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EUROpean Treatment & Reduction of Acute Coronary Syndromes cost analysis

The EUROTRACS Project

Consumers, Health, Agriculture and Food Executive Agency
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Deliverable N. D07-00

Title:
Cost-effectiveness analysis of acute coronary syndrome (ACS) procedures that lower in-hospital fatality in patients older than 34 years

July 2015

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EUROpean Treatment & Reduction of Acute Coronary Syndromes cost analysis

The EUROTRACS Project

Deliverable N. D07-00

Title:

Cost-effectiveness analysis of acute coronary syndrome (ACS) procedures that lower in-hospital fatality in patients older than 34 years

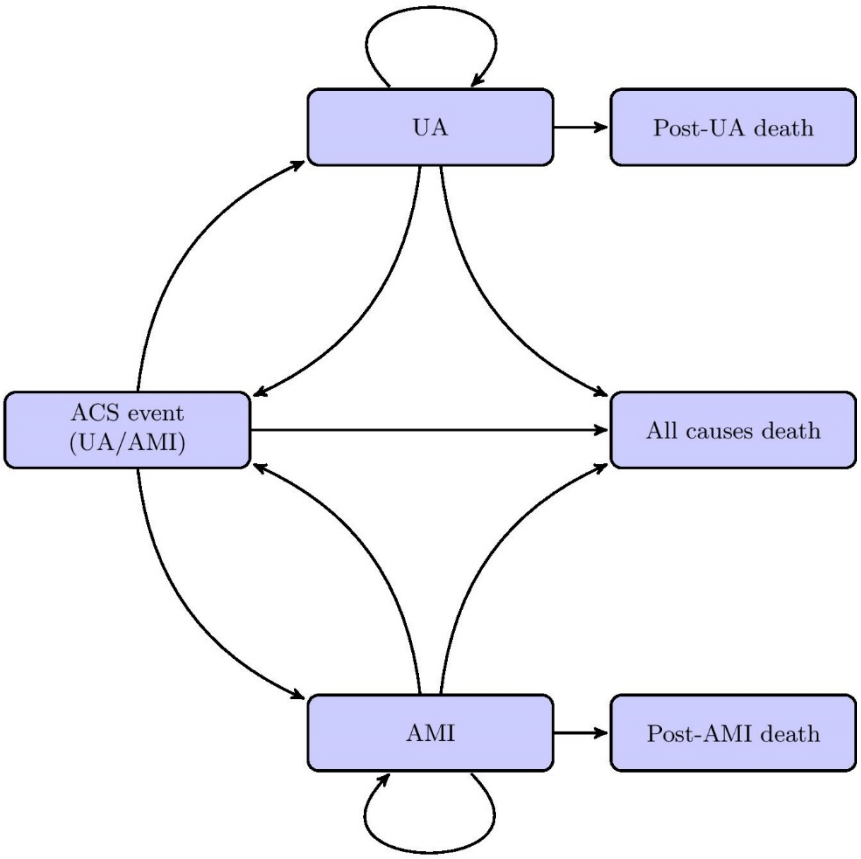
This deliverable includes in Annex I, for all countries (France, Germany, Greece, Italy, Portugal and Spain):

1. Long-term costs associated with interventions and events (disease-related and follow-up).
2. Quality-adjusted life years (QALY) gained associated to increasing use rates of revascularization in the management of patients with acute coronary syndrome (ACS).
3. Incremental cost-effectiveness ratios (ICER) (€/QALY gained).

The present deliverable summarizes the results of a cost-effectiveness analysis aimed at assessing the efficiency of increasing revascularization rates in patients with ACS.

A Markov model with annual cycles was developed based on clinical data on treatment efficacy (death risks associated to patients with/without revascularization) and the natural course of the disease, and includes data on the costs of intervention and cardiovascular (CV) events (Figure 1). The model was adapted to country-

specific context by using calibrated versions of the Framingham risk equations, risk factor prevalence and all-cause mortality rates, as well as local drug and disease costs (deliverable 3 [1]).



ACS, acute coronary syndrome; UA, unstable angina; AMI, acute myocardial infarction

Figure 1. Simplified structure of the model

Markov models are analytical tools that are particularly useful for simulating chronic health problems, and have been used on many occasions to estimate the cost-effectiveness of interventions intended to modify the natural history of patients with various disorders. Using the Markov model, in 1-year cycles, it is possible to simulate the clinical course of a patient with ACS; that is, the transition between different states of health (Figure 1), each of which is associated with a series of costs. The probability of transition can vary over time and is specific for different patient characteristics (e.g., age, gender, clinical profile, presence of CV risk factors).

Type of analysis

The model calculates the incremental cost per life year (LY) gained and cost per QALY gained associated to each intervention using the standard formula for ICER:

$$\frac{\text{Cost}_{intervention} - \text{Cost}_{no-intervention}}{\text{Effectiveness}_{intervention} - \text{Effectiveness}_{no-intervention}},$$

where $\text{Cost}_{\text{intervention}}$ and $\text{Cost}_{\text{no-intervention}}$ were the costs related to the intervention and no intervention strategies, respectively, and $\text{Effectiveness}_{\text{intervention}}$ and $\text{Effectiveness}_{\text{no-intervention}}$ were the clinical consequences in terms of LY or QALY in the two strategies. The ICER expresses the incremental cost per unit of effectiveness gained, i.e., the incremental cost per QALY gained.

Interventions compared

Several scenarios were built to depict the cost-effectiveness of revascularization based on in-hospital mortality figures for ACS patients by age group (35-64 and ≥65 years) and whether they received or not percutaneous coronary intervention (PCI). The scenarios examined were:

- use of PCI in all patients with ACS, regardless their age (scenario A),
- use of PCI in younger patients (35-64 years) (scenario B),
- use of PCI in elderly patients (≥65 years) (scenario C), and
- use of PCI in all patients for whom the intervention is most appropriate (scenario D).

We analyzed the above scenarios in two cohorts with different initial age (35 and 65).

Model parameters

The model was used to estimate the long-term costs and outcomes of the use of PCI, combining information on the effectiveness and short-term cost of this intervention, and the risk of recurrence of CV events (acute myocardial infarction -AMI- and unstable angina -UA-), and associated long-term costs for each participant country.

Reductions in in-hospital mortality associated to use of PCI depend on age group and tertiles of a propensity score (PS), obtained from previous results of the project (Table 1). All causes mortality rates were obtained from Eurostat and were referred to each country [2].

Table 1. **In-hospital fatality by PCI**

Age group	Tertile of PS	Fatality	
		no PCI	PCI
35-64	1st	3.6%	2.6%
	2nd	2.0%	1.0%
	3rd	4.3%	1.6%
≥65	1st	11.8%	6.8%
	2nd	11.4%	5.5%
	3rd	15.5%	7.4%

PS, propensity score; PCI, percutaneous coronary intervention.

The model made it possible to estimate the number of CV recurrences and their impact on quality-of-life. In order to calculate QALYs, the model assigned utility values to each health state. The utility values were obtained subtracting health state-specific disutilities (Table 2) from the utility values of general population. The utility values of general population were obtained from the Spanish National Health Survey [3].

Table 2. **Disutility values used in the model**

Health state	Disutility value[a]
UA/AMI (first year)	-0.1055
UA/AMI (subsequent years)	-0.1000

a. Adapted from: Kourlaba et al. (2012) [4] and Lindgren et al. (2007) [5].
UA, unstable angina; AMI, acute myocardial infarction.

The economic implications were assessed using two major types of healthcare costs: the initial costs of managing CV events (AMI, UA and death), and the long-term costs of follow-up for patients that survive these events. We considered the cost of revascularization with bare metal stent and drug-eluting stent for the cost of PCI. Country-specific unit costs are detailed in Annex II.

Perspective, time horizon and discounting

The analysis was carried out from the perspective of the healthcare system, with a lifetime horizon and all costs being expressed as year 2014 euros. Both costs and effects were discounted using an annual rate of 3%.

Sensitivity analysis

As uncertainty associated with the model inputs exists, univariate sensitivity analysis on several model inputs were performed to study their impact on the

results and to validate robustness of results when inputs were modified. Table 3 shows the ranges of those parameters that gave rise to more marked changes in results. Varying other parameters did not present a relevant influence in model results.

Table 3. **Parameters and ranges of the univariate sensitivity analysis**

Parameters	**Base case**	**Range**
Disutilities		
UA/AMI (first year)	-0.1055	-0.0791; -0.1319
UA/AMI (subsequent years)	-0.1000	-0.0750; -0.1250
Cost of PCI[a]	C_{PCI}	$0.75xC_{PCI}$; $1.25xC_{PCI}$
UA – annual follow-up cost	C_{UA}	$0.75xC_{UA}$; $1.25xC_{UA}$
AMI – annual follow-up cost	C_{AMI}	$0.75xC_{AMI}$; $1.25xC_{AMI}$
Annual discount rate	0.03	0.00; 0.05

a. Averaging the cost of coronary revascularization with bare metal stent and coronary revascularization with drug-eluting stent.
C_{PCI}, C_{UA}, C_{AMI} are the country-specific costs (see Appendix II).

Overview of results

Annex I shows the cost-effectiveness results by gender for each participant country with initial age 35 and 65 (all ICERs expressed in thousands of euros per QALY).

For all countries and for both men and women, the most cost-effective scenario was the scenario D (PCI in all patients for whom the intervention is most appropriate; ie, those patients with higher in-hospital fatality rates, whom are included at the 3rd tertile of PS analysis), with ICERs ranging from €6.4 to €10.5 per QALY gained for men, and from €0.7 to €3.9 per QALY gained for women, with their first CV event at their 35. When the first CV event is considered to be at age 65, the scenario D still being the most cost-effective scenario, with ICERs ranging from €6.1 to €10.0 per QALY gained for men, and from €0.8 to €4.5 per QALY gained for women.

Other scenarios also provided efficiency results showing that the use of PCI represents a good value for money in hospitalized ACS patients.

Univariate sensitivity analysis showed a high robustness of the model and the results when the most relevant parameters were ranged. ICERs remained under thresholds values of cost-effectiveness recommended by the World Health Organization [6].

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Annex I

Table 4. **Description of scenarios**

Scenarios	Description
A	PCI in all patients with ACS
B	PCI in younger patients (35-64 years)
C	PCI in elderly patients (≥65 years)
D	PCI in all patients for whom the intervention is most appropriate

Table 5. **ICER (000€/QALY gained) by country and gender (initial age 35)**

	Scenario A		Scenario B		Scenario C		Scenario D	
Country	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
France	12.8	1.2	13.6	1.1	8.6	1.3	8.0	1.1
Germany	13.4	1.1	14.3	1.1	9.7	1.2	8.5	1.1
Greece	9.8	2.0	10.3	2.0	7.0	2.1	6.6	2.0
Italy	15.1	3.9	16.0	3.9	11.4	4.2	10.5	3.9
Portugal	10.2	0.7	10.9	0.7	7.2	0.8	6.4	0.7
Spain	15.1	1.8	16.1	1.8	10.7	1.9	9.7	1.8

ICER expressed as thousands of euros per QALY gained.
Both costs and QALYs were discounted using an annual rate of 3%.
ICER, incremental cost-effectiveness ratio, QALY, quality-adjusted life year.

Table 6. **ICER (000€/QALY gained) by country and gender (initial age 65)**

	Scenario A		Scenario B[a]		Scenario C[b]		Scenario D	
Country	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
France	9.3	1.4	-	-	9.3	1.4	7.0	1.3
Germany	10.7	1.4	-	-	10.7	1.4	8.1	1.3
Greece	7.8	2.3	-	-	7.8	2.3	6.1	2.3
Italy	12.4	4.5	-	-	12.4	4.5	10.0	4.5
Portugal	8.1	0.9	-	-	8.1	0.9	6.1	0.8
Spain	11.7	2.1	-	-	11.7	2.1	8.9	2.1

a. Scenario B has not sense because the initial age is 65.
b. Scenario C is actually the same as scenario A, because the initial age is 65.
ICER expressed as thousands of euros per QALY gained.
Both costs and QALYs were discounted using an annual rate of 3%.
ICER, incremental cost-effectiveness ratio, QALY, quality-adjusted life year.

Table 7. **Results of the sensitivity analysis (initial age 35)**

		Scenario A		Scenario B		Scenario C		Scenario D	
Parameter	**Country**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
Disutilities									
	France	12.38 - 13.17	1.11 - 1.19	13.23 - 14.06	1.10 - 1.18	8.30 - 8.88	1.21 - 1.31	7.79 - 8.28	1.10 - 1.18
	Germany	13.02 - 13.85	1.10 - 1.17	13.88 - 14.75	1.07 - 1.15	9.37 - 10.02	1.18 - 1.28	8.21 - 8.73	1.07 - 1.14
	Greece	9.47 - 10.07	1.92 - 2.05	10.04 - 10.67	1.92 - 2.05	6.79 - 7.26	2.04 - 2.21	6.37 - 6.77	1.92 - 2.05
	Italy	14.67 - 15.61	3.78 - 4.04	15.57 - 16.55	3.75 - 4.00	11.04 - 11.80	3.99 - 4.32	10.20 - 10.85	3.75 - 4.01
	Portugal	9.92 - 10.56	0.70 - 0.75	10.58 - 11.24	0.68 - 0.73	7.01 - 7.50	0.76 - 0.82	6.19 - 6.58	0.67 - 0.72
	Spain	14.61 - 15.54	1.74 - 1.86	15.60 - 16.58	1.72 - 1.83	10.39 - 11.11	1.86 - 2.01	9.39 - 9.98	1.72 - 1.83
Cost of PCI									
	France	9.85 - 15.67	1.15 - 1.15	10.49 - 16.76	1.14 - 1.14	6.73 - 10.44	1.26 - 1.26	6.29 - 9.76	1.14 - 1.14
	Germany	10.37 - 16.47	1.13 - 1.14	11.01 - 17.59	1.10 - 1.11	7.65 - 11.71	1.22 - 1.24	6.64 - 10.28	1.10 - 1.10
	Greece	7.79 - 11.73	1.99 - 1.99	8.23 - 12.46	1.99 - 1.99	5.72 - 8.31	2.12 - 2.12	5.39 - 7.73	1.99 - 1.99
	Italy	12.26 - 17.99	3.90 - 3.91	12.95 - 19.14	3.87 - 3.87	9.47 - 13.35	4.15 - 4.16	8.80 - 12.22	3.87 - 3.88
	Portugal	7.87 - 12.59	0.72 - 0.74	8.36 - 13.45	0.70 - 0.71	5.69 - 8.80	0.78 - 0.80	4.97 - 7.78	0.69 - 0.70
	Spain	11.74 - 18.39	1.79 - 1.8	12.49 - 19.66	1.77 - 1.78	8.53 - 12.95	1.92 - 1.94	7.69 - 11.66	1.77 - 1.77
UA – follow-up cost									
	France	12.70 - 12.82	1.09 - 1.22	13.57 - 13.69	1.08 - 1.20	8.51 - 8.66	1.18 - 1.34	7.97 - 8.09	1.08 - 1.20
	Germany	13.37 - 13.48	1.07 - 1.19	14.25 - 14.36	1.05 - 1.17	9.61 - 9.75	1.16 - 1.30	8.40 - 8.51	1.05 - 1.16
	Greece	9.68 - 9.84	1.91 - 2.07	10.27 - 10.42	1.91 - 2.06	6.92 - 7.11	2.03 - 2.22	6.49 - 6.64	1.91 - 2.06
	Italy	15.00 - 15.24	3.78 - 4.03	15.93 - 16.16	3.75 - 3.99	11.27 - 11.55	4.00 - 4.30	10.4 - 10.63	3.75 - 4.00
	Portugal	10.19 - 10.27	0.69 - 0.77	10.87 - 10.94	0.67 - 0.74	7.20 - 7.30	0.74 - 0.84	6.34 - 6.42	0.66 - 0.74
	Spain	14.99 - 15.13	1.72 - 1.87	16.01 - 16.14	1.70 - 1.84	10.65 - 10.82	1.84 - 2.02	9.61 - 9.74	1.70 - 1.84
AMI – follow-up cost									
	France	12.56 - 12.95	0.93 - 1.37	13.43 - 13.83	0.92 - 1.36	8.41 - 8.76	1.03 - 1.49	7.83 - 8.23	0.92 - 1.36
	Germany	13.25 - 13.59	0.95 - 1.32	14.13 - 14.48	0.92 - 1.29	9.53 - 9.83	1.04 - 1.42	8.29 - 8.63	0.92 - 1.29
	Greece	9.38 - 10.14	1.57 - 2.41	9.96 - 10.73	1.57 - 2.40	6.67 - 7.35	1.69 - 2.56	6.18 - 6.95	1.57 - 2.40
	Italy	14.37 - 15.88	3.07 - 4.74	15.27 - 16.82	3.04 - 4.70	10.72 - 12.10	3.29 - 5.02	9.75 - 11.28	3.04 - 4.71
	Portugal	10.13 - 10.33	0.62 - 0.84	10.80 - 11.00	0.60 - 0.81	7.16 - 7.34	0.68 - 0.90	6.28 - 6.48	0.59 - 0.81
	Spain	14.74 - 15.38	1.44 - 2.15	15.75 - 16.40	1.42 - 2.13	10.45 - 11.03	1.56 - 2.30	9.35 - 10.00	1.42 - 2.13
Annual discount rate									
	France	9.16 - 15.80	1.24 - 1.10	9.59 - 16.67	1.22 - 1.09	8.14 - 8.90	1.32 - 1.22	5.94 - 9.70	1.22 - 1.09
	Germany	10.19 - 16.19	1.23 - 1.07	10.64 - 17.09	1.20 - 1.06	9.24 - 9.98	1.27 - 1.20	6.62 - 9.97	1.19 - 1.05
	Greece	7.50 - 11.68	2.12 - 1.91	7.82 - 12.26	2.12 - 1.91	6.75 - 7.20	2.21 - 2.06	5.28 - 7.61	2.12 - 1.91
	Italy	11.95 - 17.90	4.18 - 3.75	12.39 - 18.85	4.13 - 3.72	11.06 - 11.65	4.32 - 4.03	8.71 - 12.01	4.14 - 3.72
	Portugal	7.89 - 12.19	0.79 - 0.69	8.31 - 12.85	0.76 - 0.67	6.93 - 7.47	0.82 - 0.77	5.06 - 7.44	0.75 - 0.66
	Spain	11.22 - 18.38	1.93 - 1.72	11.67 - 19.42	1.90 - 1.70	10.25 - 11.08	2.01 - 1.88	7.45 - 11.50	1.90 - 1.70

ICER expressed as thousands of euros per QALY gained.
Both costs and QALYs were discounted using an annual rate of 3% (except in sensitivity analysis on annual discount rate).
PCI, percutaneous coronary intervention; UA, unstable angina; AMI, acute myocardial infarction; ICER, incremental cost-effectiveness ratio, QALY, quality-adjusted life year.

Table 8. **Results of the sensitivity analysis (initial age 65)**

		Scenario A		Scenario B[a]		Scenario C[b]		Scenario D	
Parameter	**Country**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
Disutilities									
	France	8.99 - 9.60	1.30 - 1.41	-	-	8.99 - 9.60	1.30 - 1.41	6.74 - 7.20	1.29 - 1.39
	Germany	10.38 - 11.09	1.30 - 1.41	-	-	10.38 - 11.09	1.30 - 1.41	7.85 - 8.39	1.26 - 1.36
	Greece	7.51 - 8.03	2.22 - 2.40	-	-	7.51 - 8.03	2.22 - 2.40	5.91 - 6.32	2.22 - 2.40
	Italy	12.04 - 12.87	4.32 - 4.67	-	-	12.04 - 12.87	4.32 - 4.67	9.68 - 10.35	4.29 - 4.64
	Portugal	7.89 - 8.43	0.83 - 0.90	-	-	7.89 - 8.43	0.83 - 0.90	5.90 - 6.31	0.79 - 0.85
	Spain	11.29 - 12.07	2.01 - 2.17	-	-	11.29 - 12.07	2.01 - 2.17	8.59 - 9.18	1.98 - 2.14
Cost of PCI									
	France	7.28 - 11.30	1.35 - 1.36	-	-	7.28 - 11.30	1.35 - 1.36	5.53 - 8.39	1.34 - 1.34
	Germany	8.45 - 13.00	1.34 - 1.36	-	-	8.45 - 13.00	1.34 - 1.36	6.49 - 9.72	1.31 - 1.31
	Greece	6.33 - 9.20	2.31 - 2.31	-	-	6.33 - 9.20	2.31 - 2.31	5.09 - 7.13	2.31 - 2.31
	Italy	10.34 - 14.55	4.48 - 4.50	-	-	10.34 - 14.55	4.48 - 4.50	8.51 - 11.50	4.46 - 4.46
	Portugal	6.38 - 9.92	0.85 - 0.88	-	-	6.38 - 9.92	0.85 - 0.88	4.84 - 7.36	0.82 - 0.82
	Spain	9.26 - 14.07	2.08 - 2.10	-	-	9.26 - 14.07	2.08 - 2.10	7.17 - 10.58	2.05 - 2.06
UA – follow-up cost									
	France	9.21 - 9.36	1.27 - 1.43	-	-	9.21 - 9.36	1.27 - 1.43	6.89 - 7.03	1.25 - 1.42
	Germany	10.66 - 10.79	1.28 - 1.42	-	-	10.66 - 10.79	1.28 - 1.42	8.04 - 8.18	1.24 - 1.38
	Greece	7.67 - 7.86	2.21 - 2.41	-	-	7.67 - 7.86	2.21 - 2.41	6.01 - 6.20	2.21 - 2.41
	Italy	12.3 - 12.59	4.33 - 4.64	-	-	12.3 - 12.59	4.33 - 4.64	9.86 - 10.15	4.30 - 4.62
	Portugal	8.10 - 8.19	0.82 - 0.91	-	-	8.10 - 8.19	0.82 - 0.91	6.05 - 6.15	0.77 - 0.87
	Spain	11.58 - 11.75	2.00 - 2.18	-	-	11.58 - 11.75	2.00 - 2.18	8.79 - 8.96	1.96 - 2.15
AMI – follow-up cost									
	France	9.08 - 9.49	1.10 - 1.60	-	-	9.08 - 9.49	1.10 - 1.60	6.76 - 7.16	1.09 - 1.58
	Germany	10.55 - 10.90	1.14 - 1.56	-	-	10.55 - 10.90	1.14 - 1.56	7.94 - 8.28	1.10 - 1.52
	Greece	7.37 - 8.15	1.83 - 2.79	-	-	7.37 - 8.15	1.83 - 2.79	5.71 - 6.50	1.83 - 2.78
	Italy	11.66 - 13.22	3.55 - 5.43	-	-	11.66 - 13.22	3.55 - 5.43	9.22 - 10.79	3.52 - 5.40
	Portugal	8.05 - 8.25	0.74 - 0.99	-	-	8.05 - 8.25	0.74 - 0.99	6.00 - 6.20	0.70 - 0.94
	Spain	11.34 - 12.00	1.68 - 2.49	-	-	11.34 - 12.00	1.68 - 2.49	8.55 - 9.21	1.65 - 2.46
Annual discount rate									
	France	8.13 - 10.11	1.39 - 1.32	-	-	8.13 - 10.11	1.39 - 1.32	6.14 - 7.54	1.38 - 1.31
	Germany	9.65 - 11.48	1.38 - 1.33	-	-	9.65 - 11.48	1.38 - 1.33	7.36 - 8.63	1.35 - 1.29
	Greece	7.03 - 8.28	2.38 - 2.26	-	-	7.03 - 8.28	2.38 - 2.26	5.60 - 6.46	2.38 - 2.26
	Italy	11.44 - 13.15	4.62 - 4.40	-	-	11.44 - 13.15	4.62 - 4.40	9.32 - 10.49	4.59 - 4.37
	Portugal	7.41 - 8.66	0.88 - 0.85	-	-	7.41 - 8.66	0.88 - 0.85	5.58 - 6.46	0.84 - 0.81
	Spain	10.41 - 12.55	2.15 - 2.05	-	-	10.41 - 12.55	2.15 - 2.05	8.00 - 9.50	2.12 - 2.01

a. Scenario B has not sense because the initial age is 65.
b. Scenario C is actually the same than scenario A, because the initial age is 65.
ICER expressed as thousands of euros per QALY gained.
Both costs and QALYs were discounted using an annual rate of 3% (except in sensitivity analysis on annual discount rate).
PCI, percutaneous coronary intervention; UA, unstable angina; AMI, acute myocardial infarction; ICER, incremental cost-effectiveness ratio, QALY, quality-adjusted life year.

Annex II

Table 9. **Unit costs by country (2014 euros)**

	unit	France	Germany	Greece	Italy	Portugal	Spain
Intervention costs							
Bare metal or drug-eluting stent	1 intervention	3,037.00	3,002.00	2,002.00	3,002.00	2,148.95	3,470.58
Balloon angioplasty	1 intervention	994.00	2,884.00	2,002.00	585.00	1,598.95	3,736.12
Acute care costs							
Surviving AMI patients with complications	1 event	3,434.00	8,100.00	1,818.00	4,700.00	3,776.00	5,018.00
Surviving AMI patients without complications	1 event	1,372.00	3,570.00	722.00	3,377.00	2,379.00	4,708.00
AMI patients who died	1 event	2,680.00	10,540.00	1,818.00	4,018.00	3,153.00	3,378.00
Surviving UA patients with complications	1 event	2,962.00	7,300.00	940.00	1,870.00	3,776.00	5,018.00
Surviving UA patients without complications	1 event	835.00	2,160.00	424.00	1,870.00	2,379.00	4,708.00
UA patients who died	1 event	823.00	13,780.00	940.00	1,870.00	3,153.00	3,378.00
Follow-up costs							
Unstable angina	1 year	1,028.60	925.94	1,270.32	1,987.98	635.07	1,169.58
Acute myocardial infarction	1 year	855.40	737.66	1,660.68	3,283.87	431.27	1,393.78

AMI, acute myocardial infarction; UA, unstable angina.