


# openheart Cost-effectiveness of stepwise provisional versus systematic dual stenting strategies in patients with distal bifurcation left main stem lesions: economic analysis of the EBC MAIN trial

Alicia Le Bras,<sup>1</sup> David Hildick-Smith,<sup>2</sup> Arnaud Nze Ossima,<sup>1</sup> Olivier Supplisson,<sup>1</sup> Mohamed Egred,<sup>3</sup> Philippe Brunel,<sup>4</sup> Adrian P Banning,<sup>5</sup> Marie-Claude Morice,<sup>6</sup> Isabelle Durand-Zaleski <sup>1,7</sup>

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For numbered affiliations see end of article.

**Correspondence to**  
Dr Isabelle Durand-Zaleski;  
[isabelle.durand-zaleski@aphp.fr](mailto:isabelle.durand-zaleski@aphp.fr)

## ABSTRACT

**Background** In patients with distal bifurcation left main stem lesions requiring intervention, the European Bifurcation Club Left Main Coronary Stent Study trial found a non-significant difference in major adverse cardiac events (MACEs, composite of all-cause death, non-fatal myocardial infarction and target lesion revascularisation) favouring the stepwise provisional strategy, compared with the systematic dual stenting.

**Aims** To estimate the 1-year cost-effectiveness of stepwise provisional versus systematic dual stenting strategies.

**Methods** Costs in France and the UK, and MACE were calculated in both groups to estimate the incremental cost-effectiveness ratio (ICER). Uncertainty was explored by probabilistic bootstrapping. The analysis was conducted from the perspective of the healthcare provider with a time horizon of 1 year.

**Results** The cost difference between the two groups was €-755 (€5700 in the stepwise provisional group and €6455 in the systematic dual stenting group,  $p$  value<0.01) in France and €-647 (€6728 and €7375, respectively,  $p$  value=0.08) in the UK. The point estimates for the ICERs found that stepwise provisional strategy was cost saving and improved outcomes with a probabilistic sensitivity analysis confirming dominance with an 80% probability.

**Conclusion** The stepwise provisional strategy at 1 year is dominant compared with the systematic dual stenting strategy on both economic and clinical outcomes.

## INTRODUCTION

There is conflicting evidence regarding the best strategy to treat bifurcation lesions. In addition to uncertain long-term benefit on outcomes, systematic

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In patients with left main stem bifurcation lesions requiring intervention, a stepwise provisional strategy resulted in fewer major adverse cardiac events (composite of all-cause death, non-fatal myocardial infarction and target lesion revascularisation) than a systematic dual stenting strategy.

### WHAT THIS STUDY ADDS

⇒ We performed an economic evaluation and found a 1 year, cost difference of €647 (France) to €755 (UK) favouring stepwise stenting.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Stepwise provisional stenting should be preferred on both economic and clinical criteria.

stenting has increased costs and potential detrimental effects. The European Bifurcation Club Left Main Coronary Stent Study (EBC MAIN), an open-label, randomised trial, found a non-significant difference in major adverse cardiac events (MACEs) favouring the with stepwise layered strategy compared with planned dual stenting.<sup>1</sup> In parallel with assessment of clinical outcomes, our objective was to estimate the incremental cost-effectiveness ratio (ICER) at 12 months, using MACE, the composite of all-cause death, myocardial infarction and target lesion revascularisation, as the effectiveness criterion. The CURE and BASKET trials have provided benchmarks for acceptable costs with an ICER

of US\$22 484 in the USA and 64 €732 in Switzerland to prevent one MACE.<sup>2,3</sup>

## METHODS

### Clinical trial

The design and results of EBC MAIN have been published.<sup>1,4</sup> The study hypothesis was that left main coronary bifurcation lesions are best treated with a planned single-stent strategy rather than a planned dual-stent strategy, with respect to death, target lesion revascularisation and myocardial infarction at 1 year. The primary study endpoint was a composite of death, myocardial infarction and target lesion revascularisation at 12 months. Secondary endpoints were: death, myocardial infarctions and target lesion revascularisation, each at 12 months; angina status, stent thrombosis, death, myocardial infarction, target lesion revascularisation at 3-year and 5-year clinical follow-up.

The study protocol was registered in the ClinicalTrials.gov registry (NCT02497014). The study was supported by an unrestricted educational grant from Medtronic. The trial was administered and overseen by a Clinical Research Organisation (Cardiovascular European Research Center, CERC, Massy, France) and the endpoints related events were adjudicated by a Clinical Events Committee and a Data and Safety Monitoring Board. An independent CoreLab analysed the procedural angiograms and all revascularisation procedures. The study protocol, clinical investigation plan and the statistical analysis plan were developed by CERC, the economic evaluation was preplanned.<sup>4</sup> In summary, 467 with true left main stem bifurcation lesions requiring intervention recruited in 11 European countries were randomly allocated to the stepwise layered provisional strategy (n=230) or the systematic dual stent strategy (n=237). The primary endpoint (a composite of death, myocardial infarction, and target lesion revascularisation at 12 months) occurred in 14.7% of the stepwise provisional group versus 17.7% of the systematic dual stent group (HR 0.8, 95% CI 0.5–1.3; p value=0.34).

### Cost-effectiveness analysis

The primary endpoint for the effectiveness was the primary clinical composite outcome of EBC MAIN defined as the composite of all-cause death, non-fatal

myocardial infarction and target lesion revascularisation (MACE), at 1 year between the stepwise provisional group and the systematic dual stenting group, calculated as the total number of events in each group divided by the total population. A within-trial cost utility analysis was not possible since no quality of life data had been collected during the trial.

The endpoint of the economic evaluation was the 12-month ICER expressed as the difference in costs divided by the difference in MACE. Total costs were estimated from the date of recruitment until the earliest of death, withdrawal and 12 months. Measures of within-trial use of hospital resources were based on routine hospital data via patient-level information and costing systems, and entries in case report forms (CRFs) for devices. The cost analysis was undertaken from a hospital perspective in the French and English settings. We selected these countries with close practice patterns because of the known negative correlation between unit costs and volume of hospital resources. We did a fully pooled analysis for resource utilisation and clinical outcomes and valued resource use at country prices. We followed the Consolidated Health Economic Evaluation Reporting Standards reporting guidelines.<sup>5</sup>

Costs for each strategy included:

- ▶ The initial procedural costs: the costs of the index hospital admission and devices used during the procedure.
- ▶ Costs of procedure-related and cardiac events during the 1-year follow-up.

Usage data for hospital resources were obtained from discharge summaries for the index admission. Repeat hospital admissions were identified from the study electronic CRF (eCRF) for adverse events. We took into account only events labelled as relevant by the clinical event committee.

The cost of the index admission were calculated based on the severity—adjusted diagnosis related groups (DRGs) obtained from the national hospital cost study<sup>6</sup> for costs in France and from the National Cost Collection for costs in the UK.<sup>7</sup> We estimated for each DRG the procedure related costs and the length of stay related costs based on the average national values, and recalculated each for the trial patients using the actual procedure duration, number of guides, stents and balloons and length of stay reported in the CRF.

**Table 1** Details of adverse events at 1 year

	Stepwise provisional (N=230)		Systematic dual (N=237)		P value
	N	Mean±SD	N	Mean±SD	
Events					
Death from any cause	7	0.03 (±0.17)	10	0.04 (±0.20)	0.50
Myocardial infarctions	26	0.11 (±0.36)	27	0.11 (±0.36)	0.98
Revascularisation	36	0.16 (±0.49)	41	0.17 (±0.48)	0.71
Stroke	2	0.01 (±0.09)	1	0.00 (±0.06)	0.55

**Table 2** Resource use, per-patient cost (inflated) in euros and clinical results by randomisation group at 1 year (intention-to-treat analysis)

	Stepwise provisional (N=230)	Systematic dual (N=237)	P value
MACEs—mean±SD	0.20 (±0.54)	0.25 (±0.60)	0.40
Initial admission days—mean±SD	3.19 (±3.67)	3.58 (±4.56)	0.30
Number of repeat hospital admissions—mean±SD	0.22 (±0.60)	0.22 (±0.61)	0.91
French costs (€)—mean±SD			
Initial admission	4874 (±3114)	5618 (±3437)	<b>0.01</b>
Intensive care unit days	337 (±792)	336 (±692)	0.98
Floor bed days	2457 (±2165)	2711 (±2603)	0.25
Procedure±	552 (±302)	616 (±352)	<b>0.04</b>
Stents	929 (±610)	1331 (±449)	<b>&lt;0.01</b>
Balloons	243 (±103)	271 (±110)	<b>&lt;0.01</b>
Guides	356 (±243)	353 (±224)	0.89
Repeat hospital admissions	826 (±2380)	837 (±2305)	0.96
Within 30 days	84 (±633)	31 (±476)	0.30
Between 30 days and 6 months	266 (±1278)	379 (±1392)	0.36
Between 6 months and 12 months	476 (±1815)	427 (±1437)	0.75
Total 1-year costs	5700 (±4081)	6455 (±4394)	0.05
UK costs (€)—mean±SD			
Initial admission	6203 (±2002)	6835 (±2173)	<b>&lt;0.01</b>
Hospitalisation±	4675 (±1808)	4880 (±2106)	0.26
Stents	929 (±610)	1331 (±449)	<b>&lt;0.01</b>
Balloons	243 (±103)	271 (±110)	<b>&lt;0.01</b>
Guides	356 (±243)	353 (±224)	0.89
Repeat hospital admissions	525 (±1589)	540 (±1553)	0.92
Within 30 days	41 (±346)	17 (±265)	0.40
Between 30 days and 6 months	176 (±875)	247 (±1002)	0.42
Between 6 months and 12 months	308 (±1219)	276 (±957)	0.75
Total 1-year costs	6728 (±2490)	7375 (±2758)	<b>&lt;0.01</b>

MACEs (major adverse cardiovascular events), including all-cause death, non-fatal myocardial infarction and target lesion revascularisation; ±: excluding the costs of stents, balloons and guides. Bold values are statistically significant.

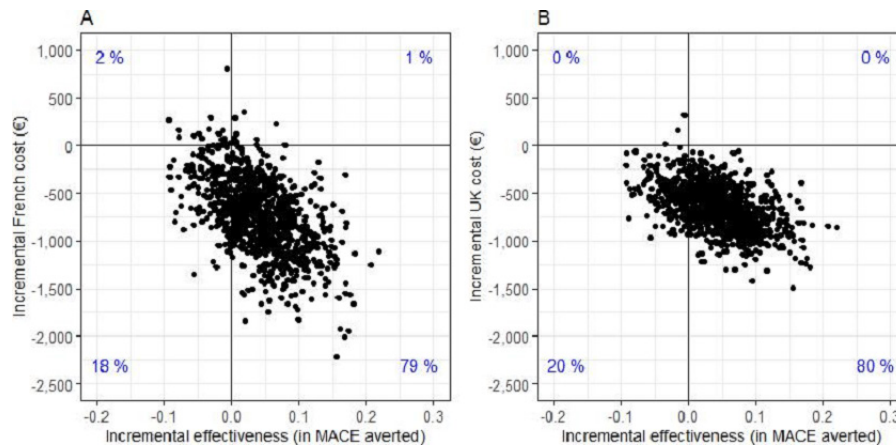
Repeat hospital admissions were identified from the study eCRF for adverse events. When multiple MACE occurred in a cluster, we assigned to each the relevant DRG and its associated costs and selected the DRG associated with the highest activity. Deaths that were not associated with a cluster of other MACE were not valued.

All unit costs for supplies and DRGs are presented in online supplemental table 1. All costs were valued at 2021 prices. UK pounds were converted into euros using the Organisation for Economic Co-operation and Development purchasing parity power £1=€1.07.<sup>8</sup> Both costs and outcomes were undiscounted because of the short time horizon. The ICER, defined as the difference in cost between the two strategies divided by the difference in effectiveness, was reported in cost per MACE averted.

### Statistical analysis

The statistical analyses were performed on the intention-to-treat (ITT) and per-protocol (PP) populations.<sup>9</sup> Multivariate imputation by chained equations was used to process missing data.<sup>10 11</sup> Imputed datasets were generated using predictive mean matching from a set of imputation models constructed from all potential prognostic factors: sex, age, site, country, time spent in the trial and by intervention group.

Cost and efficacy data were expressed as mean±SD. The cost differences between groups were compared with a sampled permutation test with 1000 replications. Group differences in MACE and repeat hospital admissions were compared with a Poisson model or a negative binomial regression. Poisson regressions assume that the variance of the distribution is equal to its mean. If this assumption was not met, we used negative binomial regression.



**Figure 1** Scatter plots of incremental cost and effectiveness of stepwise provisional strategy compared with systematic dual stenting strategy at one year on the per-protocol population. (A) Scatter plot of incremental cost and effectiveness in euros with French costs per MACE averted. (B) Scatter plot of incremental cost and effectiveness in euros with UK costs per MACE averted. MACE (major adverse cardiovascular events), all-cause death, non-fatal myocardial infarction and target lesion revascularisation.

Other quantitative data were compared by treatment group using: (1) the standard Student's t-test, when the assumptions of homogeneity (equal variances between groups) and normality were met, (2) the Welch's t-test, a parametric alternative to the t-test, when the assumption of homogeneity was not met, (3) the Mann-Whitney U test, a non-parametric test, when the dependent variable was not normally distributed.

The uncertainty of the results was analysed using a non-parametric bootstrap, which provided multiple estimates of the ICER by randomly resampling the patient population 1000 times. Results were presented as a scatter plot of 1000 ICERs on the cost-effectiveness plane and transformed into a cost-effectiveness acceptability curve based on the decision-makers' willingness to pay for an additional quality-adjusted life year. All the 95% CIs were estimated with non-parametric bootstrap. A p value less than 0.05 was considered significant.

All health economic analyses were performed using the following packages in R: Tidyverse, Boot, Janitor, Coin and Mice packages in R.<sup>12</sup>

## RESULTS

### Participants

Between February 2016 and November 2019, 467 patients with true left main stem bifurcation lesions requiring intervention were enrolled in the trial at 31 sites in 11 European countries. Among them, 230 patients were randomly assigned to receive the stepwise provisional strategy, and 237 to receive the systematic dual stenting strategy. On the PP population, the number of patients was 224 and 225, respectively.

### Effectiveness

Details of adverse events at 1 year are presented in table 1 for the ITT population and in online supplemental table 2 for the PP population. Table 1 shows the

mean number of myocardial infarctions was 0.11 ( $\pm 0.36$ ) in both groups. At 1 year, no difference was shown in adverse events.

### Service use and costs

Table 2 shows the average resource use for the stepwise provisional and systematic dual groups for the ITT analysis. Results at 1 year are presented in online supplemental table 3 for the PP population. In the ITT population, both groups have similar average length of stay for initial hospitalisation (p value=0.30) and repeat hospital admissions (p value=0.91).

At 1 year, the mean incremental cost was €-755 (95% CI €-1514–€11; p value<0.01) in France and €-647 (95% CI €-1108–€164; p value=0.08) in the UK, in favour of the stepwise provisional group (table 2). Total additional costs were mainly due to the procedure.

### Cost-effectiveness

On the ITT population, the stepwise provisional strategy is less costly and has a higher efficiency (fewer MACEs), compared with the systematic dual stenting strategy at 1 year. The ICER was -15 000 €/MACE averted in France and -12 940 €/MACE averted in UK. In other words, each MACE averted at 1 year in the stepwise provisional strategy is associated with a cost saving of €15 000 and €12 940 compared with the systematic dual stenting strategy. The set of ICERs estimated by the non-parametric bootstrap are presented by the scatterplot on the cost-effectiveness plane in figure 1 for the ITT population and in online supplemental figure 1 for the PP population; nearly 80% of these ICERs were located in the bottom right-hand quadrant. These results suggest that stepwise provisional approach has a probability close to 80% of being dominant regardless of the country or population analysed.



## DISCUSSION

To our knowledge, this is the first cost-effectiveness study conducted on patients with distal bifurcation left main stem lesions. We found that in both France and the UK the use of the stepwise layered provisional strategy had an 80% chance of being both more effective and less costly than the systematic dual stenting strategy.

The results of the economic evaluation of the EBC main trial present a different perspective from the clinical assessment by studying the joint distribution of costs and outcomes. The outcome (effectiveness criteria) used was the average number of MACE rather than the per cent of patients with MACE and the endpoint of the cost-effectiveness analysis was the cost per MACE averted. The results of the economic evaluation present information that complements the clinical evaluation by combining resource utilisation with medical outcomes and providing the likelihood that provisional stenting represents an appropriate use of healthcare budgets.

## Limitations

We have identified the following limitations. First, the time horizon chosen for the economic evaluation is 1 year. It is possible that some MACE occurred after this follow-up period. For this reason, the follow-up period is extended to 3 years. Second, costs estimates relied on a proxy for estimating the DRGs index. Therefore, they suffered from a lack of precision. Third, we used hospital costs only, under the assumption that out of hospital costs such as medications and follow-up visits would not differ between groups. Indirect costs such as loss of productivity or non-medical costs were not included with biased the results in favour of the group with the lower event rate. The study was supported by Medtronic, a device manufacturer. However, the EBC main trial was investigator-led, devised by and run through the European Bifurcation Club without participation of Medtronic in the design, analysis or interpretation of the data. Furthermore, the results do not favour the manufacturer since the better strategy required a statistically significant lower number of stents.

## CONCLUSIONS

Among patients with distal bifurcation left main stem lesions, the cost-effectiveness analysis favoured of the stepwise provisional strategy, rather than the systematic dual stenting strategy.

## Impact on daily practice

The main results of the EBC-MAIN trial showed that the stepwise provisional strategy was as effective as the systematic dual stenting strategy. With nearly 80% probability that stepwise provisional strategy is more effective and less expensive, this economic evaluation also highlighted the financial interest of the stepwise provisional strategy, which may lead the healthcare authorities to keep the stepwise provisional strategy in left main stem true bifurcation procedures.

## Author affiliations

<sup>1</sup>URCEco DRCl, Assistance Publique - Hopitaux de Paris, Paris, France

<sup>2</sup>Sussex Cardiac Centre, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK

<sup>3</sup>Cardiology, Freeman Hospital, Newcastle upon Tyne, UK

<sup>4</sup>Cardiology, Clinique de Fontaine, Dijon, France

<sup>5</sup>Cardiology, Royal Sussex County Hospital, Brighton, UK

<sup>6</sup>Cardiology, Cardiovascular European Research Center CERC, Massy, France

<sup>7</sup>University of Paris, Paris, France

**Twitter** Isabelle Durand-Zaleski @zaleski\_i

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## ORCID iD

Isabelle Durand-Zaleski <http://orcid.org/0000-0002-4078-1476>

## REFERENCES

- Hildick-Smith D, Egred M, Banning A, *et al*. The European Bifurcation club left main coronary stent study: a randomized comparison of stepwise provisional vs. systematic dual stenting strategies (EBC MAIN). *Eur Heart J* 2021;42:3829–39.
- Lamy A, Jönsson B, Weintraub WS, *et al*. The cost-effectiveness of the use of clopidogrel in acute coronary syndromes in five countries based upon the CURE study. *Eur J Cardiovasc Prev Rehabil* 2004;11:460–5.
- Brunner-La Rocca HP, Kaiser C, Bernheim A, *et al*. Cost-effectiveness of drug-eluting stents in patients at high or low risk of major cardiac events in the Basel Stent Kosteneffektivitäts trial (BASKET): an 18-month analysis. *Lancet* 2007;370:1552–9.
- Chieffo A, Hildick-Smith D. The European bifurcation club left main study (EBC MAIN): rationale and design of an international, multicentre, randomised comparison of two stent strategies for the treatment of left main coronary bifurcation disease. *EuroIntervention* 2016;12:47–52.
- Husereau D, Drummond M, Petrou S, *et al*. Consolidated health economic evaluation reporting standards (CHEERS) statement. *Value Health* 2013;16:e1–5.

- 6 ATIH. Référentiel national de Coûts des Prises en charge (ENC). Available: <https://www.scansante.fr/applications/enc-mco> [Accessed 05 May 2022].
- 7 National Health Service. National cost collection: national schedule of NHS costs for the year 2019 - 2020. Available: <https://www.england.nhs.uk/national-cost-collection> [Accessed 05 May 2022].
- 8 Organisation for Economic Co-operation and Development (OECD) purchasing power parity index. Available: <https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm> [Accessed 10 Feb 2022].
- 9 Gupta SK. Intention-to-treat concept: a review. *Perspect Clin Res* 2011;2:109–12.
- 10 White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011;30:377–99.
- 11 van S, Groothuis-Oudshoorn K. Mice: multivariate imputation by chained equations in R. *J Stat Softw* 2011;45:1–67.
- 12 R Core Team. R: A language and environment for statistical computing. Vienna, Austria R Foundation for Statistical Computing; 2020. Available: <https://www.R-project.org>

**Supplementary material****Table 1.** Unit costs used for index hospitalization and adverse events (in €)

Type of service/product/event	French unit cost (€)	UK unit cost (€)	Source
<b>Index hospitalization</b>			
Stent DES	573	573	Statutory health insurance tariffs
Catheter IVUS	454	454	Manufacturer price
Balloon	50	50	Manufacturer price
Guide wire	50	50	Manufacturer price
Catheter guide	35	35	Manufacturer price
PCI (per min) ±	Range : 2-13	NA	French national hospital cost study
Cardiology ward day ±	Range: 155-1,200	NA	French national hospital cost study
Intensive care unit day	Range: 323 - 807	NA	French DRG tariffs for public hospital

		Range :	
Hospitalization day±	NA	393 – 3,408	National schedule of NHS costs
<b>Events at 12 months</b>			
Fatal myocardial Infarction	1,773	3,133	French national hospital cost study, National schedule of NHS costs
Nonfatal myocardial Infarction without revascularization	3,183	1,449	French national hospital cost study, National schedule of NHS costs
Nonfatal myocardial Infarction with revascularization	4,882	4,781	French national hospital cost study, National schedule of NHS costs
Revascularization without Myocardial Infarction	4,144	3,086	French national hospital cost study, National schedule of NHS costs
Fatal stroke	2,739	2,399	French national hospital cost study, National schedule of NHS costs

± valued with severity-adjusted diagnosis related group cost data. DES: drug-eluting stent;

PCI: percutaneous coronary intervention



**Table 2.** Details of adverse events at one year (per protocol analysis)

	Stepwise		Systematic dual		p-value
	provisional (N = 224)		(N =225)		
	N	Mean ± sd	N	Mean ± sd	
<b>Events</b>					
• Death from any cause	6	0.03 (± 0.16)	10	0.04 (± 0.21)	0.320
• Myocardial infarctions	26	0.12 (± 0.36)	27	0.12 (± 0.36)	0.909
• Revascularization	36	0.16 (± 0.49)	39	0.17 (± 0.48)	0.785
• Stroke	2	0.01 (± 0.09)	1	0.00 (± 0.07)	0.569

**Table 3.** Resource use, per-patient cost (inflated) in € and clinical results by randomization group at one-year (per-protocol analysis)

	<b>Stepwise provisional (N = 224)</b>	<b>Systematic dual (N =225)</b>	<b>p-value</b>
<b>MACEs</b>	0.21 (± 0.55)	0.25 (± 0.61)	0.379
<b>Initial admission days</b>	3.17 (± 3.66)	3.56 (± 4.59)	0.320
<b>Number of repeat hospital admissions</b>	0.22 (± 0.61)	0.24 (± 0.62)	0.772
<b>French costs (€)</b>			
<b>Initial admission</b>	4,864 (± 3,138)	5,593 (± 3,493)	<b>0.021</b>
• Intensive care unit days	335 (± 800)	335 (± 704)	0.995
• Floor bed days	2,452 (± 2,178)	2,692 (± 2,641)	0.294
• Procedure ±	554 (± 306)	602 (± 329)	0.112
• Stents	926 (± 615)	1,337 (± 446)	<b>&lt;0.001</b>
• Balloons	243 (± 104)	272 (±110)	<b>0.004</b>
• Guides	354 (± 245)	355 (± 225)	0.956
<b>Repeat hospital admissions</b>	841 (± 2,408)	881 (± 2,357)	0.857
• Within 30 days	87 (± 642)	33 (± 488)	0.316

• Between 30 days and 6 months	266 (± 1,292)	399 (± 1,426)	0.299
• Between 6 months and 12 months	488 (± 1,837)	449 (± 1,472)	0.804
<b>Total 1-year costs</b>	<b>5,705 (± 4,125)</b>	<b>6,474 (± 4,483)</b>	<b>0.059</b>
<b>UK costs (€)</b>			
<b>Initial admission</b>	<b>6,181 (± 1,999)</b>	<b>6,802 (± 2,156)</b>	<b>0.002</b>
• Hospitalization ±	4,658 (± 1,806)	4,838 (± 2,055)	0.325
• Stents	926 (± 615)	1,337 (± 446)	<b>&lt;0.001</b>
• Balloons	243 (± 104)	272 (± 110)	<b>0.004</b>
• Guides	354 (± 245)	355 (± 225)	0.956
<b>Repeat hospital admissions</b>	<b>540 (± 1,608)</b>	<b>569 (± 1,589)</b>	<b>0.847</b>
• Within 30 days	42 (± 351)	18 (± 272)	0.415
• Between 30 days and 6 months	181 (± 886)	260 (± 1,027)	0.381
• Between 6 months and 12 months	316 (± 1,235)	290 (± 980)	0.804
<b>Total 1-year costs</b>	<b>6,721 (± 2,501)</b>	<b>7,371 (± 2,776)</b>	<b>0.009</b>

MACEs, major adverse cardiovascular events including all-cause death, non-fatal myocardial infarction, and target lesion revascularization;

±: Excluding the costs of stents, balloons and guides.



**Supplementary material****Table 1.** Unit costs used for index hospitalization and adverse events (in €)

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Nonfatal myocardial Infarction with revascularization	4,882	4,781	French national hospital cost study, National schedule of NHS costs
Revascularization without Myocardial Infarction	4,144	3,086	French national hospital cost study, National schedule of NHS costs
Fatal stroke	2,739	2,399	French national hospital cost study, National schedule of NHS costs

± valued with severity-adjusted diagnosis related group cost data. DES: drug-eluting stent;

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**Table 2.** Details of adverse events at one year (per protocol analysis)

	Stepwise		Systematic dual		p-value
	provisional (N = 224)		(N =225)		
	N	Mean ± sd	N	Mean ± sd	
<b>Events</b>					
• Death from any cause	6	0.03 (± 0.16)	10	0.04 (± 0.21)	0.320
• Myocardial infarctions	26	0.12 (± 0.36)	27	0.12 (± 0.36)	0.909
• Revascularization	36	0.16 (± 0.49)	39	0.17 (± 0.48)	0.785
• Stroke	2	0.01 (± 0.09)	1	0.00 (± 0.07)	0.569

**Table 3.** Resource use, per-patient cost (inflated) in € and clinical results by randomization group at one-year (per-protocol analysis)

	<b>Stepwise provisional (N = 224)</b>	<b>Systematic dual (N =225)</b>	<b>p-value</b>
<b>MACEs</b>	0.21 (± 0.55)	0.25 (± 0.61)	0.379
<b>Initial admission days</b>	3.17 (± 3.66)	3.56 (± 4.59)	0.320
<b>Number of repeat hospital admissions</b>	0.22 (± 0.61)	0.24 (± 0.62)	0.772
<b>French costs (€)</b>			
<b>Initial admission</b>	4,864 (± 3,138)	5,593 (± 3,493)	<b>0.021</b>
• Intensive care unit days	335 (± 800)	335 (± 704)	0.995
• Floor bed days	2,452 (± 2,178)	2,692 (± 2,641)	0.294
• Procedure ±	554 (± 306)	602 (± 329)	0.112
• Stents	926 (± 615)	1,337 (± 446)	<b>&lt;0.001</b>
• Balloons	243 (± 104)	272 (±110)	<b>0.004</b>
• Guides	354 (± 245)	355 (± 225)	0.956
<b>Repeat hospital admissions</b>	841 (± 2,408)	881 (± 2,357)	0.857
• Within 30 days	87 (± 642)	33 (± 488)	0.316

• Between 30 days and 6 months	266 (± 1,292)	399 (± 1,426)	0.299
• Between 6 months and 12 months	488 (± 1,837)	449 (± 1,472)	0.804
<b>Total 1-year costs</b>	<b>5,705 (± 4,125)</b>	<b>6,474 (± 4,483)</b>	<b>0.059</b>
<b>UK costs (€)</b>			
<b>Initial admission</b>	<b>6,181 (± 1,999)</b>	<b>6,802 (± 2,156)</b>	<b>0.002</b>
• Hospitalization ±	4,658 (± 1,806)	4,838 (± 2,055)	0.325
• Stents	926 (± 615)	1,337 (± 446)	<b>&lt;0.001</b>
• Balloons	243 (± 104)	272 (± 110)	<b>0.004</b>
• Guides	354 (± 245)	355 (± 225)	0.956
<b>Repeat hospital admissions</b>	<b>540 (± 1,608)</b>	<b>569 (± 1,589)</b>	<b>0.847</b>
• Within 30 days	42 (± 351)	18 (± 272)	0.415
• Between 30 days and 6 months	181 (± 886)	260 (± 1,027)	0.381
• Between 6 months and 12 months	316 (± 1,235)	290 (± 980)	0.804
<b>Total 1-year costs</b>	<b>6,721 (± 2,501)</b>	<b>7,371 (± 2,776)</b>	<b>0.009</b>

MACEs, major adverse cardiovascular events including all-cause death, non-fatal myocardial infarction, and target lesion revascularization;

±: Excluding the costs of stents, balloons and guides.

