggests that the rates for angina are rising.[7]

Aetiology

Cigarette smoking and other tobacco use are associated with an increase in atheroma and

TABLE 1 *Prevalence and incidence rates of AMI and angina per 10,000 person years at risk (PYAR)*[7]

	Prevalence		Incidence	
	Men	Women	Men	Women
AMI	38	20	29	16
Angina	130	98	55	49

are a major risk factor for IHD. Diabetes mellitus, hypertension, raised cholesterol, genetic predisposition, diet, lack of exercise and obesity are also risk factors.

Many of these risk factors can be modified and IHD has been identified as a major contributor to **avoidable** mortality. Reduction in circulatory disease mortality is a major UK government target in the strategy to improve the nation's health.[9]

Treatments of established IHD

Introduction

Although preventing IHD is important, this paper is concerned with the treatments that aim to reduce both the morbidity and the mortality in patients with established IHD. Treatment of IHD has many modalities:

- modification of risk factors
- medical management
- percutaneous invasive treatments (carried out by interventional cardiologists)
- surgical interventions.

Medical treatments have many mechanisms of action and rationales. They may aim to:

- reduce risk factors causing IHD
- reduce the physical demand on the heart
- improve the blood flow within the heart
- alter the clotting characteristics of blood.

There are now many well established treatments for both IHD and many of its risk factors. Many clearly contribute to both alleviation of symptoms and prevention of adverse events, such as AMI and death. The aims of treatment are to prolong life, prevent MI, prevent damage to the heart and heart failure, relieve painful and disabling angina and other symptoms, and improve quality of life.

This paper does not review the evidence for all of these treatments or discuss their relative merits, but concentrates on coronary artery stenting and the alternative established methods of revascularisation (PTCA and CABG), which are increasingly being replaced by stenting.

It is useful to have a brief overview of revascularisation techniques over the last 30 years in order to understand why stents were developed. Initially, revascularisation began in order to provide alternative therapy when medical treatments failed to control symptoms. The basic aim of all revascularisation procedures is to provide a better lumen in the vessel supplying heart muscle to improve blood flow.

CABG

CABG is a surgical technique that involves opening the chest wall and bypassing a blocked or narrowed section of a coronary artery, usually by using a vein or artery taken from elsewhere in the patient's body.

CABGs began in the late 1960s. They are carried out by cardiothoracic surgeons and can be undertaken as planned or emergency procedures. They are usually reserved for more severe cases of CAD[10] and are used to treat patients with chronic stable angina or unstable angina, following MI or following complications from PTCA. CABGs were also considered more appropriate for complex disease patterns (e.g. multi-vessel disease, disease of the left anterior descending [LAD] artery and diffuse disease). Techniques have been evolving (e.g.the development of minimally invasive CABG). The advantages and disadvantages of CABG are summarised in *Box 1*.

BOX 1 Advantages and disadvantages of CABG

Advantages

Complete relief from angina in 60–90% of patients at 1 year[11,12]

A slight decrease in mortality when compared with medical treatment[11,12]

Lower revascularisation rates after 1 year when compared with PTCA[11,13]

Disadvantages

High cost. A longer time is spent in hospital and for convalescence: the mean length of stay post-operatively in uncomplicated cases is 7–10 days[11,14]

There is a slightly higher rate of MI when compared with medical treatment[11]

Following hospital discharge, recovery takes longer after CABG when compared with PTCA[11,12,15]

Some patients are not fit enough to undergo such a major operation

In the longer term, progression of CAD often occurs in native or graft vessels[30]

PTCA

PTCA is a technique in which the narrowed or blocked part of a coronary artery is dilated by passing a radiographically guided catheter with a small balloon, usually through the femoral artery, into the narrowed section of the coronary artery. The balloon is then inflated to a high pressure for a short time. The inflated balloon produces longitudinal and circular splits in the atheromatous plaque. The balloon is then deflated and withdrawn. Because the plaque has elastic properties, it retracts where it has split leaving the coronary artery with a wider lumen than before the procedure but with a very disrupted surface.[16]

PTCA was first used in the late 1970s[17] and its use has grown steadily. PTCAs are undertaken by interventional cardiologists in a cardiac catheterisation laboratory.

PTCA is generally considered when medical treatment has failed to control symptoms.[10] It is most commonly used in single or double vessel disease.[18] Indications for PTCA have widened, and the procedure is now used to treat patients with chronic stable angina, unstable angina, stenosed CABG grafts, or cardiogenic shock, as well as patients with asymptomatic IHD and those for whom CABG is deemed inappropriate. PTCA can be repeated if symptoms return.

PTCA is also used to achieve reperfusion following MI and has the advantage of lower bleeding rates than with fibrinolytic ('clot-busting') therapy. Also, PTCA produced better short-term clinical outcomes than older fibrinolytic treatment regimens. The use of PTCA in AMI is not common because of the limited immediate availability of cardiac catheterisation laboratories and resultant delays in 'time to balloon'.[19]

The advantages and disadvantages of PTCA are summarised in *Box 2*.

When compared with medical therapy, studies have shown that PTCA is probably more successful in treating angina, but at the cost of higher subsequent rates for MI (inflating the balloon temporarily blocks blood flow through the artery, there can be acute closure of the artery, side branch occlusion or distal embolisation) and need for CABG.[21,25] Evidence suggests that more patients have angina 1 year after PTCA than after CABG, but the difference is not so marked after 3 years.[13] Mortality and MI rates are similar for both treatments but the re-intervention rates are greater for PTCA.[13] Compared with CABG, PTCA is cheaper, involves a shorter hospital stay and is less painful for the patient.[11]

Recent new antithrombotic strategies developed in conjunction with stent insertion but not used widely in PTCAs may have important implications when interpreting evidence about the relative effectiveness and adverse effects of the two technologies (see page 5).

BOX 2 Advantages and disadvantages of PTCA

Advantages

In randomised controlled trials (RCTs), PTCA has been shown to have improved outcomes compared with medical therapy[20,21]

PTCA does not require a general anaesthetic or necessitate opening the chest wall so it is useful in patients for whom operations carry a high risk

Length of stay in hospital is short (this is gradually decreasing: for elective and emegency cases, the mean was 4.3 days in 1994[22] and 3.7 days in 1996/1997[14])

PTCA can be carried out as a day case – there were 75 day cases (0.53% of all PTCA cases) in the UK in 1998[14]

It is useful for people considered not fit enough for a CABG

There is no need for prolonged convalescence

Disadvantages

Acute closure: during the procedure the artery may close abruptly, leading to an MI or, in rare cases, death. Abrupt closure during PTCA has been reported in 2–10% of patients[23] and this has required emergency CABG back-up to be available.[16,18] 'Bailout' stenting now provides an alternative to CABG in many of these cases (see 'Bailout stenting' page 4)

Restenosis: between 15 and 52% of target arteries show narrowing on angiography after a few months (restenosis) following an initial successful PTCA.[13,24] These patients may then require further treatment which could be CABG, PTCA (known as target vessel revascularisation [TVR]) or, where these options are not indicated, medical treatment. In the RITA-I RCT comparing PTCA with CABG, mortality was no different at 6 months, the incidence of angina was higher in PTCA patients, and 31% of these patients compared with 11% of CABG patients required revascularisation. Similar results have been found in meta-analysis.[13] As, however, complications following PTCA occur mostly in the first 6 months whereas complications following CABG may occur over a longer period, the picture may change to some extent when longer term follow-up from the trials becomes available

Technology under evaluation: coronary artery stents

Introduction

Coronary artery stents are short prosthetic linings for coronary arteries which are used as an adjunct to PTCA in the invasive management of CAD or are inserted directly. They were developed to address the two main disadvantages of PTCA: the need for emergency CABG if PTCA fails, and restenosis (see *Box 2*).

A coronary artery stent is a metal tube, coil or mesh that is inserted into the coronary artery via a catheter inserted into an artery in the groin or arm. Before stent placement, the artery is usually widened using a balloon. Stents are made from stainless-steel, nitinol or tantalum wire bent in a variety of ways to make coils or slotted tubes. They can have radio-opaque end markers or can be coated with heparin.[26,27] Stents are inserted into coronary arteries and expanded onto the artery wall by using the pressure from a balloon or a balloon catheter, or by retraction of a sheath.

Despite being a relatively new technology, stents are frequently used (see 'Stent rates' page 7) and are being used in an increasing range of lesions and patient subgroups. Stents are the most widely diffused of the new additions to PTCA. Since the use of stents in patients was first reported by Sigwart in 1987,[26] their design and use has been rapidly and continually evolving. The first generation of stents has now been replaced by improved designs.[28] It has been suggested that some 40 or more stents are available in Europe and elsewhere,[29] but only a limited number of these are said to be in routine use in the UK.

More than one stent may be fitted during a procedure, depending on the length of the lesion or whether there are multiple lesions suitable for stenting in different coronary arteries. The time taken to insert the stent successfully depends partly on the operator's ability and experience and partly on the anatomy of the lesion to be stented.

Causes of restenosis after PTCA are complex – the growth of new scar tissue, vessel recoil and vessel 'remodelling' (a narrowing of the lumen of a vessel which has been widened in an angioplasty) all play a role. By providing a permanent support structure or 'scaffold' for the vessel wall, it was thought that stents might reduce both vessel recoil and remodelling.

There are several strategies for the use of coronary artery stents[26,30] including bailout stenting, elective stenting and provisional stenting, which are considered below. Elective stenting is the technology that is evaluated in this report. Both bailout stenting and provisional stenting occur in the control arms of PTCA trials for ethical reasons. Moreover, provisional stenting is often the control procedure with which elective stenting is compared.

The potential advantages and disadvantages of stenting are summarised in *Box 3*.

BOX 3 Potential advantages and disadvantages of stenting

Potential advantages

Stenting takes very little longer than PTCA on its own

The use of a stent may reduce the need for subsequent repeat intervention

The stay in hospital for elective stent procedures is short (up to 3 days only, with some patients being suitable for treatment as day cases[22,31])

Stenting is suitable for some patients for whom CABG would have been indicated in preference to PTCA but who are insufficiently fit to undergo a major operation

Compared with PTCA, it diminishes the risk of having to undergo an emergency CABG

Stenting is less traumatic than CABG for the patient

Potential disadvantages

Stent thrombosis: stents are 'foreign bodies' permanently implanted into arterial walls so there is a risk of blood clots forming and blocking the coronary artery

In-stent restenosis: this occurs when there is narrowing of the lumen within a stent. Mostly this is related to overgrowth of the intima, the elastic membrane inside the artery, and is promoted by the trauma of stent insertion[32]

If the procedure is inadequate in preventing symptoms, future interventions (e.g. further PTCA) may be more difficult and patients may have to undergo open heart surgery (CABG) instead

Bailout stenting

As discussed above, PTCA can cause acute closure of an artery. Stents can be used to tack back flaps of the arterial wall caused by rupture of a plaque to keep the coronary artery open and, if successful, prevent the need for emergency CABG. This use of stents is known as 'bailout' or rescue stenting. There is no strong evidence from RCTs of the superiority of bailout stenting over emergency CABG or other emergency treatments (e.g.

prolonged perfusion balloon). However, evidence of this type would be logistically hard to obtain because of the emergency nature of the situation. Bailout stenting has received widespread acceptance as an alternative to emergency CABG. Poor outcomes associated with emergency CABG suggest that current practice seems reasonable. Bailout stenting is not considered further in this report.

Elective stenting

Elective or 'primary' stenting is the planned insertion of a stent irrespective of angioplasty results. The aim of elective stenting is to reduce the incidence of restenosis in the treated artery in the longer term compared with PTCA, thus reducing the need for further invasive intervention. Stenting can, in theory, prevent gradual closure of the artery and long-term restenosis by increasing the lumen diameter after the procedure and mechanically reinforcing the vessel wall.[33]

Elective stenting may be used in subacute IHD and also as a reperfusion therapy in the early hours of an AMI (as an alternative or in addition to fibrinolytic therapy).

Provisional stenting

Contingent use of a stent, dependent on the angiographic result of a PTCA, is known as 'provisional stenting'. Where angiography suggests that the result of a PTCA is sub-optimal, stents are used to prevent restenosis and potential acute arterial closure.

Antithrombotic therapy in stent use

Because early studies reported high rates of stent thrombosis,[34,35] aggressive antiplatelet and anticoagulant therapy, incorporating anticoagulation with heparin for up to 96 hours after deployment, was introduced to prevent these potentially fatal complications.[36] For the first few years that stents were being used, patients were given aspirin, dipyridamole, dextran, heparin, warfarin and calcium antagonists or a similar combination. The use of these regimens in early stent trials resulted in more bleeding complications and longer hospital stays with stents than with PTCA alone.[32] Antithrombotic therapy is a rapidly changing field, and regimens used in early stent trials are no longer current practice.[37] Bleeding complication rates have decreased, as the increasing use of antiplatelet therapy with aspirin and ticlopidine has meant that lower doses of anticoagulants are now current practice, resulting in decreased bleeding complications and hence shorter hospital stays.[18,38–40] Neutropenia has been reported with ticlopidine, but not with clopidogrel, another antiplatelet agent, which is now used routinely in preference.

An important development in antiplatelet therapy is the licensing of abciximab, a monoclonal antibody that inhibits platelet glycoprotein IIb/IIIa receptors, for high-risk patients undergoing PTCA. A recent RCT found a lower rate of death, MI or urgent revascularisation in stent with abciximab than in stent with placebo (5.3% compared with 10.8%; hazard ratio 0.48 [95% confidence interval, CI, 0.33 to 0.69]).[41] Six-month outcomes were reported in the EPILOG trial,[42] in which there was no difference in the pre-specified endpoint between abciximab and low-dose heparin or placebo, although there was a difference between abciximab and standard dose heparin or placebo. Attenuation of the 30-day risk difference largely resulted from the lack of any impact of abciximab on non-urgent revascularisation. The CAPTURE trial also found no difference in deaths or MI at 6 months.[43] Results in favour of abciximab at 30 days have been reported for stent subgroups in the CAPTURE and EPILOG trials,[44] but the use of stents was discouraged in these trials, so patients are unlikely to be repre-sentative. Treatment with this drug adds substantially to the cost (£670 for a typical patient; E Grant, West Midlands Drug Information Unit: personal communication, 1999), and a full evaluation of the effectiveness and cost-effectiveness of this class of drugs in the treatment of IHD is needed.

Aggressive antithrombotic strategies do not appear to have been rigorously tested in PTCA.

Developments in percutaneous coronary interventions (PCIs)

The nature and design of stents, methods of insertion and adjuvant therapies are continuously evolving. For example, manufacturers are seeking to make stents that are non-thrombogenic[32] or conformable so that 'dead space' between the stent and the vessel wall (which predisposes to clot formation) is eliminated. There are also developments in PTCA and other PCIs that do not involve stent placement. There are trials in progress comparing different stents and looking at direct stenting. New technological developments to prevent or deal with in-stent stenosis include medical treatments, laser treatments, debulking, atherectomy, cutting balloon angioplasty, stent coatings, therapeutic ultrasound and radiotherapy.[32,45]

The range of indications for which stents are being used is expanding. Proponents argue that stents not only improve the outcome in situations where PTCA would have been used previously, but also extend the range of circumstances in which PCIs are appropriate. That is to say that stents are appropriate in some of the circumstances in which CABG was indicated because of the complexity of the disease pattern (e.g. multi-vessel disease) or when PTCA was felt to be too risky.

Current service provision

Introduction

Before the introduction of stents, PTCA alone was the standard treatment, and provided an alternative to open heart surgery for many patients. Improvements in PTCA technology, the introduction of stents and adjunctive anti-thrombotic drug therapy have resulted in a rapid increase in the number of PCIs carried out, and their use in a wider range of patients.

This section will examine the current service provision and activity levels for PCIs and CABGs. However, it must be remembered that IHD is treated in every section of the NHS, especially in primary care and in non-specialist hospitals, and that any changes in service provision will have a knock-on effect on these services.

Provision of interventional or diagnostic centres

The number of centres undertaking diagnostic tests or performing interventions has increased steadily over the last decade. In 1998 there were 126 such centres in the UK,[31] 111 of which are in the NHS (46 interventional and 65 diagnostic only). All 15 centres in the private sector are interventional. The activity of NHS interventional centres also increased between 1991 and 1998 with a doubling of the mean number of PCIs undertaken per centre (from 191 in 1991 to 408 in 1998).

Cardiac catheterisations

According to national statistics, in 1996/1997 there were 57,046 NHS patient episodes categorised as cardiac catheterisations (for angiography or PCI) in the UK.[14] Of these, 42% were day cases and 68% were carried out in men. According to the British Cardiovascular Intervention Society (BCIS) returns (see below), there were 100,023 cardiac catheterisations in the NHS and private intervention centres in 1998.

Number of PCIs

PCIs include PTCA alone, atherectomy, excimer laser, rotablator and PTCA with stent. According to the audit data from the BCIS, in 1998 there were 24,899 PCIs. The number of PCIs has increased 2.5-fold from 1991 to 1998 (*Table 2*).[31]

Although there is a striking increase in PCIs, comparisons with activity levels in other countries suggest that there is potential for considerable further growth. Germany had a rate of over 1800/million population in 1998. *Figure 1* shows a comparison of the UK with the rest of Europe.

Compared with the UK, European countries such as Portugal, Italy, France and Spain have very low rates of IHD (age-adjusted mortality rates per 100,000 for men aged 45–74 years in 1990–1992: Portugal, 207; Italy, 224; France, 42; Spain, 181, England and Wales, 515; Scotland, 655). In the light of these low rates of IHD in other European countries, the UK's relatively low rate of PCI activity is even more striking.

TABLE 2 *Total UK PCI procedures*[31]

Year	No. of centres	Total no. of PCIs	Increase over previous year (%)	Rate (per million population)
1991	52	9,933	–	174
1992	52	11,575	16.5	203
1993	53	12,937	11.8	227
1994	54	14,624	13.0	256
1995	54	17,344	18.6	304
1996	53	20,511	18.1	359
1997	58	22,902	11.7	402
1998	61	24,899	8.7	437

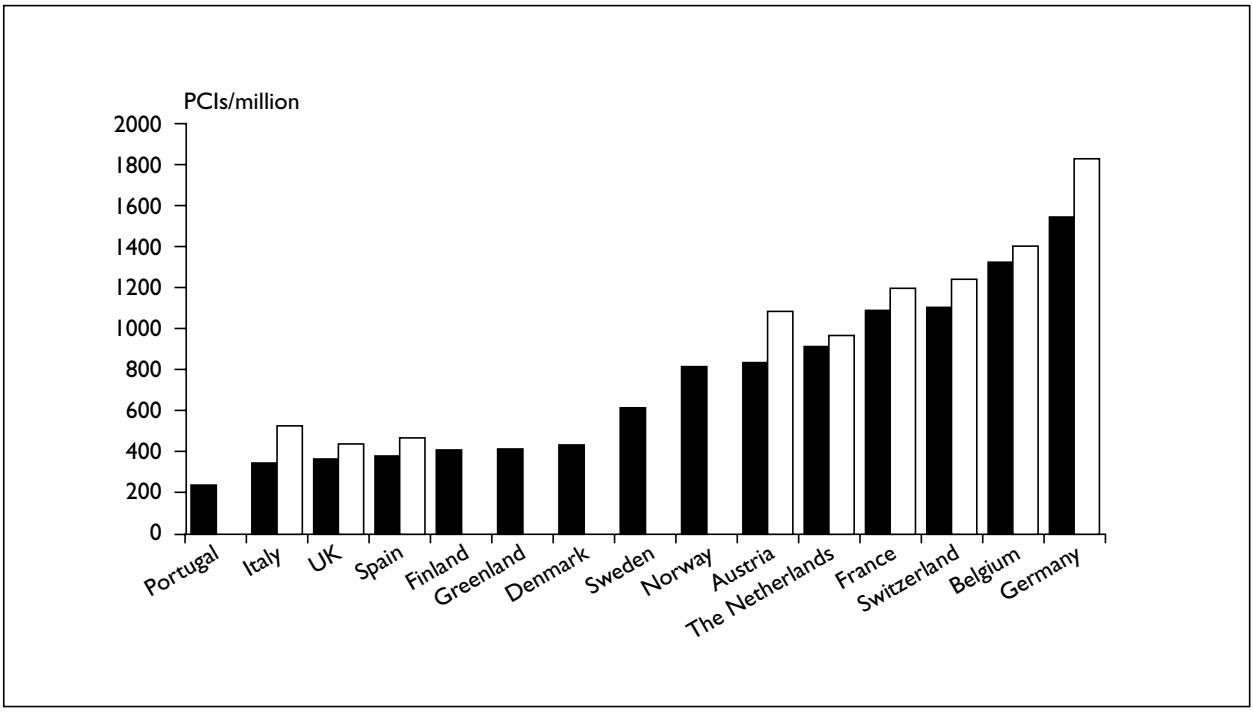


FIGURE 1 *PCIs: UK compared with other European countries 1996 (■) and 1998 (□)*

UK data[31] show that the overwhelming majority of PCIs are either PTCA alone or PTCA with stent. The BCIS audit data show that 31% of PCIs do not involve stents (i.e. approximately 17,200 procedures). National statistics show that there were 14,023 patient episodes for PTCA in 1998 with a median and modal length of stay of 1–2 days.[14]

Stent rates

The rate of stent insertion in PTCA has been increasing. The rate increased 23-fold from 13 to 302/million UK population between 1993 and 1998. The use of stents has also increased as a proportion of PCIs and now about 70% of PCIs will involve the use of stents (*Figure 2*).[31]

CABG rates

National statistics for CABGs in the UK (excluding Northern Ireland) show that there were 16,780 patient episodes in 1998, of which 13,297 (79%) were in men and 3483 (21%) were in women. The mean length of stay was 9 days.[14] These numbers give a rate of about 320/million population. Only 3.23% of these patient episodes were emergency admissions; the others were either elective (88%) or admissions from other NHS providers (8.64%).[14]

Proponents of stenting argue that rates of emergency CABG following PTCA have dropped as the percentage of PTCAs involving stents has gone up (*Figure 3*), as have repeat procedures for acute closure (*Figure 4*) and repeat procedures for restenosis (*Figure 5*).

The data in *Figures 3–5* come from the registry run by the BCIS. However, caution must be used before drawing strong conclusions from the data because complete outcome data are not received from all centres and it is possible that there is some reporting bias.

Geographical variation

There is considerable geographical variation in both patient need (for investigation and revascularisation) and service provision. The two are not necessarily correlated. Discussion with clinicians and public health consultants concerned with services for IHD suggests that revascularisation activity and guidelines for access to services and treatment in different districts may be determined more by service supply and clinician interest than by patient need. It is also possible that different attitudes to the treatment of elderly people may underlie some of difference in activity levels between areas with similar standardised mortality ratios (SMRs).

Need

There are differences in SMRs for IHD between regions in the UK. *Table 3* shows the figures for the old regional structure for 1993–1995 when SMRs ranged between 88 and 113.

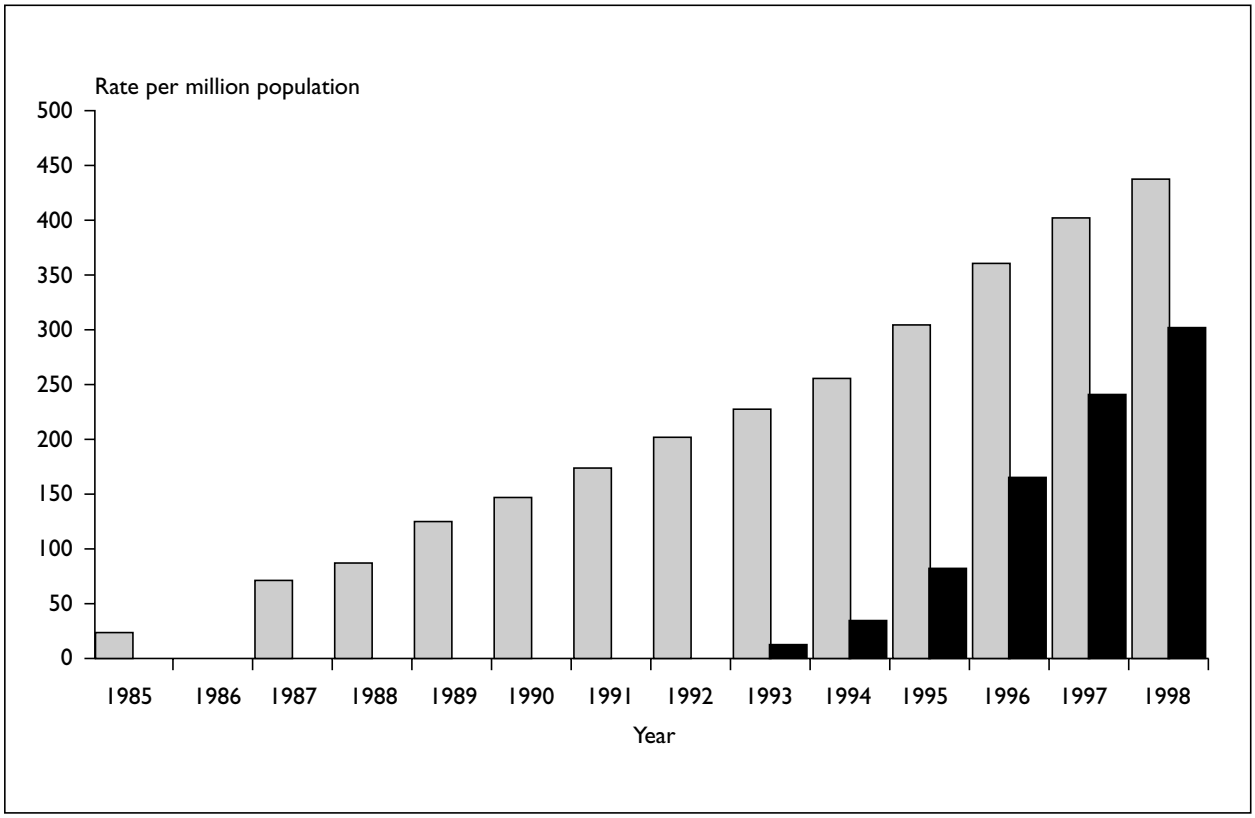


FIGURE 2 *Rates of PCIs and PTCA plus stent in the UK, 1985–1998 (□, all PCI procedures; ■, stents)*

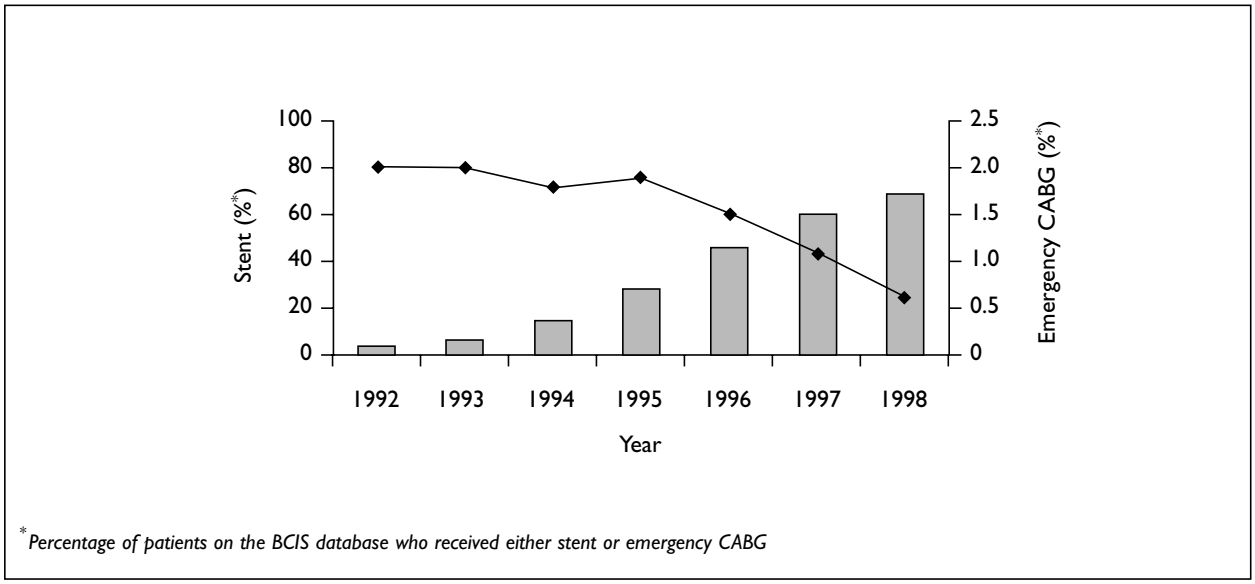
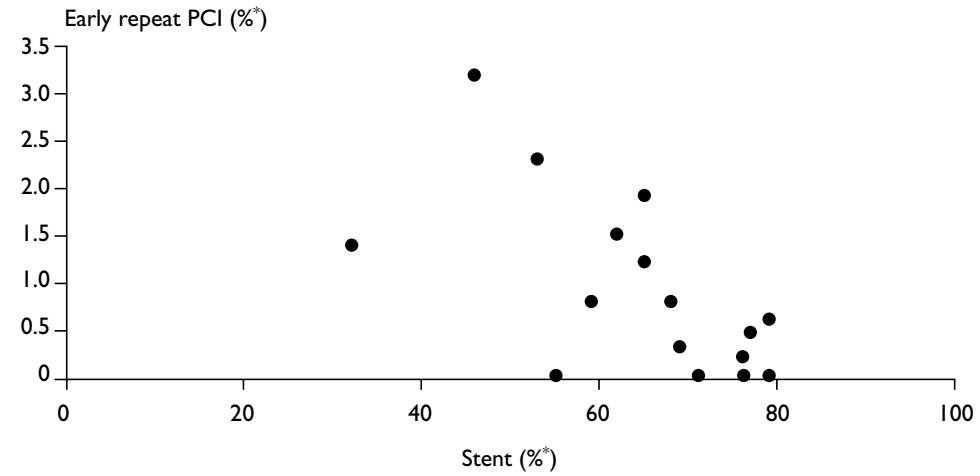


FIGURE 3 *Stenting and the need for emergency CABG (□, stent; —◆—, emergency CABG)*

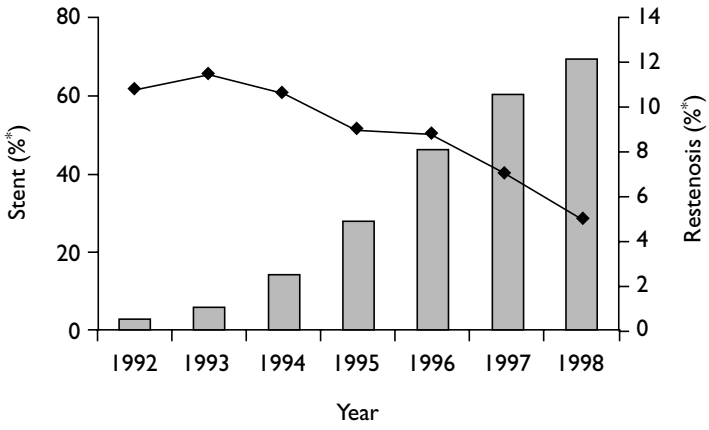
Activity

Access to facilities and revascularisation rates vary greatly across the country with a five-fold difference in revascularisation rates between different regions.[46] Similar differences can be found within regions. An example follows for the West Midlands Region for the years 1990–1997 (*Table 4*). There were over two-fold differences between districts for CABG rates, and more than six-fold differences in PTCA rates (data from Hospital Episode Statistics dataset). It can be seen from *Table 4* that access and need do not correlate: Solihull has the



*Percentage of patients on the BCIS database at each centre

FIGURE 4 *Stenting and early repeat PCI for acute closure 1998[31] (data from 16 centres)*



*Percentage of patients on the BCIS database

FIGURE 5 *Stenting and procedures for restenosis[31] (data from 25 centres) (□, stent; —◆—, restenosis)*

lowest SMR and the highest revascularisation rate, whereas Walsall has the highest SMR and the lowest revascularisation rate.

Implications for the NHS

It is reasonable to assume that populations with relatively high SMRs for IHD will require higher rates of revascularisation than populations with lower SMRs, provided that interventions are being used appropriately. Thus the comparisons of revascularisation rates in the UK with those of other European countries (*Figure 1*), suggest that there is probably under-provision of services in this country. This is true whether or not one concludes that stenting is more effective or cost-effective than PTCA alone.

TABLE 3 *SMRs for Regions in England 1993–1995*

Region	SMR for IHD, 1993–1995
Northern & Yorks	113
Trent	105
Anglia & Oxford	88
North Thames	92
South Thames	88
South West	91
West Midlands	105
North West	116

The British Cardiac Society suggested in a statement issued in 1994 that a realistic target for 1996–1997 should be 1000 revascularisations per million population (with a split of 6:4 for CABGs:PTCA).[46] A prospective study of patients referred from a random sample of general practitioners to a special open-access chest pain clinic estimated a crude annual incidence of 830/million population, of whom about one-third had exercise test results that would suggest referral for revascularisation.[47]

The National Service Framework (NSF) has been published[48] since completion of this report in December 1999. The NSF has set standards for the prevention and treatment of IHD including revascularisation. It offers advice on the indications for investigation and treatment. Now that this is available, the size, nature and location of any under-provision ought to become clearer.

TABLE 4 *Revascularisation rates and SMRs for IHD, West Midlands Region*

Health Authority	CABG/million population, 1996	PTCA/million population, 1996	Total	SMRs for IHD, 1993–1995
Region	***543***	***274***	***817***	***105***
Coventry	297	577	874	100
Warwickshire	354	589	943	92
Walsall	457	141	598	131
Sandwell	472	151	623	119
Wolverhampton	499	192	691	107
Herefordshire	522	91	613	92
South Staffordshire	523	262	785	111
North Staffordshire	537	253	790	113
Worcester	598	196	794	90
Shropshire	615	171	786	102
Birmingham	652	226	878	108
Dudley	676	256	932	104
Solihull	687	407	1094	89

Data from Hospital Episode Statistics dataset

Chapter 2
Methods

Review questions

The following questions are addressed in this review.

- What are the effects and effectiveness of elective stent insertion versus PTCA in subacute IHD, particularly stable angina and unstable angina?
- What are the effects and effectiveness of elective stent insertion versus CABG in subacute IHD, particularly stable angina and unstable angina?
- What are the effects and effectiveness of elective stent insertion versus PTCA in acute MI?
- What are best estimates of UK cost for elective stent insertion, PTCA and CABG in the circumstances of review questions 1 to 3?
- What are best estimates of cost-effectiveness and cost–utility for elective stent insertion relative to PTCA or CABG in the circumstances of review questions 1 to 3?

The methods of the reviews generally followed the guidance laid out in the West Midlands Development and Evaluation Service Handbook[49] and the NHSCRD Report No. 4.[50]

Search strategy

A scoping search was undertaken, focusing on existing reviews and other key papers, as well as the identification of RCTs likely to be included. The yield from this search and a 1998 West Midlands Development and Evaluation Committee (DEC) report on coronary artery stents[1] was used to develop the protocol for the review including inclusion and exclusion criteria and a data abstraction form. Although the scoping review identified recent systematic reviews comparing stents with PTCA,[51,52] this technology is developing so rapidly that any review quickly becomes out of date and so the existence of these systematic reviews did not preclude the need for an up-to-date review.

A search was made for RCTs comparing stents, inserted during a PTCA procedure, with PTCA alone or with CABG in any manifestation of CAD using the NHS Centre for Reviews and Dissemination search strategy for RCTs.[50] The search strategy covered the period from 1990 to November 1999, as it was in the early 1990s that work on the development of coronary artery stents first began. Key components of the formal search were as follows.

- Electronic databases were searched: MEDLINE (including Pre-MEDLINE); EMBASE; BIDS ISI; The Cochrane Library; York HTA. A combination of index terms (including 'stent' and 'coronary artery disease') and textwords (including 'stent*' and 'coronary') were used.
- A general search of Internet sites was made using medical search engines including OMNI and the general search engine Google, using general search terms such as 'cardiology' or 'stent*'. A search of specific cardiology Internet sites (including the American College of Cardiology website) was carried out.
- Contact was made with lead researchers on existing reviews and RCTs and local clinical experts.
- Handsearches of cardiology conference abstracts, in journals and on websites, were carried out.
- Handsearches were made of recent issues (1999) of cardiology journals.
- Citations were checked in reviews and RCTs identified by the searches.
- A search was made of manufacturers' submissions to NICE (see appendix 1).

For MEDLINE and EMBASE search strategies see appendix 2.

The search strategy was expanded to look for relevant economic analyses and for information to inform the economic model. Searches focused on research that reported costs and quality of life data associated with CAD and interventional cardiology.

Additional elements to the search strategy included:

- specific searches on MEDLINE for relevant cost and cost-effectiveness studies
- searching specialised health economics sources such as NHS Economic Evaluation Database (NHSEED) and the Database of Abstracts of Reviews of Effectiveness (DARE).

For cost and cost-effectiveness search strategies see appendices 3 and 4.

Inclusion and exclusion criteria (clinical effectiveness)

Two independent reviewers using explicit predetermined criteria made the inclusion and exclusion decisions. Disagreements were resolved through discussion with a third party. Inclusion and exclusion decisions were made independently of the detailed scrutiny of the results.

Inclusion criteria

Studies were only included in the final analysis of the review if they met the criteria in *Box 4*.

BOX 4 Criteria for inclusion of studies in the final analysis of clinical effectiveness

Study design	RCTs
Population	Adults with CAD in native or graft vessels. Patient groups included subacute IHD and with AMI
Intervention	Coronary artery stents inserted as an elective procedure
Comparator	Elective PTCA and CABG (i.e. established invasive treatments) including PTCA with provisional stenting (i.e. where stenting is conditional upon immediate angiographic results)
Outcomes	Studies were only included in the review if they reported results of one or more of: combined event rate (or event-free survival), death, MI (Q wave, non-Q wave and total), angina rate, target vessel revascularisation, CABG, repeat PTCA, angiographic outcomes
Reporting	Only trials that had closed and had reported results for all or almost all recruited patients were included

The primary outcomes for this review were the medium term (3 to < 12 month) and long-term (1–5 year) clinical results. The secondary outcomes were considered to be short-term (< 3 month) clinical results and the angiographic results. Although trials with only angiographic outcomes were included, preferred outcomes were patient-, rather than coronary artery-, centred. Angiographic outcomes may be biased because the stent is visible in angiographic film.

This review included RCTs that have been fully published in peer-reviewed journals and also as conference abstracts. When RCTs were published as conference abstracts only, efforts were made to obtain more complete data from the trialists by writing to the first named author. Trialists had 4–6 weeks to reply. Trials published as abstracts were only included if the trial had closed and some follow-up effectiveness results were available for all or almost all trial participants.

Exclusion criteria

The exclusion criteria were as follows.

1. RCTs that had not finished recruiting (as of latest abstract available).
2. RCTs that published interim results only.
3. RCTs that published results for only some of the trial participants.
4. RCTs for which there were no details of the numbers of patients in each arm of the trial.
5. RCTs that did not compare elective stenting with PTCA or CABG.

The review did not address:

- bailout stenting compared with PTCA (prolonged perfusion balloon) for failed initial PTCA (RCTs of bailout stenting are logistically difficult)
- stents compared with medical treatment
- stents compared with newer technologies (e.g. atherectomy, excimer laser or angioplasty cutting balloon)
- stents compared with stents (i.e. comparisons of effectiveness of different stent types).

Note was made of any RCTs found during the searches and subsequently excluded under points 1–5 above.

Inclusion and exclusion criteria (economic evaluation)

One reviewer, using explicit, predetermined criteria, made the inclusion and exclusion decisions for the cost and cost-effectiveness studies.

Studies were included in the final review if they met the criteria shown in *Box 5*.

As costs from other countries, particularly the USA, may not be comparable with costs in the UK, only costs calculated in the UK are included in the cost analysis.

BOX 5 Criteria for inclusion of studies in the final analysis of cost and cost-effectiveness

Population	Adults with CAD AND
Economic study type	Studies reporting UK costs OR
	Comparative economic evaluation combining both costs and outcomes OR
	Economic evaluation in which costs and outcomes are reported separately for the years 1998 and 1999 (to ensure current practice has been included)

This review excludes any studies published before 1996. Practice has changed significantly in recent years, in particular with respect to replacing the anti-coagulation treatment with an anti-thrombotic regimen which allows earlier discharge and fewer bleeding complications. Stent technology has changed, and the patients treated have changed from low risk (discrete single-vessel lesions) to those with more complex multi-vessel disease. The costs of the procedures are changing rapidly, so costs calculated during the last 3 years (1996–1999) only have been included.

Data abstraction (clinical effectiveness)

Two independent reviewers undertook the data abstraction using a data extraction form developed during the protocol stage of the review. Disagreements were resolved by discussion and with the aid of a third party when there was any residual discrepancy.

The following data were extracted:

- overall study design sufficient to allow an assessment of the validity of the study such as size, duration, randomisation procedure, concealment of allocation, blinding, drop-outs, crossovers, and losses to follow-up for each patient group
- details of the study populations such as percentages of patients with stable and unstable angina and previous MI
- details of the intervention such as type of stent and anticoagulation/antiplatelet treatment used
- individual outcomes measured such as use of survival analysis or event rates and the results, as percentages and/or ideally as raw numbers, plus any summary measure given (standard deviation, *p* value and CIs where possible).

Data abstraction (economic evaluation)

For the UK cost study the following data were extracted:

- source of information, reference, date, and potential problems with source
- nature of intervention costed
- nature of costing (procedure only, hospital costs or wider costs including follow-up time) and whether point estimate or range
- estimate of cost and range.

For the cost-effectiveness study the following data were extracted:

- details of the study design
- details of the study population
- details of the intervention used, for example, primary stenting, versus PTCA or secondary stenting
- details of individual outcome measures used
- details of and sources of effectiveness data in economic models
- details of sources of quality of life data
- methods of collecting cost data
- assumptions used in economic models.

Quality assessment (clinical effectiveness)

Two independent reviewers undertook the quality assessment. Disagreements were resolved by discussion and with the aid of a third party when there was any residual discrepancy.

The quality of RCTs was assessed in standard ways[50] including the use of the Jadad[53] score. A judgement on the quality and reliability of each study, and of each outcome within the study, was made on the basis of the abstracted information.

Quality assessment (economic evaluation)

The quality assessment of cost-effectiveness analyses was based on the 35-point checklist used by the *British Medical Journal* to assist referees of

economic analyses.[54,55] When studies were available only in abstract form or summarised in an industry submission there was insufficient information to do a formal quality assessment.

Data synthesis (clinical effectiveness)

Results are presented for the review questions listed above. All abstracted data were collated in summary tables indicating the general pattern of results. Where possible all results were analysed on an intention to treat basis.

Where sufficient information was available and the studies were considered sufficiently clinically and statistically homogeneous for combination to be informative, meta-analyses were carried out using Cochrane Collaboration Review Manager 3.01 software (Update Software Ltd). Analyses were made for the clinical outcome measures of death, MI, angina rate, TVR, CABG, repeat PTCA and total event rate for stents versus PTCA in IHD and following acute MI.

Possible explanations of heterogeneity were considered such as differences between the subgroups specified below and the potential impact of study quality.

In the review of stents versus PTCA in IHD, the following prespecified patient subgroups were considered:

- patients with small coronary arteries
- patients with chronic occlusion
- stenting compared to PTCA with stent insertion dependent upon immediate angiographic results (provisional stenting).

Data synthesis (economic evaluation)

The purpose of the review of economic evaluation was to document existing cost data and health economic assessments, with a view to explaining variation in them, particularly in light of the systematic review of effectiveness information in the preceding sections. These data are used to draw overall conclusions on the likely cost-effectiveness and cost–utility of the use of elective stenting in CAD. This review has not undertaken a cost–utility estimate or directly modelled the data.

Chapter 3
Results

Introduction

The clinical effectiveness and economic evaluation results are presented in separate sections of this report. Overall, 108 references were identified for this systematic review.[27,41,51,56–160]

Effectiveness results

Results of the searches

Full results of the searches are reported in appendix 2.

Excluded trials

Twenty-five RCTs were found which did not meet the inclusion criteria (15 trials of stent versus PTCA in IHD,[56–69,155,156,158,159] four trials of stent versus CABG in IHD,[70–73] three trials of stent versus PTCA in patients with MI,[74–76] and three trials of other comparisons[75,77,78]). Details of these excluded trials are shown in appendix 5 (pages 69–72).

Most of the trials were excluded because the trial had not yet finished enrolment of patients. Other reasons for exclusion included no details of number of patients in each arm of the RCT and reporting of results for only a small proportion of trial participants. Almost all of the excluded trials were reported as conference abstracts only. Where only abstracts were available, letters requesting further information were sent to first authors. For some of the fully reported trials the longer term follow-up results were only available in abstract form, but no letters were sent to the investigators in those trials. STRESS II [79] was a continuation of the STRESS trial, and data from STRESS I alone has been used here in view of the *ad hoc* decision to continue the STRESS trial and the fuller reporting of the STRESS I data.

Coronary artery stent technology is in a phase of rapid development. This is evidenced by the number of trials in progress which were excluded from this review. New evidence on all of the questions addressed is likely to become available over the coming years.

Included trials

Thirty-five RCTs were found which met the inclusion criteria for this report:

- 25 comparing elective stenting with PTCA in subacute CAD
- three comparing elective stenting with CABG (or minimally invasive CABG) in CAD
- seven comparing stents with PTCA following AMI.

Replies from authors provided substantial further information for two trials on AMI patients, STENTIM II and PASTA. A further abstract was received for the PSAAMI study.

A level of statistical significance of $p < 0.05$ has been used throughout the results.

Effectiveness of elective stenting compared with PTCA in subacute IHD

Trial reporting

Of the 25 trials in this category, 16[27,41,80–107] were fully reported in peer-reviewed journals. The remaining nine[108–117] were available as abstracts only or in a press release that appeared to use information from a conference presentation in March 1999 (OPUS; included in Cordis industry submission)[116] or from another systematic review (WIN).[51,109]

In the tables, the 25 trials are presented in the order of oldest trials first (BENESTENT[80–84] to WIDEST[111]), then subgroups of trials of: saphenous vein graft lesions (SAVED[96]), stent + abciximab versus PTCA + abciximab (EPISTENT[41,97]), chronic coronary occlusion (SICCO[98–100] to CORSICA[113]) and then elective stenting versus PTCA with provisional stenting (OCBAS[107] to OPUS[116]).

Follow-up varied from 6 months to 5 years. The clinical results tables have been split into three groups: immediate, in hospital or up to 1 month follow-up, 3 to < 12 months follow-up, and 1 to 5 years follow-up. Only the medium- and long-term results have been discussed in the results section and meta-analyses.

There were sufficient trials for the possibility of publication or small study bias to be considered in a funnel plot. The outcome chosen for the

plot was the medium-term event rate, and those trials which reported this outcome in sufficient detail to be included in a meta-analysis (see below) were included in the plot (*Figure 6*). The plot gives no clear indication of publication or small study bias.

Patients

Patient characteristics are reported in appendix 5 (pages 73–77). All of the trials included patients who could have been treated either with PTCA alone or with stents. In some of the earlier trials (BENESTENT,[80–84] Eeckhout,[90] GISSOC[101]) it was specified that all patients also had to be eligible for CABG.

The BENESTENT[80–84] trial, one of the earliest, included only patients with stable angina. All other trials included various proportions of patients with stable or unstable angina.

All trials but DEBATE II[114,115,117] (for which little information on trial design was available) and Restenosis SSG[95] excluded small coronary artery stents. The latter included only patients with restenosis following PTCA. Some trials only included new lesions (BENESTENT,[80–84] STRESS,[85–89] Eeckhout,[90] Versaci,[91] BENESTENT II,[27] AS,[110] SICCO[98–100]) whereas the other trials (which gave details) included both new and restenotic lesions.

One trial included only lesions in saphenous vein grafts (SAVED[96]). All of the other trials looked at lesions in native vessels only.

A large subgroup of eight trials included patients whose vessels had chronic and total occlusion only (SICCO,[98–100] GISSOC,[101] Hancock,[102] TOSCA,[103,104] SPACTO,[105] SARECCO,[106] STOP,[112] CORSICA[113]) whereas other trials specifically excluded total occlusion (Versaci,[91] START[93,94]).

Although four trials[57,64,65,68] considered the use of stenting in small coronary vessels, none of them could be included in the review because no complete results were available.

Most trials did not report what proportion of potential patients were eligible for the trial, or indeed what proportion of eligible patients were randomised (see appendix 5, pages 78–83). Where this was reported (Eeckhout,[90] EPISTENT,[41,97] SICCO,[98–100] Hancock,[102] TOSCA,[103,104] SPACTO,[105] OCBAS[107]), most trials appeared to have included only highly selected groups. Thus trial results may not be generalisable to typical PCI patients.

Interventions and comparators

Stents

The type of stent used in the RCTs varied but more used Palmaz-Schatz than any other stent type (see appendix 5, pages 73–77). Two of the

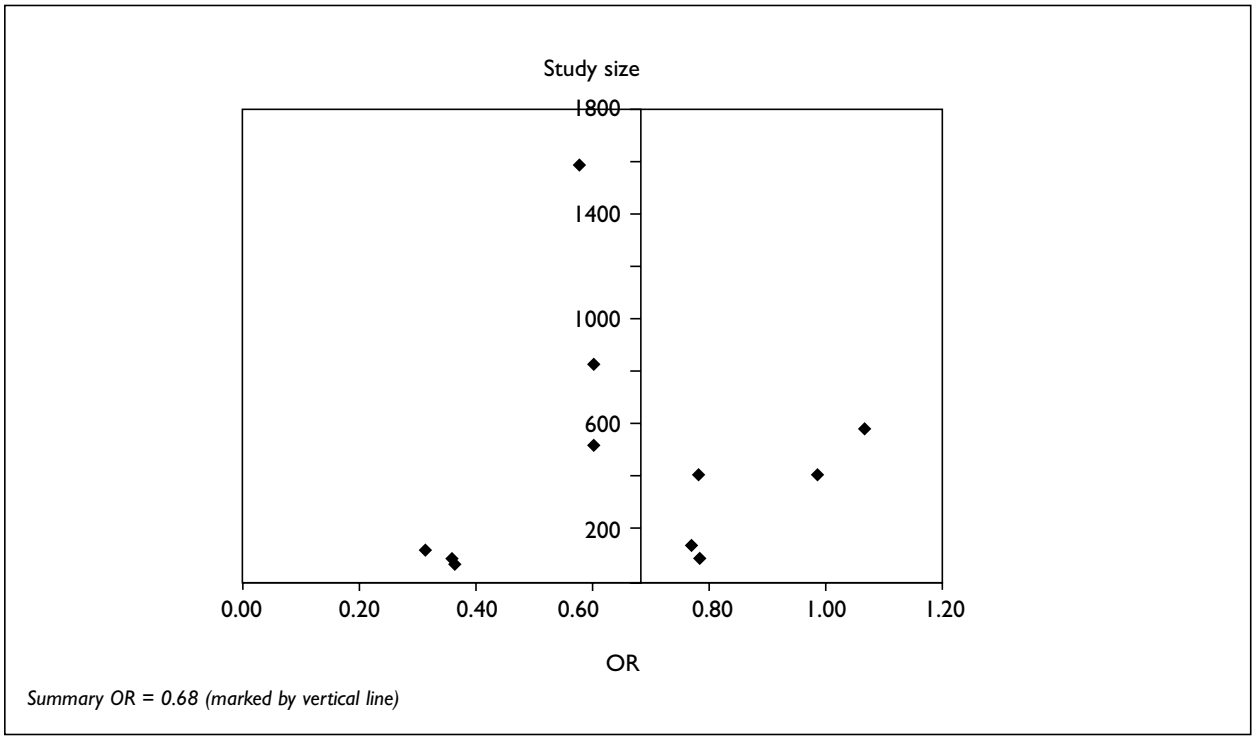


FIGURE 6 *Funnel plot: odds ratios (ORs) for 4–11 month event rate against study size – stent versus PTCA*

trials used Palmaz-Schatz heparin-coated stents (BENESTENT II,[27] TOSCA[103,104]).

Antithrombotic regimens
The standard anticoagulation/antiplatelet drug treatments have changed in the last 5 years. When the first trials were undertaken (BENESTENT,[80–84] STRESS,[85–89] Versaci,[91] START,[93,94] SAVED,[96] SICCO,[98–100] GISSOC,[101] Hancock[102]), warfarin for the stent group was standard practice but the PTCA groups did not receive the same drug treatment. Since then warfarin has not been used because of increased bleeding complications and ticlopidine has been used instead. In some trials (WIDEST,[111] TOSCA,[103,104] SPACTO[105]) the drug regimen for the stent patients changed from warfarin to ticlopidine midway through the trial. In only a few trials (AS,[110] EPISTENT,[41,97] CORSICA[113]) does it appear that the same drug regimen was given to the stent and PTCA groups (see appendix 5, pages 84–87). In the vast majority of trials antithrombotic therapy was more intensive in the stent arm than in the PTCA arm, leaving open the possibility that some of the difference in observed outcomes may be attributable to this.

In the EPISTENT[41,97] trial there was a third arm to the trial (stent + placebo) but the only results included in this review are for the stent + abciximab and PTCA + abciximab groups. Abciximab was used in a small proportion of patients in other RCTs in this review (TOSCA[103,104]).

It might be expected that bleeding complication rates and also length of hospital stay would have varied depending upon the anticoagulation regimen used.

Comparators
In most of the trials, the intention was to treat the PTCA group with PTCA only. However, some patients in the PTCA-only groups did receive stents. Patients either received emergency stent placement because the target artery had not remained patent after the PTCA (bailout stent), or a stent because there was uncertainty as to whether the artery would have remained patent (provisional stent). In these trials the number of patients in the PTCA group who received a stent was recorded as a treatment crossover. In a few of the trials (OCBAS,[107] DEBATE II,[114,115,117] OPUS[116]) the strategy of provisional stenting for an unacceptable PTCA result was part of the trial design. In these trials, patients allocated to PTCA received a stent if the immediate angiographic results were considered 'suboptimal' (not 'stent-like'), as well as when there was an emergency requirement for a bailout stent. In this review, the number of patients in the PTCA group who received a stent is recorded as a treatment crossover whatever the reason for crossover, regardless of different trial design (see appendix 5, pages 84–87). No crossovers were allowed in some trials.

The crossovers from stent to PTCA treatment ranged from 0% to 9.3%. The crossovers from PTCA to stent treatment ranged from 0% to 37%. Of the four trials with a crossover from PTCA to stents of > 30%, only one was a trial of PTCA with provisional stenting versus elective stenting.

Another important difference between trial designs is the point at which randomisation occurs. This was sometimes before catheterisation, sometimes after the guidewire had been passed, and sometimes after a successful PTCA had been achieved. The further along this pathway randomisation occurs, the more selected the patient group.

Summary
The trials are not simply comparing stenting in PTCA with PTCA alone. The interventions and comparisons in these trials are packages comprising selection at different stages in the catheterisation pathway, different policies with regard to crossover to stent in the PTCA arm of the trial, and antithrombotic regimens which in most cases were different for stent and for PTCA and which in some cases were changed part way through the trial.

Trial quality
Where reported, the baseline characteristics of stent and PTCA groups within each trial were mostly similar. Any differences are described in appendix 5 (pages 78–83). The most conspicuous difference was in the SPACTO[105] trial, in which men made up 57% of the patient population in the stent arm of the trial and 81% in the PTCA arm ($p = 0.02$), suggesting that confounding factors might not have been balanced between the trial arms.

All of the RCTs were graded using the Jadad scale[53] (see appendix 5, pages 84–87). This score incorporates points for blinding, randomisation, concealment of allocation and reporting of follow-up – all factors that have been shown to be important in prevention of bias. A score of 3 or more indicates a trial of good quality in these respects. The scores ranged from 1 to 3 only. None of the trials was described as double blind, as this would be impossible to achieve. It

appears that neither physicians nor patients were blinded to the treatment received in any of the trials. The Jadad score is included to give an indication of the quality of trial execution, but in this case it also reflects the quality of reporting, largely in those trials published only in abstract form. The main reason for a fully reported RCT receiving a score of less than 3 was because there were no details of the randomisation process. All of the RCTs reported as abstracts only had a Jadad score of 1.

The number of drop-outs after randomisation was usually very small (see appendix 5, pages 78–83).

As blinding of patients and clinicians was not possible in these trials, it is possible that some degree of bias has entered into trial execution and reporting, because trialists often have a subconscious bias in favour of the new treatment, in this case stents. This has been acknowledged by stent trialists.[27]

A further source of bias is introduced by angiographic follow-up. It is not possible to blind angiographic assessment of outcomes, but a further potentially important problem is that it is probable that healthy rather than unhealthy patients are lost to or refuse angiographic follow-up. In this review, clinical outcomes are considered to be the primary endpoints, although angiographic outcome data are reported in appendix 5 (pages 92–93).

In general, the clinical follow-up rates are high, even for long-term follow-up. Where it is completely unclear as to how many patients have been followed up, blanks have been left in the tables in appendix 5. Although percentages were sometimes given in the trial reports, absence of any absolute numbers often made it impossible to include data in the meta-analysis.

Short-term clinical outcomes

Short-term outcomes are reported in appendix 5 (pages 88–89 and 90–91). The bleeding complication rate appears to be influenced by the anticoagulant regimen, rather than by stent insertion, as it varies according to the anticoagulation used. In particular, where major bleeding complications were recorded, differences between stent and PTCA arms were minimal in those trials which did not incorporate formal anticoagulation with warfarin and used ticlopidine instead (that is, BENESTENT II,[27] EPISTENT,[41,97] and SARECCO[106]). Bleeding complications, costs and hospital stay were increased when heavy anticoagulation was used.

Definitions of major bleed varied between the trials. Where descriptions of bleeding complications were given, major bleed was taken to include any bleeding that had resource implications (e.g. need for vascular repair or blood transfusion).

Angiographic outcomes

Angiographic follow-up for all trials varied from 4 to 9 months but was mostly carried out at approximately 6 months. Initial minimal lumen diameter of the coronary artery (MLD) and percentage stenosis and follow-up restenosis rates are reported in appendix 5 (pages 92–93).

Stenting produced better post-procedural angiographic results than PTCA but the difference between the two groups declined over time. Angiographic results from the trials tend to show a statistically significant improvement for the stent group compared with the PTCA group post procedure and at follow-up (4 to 9 months), but angiographic results are not well correlated with clinical results and so will not be discussed further in this report.

Medium-term (4 to 11 months) clinical outcomes

Results covering periods of follow-up of between 4 and 11 months are reported in appendix 5 (pages 95–96 and 97–98).

Where full information on the numbers of patients in each arm and the number of events was available, trials were included in meta-analyses produced using the Cochrane Collaboration Revman 3.01 software (Update Software Ltd) and are reported in Forest plots. A fixed effect model and the Peto OR have been used. Results which were clearly based on actuarial survival analysis with variable lengths of follow-up were not included in the meta-analyses. The following outcomes were considered: composite event rates (for definition used in each trial, see appendix 5, page 94), death, MI, target vessel or lesion revascularisation (TVR or TLR), CABG, repeat PTCA and angina status. Trials are ordered as follows: general CAD trials in order of year of publication, followed by EPISTENT,[41,97] the abciximab trial, followed by chronic occlusion trials in order of year of publication.

Event rate

The medium-term event rate was the primary clinical endpoint of most trials. Composite event rates included death, MI and repeat revascularisation. The last of these accounted for the majority of the events. Details of individual

trial event rate definitions are given in appendix 5 (page 94). Composite event rates reported at between 4 and 11 months follow-up tended to favour stent (*Figure 7*), with a summary OR of 0.68 (95% CI, 0.59 to 0.78). Some heterogeneity between the ORs was present, but it was not obviously related to patient characteristics or to patient subgroups (e.g. chronic occlusion).

Two trials were neutral between stent and PTCA. They were WIN,[51,109] which appeared to have unusually high event rates and consistently different results, and TOSCA,[103,104] one of the chronic occlusion trials. The latter used a sensitive definition of MI (≥ 5 times the normal creatinine kinase [CK-MB] elevation) that might in part account for this result if stenting in itself produced CK-MB elevation. This result can also be seen in the L'Abbe plot in *Figure 8*. The event rates in the SICCO[98–100] and SPACTO[105] trials were high, consistent with the relatively longstanding and confirmed disease in patients in these trials. In the case of SPACTO,[105] this was compounded by the exclusion of patients with no angiographic follow-up (21%) from the reporting of results. BENESTENT II[27] and EPISTENT[41,97] had particularly low event rates.

Impact of crossovers on event rate

The possibility that the event rate was influenced by the proportion of PTCA patients who crossed over to stent is explored in *Figure 9* which plots crossover rates against the OR for the event rate. There is no evidence of a clear relationship between effect size and crossover, which is surprising.

Impact of method of follow-up on event rate

The BENESTENT II trial[27] provides some important information on the impact of method of follow-up on event rates. To quote the investigators, "we wanted to document the natural

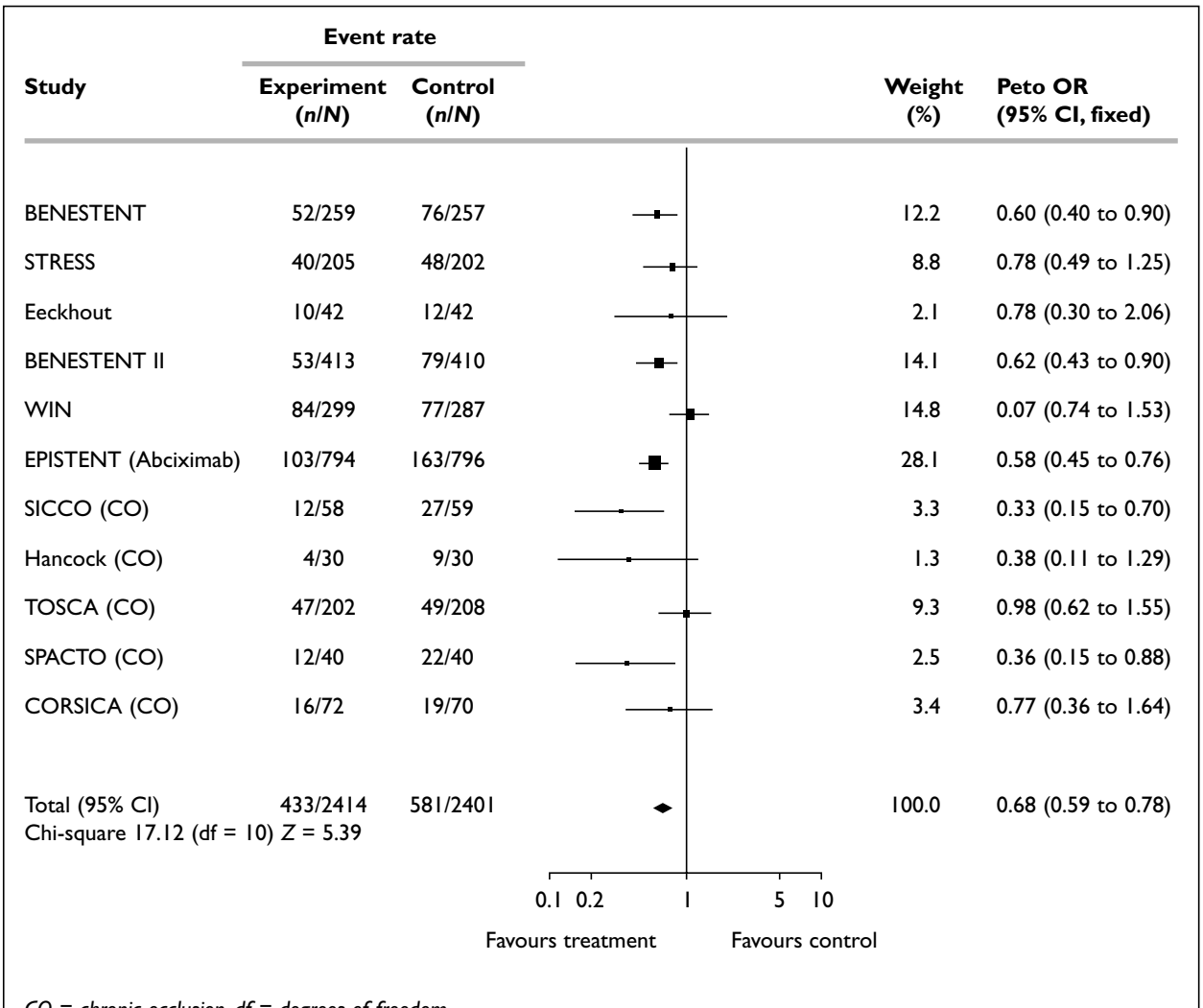


FIGURE 7 *Event rates at 4 to 11 months: stent compared with PTCA in IHD*

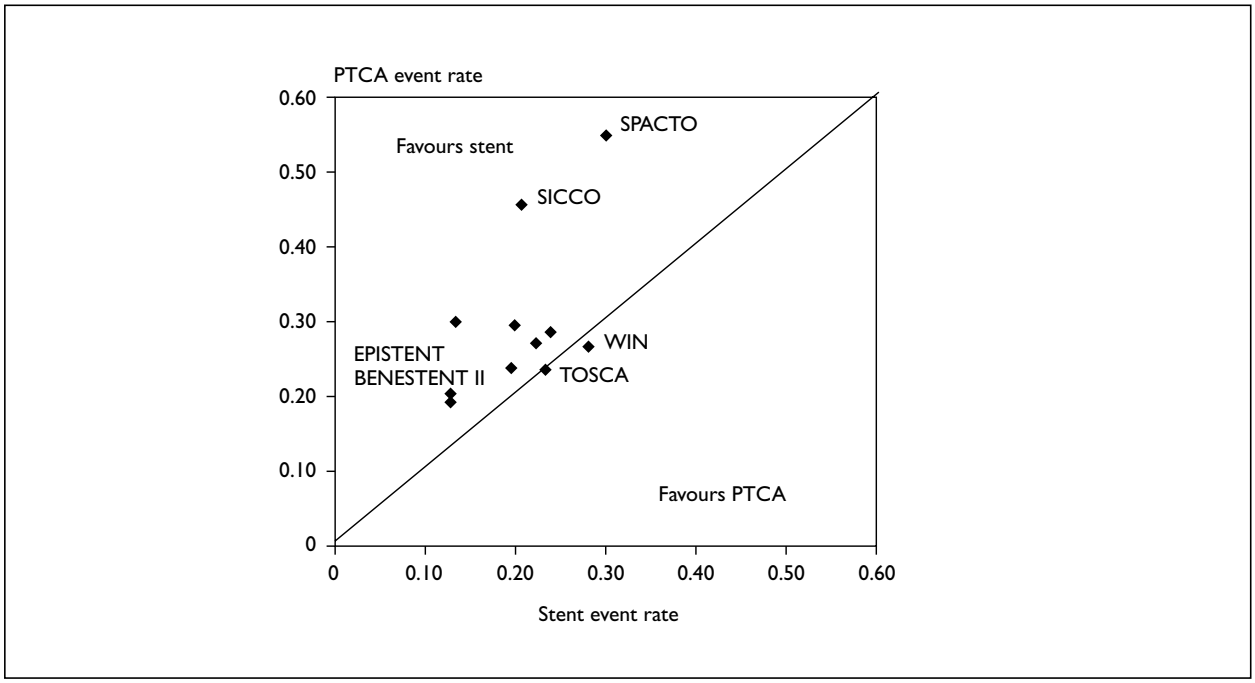


FIGURE 8 *L'Abbe plot: event rates at 4 and 11 months – stent versus PTCA*

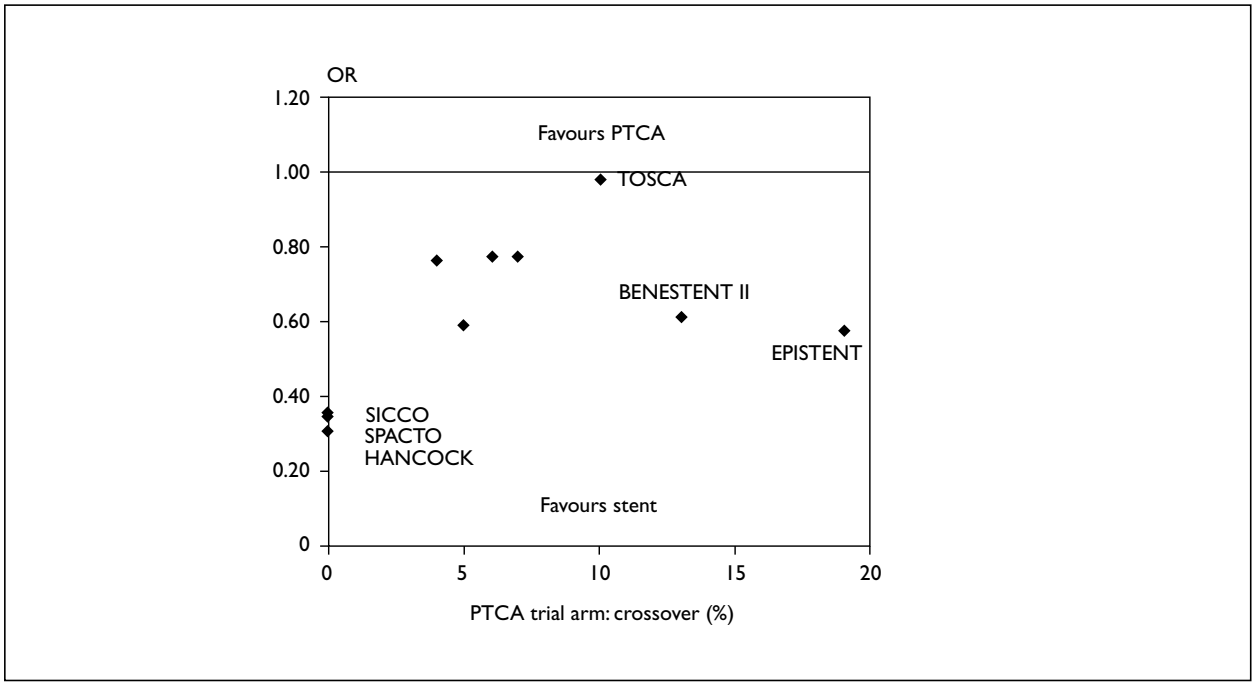


FIGURE 9 *ORs for event rates at 4–11 months – stent versus PTCA by stent crossover rate in PTCA*

TABLE 5 *Impact of method of follow-up on BENESTENT II EFS (Kaplan–Meier method) at 12 months*

	EFS (%)		
Patient group	**Stent**	**PTCA**	***p* value (log-rank test)**
All patients	84.3	77.6	0.01
Patients with angiographic follow-up	79.3	76.6	0.39
Patients with clinical follow-up alone	89.3	78.6	0.003

course of the disease and the spontaneous behaviour of the interventional cardiologists, taking into account their current psychological diagnostic and therapeutical bias". This was achieved by a sub-randomisation to clinical follow-up alone or to clinical and angiographic follow-up. The difference between the stent and PTCA arms in event free survival (EFS) was almost entirely attributable to the differences found in the group randomised to clinical follow-up alone (*Table 5*). The reason for the difference is unclear. Apart from the BENESTENT II[27] sub-randomisation, EPISTENT[41,97] was the only trial without angiographic follow-up.

Event rate summary

In summary, analysis on an intention-to-treat basis shows that stenting is associated with a reduction in clinical events in the medium term compared with PTCA. Event rates are lower overall where there is no angiographic follow-up, as a result of reduced intervention rates, but in these circumstances the relative difference in event rates is greater and favours stent. This difference could result from clinician behaviour, as well as from real need to intervene.

The separate components of the clinical event rates are considered below.

Death rate

Death rates at between 4 and 11 months for PTCA compared with stent are shown in *Figure 10*.

Death is a relatively rare outcome at this period of follow-up and as indicated by the CIs in

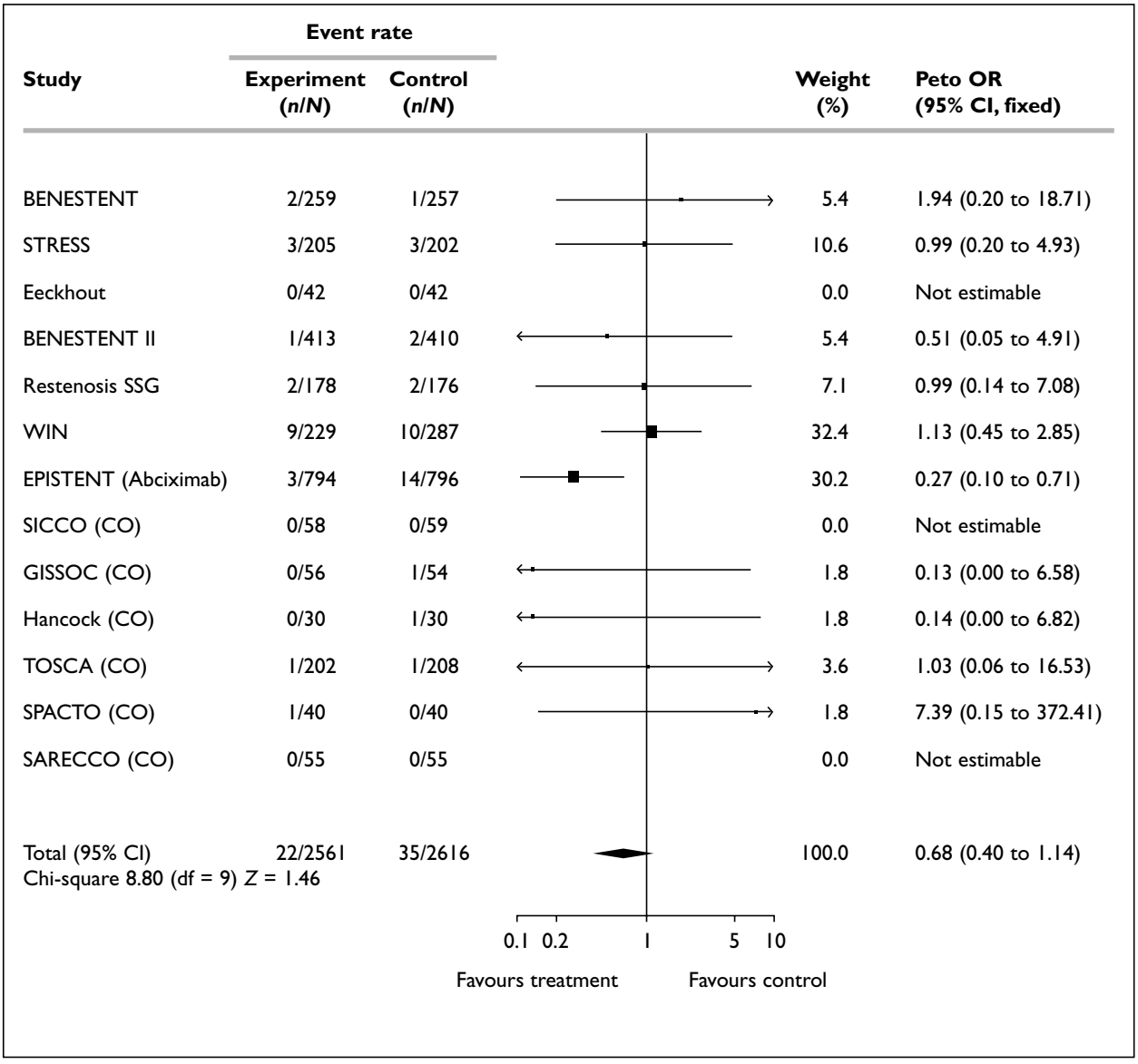


FIGURE 10 *Death rates at 4 to 11 months: stent compared with PTCA in IHD*

Figure 10, the trials are not powerful enough collectively to provide any evidence on this outcome. The high event rate in WIN[51,109] results in narrower CIs, but WIN event rates are not typical, and perhaps result from some unidentified clinical heterogeneity in a trial with limited reporting. EPISTENT,[41,97] the largest trial, shows a difference in favour of stent with abciximab in comparison to PTCA with abciximab. This finding may not be generalisable to stent and/or PTCA without abciximab. Few patients in the other trials had abciximab. The trials other than WIN[51,109] and EPISTENT,[41,97] individually or collectively, provide no evidence on the impact of stents on mortality.

MI rate

Rates of MI at between 4 and 11 months for PTCA compared with stent are shown in *Figure 11.* Where Q wave and non-Q wave MIs were reported separately, data have been combined. There may be some rounding errors from back calculation from percentages.

The trials display no statistical heterogeneity. No trial favours either stent or PTCA. As with mortality, low underlying event rates reduce the power of the trials to provide definitive information. The TOSCA[103,104] trial's definition of MI was CK-MB elevation more than five times the norm. This sensitive definition may include false positive diagnoses of MI and is inconsistent with the definitions used in the other trials. Again, the high event rate in WIN[51,109] is not typical of the other trials. WIN,[51,109] BENESTENT[80–84] and BENESTENT II[27] have relatively precise CIs and show no difference between stent and PTCA. In summary, the trials provide no evidence of an effect on MI.

Those trials that report Q-wave MI separately (*Figure 12*) have homogeneous results and show

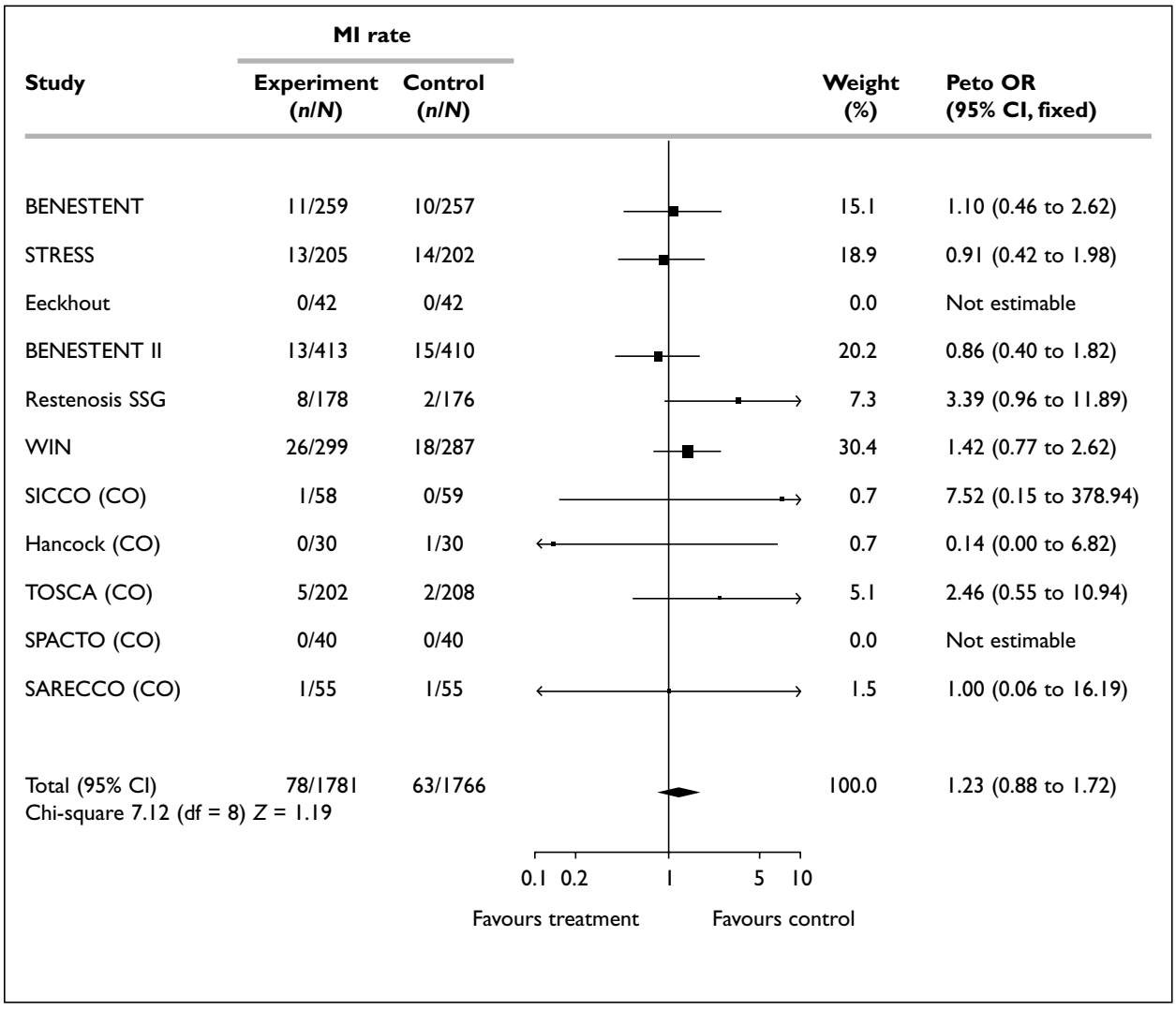


FIGURE 11 *MI rates at 4 to 11 months: stent compared with PTCA in IHD*

no difference between stent and PTCA on this more precise definition of MI.

Results for non-Q wave MI also showed no difference between stent and PTCA (*Figure 13*).

Angina rate

Only five trials reported on the angina status of the patients at 4 to 11 months, despite the important impact of this outcome on patient quality of life. Where possible, angina-free survival

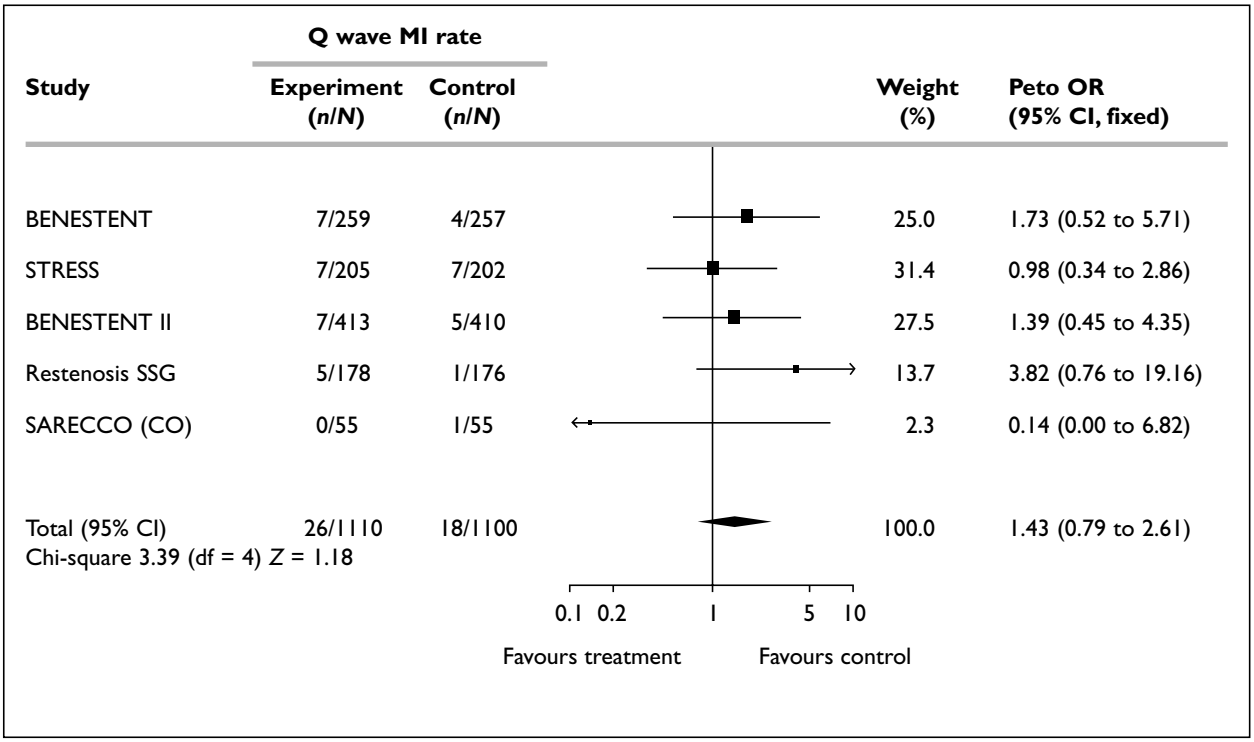


FIGURE 12 *Q wave MI rates at 4 to 11 months: stent compared with PTCA in IHD*

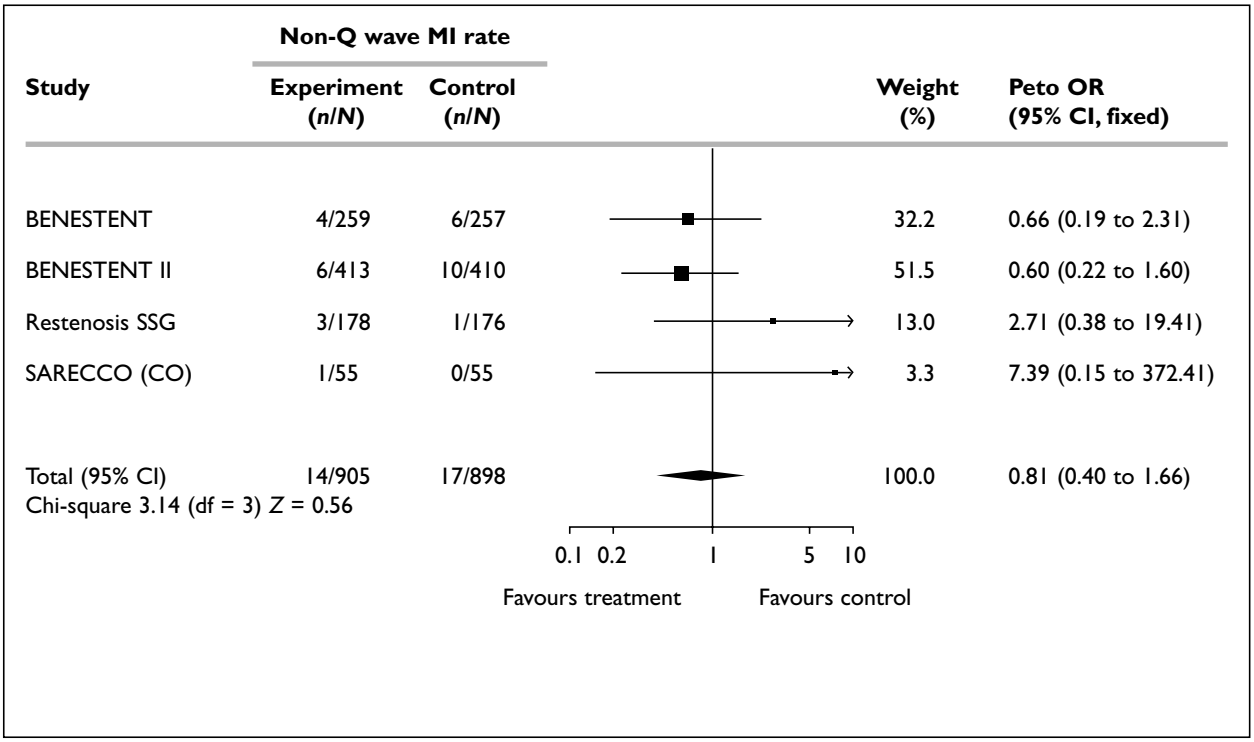


FIGURE 13 *Non-Q wave MI rates at 4 to 11 months: stent compared with PTCA in IHD*

rates have been recalculated as angina rates. The results are heterogeneous, with BENESTENT[80–84] tending to favour PTCA and the others tending to favour stent. There are statistically significant results from the BENESTENT II trial,[27] a recent and relatively good quality trial, and the SICCO trial[98–100] (*Figure 14*). There are no obvious clinical explanations for these differences. The BENESTENT II trial[27] yields a number needed to treat of 13 to achieve one extra angina-free patient at 6 months. Angina is an important outcome that occurs frequently but has been poorly evaluated. Further trials will be needed if the impact of stents on angina is to be addressed adequately.

TVR rate

TVR comprises repeat PCIs and CABGs that address restenosis in the vessel originally treated. Some trials specify TLR. TVR and TLR have been combined here. All but one of the trials favours stent (*Figure 15*). WIN[51,109] once again introduces some heterogeneity and is neutral between stent and PTCA. As a whole the results favour stent.

CABG rate

The outcome CABG includes any CABG, not just CABG procedures that address problems with the target vessel. Low event rates again mean that trial results are very imprecise (*Figure 16*). They are however consistent and homogeneous with relatively precise CIs, and collectively favour neither stent nor PTCA.

Repeat PTCA rate

The outcome PTCA includes any PTCA, not just PTCA procedures that address problems with the target vessel, except for a few of the trials in which only repeat PTCA of the target vessel was reported. Repeat PTCA was by far the more common form of repeat intervention, and trial results are accordingly more precise (*Figure 17*). There is some heterogeneity in the results: WIN[51,109] was neutral between stent and PTCA, whereas the other trials favoured stent, so that on balance stent reduces the repeat PTCA rate relative to initial PTCA (summary OR, 0.57; 95% CI, 0.48 to 0.69). Repeat PTCAs to the target vessel make the largest contribution to the event rate.

Medium-term outcomes summary

There is a lower event rate with stent than with PTCA at periods of follow-up of between 4 and 11 months. Composite event rates, however, include both deaths and MIs and re-interventions. Death and MIs might be considered the more important outcomes, but as these events are relatively rare in the trials, the trials provide no clear evidence on

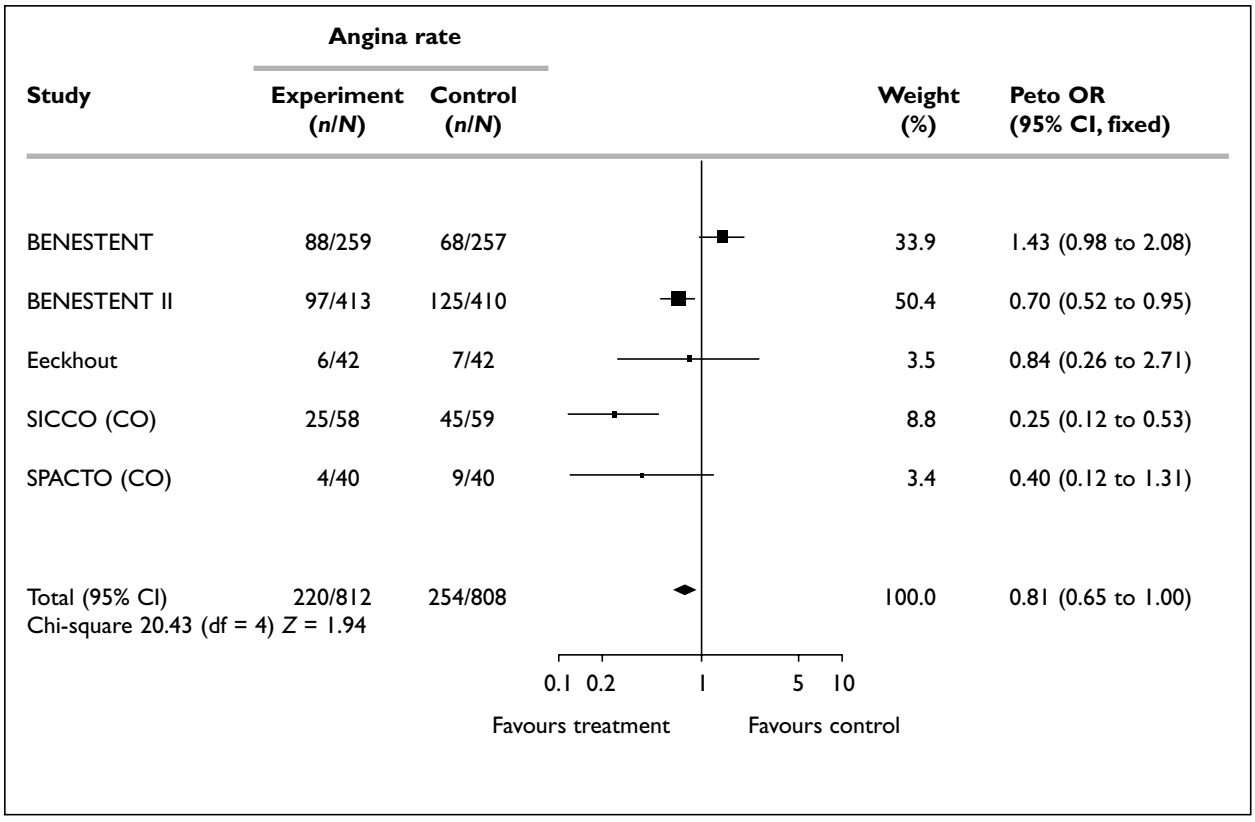


FIGURE 14 *Angina rates at 4 to 11 months: stent compared with PTCA in IHD*

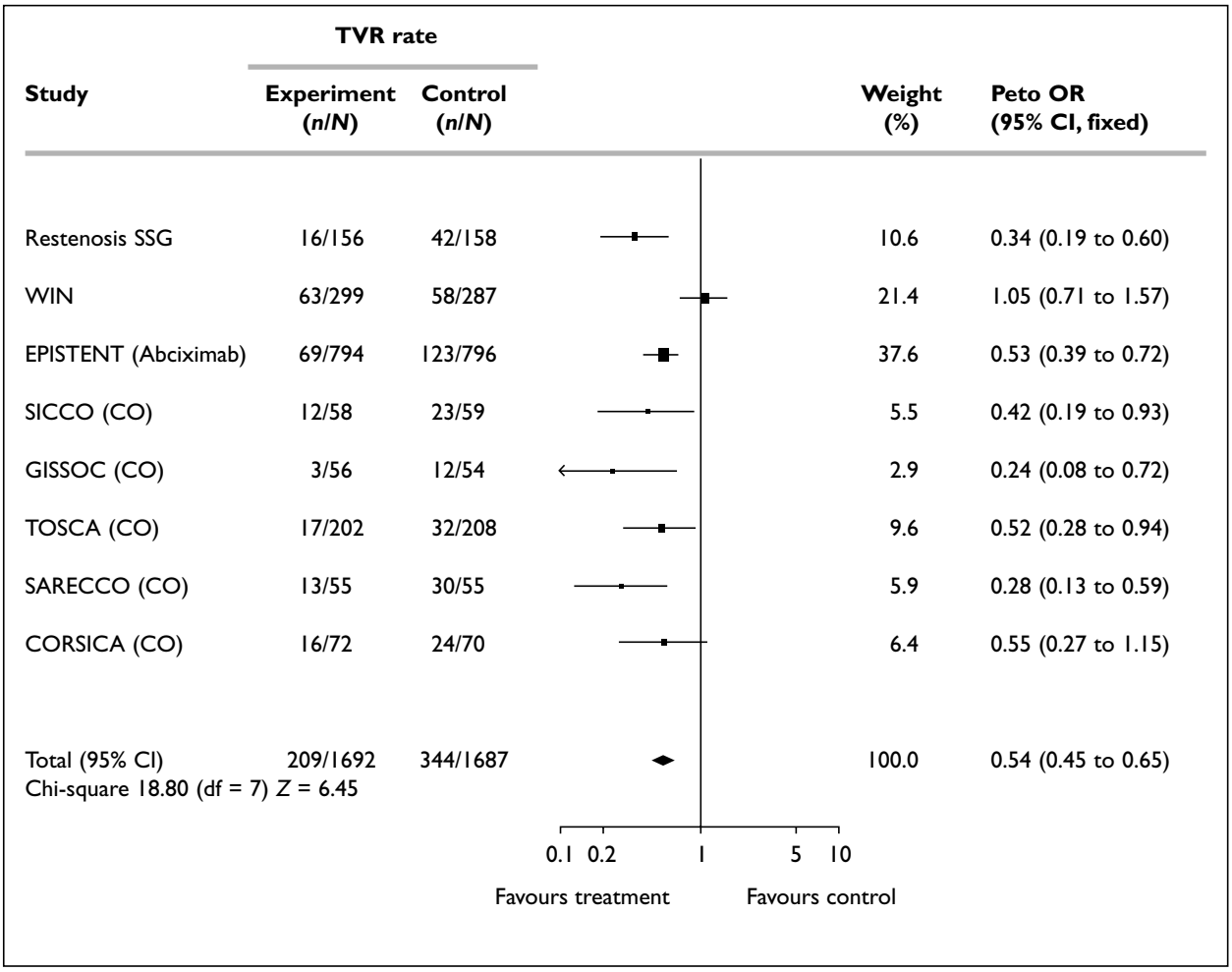


FIGURE 15 *TVR rates at 4 to 11 months: stent compared with PTCA in IHD*

either outcome. Differences in re-intervention rates largely account for the superiority of stents in the trials. This outcome is, however, potentially susceptible to bias, as clinicians might investigate PTCA patients more intensively, leading to increased intervention.

Long-term clinical outcomes

One-year follow-up information was available for the BENESTENT,[84] STRESS,[86] Versaci,[91] BENESTENT II,[27] and WIDEST[111] trials. Follow-up data were available at 2 years for the AS[110] and SARECCO[118] trials, at 3 years (plus or minus 6 months) for the SICCO trial,[99] at 4 years for the START trial[92] and at 5 years for the BENESTENT trial.[81] Follow-up at between 9 and 23 months was available for OCBAS.[107] Longer term outcomes are tabulated in appendix 5 (pages 99 and 100).

Event rate

There was some heterogeneity in the ORs for event rates (*Figure 18*), but ORs generally favoured stent, with Versaci,[91] START,[92] BENESTENT II[27] and SICCO[99] trials having statistically significant ORs in favour of stent. BENESTENT favoured stent at 1 year,[84] but there was no significant difference in the event rate for PTCA and for stent at the 5 years follow-up.[81] The 4 years follow-up of the START trial,[92] however, favoured stent.

Death rate

Even with longer follow-up, deaths occur too rarely for the trials individually to produce evidence on this outcome. The summary OR of 1.13 (95% CI, 0.67 to 1.97) shows no difference between stent and PTCA (*Figure 19*) and provides more convincing evidence than the medium-term results of stents having no impact on death rates.

MI rate

There are no differences in MI rates between stent and PTCA in any of the longer term follow-ups as shown in *Figure 20*. The summary OR was 0.95 (95% CI, 0.65 to 1.37).

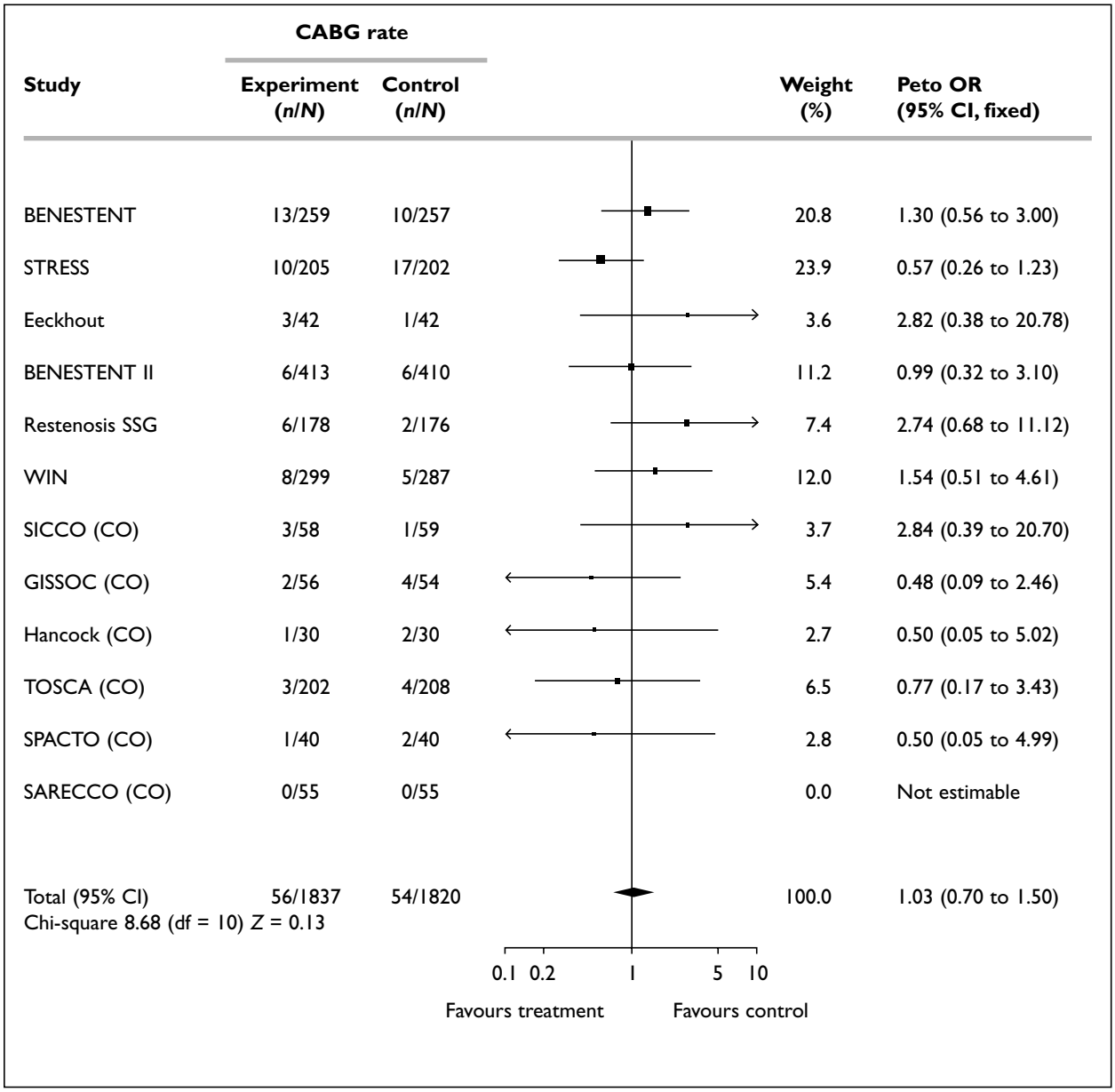


FIGURE 16 *CABG rates at 4 to 11 months: stent compared with PTCA in IHD*

In the case of BENESTENT, the non-Q wave MI rates are less at 5 years follow-up[81] than at 1 year follow-up.[84] This might result from a hierarchical definition of event rates, where only the most serious event is counted. Q wave and non-Q wave MIs are reported separately in appendix 5 (page 99).

Angina rate

Three of the four trials that reported this outcome, BENESTENT at 1 year,[84] STRESS[86] and SICCO,[99] found no difference between stent and PTCA at 1 year, 1 year and 3 years (± 6 months) respectively (*Figure 21*). The Versaci trial[91] reported a reduced OR in favour of stent at 1 year (OR, 0.36; 95% CI, 0.14 to 0.91). The trials display most heterogeneity on this outcome.

TVR rate

There was some heterogeneity in the results, but all except one trial (OCBAS[107]) favoured stent (*Figure 22*).

CABG rate

Figure 23 illustrates that there was no heterogeneity and no evidence for a difference between stent and PTCA for this outcome.

Repeat PTCA rate

There was some heterogeneity for this outcome with some trials (BENESTENT,[84] Versaci,[91]

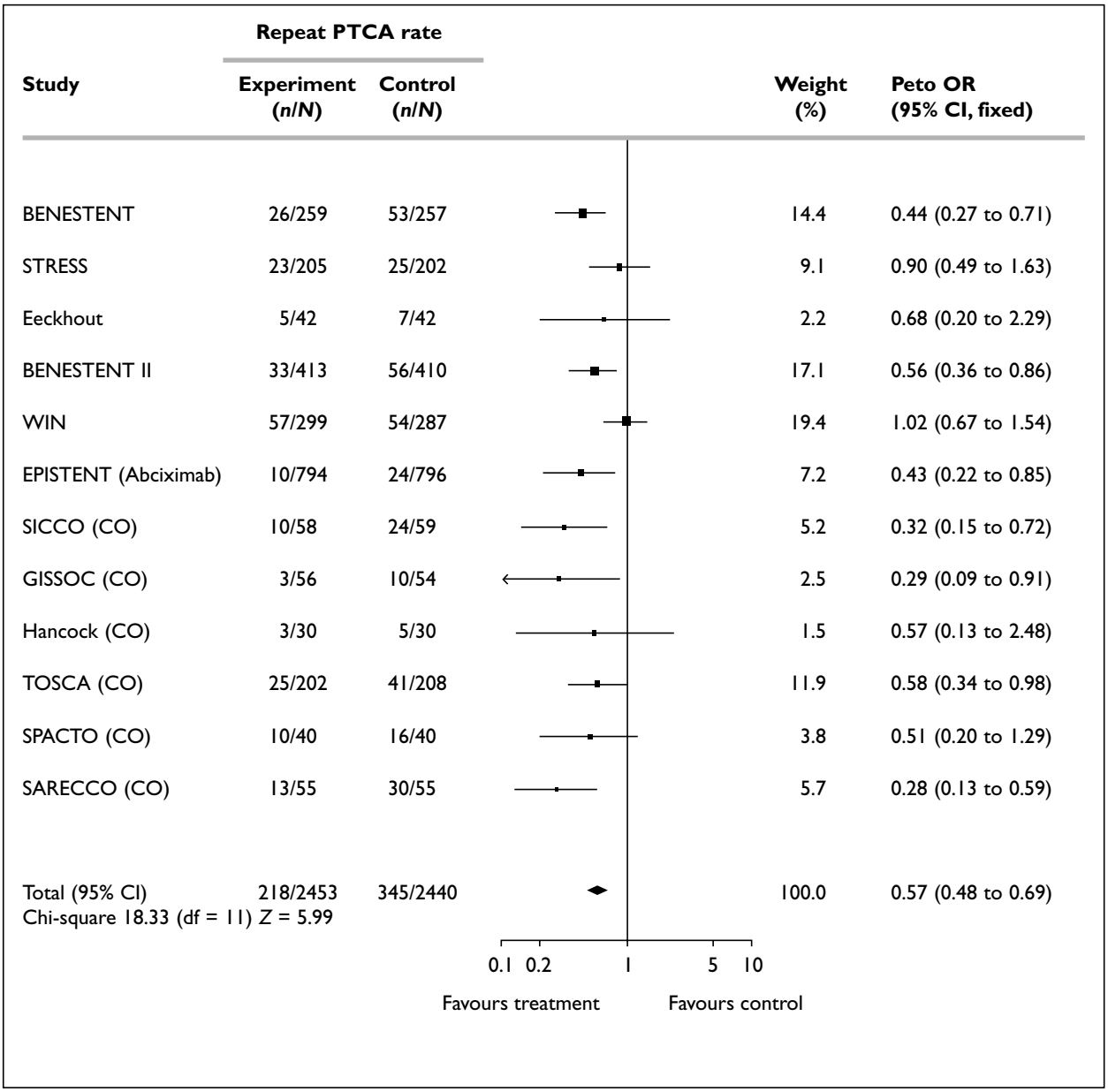


FIGURE 17 *Repeat PTCA rates at 4 to 11 months: stent compared with PTCA in IHD*

BENESTENT II[27] and SICCO[99]) favouring stent, whereas STRESS[86] and OCBAS[107] favoured neither stent nor PTCA (*Figure 24*).

Health-related quality of life

Generic and disease-specific health-related quality of life were measured at between 6 and 18 months in the STRESS trial[87] using the Short Form 36 (SF-36), a modification of the Rose Angina Questionnaire, with functional status assessed by modified versions of the Duke Activity Status Index and the Canadian Cardiovascular Society Classification. There were 160 (80%) responders out of 199 consecutive patients. The stent group had significantly better scores on the SF-36 bodily pain index. There were, however, no other differences in generic or disease-specific health-related quality of life, although 88% of the stent group reported that bodily pain did not interfere with normal work compared with 73% of the PTCA group ($p < 0.05$).

Long-term outcomes summary

Relatively few trials have yet reported long-term outcomes. Stenting was generally associated with lower event rates at 1 year or longer, although this was not the case in the only 5 year follow-up. No conclusions could be drawn on death rates, and what evidence there was indicated no difference between stents and PTCA in MI rates. Evidence

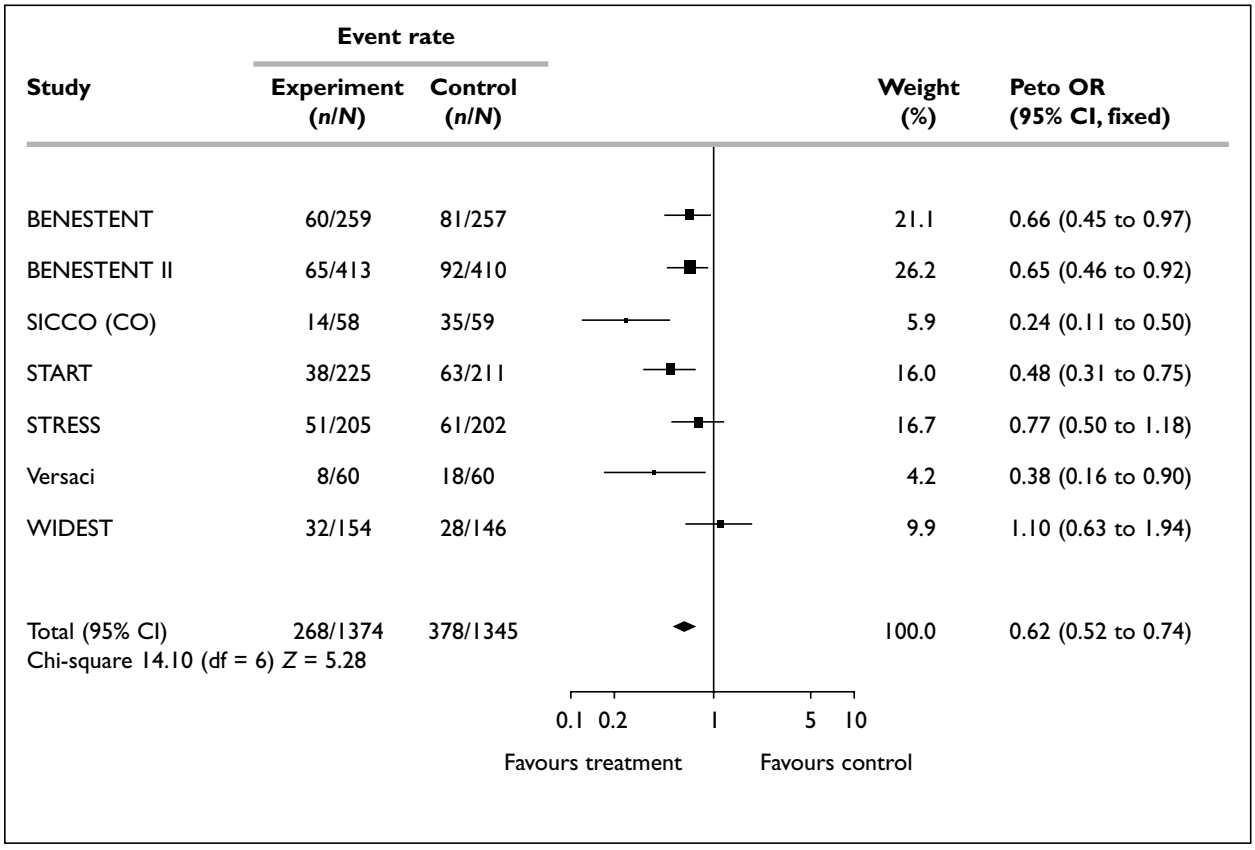


FIGURE 18 *Event rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

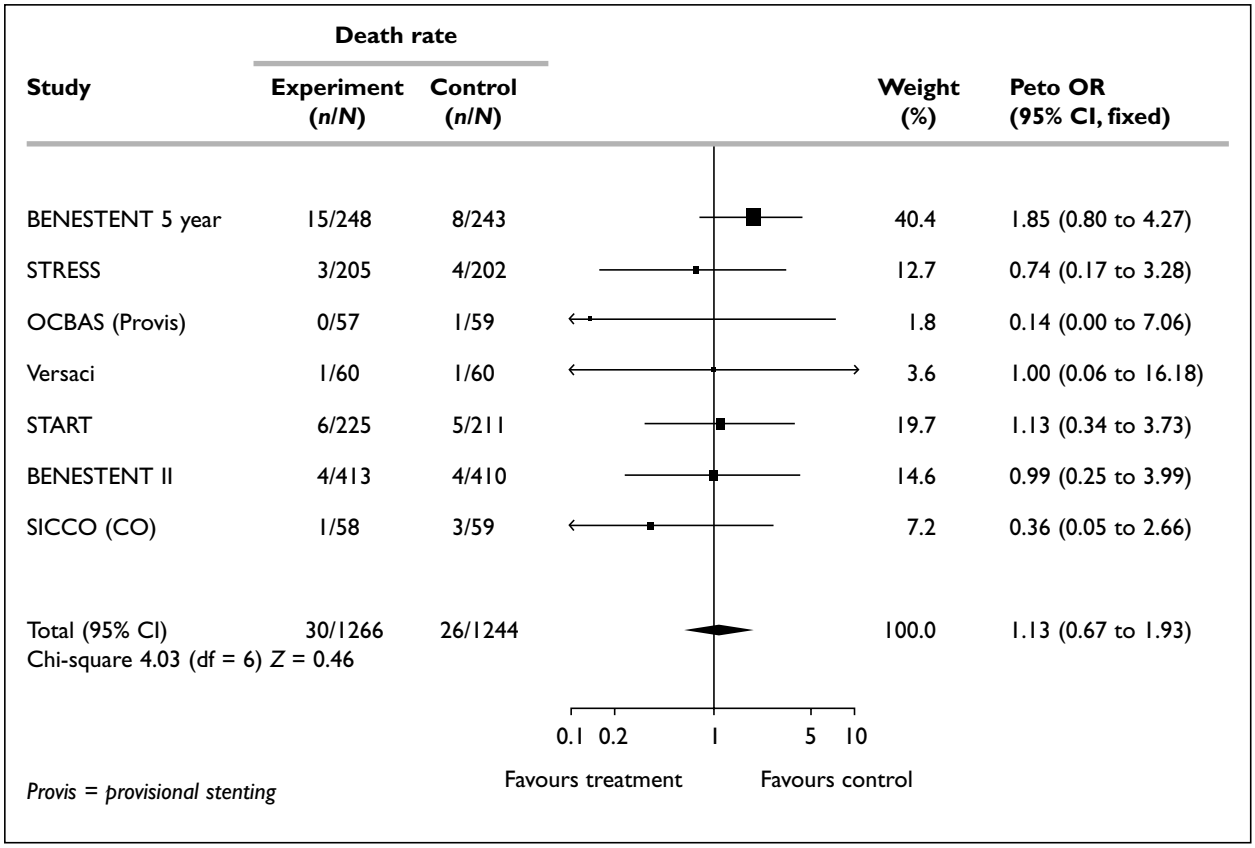


FIGURE 19 *Death rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

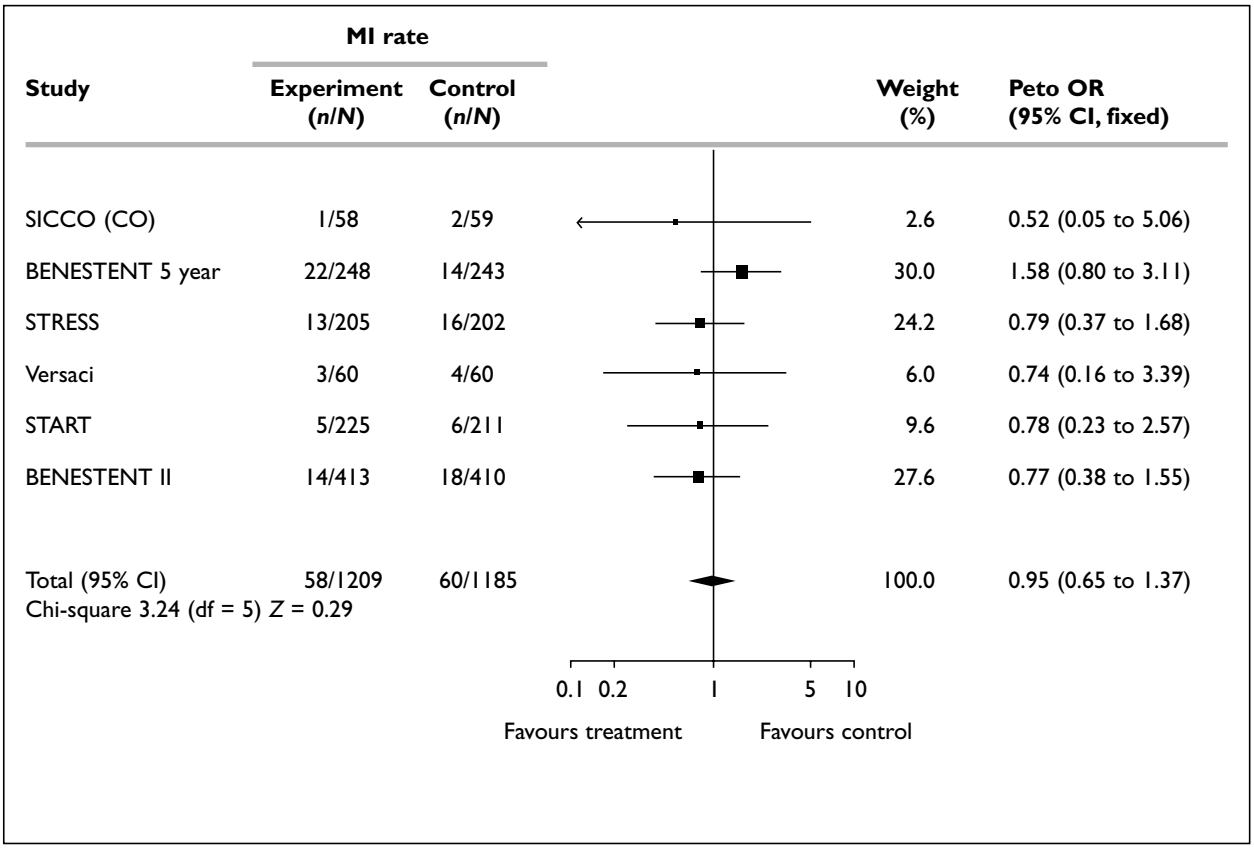


FIGURE 20 *MI rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

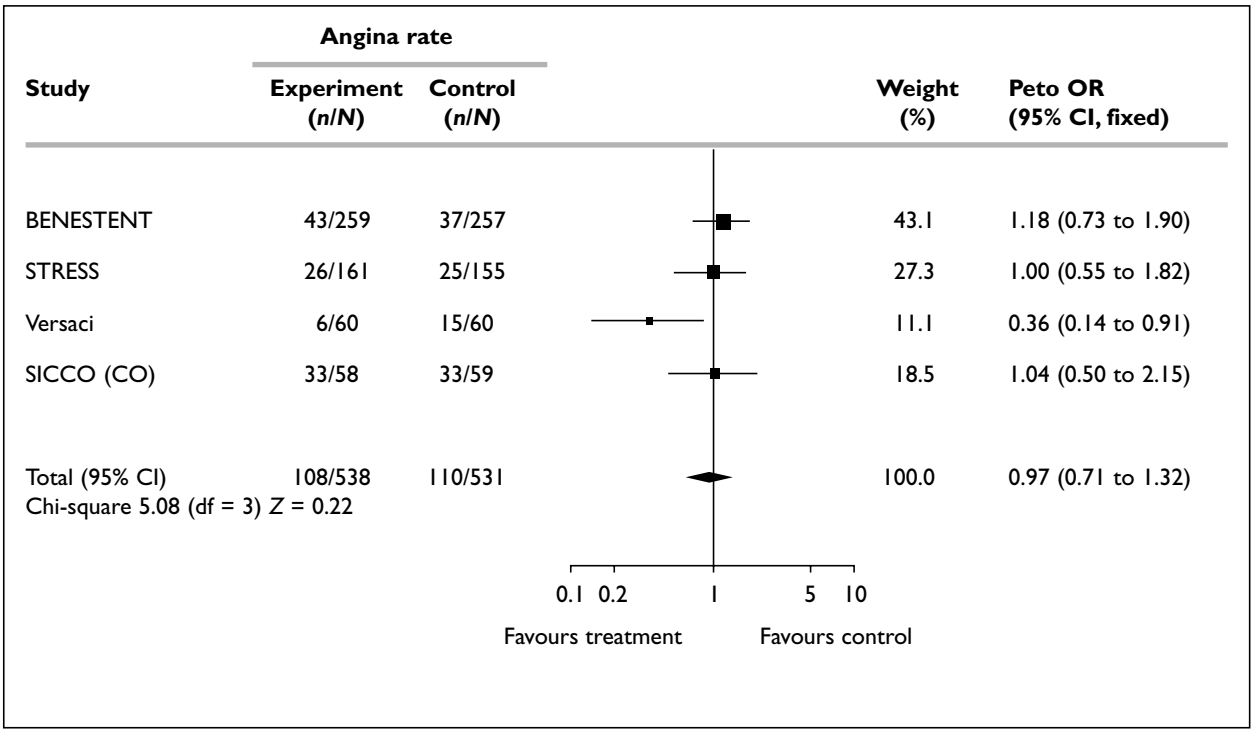


FIGURE 21 *Angina rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

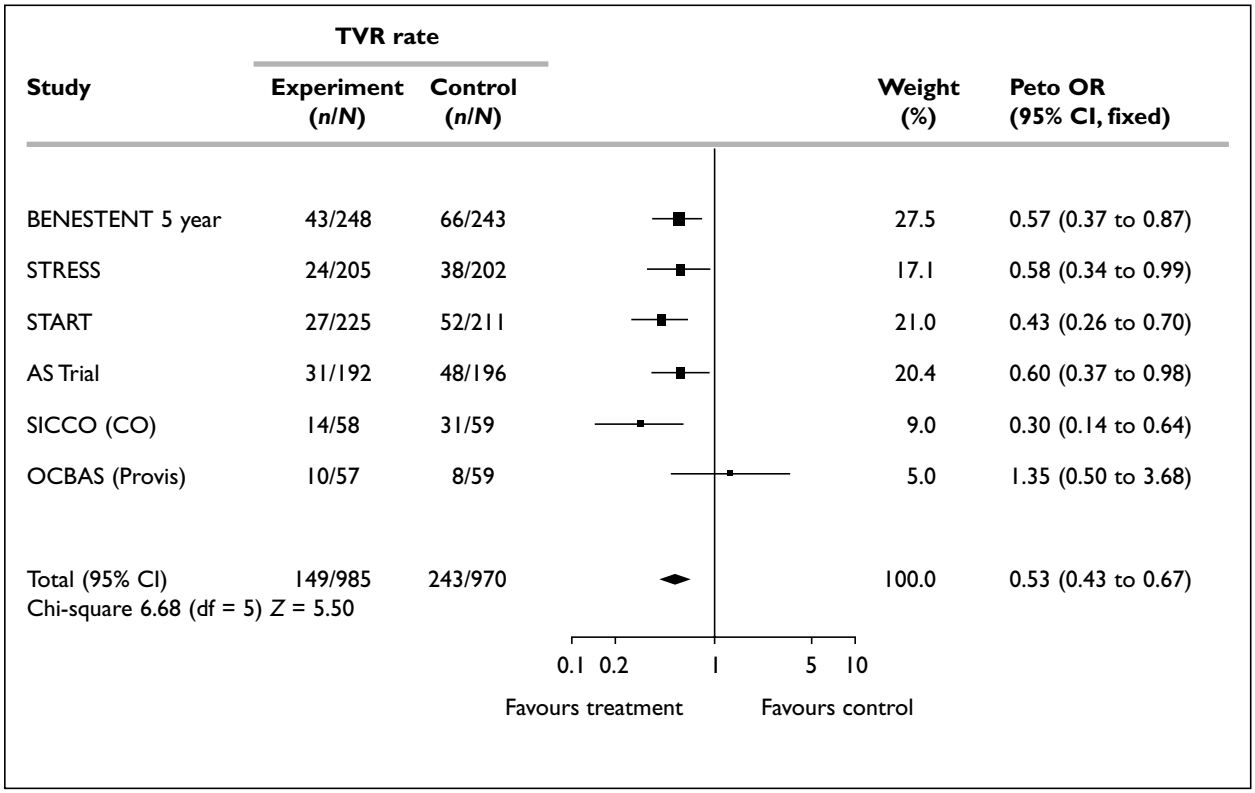


FIGURE 22 *TVR rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

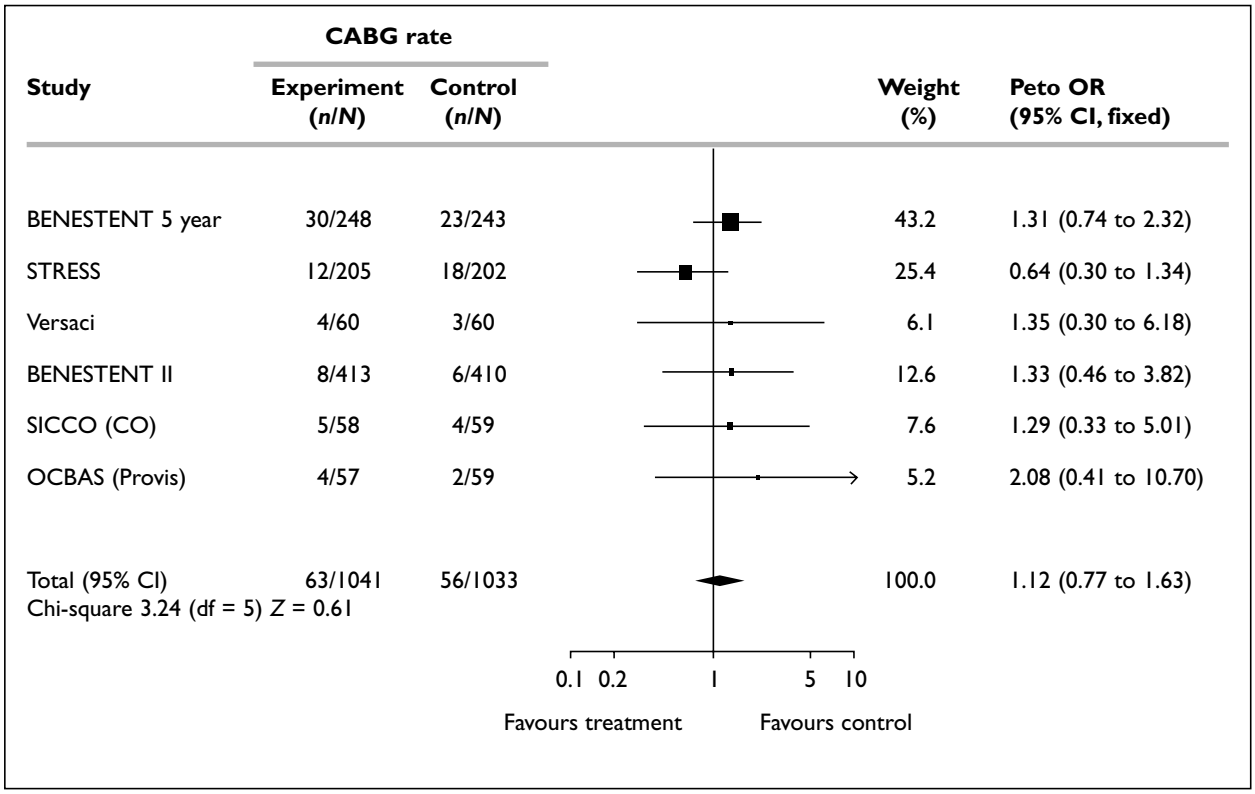


FIGURE 23 *CABG rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

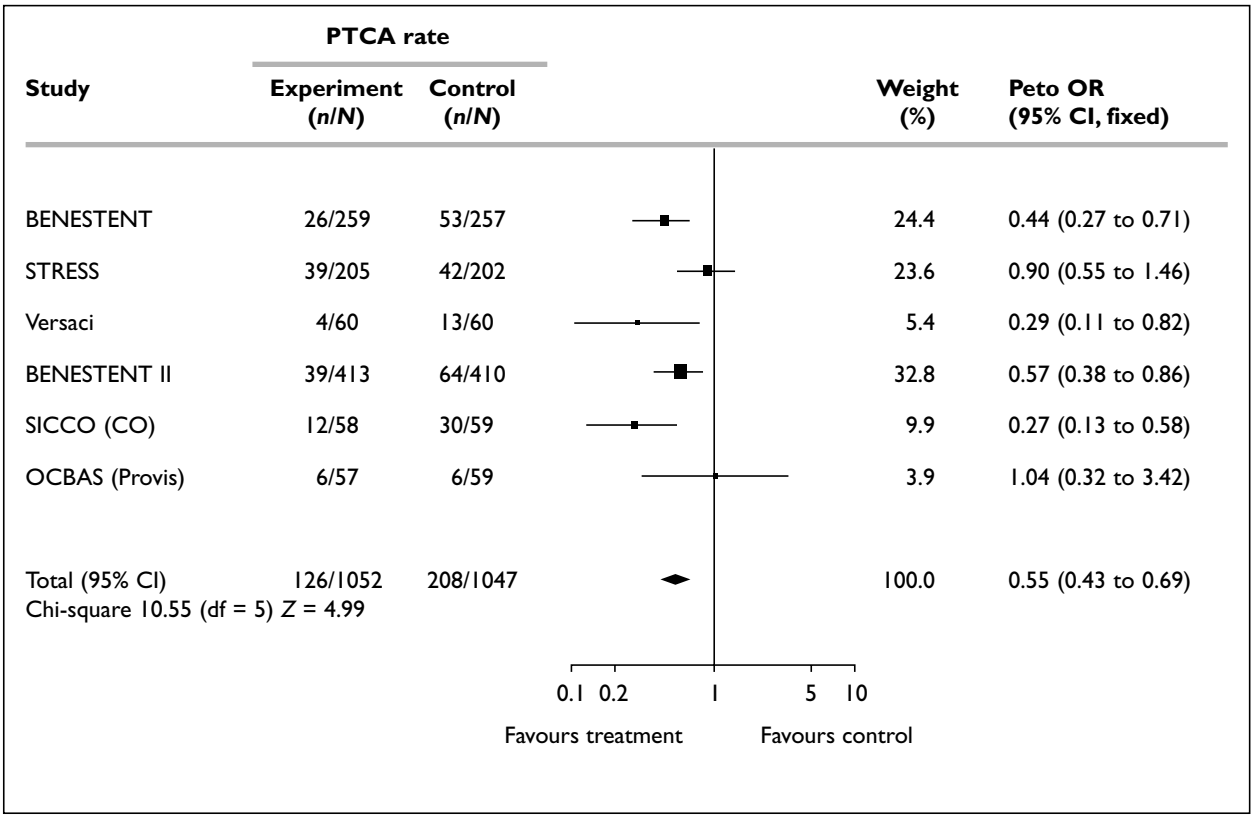


FIGURE 24 *PTCA rates, variable follow-up (≥ 1 year): stent compared with PTCA in IHD*

on angina was conflicting, although no trials favoured PTCA. Stent was associated with a relative reduction in revascularisation rates.

Summary

The trials broadly favoured stents over PTCA in trials of planned stenting. There are, however, some caveats.

- The nature of intervention meant that neither clinicians nor patients could be blinded to treatment, and so the trials may be biased in favour of stent to some degree.
- Most of the trials allowed some crossover to stent from PTCA – in some trials to the extent that effectively different stenting policies (immediate or provisional) were under review, not a straight choice between stent and PTCA.
- The trials individually and collectively did not have the statistical power to provide precise outcomes on mortality and MI, which are relatively rare but important outcomes.
- Event rates favourable to stents reflected reduced intervention rates, not reduced mortality or coronary events.
- Although angina is an important outcome, it was not often reported, results were inconsistent, and little can be said about the impact of stents on the recurrence of angina or its severity.

Effectiveness of elective stenting compared with CABG in subacute IHD

Trial reporting

Each of the three trials[120–122] is reported as an abstract only. Letters were sent to all three trialists but no replies were received.

Patients

The largest trial (ERACI II[120]) included only people with multi-vessel disease. The other two trials included LAD lesions only (see appendix 5, page 101).

Interventions

One of the trials (Spyrantis[122]) compared a new technique of minimally invasive CABG with stents. The other two trials used standard CABG (see appendix 5, page 101).

Trial quality

Because only abstracts were available, details of trial design were not available. Each of the trials had a Jadad score of 1, possibly as a consequence of lack of full publication (see appendix 5,

page 103). None of the trials reported the proportion of eligible patients randomised (see appendix 5, page 102). Baseline characteristics were reported to be similar in both arms of each of the three trials (see appendix 5, page 102). One trial, ERACI II,[120] reported statistically significant differences in favour of stent for 30-day event rate, deaths and MI. The SIMA[121] trial, however, found no such differences in in-hospital outcome (see appendix 5 pages 104 and 105).

The one trial (SIMA[121]) that reported complications found a significant difference in favour of stents for an outcome that included major bleeding and arrhythmias.

Angiographic outcomes

Angiographic follow-up is not fully reported in this group of trials. The only trial[122] to report restenosis rates at follow-up shows a larger restenosis rate for the stent group compared with the CABG group (see appendix 5, page 106).

Medium term (4 to 11 months) clinical outcomes

Very few results are available for these three trials. ERACI II[120] shows a significantly higher rate of TVR in the stent group and Spyrantis[122] shows a significantly higher rate of repeat PTCA in the stent group at 6 months follow-up (see appendix 5, page 107). No numbers for outcomes death, MI or angina rate were given in the reports of any of the trials.

No results beyond 6 months were available.

Summary

Full evaluation of stent against CABG in CAD must await completion of trials in progress and full publication.

Results so far indicate that stenting is associated with higher re-intervention rates at 6 months than CABG.

Effectiveness of stents compared with PTCA in acute MI

Trial reporting

Of the seven trials in this category, three[119,123,124] have been fully reported in peer-reviewed journals. Letters were sent to the investigator for the other four trials,[125–128] which resulted in three replies, including page proofs (PASTA[125]), a manuscript (STENTIM II[128]) and a further abstract (PSAAMI[127]). The largest trial by far in this group is the PAMI-Stent trial.[126] Although this trial appears to have finished recruiting and follow-up, it has not been fully published at the time of writing. Twenty-five abstracts were available for this trial, and those that appeared to be based on completed recruitment were used to abstract data. It was impossible to identify the number of patients in each arm of the PSAAMI trial at follow-up, and data from this trial could not be used in meta-analyses.

Patients

All of the trials include patients within 12–24 hours of MI symptom onset in whom the culprit lesion is in a 'stentable' artery. Cardiogenic shock is included in some of the trials (GRAMI,[119] FRESCO,[123] PSAAMI[127]) and excluded in others (PAMI-Stent.[126] STENTIM II[128]) (see appendix 5, pages 108–109).

Interventions and comparators

Stent

The type of stent used varied (Palmaz-Schatz, Gianturco-Roubin, Wiktor). One trial used a heparin-coated stent (PAMI-Stent[126]) and one used a silicon carbide-coated Tantal stent (PSAAMI[127]) (see appendix 5, pages 108–109).

Antithrombotic regimens

Most of the trials used ticlopidine rather than anticoagulation, but the ESCOBAR[124] trial changed from warfarin to ticlopidine after 20% patients had been treated. In the PSAAMI trial,[127] abciximab was used in approximately 50% patients (see appendix 5, pages 108–109).

Comparators

PTCA was the comparison in all trials, with stenting conditional upon initial PTCA in the PTCA arm of the STENTIM II trial[128] (appendix 5, pages 108–109).

Crossovers

Rates of crossover in the stent arms of the trials ranged from 0% to 3%, whereas in the PTCA arms they ranged from 0% to 36%. Thus in the PTCA arms of the trials, the chances of patients receiving the intervention rather than the control treatment varied (see appendix 5, page 110).

Trial quality

The Jadad scores[53] ranged from 1 to 3 (see appendix 5, page 111). It is possible that the low scores of PSAAMI[127] and PAMI-Stent[126] reflect reporting in abstract form rather than poor execution in terms of concealment of allocation and follow-up, but without full publication, quality cannot be assumed to be high. As patients and

clinicians cannot be blinded to treatment in these trials, it is possible that some degree of bias has entered into trial execution and reporting.

Short-term clinical outcomes

Two out of the three trials that reported short-term event rates (GRAMI[119] and PASTA[125]) found significant differences in favour of stent (see appendix 5, page 113). Event rate definitions are given in appendix 5 (page 94). None of the trials reported significant differences in deaths or MI, and the differences that did exist arose from differences in re-intervention rates (see appendix 5, page 113). The PAMI-Stent[126] and FRESCO[123] trials found significant differences in TVR in favour of stents.

Definitions of major bleed vary between the trials. Where descriptions of bleeding complications were given, major bleed was taken to include any bleeding that had resource implications (e.g. need for vascular repair or blood transfusion). There were no significant differences in bleeding complications reported in any of the trials (see appendix 5, page 112). This may reflect the use of ticlopidine, rather than intensive anticoagulant therapy, in these trials.

Angiographic outcomes

Angiographic results from three trials (FRESCO,[123] PASTA,[125] STENTIM II[128]) all show a statistically significant improvement for the stent group compared with the PTCA group post-procedure and at follow-up (6 months) (see appendix 5, page 114).

Clinical outcomes at 6 to 12 months

Two trials, FRESCO[123] and ESCOBAR,[124] reported at 6 months only. One trial, GRAMI,[119] reported at 1 year only, whereas PASTA,[125] PAMI-Stent[126] and PSAAMI[127] reported at 6 and 12 months. Results at both 6 months (see appendix 5, pages 115 and 116) and 12 months (see appendix 5, pages 117 and 118) are reported in the tables in appendix 5, but the results at 12 months are used in preference to those at 6 months in the meta-analyses.

Event rate

There were lower event rates in the stent group (summary OR, 0.39; 95% CI, 0.28 to 0.54) with no heterogeneity (see *Figure 25*). This yielded numbers needed to treat ranging from 4 in PASTA[125] to 12 in STENTIM II.[128]

Death rate

In all seven trials, there were no significant differences in death rates between the stent and PTCA groups. Death is a relatively rare outcome at this period of follow-up, and as indicated by the CIs in *Figure 26*, the trials are not powerful enough collectively to provide any evidence on this outcome.

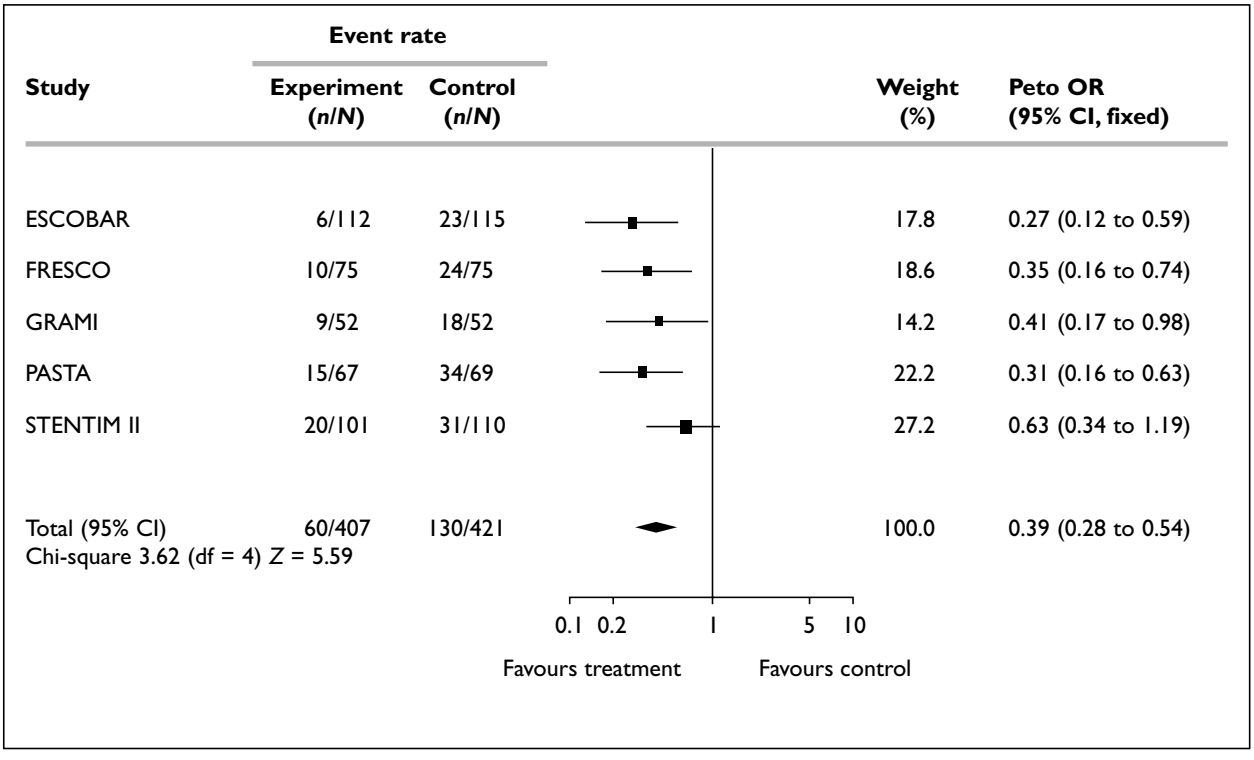


FIGURE 25 *Event rates, 6 to 12 months follow-up: stent compared with PTCA in AMI*

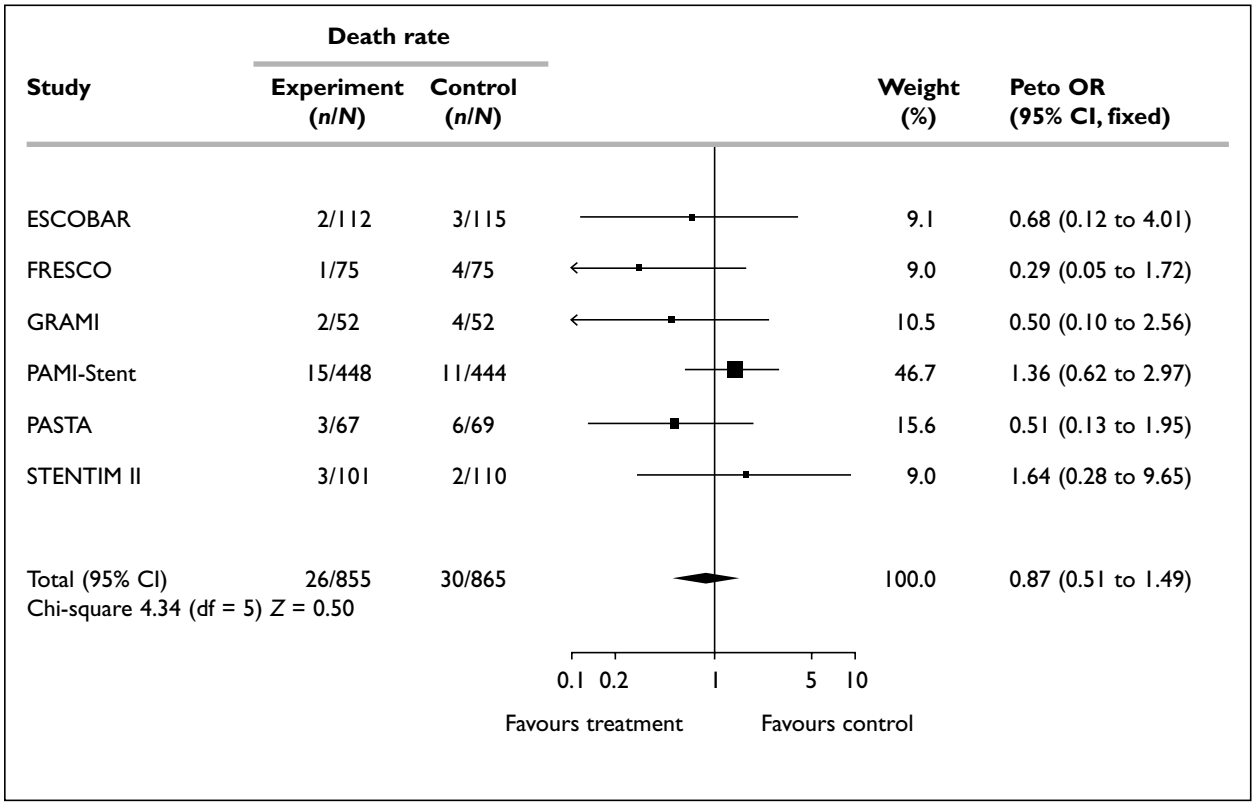


FIGURE 26 *Death rates, 6 to 12 months follow-up: stent compared with PTCA in AMI*

MI rate

As shown in *Figure 27* all trials that measured this outcome suggested benefit. However, only in ESCOBAR[124] was the result statistically significant. When the results of the trials were combined there was reduced MI in the stent group compared with the PTCA group, but it should be noted that the 95% CI for the summary OR still includes 1.0, that the result is based on a very small number of outcomes and that only

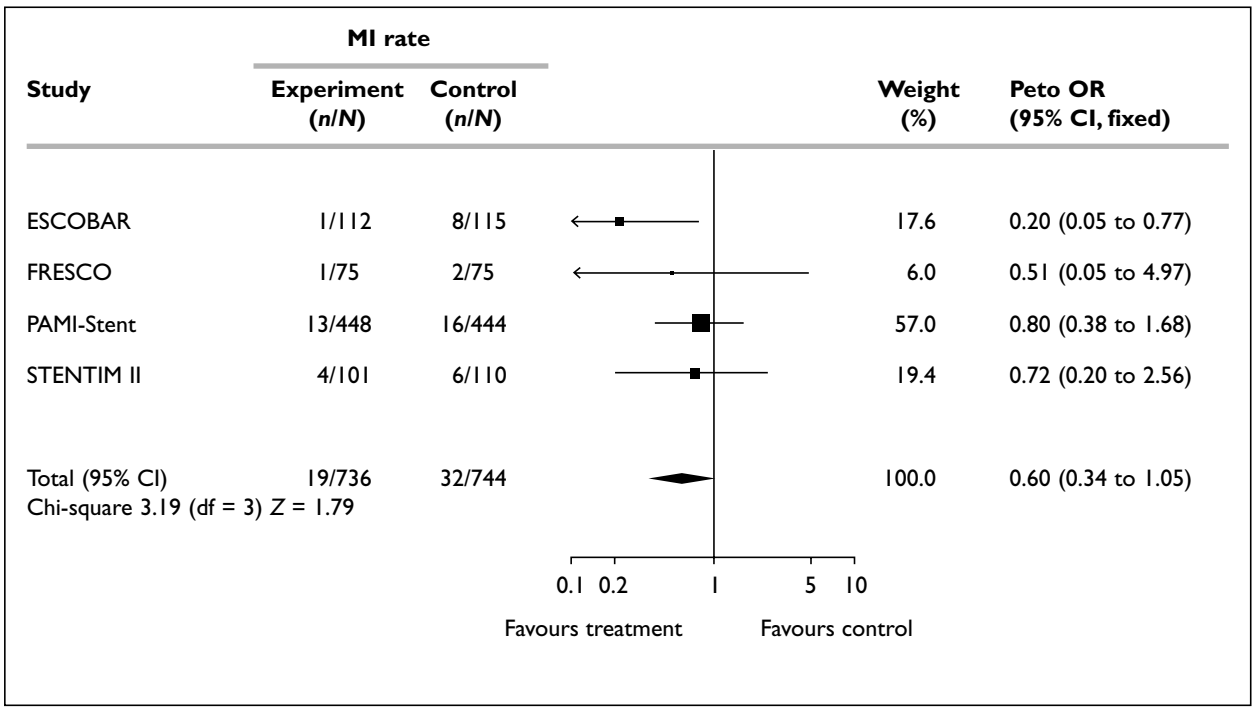


FIGURE 27 *MI rates, 6 to 12 months follow-up: stent compared with PTCA in AMI*

provisional results were available for the largest trial, PAMI-Stent.[126] Q wave and non-Q wave MI were not reported separately.

Angina rate
Only one trial reported angina rates at follow-up (PAMI-Stent[126]). There was a significant difference in angina status at 6 months, with 10.1% of the stent group having angina, in comparison with 15.5% of the PTCA group ($p < 0.05$) (calculated from reporting of diabetic and non-diabetic subgroup results).

TVR rate
When the trials were combined, there was a significant decrease in TVR rates for the stent group compared with the PTCA group (summary OR, 0.41; 95% CI, 0.31 to 0.56), with no heterogeneity in the results (see *Figure 28*).

CABG rate
There were only four CABGs in the two trials that reported this outcome, FRESCO[123] and STENTIM II,[128] and so the results provide no useful information on CABG rate.

Repeat PTCA
When the two trials reporting this outcome were combined, stenting was associated with a reduction in repeat PTCA rates with little heterogeneity (summary OR, 0.44; 95% CI 0.26 to 0.74) (see *Figure 29*).

Summary
Of seven trials, three were published in peer-reviewed publications, for two information was obtained from authors, and for two (including the largest trial) publication was only in abstract form.

The trials consistently favoured stents over PTCA in trials of stenting in acute MI. There are, however, some caveats.

- The nature of intervention meant that neither clinicians nor patients could be blinded to treatment, so that the trials may be biased in favour of stent to some degree.
- Crossover rates from PTCA to stent ranged from 0% to 36%, indicating that different policies were operating with regard to crossover to stent in the PTCA arms of the trials.
- The trials individually and collectively did not have the statistical power to provide precise outcomes on mortality.
- There were no differences between stent and PTCA in reinfarction rates.
- Event rates favourable to stents largely reflected reduced intervention rates, not reduced mortality or coronary events.

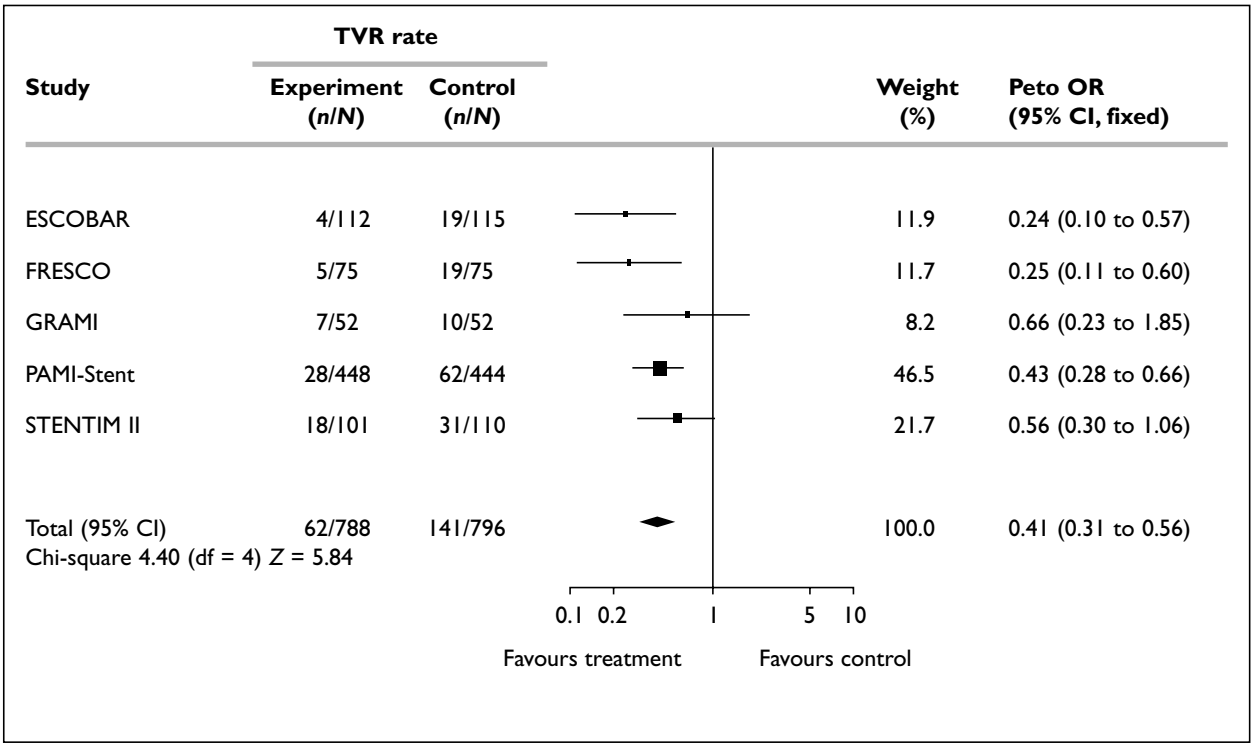


FIGURE 28 *TVR rates, 6 to 12 months follow-up: stent compared with PTCA in AMI*

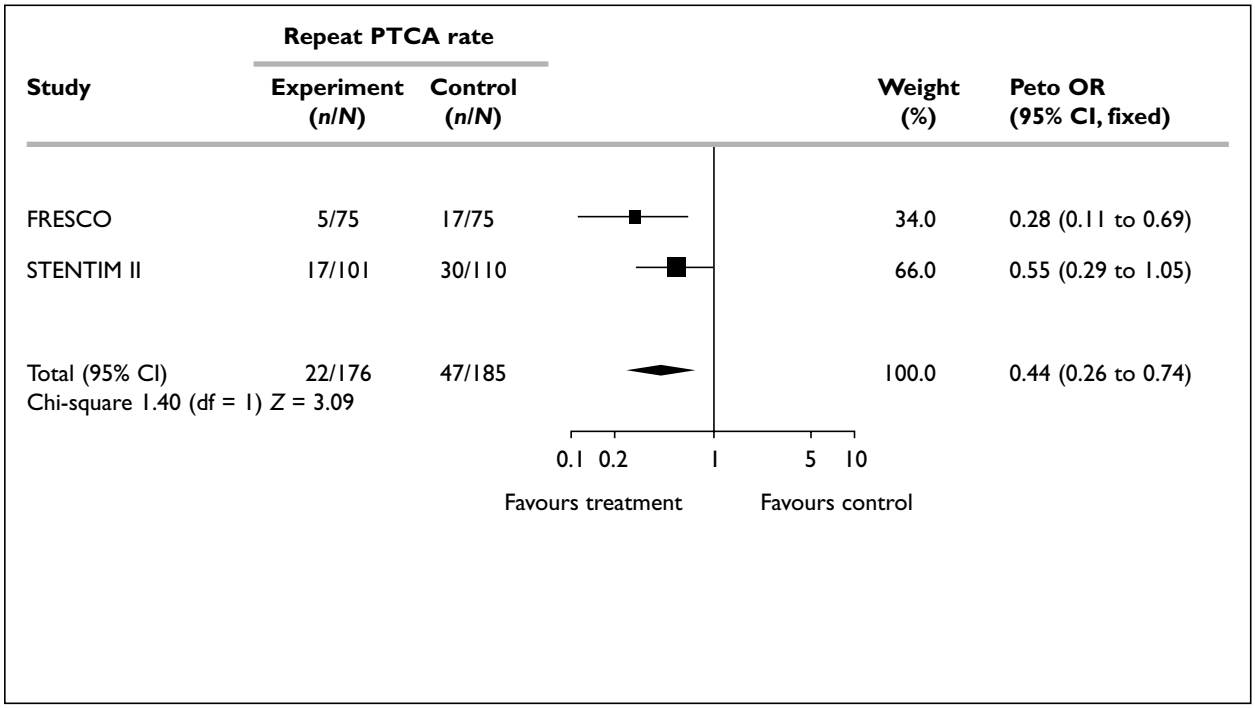


FIGURE 29 *Repeat PTCA rates, 6 to 12 months follow-up: stent compared with PTCA in AMI*

- The only trial that considered angina found in favour of stent. This trial has not as yet been fully published at the time of writing.

Results of economic evaluations review

Studies reporting costs

Number of studies

Nine studies reported the costs of PTCA in the UK. Five of these also reported stent costs and seven reported the cost of CABG. Four of the studies are included in the section on cost-effectiveness analyses. Three RCTs from the clinical effectiveness review are included in the cost-effectiveness/cost–utility review.[70,116,129]

Design of cost studies

The cost studies came from a variety of study types. Studies either presented costs only[130] or were part of cost-effectiveness studies.[1,131–137] Most provided minimal detail on costing methods used. As a result, important factors such as bailout stenting and trends towards using multiple stents may not have been taken into account. Costs were obtained from three systematic reviews.[1,132,133] The most detailed cost analysis was a micro-costing study,[131] which we have used as the pivotal study. The costs from this study lie midway in the range of hospital costs.

NHS costs for PTCA, stents and CABG

The costs for PTCA, PTCA with stent and CABG are shown in *Table 6* and in detail in appendices 6–8 (pages 119–126).

The costs in the appendices are presented in date order (earliest first). A separate table shows the current prices of some stents. The costs have been separated into three main groups for each intervention:

- Costs for the procedure include staff time and equipment costs used during the procedure itself.
- Hospital costs include length of stay in hospital and associated costs in addition to procedural costs.
- Wider costs include in addition the treatment costs incurred during the follow-up of a cohort of patients for a specified length of time following the initial procedure and include the procedure and hospital costs.

The costs should increase as more factors are taken into account. However, the summary of costs does not show this trend. Apparently, for stents the wider costs are less than the procedure costs and hospital costs. This is an anomaly resulting from the small number of studies contributing information to particular cells in *Table 6*.

TABLE 6 *Summary of costs (in £) for PTCA, stent and CABG*

	PTCA			Stents			CABG		
	Procedure only	**Hospital costs**	**Wider costs**	**Procedure only**	**Hospital costs**	**Wider costs**	**Procedure only**	**Hospital costs**	**Wider costs**
Mean	2408	2850	3156	4700*	4340	3999*	5144	6028	5065*
Range	1053–4944	1125–4325	2683–3630	–	2664–5697	2484–5290	2105–9123	3197–10,770	–
Number of data sources	7	9	2	1	5	2	5	9	1
Pivotal study[131]	–	2357	–	–	4144†	–	–	5539	–

* *Caution required in interpreting these figures as they are based on small numbers of studies (see text for further discussion)*
† *Cost for a repeat PTCA and stent*

The difference in mean hospital cost between stent and PTCA is £1490, and for the pivotal study £1787. However for the figure from the pivotal study it should noted that this is based on costs for a **repeat** PTCA with stent (mean cost £4144), and is hence likely to be an overestimate of the true difference. The difference in mean costs, for the wider cost studies, is £843. Again this may be biased by the small number of studies ($n = 2$). However, in the most recent study, examining wider costs in both PTCA and stents, the cost differential was £919.[1] Thus it seems reasonable to conclude that the cost differential between PTCA and stent is less for wider costs than for procedural costs.

PTCA procedure costs appear to increase over time. However, there are no time trends in hospital and wider costs. This is also true of the procedural, hospital and wider costs of stents. This is likely to be an artefact because of the small number of studies available. The trends of stent prices appear to be decreasing over time (information from industry data on file). The main variation in the data appears to be the variation in costs from different sources.

The difference in mean hospital cost between CABG and stent is £1688, and for the pivotal study £1395. Because of the limitations of the information available it is impossible to comment on the difference between wider costs. There do not appear to be any time trends in the procedural, hospital or wider costs but even fewer data were available than for stents versus PTCA.

Studies reporting cost-effectiveness/ cost–utility

Number of studies

A total of 16 studies that compared the cost-effectiveness of coronary stenting with PTCA were identified. In all except one, the comparison arm was PTCA, but in the OPUS study the comparison was between PTCA and provisional stenting. One further study comparing the cost-effectiveness of stenting with that of CABG in multi-vessel disease was identified.[70]

Few of the studies are directly comparable. They are based on a range of effectiveness data, costs have been collected at different time periods, they use a range of outcome measures, and the PTCA groups compared with stenting used a spectrum of policies from all PTCA, to PTCA with bailout stenting, or provisional stenting.

Study design

Six of the studies were cost-effectiveness analyses,[18,27,70,134,138–146] six were cost–utility analyses[1,133,146–150] and five reported costs and outcomes separately.[116,137,151–153] Three studies were RCTs,[27,70,116] five were observational studies[134,137,151–153] and eight used modelling techniques.[18,133,138–150]

Appendix 9 (page 127) shows the characteristics of the studies and the type of cost-effectiveness analysis used. The studies based on models are tabulated in detail in appendix 10 (pages 129–132) and the individual studies are tabulated in appendix 11 (page 133–137). We concentrated on the cost-effectiveness and cost–utility analyses. We did not examine in depth the studies in which the costs and outcomes were reported separately because they were mainly based on observational effectiveness data. These have the advantage of reporting current routine practice, and thus may produce results that are more generalisable. They have the major disadvantage of potential bias due to baseline differences in the groups. Three of the studies provide sufficient baseline

information to comment on the comparability of the groups. All report differences at baseline. Jackson and colleagues attempted to deal with the differences by undertaking a logistic regression to establish that the case-mix was independent of major outcomes.[134] Peterson and co-authors re-analysed the data using a narrow group of patients who had not had a previous revascularisation and restricting any outcomes to the target lesion.[152] This did not result in any change in the results. Palmer and co-authors did not deal with the baseline differences, except by establishing identical success and complication rates in the two groups.[137]

Quality of the studies

The quality of the studies is reported in the economic studies checklist (see appendix 14; page 141). Six of the studies reported a sensitivity analysis, with explicit assumptions. All the studies have flaws. Only one study (BENESTENT II) was an RCT with costs and outcomes collected and reported simultaneously.[27] The general pattern of quality for sources of effectiveness data (items 8–10 on checklist; see pages 141 and 142) were good but the pattern for costs considerably poorer (items 16–19; see page 142).

Source of cost data

Nine of the studies based their costings on bottom-up costing exercises[27,134,137–149,152] and five of these used European data.[27,134,137–145,148] Five studies used UK prices[1,18,133,150,153] and in three studies there was insufficient information given to determine the source of the cost data.[70,116,151] Further detail is given in appendix 12 (page 137).

Outcome measures

A range of outcome measures have been reported: event-free survival (EFS), cost per event-free survivor (cost/EFS), cost per outcome avoided, incidence of major adverse coronary events, cost per quality adjusted life-year (QALY). (EFS in the clinical effectiveness review has been taken to be the reverse of total event rate.) Appendix 13 (page 139) shows which studies have reported individual outcome measures.

EFS includes the absence of death, MI and revascularisation procedures. These outcomes were used in the three studies that used this measure to compare PTCA with stenting. Each of these outcomes carries equal weight in the outcome measure, but all of the studies reported the individual event rates separately and found that the major difference was in the revascularisation rates.

With the exception of the West Midlands DEC report,[1] the quality of life data used in all the cost–utility analyses were derived from the paper by Cohen and colleagues (1994).[154] Cohen and colleagues used data from Pliskin's study of patients with angina and made some assumptions about quality of life for three different degrees of severity of angina.

Results of cost-effectiveness analysis

The cost/EFS is largely the cost per revascularisation procedure averted (which is usually a repeat PTCA) although there are small proportions of patients with MI or deaths. There is concern about the meaning of cost/EFS when the main event being prevented is repeat PTCA which has mainly resource rather than health implications.

The cost/EFS for stents ranges from 38% higher than PTCA to 31% lower. Results from the four studies reporting this outcome are shown in *Table 7*. The differences are a function of differences both in costs and in the EFS rates. However, the majority contributor to lower costs/EFS in stent patients in recent studies appears to be a reduction in cost differential.

The earliest report used data from BENESTENT I and there is a large (55%) additional cost of stenting compared with PTCA.[146] This high cost is mainly due to the anticoagulation regimen used for BENESTENT I. The same study also used data from the BENESTENT II pilot (Phase IV) (approximately 2 years later) and compared the stenting results from this with the PTCA results of BENESTENT I. This comparison results in an 18% lower cost/EFS. The main contributor to the low cost/EFS for stenting is the large (22%) difference in EFS rates between the two groups. As the effectiveness data were not collected over the same time period, it is likely that factors other than the type of procedure affected the result. The cost difference between the stenting in the BENESTENT II pilot (Phase IV) and PTCA is much lower than for BENESTENT I and this difference is largely due to the change to an antiplatelet regimen.

Schwicker and Banz reported the largest differences in cost/EFS.[138–145] Their effectiveness estimates were derived from a literature review up to 1996 with some input from experts. Although they used quality criteria for the inclusion of studies, they also included some non-randomised trials, which may account for the larger differences in EFS rates. They also had the longest follow-up period.

TABLE 7 *Features of studies reporting EFS rates and costs*

Study	Follow-up period	EFS rate (%)			Costs		Cost-difference as % of PTCA	Cost/EFS		Difference in cost/EFS as % of PTCA
		Stents	PTCA	Difference	Stents	PTCA		Stents	PTCA	
Van Hout *et al.*[146]										
BENESTENT I	7 months	80	70	10	DFl 23,593	DFl 15,208	+55	DFl 29,000	DFl 21,000	+38
BENESTENT II pilot		92	70	22	DFl 16,663	DFl 15,208	+9.5	DFl 18,000	DFl 22,000	–18
Schwicker & Banz[138–145]										
SVD 1 year follow-up	1 year	89	76	13	DFl 12,812	DFl 12,479	+2.6	DFl 14,430	DFl 19,989	–29
SVD 3 years follow-up	3 years	82	68	14	DFl 15,126	DFl 14,885	+1.6	DFl 18,697	DFl 27,271	–31
BENESTENT II[27]	1 year	89	79	11	DFl 18,812	DFl 16,727	+2.5	DFl 21,309	DFl 21,073	+1.2
Boston Scientific[150]	1 year	84	78	6	£4918	£4662	+5.5	£5840	£6010	–2.9

SVD, single vessel coronary disease

Some figures have been rounded

Both BENESTENT II and a study by Boston Scientific reported similar costs/EFS for PTCA and stenting.[27,150] Both used the effectiveness data from BENESTENT II. Apart from the Boston Scientific study,[150] all these studies used cost data from The Netherlands, which reduces the differences between healthcare systems.

Despite the above explaining variation, the general pattern revealed is a favourable or neutral impact on cost-effectiveness. This is particularly so when account is taken of the fact that the only cost-effectiveness analysis showing markedly greater cost/EFS in the stent group relative to the PTCA group is the oldest study which least reflects current practice.

Results of cost–utility analyses

Table 8 shows the results of the studies reporting cost/QALY. This also presents the ranges of cost/QALY from the sensitivity analyses and the assumptions made in the models. Although the cost/QALY derived in the Wessex DEC study[133] is notably higher than in the other studies, the lower end of the sensitivity analysis is of a similar order as for the other results. Equally, the higher ranges of cost/QALY obtained from the studies by Guidant[148] and by Cohen and colleagues[147,149] are of a similar order to the Wessex DEC[1] result. The results are very sensitive to the assumptions used in the models, and the effectiveness and cost data used. In individual models the cost/QALY was very sensitive to the restenosis rates and the costs of stenting. This was clearly demonstrated in a model developed by Cohen and colleagues (1994).[154] The overall pattern suggests a cost/QALY difference between stents and PTCA of approximately £20,000–£30,000.

When comparing the cost–utility results between studies other assumptions are important. The Wessex DEC assumed an equal mortality rate in the PTCA and stent groups and thus only included the difference in revascularisation rates in their model.[133] The mortality rate after PTCA and stenting is approximately 1% at 1 year and thus it is a reasonable assumption to exclude deaths. When Guidant[148] excluded deaths from their model, the cost/QALY rose substantially. Although the West Midlands DEC also assumed an equal death rate at 1 year, they included a higher mortality rate in the PTCA group at 6 months follow-up.[1] Boston Scientific[150] did not have a significantly different mortality rate at 1 year. The West Midlands DEC[1] used different quality of life data for the different grades of angina reported by BENESTENT II. This is in

TABLE 8 *Analysis of cost–utility studies*

Study	Key assumptions	Difference in revascularisation rates (%)	Additional cost of stent	Cost/ QALY	Range of cost/ QALY from sensitivity analysis
Wessex DEC[133]	Patients with repeat PTCA had symptomatic restenosis with QOL valued at 0.8 Waiting-time for revascularisation 3 months Same procedural success rate in both groups Same survival rate in both groups PTCA if PTCA or stent	10.6	£1431	£250,000	£20,000–£772,000
West Midlands DEC[1]	Different QOL data used for the different grades of angina post PTCA and stent (data based on BENESTENT II results) Average EUROQOL for post-PTCA patient with angina is 0.661, and post-stent is 0.724 Death rates at 1 year are the same, at 6 months for PTCA death rate = 0.5% and for stent = 0.2% One stent used per procedure	5.6	£919	£23,000	£13,000–£53,000
Boston Scientific[150]	Deaths: 0.2% more early deaths in PTCA group Waiting-time for target-lesion revascularisation was 3 months Utility value with restenosis 0.8 QALYs 1.17 stents used per procedure	5.8	£256*	£31,500	Approx. £15,000–£82,000
Cohen *et al.*, 1997 & 1999[147,149]	55-year-old man with single vessel disease Restenosis > 50% would require revascularisation Patients with restenosis would have a max. of 3 percutaneous revascularisation attempts before CABG	16	$800	$33,700	Cost/QALY increases to $200,000 for type A mid-right coronary stenosis, with abrupt closure rate of 3% and restenosis rate of 25–30%

**This is the marginal cost of adjunctive stenting at 1 year, not the average price of a stent*

QOL, quality of life

continued

TABLE 8 contd *Analysis of cost–utility studies*

Study	Key assumptions	Difference in revascularisation rates (%)	Additional cost of stent	Cost/ QALY	Range of cost/ QALY from sensitivity analysis
Guidant[148]	No difference was assumed in death rates from primary procedures, but the submission includes the effects of higher total deaths from secondary and subsequent procedures in the absence of stents, due to higher rates of restonosis Waiting-time for target-lesion revascularisation was 3 months 2-year follow-up	10	£1041	£6812	£6813–£360,000 (if impact of deaths and CABGs and longer waiting times ignored)

contrast to the other studies, which derived their utility values for angina from Cohen and colleagues (1994).[154] Guidant[148] calculated the lowest cost/QALY. This was the lowest end of the range in their sensitivity analysis, and they took a 2-year perspective, unlike the other studies.

Stents compared with CABG in multi-vessel disease

The ARTS study[70] and Schwicker and Banz[138–145] looked at stents in comparison with CABG for multi-vessel disease. They both reported higher rates of EFS in patients following CABG. Schwicker and Banz report lower costs at 3 years follow-up in stent patients, and ARTS has similar findings for patients with two-vessel disease. Despite the lower effectiveness, stenting may be a cost-effective alternative to CABG in patients with multi-vessel disease.

Summary and implications of economic analysis

Variation is a marked feature of all the health economic data reviewed. This variation was particularly apparent between different estimates of cost, cost-effectiveness or cost–utility. There was also a contrast between the general message about efficiency provided by cost-effectiveness analyses, which presented elective stenting as efficient and having relatively minimal resource consequences, and that presented by the cost–utility estimates, which in the range of £20,000–£30,000 would be close to an important threshold distinguishing efficient from inefficient.

Although the interrelationship was only examined crudely, we believe that there are clues to the source of this contradiction.

From the analysis of cost information, hospital costs of stents remain higher than those of PTCA despite the falling costs of stents – differential of approximately £1500 to £1800. The cost differential between stents and PTCA falls when the wider costs (of follow-up and repeat revascularisation procedures) are taken into account. Taking this into account would reduce the cost differential to about £900.

This differential in costs is similar to those used in cost–utility calculations. However the cost differential used in the cost-effectiveness analyses is much narrower. In contrast to estimates of effectiveness used in all the health economic analyses, there is a marked difference in the costs used. The question arises as to which set of analyses uses the most accurate costs. This is particularly important because costing methods were rarely given in the studies reporting cost data. Thus, there was little indication of whether key factors likely to influence relative cost, such as the degree of use of bailout stenting or multiple use of stents, were taken into account. Uniquely, McKenna and colleagues[131] provided a bottom-up costing, but despite good methods, it is clear that current practice in these key respects could not be anticipated in 1997.

We believe, therefore, that the observation that the cost-effectiveness analyses tended to be based on bottom-up costings, and cost–utility estimates tended to be based on ill-defined costs or prices, suggests that greater caution should be applied to the interpretation the cost/QALY figures. This is particularly so as the utility values used to assess impact are underpinned by a limited amount

of research. Further, in the interpretation of cost/QALY figures, although the health value of the main event avoided – need for repeat PTCA – is probably correctly attributed a relatively low health value, this does not take into account the potential value of avoiding repeat PTCA to the wider healthcare system. This may be particularly pertinent in the NHS where there is evidence of significant under-provision of revascularisation procedures for severe IHD. In a situation in which there is an imperative to increase revascularisation rates, and where it may take time to develop capacity (i.e. increased numbers of centres with trained staff with the appropriate technical skills), the value of avoiding repeat PTCAs may not be truly reflected by its impact on individual health alone.

Although we tentatively favour the picture of efficiency suggested by the cost-effectiveness analyses, some caution also needs to be exercised in interpreting these. We had concern about the meaning of cost/EFS, where the main event being prevented is repeat PTCA, which arguably has greater resource consequences than personal health consequences.

On the basis of the above we conclude that there is evidence that initial costs to achieve a reduced rate of repeat PTCA may be largely off-set by the savings this brings about. However, the confidence with which this can be asserted would be greatly improved if the resource neutrality of coronary artery stents could be confirmed, using more rigorously derived cost data.

Finally, two points should be noted: firstly, that, despite some information on costs and a health economic analysis, conclusions concerning the efficiency of stenting relative to CABG are hampered by a lack of fully published effectiveness data; secondly that, although effectiveness data exist showing the relative benefit of stenting relative to PTCA in AMI, no relevant cost or health economic analyses were identified, again prohibiting conclusions.

Chapter 4

Discussion and conclusions

Results summary

Stents versus PTCA for subacute IHD (i.e. mainly angina and unstable angina)

General

It is important to remember that whatever the results of the evidence examined, we have implicitly accepted that there is a role for stenting in treating acute closure occurring during a PTCA (bailout or rescue stenting). The evidence for this is mainly observational, but convincing. The main alternative in this situation, an emergency CABG, appears to have worse outcomes, and has major resource implications.

BCIS audit data suggest that increasing stent use has been associated with a reduction in emergency CABG. However other technological advances could also contribute to this change over time. Although not part of the effectiveness review, two small trials provided little support for prolonged balloon perfusion balloon inflation as an alternative to bailout stenting.

Finally the availability of bailout stenting does not obviate the need for recourse to emergency CABG.

Effects and effectiveness

The key points are shown in *Box 6*.

Costs

The key points are presented in *Box 7*.

Cost-effectiveness and cost–utility

The key points are presented in *Box 8*.

Stents versus CABG for subacute IHD (i.e. mainly angina and unstable angina)

General

Understanding whether elective stenting is effective and cost-effective in the management of complex patterns of coronary artery occlusion, for which currently CABG is the preferred method of management, is critical to planning an appropriate balance of provision between the two main modes of coronary artery revascularisation – PTCA and CABG. The importance of this is compounded by the fact that the two sets of procedures are undertaken by different professional groups whose skills are not obviously transferable.

Effects and effectiveness

Seven randomised trials were identified (three with sufficient information to make some entry in our study characteristics table; four without such information, detailed in the table of excluded studies). Unfortunately, none of the trials have reported their results fully, although a number have completed recruitment. Currently, there is thus no rigorous evidence on the effectiveness of stents relative to CABG. However it seems likely that such evidence may become available over the next 2 years.

Costs

Cost data are available on both PTCA and CABG. All the provisos concerning the available cost data mentioned above apply.

Cost-effectiveness and cost–utility

One health economic analysis was identified. This is based on an ongoing trial, but clearly until confirmed and fully published effectiveness data are available, this analysis must be regarded as speculative.

Stents versus PTCA for acute MI

General

In order to interpret research comparing elective stenting and PTCA for acute MI, we have assumed that PCI is at least as effective and cost-effective as medical acute management of MI. Although we did not specifically review this evidence, this seems reasonably well established.

Effects and effectiveness

There are a good number of randomised trials, with more in progress. Unfortunately the results of those that have been completed are devalued by incomplete or poor reporting. Although we have not examined these studies in as much detail, most of the issues highlighted in the analysis of trials on elective stenting versus PTCA in subacute IHD seem to apply.

- The PTCA arms of most of the trials actually allow bailout or rescue stenting.
- What constitutes bailout stenting in the PTCA alone trial arms varies, and does not only include stenting for acute closure, but also for suboptimal PTCA results.

BOX 6 Stents versus PTCA for subacute IHD: key points on effects and effectiveness

- There is a good volume of randomised trials, with many more in progress. Unfortunately the results of those that have been completed are in many cases devalued by incomplete or poor reporting.
- Interpretation of the available published trials is complicated by considerable clinical heterogeneity manifested by important differences in:
  - IHD sub-types investigated
  - stenting strategies used
  - anticoagulation strategies used.
- The PTCA arms of most of the trials actually allow use of stents when acute closure occurs during the angioplasty procedure (bailout stenting). Thus it is inaccurate to interpret the results of the trials as the impact of stents versus no stents.
- Further, the definition of what constitutes bailout stenting varies. In some trials, stenting occurring in the control arm appears to have been undertaken not just for acute closure but also for sub-optimal PTCA results.
- Thus, effectively trials compare treatment packages comprising:
  - the PCI
  - rules for and patient preference for crossover
  - antithrombotic therapy.
- There is a consistent difference between treatment and control groups other than use of stents, especially in the use of more intensive antithrombotic therapy. This could account for some of the difference in observed outcome, currently wholly attributed to stent use alone.
- Aside from the quality of reporting, the quality of trial conduct also needs to be taken into account. Randomisation processes were often inadequately reported or sub-optimal. Further, steps to increase the objectivity of outcome assessment, although difficult, were rarely attempted. This is important to maintain validity, as in the absence of blinding there is clear risk of decisions to re-intervene being heavily influenced by whether a patient was allocated to elective stenting or PTCA alone.
- Although the above points introduce important sources of uncertainty, the following effects appear to have been established:
  - stents decrease total event rates (generally consisting of death, MI and need for re-intervention [either repeat PTCA or CABG]); the summary OR from the meta-analysis is 0.68 (95% CI, 0.59 to 0.78)
  - the main component of this decrease is reduced numbers of repeat PTCAs; the summary OR is 0.57 (95% CI, 0.48 to 0.69)
  - because of the relative rarity of events, it is impossible to be categorical about whether there is any impact on deaths, MIs and CABGs
  - it is impossible to be categorical about the effect on being angina-free because relatively few trials have measured this outcome.
- This pattern exists whether outcomes are examined in the medium term (4–11 months) or the long-term (1–5 years).
- The general consistency of the results, with the possible exception of the effect on angina status, suggests that the marked clinical heterogeneity noted may not be as important in assessing the effectiveness of elective stenting as it might at first appear.
- Although not conclusive, there is no obvious evidence of publication bias.
- There is insufficient evidence to draw conclusions on whether provisional stenting (observing initial PTCA result, and only inserting a stent if deterioration in the initial result occurs) is an effective or cost-effective strategy relative to routine insertion of stents.
- There is insufficient evidence to draw conclusions on use of stents in small coronary arteries (where the lumen of the coronary artery is < 3 mm).

BOX 7 Stents versus PTCA for subacute IHD: key points on costs

- There is a considerable amount of recent, routine and published cost data.
- Whether considering the procedure costs, the hospital costs or the wider costs of stents relative to PTCA, there is uncertainty, manifest by wide variation.
- Some of this variation is likely to be due to costing method, although it is difficult to substantiate this owing to poor reporting of the method by which costs or prices were derived. We have placed greatest reliance on explicit methods, which in practice meant weighting more highly bottom-up or micro-costing exercises.
- It is unclear to what extent the following potentially very influential factors on cost have been taken into account:

  – established use of stents in routine PTCA practice, particularly for bailout stenting

  – trends towards using multiple stents.
- Failure to take account of the first of the above would have a tendency to overestimate the cost differential; failure to take account of the second would have a tendency to underestimate the cost differential.
- With these provisos, there is a cost differential, stents costing more than PTCA. The cost differential is smaller when wider costs are taken into account.

BOX 8 Stents versus PTCA for subacute IHD: key points on cost-effectiveness and cost–utility

- There is a considerable volume of recent published health economic analyses, relating effectiveness and costs in:

  – cost-effectiveness analyses, particularly expressing cost/EFS

  – cost–utility analyses, expressed as cost/QALY.
- On appraisal, all analyses examined had important weaknesses.
- The overall pattern from cost-effectiveness analyses is that cost/EFS is less for elective stenting than PTCA, particularly in more recent analyses. In these the increased initial costs of stents are almost completely offset by savings resulting from reduced need for revascularisation.
- Although there was some concern about the interpretation of the measure cost/EFS, where the main event being prevented is repeat PTCA, the implication is that use of stents, at least in the context of the trials on which the cost-effectiveness analyses were based, could be cost-neutral.
- The overall pattern from cost–utility analyses is less easy to discern, there being much wider variation, but marginal cost/QALY in the region of £20,000–30,000 are typical.
- Thus the cost–utility analyses appear less encouraging, partly reflecting the apparently low perceived personal health value of requiring a repeat PTCA after the initial procedure. However, there is very little evidence in the literature on the impact of stents on quality of life.
- The view of the general efficiency of elective stenting thus seems to be dependent on the type of analysis used. Based on a limited exploration of the data we believe that this difference could arise from general differences in cost differential between stents and PTCA. The cost-effectiveness analyses tend to use bottom-up costing; the cost–utility analyses tend simply to use prices. We believe the latter method of costing is less likely to take into account important factors influencing cost.
- A further important issue relevant to the interpretation of cost/QALY figures, is that although the health value of the main event avoided – need for repeat PTCA – is correctly attributed a relatively low health value, this does not take into account the potential value of avoiding repeat PTCA to the wider healthcare system. This may be particularly pertinent in the NHS where there is evidence of significant under-provision of revascularisation procedures for severe IHD. In a situation where there is an imperative to increase revascularisation rates, and where it may take time to develop capacity (i.e. increased numbers of staff with the appropriate staff with the appropriate technical skills), the value of avoiding repeat PTCAs may not be truly reflected by its impact on individual health alone.

- Randomisation processes were often inadequately reported or sub-optimal, and steps to reduce the bias introduced by the difficulty of blinding to treatment allocation was rarely attempted.

Similarly, although the above points introduce uncertainty, the following effects appear to have been established.

- Elective stenting decreases total event rates (generally consisting of death, MI and need for re-intervention [either repeat PTCA or CABG]). The summary OR from the meta-analysis is 0.39 (95% CI, 0.28 to 0.54).
- The main component of this decrease is reduced numbers of repeat PTCAs. The summary OR is 0.44 (95% CI, 0.26 to 0.74).
- Because of the relative rarity of events, it is impossible to be categorical about whether there is any impact on deaths, MIs and CABGs.
- It is impossible to be categorical about the effect on being angina-free because relatively few trials have measured this outcome, although one large trial found a significant difference in favour of stents.[126]

Costs

No cost data specific to the use of stents or PTCAs in the context of acute MI were identified.

Cost-effectiveness and cost–utility

Similarly, no health economic evaluations of the use of PTCA in comparison with stents in the context of acute MI were identified. The absence of such information is critical because of the major structural and resource implications of widespread use of either PTCA or stenting immediately after MI.

Potential methodological strengths and weaknesses of the technology assessment

Strengths

We identify the following methodological features as being particularly robust:

- a series of clearly defined questions
- a comprehensive search strategy incorporating both published and partially published material
- duplicate application of inclusion and exclusion criteria
- detailed assessment of included study quality
- duplicate data abstraction
- use of meta-analysis to amplify the assessment of patterns of results across several trials assessing the same intervention.

Potential weaknesses

In systematic reviews, publication bias is always a potential problem, and although the comprehensive search strategy is a defence against this and the funnel plot showed no obvious evidence of publication bias, the possibility of it can never be completely excluded. Related to this is the major constraint of the lack of complete information on finished trials. The response to requests for further information from lead authors was poor but understandable given the relatively short time-scales involved. Collecting missing outcome data could be important for two reasons:

- it might allow more definitive conclusions on rarer outcomes like deaths, MI and repeat CABG
- it might provide reassurance that there is no selective reporting (i.e. reporting only outcomes that show the intervention in its most favourable light).

Ideally it would have been useful to explore completely the influence of different variables on the pattern of effectiveness results using meta-regression. However, although available time was a limiting factor, so too was availability of complete data, which as indicated above was outside our control.

In the review of economic evaluations, quality of available cost data was a major limitation. Without clear methods it is impossible to assess the degree to which important costs have or have not been included. Not undertaking our own de novo modelling of costs and effects might also be construed as a limitation, but our own view was that in the time available we could not overcome a major short-coming of the cost–utility estimates (in particular, poor assessment of costs using micro-costing techniques). Finally, as for the effectiveness data, additional efforts to explore the differences between the various economic evaluations identified could have increased the certainty of some of our conclusions on the general efficiency of elective stenting.

Important issues not addressed by this health technology assessment

Key issues that this assessment did not encompass include the following.

- The evidence base for use of stents for bailout stenting.

- The relative effectiveness of different stent types.
- The effectiveness of PTCA + stents in those patients for whom the risk from PTCA and/or CABG is currently perceived to be too great. These patients can currently only be offered medical therapy, which in the specific situation is unlikely to be offering complete relief of symptoms attributable to IHD.
- The evidence base for newer technologies (e.g. laser and minimally invasive CABG). However, although possible in theory, we are not convinced that it is possible to predict how stenting will relate to developing technologies, particularly whether it will be superseded, and if so when.
- The impact on PCI of different anti-thrombotic regimens, particularly glycoprotein IIb/IIIa inhibitors. The assessment also did not address the issue of whether the newer anti-thrombotic regimens added to PTCA alone without use of stents may achieve some of the benefit currently attributed wholly to stent use.

Conclusions

- In subacute IHD, especially stable angina and unstable angina, there is evidence for the effectiveness of a strategy of using stents rather than PTCA plus recourse to bailout stenting when acute closure occurs.
- The main impact is on reduced need for repeat PTCA.
- Although based on RCTs, the available research is open to bias and hence there is not complete certainty.
- Our tentative view is that used in these conditions and this way, stents are likely to represent an efficient use of resources.
- However, the confidence with which the last conclusion can be made would be greatly improved if the resource neutrality of stents could be confirmed, using more rigorously derived cost data.
- The evidence on the relative effectiveness and efficiency of stents used provisionally is inconclusive.
- Outside the use of stents in subacute IHD, the effectiveness and/or efficiency of stents use is not known.

Implications of assessment findings

NHS

- The main conclusions relate to an area of practice – elective stenting for stable and unstable angina – which is already well established. In this sense the findings of this report serve to confirm that the trend for increasing use of stents is reasonable, with the important proviso that its cost neutrality is confirmed. If this is the case, complete diffusion of the technology should have minimal consequences.
- Unfortunately, research on effectiveness, cost-effectiveness and cost–utility is not available to address whether further expansion of stenting beyond these indications should be encouraged or discouraged.
- For many important stenting applications, research appears to be ongoing (see pages 5 and 15), suggesting a further reassessment of available research evidence and health economic evaluations would be valuable in 1 to 2 years' time. This is particularly true for the following areas:
  - use of stents provisionally
  - assessment of the relative impact of different types of stents
  - use of PTCA + stents relative to medical therapy in patients thought to be unsuitable for PTCA and/or CABG
  - use of stents relative to CABG in subacute IHD with complex patterns of occlusion
  - use of stents in acute manifestations of IHD, especially acute MI.
- In our opinion, further expansion of stent use in these areas should await the reassessments.
- In addition, there are a few areas where little if any research appears to be on-going, and these are described in detail in implications for future research.

Patients and carers

- Making individual decisions on the most appropriate treatment for severe IHD is difficult, both because of the highly technical nature of the subject and because of the perceived severity of the circumstances in which patients are required to make that decision.
- Because individuals are being required to make such decisions, an important task is to convey information about the relative benefits and drawbacks of PTCA + stents or CABG, clearly indicating the circumstances in which the balance of these might favour one or other option. A concern is that stents might be misperceived as a panacea.

Implications for future research

A general message from this assessment is to give a clear indication to researchers and industry that complete reporting of any trial data is essential.

Even if a peer-reviewed publication is not feasible, a properly prepared manuscript should be readily available which gives details about method and results, including information on all outcomes measured in all patients who were initially randomised. Conference abstracts and press releases are insufficient, and effectively lead to the exclusion of potentially valuable information in this sort of exercise.

Specifically, we believe the following areas in relation to the use of stents need to be addressed:

- better cost data, using explicit micro-costing
- impact of stents on severity of angina and quality of life
- effectiveness of newer technologies.

Finally, such is the importance of clearly establishing the effectiveness and efficiency of stents compared with CABG that careful consideration should also be given to whether further targeted research would be valuable in this area too, despite the fact that there is considerable ongoing research on this topic.

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References

1. Meads C, Cummins C, Stevens A. Coronary artery stents. Birmingham: Department of Public Health and Epidemiology, University of Birmingham; 1998 (West Midlands Development and Evaluation Service Report No. 9).
2. Office for National Statistics. Mortality statistics: general. Review of the Registrar General on Deaths in England and Wales; 1997. London: The Stationery Office; 1999 (Series DH1; No. 30).
3. Public Health Common Data Set 1996. Vol. IV. London: Department of Health; 1997.
4. Sans S, Kesteloot H, Kromhout D. The burden of cardiovascular diseases mortality in Europe. *Eur Heart J* 1997;**18**:1231–48.
5. World Health Organization. The world health report 1999: making a difference. Geneva: World Health Organization; 1999.
6. Health survey for England: cardiovascular disease '98. London: Department of Health; 1999.
7. McCormick A, Fleming D, Charlton J. Morbidity statistics from general practice: fourth national study 1991–1992. London: HMSO, 1995 (Series MB5; No. 3).
8. Office for National Statistics. The health of adult Britain 1841–1994. Volume 2, Chapters 15–27. London: The Stationery Office; 1997 (Decennial Supplement No. 13).
9. Saving lives: our healthier nation. Presented to Parliament by the Secretary of State for Health by command of Her Majesty, July 1999. London: The Stationery Office; 1999 (CM 4386).
10. Cleland JG. Can improved quality of care reduce the costs of managing angina pectoris. *Eur Heart J* 1996;**17**(Suppl. A):29–40.
11. Pocock SJ, Henderson RA, Seed P, Treasure T, Hampton JR. Quality of life, employment status and anginal symptoms after coronary angioplasty or bypass surgery. 3 year follow up in the Randomised Intervention Treatment of Angina (RITA) trial. *Circulation* 1996;**94**:135–42.
12. Bliley AV, Ferrans CE. Psychologic aspects of cardiovascular care. *Heart Lung* 1993;**22**:193–9.
13. Pocock SJ, Henderson RA, Rickards AF, Hampton JR, King SB, Hamm CW, *et al.* Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. *Lancet* 1995;**346**:1184–9.
14. CHKS Ltd. Acute Care 97/98. Healthcare Resource Groups. National Statistics 1996/97. London: Financial Times Healthcare; 1997.
15. Coronary angioplasty versus coronary artery bypass surgery: the Randomised Intervention Treatment of Angina (RITA) trial. *Lancet* 1993;**341**:573–80.
16. Working Party of the British Cardiac Society. Coronary angioplasty in the United Kingdom. Report of a Working Party of the British Cardiac Society. *Br Heart J* 1991;**66**:325–31.
17. New device therapy for coronary artery disease (revisited). New Dev Med Drug Ther [serial online] Sep/Dec 1996. Available from: http://www.medpub.com/7feat1.htm
18. Scottish Health Purchasing Information Centre. Stents for coronary artery disease. Aberdeen: Scottish Health Purchasing Information Centre; 1996.
19. White H. Future of reperfusion therapy for myocardial infarction. *Lancet* 1999;**354**:695–7.
20. Parisi AF, Folland E, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of single vessel coronary artery disease. *N Engl J Med* 1992;**326**:10–16.
21. RITA-2 trial participants. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA 2) trial. *Lancet* 1997;**350**:461–8.
22. CHKS Ltd. Acute Care 95. Healthcare Resource Groups. National Statistics 1994/5. Alcester: CHKS Ltd; 1995.
23. Stauffer J, Eeckhout E, Goy J, Nacht C, Vogt P, Kappenberger L. Major dissection during coronary angioplasty: outcome using prolonged balloon inflation versus coronary stenting. *J Invasive Cardiol* 1995;**7**:221–7.
24. Legrand V, Raskinet B, Laarman G, Danchin N, Morel MA, Serruys PW. Diagnostic value of exercise electrocardiography and angina after coronary artery stenting. *Am Heart J* 1997;**133**:240–8.
25. Gunnell D, Harvey I, Smith L. The invasive management of angina: issues for consumers and commissioners. *J Epidemiol Community Health* 1995;**49**:335–43.
26. Pepine CJ, Holmes DR. ACC Expert Consensus Document. Coronary artery stents. *J Am Coll Cardiol* 1999;**28**:782–94.

27. Serruys PW, van Hout B, Bonnier H, Legrand V, Garcia E, Macaya C, *et al.* Randomised comparison of implantation of heparin-coated stents with balloon angioplasty in selected patients with coronary artery disease (Benestent II). *Lancet* 1998;**352**:673–81.

28. Gershlick AH. Evidence based data to support the use of stents in clinical practice [online]. British Cardiovascular Intervention Society, 1999. [Intracoronary stents: BCIS submission to NICE.] Available from: http//:www.bcis.org.uk/

29. Butman SM. (Almost) all you ever wanted to know about stents [book review]. *Lancet* 1999;**354**:80.

30. Cohen E, Schwartz L. Coronary artery stenting: indications and cost implications. *Prog Cardiovasc Dis* 1996;**39**:83–110.

31. BCIS audit returns of interventional procedures 1998. [online]. [Copy of a presentation made at Leicester, October 1999 by Mark de Belder on behalf of the Council of the British Cardiovascular Intervention Society.] Available from: http://www.bcis.org.uk/audit/oct99.html

32. Sigwart U. Prevention of restenosis after stenting. *Lancet* 1999;**354**:269–70.

33. Ozaki Y, Violaris AG, Serruys PW. New stent technologies. *Prog Cardiovasc Dis* 1996;**39**:129–40.

34. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. *N Engl J Med* 1987;**316**:701–6.

35. Serruys PW, Strauss BH, Beatt KJ, Bertrand ME, Puel J, Rickards AF, *et al.* Angiographic follow-up after placement of a self-expanding coronary artery stent. *N Engl J Med* 1991;**324**:13–17.

36. Uren NG, Chronos NA. Intracoronary stents. *BMJ* 1996;**313**:892–3.

37. Hirsh J, Weitz JI. New antithrombotic agents. *Lancet* 1999;**353**:1431–6.

38. Popma JJ, Lansky AJ, Ito S, Mintz GS, Leon MB. Contemporary stent designs: technical considerations, complications, role of intravascular ultrasound and anticoagulation therapy. *Prog Cardiovasc Dis* 1996;**39**:111–28.

39. Hall P, Nakamura S, Maiello LO, Blengino S, Martini G, Ferraro MC. A randomised comparison of combined ticlopidine and aspirin therapy versus aspirin therapy alone after successful intravascular ultrasound guided stent implication. *Circulation* 1996;**93**:215–22.

40. Schomig A, Newman FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, *et al.* A randomised comparison of antiplatelet and anticoagulant therapy after the placement of coronary artery stents. *N Engl J Med* 1996;**334**:1084–9.

41. The Epistent Investigators. Randomised placebo-controlled and balloon angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein-IIb/IIIa blockade. *Lancet* 1998;**352**:87–92.

42. The EPILOG Investigators. Platelet glycoprotein IIb/IIIa receptor blockade and low dose heparin during percutaneous coronary revascularisation. *N Engl J Med* 1997;**336**:1689–96.

43. Randomised placebo controlled trial of Abciximab before and during coronary intervention in refractory unstable angina: the CAPTURE study. *Lancet* 1997;**349**:1429–35.

44. Chronos N, Vahanian A, Betriu A, Emanuelsson H, Goldberg S, Gulba D, *et al.* Use of Abciximab in interventional cardiology. *Eur Heart J* 1998;**19** (Suppl D):D31–D39.

45. Laramore GE, Stelzer KJ. Radiation therapy for benign disease: an old area revisited. *Lancet* 1998;**352**:834–5.

46. British Cardiac Society. Council statement on the demand and need for cardiac services and the development of a waiting list strategy for cardiac disease – July 1994 [online]. Available from: http://www.bcs.com/publications/

47. Ghandi MM, Lampe FC, Wood DA. Incidence, clinical characteristics, and short-term prognosis of angina pectoris. *Br Heart J* 1995;**73**:193–8.

48. Milburn A. How to beat heart disease and inequality. *The Observer* 12 Dec 1999.

49. Burls A, Cummins C, Fry-Smith A, Gold L, Hyde C, Jordan R, *et al.* West Midlands Development and Evaluation Service handbook. Version 2.2, 2000. Birmingham: Department of Public Health and Epidemiology, University of Birmingham; 2000.

50. NHS Centre for Reviews and Dissemination. Undertaking systematic reviews of research on effectiveness: CRD guidelines for those carrying out or commissioning reviews. York: NHS Centre for Reviews and Dissemination, University of York; 1996 (CRD Report 4).

51. Perleth M, Kochs G. Stenting versus Ballondilatation bei korondrer Herzkrankheit. Systematisch Übersichten zur medizinischen Effektivität und zur Kosten-Effektivität. [Stenting versus percutaneous transluminal coronary angioplasty (PTCA) for coronary artery disease: results of a systematic review] [in German] [online]. Cologne: Deutsches Institut fur Medizinische Dokumentation und Information; 1999. Available from: http://www.dimdi.de/

52. Mehta RH, Bates ER. Coronary stent implantation in acute myocardial infarction. *Am Heart J* 1999;**137**:603–11.

53. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, *et al.* Assessing the quality of reports of randomised clinical trials: is blinding necessary? *Controlled Clin Trials* 1996;**17**:1–12.

54. NHS Centre for Reviews and Dissemination. Making cost effectiveness information accessible: the NHS Economic Evaluation Database project. York: NHS Centre for Reviews and Dissemination, 1996 (CRD Report 6).

55. Drummond MF, Jefferson TO. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The Economic Evaluation Working Party. *BMJ* 1996;**313**:275–83.

56. Isley C. Additional value of NIR stents for treatment of long coronary lesions. ADVANCE [online]. Abstract from: National Research Register Project N0201048162. Available from: http://www.update-software.com/National/nrr-frame.html

57. Koning R, Khalife K, Gilard M, Commeau P, Lipiecki J, Bedossa M, *et al.* The BESMART study: in-hospital clinical and angiographic results. *Eur Heart J* 1999;**20** (Abstract Suppl. August/September):383.

58. Ambrose JA, Sharma SK, Marmur JD, Garcia AR, Cooke TP, Duvvuri S, *et al.* Balloon optimization vs stent study (BOSS): a prospective randomised trial. *Circulation* 1997;**96**(Suppl 1):I-592.

59. Rothman M. Coating of stents – balloon angioplasty vs heparin-coated and non-coated coronary stents (COAST) [online]. Abstract from: National Research Register Project N0205019136. Available from: http://www.update.software.com/National/nrr-frame.html

60. Moussa I, Colombo A, Di Francesco L, Di Mario C, Jain A, de Leso JS, *et al.* Is Doppler-guided balloon angioplasty with conditional stenting a viable option in diabetic patients? A subanalysis of the DESTINI trial. *Eur Heart J* 1999;**20** (Abstract Suppl. August/September):605.

61. FR.O.S.T. Study Group. The French Randomised Optimal Stenting Trial (FR.O.S.T.) final results of a multicenter, prospective, randomized study comparing systematic stenting to angiography/coronary flow reserve guided stenting. The FR.O.S.T. Study Group. *Circulation* 1998;**98**(Suppl. 1):1–228.

62. Hibi K, Kobayashi Y, Maehara A, Oshima S, Kato K, Takazawa J, *et al.* A randomized comparison of the effects of gradual inflation at optimum pressure versus stent implantation on early and late outcome [online]. Abstract from the 48th Annual Scientific Session. American College of Cardiology, New Orleans, Louisiana March 7–10 1999. Abstract No. 1189-48. Available from: http://ex2.excerptamedica.com/99acc/abstracts/abs1189-48.html

63. Tamai H, Tsuchigane E, Suzuki T, Nishikawa H, Fujii K, Aizawa T, *et al.* Interim results from Mayo Japan investigation for chronic total occlusion (MAJIC). *Circulation* 1998;**98**(Suppl. 1):1-639–40.

64. Garcia E, Gomez-Recio M, Pasalodos J, Bethancourt A, Zeuco J, Iniguez A. Immediate results of the RAP study: a randomized trial that compares stent and balloon angioplasty in small vessels. *Eur Heart J* 1999;**20** (Abstract Suppl. August/September):385.

65. Schalij M, Douchet S, De Bruyne B, Vrolix M, Hilton D, Chenu P, *et al.* Stenting of small coronary arteries: interim report from a randomized multicenter trial in patients with a vessel reference diameter of 2.3–2.9mm. The SISA study. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):386.

66. Cumberland D. Sub-Optimal Angioplasty Result Study (SOAR study) [online]. Abstract from: National Research Register Project N0164012429. Available from: http://www.update-software.com/National/nrr-frame.html

67. Haude M, Erbel R, Hoepp HW, Heublein B, Sigmund M, Meyer J, *et al.* STENT-BY study: a prospective randomized trial comparing immediate stenting versus conservative treatment strategies in abrupt vessel closure or symptomatic dissections during coronary balloon angioplasty. *Eur Heart J* 1996;**17**(Abstract Suppl. August):172.

68. Koolen JJ, Bonnier JJ, Hanekamp CE. Small Vessel Study: a prospective randomised controlled multicenter trial. Protocol. Berlin: Biotronik; [date unknown].

69. Chauhan A, Penn IM, Ricci DR, Buller CE, Almond DG, Lazzam C, *et al.* Coronary artery stenting reduces late clinical events in restenosis lesions: final results from the trial of angioplasty and stents in Canada (TASC I). *Heart* 1996;**75**(Suppl. 1):45.

70. Serruys PW, Unger F, van Herwerden L, Mohr F, Simon R, Wijns W, *et al.* Arterial Revascularisation Therapy Study: The ARTS Study, a randomised trial of by-pass surgery versus stenting in multivessel coronary disease. *Circulation* 1998;**98** (Suppl. 1):1–498.

71. Morrison DA. Angina with Extremely Serious Operative Mortality Evaluation AWESOME [online]. Abstract from Cardiosource. Available from: http://206,137.72.17/trials/trialview.asp?uid=29471

72. Angelini G. A multi-centre randomised controlled trial of minimally invasive by-pass grafting vs angioplasty with stenting for single vessel disease of the left anterior descending coronary artery [online]. Abstract from NHS R&D Health Technology Assessment Programme 3 list of commissioned HTA projects. Project 96/04/06. Available from: http://www.hta.nhsweb.nhs.uk/projdets/960406.htm

73. Sigwart U, Stables RH. Stent or surgery SoS [online]. Abstract from Cardiosource. Available from: http://206.137.72/trials/trialview.asp?uid=29172

74. Schwimmbeck P, Spencker S, Hohmann C, Horstkotte D, Behrens S, Pauschinger M, *et al.* Heparinized stents in acute myocardial infarction: first results from the BESSAMI (Berlin Stent Study in Acute Myocardial Infarction) trial. *Eur Heart J* 1999;**20** (Abstract Suppl. August/September):170.

75. Kutryk M, Serruys PW. Coronary stenting: current perspectives. London: Martin Dunitz; 1999.

76. Kawashima A, Ueda K, Nishida Y, Inoue N, Uemura S, Miyazaki H, *et al.* Quantitative angiographic analysis of restenosis of primary stenting using Wiktor stent for acute myocardial infarction: results from a multicenter randomized PRISAM Study. *Circulation* 1998;**98**(Suppl. 1):1–153.

77. Rodriguez AE, Santaera O, Larribau M, Fernandes M, Sarmiento R, Balino NP, *et al.* Coronary stenting decreases restenosis in lesions with early loss in luminal diameter 24 hours after successful PTCA. *Circulation* 1995;**91**:1397–402.

78. Ricci RD, Buller CE, O'Neill B, Foster C, Amond D, Lazzam C, *et al.* Coronary stent vs prolonged perfusion balloon for failed coronary angioplasty – a randomized trial. *Circulation* 1994;**90** Part 2:I-651.

79. Wong SC, Zidar JP, Chuang YC, Schatz RA, Goldberg S, Baim DS, *et al.* Stents improve late clinical outcomes: results from the combined (1+11) STent REStenosis Study. *Circulation* 1995;**92**(Suppl. 1):1–281.

80. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, *et al.* A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. *N Engl J Med* 1994;**331**:489–95.

81. Serruys PW, The BENESTENT-1 study group. Continued benefit of coronary stenting versus balloon angioplasty: five-year clinical follow-up of BENESTENT trial. *Eur Heart J* 1999;**20** (Abstract Suppl. August/September):136.

82. Foley DP, Serruys PW. Provisional stenting-stent like balloon angioplasty: evidence to define the continuing role of balloon angioplasty for percutaneous coronary revascularisation. *Semin Intervent Cardiol* 1996;**1**:269–73.

83. Keane D, Azar AJ, de Jaegere P, Rutsch W, de Bruyne B, Legrand V, *et al.* Clinical and angiographic outcome of elective stent implantation in small coronary vessels: an analysis of the BENESTENT trial. *Semin Intervent Cardiol* 1996;**1**:255–62.

84. Macaya C, Serruys PW, Ruygrok P, Suryapranata H, Mast G, Klugmann S, *et al.* Continued benefit of coronary stenting versus balloon angioplasty: one year clinical follow up of BENESTENT trial. *J Am Coll Cardiol* 1996;**27**:255–61.

85. Fischman DL, Leon MB, Baim DS, Schatz RA, Savage MP, Penn I, *et al.* A randomised comparison of coronary stent placement and balloon angioplasty in the treatment of coronary artery disease. *N Engl J Med* 1994;**331**:496–501.

86. George CJ, Baim DS, Brinker JA, Fischman DL, Goldberg S, Holubkov R, *et al.* One year follow-up of the stent restenosis (STRESS 1) Study. *Am J Cardiol* 1998;**81**:860–5.

87. Krumholz HM, Cohen DJ, Williams C, Baim DS, Brinker JA, Cabin H, *et al.* Health after coronary stenting or angioplasty: results from the Stent Restenosis Study. *Am Heart J* 1997;**34**:337–44.

88. Cohen DJ, Krumholz HM, Sukin CA, Ho KK, Siegrist RB, Cleman M, *et al.* In-hospital and one-year economic outcomes after coronary stenting or balloon angioplasty: results from a randomized clinical trial. *Circulation* 1995;**92**:2480–7.

89. Slota PA, Fischman DL, Savage M, Rake R, Goldberg S. Frequency and outcome of development of coronary artery aneurysm after intracoronary stent placement and angioplasty. *Cardiology* 1997;**79**:1104–6.

90. Eeckhout E, Stauffer J-C, Vogt P, Debbas N, Kappenberger L, Goy J-J. Comparison of elective Wiktor stent placement with conventional balloon angioplasty for new-onset lesions of the right coronary artery. *Am Heart J* 1996;**132**:263–8.

91. Versaci F, Gaspardone A, Tomai F, Crea F, Chiariello L, Gioffre P. A comparison of coronary artery-stenting with angioplasty for isolated stenosis of the proximal left anterior descending coronary artery. *N Engl J Med* 1997;**336**:817–22.

92. Masotti M, Serra A, Fernandez-Aviles F, Alonso J, Gimeno F, Colman T, *et al.* Four years follow-up of the START trial, a randomized stenting versus PTCA study. *Eur Heart J* 1999;**20** (Abstract Suppl. August/September):533.

93. Bertrui A, Serra A, Masotti M, Delcan JL, Garcia E, Colman T, *et al.* The Spanish Trial: are national randomized trials a necessary evil? *J Intervent Cardiol* 1994;**7**:347–53.

94. Masotti M, Serra A, Betriu A. Stent en lesiones coronarias de novo: metaanalisis. [Stents for new coronary lesions: meta-analysis.] [In Spanish.] *Rev Esp Cardiol* 1997;**50**(Suppl. 2):3–9.

95. Erbel R, Haude M, Hopp HW, Franzen D, Rupprecht HJ, Heublin B, *et al.* Coronary-artery stenting compared with balloon angioplasty for restenosis after initial balloon angioplasty. *N Engl J Med* 1998;**339**:1672–8.

96. Savage MP, Douglas JS, Fischman DL, Pepine CJ, King SB, Werner JA, *et al.* Stent placement compared with balloon angioplasty for obstructed coronary bypass grafts. *N Engl J Med* 1997;**337**: 740–6.

97. L'Allier PL, Cura FA, Sapp S, Lincoff MA, Topol EJ. EPISTENT: a large scale randomized trial of primary versus provisional coronary stenting with background platelet glycoprotein IIb/IIIa blockade [online]. Abstract from the 48th Annual Scientific Session. American College of Cardiology, New Orleans, Louisiana. March 7–10 1999. Abstract No. 81-4. Available from: http://ex2-excerptamedica.com/99acc/abstracts/abs81-4.html

98. Sirnes PA, Golf S, Myreng Y, Molstad P, Emanuelsson H, Albertsson P, *et al.* Stenting in chronic coronary occlusion (SICCO): a randomised, controlled trial of adding stent implantation after successful angioplasty. *J Am Coll Cardiol* 1996;**28**:1444–51.

99. Sirnes PA, Golf S, Myreng Y, Molstad P, Albertsson P, Mangschau A, *et al.* Sustained benefit of stenting chronic coronary occlusion: long-term clinical follow-up of the stenting in chronic coronary occlusion (SICCO) study. *J Am Coll Cardiol* 1998;**32**:305–10.

100. Sirnes PA, Molstad P, Myreng Y, Golf S. Predictors for restenosis after angioplasty of chronic coronary occlusions. *Int J Cardiol* 1998;**67**:111–18.

101. Rubartelli P, Niccoli L, Verna E, Giachero C, Zimarino M, Fontanelli A, *et al.* Stent implantation versus balloon angioplasty in chronic coronary occlusions: results from the GISSOC trial. *J Am Coll Cardiol* 1998;**32**:90–6.

102. Hancock J, Thomas MR, Holmberg S, Wainwright RJ, Jewitt DE. Randomised trial of elective stenting after successful percutaneous transluminal coronary angioplasty of occluded coronary arteries. *Heart* 1998;**79**:18–23.

103. Buller CE, Dzavik V, Carere RG, Mancini J, Barbeau G, Lazzam C, *et al.* Primary stenting versus balloon angioplasty in occluded coronary arteries: the Total Occlusion Study of Canada (TOSCA). *Circulation* 1999;**100**:236–42.

104. Dzavik V, Carere RG, Teo KK, Knudtson ML, Marquis JF, Buller CE. An open design, multicentre, randomized trial of percutaneous transluminal coronary angioplasty versus stenting, with a heparin-coated stent, of totally occluded coronary arteries: rationale, trial design and baseline patient characteristics. *Can J Cardiol* 1998;**14**:825–32.

105. Hoher M, Wohrle J, Grebe OC, Kochs M, Osterhues HH, Hombach V, *et al.* A randomized trial of elective stenting after balloon recanalization of chronic total occlusions. *J Am Coll Cardiol* 1999;**34**:722–9.

106. Sievert H, Rodhe S, Utech A, Schulze R, Scherer D, Merle H, *et al.* Stent or angioplasty after recanalization of chronic coronary occlusions? (The SARECCO trial). *Am J Cardiol* 1999;**84**:386–90.

107. Rodriguez A, Ayala F, Bernardi V, Santaera O, Marchand E, Pardinas C, *et al.* Optimal coronary balloon angioplasty with provisional stenting versus primary stent (OCBAS). *J Am Coll Cardiol* 1999;**32**:1351–7.

108. Knight CJ, Curzen N, Groves PH, Patel DJ, Goodall AH, Wright C, *et al.* Stenting suboptimal results following balloon angioplasty significantly reduces restenosis: results of a single centre randomised trial. *Circulation* 1997;**96** (Suppl. 1):1–709.

109. Bilodeau L, Schreiber T, Hilton JD, Rosenblum S, Mehta S, McIvor M, *et al.* The wallstent in native coronary arteries (WIN) multicentre randomized trial: in-hospital acute results. *Eur Heart J* 1998; **19**(Abstract Suppl. August):48.

110. Witowski W, Ruzyllo W, Gil R, Purzycki Z, Kosmider M, Polonski L, *et al.* A randomized comparison of elective stenting versus balloon angioplasty with two years follow-up. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):136

111. Fluck DS, Chenu P, Street J, Balcon R, Layton CA. Is "bail-out" stenting the effective option? The widest trial. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):26.

112. Lotan C, Hendler A, Turgeman Y, Ayzenberg O, Beyar R, Disegni E, *et al.* The STOP study: a randomized multicenter Israeli study for Stents in Total Occlusion and restenosis Prevention – final report. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):156.

113. Guerin Y, Chevalier B, Tron C, Commeau P, Brunel P, Metzger JP, *et al.* Preliminary results of a randomized study between balloon versus stent in chronic coronary occlusion. *Circulation* 1997;**96**(Suppl. 1):1–268.

114. Serruys PW, de Bruyne B, Gurne O, Pijls N, Belardi J, van Es GA, *et al.* DEBATE II: "DESTINIsation" of the DEBATE II trial data. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):650.

115. Serruys PW, de Bruyne B, Sousa E, Piek JJ, Muramatsu T, Vrints C, *et al.* DEBATE II – final results of the 6-month follow-up. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):371.

116. Weaver WD. Optimal angioplasty versus primary stenting (OPUS). *J Am Coll Cardiol* 1999;**34**:1.

117. de Bruyne B, Groothuis W, Sousa E, Seabra-Gomes R, Vrints C, Piek JJ, *et al.* DEBATE II: a randomized study to evaluate provisional stenting after guided balloon angioplasty. *Circulation* 1998;**98**(Suppl. 1):1–498.

118. Sievert H, Rohde S, Utech A, Schulze R, Spies H, Ensslen R, *et al.* Stent implantation after successful balloon angioplasty of a chronic coronary occlusion (SARECCO): 2 years follow-up. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):137.

119. Rodriguez AE, Bernardi V, Fernandez M, Mauvecin C, Ayala F, Santaera O, *et al.* In-hospital and late results of coronary stents versus conventional balloon angioplasty in acute myocardial infarction (GRAMI) trial. *Am J Cardiol* 1998;**81**:1286–91.

120. Rodriguez AE, Santaera O, Grinfeld L, Bernardi V, Baldi J, Navia J, *et al.* Argentine randomized study optimal coronary balloon angioplasty and stenting versus coronary bypass surgery in multiple vessel disease (ERACI II): acute and mid term outcome. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):137.

121. Goy J-J, Kaufman U, Bertel O, Gaspardone A, Meier B, Garachemani A, *et al.* Design and acute results of the SIMA trial. *Circulation* 1998;**98** (Suppl. 1):1–349.

122. Spyrantis N, Diegeler A, Lauer B, Hambrecht R, Mohr F-W, Schuler G. Minimal invasive bypass surgery versus stent implantation in proximal high-grade lesions of the left anterior descending coronary artery. *Eur Heart J* 1999;**20**(Abstract Suppl. August/September):136.

123. Antoniucci D, Santoro G, Bolognese L, Valenti R, Trapani M, Fazzini P. A clinical trial comparing primary stenting of the infarct related artery with optimal primary angioplasty for acute myocardial infarction. *J Am Coll Cardiol* 1998;**31**:1234–9.

124. Suryapranata H, van't Hof A, Hoorntje J, de Boer M, Zijlstra F. Randomised comparison of coronary stenting with balloon angioplasty in selected patients with acute myocardial infarction. *Circulation* 1998;**97**:2502–5.

125. Saito S, Hosokawa G, Tanaka S, Nakamura S. Primary stent implantation is superior to balloon angioplasty in acute myocardial infarction: final results of the primary angioplasty versus stent implantation in acute myocardial infarction (PASTA) trial. *Cathet Cardiovasc Intervent* 1999;**48**:262–8.

126. Grines CL, Cox DA, Garcia E, Stone G, Mattos L, Katz S, *et al.* Stent PAMI: primary endpoint results of a multicenter randomized trial of heparin coated stenting vs primary PTCA for AMI. *Circulation* 1998;**98**(Suppl. 1):1–22.

127. Scheller B, Hennen B, Severin-Kneib S, Markwirth T, Doerr T, Berg G, *et al.* Follow-up of the PSAAMI study population (primary stenting vs angioplasty in acute myocardial infarction) [online]. Abstract from the 48th Annual Scientific Session. American College of Cardiology, New Orleans, Louisiana. March 7–10 1999. Abstract No. 1038-95. Available from: http://ex2.excerptamedica.com/99acc/abstracts/abs1038-96.html

128. Maillard L, Hamon M, Khalife K, Steg PG, Beygui F, Guermonprez JL, *et al.* A comparison of systematic stenting and conventional balloon angioplasty during primary PTCA for acute myocardial infarction. *J Am Coll Cardiol* 2000; in press.

129. Serruys PW, Sousa E, Belardi J, Nobuyoshi M, Probst P, Gulba DC, *et al.* BENESTENT-II trial: subgroup analysis of patients assigned either to angiographic and clinical follow-up or clinical follow-up alone. *Circulation* 1997;**96**(Suppl. 1): 1-653-54.

130. The New NHS Reference Costs [online]. Accessed 30/11/99. London: NHS Executive; [date unknown]. Available from: http:www.doh.gov.uk/nhsexec/refcosts.htm

131. McKenna M, Wheeldon N, Buxton M. Costing cardiac revascularisation for economic evaluation: micro-costing versus routine data? *Br J Med Econ* 1997;**11**:65–79

132. Nicholson T, Stein K. Low molecular weight heparins compared with unfractionated heparin for unstable angina and non-Q wave myocardial infarction. Southampton: Wessex Institute for Health Research and Development; 1999 (DEC Report No. 93).

133. Chase D, Best L, Milne R. Stents for coronary artery disease (CAD). Southampton: Wessex Institute for Health Research and Development; 1998 (DEC Report No. 87).

134. Jackson M, Wilkinson I, Ord K. Cost effectiveness of coronary artery stenting [copy of a presentation given at the Health Services Research Centre, University of Birmingham, Nov 1998].

135. Cotton JM, de Belder A, Wainwright RJ. Stenting strategies in coronary artery disease – a cost-effective analysis. *Heart* 1999;**81**(Suppl. 1):28.

136. Haywood GA, Turner M, Gilbert TJ, Burrell CJ. Cost effectiveness of intracoronary stents: a British perspective. *Heart* 1999;**81**(Suppl. 1):53.

137. Palmer N, Fort S, Starkey I, Shaw T, Northridge D. Should use of intracoronary stents during percutaneous revascularisation be restricted? [letter]. *Lancet* 1998;**351**:416–17.

138. Banz K, Schwicker D. Cost-effectiveness of Palmaz-Schatz stenting for patients with coronary artery disease in France. *J Invasive Cardiol* 1997;**9** (Suppl. A):17A–22A.

139. Banz K, Schwicker D. Cost-effectiveness of Palmaz-Schatz stenting for patients with coronary artery disease in Germany. *J Invasive Cardiol* 1997;**9** (Suppl. A):23A–28A.

140. Banz K, Schwicker D. Cost-effectiveness of Palmaz-Schatz stenting for patients with coronary artery disease in Italy. *J Invasive Cardiol* 1997;**9** (Suppl. A):29A–34A.

141. Banz K, Schwicker D. Cost-effectiveness of Palmaz-Schatz stenting for patients with coronary artery disease in the Netherlands. *J Invasive Cardiol* 1997;**9**(Suppl. A):35A–40A.

142. Banz K, Schwicker D. Cost-effectiveness of Palmaz-Schatz stenting for patients with coronary artery disease in Spain. *J Invasive Cardiol* 1997;**9** (Suppl. A):41A–46A.

143. Schwicker D, Banz K. New perspectives on the cost-effectiveness of Palmaz-Schatz coronary stenting, balloon angioplasty and coronary artery bypass surgery – a decision model analysis. *J Invasive Cardiol* 1997;**9**(Suppl. A):7A–16A.

144. Popma JJ, Lansky AJ, Laird JR, Leon MB. A critical appraisal of decision analytic models to evaluate the cost-effectiveness of stenting. *J Invasive Cardiol* 1997;**9**(Suppl. A):3A–6A.

145. Schwicker D, Banz K. New perspectives on the cost-effectiveness of Palmaz-Schatz coronary stenting, balloon angioplasty, and coronary artery bypass surgery. *J Invasive Cardiol* 1997;**9** (Suppl. A):47A–48A.

146. Van Hout B, van der Woude T, de Jaegere P, van den Brand H, van Es GA, Serruys PW, *et al.* Cost effectiveness of stent implantation versus PTCA: the BENESTENT experience. *Semin Intervent Cardiol* 1996;**1**:263–8.

147. Cohen D, Sukin C. Cost effectiveness of coronary interventions. *Heart* 1997;**78**(Suppl. 2):7–10.

148. Guidant. Industry submission to NICE. 1999.

149. Cohen DJ, Sukin CA. Evaluation of the cost-effectiveness of coronary stenting: a societal perspective. *Am Heart J* 1999;**137**:S133–S137.

150. Boston Scientific. Industry submission to NICE. 1999.

151. Farshid A, Leong B, Pitney M, McCredie R, Allan R. Impact of an aggressive stenting strategy on initial and one-year follow-up costs in patients undergoing coronary angioplasty. *Aust NZ Med J* 1999;**29**:243–8.

152. Peterson ED, Cowper PA, DeLong ER, Zidar JP, Stack RS, Mark DB. Acute and long-term cost implications of coronary stenting. *J Am Coll Cardiol* 1999;**33**:1610–18.

153. Kurbaan AS, Bowker TJ, Isley CD, Kunz RA, Sigwart U, Rickards AF. Is coronary stenting cost effective? A comparison of the CABRI Trial and NEXT Registry. *Circulation* 1998;**98**(Suppl. 1):1–500

154. Cohen DJ, Breall JA, Ho KK, Kuntz RE, Goldman L, Baim DS, *et al.* Evaluating the potential cost-effectiveness of stenting as a treatment for symptomatic single-vessel coronary disease. *Circulation* 1994;**89**:1859–74.

155. Di Mario C, Moses J, Anderson T, Bonan R, Muramatsu T, Colombo A, *et al.* Multicenter randomized comparison of early clinical events after primary stenting or balloon angioplasty in 619 patients. On behalf of the DESTINI CFR Study Group. *Circulation* 1998;**98**(Suppl. 1):1–228.

156. Cohen DJ, Taira D, Di Mario C, Colombo A, Kern MJ, Jacobs C, *et al.* In-hospital and 6-month follow-up costs of universal vs provisional stenting: results from the DESTINI trial. *Circulation* 1998;**98**(Suppl. 1):1–499

157. Toutouzas K, Stefanadis C, Tsiamis E. Stents coated by an autologous arterial graft: the first application in human coronary arteries. *J Am Coll Cardiol* 1998;**31**(Suppl.):351A.

158. Sato Y, Nosaka H, Kimura T, Nobuyoshi M. Randomized comparison of balloon angioplasty versus coronary stent implantation for total occlusion. *J Am Coll Cardiol* 1996;**27**(Suppl. A):152A.

159. Penn IM, Ricci DR, Almond DG, Lazzam C, Marquis J-F, Webb JG, *et al.* Coronary artery stenting reduces restenosis: final results from the Trial of Angioplasty and Stents in Canada (TASC)1. *Circulation* 1995;**92**(Suppl. 1):1–279.

160. Cohen DJ, Breall JA, Ho KK, Weintraub RM, Kuntz RE, Weinstein MC, *et al.* Economics of elective coronary revascularisation. Comparison of costs and charges for conventional angioplasty, directional atherectomy, stenting and bypass surgery. *J Am Coll Cardiol* 1993;**22**:1052–9.

Appendix 1

Manufacturers' submissions

All of the submissions were used in the review to look for new data that met the inclusion/exclusion criteria of the review for both effectiveness studies and economic evaluations.

The table below details those submissions with original data (not available elsewhere) that were used in the review.

TABLE 9 *Submissions with original data (not available elsewhere) used in the review*

Company	Effectiveness	Data extracted cost	Economic evaluation
Biocompatibles Ltd	–	✔	✔
Biotronik UK Ltd	✔ (SVS)	✔	–
Boston Scientific	–	✔	✔
Cook (UK) Ltd	–	–	–
Cordis	✔ (OPUS)	–	✔
Guidant Ltd	–	–	✔
Jomed UK Ltd	–	✔	–
Medtronic AVE	–	–	–
Sorin Biomedica UK Ltd	–	✔	–

Appendix 2

Effectiveness search strategy

TABLE 10 *Electronic databases searched*

Database	Years/date searched	Search strategy	Results	
			Total no. references	No. of RCTs found†
MEDLINE	1989–Nov 1999	See *Table 12*	199	19
BIDS ISI	1989–Nov 1999	Coronary + stent$ + trial$	302	4
EMBASE	1980–Sept 1999	See *Table 13*	209	0
HealthSTAR non-MEDLINE	1992–Sept 1999	Stents and coronary and trial	12	0
Cochrane Library	1999 Issue 4	Stents	266	0
York HTA	Sept 1999	Stent$	25	0
York DARE	Sept 1999	Stent$	14	0
American College of Cardiology conference abstracts	48th Scientific Session, 1999	Stents	224	6
Google web browser	Oct 1999	Stents	2128 (first 100 investigated)	2
Cardiosource (http://www.cardiosource.com)	Oct 1999	Stents	32	3
National Research Register	Nov 1999	Stent*	203	3

† *In addition to those found in MEDLINE*

TABLE 11 *Handsearch of conference abstracts/reviews*

Conference/review	Year	No. of RCTs found
Circulation **98**(17)	1998	9
Circulation **96**	1997	4
Circulation **94**(8)	1996	0
European Heart Journal **20**	1999	5
European Heart Journal **19**	1998	0
European Heart Journal **18**	1997	0
Coronary stenting current perspectives[75]	1998	2
Perleth M, Kochs G. Systematic review[51]	1999	4

TABLE 12 *MEDLINE effectiveness search strategy*

	Search history	Results
1	Randomized controlled trial.pt.	119,196
2	Randomized controlled trials.sh.	13,626
3	Random allocation.sh.	39,176
4	Double blind method.sh.	56,793
5	Single blind method.sh.	4,547
6	1 or 2 or 3 or 4 or 5	169,645
7	Animal.sh.	2,922,596
8	Human.sh.	6,575,986
9	7 not (7 and 8)	2,323,349
10	6 not 9	160,831
11	Exp stents/	8,056
12	Exp angioplasty, transluminal, percutaneous coronary/ or exp atherectomy, coronary/ or exp coronary aneurysm/ or exp coronary angiography/ or exp coronary arteriosclerosis/ or exp coronary artery bypass/ or exp coronary care units/ or exp coronary circulation/ or exp coronary disease/ or exp coronary thrombosis/ or exp coronary vasospasm/ or exp coronary vessel abnormalities/ or exp coronary vessels/ or exp internal mammary-coronary artery anastomosis/	155,820
13	10 and 11 and 12	164
14	STENT$.mp	11,636
15	10 or 14	11,636
16	10 and 12 and 15	199

TABLE 13 *EMBASE search strategy*

	Search history	Results
1	Exp randomized controlled trial/	39,332
2	Exp controlled study/	888,862
3	Randomised controlled trial$.tw.	1,439
4	Exp randomisation/	2,454
5	Exp double blind procedure/	32,633
6	Exp single blind procedure	2,400
7	1 or 2 or 3 or 4 or 5 or 6	900,571
8	Exp stent/ or 'stents'.mp.	7,891
9	Exp coronary artery/ or exp coronary artery aneurysm/ or exp coronary artery anomaly/ or exp coronary artery atherosclerosis/ or exp coronary artery blood flow/ or exp coronary artery bypass graft/ or exp coronary artery bypass surgery/ or exp coronary artery circumflex branch/ or exp coronary artery collateral circulation/ or exp coronary artery constriction/ or exp coronary artery dilatation/ or exp coronary artery disease/ or exp coronary artery fistula/ or exp coronary artery ligation/ or exp coronary artery obstruction/ or exp coronary artery pressure/ or exp coronary artery recanalisation/ or exp coronary artery spasm/ or exp coronary artery surgery/ or exp coronary artery thrombosis/ or exp coronary blood vessel/ or exp coronary care unit/ or exp coronary haemodynamics/ or exp coronary reperfusion/ or exp coronary risk/ or exp coronary sinus blood flow/ or exp coronary vascular resistance/ or exp coronary vasodilating agent/ or exp coronary vessel malformation/ or exp left anterior descending coronary artery/ or exp left coronary artery/ or exp right coronary artery/ or exp transluminal coronary angioplasty.	147,626
10	7 and 8 and 9	410
11	Limit 10 to yr=1997-2000	235
12	Limit 11 to human	209

Appendix 3

Cost search strategy

TABLE 14 *Electronic databases searched*

Database	Years/date searched	Search strategy	Results	
			Total no. references	No. cost studies found*
MEDLINE	1960–Nov 1999	See *Table 16*	35	0
NHSEED	Nov 1999	Stent$	41	1
MEDLINE effectiveness search	See effectiveness search strategy (appendix 2)	See effectiveness search strategy (appendix 2)	See effectiveness search strategy (appendix 2)	2
HM Government, NHS Executive – reference costs[130]	1999	N/A	N/A	1

**In addition to MEDLINE cost search (*Table 16*)*

N/A, not applicable

TABLE 15 *Handsearch of conference abstracts/reviews*

Conference/review	Year	No. of cost studies found*
West Midlands DEC coronary artery stents[1]	1998	1
Wessex DEC coronary artery stents[133]	1998	1
Wessex DEC LMW heparins[132]	1999	1
European Heart Journal **20**	1999	2

**In addition to MEDLINE cost search (*Table 16*)*

LMW heparins, low molecular weight heparins

TABLE 16 *MEDLINE cost search strategy*

	Search history	Results
1	Exp 'costs and cost analysis'/ or exp direct service costs/ or exp health care costs / or exp hospital costs/	15,858
2	Exp stents/ or 'stent'.mp	4,987
3	Exp angioplasty, transluminal, percutaneous coronary/ or exp atherectomy, coronary/ or exp coronary aneurysm/ or exp coronary angiography/ or exp coronary arteriosclerosis/ or exp coronary artery bypass/ or exp coronary care units/ or exp coronary circulation/ or exp coronary disease/ or exp coronary thrombosis/ or exp coronary vasospasm/ or exp coronary vessel abnormalities/ or exp coronary vessels/ or exp internal mammary-coronary artery anastomosis/	24,555
4	1 and 2 and 3	43
5	Limit 4 to English language	35

Appendix 4

Economic evaluation search strategy

TABLE 17 *Electronic databases searched*

Database	Years/date searched	Search strategy	Results	
			Total no. references	No. cost–utility/ cost-effectiveness studies found*
MEDLINE	1960–Nov 1999	See *Table 19*	59	5
NHSEED	Nov 1999	Stent$	41	1
MEDLINE effectiveness search	See effectiveness search strategy (appendix 2)	See effectiveness search strategy (appendix 2)	See effectiveness search strategy (appendix 2)	1

**In addition to MEDLINE cost-effectiveness search (*Table 19*)*

TABLE 18 *Handsearch of systematic reviews*

Review	Year	No. cost–utility/cost-effectiveness studies found*
West Midlands DEC, coronary artery stents[1]	1998	4
Perleth M, Kochs G. Systematic review[51]	1999	1
Industry submissions	1999	4

**In addition to MEDLINE cost-effectiveness search (*Table 19*)*

TABLE 19 *MEDLINE cost-effectiveness search strategy*

	Search history	Results
1	Exp stents/ or 'stent'.mp	10,178
2	Exp angioplasty, transluminal, percutaneous coronary/ or exp atherectomy, coronary/ or exp coronary aneurysm/ or exp coronary angiography/ or exp coronary arteriosclerosis/ or exp coronary artery bypass/ or exp coronary care units/ or exp coronary circulation/ or exp coronary disease/ or exp coronary thrombosis/ or exp coronary vasospasm/ or exp coronary vessel abnormalities/ or exp coronary vessels/ or exp internal mammary-coronary artery anastomosis/	156,431
3	1 and 2	2,477
4	exp cost allocation/ or exp cost control/ or exp cost of illness/ or exp cost savings/ or exp cost sharing/ or exp cost-benefit analysis/ or exp 'costs and cost analysis'/ or exp technology, high-cost/	60,221
5	exp cost-benefit analysis/ or exp health care costs or exp quality of life/ or exp quality-adjusted life years/	44,540
6	4 or 5	78,748
7	3 and 6	59

Appendix 5

Tables of results of review of effectiveness

TABLE 20 *Excluded RCTs: IHD, stent versus PTCA*

Study acronym or author	Patient group	Intervention	Comparator(s)	Reason for exclusion
ADVANCE[56]	IHD	Stent	PTCA	No patient follow-up information
BESMART[57]	IHD in small arteries	Stent (Bestent)	PTCA	Allocation of patients not complete
BOSS[58]	IHD	Stent (Palmaz-Schatz)	PTCA (Optimal)	Allocation of patients not complete
COAST[59]	Details not available	Stent (coated Jostent)	(a) PTCA (b) Non-coated stent	Allocation of patients not complete
DESTIN[160,155,156]	IHD	Elective stent	PTCA with provisional stent	Results for only some of the trial participants
FROST[61]	IHD	Stent	Optimal PTCA	Results at 6 months for only half trial participants
GIPSI[62]	IHD	Stent	PTCA (gradual inflation at optimum pressure)	Allocation of patients not complete
MAJIC[63]	IHD with CO	Stent (Wiktor)	PTCA	Allocation of patients not complete
RAP[64]	IHD in small arteries	Stent (Bestent)	PTCA	Allocation of patients not complete
Sato[158]	IHD with CO	Stent	PTCA	No patient numbers in either arm
SISA[65]	IHD in small arteries	Stent (Bestent)	PTCA	Allocation of patients not complete
SOAR[66]	IHD	Stent	PTCA	Allocation of patients not complete
STENT-BY[67]	IHD	Stent (Palmaz-Schatz)	PTCA	No patient numbers in each arm
SVS[68]	IHD in small arteries	Stent	PTCA	Allocation of patients not complete
TASC[169,159]	IHD	Stent (Palmaz-Schatz)	PTCA	No patient numbers in each arm

CO, chronic coronary occlusion

TABLE 21 *Excluded RCTs: IHD, stent versus CABG*

Study acronym or author	Patient group	Intervention	Comparator(s)	Reason for exclusion
ARTS[70]	IHD (SA/UA)	Stent (Palmaz-Schatz Crown + Crossflex, multiple)	CABG	No details of number of patients in each group (N.B. industry submission data)
AWESOME[71]	IHD (unstable myocardial ischaemia)	Stents, rotablator or laser	CABG	Allocation of patients not complete
MIDCAB[72]	IHD	Stent	Minimally invasive CABG	Allocation of patients not complete
SOS[73]	IHD	Stent	CABG or minimally invasive CABG	Allocation of patients not complete

SA, stable angina; UA, unstable angina

TABLE 22 *Excluded RCTs: AMI, stent versus PTCA*

Study acronym or author	Patient group	Intervention	Comparator(s)	Reason for exclusion
BESSAMI[74]	AMI	Stent (heparinised Wiktor)	PTCA	Allocation of patients not complete
CADILLAC[75]	AMI	Stent ± abciximab	PTCA ± abciximab	Allocation of patients not complete
PRISAM[76]	AMI	Stent (Wiktor)	PTCA	Allocation of patients not complete

TABLE 23 *Excluded RCTs: IHD, other comparisons*

Study acronym or author	Patient group	Intervention	Comparator(s)	Reason for exclusion
Rodriguez *et al.*[77]	IHD	Stent (Giantunco-Roubin)	Medical treatment	Trial of stent versus medical
GRACE[75]	IHD with failed PTCA	Stent (Gianturco-Roubin)	PTCA (prolonged perfusion balloon)	Allocation of patients not complete
TASC II[78]	IHD with failed PTCA	Stent (Palmaz-Schatz)	PTCA (prolonged perfusion balloon)	Trial of bailout stenting (not elective stenting)

TABLE 24 *Included RCTs: IHD, stents versus PTCA – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
BENESTENT[80–84]	IHD SA	Single and multiple, new lesion, native coronary artery < 15 mm long, > 3 mm diameter	Ostial, bifurcation, severe vessel tortuosity, presence of thrombus, contraindication to anticoagulation/ antiplatelet treatment	Stent (Palmaz-Schatz)	Aspirin, dipyridamole, dextran, heparin, warfarin, calcium antagonists	PTCA	Aspirin, dipyridamole, heparin, calcium antagonists
STRESS[85–89]	IHD	New lesions, native coronary artery, > 70% stenosis, < 15 mm long, > 3 mm diameter	MI within 7 days, contraindications to anticoagulation. LVEF < 40%. Thrombus, multiple focal lesions, diffuse disease, serious disease in L main artery, ostial, severe vessel tortuosity	Stent (Palmaz-Schatz)	Aspirin, dipyridamole, calcium antagonists, dextran 40, heparin, warfarin	PTCA	Aspirin
STRESS II[79]	IHD	New lesions, native coronary artery, > 70% stenosis, < 15 mm long, > 3 mm diameter	MI within 7 days, contraindications to anticoagulation. LVEF < 40%. Thrombus, multiple focal lesions, diffuse disease, serious disease in L main artery, ostial, severe vessel tortuosity	Stent (Palmaz-Schatz)	Aspirin, dipyridamole, calcium antagonists, dextran 40, heparin, warfarin	PTCA	Aspirin
Eeckhout *et al.*[90]	IHD Angina	Symptomatic and documented angina, new onset stenosis of R coronary artery only	Contraindication to anticoagulation, evolving MI, previous extensive inferior myocardial necrosis, at risk of loss to follow-up, poor candidates for CABG, vessel < 3 mm diameter, > 20 mm long, ostial, thrombus, vessel tortuosity	Stent (Wiktor)	Aspirin, nifedipine, heparin, acenocoumarol, dipyridamole	PTCA	Aspirin, nifedipine, heparin, calcium channel blocker
Versaci *et al.*[91]	IHD	Angina, ± documented myocardial ischaemia, new lesion in proximal LAD artery < 15 mm long, > 3 mm diameter, LVEF > 40%	MI within 1 month, contraindication to anticoagulation, ostial, major branch within target lesion, total occlusion, severe vessel tortuosity	Stent (Palmaz-Schatz)	Aspirin, diltiazem, heparin, warfarin	PTCA	Aspirin, diltiazem, heparin

LVEF = left ventricular ejection fraction (measure of heart performance); L, left; R, right

continued

TABLE 24 contd *Included RCTs: IHD, stents versus PTCA – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
START[92–94]	IHD	Angina or objective evidence of ischaemia. New lesion, stenosis > 70%, < 15 mm long, > 3 mm diameter, > 1 lesion per patient allowed to be randomised	Ostium, side branch > 2.5 mm, total occlusion, heavy calcification, vessel tortuosity, stenosis of L main, > 25% cardiogenic shock, life-threatening condition, MI within 1 week, contraindication to anticoagulation	Stent (Palmaz-Schatz)	Aspirin, heparin, dipyridamole, calcium channel antagonist, dextran 40, warfarin	PTCA	Not clearly reported
Knight *et al.*[108]	IHD	Suboptimal result of PTCA	NR	Stent (Palmaz-Schatz)	NR	PTCA	NR
BENESTENT II[27]	IHD	Stable or unstable angina, new lesions (≥ 1) suitable for CABG < 18 mm long > 3 mm diameter	Contraindication to antiplatelet treatment, L main lesion, bifurcation, graft vessel lesion, LVEF < 30%, evolving MI within 1 week	Heparin-coated stent (Palmaz-Schatz)	Heparin, ticlopidine, aspirin	PTCA	Heparin, aspirin
RSSG[95]	IHD	Single lesion re-narrowed following previous successful PTCA > 50% < 10 mm long. Angina or abnormal stress test	None	Stent (Palmaz-Schatz)	Aspirin, heparin, phenprocoumon	PTCA	Aspirin, heparin
WIN[51,109]	IHD	New or restenotic lesions, > 3 mm diameter, < 22 mm long	Ostial, bifurcation lesions, LVEF < 35%	Stent (Wall stent)	NR	PTCA	NR
AS Trial[110]	IHD	Single new lesions, native arteries	None	Stent (Palmaz-Schatz)	Ticlopidine, ASA (probably aspirin)	PTCA	Ticlopidine, ASA (probably aspirin)

LVEF = left ventricular ejection fraction (measure of heart performance); L, left; R, right; NR, not reported

continued

TABLE 24 contd *Included RCTs: IHD, stents versus PTCA – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
WIDEST[111]	IHD	New lesion, native artery	NR	Stent (Wiktor)	Decided by physician	PTCA	Decided by physician
SAVED[96]	IHD in vein graft	Angina or objective evidence of myocardial ischaemia. Stenosis > 60%, diameter 3.0–5.0 mm	MI within 7 days. Contraindications to anticoagulation, LVEF > 25%, diffuse disease needing > 2 stents, thrombus, outflow obstruction of graft	Stent (Palmaz-Schatz)	Aspirin, dipyridamole, dextran 40, heparin, warfarin	PTCA	Aspirin (if bailout, had warfarin and dipyridamole)
EPISTENT[41,97]	IHD	Stenosis > 60% target vessel	Unprotected L main stem artery, bleeding diathesis, intracranial neoplasm, CVA within 2 years, uncontrolled hypertension, recent surgery, PTCA within 3 months, taking warfarin	Stent + abciximab (Palmaz-Schatz and others not specified)	Aspirin, ticlopidine, heparin	PTCA + abciximab	Aspirin, ticlopidine, heparin
SICCO[98–100]	IHD with occluded artery	Aged > 18 years, PTCA of occluded artery (total + functional; i.e. TIMI 0 or 1), native artery, previously undilated lesion, reference diameter > 2.5 mm	Occlusions < 2 weeks old, unable to take anticoagulation, in another RCT, unlikely to return for follow-up, reference diameter < 2.5 mm, indication for bailout stenting (major dissection), previously dilated segments, complex anatomy, poor distal runoff, thrombus	Stent (Palmaz-Schatz) Randomised after PTCA completed	Aspirin, heparin, dextran, dipyridamole, warfarin, calcium channel antagonists	No stent	Aspirin, heparin, calcium channel antagonists
GISSOC[101]	IHD with occluded artery	Absolute or functional occlusion (TIMI 0 or 1), all suitable for CABG (Occlusion duration from angiographic and/or clinical follow-up)	AMI within 30 days, acute angina at rest 7 days, contraindication to anticoagulation, total occlusions at site of previous PTCA, complex dissection, occlusions for < 30 days, significant L main disease, < 3 mm diameter, > 13 mm long, tortuous, side branch	Stent (Palmaz-Schatz) Randomised after PTCA completed	Aspirin, calcium channel blocker, heparin, warfarin, ± dextran, dipyridomole	No stent	Aspirin, calcium channel blocker, heparin

LVEF, left ventricular ejection fraction (measure of heart performance); L, left; R, right; NR, not reported; CVA, cerebro-vascular accident (stroke); TIMI, Thrombolysis In Myocardial Infarction flow grade: 0 (poor) – 4 (good)

continued

TABLE 24 contd *Included RCTs: IHD, stents versus PTCA – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
Hancock *et al.*[102]	IHD with CO	Complete obstruction, TIMI 0 or 1, > 3 days old, successful initial PTCA result with TIMI grade 3 flow distal to occlusion	Bailout, stent occlusions, poor distal flow after PTCA, stent thrombosis, graft (CABG), AMI, thrombus, < 3 mm diameter, contraindication to anticoagulation	Stent (Palmaz-Schatz) Randomised after PTCA completed	Heparin, aspirin, warfarin	No stent	Heparin, aspirin
TOSCA[103,104]	IHD with total CO	TIMI 0 or 1. > 3 mm diameter, native artery, suitable for stenting, can cross lesion with guidewire	< 72 hours from onset of ST elevation, thrombus, previously revascularised occlusion, uncontrolled heart failure or shock, unsuitable for 6 month angioplasty, child-bearing potential	Heparin-coated stent (Palmaz-Schatz)	Aspirin, ticlopidine (in 93% of patients), abciximab (in 3% of patients)	PTCA	Aspirin, ticlopidine (in 57% of patients), abciximab (in 3% of patients)
SPACTO[105]	IHD with CO	TIMI = 0 only, event > 28 days, occlusion diagnosed by angiography, myocardial scentigraphy, reference diameter < 2.7 mm	Contraindication to anticoagulation, renal failure, recent CVA	Stent (Wiktor-GX) Randomised after PTCA completed	Aspirin, heparin, phenprocoumon (in 40% patients), ticlopidine (in 60% patients)	No stent	Aspirin, heparin, ticlopidine, phenprocoumon. (Fewer patients than in stent group, $p < 0.01$)
SARECCO[106]	IHD with CO	TIMI grade 0, for > 1 wk estimated from clinical history or angiography, vessel > 2.5 mm diameter, (long lesions, diffuse, thrombus included)	Contraindication to anticoagulation, AMI, CABG, severe vessel tortuosity, infarction lesions, residual stenosis > 50% after PTCA	Stent (mixed types) Randomised after PTCA completed	Aspirin, heparin, ticlopidine	No stent	Aspirin, heparin
STOP[112]	IHD with CO	CO > 10 days	NR	Stent (AVE Micro stent) Randomised after PTCA completed	NR	No stent	NR

continued

TABLE 24 contd *Included RCTs: IHD, stents versus PTCA – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
CORSICA[113]	IHD with CO	> 15 days lesion, stable + satisfactory results of PTCA	Not clearly reported	Stent (Palmaz-Schatz) Randomised after PTCA completed	Aspirin, ticlopidine	No stent	Aspirin, ticlopidine
OCBAS[107]	IHD (symp-tomatic)	Successful PTCA with good immediate angiographic result, (i.e. residual diameter stenosis < 30%, no dissection)	Lesions > 20 mm long, reference diameter < 2.5 mm, diffuse or severe L main disease, severe vessel tortuosity, acute complications from PTCA, suboptimal PTCA result, initial stent treatment, contra-indications to anticoagulant/anti-platelet treatment, non-cardiac illness, < 1 year life expectancy, in another RCT	Stent (mixed types) Randomised after stable PTCA result obtained	Aspirin, heparin, ticlopidine, calcium channel antagonists	Repeat PTCA and stent if deterioration (provisional stenting)	Aspirin, heparin, ticlopidine, calcium channel antagonists
DEBATE II[114,115,117]	IHD	Eligible for angioplasty or stent, M + F, aged 18–150 years	NR	Stent (not specified)	NR	'Guided PTCA'	NR
OPUS[116] *	IHD	Single vessel, < 20 mm long, > 3 mm diameter, > 70% stenosis, potentially treatable by PTCA or stent, age 21–81 years	MI within < 24 hours	Stent (Palmaz-Schatz) Randomised after stable PTCA results obtained	Not clearly reported	Repeat PTCA and stent if deterioration (provisional stenting)	Not clearly reported

TABLE 25 *Included RCTs: stents vs PTCA for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
BENESTENT[80–84]	NR	520	262 (259)*	258 (257)	57.5 19% F	SA, 100% UA, 0% PMI, 19.4% AMI, – CO, –	No significant differences	3/262 (1.1%) 24/259 (9.3%)	1/258 (0.4%) 16/257 (6.2%)
STRESS[85–89]	NR	410	207 (205)	203 (202)	60 22% F	SA, 52.6% UA, 47.4% PMI, 73/407 AMI, – CO, –	More men in stent group ($p < 0.05$)	2/207 (1.0%) 8/205 (3.9%)	1/203 (0.5%) 21/202 (10.4%)
STRESS I + II[79]	NR	189	100	89	NR	SA, – UA, – PMI, – AMI, – CO, –	NR	NR	NR
Eeckhout *et al.*[90]	204	84	42	42	58 19% F	SA, 85.7% UA, 14.3% PMI, 36.8% AMI, – CO, –	No significant differences	0 2/42 (4.8%)	0 3/42 (7.1%)
Versaci *et al.*[91]	204	120	60	60	56.5 12.5% F	SA, 82.5% UA, 17.5% PMI, 26.5% AMI, 0% CO, 0%	No significant differences	2/60 (3.3%) 3/60 (5.2%)	2/60 (3.3%) 4/60 (6.9%)

**In brackets, number on which results were reported (i.e. different from number randomised)*

PMI, previous myocardial infarction

continued

TABLE 25 contd *Included RCTs: stents vs PTCA for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
START[92–94]	NR	452	229	223	58.5 14% F	SA, – UA, 72% PMI, 32% AMI, 0% CO, 0%	No particular differences between groups	NR	NR
Knight *et al.*[108]	143	77	37	38	59 22% F	SA, – UA, – PMI, – AMI, – CO, –	NR	NR	NR
BENESTENT II[27]	NR	827 (823)*	414 (413)	413 (410)	54.5 21.5% F	SA, 50.3% UA, 42.2% PMI, 14.1% AMI, – CO, – Other: Silent ischaemia, 6.2%	More women in stent group, older in PTCA group	1/414 (0.2%) 14/413 (3.4%)	3/413 (0.7%) 57/410 (13.9%)
RSSG[95]	NR	383	178	176	59.5 19.2% F	SA, – UA, 19.2% PMI, 39.0% AMI, – CO, –	No obvious significant differences	13/191 (6.8%) 12/178 (6.7%)	16/192 (8.3%) 2/176 (1.1%)
WIN[51,109]	NR	586	299	287	NR	SA, – UA, 83% PMI, – AMI, – CO, –	NR	NR	NR 94/287 (32.7%)

In brackets, number on which results were reported (i.e. different from number randomised)

continued

TABLE 25 contd *Included RCTs: stents vs PTCA for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
AS Trial[110]	NR	388	192	196	NR	SA, – UA, – PMI, – AMI, – CO, –	Well matched in clinical and angiographic parameters	NR	NR
WIDEST[111]	400 to be randomised	300	154	146	NR	SA, – UA, – PMI, – AMI, – CO, –	No significant differences	0 8/154 (5.2%)	0 46/146 (31.5%)
SAVED[96]	NR	220	110	110	66 19.5% F	SA, ?20.5% UA, 79.5% PMI, 69% AMI, – CO, –	Higher rate diabetics in PTCA group (p = 0.05)	2/110 (1.8%) 3/108 (2.8%)	3/110 (2.7%) 4/107 (3.7%)
EPISTENT[41,97]	NR	2399	794	796	59.5 24.8% F	SA, 43.9% UA, 55.5% PMI, 32.5% AMI, 16.5% (within 7 days) CO, – Other: 0.6% without angina	No significant differences	10/794 (1.3%) 21/794 (2.7%)	11/796 (1.4%) 154/796 (19.3%)
SICCO[98–100]	590 (from 3080 patients with PTCA)	Not stated	58	59	57.8 18% F	SA, 100% UA, – PMI, 62.4% AMI, – CO, 100%	No obvious differences	1.7%	Combined 2 (1.7%) 0%

continued

TABLE 25 contd *Included RCTs: stents vs PTCA for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
GISSOC[101]	111	Not stated	56	54	57.6 15.5% F	SA, 86.4% UA, 9.1% PMI, 68.2% AMI, – CO, 100% Other: no angina, 4.5%	Higher baseline previous MI, single vessel disease and left circumflex coronary artery occlusion in PTCA group, higher hypercholesterolaemia and RCA in stent group (NS)	0 0	1.8% 1.9%
Hancock *et al.*[102]	187	60	30	30	60.5 36.7% F	SA, – UA, – PMI, – AMI, – CO, 100%	NR	0 0	0 0
TOSCA[103,104]	738	Not stated	202	208	57.6 18.0% F	SA, 82.7% UA, – PMI, 67.1% AMI within 6 weeks, 30.2% CO, 100%	No significant differences	0 8/202 (4.0%)	0 20/208 (9.6%)
SPACTO[105]	223	85	42	43	62.2 28.9% F	SA, 90.6% UA, 9.4% PMI, 42.3% AMI, – CO, 100%	Significantly more women in stent group (p = 0.02)	0 1/42 (2.4%)	0 7/43 (16.3%)

NS, not statistically significant

continued

TABLE 25 contd *Included RCTs: stents vs PTCA for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
SARECCO[106]	NR	111	55	55	60.5 28.2% F	SA, NR UA, NR PMI, 49.1% AMI, – CO, 100%	None	0 1 (1.8%)	0 0
STOP[112]	NR	96	48	48	59.3 16.7% F	SA, – UA, – PMI, – AMI, – CO, –	NR	NR	NR
CORSICA[113]	NR	142	72	70	NR	SA, – UA, – PMI, – AMI, – CO, –	Baseline clinical + angiographic data including TIMI 0 and occlusion duration – no significant differences	NR	NR
OCBAS[107]	206	Not stated	57	59	57.2 16.4% F	SA, 10.3% UA, 80.2% PMI, 21.6% AMI, 9.5% CO < 1 month, 12.9%	No significant differences	0% 0%	0% 8/59 (13.5%)
DEBATE II[114,115,117]	626	620	97	523	NR	SA, – UA, – PMI, – AMI, – CO, –	NR	Combined 16/523 (3.1%) NR	

continued

TABLE 25 contd *Included RCTs: stents vs PTCA for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
DEBATE II[114,115,117]	626	383	189	194	NR	SA, – UA, – PMI, – AMI, – CO, –	NR	Combined 16/523 (3.1%) NR	
OPUS[116*]	NR	479	230	249	NR	SA, – UA, – PMI, – AMI, – CO, –	2 groups 'comparable' re demographics and cardiovascular risk factors	0 0	0 37%

**Some information from press release in Cordis industry submission*

TABLE 26 *Included RCTs: stents vs PTCA for IHD – design, quality and execution*

Study acronym or author	Multicentre?	Method of randomisation	Description of withdrawals and dropouts?	Jadad score	'Adjuncts' in intervention group, not received by control group	Departures from intervention indicated	Departures from control indicated
BENESTENT[80–84]	Yes	Block by telephone	Yes	3	1000 ml dextran infusion peroperatively; warfarin to achieve INR of 2.5 to 3.5 for 3 months postoperatively	5% received PTCA; 3% eCABG; 1% treated medically	5% received stent (most bailout); 1% eCABG
STRESS[85–89]	Yes	Block, sealed envelope	Yes	3	Dipyridamole 25 mg tds and calcium channel antagonist commenced preoperatively; dextran and possibly heparin peroperatively; dipyridamole and warfarin to achieve INR of 2.0 to 3.5 for 1 month postoperatively	3% received PTCA	6% received bailout stent
STRESS II[79]	Yes	Block, sealed envelope	No	1	As for STRESS	–	–
Eeckhout *et al.*[90]	No	Not stated	Yes	2	Higher dose aspirin (> 250 mg vs 100 mg), dipyridamole 25 mg tds and acenocoumarol to maintain INR > 2.5. All postoperatively for 6 months	2% received PTCA; 2% eCABG	7% received bailout stent
Versaci *et al.*[91]	No	Not stated	Yes	2	Warfarin to maintain INR at 2.5 to 3.5 for 3 months postoperatively	5% received eCABG	3% received bailout stent; 3% eCABG
START[92–94]	Yes	Sealed envelope	No	3	Procedures used in control group not precisely defined. Unable to assess whether the rigorous anticoagulation regimen used in stent group was also used in control group	1% received bailout stent (unclear what is meant by this); 1% eCABG	15% received bailout stent

eCABG, emergency CABG; INR, International Normalised Ratio

continued

TABLE 26 contd *Included RCTs: stents vs PTCA for IHD – design, quality and execution*

Study acronym or author	Multicentre?	Method of randomisation	Description of withdrawals and dropouts?	Jadad score	'Adjuncts' in intervention group, not received by control group	Departures from intervention indicated	Departures from control indicated
Knight *et al.*[108]	No	Not stated	No	1	No detail on procedures in intervention or control group	No information on crossovers	
BENESTENT II[27]	Yes	Block by telephone	Yes	3	Ticlopidine 25 mg od for 1 month postoperatively	1% received non-heparin coated stent; 2% PTCA; 1% eCABG	13% received bailout stent; 1% eCABG
RSSG[95]	Yes	Not stated	Yes	2	Phenprocoumon to maintain INR at 2.0 to 3.5 for 3 months postoperatively	1% received eCABG	6% received bailout stent; 1% eCABG
WIN[51,109]	Yes	Not stated	No	1	–	–	32.7% received stent
AS Trial[110]	Yes	Not stated	No	1	No apparent differences, but minimal detail on procedures in intervention or control group	No information on crossovers	
WIDEST[111]	Yes	Not stated	No	1	No detail on procedures in intervention or control group	2% 'crossovers' (presumed PTCA); 3% 'failures' (presumed eCABG)	30% received bailout stent, of whom 3% were 'failures' (presumed eCABG)
SAVED[96]	Yes	Not stated	Yes	2	Aspirin 325 mg and dipyridamole 75 mg per day preoperatively; dextran and heparin infusions peroperatively; warfarin and dipyridamole for 1 month post-operatively. (Bailout stents received the additional warfarin and dipyridamole postoperatively)	2% received PTCA; 1% eCABG	7% received bailout stent; 2% eCABG; 2% medical treatment
EPISTENT[41,97]	Yes	Telephone hotline	Yes	3	Ticlopidine 250 mg bd (at investigator's discretion)	3% not stented – no information on alternative treatments offered	19% received bailout stent

continued

TABLE 26 contd *Included RCTs: stents vs PTCA for IHD – design, quality and execution*

Study acronym or author	Multicentre?	Method of randomisation	Description of withdrawals and dropouts?	Jadad score	'Adjuncts' in intervention group, not received by control group	Departures from intervention indicated	Departures from control indicated
SICCO[98–100]	Yes	Block, sealed envelope	Yes	3	Dextran peroperatively; dipyridamole 75 mg tds and warfarin to maintain INR at 3.5 to 4.0 for 3 months postoperatively	2% not stented – no information on alternative treatments offered	No deviations from allocated control treatment
GISSOC[101]	Yes	Sealed envelope	Yes	3	Warfarin to maintain INR at 2.5 to 3.5 for 1 month postoperatively. Dextran peroperatively, and dipyridamole postoperatively at investigator's discretion	No deviations from allocated intervention treatment	2% received bailout stent
Hancock *et al.*[102]	No	Not stated	Yes	2	Warfarin to maintain INR at > 2.0 postoperatively	No deviations from allocated intervention treatment	No deviations from allocated control treatment
TOSCA[103,104]	Yes	Not stated	Yes	2	Ticlopidine postoperatively (93% received this in intervention group; 57% in control)	4% 'crossover' (presumed PTCA)	10% 'crossover' (presumed bailout stent)
SPACTO[105]	Yes	Not stated	Yes	2	Ticlopidine postoperatively (57% received this in intervention group; 19% in control); phenprocoumon postoperatively (43% received this in intervention group; 16% in control)	2% not stented – no information on alternative treatments offered	16% received bailout stenting
SARECCO[106]	Yes	Not stated (separately for each centre)	Yes	2	No apparent differences, particularly in anticoagulation regimens	2% not stented – no information on alternative treatments offered	No deviations from allocated control treatment
STOP[112]	Yes	Not stated	No	1	No detail on procedures in intervention or control group	No information on crossovers	

continued

TABLE 26 contd *Included RCTs: stents vs PTCA for IHD – design, quality and execution*

Study acronym or author	Multicentre?	Method of randomisation	Description of withdrawals and dropouts?	Jadad score	'Adjuncts' in intervention group, not received by control group	Departures from intervention indicated	Departures from control indicated
CORSICA[113]	Yes	Not stated	No	1	No apparent differences, but minimal detail on procedures in intervention or control group	No deviations from allocated intervention treatment	4% received bailout stenting
OCBAS[107]	Yes	Sealed envelope	Yes	3	Ticlopidine 250 mg bd postoperatively for 1 month to patients receiving stents	No deviations from allocated intervention treatment	No deviations from allocated control treatment
DEBATE II[114,115,117]	Yes	Double randomisation process	Yes	1	No detail on procedures in intervention or control group	No apparent deviations from allocated intervention treatment, but minimal information	24% received bailout stent
DEBATE II[114,115,117]	Yes	Double randomisation process	Yes	1	No detail on procedures in intervention or control group	No information on crossovers	
OPUS[116] *	Yes	Not stated	No	1	No detail on procedures in intervention or control group	1% not stented – no information on alternative treatments offered	No deviations from allocated control treatment

*Some information from press release in the Cordis industry submission

TABLE 27 *Included RCTs: stents vs PTCA for IHD – short-term clinical results*

Study acronym or author	Procedure	Follow-up	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Major bleed	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
BENESTENT[80–84]	Stent	In hospital	259	0	0	9	–	5	1.9	4	1.5	35*	13.5
	PTCA		257	0	0	8	–	2	0.8	6	2.3	8*	3.1
STRESS[85–89]	Stent	14 days	205	0	0	11	5.4	6	2.9	NR		NR	
	PTCA		202	3	1.5	10	5.0	6	3.0	NR		NR	
STRESS II[79]	Stent	In hospital	100	STRESS II patients cannot be distinguished from STRESS patients, so no data reported here									
	PTCA		89										
Eeckhout *et al.*[90]	Stent	In hospital	42	0	0	0	0	NR		NR		6–9	–
	PTCA		42	0	0	0	0					1	2.3
Versaci *et al.*[91]	Stent	In hospital	60	0	0	1	–	1	1.7	0	0	4	6.7
	PTCA		60	0	0	1	–	0	0	1	1.7	0	0
START[92–94]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
Knight *et al.*[108]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
BENESTENT II[27]	Stent	30 days	413	0	0	11	–	5	1.2	6	1.5	5	1.2
	PTCA		410	1	0.2	13	–	4	1.0	9	2.2	4	1.0
RSSG[95]	Stent	In hospital	178	2	1.1	7	–	5	2.8	2	1.1	11*	6.2
	PTCA		176	1	0.6	2	–	1	0.6	1	0.6	1*	0.6
WIN[51,109]	Stent	30 days	299	1	0.4	16	7.0	NR		NR		NR	
	PTCA		287	1	0.4	13	5.5						
AS Trial[110]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
WIDEST[111]	Stent	In hospital	154	0	0	NR		NR		NR		NR	
	PTCA		146	1	0.7								

*$p < 0.05$, stent compared with PTCA

continued

TABLE 27 contd *Included RCTs: stents vs PTCA for IHD – short-term clinical results*

Study acronym or author	Procedure	Follow-up	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Major bleed	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
SAVED[96]	Stent	30 days	108	2	1.9	4	–	2	1.9	2	1.9	17*	15.7
	PTCA		107	2	1.9	8	–	1	0.9	7	6.5	5*	4.7
EPISTENT[41,97]	Stent	30 days	794	2	0.3	36	4.5	7	0.9	28	3.5	6	0.8
	PTCA		796	6	0.8	42	5.3	12	1.5	29	3.7	5	0.6
SICCO[98–100]	Stent	14 days	58	0	0	1	1.7	NR		NR		11*	19.0
	PTCA		59	0	0	0	0					1*	1.7
GISSOC[101]	Stent	In hospital	56	–	–	–	–	NR		NR		4	7.1
	PTCA		54	–	–	–	–					0	0
Hancock *et al.*[102]	Stent	In hospital	30	0	0	0	0	NR		NR		1	3.3
	PTCA		30	0	0	1	3.3					0	0
TOSCA[103,104]	Stent	In hospital	202	0	0	2	1.0	NR		16	7.9	NR	
	PTCA		208	0	0	1	0.5			4	2.4		
SPACTO[105]	Stent	In hospital	42	NR		NR		NR		NR		5	11.6
	PTCA		43									2	4.8
SARECCO[106]	Stent	14 days	55	0	0	1	1.8	0	0	1	1.8	0	0
	PTCA		55	0	0	1	1.8	1	1.8	0	0	0	0
STOP[112]	Stent	In hospital	48	NR		NR		NR		NR		NR	
	PTCA		48										
CORSICA[113]	Stent	30 days	72	NR		NR		NR		NR		NR	
	PTCA		70										
OCBAS[107]	Stent	In hospital	57	0	0	1	–	0	0	1	1.8	NR	
	PTCA		59	0	0	0	–	0	0	0	0		
DEBATE II[114,115,117]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
OPUS[116†]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												

*$p < 0.05$, stent compared with PTCA

†Some information from press release in the Cordis industry submission

TABLE 28 *Included RCTs: stents vs PTCA for IHD – short-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
BENESTENT[80–84]	Stent	18	6.9	NR		8	3.1	1	0.4
	PTCA	16	6.2			4	1.6	3	1.2
STRESS[85–89]	Stent	12	5.9	NR		5	2.4	9	4.4
	PTCA	16	7.9			8	4.0	4	2.0
STRESS II[79]	Stent	STRESS II patients cannot be distinguished from STRESS patients, so no data reported here							
	PTCA								
Eeckhout *et al.*[90]	Stent	3	7.1	NR		1	2.3	NR	
	PTCA	3	7.1			0	0		
Versaci *et al.*[91]	Stent	NR		NR		3	5.0	NR	
	PTCA					2	3.3		
START[92–94]	Stent	NR		NR		NR		NR	
	PTCA								
Knight *et al.*[108]	Stent	NR		NR		NR		NR	
	PTCA								
BENESTENT II[27]	Stent	16	3.9	NR		3	0.7	2	0.5
	PTCA	21	5.1			2	0.5	5	1.2
RSSG[95]	Stent	NR		5	2.8	4	2.2	NR	
	PTCA			1	0.6	1	0.6		
WIN[51,109]	Stent	22	9.6	NR		2	0.9	6	2.6
	PTCA	13	5.5			4	1.7	2	0.9
AS Trial[110]	Stent	NR		NR		NR		NR	
	PTCA								
WIDEST[111]	Stent	6	3.9	NR		NR		NR	
	PTCA	5	3.4						
SAVED[96]	Stent	6	5.6	NR		2	1.9	1	0.9
	PTCA	11	10.3			4	3.7	1	0.9
EPISTENT[41,97]	Stent	51	6.4	NR		6	–	NR	
	PTCA	73	9.2			5	–		
SICCO[98–100]	Stent	3	5.2	2	3.4	1	0.8	5	0.6
	PTCA	2	3.4	2	3.4	0	0.6	10	1.3
GISSOC[101]	Stent	NR		NR		–	1.7	1	1.7
	PTCA					–	0	2	3.4
Hancock *et al.*[102]	Stent	NR		NR		0	–	NR	
	PTCA					0	–		
TOSCA[103,104]	Stent	NR		1	0.5	1	0	0	0
	PTCA			5	2.4	0	0	1	3.3
SPACTO[105]	Stent	NR		NR		–	0.5	1	1.0
	PTCA					–	0	5	2.4
SARECCO[106]	Stent	NR		NR		0	–	NR	
	PTCA					0	–		

continued

TABLE 28 contd *Included RCTs: stents vs PTCA for IHD – short-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
STOP[112]	Stent	NR		NR		–	0	0	0
	PTCA					–	0	4	7.2
CORSICA[113]	Stent	0*	0	NR		NR		NR	
	PTCA	12*	17.1						
OCBAS[107]	Stent	NR		NR		0	–	NR	
	PTCA					–	–		
DEBATE II[114,115,117]	Stent	NR		NR		NR		NR	
	PTCA								
OPUS[116†]	Stent	NR		NR		–	0	NR	
	PTCA					–	–		

*$p < 0.05$, stent compared with PTCA

†*Some information from press release in the Cordis industry submission*

TABLE 29 *Included RCTs: stents vs PTCA for IHD – angiographic follow-up*

Study acronym or author	Period of follow-up (for MLD/ for restenosis)	Loss to follow-up (*n*/*n* on which results reported [%])		Stent MLD (mm) and % stenosis		PTCA MLD (mm) and % stenosis		Stent restenosis at follow-up		PTCA restenosis at follow-up	
		Stent	PTCA	Mean	SD/range	Mean	SD/range	*n*	%	*n*	%
BENESTENT[80–84]	In hospital/6 months	22/259 (8.5%)	17/257 (6.6%)	2.48* 22%	0.39 8%	2.05* 33%	0.33 8%	22*	8.5%	32*	12.5%
STRESS[85–89]	14 days/6 months	29/205 (14.1%)	44/202 (21.8%)	2.49* 19%*	0.43 11%	1.99* 35%*	0.47 14%	–	31.6%	–	42.1%
Eeckhout *et al.*[90]	In hospital/6 months	2/42 (4.8%)	2/42 (4.8%)	2.87* 25%*	2.66–2.96 23–28%	2.37* 32%*	2.33–2.61 29–35%	19	47.5%	14	35.0%
Versaci *et al.*[91]	In hospital/1 year	11/60 (18.3%)	16/60 (26.7%)	2.8* 17%*	0.6 14%	2.1* 34%*	0.5 13%	–	19%*	–	40%*
START[92–94]	In hospital/6 months	NR	NR	2.84 12%	0.5 10%	2.27 26%	0.5 13%	–	22%	–	37%
Knight *et al.*[108]	N/A/6 months	NR	NR	NR		NR		–	22%*	–	45%*
BENESTENT II[27]	30 days/12 months	Combined 66/823 (8.0%)		2.69* 16%*	0.37 7%	2.13* 29%*	0.39 8%	–	16%	–	31%
RSSG[95]	In hospital/6 months	22/178 (12.4%)	18/176 (10.2%)	3.02 6%	0.43 14%	2.23 30%	0.57 17%	–	18%*	–	32%*
WIN[51,109]	In hospital/6 months	NR	NR	2.56 65%	– –	2.34 66%	– –	–	39%	–	39%
AS Trial[110]	N/A/6 months	NR	NR	NR		NR		–	18.82%*	–	24.74%*
WIDEST[111]	N/A/1 year	Combined 37/300 (12.3%)		NR		NR		–	21.6%	–	17.3%
SAVED[96]	In hospital 30 days/6 months	22/108 (20.4%)	27/107 (25.2%)	2.81* 12%*	0.49 13%	2.16* 32%*	0.57 17%	32	37%	37	46%

*p < *0.05, stent compared with PTCA*

SD, standard deviation

continued

TABLE 29 contd *Included RCTs: stents vs PTCA for IHD – angiographic follow-up*

Study acronym or author	Period of follow-up (for MLD/ for restenosis)	Loss to follow-up (*n*/*n* on which results reported [%])		Stent MLD (mm) and % stenosis		PTCA MLD (mm) and % stenosis		Stent restenosis at follow-up		PTCA restenosis at follow-up	
		Stent	PTCA	Mean	SD/range	Mean	SD/range	*n*	%	*n*	%
EPISTENT[41,97]	NR	NR	NR	NR		NR		NR		NR	
SICCO[98–100]	14 days/6 months	21.7%	21.7%	2.78* 19%*	0.49 10%	2.13* 34%*	0.58 11%	17*	28%	43*	72%
GISSOC[101]	In hospital/9 months	11%	13%	2.46* 18.2%*	0.5 11.2%	1.91* 34.5%*	0.49 10.3%	–	32.0%	–	68.1%
Hancock *et al.*[102]	In hospital/6 months	1/30 (3.3%)	2/30 (6.7%)	3.3* –1.4%*	–	2.8* 20.3%*	–	8*	28%	16*	57%
TOSCA[103,104]	In hospital/6 months	0	0	2.45* 27%*	0.59 17%	1.97* 38%*	0.46 15%	–	55%*	–	70%*
SPACTO[105]	In hospital/6 months	Combined 21%		2.51* 14.6%*	0.41 10.3%	1.89* 29.4%*	0.53 10.9%	–	32.4%*	–	63.6%
SARECCO[106]	In hospital/4 months	?0	?0	2.54* 3%*	0.53 14%	1.85* 21%*	0.44 13%	13*	26%	32*	62%
STOP[112]	NR/6 months	Combined 27/96 (28.1%)		3.13*	–	2.42*	–	–	42.1%	–	71%
CORSICA[113]	NR	NR	NR	NR		NR		NR		NR	
OCBAS[107]	NR/6 months	1/57 (1.8%)	3/59 (5.1%)	2.7 12.8%	0.59 9%	2.2 22.1%	0.49 11%	11	19.6%	9	16.1%
DEBATE II[114,115,117]	NR	NR	NR	NR		NR		NR		NR	
OPUS[116 †]	NR	NR	NR	NR		NR		NR		NR	

* $p < 0.05$, *stent compared with PTCA*
† *Some information from press release in the Cordis industry submission*

TABLE 30 *Included RCTs: 'event rate' definitions*

Study acronym/author	Event rate definition
AS Trial[110]	Death, CVA, Q wave MI, TLR
BENESTENT[80–84]	All deaths, CVA, MI (Q and non-Q), CABG, PTCA of previously treated lesion
BENESTENT II[27]	Death, CVA, MI, CABG, PTCA, treatment crossover
CORSICA[113]	MACCE – not defined
DEBATE II[114,115,117]	MACE – not defined
Eeckhout *et al.*[90]	Death, CVA, MI, CABG, PTCA, treatment crossover
EPISTENT[41,97]	Any death, MI, severe ischaemia requiring CABG or PTCA
GISSOC[101]	Not defined
Hancock *et al.*[102]	Death, MI, CABG, PTCA
Knight *et al.*[108]	Not defined
OCBAS[107]	Death, MI, angina, TVR
OPUS[116*]	Death, MI, CABG, TVR
Restenosis SSG[95]	Death, MI, CABG, PTCA of target vessel
SARECCO[106]	Death, MI, CABG, PTCA, diameter stenosis > 50%
SAVED[96]	Death, MI, CABG, TVR
SICCO[98–100]	MACE – cardiac death, lesion related MI, lesion related CABG or PTCA, angiographic evidence of occlusion
SPACTO[105]	Death, MI, CABG, PTCA, recurrence of angina
START[92–94]	Sum of death, MI, TLR
STOP[112]	Not defined
STRESS[85–89]	All deaths, CVA, MI, CABG, PTCA
STRESS II[79]	As for STRESS
TOSCA[103,104]	Death, MI, any revascularisation
WIDEST[111]	Death, MI, vessel occlusion, CABG, PTCA
WIN[51,109]	MACE – not defined
Versaci *et al.*[91]	Death, MI, recurrence of angina
ERACI II[120]	MACE – death, MI, TLR by CABG or PTCA
SIMA[121]	Major cardiac events – not defined
Spyrantis *et al.*[122]	Not defined
ESCOBAR[124]	Death, MI, TVR by CABG or PTCA
FRESCO[123]	Death, MI, TVR from ischaemia
GRAMI[119]	Death, MI, repeat revascularisation
PAMI-Stent[126]	Death, CVA, MI, ischaemia driven TVR
PASTA[125]	Cardiac death, MI, TLR
PSAAMI[127]	Death, CVA, MI, ischaemic TVR
STENTIM II[128]	Death, MI, TLR by CABG or PTCA

**Some information from press release in the Cordis industry submission*

MACCE, major adverse coronary and cerebrovascular events; MACE, major adverse coronary events

TABLE 31 *Included RCTs: stents vs PTCA for IHD – medium-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Angina	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
BENESTENT[80–84]	Stent	6 months	259	2	0.8	11	–	7	2.7	4	1.5	88	34.0
	PTCA		257	1	0.4	10	–	4	1.6	6	2.3	68	26.5
STRESS[85–89]	Stent	8 months	205	3	1.5	13	6.3	7	3.4	NR		–	21.1
	PTCA		202	3	1.5	14	6.9	7	3.5			–	28.9
STRESS II[79]	Stent	10 months	100	STRESS II patients cannot be distinguished from STRESS patients, so no data reported here									
	PTCA		89										
Eeckhout *et al.*[90]	Stent	6 months	42	0	0	0	0	NR		NR		6	14.3
	PTCA		42	0	0	0	0					7	16.7
Versaci *et al.*[91]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
START[92–94]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
Knight *et al.*[108]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
BENESTENT II[27]	Stent	6 months	413	1	0.2	13	–	7	1.7	6	1.5	97	23.5
	PTCA		410	2	0.5	15	–	5	1.2	10	2.4	125	30.5
RSSG[95]	Stent	6 months	178	2	1.1	8	–	5	2.8	3	1.7	NR	
	PTCA		176	2	1.1	2	–	1	0.6	1	0.6		
WIN[51,109]	Stent	6 months	299	9	3.0	26	8.7	NR		NR		NR	
	PTCA		287	10	3.5	18	6.3						
AS Trial[110]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
WIDEST[111]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												

continued

TABLE 31 contd *Included RCTs: stents vs PTCA for IHD – medium-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Angina	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
SAVED[96]	Stent	8 months	108	–	7	NR		–	5	–	6	NR	
	PTCA	(4–8)†	107	–	9			–	4	–	11		
EPISTENT[41,97]	Stent	6 months	794	3	0.4	NR		NR		NR		NR	
	PTCA		796	14	1.8								
SICCO[98–100]	Stent	6 months	58	0	0	1	1.7	NR		NR		25*	56.9
	PTCA		59	0	0	0	0					45*	76.3
GISSOC[101]	Stent	9 months	56	0	0	–	–	0	0	NR		NR	
	PTCA		54	1	1.9	–	–	0	0				
Hancock *et al.*[102]	Stent	6 months	30	0	0	0	0	NR		NR		NR	
	PTCA		30	1	3.3	1	3.3						
TOSCA[103,104]	Stent	6 months	202	1	0.5	5	2.5	NR		NR		NR	
	PTCA		208	1	0.5	2	1.0						
SPACTO[105]	Stent	6 months	40/42	1	2.5	0	0	NR		NR		4	7.5
	PTCA		40/43	0	0	0	0					9	22.5
SARECCO[106]	Stent	4 months	55	0	0	1	1.8	0	0	1	1.8	NR	
	PTCA		55	0	0	1	1.8	1	1.8	0	0		
STOP[112]	Stent	6 months	?48	NR		NR		NR		NR		NR	
	PTCA		?48										
CORSICA[113]	Stent	6 months	72	NR		NR		NR		NR		NR	
	PTCA		70										
OCBAS[107]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
DEBATE II[114,115,117]	Stent	6 months	97	NR		NR		NR		NR		NR	
	PTCA		523										
DEBATE II[114,115,117]	Stent	6 months	189	NR		NR		NR		NR		NR	
	PTCA		194										
OPUS[116] ‡	Stent	6 months	230	NR		NR		NR		NR		NR	
	PTCA		249										

*p < *0.05, stent compared with PTCA*

†*From life-table; minimum and maximum length of follow-up*

‡*Some information from press release in the Cordis industry submission*

TABLE 32 *Included RCTs: stents vs PTCA for IHD – medium-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
BENESTENT[80–84]	Stent	52*	20.1	NR		13	5.0	26*	10.0
	PTCA	76*	29.6			10	3.9	53*	20.6
STRESS[85–89]	Stent	40	19.5	NR		10	4.9	23	11.2
	PTCA	48	23.8			17	8.4	25	12.4
STRESS II[79]	Stent	STRESS II patients cannot be distinguished from STRESS patients, so no data reported here							
	PTCA								
Eeckhout *et al.*[90]	Stent	10	23.8	NR		3	7.1	5	11.9
	PTCA	12	28.6			1	2.3	7	16.7
Versaci *et al.*[91]	Stent	NR		NR		NR		NR	
	PTCA								
START[92–94]	Stent	NR		NR		NR		NR	
	PTCA								
Knight *et al.*[108]	Stent	NR		NR		NR		NR	
	PTCA								
BENESTENT II[27]	Stent	53*	12.8	NR		6	1.5	33	8.0
	PTCA	79*	19.3			6	1.5	56	13.7
RSSG[95]	Stent	–	16.0*	16/156*	10.3	6/178	3.4	NR	
	PTCA	–	27.8*	42/158*	26.6	2/176	1.1		
WIN[51,109]	Stent	84	28.1	63	21.1	8	2.7	57	19.1
	PTCA	77	26.8	58	20.2	5	1.7	54	18.8
AS Trial[110]	Stent	–	13.23	NR		NR		NR	
	PTCA	–	21.16						
WIDEST[111]	Stent	NR		NR		NR		NR	
	PTCA								
SAVED[96]	Stent	–	26*	–	17	–	7	–	13
	PTCA	–	39*	–	26	–	12	–	16
EPISTENT[41,97]	Stent	103	13.0	69	8.7	NR		NR	
	PTCA	163	20.5	123	15.4				
SICCO[98–100]	Stent	12	20.7	12	–	3	5.2	10	17.2
	PTCA	27	45.8	23	39.0	1	1.7	24	40.7
GISSOC[101]	Stent	NR		3*	5.4	2	3.6	3	5.4
	PTCA			12*	22.2	4	7.4	10	18.5
Hancock *et al.*[102]	Stent	4	13.3	NR		1	3.3	3	10.0
	PTCA	9	30.0			2	6.7	5	16.7
TOSCA[103,104]	Stent	47	23.3	17*	8.4	3	1.5	25	12.4
	PTCA	49	23.6	32*	15.4	4	1.9	41	19.7
SPACTO[105]	Stent	12*	30.0	NR		1	2.5	10	25.0
	PTCA	22*	55.0			2	5.0	16	40.0
SARECCO[106]	Stent	NR		13*	23.6	0	0	13*	26.6
	PTCA			30*	54.5	0	0	30*	54.5

*$p < 0.05$, stent compared with PTCA

continued

TABLE 32 contd *Included RCTs: stents vs PTCA for IHD – medium-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
STOP[112]	Stent	NR		–	18.9	NR		NR	
	PTCA			–	38.7				
CORSICA[113]	Stent	16	22.2	16	22.2	NR		NR	
	PTCA	19	27.1	24	34.3				
OCBAS[107]	Stent	NR		NR		NR		NR	
	PTCA								
DEBATE II[114,115,117]	Stent	–	9	NR		NR		NR	
	PTCA	–	12						
DEBATE II[114,115,117]	Stent	–	5.3	NR		NR		NR	
	PTCA	–	15.5						
OPUS[116 †]	Stent	–	6.1*	–	3.5*	NR		NR	
	PTCA	–	14.9*	–	9.7*				

*p < *0.05, stent compared with PTCA*

† *Some information from press release in the Cordis industry submission*

TABLE 33 *Included RCTs: stents vs PTCA for IHD – long-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Angina	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
BENESTENT[84]	Stent	1 year	259/259	3	1.2	13	–	9	3.5	4	1.5	43	17.8
	PTCA		257/257	2	0.8	11	–	5	1.9	6	2.3	37	14.4
BENESTENT[81]	Stent	5 years	248/259	15	6.0	22	–	19*	7.7	3	1.2	NR	
	PTCA		243/257	8	3.3	14	–	8*	3.3	6	2.5		
STRESS[86,88]	Stent	1 year	205/205	3	1.5	13	6.3	7	3.4	NR		26/161	16.1
	PTCA		202/202	4	2.0	16	7.9	7	3.5			25/155	16.1
STRESS II[79]	Stent	1 year	100	STRESS II patients cannot be distinguished from STRESS patients, so no data reported here									
	PTCA		89										
Versaci *et al.*[91]	Stent	1 year	60/60	1	1.7	3	5.0	NR		NR		6*	10.0
	PTCA		60/60	1	1.7	4	6.7					15*	25.0
START[92]	Stent	4 years	225/229	6	2.7	5	2.2	NR		NR		NR	
	PTCA		211/223	5	2.4	6	2.8						
BENESTENT II[27]	Stent	1 year	413/413	4	1.0	14	3.4	8	1.9	6	1.5	NR	
	PTCA		410/410	4	1.0	18	4.4	6	1.5	12	2.9		
AS Trial[110]	Stent	2 years	–	1	0.52	–	–	2	1.04	NR		NR	
	PTCA		–	0	0	–	–	2	1.02				
WIDEST[111]	Stent	1 year	154	NR		NR		NR		NR		NR	
	PTCA		146										
SICCO[99]	Stent	3 years	58	1	1.7	1	1.7	–	–	–	–	33	56.8
	PTCA	(± 6 months)	59	3	5.1	2	3.4	–	–	–	–	33	55.9
SARECCO[106]	Stent	2 years	55	NR		NR		NR		NR		NR	
	PTCA		55										
OCBAS[107]	Stent	9–23 months	57	0	0	NR		NR	1	1.8		NR	
	PTCA		59	1	1.7				1	1.7			

*$p < 0.05$, *stent compared with PTCA*

TABLE 34 *Included RCTs: stents vs PTCA for IHD – long-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
BENESTENT[84]	Stent	60*	23.2	NR		18	6.9	26*	10.0
	PTCA	81*	31.5			13	5.1	53*	20.6
BENESTENT[81]	Stent	86	34.7	43*	17.3	30	12.1	NR	
	PTCA	96	29.5	66*	27.2	23	9.5		
STRESS[86,88]	Stent	51	24.9	24	11.7	12	5.8	39	19.0
	PTCA	61	30.2	38	17.3	18	8.9	42	20.8
STRESS II[79]	Stent	STRESS II patients cannot be distinguished from STRESS patients, so no data reported here							
	PTCA								
Versaci *et al.*[91]	Stent	8*	13.3	NR		4	6.7	4	6.7
	PTCA	18*	30.0			3	5.0	13	21.7
START[92]	Stent	38*	16.9	27*	12.0	NR		NR	
	PTCA	63*	29.9	52*	24.6				
BENESTENT II[27]	Stent	65*	15.7	NR		8	1.9	39	9.4
	PTCA	92*	22.4			6	1.5	64	15.6
AS Trial[110]	Stent	–	16.93*	31*	16.15	–	–	–	–
	PTCA	–	26.46*	48*	24.5	–	–	–	–
WIDEST[111]	Stent	32	20.8	NR		NR		NR	
	PTCA	28	19.2						
SICCO[99]	Stent	14*	24.1	14*	24.1	5	8.6	12	20.7
	PTCA	35*	59.3	31*	52.5	4	6.8	30	50.8
SARECCO[106]	Stent	–	26.0	NR		NR		NR	
	PTCA	–	52.0						
OCBAS[107]	Stent	–	19.2	10	17.5	4	7.0	6	10.5
	PTCA	–	16.9	8	13.6	2	3.4	6	10.2

*$p < 0.05$, stent compared with PTCA

TABLE 35 *Included RCTs: stents vs CABG for IHD – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
ERACI II[120]	IHD	Multi-vessel disease	–	Stent	NR	CABG	NR
SIMA[121]	IHD	Isolated LAD stenosis LVF > 0.45	–	Stent	NR	CABG	NR
Spyrantis *et al.*[122]	IHD	Proximal high grade lesions of LAD artery	–	Stent	NR	Minimal invasive CABG	NR

LVF, left ventricular function

TABLE 36 *Included RCTs: stents vs CABG for IHD – numbers randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	CABG				Stents	CABG
ERACI II[120]	NR	450	225	225	NR	SA, – UA, 86.6% PMI, – AMI, – CO, –	Basal demographic and angiographic characteristics similar	NR	NR
SIMA[121]	–	123	63	60	NR	SA, – UA, – PMI, – AMI, – CO, –	Characteristics similar in 2 groups	0 0	0 5/60 (8.3%)
Spyrantis *et al.*[122]	NR	136	71	65	NR	SA, – UA, – PMI, – AMI, – CO, –	All patients had stress-induced angina pectoris	0 0	0 3 conventional CABG

TABLE 37 *Included RCTs: stents vs CABG for IHD – design, quality and execution*

Study acronym or author	Multicentre?	Method of randomisation	Description of withdrawals and dropouts?	Jadad score
ERACI II[120]	Yes	Not stated	No	1
SIMA[121]	Yes	Not stated	No	1
Spyrantis *et al.*[122]	No	Not stated	No	1

TABLE 38 *Included RCTs: stents vs CABG for IHD – short-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Major bleed	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
ERACI II[120]	Stent	30 day	225	2*	0.9	2*	0.9	NR		NR		NR	
	CABG		225	13*	5.7	13*	5.7						
SIMA[121]	Stent	In hospital	63	1	1.6	3	–	0	0	3	4.8	2*	3.2
	CABG		60	0	0	2	–	1	1.7	1	1.7	18*	30.0
Spyrantis *et al.*[122]	Stent	In hospital	71	NR		NR		NR		NR		NR	
	CABG		65										

*$p < 0.05$, stent compared with CABG

TABLE 39 *Included RCTs: stents vs CABG for IHD – short-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
ERACI II[120]	Stent	8*	3.6	NR		NR		NR	
	CABG	28*	12.5						
SIMA[121]	Stent	4	6.3	NR		NR		NR	
	CABG	2	3.0						
Spyrantis *et al.*[122]	Stent	NR		NR		0	0	NR	
	CABG					2	3.1		

* $p < 0.05$, *stent compared with CABG*

TABLE 40 *Included RCTs: stents vs CABG for IHD – angiographic follow-up results*

Study acronym or author	Period of follow-up (for MLD/ for restenosis)	Loss to follow-up (*n*/*n* on which results reported [%])		Stent MLD (mm) and % stenosis		CABG MLD (mm) and % stenosis		Stent restenosis at follow-up		CABG restenosis at follow-up	
		Stent	CABG	Mean	SD/range	Mean	SD/range	*n*	%	*n*	%
ERACI II[120]	NR	NR	NR	NR		NR		NR		NR	
SIMA[121]	In hospital/N/A	NR	NR	3.0 9%	2.7–3.2 7–13%	N/A		NR		NR	
Spyrantis *et al.*[122]	N/A/6 months	21/71 (29.6%)	32/65 (49.2%)	NR		NR		18	36%	5	15%
There were no significant differences (p > *0.05*)											

TABLE 41 *Included RCTs: stents vs CABG for IHD – medium-term event rates and re-intervention*

Study acronym or author	Intervention/ time	No. followed up	Event rate		TVR		CABG		PTCA	
			n	%	*n*	%	*n*	%	*n*	%
ERACI II[120]	Stent/6 months	225	NR		–	13.7*	–	–	–	–
	CABG	225			–	4.8*	–	–	–	–
SIMA[121]	Stent	–	NR		NR		NR		NR	
	CABG	–								
Spyrantis *et al.*[122]	Stent/6 months	50	NR		NR		NR		14*	28.0
	CABG	33							3*	9.1

*p < *0.05, stent compared with CABG*

TABLE 42 *Included RCTs: stents vs PTCA for AMI – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
GRAMI[119]	AMI	Angiography within 24 hr MI symptom onset – chest pain > 30 mins, ST elevation or ST depression, age < 75 years (cardiogenic shock, previous CABG, any length stenosis included)	Bleeding risk prohibiting heparin/ antiplatelet treatment, non-cardiac illness with survival < 1 year. Reference vessel diameter < 2.5 mm, severe (> 50%) stenosis, left main, severe multi-vessel disease, culprit vessel stenosis < 50%	Stent (Gianturco-Roubin II)	I.v. nitroglycerine, aspirin, ticlopidine, heparin	PTCA	I.v. nitroclycerine, aspirin, ticlopidine, heparin
FRESCO[123]	AMI	Chest pain > 30 min with ST elevation, within 6 hr symptom onset or 6–24 hr of continuing ischaemia inc. cardiogenic shock; (any age, diffuse, tortuous, thrombus included)	Previous fibrinolytic treatment, stenosis < 70%, diameter < 2.5 mm, non-optimal PTCA	Stent (Gianturco-Roubin)	Heparin, aspirin, ticlopidine	PTCA	Heparin, aspirin, ticlopidine
ESCOBAR[124]	AMI	Within 6 hr symptom onset or 6–24 hr ongoing ischaemia, native artery suitable for stenting; (previous CABG, PTCA, MI included)	In another study, life expectancy < 1 year, unprotected L main disease, severe multi-vessel disease, bifurcation, diffuse disease, vessel tortuosity, no re-flow, thrombus	Stent (Palmaz-Schatz)	Heparin, aspirin, warfarin in 21%, ticlopidine in 79%	PTCA	Heparin
PASTA[125]	AMI	Diagnosis of MI by (a) chest pain > 30 min unresponsive to nitroglycerine; (b) ECG, ST elevation > 1 mm in > 2 leads; (c) CAG findings. Culprit lesion occluded or narrowed with flow < TIMI 2. Diameter > 2.5 mm	Excessive tortuosity, calcification proximal to stenosis	Stent (Palmaz-Schatz)	Aspirin, ticlopidine 200 mg, heparin	PTCA	Aspirin. heparin

continued

TABLE 42 contd *Included RCTs: stents vs PTCA for AMI – patient characteristics and intervention*

Study acronym or author	Patient group	Inclusion criteria	Exclusion criteria	Intervention	Antithrombotics (intervention group)	Comparator(s)	Antithrombotics (comparator group)
PAMI-Stent[126]	AMI	Within 12 hr MI onset. Reference diameter 3–4.5 mm, lesions can be covered by 2 stents max	High likelihood of CABG within 6 months, cardiogenic shock, prior thrombolysis, contra-indication to antiplatelet treatment, excessive tortuosity, major side branch within lesion	Heparin-coated stent (Palmaz-Schatz)	Heparin	PTCA	Heparin
PSAAMI[127]	AMI	Angiography within 24 hr onset, stenosis > 70% or TIMI flow < 3 in infarct-related vessel (cardiogenic shock included)	–	Silicon carbide-coated stent (Tantal)	Abciximab in 48%	PTCA	Abciximab in 48%
STENTIM II[128]	AMI	Within 12 hr onset, ECG and enzyme confirmation of MI, vessel diameter < 3 mm, TIMI flow < 3, culprit lesion stenosis > 70%	In another study within 1 month, previous thrombolytic treatment, contraindication to antiplatelet treatment, cardiogenic shock, CABG or PTCA within 6 months, multiple vessel disease, bifurcation, left main, calcified lesions. Infarct-related artery unidentifiable	Stent (Wiktor)	Aspirin, heparin, ticlopidine, ACE inhibitors, beta blockers, abciximab (3%)	PTCA + provisional stent	Aspirin, heparin, ACE inhibitors, beta blockers, abciximab (2.7%)

TABLE 43 *Included RCTs: stents vs PTCA for AMI – number randomised and baseline characteristics*

Study acronym or author	No. of patients eligible	Total no. randomised	No. randomised to:		Mean age (years)/sex	Baseline characteristics	Relevant differences between trial arms at baseline	Dropouts (*n*/*n* randomised [%]) Crossovers (*n*/*n* results reported for [%])	
			Stents	PTCA				Stents	PTCA
GRAMI[119]	116	104	52	52	58.5 16.3% F	SA, – UA, – PMI, 10.6% AMI, 10% CO, –	More hypertension in stent group ($p < 0.03$)	0 1/52 (1.9%)	0 17/52 (32.7%)
FRESCO[123]	223	150	75	75	61.5 22.7% F	SA, – UA, – PMI, 8% AMI, 100% CO, –	More diabetics in stent group (p = NS). More current anterior MI stent group ($p < 0.05$)	0 0 0 0	
ESCOBAR[124]	532 (498 angio-graphy)	227	112	115	58 15.9% F	SA, – UA, – PMI, 13.2% AMI, 100% CO, –	No significant differences in patient demographic or clinical characteristics	0 2/112 (1.8%)	0 15/115 (13.0%)
PASTA[125]	230	142	70	72	67.3 28.7% F	SA, – UA, – PMI, 5.9% AMI, 100% CO, –	No significant differences	3/70 (4.3%) 1/67 (1.5%)	3/72 (4.2%) 7/69 (10.1%)
PAMI-Stent[126]	1458	900	452	448	60 ?% F	SA, – UA, – PMI, – AMI, – CO, –	Well matched except age (stent group older, $p = 0.03$) and time to presentation (stent group took longer $p = 0.06$)	NR 1.3%	NR 67/448 (15.1%)
PSAAMI[127]	134	88	44	44	60 24% F	SA, – UA, – PMI, 9.0% AMI, 100% CO, –	No significant differences for demographic or angiographic data	NR 1/44 (27.3%)	NR 12/44 (27.3%)
STENTIM II[128]	NR	216	101	110	57.4 18.4% F	SA, – UA, – PMI, 4.7% AMI, 100% CO, –	2 groups similar	3/104 (2.9%) 3/101 (3.0%)	2/112 (1.8%) 40/110 (36.4%)

TABLE 44 *Included RCTs: stents vs PTCA for AMI – design, quality and execution*

Study acronym or author	Multicentre?	Method of randomisation	Description of withdrawals and dropouts?	Jadad score
GRAMI[119]	Yes	Not stated	Yes	2
FRESCO[123]	No	Sealed envelope	Yes	3
ESCOBAR[124]	No	Closed envelope	Yes	3
PASTA[125]	Yes	Not stated	Yes	2
PAMI-Stent[126]	Yes	Not stated	No	1
PSAAMI[127]	Yes	Not stated	No	1
STENTIM II[128]	Yes	By computer	Yes	3

TABLE 45 *Included RCTs: stents vs PTCA for AMI – short-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Major bleed	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
GRAMI[119]	Stent	In hospital	52	2	3.8	0	0	NR		NR		1	1.9
	PTCA		52	4	7.6	4	7.6					1	1.9
FRESCO[123]	Stent	30 days	75	0	0	1	1.3	NR		NR		3	4.0
	PTCA		75	3	4.0	2	2.7					3	4.0
ESCOBAR[124]	Stent	In hospital	112	2	1.8	1	0.9	NR		NR		7	6.2
	PTCA		115	3	2.6	5	4.3					1	0.9
PASTA[125]	Stent	In hospital	67	3	4.5	2	3.0	NR		NR		1	1.5
	PTCA		69	5	7.2	3	4.3					1	1.5
PAMI-Stent[126]	Stent	30 days	452	16	3.5	NR		NR		NR		NR	
	PTCA		448	8	1.8								
PSAAMI[127]	Stent	NR	NR	NR		NR		NR		NR		NR	
	PTCA												
STENTIM II[128]	Stent	In hospital	101	1	1.0	4	4.0	NR		NR		2	2.0
	PTCA		110	0	0	4	3.6					2	1.8
There were no significant differences (p > 0.05)													

TABLE 46 *Included RCTs: stents vs PTCA for AMI – short-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
GRAMI[119]	Stent	2*	3.8	NR		1	1.9	0	0
	PTCA	10*	19.2			2	3.8	3	5.7
FRESCO[123]	Stent	NR		1*	1.3	0	0	1*	1.3
	PTCA			9*	12.0	0	0	9*	12.0
ESCOBAR[124]	Stent	NR		NR		1	0.9	0	0
	PTCA					0	0	5	4.3
PASTA[125]	Stent	4*	6.0	4	6.0	NR		NR	
	PTCA	13*	18.8	9	13.0				
PAMI-Stent[126]	Stent	NR		4*	0.9	NR		NR	
	PTCA			16*	3.6				
PSAAMI[127]	Stent	NR		NR		NR		NR	
	PTCA								
STENTIM II[128]	Stent	5	5.0	5	5.0	0	0	5	5.0
	PTCA	6	5.5	6	5.4	0	0	6	5.4

*$p < 0.05$, stent compared with PTCA

TABLE 47 *Included RCTs: stents vs PTCA for AMI – angiographic follow-up results*

Study acronym or author	Period of follow-up (for MLD/ for restenosis)	Loss to follow-up (*n*/*n* on which results reported [%])		Stent MLD (mm) and % stenosis		PTCA MLD (mm) and % stenosis		Stent restenosis at follow-up		PTCA restenosis at follow-up	
		Stent	PTCA	Mean	SD	Mean	SD	*n*	%	*n*	%
GRAMI[119]	NR	NR	NR	NR		NR		NR		NR	
FRESCO[123]	30 days/6 months	94%	95%	3.06*	0.71	2.58*	1.08	12*	16	29*	38.7
ESCOBAR[124]	NR	NR	NR	NR		NR		NR		NR	
PASTA[125]	In hospital/ 6 months	17/67 (25.4%)	39/69 (56.5%)	2.85* 9.8%	0.62 12.4%	2.08* 30.6%	0.82 30.6%	–	17.0*	–	37.5*
PAMI-Stent[126]	30 days/N/A	NR	NR	2.56*	0.47	2.10*	0.45	NR		NR	
PSAAMI[127]	NR	NR	NR	NR		NR		NR		NR	
STENTIM II[128]	In hospital/ 6 months	Combined 10%		2.96* 19.44%*	0.43 8.08%	2.95* 28.45%*	0.46 10.79%	–	25.3*	–	39.6*

*$p < 0.05$, *stent compared with PTCA*

TABLE 48 *Included RCTs: stents vs PTCA for AMI – medium-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Angina	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
GRAMI[119]	Stent PTCA	NR	NR	NR		NR		NR		NR		NR	
FRESCO[123]	Stent PTCA	6 months	75 75	1 4	1.3 5.3	1 2	1.3 2.7	NR		NR		NR	
ESCOBAR[124]	Stent PTCA	6 months	112 115	2 3	1.8 2.6	1* 8*	0.9 7.0	NR		NR		NR	
PASTA[125]	Stent PTCA	6 months	67 69	3 5	4.5 7.2	– –	– –	NR		NR		NR	
PAMI-Stent[126]	Stent PTCA	6 months	448 444	15 11	3.3 2.4	13 16	2.8 3.6	NR		NR		45 68	10.0 15.3
PSAAMI[127]	Stent PTCA	6 months	44 44	– –	7 11	– –	2 9	NR		NR		NR	
STENTIM II[128]	Stent PTCA	6 months	101 110	2 1	2.0 1.0	4 6	4.0 5.5	NR		NR		NR	

*$p < 0.05$, stent compared with PTCA

TABLE 49 *Included RCTs: stents vs PTCA for AMI – medium-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
GRAMI[119]	Stent	NR		NR		NR		NR	
	PTCA								
FRESCO[123]	Stent	10*	13.3	5*	6.7	0	0	5*	6.7
	PTCA	24*	32.0	19*	25.3	2	2.7	17*	22.7
ESCOBAR[124]	Stent	6*	5	4*	3.6	NR		NR	
	PTCA	23*	20	19*	16.5				
PASTA[125]	Stent	14*	20.9	NR		NR		NR	
	PTCA	32*	46.4						
PAMI-Stent[126]	Stent	NR		28	6.2	NR		NR	
	PTCA			62	13.9				
PSAAMI[127]	Stent	–	25*	NR		NR		NR	
	PTCA	–	61*						
STENTIM II[128]	Stent	19	18.8	17	16.8	1	1.0	16*	15.8
	PTCA	30	27.3	29	26.4	0	0	29*	26.4

*$p < 0.05$, stent compared with PTCA

TABLE 50 *Included RCTs: stents vs PTCA for AMI – long-term clinical results*

Study acronym or author	Procedure	Follow-up time	No. followed up	Death		MI		Q wave MI		Non-Q wave MI		Angina	
				n	%	*n*	%	*n*	%	*n*	%	*n*	%
GRAMI[119]	Stent	1 year	52	2	3.8	NR		NR		NR		NR	
	PTCA		52	4	7.6								
PASTA[125]	Stent	1 year	67	3	4.5	NR		NR		NR		NR	
	PTCA		69	6	8.7								
STENTIM II[128]	Stent	1 year	101	3	3.0	4	4.0	NR		NR		NR	
	PTCA		110	2	1.9	6	5.5						
There were no significant differences ($p > 0.05$)													

TABLE 51 *Included RCTs: stents vs PTCA for AMI – long-term event rates and re-intervention*

Study acronym or author	Procedure	Event rate		TVR		CABG		PTCA	
		n	%	*n*	%	*n*	%	*n*	%
GRAMI[119]	Stent	9*	17.3	7	13.5	NR		NR	
	PTCA	18*	34.6	10	19.2				
PASTA[125]	Stent	15*	22.4	NR		NR		NR	
	PTCA	34*	49.3						
STENTIM II[128]	Stent	20	19.8	18	17.8	1	1.0	17	16.8
	PTCA	31	28.2	31	28.2	1	0.9	30	27.3

*$p < 0.05$, stent compared with PTCA

Appendix 6

PTCA costs

TABLE 52 *PTCA: cost of procedure only*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
Jackson *et al.* Cost-effectiveness of coronary artery stents[134]	Hospital in North West Region	?Elective	1053	1996–1997	Initial procedure resource costs only
Palmer *et al.*[137]	Edinburgh	?Elective	1234 (SD, 1249)	(publ. 1998)	Consecutive series of PTCA in one centre, but includes stenting in 42% cases
Wessex DEC Report No. 93. LMW heparins[132]	Hospital in S. of England	Emergency	2955	1998	Figures for procedure (not HRG). Figures obtained in 1998, but not clear to which financial year they relate. (Also not clear whether they include stent cost.)
	RITA trial, non-London Hospital	Elective	1767		Figures out of date (1993–1994)
		Elective	2060	1999	1993–1994 figures compounded for inflation to 1998–1999 using annual % increases for hospital and community health services pay and prices index. This does not reflect experience since 1994 as costs have not increased at the index rate
New 1999 NHS Reference Costs[130]	From all 249 NHS Trusts	?Elective	2673 680–4944	1999	
Haywood *et al.*[136]	Hospital in S&W Region	?Elective	2684	(publ. 1999)	Current contract price at one centre. ?From 1998/1999 financial year. What the price includes is not specified
Cotton *et al.*[135]	?	?Elective	4200	(publ. 1999)	No definition of cost

TABLE 53 *PTCA: hospital costs*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
McKenna *et al.*[131]	4 cardiology centres in London, N Eng. and Scot.	Elective initial including LoS	2357 2195–2566	1995/1996 (publ. 1997)	Micro-costing study using current costs for 1995/1996. Includes all procedures, staff time, laboratory tests and medications. Includes comparison of micro-costing cost and ECR for the four cardiology centres
		Elective repeat including LoS	2929 2527–3666		
McKenna *et al.*[131]	13 major UK cardiac centres	?Elective (standard/simple)	2780 2024–3995	1995/1996 (publ. 1997)	Results of a survey for ECR prices in financial year 1995–1996
	3 of the centres	?Elective (complex)	4037 3852–4260	1995/1996 (publ. 1997)	Gave separate prices for complex as opposed to simple PTCA. No definition of complex given
Wessex DEC report No. 93. LMW heparins[132]	Acute care 1997/98	Elective and emergency (including LoS)	4075 2075–4325 2075 1175–4325	1997/1998	Based on 1996–1997 figure. Range is 25–75th centiles. Costs not wholly representative of hospitals throughout the UK. Covers approx 60% of all acute hospital episodes from GB (not NI)
	ESSENCE trial	?Elective including LoS	2523	?Date	Unclear whether cost elective or includes LoS. Data taken from unpublished PhD thesis
Wessex DEC report No. 87. Coronary artery stents[133]	South and West Region	Elective PTCA without stent	1125–2907	?1996/1997	Costs from two hospitals' consultants (cardiologists). It was assumed that costs included hospital stay and anti-platelet treatment. ?From 1996/1997 financial year. Do not correlate with hospital's finance departments
West Midlands DEC report No. 9. Coronary artery stents[1]	Hospital in West Midlands	Elective including LoS	2628	1997	DHA tariffs. Figures obtained July 1997 then compounded for inflation using annual % increase in retail prices index for 1998. Assumed to also include equipment costs
		Emergency including LoS	2760		
Wessex DEC report No. 93. LMW heparins[132]	Hospital in south of England	Elective	2486	1998	Based on HRGs (E15 and E04) – unclear how derived, since mean LoS is 2.31–4.2 days. Figures obtained in 1998 but unclear whether for 1997–1998 or 1998–1999 financial year
		Emergency	2678		
	RITA trial, Non-London Hospital	Elective including LoS	3024	1993–1994	Figures out of date
		Elective including LoS	3526	1998–1999	1993–1994 figures compounded for inflation to 1998–1999 using annual % increases for hospital and community health services pay and prices index. This does not reflect experience since 1994 as costs have not increased at the index rate

LoS, length of stay

TABLE 54 *PTCA: wider costs*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
Jackson *et al*. Cost-effectiveness of coronary artery stents[134]	Hospital in North West Region	Elective and emergency	2683	1996–1997	Figures relate to two financial years covering the period 1/9/1996 to 31/7/1997; covers all events over initial procedure and follow up of 6 months
West Midlands DEC report No. 9. Coronary artery stents[1]	Hospital in West Midlands	Elective including LoS	3630	1998 (publ. 1998)	Includes costs for all events over initial procedure and follow-up of 1 year. Based on follow-up data from BENESTENT II trial

Appendix 7

Stents costs

TABLE 55 *Stents: cost of procedure only*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
Cotton *et al.*[135]		?Elective	4200 + 500	(publ. 1999)	No definition of cost. Presumes cost of stenting is cost of the stent itself plus cost of PTCA procedure

TABLE 56 *Stents: hospital costs*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
McKenna *et al.*[131]	4 cardiology centres in London, North of England and Scotland	Elective repeat PTCA with stent including LoS	4144 3221–5123	1995/1996 (publ. 1997)	Micro-costing study using current costs for 1995/1996. Includes all procedures, staff time, laboratory tests and medications
	3 of 13 major cardiac centres in UK	Elective	3874–4614 + cost of stent	1995/1996 (publ. 1997)	Results of a survey for ECR prices in financial year 1995–1996
		Emergency	3574		
Wessex DEC report No. 87. Coronary artery stents[133]	South and West Region	Elective	2664–4232	1996/1997	Costs from two hospitals' consultants (cardiologists). It was assumed that costs included hospital stay and anti-platelet treatment. ?From 1996/1997 financial year. Do not correlate with hospital's finance departments
West Midlands DEC report No. 9. Coronary artery stents[1]	Hospital in West Midlands	Single, elective including LoS	4054	1998 (publ. 1998)	DHA tariffs. Figures obtained July 1997 then compounded for inflation using annual % increase in retail prices index for 1998. Assumed to also include equipment costs
		Single, emergency including LoS	4754		
	Hospital in West Midlands	Double, elective including LoS	4808	1998 (publ. 1998)	DHA tariffs. Figures obtained July 1997 then compounded for inflation using annual % increase in retail prices index for 1998. Assumed to also include equipment costs
		Double, emergency including LoS	5697		

TABLE 57 *Stents: wider costs*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
Jackson *et al.* Cost-effectiveness of coronary artery stents[134]	Hospital in North West Region	Elective and emergency	3675	1996/97	Figures relate to two financial years covering the period 1/9/1996 to 31/7/1997; covers all events over initial procedure and follow up of 6 months
		?Elective	2484		Initial procedure resource costs only
West Midlands DEC report No. 9. Coronary artery stents[1]	Hospital in West Midlands	Single, elective including LoS	4549	1998 (publ. 1998)	Includes costs for all events over initial procedure and follow-up of 1 year. Based on follow-up data from BENESTENT II trial
		Double, elective including LoS	5290		

TABLE 58 *Stent prices*

Company	List price	Selling price/other information
Biotronik	Not given	Data on file
Boston Scientific	NIR £1000–£1440 (median £1200) Wallstent £1200	Data on file
Jomed	Not given	Data on file
Sorin Biomedica	Carbostent £650 + VAT	No information

Appendix 8

CABG costs

TABLE 59 *CABG: cost of procedure only*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
Wessex DEC report No. 93. LMW heparins[132]	Hospital in south of England	Emergency including LoS	5941	1998	Figures for procedure (not HRG). Figures obtained in 1998, but not clear which financial year they relate to. (Also not clear whether they include stent cost.)
	RITA trial, non-London Hospital	Elective Elective	2105 2454	1998	1993–1994 figures compounded for inflation to 1998–1999 using annual % increases for hospital and community health services pay and prices index. This does not reflect experience since 1994 as costs have not increased at the index rate
New NHS Reference Costs 1999[130]	From all 249 NHS Trusts	?Elective	6105 2296–9123	1999	
Haywood *et al.*[136]	Hospital in South and West Region	Elective Emergency	5905 8000	(publ. 1999)	Current contract price at one centre. ?From 1998/1999 financial year. What the price includes is not specified
Cotton *et al.*[135]		?Elective	5500	(publ. 1999)	No definition of cost

TABLE 60 *CABG: hospital costs*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
McKenna *et al.*[131]	4 cardiology centres in London, North of England and Scotland	Elective including LoS	5539 3728–7283	1995/1996 (publ. 1997)	Micro-costing study using current costs for 1995/1996. Includes all procedures, staff time, laboratory tests and medications. Includes comparison of micro-costing cost and ECR for the four cardiology centres
		Emergency following PTCA including LoS	5179 3421–7083		
	13 major cardiac centres in UK	Elective (standard/ routine)	6502 4755–8750	1995/1996 (publ. 1997)	Results of a survey for ECR prices in financial year 1995–1996
	6 of the centres	?Elective (complex/repeat/ emergency)	8268 6755–10,770	1995/1996 (publ. 1997)	Gave separate prices for complex as opposed to simple PTCA. No definition of complex given
Wessex DEC report No. 93. LMW heparins[132]	Acute care 1997/1998	Elective including LoS	7650 5875–8150	1996–1997	Based on 1996–1997 figure. Range is 25–75th centiles. Costs not wholly representative of hospitals throughout the UK. Covers approx 60% of all acute hospital episodes from GB (not NI)
		Emergency including LoS	7650 5600–8375		
	ESSENCE trial	?Elective including LoS	4705	?Date	Unclear whether cost elective or includes LoS. Data taken from unpublished PhD thesis
West Midlands DEC report No. 9. Coronary artery stents[1]	Hospital in West Midlands	Elective including LoS	4825	1998 (publ. 1998)	DHA tariffs. Figures obtained July 1997 then compounded for inflation using annual % increase in retail prices index for 1998. Assumed to also include equipment costs
		Emergency including LoS	6431		
Wessex DEC report No. 93. LMW heparins[132]	Hospital in south of England	Elective including LoS	3197	1998	Based on HRGs (E15 and E04) – unclear how derived, since mean LoS is 2.31–4.2 days. Figures obtained in 1998 but unclear whether for 1997–1998 or 1998–1999 financial year
	RITA trial, non-London Hospital	Elective including LoS	5722		Figures out of date (1993–1994)
		Elective including LoS	6672	1998–1999	1993–1994 figures compounded for inflation to 1998–1999 using annual % increases for hospital and community health services pay and prices index. This does not reflect experience since 1994 as costs have not increased at the index rate

TABLE 61 *CABG: wider costs*

Reference	Source	Procedure	Estimated cost range (£)	Date	Potential problems with source
West Midlands DEC report No 9. Coronary artery stents[1]	Hospital in West Midlands	Elective including LoS	5065	1998 (publ. 1998)	Includes costs for all events over initial procedure and follow-up of 1 year. Based on follow-up data from meta-analyses of CABG vs PTCA

Appendix 9

Study types of economic analyses

TABLE 62 *Summary of study types in economic analyses*

Economic analysis	Type of study		
	RCT	**Observational study**	**Model**
Cost-effectiveness analysis	BENESTENT II[27] Serruys *et al.* (vs CABG for MVD)[70]	Jackson *et al.*[134]	Van Hout *et al.*[146] SHPIC *et al.*[18] Schwicker & Banz[138–145]
Cost–utility analysis			Van Hout *et al.*[146] Cohen & Sukin, 1997 and 1999[147,149] Wessex DEC[133] West Midlands DEC[1] Guidant[148] Boston Scientific[150]
Costs and outcomes reported separately	OPUS[116]	Peterson *et al.*[152] Palmer *et al.*[137] Farshid *et al.*[151] Kurbaan *et al.*[153]	

MVD, multivessel coronary disease

Appendix 10

Summary table of economic analyses (models)

TABLE 63 *Summary table of economic analyses (models)*

Study (perspective)	Study aim	Modelling methods	Sources of data	Time horizon	Results	Conclusions
Van Hout *et al.* (BENESTENT)[146] (Third party payer)	To examine relative cost-effectiveness of: (i) conventional PTCA; (ii) stenting	Trial data from BENESTENT I and phase IV pilot phase of BENESTENT II used (this used no anticoagulation)	BENESTENT I and BENESTENT II pilot Costs collected for BENESTENT I per patient and procedure in Dutch hospital. (Costs in Dutch Florins)	7 months	EFS: BENESTENT I – PTCA, 70%; stent, 80%; BENESTENT II pilot – PTCA, 86%; stent, 92%. Cost/EFS (DFl): BENESTENT I – PTCA, 21,000; stent, 29,000; BENESTENT II pilot – PTCA, 22,000; stent, 18,000. Additional costs/additional EFS (DFl): BENESTENT I – PTCA, baseline; stent, 88,000; BENESTENT II pilot – PTCA, 28,000; stent, 6700.	Uncertainty remains about cost-effectiveness of PTCA and stenting. Care required with generalisability as not all patients will fulfil BENESTENT inclusion criteria
Schwicker and Banz[138–145] (Third party payer)	To examine the cost-effectiveness of stenting vs PTCA and CABG for (i) SVD and (ii) MVD in France (Fr), Germany (G), Italy (I), The Netherlands (N) and Spain (Sp)	(i) Decision analytic model; (ii) Markov post-revascularisation model	Effectiveness data: literature review to 1996 with assessment of quality of studies and some expert opinion. For MVD, effectiveness data from observational studies Costs: in-hospital costs from BENESTENT II, cost data collected in 2 hospitals in each country	3 years	EFS = absence of death, MI or revascularisation. EFS for SVD – stent, 82%; PTCA, 68%; EFS for MVD – stent, 76%; PTCA, 37%; CABG, 90%. **SVD: costs/EFS** *PTCA* / *Stent* / *% diff.* France (FF) 81K / 55K / 32.2 Germany (DM) 28K / 18K / 36.8 Italy (DM) 27K / 18K / 32.9 Spain (Ptas) 2578K / 1711K / 33.6 Netherlands (DFl) 27K / 19K / 31.5 **MVD: costs/EFS** *PTCA* / *Stent* / *CABG* France (FF) 192K / 83K / 99K Germany (DM) 69K / 27K / 38K Italy (DM) 69K / 27K / 38K Spain (Ptas) 5869K / 2654K / 2198K Netherlands (DFl) 72K / 30K / 41K	SVD: Costs of stenting and PTCA are almost equivalent due to reduced revascularisations. Stents superior to PTCA in EFS, and 25–30% lower cost/EFS. Results consistent across all 5 countries. MVD: CABG superior in EFS at 3 years. Stenting is cost-effective alternative to CABG because of lower costs

continued

TABLE 63 contd *Summary table of economic analyses (models)*

Study (perspective)	Study aim	Modelling methods	Sources of data	Time horizon	Results	Conclusions
SHPIC[18] (Third party payer)	To examine the cost-effectiveness of PTCA, stenting and CABG	Effectiveness data from BENESTENT I and STRESS combined. (Published studies up to 1996)	Effectiveness data from BENESTENT I and STRESS Costs – used extra-contractual referral prices and contract prices (1997)	Not clear, probably 6–7 months (same as BENESTENT and STRESS)	Cost/second procedure averted in stent recipients = £20,700 compared with PTCA patients Marginal cost of stenting £1124 No account taken of superior angina relief in stented patients	With fall in cost of stents there will be changes in these costings Need for RCT of patients with different risk profiles
Wessex DEC[133] (Third party costs)	To examine relative cost–utility of: conventional PTCA and PTCA with stenting	(i) Model based on BENESTENT I (ii) Sensitivity analysis	Effectiveness data from BENESTENT I and Versaci study Costs from S&W Region (1996/1997) Utility values from Cohen 1994	1 year	Cost/QALY of stenting compared with PTCA £250,000	Sensitivity analysis produced values of £20,000–£727,000/QALY Model sensitive to rate of symptomatic restenois and waiting time for revascularisation
West Midlands DEC[1] (Third party costs)	To examine relative cost-effectiveness of: (i) conventional PTCA; (ii)PTCA with stenting; (iii) CABG	(i) Decision analytic model (ii) Sensitivity analysis (Assumption of only 1 stent used per person)	Effectiveness data based on BENESTENT II trial Costs from elective and emergency DHA tariff prices for University Hospital NHS Trust 1998	1 year	QALYs compared with medical treatment: PTCA. 0.079; stent, 0.119; CABG, 0.136. Costs/100 patients: PTCA, £363,000; stent, £455,000; 2 stents, £529,000; CABG, £506,000. Incremental cost/QALY for single stent over PTCA ranged from £15,268 to £30,951	QALYs from PTCA and stents are similar, but stents are associated with higher costs

continued

TABLE 63 contd *Summary table of economic analyses (models)*

Study (perspective)	Study aim	Modelling methods	Sources of data	Time horizon	Results	Conclusions
Guidant[148] (Cost to NHS)	To establish the relative costs of stenting and PTCA	(i) Decision analysis (ii) Sensitivity analysis	Effectiveness data from Cohen (1994) and Henderson (1998) Costs: Bottom-up costing exercise based on a London teaching hospital + NHS unit costs 1997/1998 Utility values from Cohen (1994)	2 years	Marginal cost/QALY of PTCA relative to stenting = £6812	Sensitivity analysis presented. Model very sensitive to assumptions If restricted to effects of PTCA and stents only (i.e. ignoring deaths, CABGs and longer wait) then cost/QALY = £360,000
Boston Scientific[150] (Cost to NHS)	To establish the incremental cost–utility of (i) elective stenting and (ii) PTCA with only bail-out stenting allowed	Life expectancy of 60-year-old man with IHD (i) Decision analysis (ii) Sensitivity analysis	Effectiveness data from BENESTENT II Cost data from NHS and literature. (1996 cost inflated by 5%) Utility values from Cohen (1994)	1 year	Marginal cost of adjunctive stent at 1 year is £256, or 5.5% to 1 year cost of PTCA alone Incremental QALYs for stent = 0.0081 in treatment year Incremental cost/QALY = £31,508 (life expectancy) £/EFS: PTCA, £6010; stent, £5836. (Events = death, MI, CABG, repeat PTCA)	Initial costs of PTCA + stent are higher, but some costs are offset by reduced number of revascularisations Decision analysis most sensitive to waiting time for a repeat target lesion revacularisation (i.e. £20,000–80,000/QALY), restenosis rates and stent cost
Cohen 1997 and 1999[147,149]	To examine relative cost-effectiveness of (i) conventional PTCA and (ii) stenting in symptomatic SVD	Theoretical 55-year-old man with symptomatic SVD (i) decision analytic model (ii) assumptions tested using sensitivity analysis	Effectiveness data from BENESTENT I and STRESS) QALYs from Pliskin (1981) Costs from 1996 Beth Israel Hospital (Costs in 1996 US$)	1 year	Cost/QALY $33,700 Sensitivity analysis of abrupt closure and restenosis rates. Cost/QALY increases to $200,000 for type A mid-right coronary stenosis, with abrupt closure rate of 3% and restenosis rate of 25–30%	Stenting is more expensive than PTCA, even in the long-term. Its cost-effectiveness compares favourably with other medical procedures

Appendix 11

Summary of economic analyses (individual studies)

TABLE 64 *Summary table of economic analyses (individual studies)*

Study (perspective)	Study characteristics	Treatment groups	Baseline characteristics	Follow-up (duration of costing)	Results	Conclusions
BENESTENT II[27] (Third party costs)	To examine relative cost-effectiveness of: (i) PTCA with provisional stenting if necessary (ii) primary stenting with heparin-coated stent RCT with factorial design; follow-up by angiography or clinical Bottom-up costing exercise	PTCA 413 patients (201 clinical follow-up) Primary stenting 414 (205 clinical follow-up)	See *Table 24* 93% patients had single lesions	1 year (1 year)	Average cost/patient (DFI): primary stent, 18,812, PTCA, 16,727 EFS: primary stent, 89.3%; PTCA, 78.6% Costs/EFS (DFI): primary stent, 21,309; PTCA, 21,073	Primary stenting is more effective and more costly than PTCA
Jackson *et al.*[134] (Tertiary centre costs only)	Retrospective cohort study to examine the cost-effectiveness of stenting ≥ 50% coronary artery lesions with non-stented alternatives UK Bottom-up costing exercise	467 non-stented: 361 stented	Registry data, so representitive of all cardiologists' practice. Stented group had higher New Zealand priority score, and more complex lesions Baseline costs 1996/1997	1 year	Cost/outcome avoided: revascularisation £11,065; first-time target lesion re-intervention, £12,448; all interventional cardiology, £19,917 Cost-effectiveness ratios for stenting: all interventional cardiology, £22,463; CABG, £57,931; all revascularisations, £13,214	Cost-effectiveness of stenting questionable in 1996/1997. Most sensitive to stent price

continued

TABLE 64 contd *Summary table of economic analyses (individual studies)*

Study (perspective)	Study characteristics	Treatment groups	Baseline characteristics	Follow-up (duration of costing)	Results	Conclusions
Serruys *et al.* (ARTS)[70] (NR)	Prospective multi-centre RCT of stenting vs CABG in MVD Unclear how costs were derived (insufficient evidence in abstract)	1200 patients with 2 and 3 vessel disease	Insuffficient data (abstract and press release only)	1 year (1 year)	EFS for major cardiac and cerebral events: stents, 73.7%; CABG, 87.8%. *Cost ($) / CE ratio* Stents: 2-vessel low cost 16,638 / 20,586 2-vessel high cost 19,297 / 23,875 3-vessel low cost 20,456 / 25,322 3-vessel high cost 24,566 / 30,397 CABG 21,350 / 24,348	Stenting provides net saving at 1 year of 2965 Euro (~ $3100)
Weaver *et al.*[116] (OPUS I) (Third party payer)	Multicentre RCT of primary stenting vs PTCA with provisional stenting if necessary 1996–1998 Unclear how costs were derived (insufficient evidence in abstract)	479 patients, aged 21–81 years; primary stent 230 (99% had stent); PTCA 249 (37% had stent)	Patients with stable or unstable angina or MI > 24 hr previously, or evidence of ischaemia Arteries ≥ 3 mm, lesions ≈ 20 mm with mild or no calcification, = 70% stenosis	6 months (6 months)	Incidence of death, MI and target vessel revascularisation: primary stenting 6.1%; provisional stenting 14.9% (p = 0.003). Difference mainly due to fewer revascularisations Primary stenting US$284 less expensive than PTCA with provisional stenting at 6 months (primary stenting $10,206 vs $10,490 for provisional stenting)	Primary stenting is more effective and less costly than PTCA with provisional stenting at 6 months
Peterson *et al.*[152] (Third party payer)	Observational study examining the costs and effectiveness of PTCA and stent 1995–1996 Costs: bottom-up exercise using accountancy system	348 patients who received stents and 159 PTCA treated at single centre in the USA	Mean age 61 years, all received Palmaz-Schatz stent. Patients excluded if: balloon < 2.7 mm, left main or saphenous vein graft disease, within 2 days of AMI, or required a CABG just after the procedure	6 months and 1 year	Costs at 1 year: stent, US$22,140; PTCA, $22,571. Outcomes: *Stent %* / *PTCA %* / *p value* Readmission 29 / 42 / 0.006 Cardiac-catheterisation 27 / 43 / 0.001 Revascularisation 14 / 30 / 0.001 Death 3 / 3 / 0.7 MI 2 / 5 / 0.04 In employment 75 / 63 / 0.06	In contemporary practice, coronary stenting appears to lead to improved patient outcomes without increasing long-term resource requirements when compared with PTCA

continued

TABLE 64 contd *Summary table of economic analyses (individual studies)*

Study (perspective)	Study characteristics	Treatment groups	Baseline characteristics	Follow-up (duration of costing)	Results				Conclusions
Palmer *et al.*[137] (Third party payer)	Historical cohort study to compare the costs and outcomes of routine PTCA in 1994 (with low % stent usage) and 1996 (with higher stent usage)	100 consecutive patients treated with single vessel PTCA procedures in a single centre in Scotland in 1994 and 1996	In 1994 15% of PTCA patients received a stent; in 1996 42% received a stent	6 months?	Outcomes: Clinical restenosis Repeat angioplasty Costs (£)	*1994* 21% 26% 1340	*1996* 35% 9% 1234	p *value* 0.04 0.03 –	The increase in coronary stent use between 1994 and 1996 was associated with better outcomes for patients, but no increase in procedural costs
Farshid *et al.*[151] (Data from Bio-compatibles, not original paper) (NR)	Observational study to compare the costs and outcomes of a conservative stenting policy in 1995 with an elective stenting policy in 1996	1995: *n* = 347; 1996: *n* = 401	In 1995 22% of patients received a stent; 66% in 1996	1 year	Clinical restenosis Target lesion revascularisation Cost (A$)	*1995* 16.7% 14.7% 5972	*1996* 8.5% 8.5% 5994		
Kurbaan *et al.*[153] (from conference abstract only) (NR)	Observational study to compare the outcomes and costs of PTCA (1988–1992) and stenting (since 1996) Average UK costs used (US$)	PTCA: *n* = 510 Stent: *n* = 264 All patients treated in European centres	All patients fulfilled the CABRI inclusion criteria	Stents 6 months, not clear for PTCA group	Death (%) MI (%) Revascularisation: – percutaneous (%) – CABG (%) Price (US$)	*PTCA* 3.3 4.4 16.6 14.9 5000	*Stents* 0.8 0.8 7.2 1.9 10,000		Because of the reduced rate of revascularisations in the stented patients up to US$1770 can be recovered from the cost of stenting in the first 6 months

Appendix 12

Source of cost data for economic analyses

TABLE 65 *Sources of cost data for economic analyses*

Source of cost data	Study
Bottom-up costing exercise in Europe	BENESTENT II (CEA)[27] Jackson *et al.* (CEA)[134] Schwicker & Banz (CEA) (combined with UK prices)[138–145] Guidant (CU)[148]
Bottom-up costing exercise in USA, or Canada	Cohen *et al.* (1997 and 1999) (CU)[147,149] Van Hout *et al.* (CEA)[146]
UK prices	SHPIC (CU)[18] Wessex DEC (CU)[133] West Midlands DEC (CU)[1] Boston Scientific (CU)[153]
Not clear	Serruys *et al.*[70] OPUS[116]
CEA, cost-effectiveness analysis; CU, cost–utility analysis	

Appendix 13

Outcome measures reported by individual economic analyses

TABLE 66 *Outcome measures reported by individual economic analyses*

Outcome measure	Study
EFS rate	BENESTENT II[27] Serruys *et al.* (vs CABG for MVD)[70] Van Hout *et al.*[146] Schwicker and Banz[138–145] Boston Scientific[150]
Cost/EFS	BENESTENT II[27] Van Hout *et al.*[146] Schwicker & Banz[138–145] Boston Scientific[150]
Cost/outcome avoided	Jackson *et al.*[134] SHPIC[18]
Cost/QALY	Van Hout *et al.*[146] Cohen *et al.* (1997 and 1999)[147,149] Wessex DEC[133] West Midlands DEC[1] Guidant[148] Boston Scientific[150]

Appendix 14

Quality assessment of included economic studies

TABLE 67 *Quality assessment: design and methods*

	Checklist items*								
Article	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
West Midlands DEC[1]	Yes	Yes	N/C	Yes	Yes	Yes	No	Yes	Yes
Wessex DEC[133]	Yes	Yes	N/S	Yes	Yes	Yes	No	Yes	Yes
Boston Scientific[150]	Yes	Yes	N/C	Yes	Yes	Yes	No	Yes	N/A
Guidant[148]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	N/A
Serruys *et al.*[70]	Yes	No	No	Yes	Yes	No	No	Yes	N/C
Van Hout *et al.*[146]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Schwicker & Banz[138–145]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	N/A
Jackson *et al.*[134]	Yes	Yes	N/C	Yes	N/C	Yes	No	Yes	N/C
SHPIC[18]	Yes	No	No	Yes	Yes	Yes	No	Yes	N/A
OPUS/Weaver *et al.*[116]	Yes	Yes	No	N/C	Yes	N/C	No	Yes	N/C
BENESTENT II[27]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Peterson *et al.*[152]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Palmer *et al.*[137]	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes
Cohen *et al.* (1999)[149]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	N/A

* *1. Research question stated*
2. Economic importance of research question stated
3. Viewpoint(s) of analysis clearly stated and defined
4. Rationale for choosing alternative programmes or interventions compared stated
5. Alternatives being compared clearly described
6. Form of economic evaluation used stated
7. Choice of form of economic evaluation justified in relation to questions addressed
8. Source(s) of effectiveness estimates are stated
9. Details of design and results of effectiveness study given (if based on single study)

N/C, not clear; N/S, not stated

The articles by Farshid et al.[151] *and Kurbaan* et al.[153] *are not included in the quality checklist, because of insufficient data*

TABLE 68 *Quality assessment: data collection*

	Checklist items*											
Article	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**
West Midlands DEC[1]	N/A	Yes	No	Yes	N/A	N/A	No	No	Yes	N/A	Yes	Yes
Wessex DEC[133]	N/A	Yes	Yes	No	N/A	N/A	No	No	Yes	N/A	Yes	Yes
Boston Scientific[150]	N/A	Yes	Yes	Yes	N/A	N/A	No	No	Yes	Yes	Yes	Yes
Guidant[148]	N/A	Yes	No	No	N/A	N/A	Yes	Yes	Yes	N/A	Yes	Yes
Serruys *et al.*[70]	N/A	N/C	No	No	N/A	N/A	No	No	No	No	N/A	N/A
Van Hout *et al.*[146]	N/C	Yes	N/A	N/A	N/A	N/A	Yes	Yes	Yes	No	N/A	N/A
Schwicker & Banz[138–145]	N/A	Yes	N/A	N/A	N/A	N/A	Yes	Yes	Yes	No	Yes	Yes
Jackson *et al.*[134]	N/C	Yes	N/A	N/A	N/A	N/A	Yes	Yes	No	No	N/A	N/A
SHPIC[18]	N/A	Yes	N/A	N/A	N/A	N/A	No	Yes	No	N/A	N/C	No
OPUS/Weaver *et al.*[116]	N/A	Yes	N/A	N/A	N/A	N/A	No	No	No	No	N/A	N/A
BENESTENT II[27]	N/A	Yes	N/A	N/A	N/A	N/A	Yes	Yes	Yes	No	N/A	N/A
Peterson *et al.*[152]	N/A	Yes	N/A	N/A	Yes	No	No	Yes	Yes	N/A	N/A	N/A
Palmer *et al.*[137]	N/A	Yes	N/A	N/A	N/A	N/A	No	N/C	Yes	Yes	N/A	N/A
Cohen *et al.* (1999)[149]	No	Yes	No	No	N/A	N/A	Yes	Yes	Yes	N/A	Yes	Yes

* *10. Details of method of synthesis or meta-analysis of estimates given (if based on overview of number of effectiveness studies)*
11. Primary outcome measure(s) for economic evaluation clearly stated
12. Methods to value health states and other benefits stated
13. Details of subjects from whom valuations were obtained given
14. Productivity changes (if included) reported separately
15. Relevance of productivity changes to study question discussed
16. Quantities of resources reported separately from their unit costs
17. Methods for estimation of quantities and units costs described
18. Currency and price data recorded
19. Details of currency and price adjustments for inflation or currency conversion given
20. Details of any model used given
21. Choice of model used and key parameters on which it is based justified

TABLE 69 *Quality assessment: analysis and interpretation of results*

	Checklist items*													
Article	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**
West Midlands DEC[1]	Yes	N/A	N/A	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Wessex DEC[133]	Yes	N/A	N/A	N/A	N/A	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Boston Scientific[150]	Yes	N/A	N/A	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Guidant[148]	Yes	Yes	No	N/A	No	Yes	Yes	N/C	Yes	Yes	No	Yes	Yes	Yes
Serruys *et al.*[70]	Yes	No	N/A	No	No	N/A	N/A	N/A	N/A	No	N/C	Yes	Yes	N/C
Van Hout *et al.*[146]	Yes	N/A	N/A	No	No	No	N/A	N/A	N/A	Yes	Yes	Yes	Yes	Yes
Schwicker & Banz[138–145]	Yes	N/A	N/A	No	No	N/A	N/A	N/A	Yes	No	Yes	Yes	Yes	Yes
Jackson *et al.*[134]	Yes	N/A	N/A	Yes	No	N/A	N/A	Yes	Yes	N/C	Yes	Yes	Yes	N/C
SHPIC[18]	No	No	N/A	No	N/A	N/C	N/C	Yes	Yes	Yes	No	Yes	Yes	Yes
OPUS/Weaver *et al.*[116]	Yes	N/A	N/A	No	N/A	N/A	N/A	N/A	Yes	N/C	No	Yes	Yes	Yes
BENESTENT II[27]	Yes	No	N/A	No	N/A	No	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes
Peterson *et al.*[152]	Yes	N/A	N/A	No	N/A	N/A	N/A	N/A	Yes	No	No	Yes	Yes	No
Palmer *et al.*[137]	N/C	N/A	N/A	No	N/A	N/A	N/A	N/A	Yes	No	No	Yes	Yes	No
Cohen *et al.* (1999)[149]	No	N/A	N/A	No	N/A	Yes	No	No	Yes	No	No	Yes	Yes	No

* *22. Time horizon of costs and benefits states*
23. Discount rate(s) stated
24. Choice of rate(s) justified
25. Explanation given if costs or benefits not discounted
26. Details of statistical tests and CIs given for stochastic data
27. Approach to sensitivity analysis given
28. Choice of variables for sensitivity analysis justified
29. Ranges over which variables are varied stated
30. Relevant alternatives compared
31. Incremental analysis reported
32. Major outcomes presented in dis-aggregated as well as aggregated form
33. Answer to study question given
34. Conclusions follow from data reported
35. Conclusions accompanied by appropriatecaveats

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We look forward to hearing from you.

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