Economic evaluation of complete revascularisation for patients with multi-vessel disease undergoing primary percutaneous coronary intervention

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Contributors

GRB, MF, GPM, NC and AHG were involved in the study conception and design. GRB and LI analysed the data. GRB, LI, MRF, GPM and AHG wrote the draft paper. All authors revised and approved the final version of the paper.

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Key words: Economic evaluation; Myocardial infarction; Revascularization; Percutaneous coronary intervention

Abstract

Objective

To determine the cost-effectiveness of complete revascularisation at index admission compared to infarct-related artery (IRA) treatment only, in patients with multi-vessel disease undergoing Primary percutaneous coronary intervention (P-PCI) for ST-segment elevation Myocardial Infarction (STEMI).

Methods

Economic evaluation of a multi-centre randomised trial comparing complete revascularisation at index admission to IRA-only P-PCI in patients with multi-vessel disease (12 month follow-up). Overall hospital costs (costs for P-PCI procedure(s), hospital stay and any subsequent readmissions) were estimated. Outcomes were major adverse cardiac events (MACE, a composite of all-cause death, recurrent myocardial infarction, heart failure, and ischemia-driven revascularisation) and quality-adjusted life years (QALYs) derived from the EQ-5D-3L. Multiple imputation was undertaken. The mean incremental cost and effects, with associated 95% confidence intervals (95%CI), the incremental cost-effectiveness ratio (ICER) and the cost-effectiveness acceptability curve (CEAC) were estimated.

Results

Based on 296 patients, the mean incremental overall hospital cost for complete revascularisation was estimated to be –£215.96 (–£1,390.20 to £958.29), compared to IRA-only, with a per-patient mean reduction in MACE events of 0.170 (0.044 to 0.296) and a QALY gain of 0.011 (-0.019 to 0.041). According to the CEAC, the probability of complete revascularisation being cost-effective was estimated to be 72.0% at willingness to pay of £20,000 per QALY.

Conclusions

Complete revascularisation at index admission was estimated to be more effective (in terms of MACE and QALYs) and cost-effective (overall costs were estimated to be lower and complete revascularisation thereby dominated IRA-only). There was, however, some uncertainty associated with this decision.

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Introduction

Cardiovascular disease is a leading cause of mortality in the UK, with more than 150,000 deaths each year and annual costs >£15 billion [1]. Primary percutaneous coronary intervention (P-PCI) is the standard treatment for patients presenting with ST-segment elevation Myocardial Infarction (STEMI), with >90,000 such procedures undertaken in the UK each year [2]. P-PCI involves inserting a catheter via the groin or arm. A small balloon is then inflated in the narrowed artery to move the obstructing fatty tissue/clot, and to widen the artery. Usually, at least one stent is then permanently implanted to hold the artery open, and improve blood flow to the heart [2]. Of patients presenting with STEMI, 40-65% are estimated to have bystander stenosis in non-infarct related arteries (N-IRA) (multi-vessel disease) [3]. Until recently, treatment of the infarct-related artery (IRA) alone was the internationally recommended strategy [4,5,6]. However, there is growing trial evidence [7,8,9] that the additional treatment of N-IRA (complete revascularisation) is associated with fewer adverse cardiac events, and previous "do-not-do" guidance by the American College of Cardiology has now been withdrawn [10]. While these results need to be confirmed in larger trials, the emerging clinical evidence presents the opportunity to examine the cost-effectiveness of complete versus infarct-only revascularisation. Revascularisation may be associated with increased initial procedure costs, but it is important to also assess whether these costs are off-set by reduced future hospital admissions and fewer adverse events. Here, we report an economic evaluation [11,12], which was conducted alongside the CvLPRIT trial [8], to assess whether complete revascularisation constitutes a cost-effective use of health care resources. We are not aware of any previous economic evaluations of complete revascularisation in this patient group.

Methods

Participants

As previously described [8], the CvLPRIT study was a multi-centre randomised trial comparing complete revascularisation to IRA-only P-PCI for patients with bystander multi-vessel coronary artery disease. Patients were eligible if, following angiography, at least one other artery had a significant (70%) stenosis in addition to the occluded IRA. Inclusion and exclusion criteria are listed in the

Supplementary Table. Patients were randomised to either the IRA-only strategy or to complete revascularisation, undertaken either at the time of P-PCI or during that index admission. Randomisation was via an automated 24-hour telephone randomisation system and stratified by infarct location (anterior/non-anterior) and symptom onset (≤3 hours or >3 hours). Patients were followed up for 12 months post-randomisation. The study was approved by the NRES Committee East Midlands Derby (Ref: 11/H0405/4).

<Insert Supplementary Table link here>

Costs

Costs were estimated from the perspective of the UK National Health Service (NHS). Specifically, index admission P-PCI procedure(s) costs (based on procedure time, consumables and equipment (e.g. catheter, balloon and stents) used for both IRA and any N-IRA interventions performed, for both the initial procedure and any staged procedure), hospital length of stay costs (including time in critical care/high dependency and/or intensive care) and the costs of any hospital readmissions were estimated. All centres were asked to prospectively collect detailed information on the PCI procedure and admission on study specific case record forms. Follow-up data (including hospital re-admissions) was subsequently collected via telephone (6-month post-randomisation) and face-to-face appointment (12-month post-randomisation). Unit costs were assigned to all items of resource use (£GBP for the 2012-13 financial year). Where national unit cost data [13,14,15] were not available, for example for stents and other P-PCI devices, we conducted a survey of participating centres to estimate the average cost for each item. Index admission (P-PCI procedure(s) and hospital length of stay) and readmission costs were combined to estimate overall hospital costs.

In a subsample of sites (3 out of the 7 centres) all patients were also asked to complete an additional resource use questionnaire at the 12month visit. They were asked to report i) all post-discharge health professional visits in the previous 12 months, ii) whether they were in paid employment at the point of randomisation and iii) whether they had returned to work at the 12 month follow-up point. Only the first 3 enrolled sites were asked to complete the additional resource use questionnaire due to the associated burden for staff and patients. Other sites which came on board later to boost recruitment were not asked to complete the additional resource use questionnaire. Health professional visits (including General Practitioner (GP) visits, outpatient attendances, and therapist contacts) were

costed as above and added to overall hospital costs in order to estimate overall NHS and Personal Social Services (PSS) costs.

Outcomes

The primary outcome measure was MACE occurring within 12 months of randomisation (a composite of all-cause mortality, recurrent MI, heart failure and need for repeat revascularisation (PCI or CABG)), as defined in Appendix 2 of the main trial paper [8]. Hospitals recorded MACE data, informed by telephone contact with the patients at 6 months post-randomisation and hospital visits at approximately 12 months. Clinicians blinded to the randomisation group adjudicated all MACE. All MACE events over the 12 month follow-up period were included in the cost-effectiveness analyses (the primary endpoint in the clinical paper was time-to-first MACE event [8]). In line with the National Institute for Health and Clinical Excellence (NICE) methods guide [12], quality of life was measured using the EQ-5D-3L [16] at initial discharge (baseline) and at 12 months post-intervention. Utility scores (a scale where zero is equal to death and one is full health) [11] were derived from the UK York A1 tariff [17] and converted into Quality Adjusted Life Years (QALYs) using the area under the curve approach, with linear interpolation between the baseline EQ-5D and 12 month follow-up point [18]. For patients who died during follow-up, an EQ-5D score of zero was assigned at their date of death [19].

Analyses

Missing data is common in randomised trials and can lead to bias and lack of precision [20]. As recommended for within-trial analysis of cost-effectiveness [20], patterns of missing data were examined to infer the assumed missing data mechanism and complete case analysis [21] did not constitute the base-case analysis. Health professional visit costs were only requested for 3 of the centres and these costs only constituted a small component of the total cost (see Results). Pragmatically it was therefore considered inappropriate to undertake either complete case analysis or imputation for this variable and no further analysis was thereby undertaken for health professional visit costs or overall NHS and Personal Social Services (PSS) costs. To impute missing data, multiple imputation (MI) was undertaken [20], where the *mi impute* command (Stata 12.1 [22]) was used to create twenty datasets (a rule of thumb is that the number of data sets should equal the percentage of

missing data [23]) which were then pooled using Rubin's rules [24]. In addition to the costs (procedure time, consumables and equipment, length of stay and readmissions) and outcomes (baseline and 12 month EQ-5D scores), the MI model included variables associated (p-value <0.10) with missing data, costs or outcomes (time since symptom onset at randomisation (≤3 hours or >3 hours), infarct location (anterior/nonanterior), previous medical history of treated hypercholesterolemia, previous medical history of treated diabetes, age, death, centre, sex and treatment allocation). Baseline and 12 month EQ-5D scores were included, rather than individual dimension scores, as if there was missing EQ-5D data it was generally for the whole questionnaire. However disaggregated costs were used (and then combined to estimate overall hospital costs) as different resource items had different levels of missing data.

Cost and outcome data was analysed simultaneously using bivariate regression, which is generally robust for skewed data and allows for any correlation between costs and effects [25]. We followed the intention-to-treat approach, where patients were analysed according to the group to which they were allocated (regardless of treatment received). All the regressions included age and sex as covariates. The QALY regression also included the baseline EQ-5D as a covariate [18]. This enabled the mean incremental cost between the two groups (mean difference in cost) and the mean incremental effect (the mean difference in both the total number of MACE events / QALYs) to be estimated.

The incremental cost-effectiveness ratio (ICER), defined as mean incremental cost/mean incremental effect [12], for complete revascularisation, compared to IRA-only, was subsequently estimated. If one intervention was both less costly and more effective this was not necessary as that intervention would be categorised as dominant [11]. The ICER can be used to assess whether the extra cost of the intervention (in this case, complete revascularisation), constitutes value for money. In the UK, NICE refers to a cost-effectiveness threshold (λ) value of £20,000-30,000 per QALY [12]. As such, if complete revascularisation had an ICER (incremental cost per QALY) below this level we would consider it to be cost-effective.

In order to estimate the level of uncertainty associated with the decision regarding cost-effectiveness, bootstrap resampling [26] (with 250 replications drawn from each of the 20 imputed datasets [20]) was

used to depict results on the cost-effectiveness plane and the cost effectiveness acceptability curve (CEAC). The cost-effectiveness plane depicts estimates of the mean incremental cost and mean incremental effect [27], whereas the CEAC depicts the probability of the intervention being cost-effective at various 'willingness to pay' thresholds compared to standard care [28]. Additionally, the expected value of perfect information (EVPI), which provides a guide to the upper limit of the value of further research [29], was also calculated at an λ value of £20,000 per QALY.

Finally, sensitivity analyses were undertaken in order to assess the robustness of the above base-case analysis conclusions to changes in key assumptions [11]. First (SA1), a *per protocol* analysis was conducted, excluding patients who did not receive the intervention to which they were allocated (crossovers). Second (SA2), a complete case analysis [21] was conducted for comparison, where patients were only included if they had available data for all costs and outcomes. All analyses were performed in Stata version 12.1 [22] and due to the 12-month follow-up period, no discounting [11] was undertaken.

Results

Participants

Recruitment took place between May 2011 and May 2013 at seven participating UK centres. In total 296 patients were randomised. Baseline demographics and clinical characteristics were similar in both arms, 85.3% of complete revascularisation patients were male and the mean age was 64.6 years, compared to 76.7% males for IRA-only and a mean age of 65.3 years. In the 12-month follow-up period, 14 died and 19 were lost to follow-up. A national database search indicated none of these lost to follow-up patients died during the study period [8].

Costs

Table 1 summarises the levels of resource use for both groups based on available data. Mean P-PCI procedure(s) time (including any staged procedures) was higher in the complete revascularisation arm (76.6 minutes compared with 45.2 minutes for IRA-only, $p<0.001$), as were the number of stents (2.84 per patient versus 1.45, $p<0.001$). Other resource item use was broadly similar between arms (see Table 1).

<Insert Table 1 here>

The unit costs attached to each item of resource use are detailed in Table 2. Total costs were subsequently estimated (see Table 3), where mean P-PCI procedure(s) costs were lower for IRA-only patients, though mean index admission length of stay costs and MACE readmission costs were both slightly higher for IRA-only patients (see Table 3). Mean overall hospital costs were estimated to be higher for complete revascularisation patients (£5,552 complete (n=121); £4,919 IRA-only (n=116)), though there was no statistically significant difference between the two groups.

<Insert Table 2 here>

<Insert Table 3 here>

In relation to the additional resource use questionnaire, health professional visit data was provided by 48 of the 88 complete revascularisation patients (54.5%) from whom details were requested, compared to 48/92 (52.2%) IRA-only patients. Additionally, as they would have had no (post-discharge) health professional visits, these costs were set to zero for the patients who died within their index admission (n=5 IRA-only). The mean number of health professional visits in the 12-month follow-up period was 8.7 in the complete revascularisation arm, compared to 10.6 in the IRA arm only. The associated mean costs were £422 (n=48) and £480 (n=53), respectively. When health professional visit costs were added to overall hospital costs in order estimate overall NHS and PSS costs, these were estimated to be £5,814 (n=41) for complete revascularisation and £5,089 (n=42) for IRA-only (see Table 3).

The two employment questions within the additional resource use questionnaire were completed by 48/88 (54.5%) complete revascularisation patients and 48/92 (52.2%) IRA-only patients at the 12-month follow-up point. Of the 25 complete revascularisation patients who reported that they were in employment at the time of their heart attack, 20 reported they had returned to work at the 12-month follow-up point. In the IRA-only arm 15 out of 23, who reported that they were in employment at the time of their heart attack, reported that they had returned to work.

Outcomes

Table 4 summarises clinical outcomes for both groups, based on available data. Over the 12-month follow-up period, the mean number of MACE events was significantly lower in the complete

revascularisation arm (0.14 per patient, 19 events in total) compared with IRA-only (0.30 per patient, 41 events in total). In terms of health-related quality of life, EQ-5D-3L scores were slightly, non-significantly higher for complete revascularisation patients at both baseline and at 12-month follow-up.

<Insert Table 4 here>

Analyses

Table 5 presents estimates of the mean incremental cost and incremental effect (MACE or QALY), generated from bivariate regression, along with ICER and CEAC estimates. For the base-case (intention to treat) and SA1 (per protocol), complete revascularisation was estimated to dominate IRA-only, both in term of MACE events and QALYs, as it had both lower mean costs and higher mean effects. Significantly fewer MACE occurred in the complete revascularisation arm, there was no significant difference between groups with regard to either overall hospital costs or QALYs.

<Insert Table 5 here>

In terms of uncertainty, 49.0% of the cost-effect pairs on the cost-effectiveness plane were located in the south east quadrant, where complete revascularisation would be estimated to have both lower mean costs and higher mean effects. However, there was wide variation in the bootstrap estimates of both the mean incremental cost and mean incremental QALY gain (see Figure 1). Similarly, according to the CEAC, at £20,000 per QALY, the probability that complete revascularisation was more cost-effective than IRA-only was approximately 70%, indicating there was some uncertainty associated with this decision (See Supplementary figure). Additionally, the EVPI (per patient) was estimated to be £82.73. On the assumption that about one-third of the 90,000 annual P-PCI procedures for STEMI would be eligible for complete revascularization [8], then over 10 years the population EVPI would be estimated to be approximately £25 million (at a willingness to pay of £20,000 per QALY).

<Insert Figure 1 here>

<Insert Supplementary Figure link here>

As in the base-case analyses, all sensitivity analyses estimated that there was a non-significant difference in mean costs and QALYs, but a significant reduction in MACE events in patients undergoing complete revascularisation compared to IRA-only PCI (see Table 5). For base case and SA1, costs were higher in the IRA-only group, however in SA2 (complete case) costs were higher in the intervention arm. This was largely due to two participants in the IRA-only group with very high (>£50,000) costs. These participants were excluded from SA2 because some cost components were

missing, however their known costs were used to estimate the imputation models, and they were included in base case and SA1 analysis.

Discussion

Main findings

Based on evidence provided from the CvLPRIT trial [8], as complete revascularisation had both lower mean costs and higher mean effects compared to IRA-only, we would estimate complete revascularisation to be cost-effective. However, there is some uncertainty associated with this decision. For example, according to the CEAC it was estimated that there was approximately a 30% chance (at a willingness to pay of £20,000 per QALY) of making the wrong decision by implementing complete revascularization, and the population EVPI was estimated to be approximately £25 million .

Comparisons with other studies

We are not aware of any previous economic evaluations which have compared complete revascularisation to IRA-only for STEMI patients with multi-vessel disease. The findings of this study are however consistent with previous clinical evidence, that suggests complete revascularisation reduces future MACE [7,9,30,31] (with associated reduced hospital re-admission costs), and also improves quality of life (according to the Seattle Angina Questionnaire (SAQ)) [32]. There are few well conducted economic analyses of P-PCI, especially in the context of randomised trials. When compared with thrombolysis, P-PCI has higher initial costs that are offset by reduced downstream costs and complications [33,34]. In the CADILLAC trial, P-PCI with stenting was shown to be cost effective compared to plain balloon angioplasty [35]. Though they are based on different treatment comparisons, and the results may not be generalisable to the population within our study, these previous studies indicate that better revascularisation in the context of STEMI can be cost-effective, in spite of higher initial costs.

Study limitations

In line with good practice recommendations for cost-effectiveness analyses [36], we concentrated on large cost drivers and excluded resources that were not expected to differ between the two treatment arms (e.g. routine monitoring scans or tests). That said, a potential limitation is that a narrow health

sector cost perspective was taken, particularly as only patients in 3 centres were asked to complete the additional self-report questionnaire (reporting health professional visits and employment status). These costs were excluded from subsequent analyses, the results in Table 3 indicate that these were not the main cost drivers for responding patients. With regard to health-related quality of life, QALY scores were only available for ~70% of participants (see Table 4). Some of the missing EQ-5D baseline data may be due to the patient being discharged at short notice, or at the weekend when a research nurse was not available.

A further potential limitation is that our analysis is based on the evidence generated by one trial [8] and therefore may not incorporate all relevant evidence [37]. That said, a recent meta-analysis [31] shows that our trial results are in keeping with the few trials that have been conducted in this area. Similarly, it could be argued that the conclusions might differ if results were estimated over a longer follow-up period. However, if the treatment effect was maintained beyond 12 months, the conclusions would be unchanged as extrapolation would increase the QALY gain, improving the estimated level of cost-effectiveness. The main strength of this economic analysis is that it is based on a randomised study [8], an advance on observational studies that may not control for confounding factors [30].

Conclusions

Based on an economic evaluation of the CvLPRIT trial [8] we have shown that, in a population of patients with STEMI and multi-vessel disease, complete revascularisation undertaken during the index admission was more effective in terms of fewer MACE, and had an incremental QALY gain, compared with IRA-only revascularisation. As higher procedure costs are broadly off-set by lower readmission rates, such that overall costs are similar, these data suggest that complete revascularisation constitutes a cost-effective treatment option for STEMI patients with multi-vessel disease. That said, the CEAC and EVPI values suggest there is some uncertainty associated with this decision.

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Competing interests

(All outside the submitted work) MF reports grants personal fees from Astra Zeneca and grants from Novartis. NC reports grants and personal fees from Boston Scientific, grants and personal fees from Haemonetics, grants and personal fees from HeartFlow, grants and personal fees from St Jude Medical, non-financial support from Volcano, personal fees and non-financial support from Abbott Vascular. No others declared.

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Table 1 – Levels of resource use

Resource use, N/mean (SD) [n]	Complete [n=150]	IRA-only [n=146]
IRA only, N	11 (Crossover) [n=150]	139 [n=146]
N-IRA completed in same sitting, N	97 [n=150]	7 (Crossover) [n=146]
N-IRA completed in separate (staged) sitting, N	42 [n=150]	0 [n=146]
P-PCI procedure time, mean (minutes)	59.92 (29.37) [n=140]	45.19 (17.60) [n=132]
Staged N-IRA procedure time, mean (minutes)	53.89 (29.10) [n=36 of 42]	-
P-PCI and any staged N-IRA procedure time, mean (minutes)	76.65 (41.20) [n=135]	45.19 (17.60) [n=132]
Glycoprotein IIb/IIIa inhibitors (GPI agents), N	46 [n=145]	44 [n=134]
Bivalirudin, N	78 [n=139]	63 [n=128]
Bare metal stents, N	9 [n=147]	13 [n=140]
Drug-eluting stents, N	141 [n=147]	127 [n=140]
Total number of stents, mean (number used per patient)	2.84 (1.26) [n=147]	1.45 (0.90) [n=140]

Thrombus aspiration, N	93 [n=145]	102 [n=140]
Radial access, N	112 [n=146]	99 [n=140]
Initial hospital length of stay per patient, mean (days)	3.89 (4.26) [n=148]	5.10 (10.33)† [n=140]
Readmissions (all), length of stay per patient, mean (days)	1.47 (3.70) [n=139]	1.66 (4.08) [n=138]

N=number of patients in receipt; n=number of patient for whom data were available; SD=standard deviation; IRA= infarct-related artery; N-IRA=non infarct-related artery; P-PCI=Primary percutaneous coronary intervention; † 1 IRA patient had an index admission length of stay of 65 days and another 104 days – if this data is removed the IRA mean is 3.96 days, the median value in both arms is 3 days.

Table 2 – Unit costs

Resource use	Unit cost
Index admission costs	
P-PCI Procedure time cost (per minute)	£5.94*
Glycoprotein IIb/IIIa inhibitor: Abciximab	£710.15*†[15]
Bivalirudin	£426.25*‡[15]
Bare metal stent	£97.50*
DES stents	£301.88*
Femoral access	£46.86*
Radial access	£26.50*
Thrombus aspiration catheter	£160.00*
Disposables× (cost per sitting)	£154.50*
Bed day – standard care	£379.40[13]
Bed day – high dependency	£851.89[13]
Bed day – intensive care	£1,236.48[13]
Readmissions Costs (up to 12 months follow-up)	
Bed day (non-MACE)	£265.06[13]
Myocardial infarction	£1,710.18 + £224.15 per day if >5 days[13]
Heart failure	£2,168.19 + £280.56 per day if >5 days[13]
Revascularisation: PCI	£2,016.59 + £379.40 per day if >5 days[13]
Revascularisation: CABG	£9,002.01 + £388.82 per day if >5 days[13]
Health professional visits (most commonly reported)	
Cardiologist	£125.89[13]
Hospital nurse	45.00[14]
General Practitioner (GP)	25.00[14]

P-PCI=Primary percutaneous coronary intervention; CABG=Coronary artery bypass grafting; MACE =major adverse cardiac event; Sources/assumptions:*Based on survey of participating centres; †2.8 vials per sitting; ‡ 1.38 vials per sitting; × Balloon, sheath, catheter

Table 3 – Summary costs

Cost component: mean (SD) [n]	Complete	IRA-only	P-value
P-PCI procedure(s) time	£455.37 (£244.77) [n=135]	£268.46 (£104.55) [n=132]	<0.001
P-PCI procedure(s) consumables and equipment	£1,695.95 (£583.41) [n=137]	£1,183.98 (£467.88) [n=128]	<0.001
Index admission – hospital length of stay	£2,830.98 (£2,091.97) [n=148]	£3,605.11 (£6,231.66) [n=140]	0.164
Total Index admission cost	£4,890.12 (£2,097.54) [n=129]	£4,668.21 (£5,048.39) [n=121]	0.654
MACE readmissions	£277.92 (£1,264.14) [n=139]	£400.88 (£1,232.14) [n=138]	0.413
Other hospital readmissions	£310.83 (£935.73) [n=139]	£251.62 (£668.20) [n=138]	0.545
Overall hospital costs	£5,551.70 (£2,974.40) [n=121]	£4,918.60 (£2,449.29) [n=116]	0.074
Health Professional visits	£422.07 (£385.47) [n=48]	£480.43 (£368.74) [n=53]	0.440
Overall NHS and PSS costs	£5,814.25 (£3,041.03) [n=41]	£5,089.17 (£2,101.78) [n=42]	0.212

n=number of patient for whom data were available; SD=standard deviation; P-PCI=Primary percutaneous coronary intervention; PSS=Personal Social Services

Table 4 – Outcomes

item, N/mean (SD) [n]	Complete [n=150]	IRA-only [n=146]	P-value
Baseline EQ-5D-3L score, mean	0.824 (0.216) [n=116]	0.791 (0.295) [n=116]	0.287
12 month EQ5D-3L score, mean	0.837 (0.256) [n=122]	0.798 (0.311) [n=115]	0.295
QALY score, mean	0.833 (0.204) [n=103]	0.801 (0.258) [n=100]	0.339
MACE,N	19 [n=139]	41 [n=138]	0.016*
Death, N	4 [n=150]	10 [n=146]	0.098
Heart Failure, N	6 [n=139]	11 [n=138]	0.259
Myocardial infarction, N	1 [n=139]	3 [n=138]	0.312
Revascularisation, N	8 [n=139]	17 [n=138]	0.079

n=Number for whom data were available; N=number of events; SD=standard deviation; * Statistically significant p<0.05; MACE=major adverse cardiac events; QALY=Quality Adjusted Life Years truncated at 12months

Table 5 – Estimates of incremental cost, incremental effect and cost-effectiveness of complete revascularisation in the base-case and sensitivity analyses

Analysis (Nc,Ni)	Incremental cost (95% CI)	Incremental effect (95% CI)	ICER	CEAC*
		MACE		
Base-case: imputed (150, 146)	-£215.96	-0.170	Dominant	
	(-£1,390.20 to £958.29)	(-0.044 to -0.296)		
SA1: imputed per protocol: (139, 139)	-£534.89	-0.201	Dominant	
	(-£1,730.65 to £660.88)	(-0.070 to -0.331)		
SA2: complete case: (121, 116)	£590.63	-0.156	£3,776.87	
	(-£91.02 to £1,272.27)	(-0.023 to -0.290)		
		QALYs		
Base-case: imputed (150, 146)	-£215.96	0.011	Dominant	72.0%
	(-£1,390.20 to £958.29)	(-0.019 to 0.041)		
SA1: imputed per protocol: (139, 139)	-£534.89	0.012	Dominant	84.4%
	(-£1,730.65 to £660.88)	(-0.019 to 0.043)		
SA2: complete case: (89, 86)	£446.65	0.021	£21,495.69	45.3%
	(-£151.55 to £1,044.86)	(-0.018 to 0.060)		

95% CI=95% confidence interval; ICER =incremental cost-effectiveness ratio; Dominant = lower mean costs and higher mean effect; Nc (Ni) =Number randomised to complete revascularisation (IRA only) who were included in the analysis; SA1 and SA2 refer to the first and second sensitivity analyses described in the Methods; MACE=major adverse cardiac events; QALY=Quality Adjusted Life Years truncated at 12months; *probability of bring cost-effective on the cost-

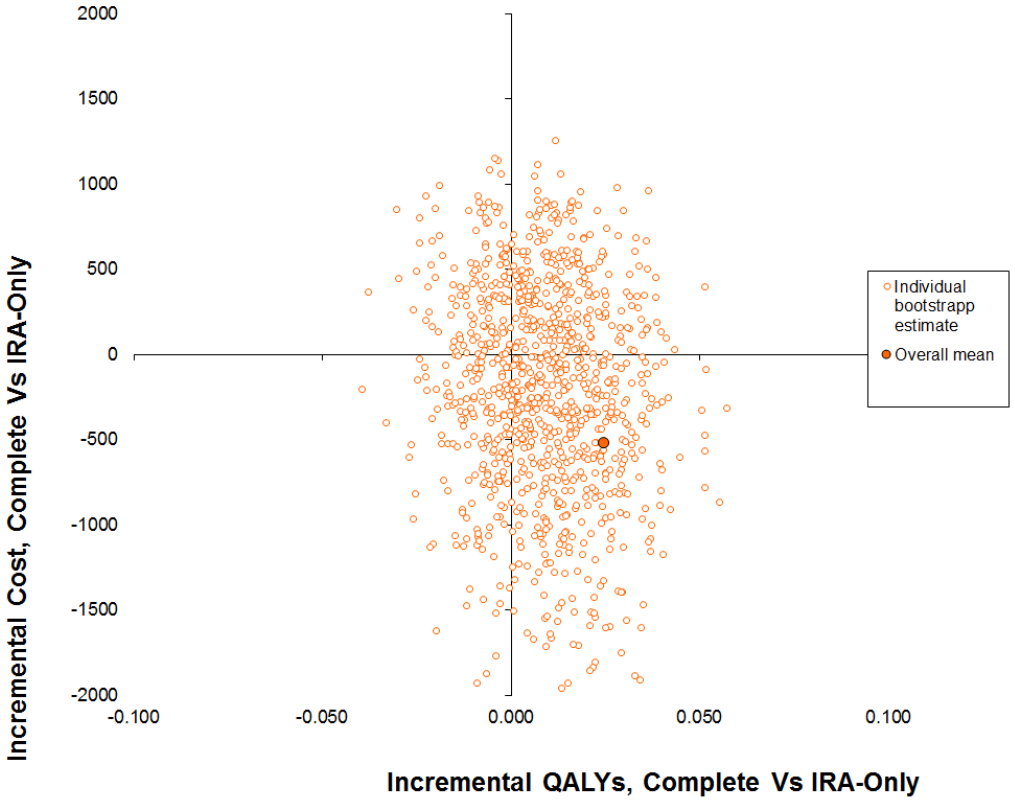
effectiveness acceptability curve (CEAC) at the threshold (λ) of £20,000 per QALY;

Supplementary Table: Inclusion and Exclusion criteria

Inclusion criteria
Suspected or proven acute myocardial infarction; Significant ST elevation or left bundle branch block (LBBB) on electrocardiogram (ECG) (in cases of LBBB, angiographic confirmation of infarct-related artery (IRA) occlusion is required)
< 12 hrs of symptom onset
Scheduled for Primary percutaneous coronary intervention (P-PCI) for clinical reasons
Provision of verbal assent followed by written informed consent
Multivessel coronary artery disease at angiography defined as:
IRA plus at least one non-infarct related epicardial artery (N-IRA) with at least one lesion deemed angiographically significant (>70% diameter stenosis in one plane or > 50% in 2 planes).
The N-IRA should be a major (>2mm) epicardial coronary artery or branch (>2mm) and be suitable for stent implantation.
Exclusion criteria
Any exclusion criteria for P-PCI
<18 years
Clear indication for, or contraindication to, multi vessel P-PCI according to operator judgement
Previous Q wave myocardial infarction
Patients with prior CABG (Coronary artery bypass grafting)
Cardiogenic Shock
Ventricular septal defect (VSD) or moderate/severe mitral regurgitation
Chronic kidney disease (Creatinine (Cr)>200µmol/l or eGFR (estimated Glomerular Filtration Rate<30ml/min/1.73m^2)
Suspected or confirmed thrombosis of a previously stented artery
Where the only significant N-IRA lesion is a chronic total occlusion

Figure Legends

Figure 1. Bootstrapp estimates (and overall mean) of the incremental cost and effect of complete revascularisation compared to IRA-only, depicted on the cost-effectiveness plane



Supplementary figure for the web. Cost effectiveness acceptability curve: estimated probability of complete revascularisation being cost-effective at different levels of cost-effectiveness. The base-case (solid line), and sensitivity analyses 1 (per protocol: dashed) and 2 (complete case: dotted line).