

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Spaulding C, Daemen J, Boersma E, Cutlip DE, Serruys PW. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007;356:989-97.

## Online Supplementary Appendix

### Death narratives and stent thrombosis adjudication; subgroup analyses; and event rates in patients with and without diabetes mellitus

**Appendix Table 1. Non-cardiovascular causes of death with stent thrombosis adjudication in patients receiving a SES (n=27)**

Days post procedure	Age at inclusion	Diabetes	Narrative	Stent thrombosis adjudication according to the ARC definitions
91	84	No	Intracranial hemorrhage	No ST
127	67	No	Metastatic renal cell carcinoma	No ST
203	79	Yes	Septicaemia	No ST
239	73	No	Fall; subdural hematoma	No ST
277	54	Yes	Osteomyelitis post amputation	No ST
330	65	No	Colon cancer	No ST
333	56	Yes	Subarachnoidal hemorrhage	No ST
388	77	No	Cerebral vascular accident	No ST
438	70	No	Metastatic lung cancer	No ST

467	70	No	Chronic lung disease, pneumonia	No ST
524	69	No	Cerebrovascular accident	No ST
572	65	Yes	Respiratory failure	No ST
596	67	No	Metastatic prostate carcinoma	No ST
601	81	No	End stage chronic lung disease	No ST
619	69	No	Metastatic lung cancer	No ST
723	54	Yes	Car accident	No ST
786	79	No	End stage chronic lung disease	No ST
855	78	No	Metastatic oropharynx epidermoid carcinoma	No ST
982	70	No	Dementia, seizure disorder	No ST
1054	73	No	Pulmonary infection	No ST
1122	74	Yes	Lymphoma	No ST
1261	74	Yes	Pancreatic cancer	No ST
1299	54	No	Lung cancer	No ST
1309	77	Yes	Respiratory failure	No ST
1368	75	No	Respiratory failure	No ST
1435	71	No	Renal cell carcinoma	No ST
1439	51	No	Colon carcinoma	No ST

**Appendix Table 2. Non-cardiovascular causes of death with stent thrombosis adjudication in patients receiving a BMS (n=23)**

<b>Days post procedure</b>	<b>Age at inclusion</b>	<b>Diabetes</b>	<b>Narrative</b>	<b>Stent thrombosis adjudication according to the ARC definitions</b>
52	70	No	Metastatic lung cancer	No ST
168	71	No	Bleeding from a gastric ulcer	No ST
306	53	Yes	Lung cancer	No ST
369	81	No	Lung cancer	No ST
558	65	No	Multiple myeloma	No ST
624	64	No	Glioblastoma multiforme	No ST
758	70	No	Pancreatic cancer	No ST
766	56	No	Gastric cancer	No ST
789	67	No	Intracranial hemorrhage	No ST
818	77	No	Stent thrombosis after stopping aspirin and clopidogrel for upper gastrointestinal bleeding at 278 days. Ischemic bowel with perforation as cause of death	Definite ST
862	67	Yes	Cerebrovascular accident	No ST
973	54	No	Perforation of gastric ulcer	No ST
1091	88	No	Skin cancer with metastases	No ST
1142	83	No	Progressive dementia, urosepsis	No ST
1167	52	No	Brain tumor	No ST
1200	78	No	Perforated peptic ulcer and upper gastrointestinal bleeding	No ST
1250	77	Yes	Pneumothorax	No ST
1253	84	No	Hip surgery with post-operative	No ST

			complications ; autopsy negative for ST	
1290	89	No	Pneumonia	No ST
1323	68	No	Metastatic lung cancer	No ST
1358	71	No	Lymphoma	No ST
1367	71	Yes	Urinary tract infection - sepsis	No ST
1427	74	No	Metastatic lung cancer	No ST

**Appendix Table 3. Cardiovascular causes of death with stent thrombosis adjudication in patients receiving a SES (n=30)**

<b>Days post procedure</b>	<b>Age at inclusion</b>	<b>Diabetes</b>	<b>Narrative</b>	<b>Stent thrombosis adjudication according to the ARC definitions</b>
1	53	Yes	Post procedure intracerebral hemorrhage	No ST
167	80	No	A repeat angiography performed 167 days post-procedure found no restenosis at the site of the target lesion on the LAD. During the procedure, an intracoronary ultrasound was performed. Occlusive dissection appeared on the LAD. PTCA was performed, acute MI and death occurred after the procedure	No ST
198	83	No	Possible intake of benzodiazepines, urinary tract infection, liver dysfunction, renal failure pneumonia and heart failure	No ST
299	74	No	Out of hospital cardiac arrest. No autopsy performed	Possible ST
465	70	Yes	The patient was reported as having acute shortage of breath and died shortly after. No autopsy was	Possible ST

			performed.	
542	57	No	A non-Q wave MI occurred 539 days after the index procedure. An angiogram was performed 542 days post-procedure and showed an occluded target lesion.  An attempt to open the occlusion failed. Death occurred on the same day	Definite ST
545	65	Yes	The patient complained of chest pain and sustained an out of hospital cardiac arrest. An autopsy was not performed.	Possible ST
702	65	No	Out of hospital cardiac arrest. The patient was transported to a hospital by an emergency medical team and pronounced dead at arrival. An autopsy was not performed.	Possible ST
734	73	Yes	When the patient's referring physician was contacted for 3 year follow-up, the physician reported the patient had expired in 2003. No autopsy was performed.	Possible ST
759	68	Yes	Found dead in her car with no obvious injuries. An autopsy was not performed.	Possible ST
776	67	No	Complications of coronary artery bypass surgery for performed for progression of coronary artery disease.	No ST
800	80	Yes	Patient found dead at home. An autopsy was not performed	Possible ST
802	67	No	Stent thrombosis with acute myocardial infarction and cardiogenic shock	Definite ST
806	88	No	The patient was admitted to an outlying facility for a cerebrovascular accident. During the hospital stay he experienced a Q-wave MI which was not properly	Possible ST

			documented (no ECG available) and died	
823	75	Yes	The patient had revascularization of non-target lesions 23 and 26 months after the index procedure, sustained a MI in the territory of the non-target vessel and died suddenly three weeks after the non-target revascularization procedure.	No ST
887	80	Yes	Died at home. The cause of death noted on the death certificate was “sudden death”	Possible ST
917	47	No	10 days after the implantation of the stent on the proximal LAD, the patient suffered a non-Q wave anterior MI. Thrombolytic therapy was given in another site and the patient was transferred. 10 days after the non-Q wave infarction, a coronary angiogram revealed a patent stent and a 40-50% stenosis downstream. PCI was performed on the mid-LAD. A cerebro-vascular accident occurred 104 days after the index procedure. No-Q waves were reported 653 and 711 days post-procedure. Repeat catheterization was not performed. The patient died of heart failure 917 days post-procedure.	Probable ST
961	71	Yes	Heart failure, arrhythmia, kidney failure and septicemia	No ST
1074	73	Yes	Found unresponsive at home and resuscitation attempts were unsuccessful. An autopsy was not performed	Possible ST
1085	79	No	Found dead at home. An autopsy was not performed	Possible ST
1086	52	No	Died at home. No information on the cause of death available. An autopsy was not performed	Possible ST

1133	92	No	Progressive heart failure	No ST
1179	66	No	The clinical site reported that during a review of the hospital computer system it was discovered that the patient was recorded as dead. A death certificate was not available, and the clinical site confirmed that no further data would be forthcoming.	Possible ST
1234	68	No	Dementia and progressive heart failure	No ST
1300	80	Yes	The patient expired at home. The Death Form and Death Certificate noted that the cause of death was an acute myocardial infarction. No autopsy was performed.	Possible ST
1313	54	Yes	At the time of the four year follow-up contact, the investigational site discovered via the national social security registry that the patient had died. No further information was obtained.	Possible ST
1376	70	No	Prosthetic valve endocarditis	No ST
1389	68	Yes	Heart Failure	No ST
1416	64	Yes	The patient was admitted to the coronary care unit because of acute shortage of breath, intubated on arrival and died shortly after. No autopsy was performed.	Possible ST
1428	67	Yes	Heart failure – bilateral pneumonia	No ST

**Appendix Table 4. Cardiovascular causes of death with stent thrombosis adjudication in patients receiving a BMS (n=23)**

<b>Days post procedure</b>	<b>Age at admission</b>	<b>Diabetes</b>	<b>Narrative</b>	<b>Stent thrombosis adjudication according to the ARC definition</b>
30	79	No	Sudden death at home. An autopsy was not performed	Probable ST
45	62	Yes	The patient died during a trip to a foreign country. The exact cause of death is unknown.	Possible ST
97	57	No	Out of hospital cardiac arrest. An autopsy was not performed	Possible ST
140	54	Yes	Patient found dead at home. No resuscitation was attempted. An autopsy was not performed.	Possible ST
517	73	No	Felt suddenly sick, went to bed and was found shortly after in deep coma and died. An autopsy was not performed	Possible ST
553	69	No	Restenosis. Died of complications of coronary artery bypass surgery.	No ST
574	62	No	The patient was found lying face down next to a capsized sailboat. Sudden death was suspected and adjudicated as cardiac.	Possible ST
578	69	No	Progressive heart failure and skin malignancy	No ST
613	73	Yes	MI in the territory of the implanted stent 16 days after the procedure. Sudden death at home. An autopsy was not performed	Probable ST
664	81	No	Progressive heart failure	No ST

799	66	No	Died suddenly at home. An autopsy was not performed	Possible ST
804	50	No	At 196 days: occlusive restenosis with no ischemia. PCI failed to reopen the occlusion. Unexplained death at home 804 days after the index procedure.. Since the stent was previously occluded by restenosis, the event was adjudicated as a cardiac death and no stent thrombosis	No ST
818	66	No	Sudden death at home. An autopsy showed recent myocardial infarction in the territory of a non target vessel.	No ST
855	50	Yes	PCI of the target lesion was performed 280 and 763 days post-procedure. PCI was also performed on non-target lesions 280, 337 and 659 days post-procedure Sudden death at home occurred 855 days after the index procedure. An autopsy was not performed.	Possible ST
942	55	No	Circumstances of death unknown	Possible ST
1012	80	No	Died suddenly at home. An autopsy was not performed	Possible ST
1048	49	No	Circumstances of death unknown. The death certificate mentions previous and acute MI. An autopsy was not performed	Possible ST
1067	72	No	Suddenly felt sick, was taken to a hospital were he died shortly after arrival. An autopsy was not performed	Possible ST
1081	70	No	Rupture of ventricular aneurysm	No ST

1313	53	No	Found dead in the passenger seat of his car, motor not running, no sign of collision. An autopsy ruled out stent thrombosis	No ST
1381	81	Yes	MI in the territory of the implanted stent 85 days after the procedure. Sudden death 1381 post-procedure. An autopsy was not performed.	Probable ST
1391	66	Yes	Died suddenly at home. An autopsy was not performed	Possible ST
1404	64	No	At four years follow-up, the study investigator found her name on a national death registry. The cause and circumstances of death are unknown.	Possible ST

SES indicated sirolimus-eluting stent, BMS bare metal stent, MI myocardial infarction, ST stent thrombosis, TVR target vessel revascularization, CVA cerebrovascular accident.



Legend for Appendix Figure 1:

**All-cause mortality in selected subgroups.**

Exploratory analyses to evaluate possible heterogeneity in treatment effects on mortality according to the trial of enrolment and the following 10 clinically relevant characteristics: age, sex, diabetes, previous MI, dyslipidemia, hypertension, heart failure, Canadian Cardiovascular Society angina classification, number of diseased vessels and left ventricular ejection fraction. The size of the squares corresponds to the amount of statistical information. For the continuous variables (age and left ventricular ejection fraction), medians were used as cut-off. Results of tests for heterogeneity in treatment effect were considered significant if P was <0.01.

MI=myocardial infarction, CCS= Canadian Cardiovascular Society, LVEF=left ventricular ejection fraction.

**Appendix Table 5. Incidence of death, myocardial infarction and stent thrombosis at four-year follow-up in patients with and without diabetes mellitus**

	Patients with diabetes mellitus					Patients without diabetes mellitus					P for interaction	
	Events at 4-year follow-up				AdjustedHR (95% CI)	Events at 4-year follow-up				AdjustedHR (95% CI)		
	SES (195 patients)		BMS (233 patients)			SES (683 patients)		BMS (635 patients)				
	N	%	N	%	N	%	N	%				
Death	23	12.2	10	4.4	2.9 (1.38-6.1)	34	5.1	36	5.8	0.88 (0.55-1.41)	0.008	
Cardiovascular	14	7.7	6	2.7	3.0 (1.14-7.7)	15	2.3	17	2.8	0.82 (0.41-1.64)	0.033	
Non-cardiovascular	9	4.9	4	1.8	2.8 (0.87-9.2)	19	2.9	19	3.2	0.93 (0.49-1.76)	0.11	
Myocardial infarction	12	6.5	19	8.2	0.75 (0.37-1.55)	43	6.4	34	5.5	1.19 (0.76-1.87)	0.29	
Q wave MI	5	2.7	1	0.4	6.3 (0.73-54)	13	2.0	10	1.6	1.22 (0.53-2.8)	0.16	
Non-Q wave MI	7	3.8	18	7.8	0.46 (0.19-1.11)	30	4.5	25	4.0	1.13 (0.66-1.91)	0.088	
Death or Q-wave MI	26	13.8	10	4.4	3.3 (1.59-6.9)	44	6.6	45	7.3	0.91 (0.60-1.39)	0.003	
Death or any MI	31	16.4	26	11.3	1.43 (0.85-2.4)	69	10.3	64	10.3	1.01 (0.72-1.42)	0.28	
Thrombosis by Protocol definition												
Acute ST (within 24 hours)	0	-	0	-	-	0	-	0	-	-		
Subacute ST (within 1 - 30 days)	1	0.5	0	-	-	3	0.4	1	0.2	2.8 (0.29-27)	1.0	
Late ST (after 30 days)	1	0.6	1	0.4	1.19 (0.07-19)	5	0.8	3	0.5	1.57 (0.37-6.6)	0.86	
Thrombosis by ARC definitions												
Acute ST (within 24 hours)	0	-	0	-	-	0	-	0	-	-		
Subacute ST (within 1 - 30 days)	1	0.5	2	0.9	0.62 (0.06-6.8)	3	0.4	1	0.2	2.8 (0.29-27)	0.37	
Late ST (within 30 days - 1 year)	0	-	4	1.7	-	2	0.3	7	1.1	0.27 (0.06-1.28)	0.99	

Very late ST (after 1 year)	11	6.1	3	1.4	4.7 (1.31-17)	12	1.9	11	1.8	1.02 (0.45-2.3)	0.048
Definite ST	2	1.1	1	0.4	2.5 (0.22-27)	8	1.2	6	1.0	1.25 (0.43-3.6)	0.62
Definite or probable ST	2	1.1	5	2.2	0.49 (0.10-2.5)	11	1.7	10	1.6	1.03 (0.44-2.4)	0.43
Any ST	12	6.6	9	3.9	1.64 (0.70-3.9)	18	2.8	19	3.1	0.88 (0.46-1.68)	0.26

SES indicates sirolimus-eluting stent, BMS bare metal stent, HR hazard ratio, CI confidence interval, MI myocardial infarction, ST stent thrombosis, ARC academic research consortium.