

- Smith SC Jr, Dove JT, Jacobs AK, Kennedy JW, Kereiakes D, Kern MJ, et al. ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines)—executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and Interventions. *Circulation* 2001;103(24):3019-41.
- Casula R, Athanasiou T, Foale R. Recent advances in minimal-access cardiac surgery using robotic-enhanced surgical systems. *Expert Rev Cardiovasc Ther* 2004;2:589-600.
- Nordmann AJ, Briel M, Bucher HC. Mortality in randomized controlled trials comparing drug-eluting vs. bare metal stents in coronary artery disease: a meta-analysis. *Eur Heart J* 2006. 27 (23):2784-814.
- Rao C, Aziz O, Panesar SS, Jones C, Morris S, Darzi A, et al. Cost effectiveness analysis of minimally invasive internal thoracic artery bypass versus percutaneous revascularisation for isolated lesions of the left anterior descending artery. *BMJ* 2007; doi: 10.1136/bmj.39112.480023.BE.

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## Cost effectiveness analysis of minimally invasive internal thoracic artery bypass versus percutaneous revascularisation for isolated lesions of the left anterior descending artery

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### ABSTRACT

**Objective** To compare the cost effectiveness of percutaneous transluminal coronary artery stenting with minimally invasive internal thoracic artery bypass for isolated lesions of the left anterior descending artery.

**Design** Cost effectiveness analysis.

**Data sources** Embase, Medline, Cochrane, Google Scholar, and Health Technology Assessment databases (1966-2005), and reference sources for utility values and economical variables.

**Methods** Decision analytical modelling and Markov simulation were used to model medium and long term costs, quality of life, and cost effectiveness after either intervention using data from referenced sources. Probabilistic sensitivity and alternative analyses were used to investigate the effect of uncertainty about the value of model variables and model structure.

**Results** Stenting was the dominant strategy in the first two years, being both more effective and less costly than bypass surgery. In the third year bypass surgery still remained more expensive but became marginally more effective. As the incremental cost effectiveness was £1 108 130.40 (€1 682 146.00; \$2 179 194) per quality adjusted life year (QALY), the additional effectiveness could not be said to justify the additional cost at this stage. By five years, however, the incremental cost effectiveness ratio of £28 042.95 per QALY began to compare favourably with other interventions. At 10 years the additional effectiveness of 0.132 QALYs (range -0.166 to 0.430) probably justified the additional cost of £829.02 (range £205.56 to £1452.48), with an incremental cost effectiveness of £6274.02 per QALY. Sensitivity and alternative analysis showed the results were sensitive to the time horizon and stent type.

**Conclusions** Minimally invasive left internal thoracic artery bypass may be a more cost effective medium and long term alternative to percutaneous transluminal coronary artery stenting.

### INTRODUCTION

A meta-analysis of randomised trials suggested that minimally invasive internal thoracic artery bypass for isolated lesions of the left anterior descending artery resulted in fewer complications in the mid-term than did transluminal stenting.<sup>1</sup> We compared the cost effectiveness of the two interventions and determined whether this translated into differences in quality of life.

### METHODS

We calculated the incidences of clinical outcomes of interest from the meta-analysis weighted means data.<sup>1</sup> We used decision analysis and Markov simulation to model long term outcomes of interventions in the absence of empirical long term follow-up data.<sup>2</sup> We used quality adjusted life years (QALYs) and cost as measures of effect and the incremental cost effectiveness ratio to assess whether improved efficacy justified increased cost. To investigate the uncertainty of our results we used sensitivity and alternative analysis.

### Model structure and variables

The model we used is on bmj.com. The base case analysis was for a 61 year old male cohort, the average age of patients in the included studies. We carried out the analysis for a 10 year time horizon, with one year Markov cycles. Costs and effects were discounted at 3.5%.

We converted the incidences of outcomes into transition probabilities<sup>3</sup> with the exception of perioperative death and cerebrovascular event, which we assumed to always occur within the first cycle. See bmj.com for sources of transition probabilities for baseline mortality, the likelihood of death after myocardial infarction and cerebrovascular event, confidence intervals for these values, and a table showing the variables used in the analysis.

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We valued one year of good cardiac health at 0.86 QALYs. Patients undergoing either intervention were assumed to have had angina for six weeks before the procedure, incurring a disutility of 0.02 QALYs for six weeks. Patients incurred a disutility of 0.012 QALYs for 13 weeks when surviving bypass surgery, 0.0035 QALYs for six weeks when surviving transluminal stenting, and 0.1 QALYs for 13 weeks when surviving myocardial infarction. Patients surviving a cerebrovascular event incurred a permanent disutility of 0.3 QALYs (0.33 QALYs after a second stroke).

We carried out the analysis from a UK health service perspective. Costs are in pounds sterling, with incremental cost effectiveness ratios in pounds sterling per QALY. The cost of a cerebrovascular event was set at £1586 (€2405; \$3107) and a myocardial infarction at £453.13.<sup>4</sup>

#### Sensitivity analysis and uncertainty

We examined the combined effect of uncertainty about model variables using Monte-Carlo simulation,<sup>2</sup> with 1000 iterations in each loop.

Uncertainty was investigated with a cost effectiveness acceptability curve.<sup>2</sup> The curve shows how the certainty for an intervention being more cost effective varies as the amount a healthcare provider is prepared to pay for an improvement of 1 QALY increases.

#### Alternative analysis

To investigate the effect of demographics we carried out analyses with published values for baseline mortality for men aged 51, 61, and 71 and for women aged 61.<sup>5</sup> We accounted for the cost of the procedures to the NHS and to society. Our analysis was for different time horizons between 0 and 15 years.

As data were not available after three years for all outcomes we investigated the uncertainty about long term reintervention rates by carrying out a pessimistic scenario, where the same reintervention rate was used after two years for both interventions. To investigate the possible effect of drug eluting stents we carried out three analyses. In the first we extrapolated data on the efficacy of the stents for one year follow-up from a meta-analysis.<sup>6</sup> We assumed that reintervention rates were the same in both groups and that the incidence of myocardial infarction and cerebral events with transluminal stenting was half that with bare metal stents (base case). In the second analysis we combined the cost of drug eluting stents with the incidence of reintervention and the composite outcome using bare metal stents (base case). Finally, we assumed the rates of reintervention and the composite outcome to be halfway between the previous two analyses. We assumed the incremental cost of drug eluting stents to be £200 compared with bare metal stents and the cost of daily clopidogrel in the year after insertion of a drug eluting stent to be £460.29.<sup>7</sup>

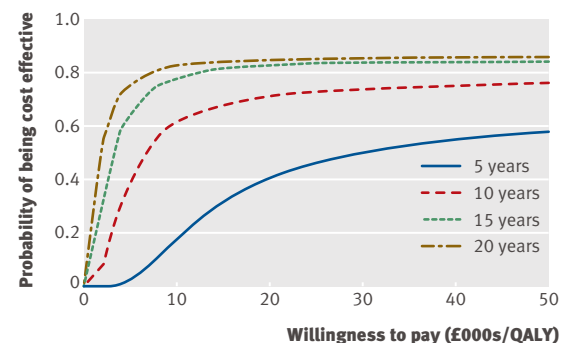
## RESULTS

Transluminal stenting cost £6317.07 per patient and minimally invasive internal thoracic coronary artery bypass cost £7146.09 per patient (6.718 and 6.850 QALYs per patient respectively over 10 years), representing a gain of 0.132 QALYs (range -0.166 to 0.430) with surgical bypass and an incremental cost of £829.02 (range £205.56 to £1452.48), with an incremental cost effectiveness ratio of £6274.02 per QALY.

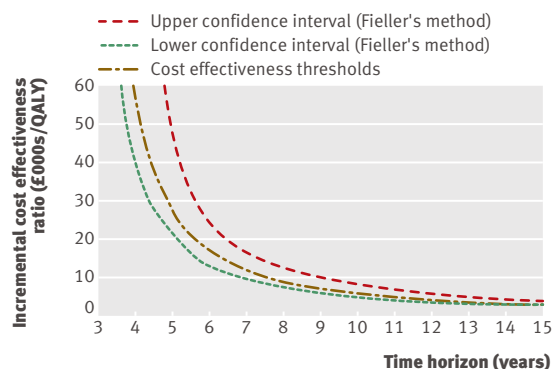
No significant uncertainty was associated with the incremental cost effectiveness ratio (see [bmj.com](http://bmj.com)). Figure 1 shows the cost effectiveness acceptability curve.

As the time horizon increased, minimally invasive internal thoracic artery bypass became more effective, overtaking transluminal stenting after three years (fig 2). Beyond this, surgical bypass became more effective but was more expensive than stenting. The incremental cost effectiveness ratio per QALY was £28 042.95 at five years, £17 474.26 at six years, £6274.02 at 10 years, and £2878.98 at 15 years. The incremental cost effectiveness ratio of £10 354.79 per QALY at 10 years in the pessimistic analysis suggests that although the results may be sensitive to uncertainty about the long term reintervention rates, surgical bypass remained the most cost effective alternative at 10 years even when the reintervention rates and incidence of complications were considered to be the same after two years. Uncertainty about utility variables had little effect on the results. The results were insensitive to demographics (incremental cost effectiveness ratio £5808.22 per QALY in women, £6435.37 in 71 year olds, and £5723.57 in 51 year olds). The additional cost of absence from work after surgical bypass was offset by the societal cost of more frequent reintervention after stenting, resulting in a lower incremental cost (£776.65) and incremental cost effectiveness ratio (£5499.45 per QALY) in the societal perspective analysis compared with the base case.

The results of the alternative analysis for drug eluting stents differed most from the base case. In the first analysis, transluminal stenting was £686.04 cheaper



**Fig 1** Cost effectiveness acceptability curves for different time horizons, showing certainty with which minimally invasive internal thoracic artery bypass is the most cost effective intervention as amount healthcare providers are prepared to pay for one QALY varies



**Fig 2** | Effect of time horizon on incremental cost effectiveness ratio for minimally invasive internal thoracic artery bypass compared with transluminal stenting

and 0.042 QALYs more effective. In the second analysis, surgical bypass was more expensive but more effective (incremental cost effectiveness ratio £6970.58 per QALY). In the third analysis, surgical bypass was most cost effective (incremental cost effectiveness analysis £302.53 per QALY).

## DISCUSSION

Although percutaneous transluminal coronary artery stenting for patients with lesions of the left anterior descending artery is initially cheaper and more effective than minimally invasive internal thoracic artery bypass, the latter is more cost effective long term, with an incremental cost effectiveness ratio at 10 years of £6274.02 per QALY. The absolute difference in effect between the interventions is small at 10 years, but probabilistic sensitivity analysis suggests with 71.1% certainty that surgical bypass is the most cost effective alternative at a cost effectiveness threshold of £20 000 per QALY and 73.4% at £30 000 per QALY.

Several factors should be considered. Firstly, beyond six years the incremental cost effectiveness ratio of surgical bypass compares favourably with other interventions and becomes more effective the longer a patient lives. Secondly, that results were sensitive to uncertainty of the variables could be largely due to the uncertainty about complication rates after intervention. Thirdly, myocardial infarction and stroke are poorly reported. Fourthly, alternative analysis suggests that these results are not sensitive to

demographics, uncertainty about long term re-intervention rates, or the utility of different health states. Finally, many of the assumptions were biased towards stenting, increasing the robustness of the finding that surgical bypass is more cost effective.

The findings of this study are less equivocal than published data on the two interventions in multiple vessel disease.<sup>8</sup> This may be a reflection of varying population characteristics of patients with single and multiple vessel disease,<sup>9</sup> but also may be due to other methodological limitations. Variables in this study were obtained from meta-analysed data, and the confidence intervals reflect the uncertainty. The event rates used by Yock et al<sup>8</sup> were based on modifications to data from two trials,<sup>10,11</sup> and used values that did not directly compare stenting with bypass grafting.<sup>12,13</sup> Despite the uncertainty with many of the variables in our model the values provide contemporary estimates of event rates.<sup>14-16</sup> Similarly, the utility and cost estimates may represent truer estimates, from an NHS perspective in a contemporary UK population.

## Study limitations

Our study has several limitations. Firstly, results were limited by the accuracy of the model structure and estimates of the variables. Secondly, transition probabilities were based on meta-analytical data,<sup>1</sup> which for variables with low event rates resulted in higher uncertainty. Thirdly, without long term follow-up data the model structure could not be validated; we investigated potential bias towards surgical bypass using alternative analysis. Finally, we did not carry out an analysis of the effects on budgets.

## Implications for practice

That minimally invasive internal thoracic artery bypass could be a more cost effective long term intervention than transluminal stenting has important implications. These results do not, however, account for the increased use of drug eluting stents over bare metal stents.<sup>6</sup> As data beyond one year are lacking on outcomes comparing transluminal stenting using drug eluting stents with bare metal stents and no data are available comparing transluminal stenting using drug eluting stents with minimally invasive internal thoracic artery bypass, rigorous comparison of the two interventions is not possible.

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**Competing interests:** None declared.

**Ethical approval:** Not required.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

Surgical bypass may offer a more favourable long term outcome for multiple vessel coronary disease compared with percutaneous interventions

Minimally invasive left internal thoracic artery bypass results in fewer mid-term complications than transluminal stenting

## WHAT THIS STUDY ADDS

Minimally invasive left internal thoracic artery bypass is more effective in the long term, justifying its initial additional cost

These findings do not take into account the effect of drug eluting stents, for which data on long term effectiveness are awaited

1 Aziz O, Rao C, Panesar SS, Jones C, Morris S, Darzi A, et al. Meta-analysis of minimally invasive internal thoracic artery bypass versus percutaneous revascularisation for isolated lesions of the left anterior descending artery. *BMJ* 2007;doi:10.1136/bmj.39106.476215.BE.

2 Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddard GL. *Methods for the economic evaluation of health care programmes*. 3rd ed. Oxford: Oxford University Press, 2004.

- 3 Petitti DB. *Meta-analysis, decision analysis and cost-effectiveness analysis: methods for quantitative synthesis in medicine*. 2nd ed. New York: Oxford University Press, 2000.
- 4 Reeves BC, Angelini GD, Bryan AJ, Taylor FC, Cripps T, Spyt TJ, et al. A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery. *Health Technol Assess* 2004;8(16):1-43.
- 5 UK Government Actuary's Department. *Interim life tables 2005*. London: GAD, 2006.
- 6 Roiron C, Sanchez P, Bouzamondo A, Lechat P, Montalescot G. Drug eluting stents: a meta-analysis of randomised controlled trials. *Heart* 2006;92(5):641-9.
- 7 British Medical Association, Royal Pharmaceutical Society of Great Britain. *British national formulary*. London: BMA, RPS, 2006. (No 51.)
- 8 Yock CA, Boothroyd DB, Owens DK, Garber AM, Hlatky MA. Cost-effectiveness of bypass surgery versus stenting in patients with multivessel coronary artery disease. *Am J Med* 2003;115(5):382-9.
- 9 Zimmerman FH, Cameron A, Fisher LD, Grace NG. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). *J Am Coll Cardiol* 1995;26:654-61.
- 10 Bypass Angioplasty Revascularization Investigators. Seven year outcome in the bypass angioplasty revascularization investigation (BARI) by treatment and diabetic status. *J Am Coll Cardiol* 2000;35:1122-9.
- 11 King SB III, Kosinski AS, Guyton RA, Lembo NJ, Weintraub WS. Eight-year mortality in the Emory angioplasty versus surgery trial (EAST). *J Am Coll Cardiol* 2000;35:1116-21.
- 12 George CJ, Baim DS, Brinker JA, Fischman DL, Goldberg S, Holubkov R, et al. One-year follow-up of the stent restenosis (STRESS I) study. *Am J Cardiol* 1998;81:860-5.
- 13 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. Benestent Study Group. *J Am Coll Cardiol* 1996;27:255-61.
- 14 Niinami H, Takeuchi Y, Ichikawa S, Suda Y. Partial median sternotomy as a minimal access for off-pump coronary artery bypass grafting: feasibility of the lower-end sternal splitting approach. *Ann Thorac Surg* 2001;72(3):S1041-5.
- 15 Casula R, Athanasiou T, Foale R. Recent advances in minimal-access cardiac surgery using robotic-enhanced surgical systems. *Expert Rev Cardiovasc Ther* 2004;2:589-600.
- 16 Popma JJ, Kantz RE, Baim DS. Editorial: a decade of improvement in the clinical outcomes of percutaneous coronary interventions for multi-vessel coronary artery disease. *Circulation* 2002;106:1592-4.

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## Cost effectiveness of clinically appropriate decisions on alternative treatments for angina pectoris: prospective observational study

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### ABSTRACT

**Objective** To assess whether revascularisation that is considered to be clinically appropriate is also cost effective.

**Design** Prospective observational study comparing cost effectiveness of coronary artery bypass grafting, percutaneous coronary intervention, or medical management within groups of patients rated as appropriate for revascularisation.

**Setting** Three tertiary care centres in London.

**Participants** Consecutive, unselected patients rated as clinically appropriate (using a nine member Delphi panel) to receive coronary artery bypass grafting only (n=815); percutaneous coronary intervention only (n=385); or both revascularisation procedures (n=520).

**Main outcome measure** Cost per quality adjusted life year gained over six year follow-up, calculated with a National Health Service cost perspective and discounted at 3.5%/year.

**Results** Coronary artery bypass grafting cost £22 000 (€33 000; \$43 000) per quality adjusted life year gained compared with percutaneous coronary intervention among patients appropriate for coronary artery bypass grafting only (59% probability of being cost effective at a cost effectiveness threshold of £30 000 per quality adjusted life year) and £19 000 per quality adjusted life year gained compared with medical management among those appropriate for both types of revascularisation (probability of being cost effective 63%). In none of the three appropriateness groups was percutaneous coronary intervention cost effective at a

threshold of £30 000 per quality adjusted life year. Among patients rated appropriate for percutaneous coronary intervention only, the cost per quality adjusted life year gained for percutaneous coronary intervention compared with medical management was £47 000, exceeding usual cost effectiveness thresholds; in these patients, medical management was most likely to be cost effective (probability 54%).

**Conclusions** Among patients judged clinically appropriate for coronary revascularisation, coronary artery bypass grafting seemed cost effective but percutaneous coronary intervention did not. Cost effectiveness analysis based on observational data suggests that the clinical benefit of percutaneous coronary intervention may not be sufficient to justify its cost.

### INTRODUCTION

Guidelines based on clinical appropriateness criteria are widely used to inform decisions about practice but are insufficient grounds for allocating healthcare resources. Although consensus exists that cost effectiveness analysis is needed to maximise the health gains achieved from a limited budget, how closely formally measured clinical appropriateness accords with cost effectiveness is not known. No three way randomised comparisons of the cost effectiveness of medical management, percutaneous management, and coronary artery bypass grafting exist.<sup>1</sup> We studied three management strategies for coronary disease: coronary artery bypass grafting, percutaneous management, and medical management.