National Institute for Health and Care Excellence

Final

Acute coronary syndromes

[F] Evidence review for the clinical and cost-effectiveness of drug-eluting stents

NICE guideline NG185

Intervention evidence review

November 2020

Final

This evidence review was developed by the National Guideline Centre based at the Royal College of Physicians

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The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

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1 Drug eluting stents

1.1 Review question: What is the clinical and cost effectiveness of drug-eluting stents in adults with acute coronary syndromes, including those with unstable angina or NSTEMI undergoing percutaneous coronary intervention and those with STEMI undergoing primary percutaneous coronary intervention?

1.2 Introduction

In 2008 drug-eluting stents were recommended in certain circumstances by NICE technology appraisal 152 'Drug-eluting stents for the treatment of coronary artery disease':

- Drug-eluting stents are recommended for use in percutaneous coronary intervention for the treatment of coronary artery disease, within their instructions for use, only if:
  - the target artery to be treated has less than a 3-mm calibre or the lesion is longer than 15 mm, and
  - the price difference between drug-eluting stents and bare-metal stents is no more than £300.[81]

This was on the basis of a systematic review of the evidence and cost effectiveness modelling. However, since then drug-eluting stents have continued to develop and new studies have been published. Audit data from 2016 reported that 92% of PCIs used stents and 90% used drug eluting stents and this varied only slightly by indication (that is, it was 89% in PPCI for STEMI).

This guideline will review the evidence for drug eluting stents compared to bare metal stents in people with ACS and partially update and replace the recommendations from TA152. It is important to note that TA152 covered all PCI whereas this guideline will only be updating recommendations in relation to people with ACS.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	Patients with UA/NSTEMI and those with STEMI intended for treatment with a stent
Intervention(s)	Drug eluting stents including: • Sirolimus • Everolimus • Paclitaxel • Rapamycin • Paclitaxel & Cilostazol • Ridaforolimus • Novolimus • Zotarolimus

Comparison(s)	Bare metal stents including: • Cobalt Chronium • Platinium Chronium • Stainless Steel
Outcomes	**CRITICAL** Time points: early ≤1 and later >1-3 year • All-cause mortality • Cardiac mortality • TVF- target vessel failure • TLR and TVR – target lesion and target vessel revascularisation • Stent thrombosis (definite and/or probable) (record if assessed using optical coherence tomography (OCT), Intravascular ultrasound (IVUS) or angiography) • Myocardial infarction • Health-related quality of life including EQ5D and SF-36. **MPORTANT** • Bleeding- Where possible, bleeding outcomes will be categorised into: ○ Major bleeding (including BARC 3-5 and as reported by author) ○ Minor bleeding (including BARC 2, TIMI and as reported by author). The following hierarchy of bleeding scales will be used: ○ BARC ○ Author's definition ○ TIMI ○ GUSTO • MLD - Minimal lumen diameter (measuring how much restenosis there is)- surrogate marker for TLR and TVR
Study design	• Randomised Controlled Trials (RCT) • Systematic Reviews (SR) of RCTs

1.4 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual.[28] Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

1.5 Clinical evidence

1.5.1 Included studies

Twenty-nine trials (fifty papers) were included in the review; [7, 13, 14, 17-19, 22, 27, 32-36, 46, 47, 55-57, 61, 67, 73, 75, 76, 88-91, 94-96, 100, 102-105, 109, 111-114, 116, 121-126, 128, 131, 133] that evaluated drug-eluting stents versus bare metal stents. Evidence from these studies is summarised in the clinical evidence summary below (Table 4).

One relevant Cochrane review was identified for this evidence review.[42] This Cochrane review's PICO was similar to the PICO developed by the guideline committee. However, the Cochrane review did not have an upper limit for the outcome time-points. As seen in Table 1, the guideline committee agreed on reviewing outcome data that was reported up to 3 years. The studies included in the Cochrane were reviewed and included if applicable.

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix H.

1.5.2 Excluded studies

See the excluded studies list in appendix I.

1.5.3 Summary of clinical studies included in the evidence review

Table 2: Summary of evaluated outcomes in included studies

Study	No. of participants	Country	All-cause mortality		Cardiac mortality		TVF		TLR/TVR		MI		Stent thrombosis		MLD		Bleeding	
			1 yr	+1 yr	1 yr	+1 yr	1 yr	+1 yr	1 yr	+1 yr	1 yr	+1 yr	1 yr	+1 yr	1 yr	+1 yr	1 yr	+1 yr
Brilakis 2009[19]: SOS	80	USA, Greece	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N
Brilakis 2018[17]: DIVA	597	USA	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	N	N	Y	Y
Chechi 2007[27]	80	Italy	Y	N	N	N	N	N	Y	N	Y	N	Y	N	Y	N	N	N
de Belder 2014[32]: XIMA	800	UK, Spain	Y	N	Y	N	N	N	Y	N	Y	N	N	N	N	N	Y	N
Di Lorenzo 2009[34]: PASEO	270	Italy	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	Y	N	N	N	N
Diaz de la Llera 2007[35]	120	Spain	Y	N	N	N	N	N	Y	N	N	N	Y	N	N	N	N	N
Guagliumi 2010[46]: OCTAMI	44	USA, Italy	Y	N	N	N	N	N	Y	N	Y	N	Y	N	N	N	N	N
Han 2007[47]	200	Chile	N	N	Y	N	N	N	N	N	Y	N	Y	N	N	N	N	N
Kaiser 2010[55]: BASKET-PROVE	2314	Multinational	N	Y	N	Y	N	N	N	Y	N	N	N	Y	N	N	N	N
Kaiser 2015[56]: BASKET-PROVE II	2291	Multinational	N	Y	N	Y	N	N	N	Y	N	Y	N	Y	N	N	N	N
Kelbaek 2008[61]: DEDICATION	626	Denmark	Y	Y	Y	Y	N	N	Y	Y	Y	Y	N	N	Y	N	N	N
Laarman 2006[67]: PASSION	619	Netherlands	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	N	N	N	N
Menichelli 2007[76] : SESAMI	320	Italy	Y	Y	N	N	N	N	Y	Y	Y	Y	Y	Y	N	N	N	N
Raber 2012[90]: COMFORTABLE	1161	Multinational	Y	Y	Y	Y	N	N	N	Y	N	N	Y	Y	Y	Y	N	N

Study	No. of participants	Country	All-cause mortality		Cardiac mortality		TVF		TLR/TVR		MI		Stent thrombosis		MLD		Bleeding	
Remkes 2016[94]: ELISA 3 trial	474	Netherlands	N	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	N
Ribamar Costa 2012[95]	40	Brazil	Y	N	N	N	N	N	N	N	Y	N	Y	N	Y	N	N	N
Ribichini 2011[96]: CEREA-DES	250	Italy	Y	N	Y	N	N	N	Y	N	Y	N	N	N	N	N	N	N
Rodriguez 2011[100]: EUCATAX	422	Argentina	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	N	N	N	N
Sabate 2012[104] EXAMINATION	1498	Spain, Italy, Netherlands	Y	Y	Y	Y	N	N	Y	Y	N	N	Y	Y	N	N	Y	Y
Sanchez 2010[105]: GRACIA-3	433	Spain	N	N	Y	N	N	N	N	N	Y	N	Y	N	Y	N	Y	N
Spaulding 2006[109]: TYPHOON	715	Multinational	Y	N	Y	N	Y	N	N	N	Y	N	Y	N	Y	N	N	N
Steinwender 2008[111]	16	Austria	Y	N	N	N	N	N	N	N	N	N	Y	N	Y	N	N	N
Stone 2009[112]: HORIZONS-AMI	3006	Multinational	Y	Y	Y	Y	N	N	Y	Y	N	N	Y		Y	N	N	Y
Strozzi 2007[116]	119	Croatia	Y	N	N	N	N	N	Y	N	Y	N	N	N	Y	N	N	N
Valgimigli 2008[122]: MULTISTRATEGY trial	744	Multinational	Y	Y	Y	Y	N	N	Y	Y	Y	N	N	Y	N	N	Y	N
Valgimigli 2014[126]: PRODIGY	2013	Italy	N	N	N	N	N	Y	N	N	N	N	N	Y	N	N	N	N
Valgimigli 2015[125]: ZEUS trial	1606	Multinational	Y	N	Y	N	N	N	Y	N	Y	N	Y	N	N	N	Y	N
van der Hoeven 2008[128]: MISSION	310	Netherlands	Y	Y	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	N	N	N
Wijnbergen 2012[133]: DEBATER	907	Netherlands	Y	N	N	N	N	N	Y	N	N	N	Y	N	N	N	Y	N

Green boxes = study evaluated outcome; Grey boxes = study did not evaluate outcome; Y= yes (evaluated) N=no (not evaluated)

Table 3: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Brilakis 2009[19]: SOS trial Brilakis, 2011[18]	Intervention (n=39): Drug-eluting stents: paclitaxel-eluting stents Comparison (n=41): Bare metal stents (type of bare metal stent used was unspecified in study)	n=80 People with 1 or more 50% to 99% de novo or re-stenotic lesions in an SVG that were between 2.5 and 4.0 mm in diameter and need for percutaneous coronary intervention (PCI) Unstable angina: 37.5% Non-STEMI: 22.5% Age (mean): 66.5 years Gender (male to female ratio): 80:0 Ethnicity: White 94%, Black 2.5%, Hispanic 1.5% USA and Greece	All-cause mortality at 1 year and 35 months Myocardial infarction at 1 year and 35 months Target vessel revascularisation at 1 year and 35 months Target lesion revascularisation at 1 year and 35 months Target vessel failure at 1 year and 35 months Stent thrombosis (definite or probable) at 1 year and 35 months Minimal luminal diameter (in-segment, proximal edge, in-stent, distal edge) at 1 year and 35 months	
Brilakis 2018[17]: DIVA trial	Intervention (n=292): Drug-eluting stents: Any drug-eluting stent that was approved by the US Food and Drug Administration and clinically	n=597 People with at least one significant de-novo SVG lesion (50–99% stenosis of a 2·25–4·5 mm diameter SVG) requiring	All-cause mortality at 1 year Cardiac mortality at 1 year Myocardial infarction at 1 year	

Study	Intervention and comparison	Population	Outcomes	Comments
	available at the time of enrolment could be used Comparison (n=305): Bare metal stents: Any bare metal stent that was approved by the US Food and Drug Administration and clinically available at the time of enrolment could be used	percutaneous coronary intervention Unstable angina: 31% NSTEMI: 23.5% Age (mean): 68.6 years Gender (male to female ratio): Ethnicity: White 88.5%, Black 8.5%, Hispanic 5.5% USA	Target vessel revascularisation at 1 year Target lesion revascularisation at 1 year Stent thrombosis (definite and definite or probable) at 1 year Post-procedural bleeding at 1 year	
Chechi 2007[27]	Intervention (n=40): Drug-eluting stents: paclitaxel-eluting stents Comparison (n=40): Bare metal stents (type of bare metal stent used was unspecified in study)	n=80 People with chest pain persisting for ≥30 minutes associated with ST elevation Age (mean): 60.7 years Gender (male to female ratio): 66:14 Ethnicity: Not reported Italy	All-cause mortality at 7 months Target lesion revascularisation at 7 months Target vessel revascularisation at 7 months Myocardial infarction at 7 months Minimal lumen diameter at 7 months	Included in Cochrane Review (STEMI patients)
de Belder 2014[32]: XIMA trial	Intervention (n=399): Drug-eluting stents: everolimus-eluting stents Comparison (n=401):	n=800 People with non–ST-segment elevation myocardial, infarction, unstable angina, and stable angina	All-cause mortality at 1 year Cardiac mortality at 1 year Target vessel revascularisation at 1 year	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	Bare metal stents (type of bare metal stent used was unspecified in study)	Age (mean): 83.5 years Gender (male to female ratio): 480:320 Ethnicity: Not reported Multinational (United Kingdom and Spain)	Myocardial infarction at 1 year Major bleeding at 1 year	
Di Lorenzo 2009[34]: PASEO trial Di Lorenzo 2009[33]	Intervention 1 (n=90): Drug-eluting stents: paclitaxel-eluting stents Intervention 2 (n=90): Drug-eluting stents: sirolimus-eluting stents Comparison (n=90): Bare metal stents (type of bare metal stent used was unspecified in study)	n=270 People with chest pain for more than 30 minutes and ST-segment elevation Age (mean): 62.5 years Gender (male to female ratio): 190:80 Ethnicity: Not reported Italy	All-cause mortality at 1 year, 2 years Target lesion vascularisation at 1 year and 2 years Myocardial infarction (re-infarction) at 1 year and 2 years Stent thrombosis (definite, probable and possible) at one1 year, 2 years	Included in Cochrane Review (STEMI patients)
Diaz de la Llera 2007[35]	Intervention (n=60): Drug-eluting stents: sirolimus-eluting stents Comparison (n=60): Bare metal stents (type of bare	n=120 People with STEMI who were candidates for primary angioplasty Age (mean): 64.5 years Gender (male to female ratio): 95:19	All-cause mortality at 1 year Target vessel revascularisation at 1 year Stent thrombosis (late and acute or subacute) at 1 year	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	metal stent used was unspecified in the study)	Ethnicity: Not reported Spain		
Guagliumi 2010[46]: OCTAMI trial	Intervention (n=33): Drug-eluting stents: zotarolimus-eluting stents Comparison (n=11): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=44 People presented with STEMI <12 h after symptom onset (prolonged chest pain for more than 20 min, unresponsive to nitroglycerin, and ST-segment elevation Age (mean): 61.1 years Gender (male to female ratio): 34:10 Ethnicity: Not reported Italy and USA	All-cause mortality at 1 year Target lesion revascularisation at 1 year Target vessel revascularisation at 1 year Myocardial infarction at 1 year	Included in Cochrane Review (STEMI patients)
Han 2007[47]	Intervention (n=100): Drug-eluting stents: tacrolimus-eluting stents Comparison (n=100): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=200 People with symptomatic or documented myocardial ischemia, including acute myocardial infarction Age (mean): 58.4 years Gender (male to female ratio): 153:47 Ethnicity: Not reported Chile	Cardiac mortality at 8 months Myocardial infarction at 8 months	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
Kaiser 2010[55]: BASKET-PROVE trial	Intervention 1 (n=775): Drug-eluting stents: first-generation sirolimus-eluting stents Intervention 2 (n=774): Drug-eluting stents: second-generation everolimus-eluting stent Comparison (n=765): Bare metal stents – cobalt chromium	n=2314 People who presented with chronic or acute coronary disease, who underwent angioplasty with stenting Unstable angina/NSTEMI: 32.3% NSTEMI: 32% Age (mean): 66.5 years Gender (male to female ratio): 1759: 555 Ethnicity: Not reported Switzerland, Denmark, Austria, and Italy	All-cause mortality at 2 years Cardiac mortality at 2 years Myocardial infarction at 2 years Target vessel revascularisation at 2 years Stent thrombosis (definite; definite or possible) at 2 years Major bleeding at 2 years Minor bleeding at 2 years	Included in Cochrane Review (STEMI patients)
Kaiser 2015[56]: BASKET-PROVE II trial	Intervention 1 (n=765): Drug-eluting stents: second-generation biolimus-A9–eluting biodegradable-polymer stainless-steel stents Intervention 2 (n=765) Drug-eluting stents: second-generation everolimus-eluting durable-polymer cobalt-chromium stents Comparison (n=761):	n=2291 People presenting with chronic or acute coronary artery disease requiring angioplasty and stenting STEMI: 29% NSTEMI: 34% Age (mean): 62.5 years Gender (male to female ratio): Ethnicity: 1787: 504 Switzerland, Denmark, Germany, and Austria	All-cause mortality at 2 years Cardiac mortality at 2 years Myocardial infarction at 2 years Target vessel revascularisation at 2 years Stent thrombosis (definite; definite or possible at 2 years	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	Bare metal stents: newest-generation thin-strut BMS coated with a biocompatible silicone-carbide layer			
Kelbaek 2008[61]: DEDICATION trial Kaltoft 2010[57]	Intervention (n=313): Drug-eluting stents: mixed use of drug eluting stents (47% were sirolimus-eluting, 40% were paclitaxel-eluting, and 13% were zotarolimus-eluting stents Comparison (n=313): Mixed use of bare metal stents (38% were made of cobalt alloy, 39% were stainless steel stents, and 23% were miscellaneous stainless steel stents	n=626 People with chest pain of >30 minute duration who had a cumulated ST-segment elevation Age (mean): 62.05 years Gender (male to female ratio): 458:168 Ethnicity: Not reported Denmark	All-cause mortality at 1 year and 3 years Cardiac mortality at 1 year and 3 years Target lesion revascularisation at 1 year and 3 years Target vessel revascularisation at 1 year and 3 years Myocardial infarction at 1 year and 3 years Minimal lumen diameter (in-lesion zone and in-stent zone) at 8 months	Included in Cochrane Review (STEMI patients)
Laarman 2006[67]: PASSION trial Dirksen 2008[36]	Intervention (n=310): Drug-eluting stents: paclitaxel-eluting stents Comparison (n=309):	n=619 People who had an acute myocardial infarction with ST-segment elevation (>20 minutes of chest pain and ST-segment elevation	All-cause mortality at 1 year and 2 years Cardiac mortality at 1 year and 2 years Target lesion revascularisation at 1 year and 2 years	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	Bare metal stents (type of bare metal stent used was unspecified in the study)	Age (mean): 61 years Gender (male to female ratio): 470:149 Ethnicity: Not reported Netherlands	Myocardial infarction (recurrent) at 1 year and 2 years	
Menichelli 2007[76] : SESAMI trial Violini 2010[131]	Intervention (n=160): Drug-eluting stents: sirolimus-eluting stents Comparison (n=160): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=320 People who had symptoms of acute MI for ≥30 minutes but ≤12 hours, and had ≥1 mm ST-segment elevation Age (median): 62.5 years Gender (male to female ratio): 128:32 Ethnicity: Not reported Italy	All-cause mortality at 1 year and 3 years Target lesion revascularisation at 1 year and 3 years Target vessel revascularisation at 1 year and 3 years Myocardial infarction (re-infarction) at 1 year and 3 years Stent thrombosis (definite) at 1 year and 3 years	Included in Cochrane Review (STEMI patients)
Raber 2012[90]: COMFORTABLE trial Magro 2014[73] Raber 2016[88] Raber 2014[91], Raber 2012[89]	Intervention (n=578): Drug-eluting stents: eluting biolimus from a biodegradable polylactic acid polymer Comparison (n=583): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=1161 People with symptom onset within 24 hours and ST segment elevation Age (mean): 60.6 years Gender (male to female ratio): 918:243 Ethnicity: Not reported	All-cause mortality at 1 year and 2 years Cardiac mortality at 1 year and 2 years Target lesion revascularisation at 1 year and 2 years Target vessel revascularisation at 2 years	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
		Multinational (11 centres across: Denmark, Israel, Netherlands, Serbia, Switzerland, United Kingdom)	Stent thrombosis (definite and probable) at 1 year and 2 years Minimal lumen diameter (in stent, in segment) at 12 months	
Remkes 2016[94]: ELISA 3 trial	Intervention (n=234): Drug-eluting stents: everolimus-eluting stents Comparison (n=240): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=474 People with NSTEMI hospitalised with ischaemic chest pain or dyspnoea at rest, with the last episode occurring 24 hours or less Age (mean): 65.27 years Gender (male to female ratio): 351:123 Ethnicity: Not reported Netherlands	Target vessel revascularisation at 2 years Minimal lumen diameter at 9 months	Included in Cochrane Review (STEMI patients)
Ribamar Costa 2012[95]	Intervention (n=20): Drug-eluting stent (unspecified), study reports Cypher Select. Comparison (n=20): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=40 People with ST-segment elevation myocardial infarction (MI) treated in the very early phase (primary or rescue percutaneous coronary intervention [PCI]), restenotic lesions, lesions located at grafts and at the left main stem Age (mean): 56.3 years	All-cause mortality at 1 year Myocardial infarction at 1 year Stent thrombosis at 1 year Minimal lumen diameter (proximal edge and distal edge) at 1 year	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
		Gender (male to female ratio): 28:12 Ethnicity: Not reported Brazil		
Ribichini 2011[96]: CEREA-DES trial	Intervention (n=125): Drug-eluting stents: paclitaxel-eluting stents or the sirolimus-eluting stents Comparison (n=125): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=250 People showing significant coronary artery disease (either single or multi-vessel involvement), with signs or symptoms of myocardial ischemia, amenable for PCI Unstable angina: 30.8% NSTEMI: 26.8% Age (mean): 63.99 years Gender (male to female ratio): 210:40 Ethnicity: Not reported Italy	All-cause mortality at 1 year Cardiac mortality at 1 year Myocardial infarction (non–Q-wave and Q-wave) at 1 year Target lesion revascularisation at 1 year Target vessel revascularisation at 1 year	
Rodriguez 2011[100]: EUCATAX trial	Intervention (n=211): Drug-eluting stents: paclitaxel-eluting stents coated with a biodegradable polymer and glycocalyx Comparison (n=211):	n=422 People with a de novo stenosis in a major coronary artery Unstable angina: 63.3% Age (mean): 64.3 years Gender (male to female ratio): 343:79	All-cause mortality at 1 year Cardiac mortality at 1 year Myocardial infarction (acute) at 1 year Target vessel revascularisation at 1 year	

Study	Intervention and comparison	Population	Outcomes	Comments
	Bare metal stents (type of bare metal stent used was unspecified in the study)	Ethnicity: Not reported Argentina	Target vessel failure at 1 year	
Sabate 2012[104] EXAMINATION trial Sabate 2011[103] Sabate, 2014[102] (2 year results) Brugaletta 2012[22]:	Intervention (n=751): Drug-eluting stents: everolimus-eluting stents Comparison (n=747): Bare metal stents – cobalt chromium balloon expandable bare metal stent	n=1498 People with STEMI within the first 48 hours after symptom onset, requiring emergent percutaneous coronary intervention Age (mean): 61.2 years Gender (male to female ratio): 1244:254 Ethnicity: Not reported Spain, Italy, Netherlands	All-cause mortality at 1 year and 2 years Cardiac mortality at 1 year and 2 years Target lesion revascularisation at 1 year and 2 years Target vessel revascularisation at 1 year and 2 years Myocardial infarction at 1 year and 2 years Stent thrombosis (definite/definite and probable) at 1 year and 2 years Major bleeding at 1 year and 2 years Minor bleeding at 1 year and 2 years	Included in Cochrane Review (STEMI patients)
Sanchez 2010[105]: GRACIA-3 trial	Intervention (n=217): Drug-eluting stents: paclitaxel-	n=433 People with symptom onset within	Cardiac mortality at 1 year Myocardial infarction at 1 year	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	eluting stent with or without tirofiban. Comparison (n=216): Bare metal stents (type of bare metal stent used was unspecified in the study) - with or without tirofiban.	12 hours, chest pain lasting more than 20 minutes and ST-segment elevation. Age (mean): 61 years Gender (male to female ratio): 358/75 Ethnicity: Not reported Spain	Stent thrombosis (definite and probable) at 1 year Minor bleeding at 1 year Minimal lumen diameter at 1 year Major bleeding at 1 year	
Spaulding 2006[109]: TYPHOON 2006 trial	Intervention (n=356): Drug-eluting stents: sirolimus-eluting stent Comparison (n=359): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=715 People with symptoms which began less than 12 hours before catheterization and if the electrocardiogram showed ST segment elevation Age (mean): 59.3 years Gender (male to female ratio): 558:157 Ethnicity: Not reported Multinational (Australia, Czech Republic, Denmark, France, Germany, Hungary, Israel, Italy, Latvia, Netherlands, Poland, Portugal, Spain, Switzerland, United Kingdom)	All-cause mortality at 1 year Cardiac mortality at 1 year Target vessel failure at 1 year Myocardial infarction (recurrent) at 1 year Stent thrombosis at 1 years Minimal lumen diameter (in stent and in lesion) at 8 months	Included in Cochrane Review (STEMI patients)
Steinwender 2008[111]	Intervention (n=8):	n=16	All-cause mortality at 6 months	Included in Cochrane Review

Study	Intervention and comparison	Population	Outcomes	Comments
	Drug-eluting stents: sirolimus-eluting stents Comparison (n=8): Bare metal stents (type of bare metal stent used was unspecified in the study)	People with a first ST-elevation anterior myocardial infarction Age (mean): 55.5 years Gender (male to female ratio):12:4 Ethnicity: Not reported Austria	Minimal lumen diameter at 6 months	(STEMI patients)
Stone 2009[112]: HORIZONS-AMI trial Mehran 2008[75] Stone 2010[113] Stone 2011[114]	Intervention (n=2257): Drug-eluting stents: paclitaxel-eluting stents Comparison (n=749): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=3006 People presenting with ST-segment elevation myocardial infarction Age (mean): 59.6 years Gender (male to female ratio): Ethnicity: Not reported Multinational (Argentina, Austria, Germany, Israel, Italy, Netherlands, Norway, Poland, Spain, United Kingdom, USA)	All-cause mortality at 1 year and 3 years Cardiac mortality at 1 year and 3 years Target lesion revascularisation at 1 year and 3 years Target vessel revascularisation (ischemia-driven) at 1 year and 3 years Stent thrombosis at 1 year and 3 years Major bleeding (including CABG) at 3 years Minimal lumen diameter at 1 year	Included in Cochrane Review (STEMI patients)
Strozzi 2007[116]	Intervention (n=39): Drug-eluting stents: sirolimus-	n=119 People with a diagnosis of acute	All-cause mortality at 6 months Target lesion revascularisation at	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	eluting stents Comparison (n=40): Bare metal stents (type of bare metal stent used was unspecified in the study)	coronary syndrome included acute myocardial infarction with ST elevation, prolonged angina for more than 20 minutes, or recurrent episodes at rest with indicators of cardiac ischemia or injury Age (mean): 57.8 years Gender (male to female ratio): 95:24 Ethnicity: Not reported Croatia	6 months Myocardial infarction at 6 months Minimal lumen diameter at 6 months	
Valgimigli 2008[122]: MULTISTRATEGY trial Valgimigli 2013[121]	Intervention (n=372): Drug-eluting stents: sirolimus-eluting stents Comparison (n=372): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=744 People with chest pain for longer than 30 minutes with an electrocardiographic ST-segment elevation Age (mean): 63.9 years Gender (male to female ratio): 565:179 Ethnicity: Not reported Multinational (16 centres in: Italy, Argentina and Spain)	All-cause mortality at 8 months and 3 years Cardiac mortality at 3 years Target vessel revascularisation at 8 months and 3 years Myocardial infarction at 8 months Stent thrombosis (definite and/or probable) at 3 years Major bleeding at 30 days Minor bleeding at 30 days	Included in Cochrane Review (STEMI patients)
Valgimigli 2014[126]:	Intervention 1 (n=1508):	n=2013	Target lesion revascularisation at	Included in

Study	Intervention and comparison	Population	Outcomes	Comments
PRODIGY trial Valgimigli 2010[123]	Drug-eluting stents: everolimus-eluting stents, paclitaxel-eluting stents or zotarolimus eluting stents Intervention 2 (n=505): Drug-eluting stents: paclitaxel-eluting stents Intervention 3 (n=502): Drug-eluting stents: zotarolimus-eluting stents Comparison (n=505): Third-generation thin-strut bare metal stents(metal not specified in the study)	People with chronic stable coronary artery disease or acute coronary syndromes, including non–ST-segment elevation myocardial infarction (MI) and ST-segment elevation MI ACS: 73% NSTEMI:22.5% STEMI:32.3% Unstable angina:18.5% Age (mean): 68.5 years Gender (male to female ratio): 1538:465 Ethnicity: Not reported Italy	2 years Target vessel revascularisation at 2 years Stent thrombosis (definite or probable) at 2 years	Cochrane Review (STEMI patients)
Valgimigli 2015[125]: ZEUS trial Valgimigli 2013[124]	Intervention (n=802): Drug-eluting stents: zotarolimus-eluting stents Comparison (n=804): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=1606 People who underwent elective, urgent, or emergent percutaneous coronary intervention with intended stent implantation 63.3% ACS, 16% unstable angina, 27.5% NSTEMI, 19% STEMI Age (median): 71.8 years	All-cause mortality at 1 year Cardiac mortality at 1 year Target vessel revascularisation at 1 year Target lesion revascularisation at 1 year	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
		Gender (male to female ratio): 1133:473 Ethnicity: Not reported Multinational (Netherlands, Italy, Greece, Hungary, Ireland, Switzerland, Portugal, Belgium)	Myocardial infarction at 1 year Stent thrombosis (definite and possible) at 1 year Bleeding at 1 year	
van der Hoeven 2008[128]: MISSION trial Atary 2010[7] Boden 2011[13] Boden 2012[14]	Intervention (n=158): Drug-eluting stents: sirolimus-eluting stents Comparison (n=152): Bare metal stents (type of bare metal stent used was unspecified in the study)	n=310 People with STEMI symptoms which started 9 hours before primary percutaneous coronary intervention Age (mean): 59.2 years Gender (male to female ratio): 241:69 Ethnicity: Not reported Netherlands	All-cause mortality (cardiac and non-cardiac) at 1 year and 3 years Cardiac mortality at 1 year and 3 years Target vessel failure at 1 years and 3 years Myocardial infarction (recurrent MI spontaneous and procedure related) at 1 year and 3 years Stent thrombosis (definite) at 3 years Minimal lumen diameter (in-stent and in-segment) at 1 year	Included in Cochrane Review (STEMI patients)
Wijnbergen 2012[133]: DEBATER trial	Intervention (n=441): Drug-eluting stents: sirolimus-eluting stent	n=907 People with STEMI, who resented within 12 hours of onset of symptoms	All-cause mortality at 1 year Target vessel revascularisation at 1 year	Included in Cochrane Review (STEMI patients)

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=466): Bare metal stent (type of bare metal stent used was unspecified in the study – choice of the bare metal stent was left to the discretion of the operator)	Age (mean): 61 years Gender (male to female ratio): 668:202 Ethnicity: Not reported Netherlands	Stent thrombosis (definite and probable) at 1 year Bleeding at 1 year	

See appendix D for full evidence tables.

1.5.4 Quality assessment of clinical studies included in the evidence review

Table 4: Clinical evidence summary: Drug eluting stents (DES) versus bare metal stents (BMS)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with BMS	Risk difference with DES (95% CI)
All-cause mortality	14049 (22 studies) up to 1 year	⊕⊕⊖⊖ LOW[1,3] due to risk of bias, imprecision	N/A[5]	49 per 1000	2 fewer per 1000 (from 9 fewer to 5 more)
All-cause mortality	12999 (12 studies) 1-3 years	⊕⊕⊖⊖ LOW[1,2] due to risk of bias, imprecision	RR 0.87 (0.75 to 1.01)	57 per 1000	7 fewer per 1000 (from 14 fewer to 1 more)
Cardiac mortality	12117 (14 studies) up to 1 year	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 0.98 (0.82 to 1.17)	39 per 1000	1 fewer per 1000 (from 7 fewer to 7 more)
Cardiac mortality	12416 (10 studies)	⊕⊕⊖⊖ LOW[1,2]	RR 0.85 (0.70 to 1.03)	37 per 1000	6 fewer per 1000 (from 11 fewer to 1 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with BMS	Risk difference with DES (95% CI)
	1-3 years	due to risk of bias, imprecision			
Target vessel failure	2041 (4 studies) up to 1 year	⊕⊖⊖⊖ VERY LOW[1,2,4] due to risk of bias, inconsistency, imprecision	RR 0.62 (0.44 to 0.88)	164 per 1000	62 fewer per 1000 (from 20 fewer to 92 fewer)
Target vessel failure	703 (3 studies) 1-3 years	⊕⊕⊕⊖ MODERATE[1] due to risk of bias	RR 0.55 (0.41 to 0.74)	259 per 1000	117 fewer per 1000 (from 67 fewer to 153 fewer)
Target vessel revascularisation	12858 (18 studies) up to 1 year	⊕⊕⊕⊖ MODERATE[1] due to risk of bias	RR 0.52 (0.46 to 0.59)	100 per 1000	48 fewer per 1000 (from 41 fewer to 54 fewer)
Target vessel revascularisation	15141 (13 studies) 1-3 years	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 0.52 (0.47 to 0.57)	129 per 1000	62 fewer per 1000 (from 55 fewer to 68 fewer)
Stent thrombosis - definite or probable	11405 (12 studies) up to 1 year	⊕⊕⊖⊖ LOW[1,2] due to risk of bias, imprecision	RR 0.71 (0.57 to 0.89)	34 per 1000	10 fewer per 1000 (from 4 fewer to 15 more)
Stent thrombosis - definite or probable	14390 (12 studies) 1-3 years	⊕⊕⊖⊖ LOW[1,2] due to risk of bias, imprecision	RR 0.80 (0.64 to 0.99)	28 per 1000	6 fewer per 1000 (from 0 fewer to 10 fewer)
Myocardial infarction	10780 (20 studies) up to 1 year	⊕⊕⊖⊖ ⊕⊕⊕⊖ MODERATE[1] due to risk of bias	N/A[5]	46 per 1000	18 fewer per 1000 (from 12 fewer to 23 fewer)
Myocardial infarction	9456 (10 studies) 1-3 years	⊕⊕⊖⊖ LOW[1,2] due to risk of bias,	RR 0.66 (0.53 to 0.83)	41 per 1000	14 fewer per 1000 (from 7 fewer to 19 fewer)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with BMS	Risk difference with DES (95% CI)
		imprecision			
Bleeding - Unspecified	1467 (2 studies) up to 1 year	⨁⨀⨀⨀ VERY LOW[1,2] due to risk of bias, imprecision	RR 0.73 (0.41 to 1.31)	35 per 1000	9 fewer per 1000 (from 20 fewer to 11 more)
Bleeding - Major	7395 (6 studies) up to 1 year	⨁⨁⨀⨀ LOW[1,2] due to risk of bias, imprecision	RR 0.79 (0.56 to 1.11)	20 per 1000	4 fewer per 1000 (from 9 fewer to 2 more)
Bleeding - Minor	6595 (5 studies) up to 1 year	⨁⨁⨀⨀ LOW[1,2] due to risk of bias, imprecision	RR 0.84 (0.63 to 1.12)	32 per 1000	5 fewer per 1000 (from 12 fewer to 4 more)
Bleeding - Major	5104 (2 studies) 1-3 years	⨁⨀⨀⨀ VERY LOW[1,2,4] due to risk of bias, inconsistency, imprecision	RR 0.99 (0.63 to 1.57)	54 per 1000	1 fewer per 1000 (from 20 fewer to 31 more)
Bleeding - Minor	2314 (1 study) 1-3 years	⨁⨀⨀⨀ VERY LOW[1,2] due to risk of bias, imprecision	RR 0.91 (0.47 to 1.78)	17 per 1000	2 fewer per 1000 (from 9 fewer to 13 more)
Minimal luminal diameter - In-segment	346 (2 studies) up to 1 year	⨁⨁⨁⨀ MODERATE[1] due to risk of bias		The mean minimal luminal diameter - in-segment in the control groups was 1.745 mm	The mean minimal luminal diameter - in-segment in the intervention groups was 0.53 higher (0.4 to 0.65 higher)
Minimal luminal diameter - In-stent	1103 (5 studies) up to 1 year	⨁⨁⨁⨀ MODERATE[1] due to risk of bias		The mean minimal luminal diameter - in-stent in the control groups	The mean minimal luminal diameter - in-stent in the intervention groups was 0.68 higher

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with BMS	Risk difference with DES (95% CI)
				was 1.75 mm	(0.60 to 0.77 higher)
Minimal luminal diameter - In-lesion	695 (2 studies) up to 1 year	⨁⨁⊖⊖ LOW[1,2] due to risk of bias, imprecision		The mean minimal luminal diameter - in-lesion in the control groups was 1.84 mm	The mean minimal luminal diameter - in-lesion in the intervention groups was 0.43 higher (0.32 to 0.53 higher)
Minimal luminal diameter - Proximal edge	37 (1 study) up to 1 year	⨁⨁⊖⊖ LOW[1,2] due to risk of bias, imprecision		The mean minimal luminal diameter - proximal edge in the control groups was 2.86 mm	The mean minimal luminal diameter - proximal edge in the intervention groups was 0.12 lower (0.45 lower to 0.21 higher)
Minimal luminal diameter - Distal edge	40 (1 study) up to 1 year	⨁⊖⊖⊖ VERY LOW[1,2] due to risk of bias, imprecision		The mean minimal luminal diameter - distal edge in the control groups was 2.85 mm	The mean minimal luminal diameter - distal edge in the intervention groups was 0.05 lower (0.39 lower to 0.29 higher)
Minimal luminal diameter - Unspecified	5273 (7 studies) up to 1 year	⨁⊖⊖⊖ VERY LOW[1,2,4] due to risk of bias, inconsistency, imprecision		The mean minimal luminal diameter - unspecified in the control groups was 2.25 mm	The mean minimal luminal diameter - unspecified in the intervention groups was 0.18 higher (0.05 to 0.32 higher)

1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
3 Imprecision was assessed by calculating the optimal information size and graded as follows: <80% - very serious imprecision, 80-90%- serious imprecision, >90%– no imprecision

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with BMS	Risk difference with DES (95% CI)
4 Downgraded by 1 or 2 increments because heterogeneity, I2= > 50%, p= > 0.04, unexplained by subgroup analysis 5 No relative effect due to 0 events. Risk difference calculated in Review Manager					

See appendix F for full GRADE tables.

1.6 Economic evidence

1.6.1 Included studies

Five health economic studies with the relevant comparison were included in this review.[24, 48, 81, 93, 106, 135, 137] Note that two papers were identified for one study as one of these (Hill 2007[48]) is the analysis undertaken to inform TA152.[81] These are summarised in the health economic evidence profile below (Table 5) and the health economic evidence tables in Appendix H:.

1.6.2 Excluded studies

Fifteen economic studies relating to this review question were excluded due to a combination of methodological limitations and the availability of more applicable evidence.[8-10, 20, 21, 39, 45, 52, 54, 65, 69, 87, 117, 118, 129] These are listed in Appendix I:, with reasons for exclusion given. Generally, these were studies that were published before the technology appraisal analysis, used treatment effects that were from clinical studies that did not meet the inclusion criteria or did not use QALYs.

See also the health economic study selection flow chart in Appendix G:.

1.6.3 Summary of studies included in the economic evidence review

Table 5: Health economic evidence profile: drug-eluting stents versus bare metal stents

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Canoui-Poitrine 2009[24] (France)	Partially applicable[(a)]	Potentially serious limitations[(b)]	• Within-trial analysis of French subgroup of the TYPHOON RCT with probabilistic analysis. QALYs estimated by attributing a QALY loss to all adverse events that occurred during follow-up.[(c)] • Cost-utility analysis (QALYs) / cost-effectiveness analysis (TVR avoided) • Population: people presenting with STEMI less than 12 hours after the onset of chest pain, undergoing PCI. • Comparators: 1. Bare metal stents 2. Drug eluting stents (sirolimus) • Follow-up: 1 year	£911[(d)]	-0.0006 QALYs -15.6% TVR	BMS dominates DES (lower cost and higher QALYs) £5,842 per repeat TVR avoided	No probabilistic analysis for QALY analysis. 54.9% of ICERs estimated remain under the threshold of £7,980 per repeat TVR avoided. One person in the DES arm had a heart transplant which considerably increased costs of the DES arm. Removing this incident resulted in an ICER of £4,635 per TVR avoided.
Hill 2007[48] (UK) *ERG analysis for*	Partially applicable[(e)]	Potentially serious limitations[(f)]	• Decision analytic model based around differences in repeat revascularisation within 12 months.	*Narrow effectiveness*[(g)] Taxus =	*Narrow effectiveness*[(g)] 0.002444	*Narrow effectiveness*[(g)] Taxus = £348,700	No probabilistic analysis. A wide range of sensitivity analyses around baseline risks, relative risks, costs,

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
NICE TA152			QALY differences arise due to lower QOL weights being attributed to those that have a repeat revascularisation. Mortality and long-term morbidity assumed to be unaffected. • Cost-utility analysis (QALYs) • Population: people with coronary artery disease revascularised in NHS hospitals - non-elective index PCI results presented here (assumed to equate to ACS) • Comparators: 1. Bare metal stents 2. Drug eluting stents (Taxus, Cypher) • Time horizon: 1 year	£852[h] Cypher = £919[h] *Broad effectiveness*[g] Taxus = £795[h] Cypher = £861[h]	QALYs *Broad effectiveness*[g] 0.003251 QALYs	Cypher = £376,100 *Broad effectiveness*[g] Taxus = £244,400 Cypher = £264,800	utilities and other inputs were undertaken. The ICERs ranged from £185,300 to £702,200 per QALY gained. Additional results are presented after this table. A scenario exploring the absolute risk and difference in the costs of BMS and DES was undertaken. This showed that for non-elective patients with an absolute risk of 18% or more and a price difference of £300 the ICER ranged from DES being dominant to £24,000. This led to the previous recommendation in NICE TA152. A breakdown of these results is demonstrated in Table 7.
Schur 2018[106] (Spain)	Partially applicable[i]	Potentially serious limitations[j]	• Within-trial analysis of the EXAMINATION RCT 5 year data with modelled extrapolation and probabilistic analysis; incorporates mortality, MI, stent thrombosis	£455[k]	0.10 QALYs	£4,180 per QALY gained	86.9% of simulations were below a threshold of £26,467 per QALY gained. ICERs in sensitivity analyses ranged from ~£3000 to ~£8000 per

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
			and revascularisation. • Cost-utility analysis (QALYs) • Population: STEMI within the first 48 hours requiring emergent PCI (with vessel sizes of 2.25 to 4.00mm); 85% PPCI. • Comparators: 1. Bare metal stents 2. Drug eluting stents (everolimus) • Time horizon: lifetime (with treatment effect duration 5 years)				QALY gained. Analyses varying the different in stent costs found that if this was £116 there was no difference in lifetime costs.
Wisloff 2013[135] (Norway)	Partially applicable[l]	Potentially serious limitations[m]	• Decision analytic model with treatment effects obtained from a published network meta-analysis, this included mortality, myocardial infarction and revascularisation. • Cost-effectiveness analysis (life years) • Population: people with STEMI, NSTEMI, unstable or stable angina undergoing PCI with stent • Comparators: 1. Bare metal	2−1: -£1,473[n] 3-1: -£223[n] 3−2: £1,250[n]	2−1: 0.003 life years 3-1: 0.151 life years 3−2: 0.148 life years	DES dominates (lower costs and higher life years) BMS 3 vs 2: £9,553 per life year gained	With a cost effectiveness threshold of <£8,571per life year gained SES had highest probability of being cost-effective. With a cost effectiveness threshold of >£8,571per life year gained PES had the highest probability of being cost-effective. An analysis was conducted assuming lifetime treatment effectiveness of DES demonstrated that PES was the most cost-effective option.

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
			stents 2. Drug-eluting stents (sirolimus) 3. Drug-eluting stents (paclitaxel) • Time horizon: lifetime (with treatment effect for 5 years)				
Zbinden 2017[137] (Switzerland)	Partially applicable[o]	Potentially serious limitations[p]	• Within-trial analysis of a subgroup of BASKET-PROVE RCT with probabilistic analysis • Cost-utility analysis (QALYs) based on within-trial analysis of EQ-5D data; also cost-effectiveness analysis (target lesion revascularisations avoided) • Population: people with stable CAD or ACS undergoing PCI with at least one stent with a diameter ≥3mm and ≤15 mm lesion • Comparators: 1. Bare metal stents 2. Drug eluting stents (Cypher, Xience) • Follow-up: 2 years	£75[q]	0.005 QALYs 0.083 TLRs avoided	£15,105 per QALY gained £1,986 per TLR avoided	**QALY analysis** Probability DES cost effective (£26,486 threshold): 52.0% **TLR avoided analysis** Probability DES cost effective (£5,297 threshold): 88.2% No deterministic sensitivity analysis.

Abbreviations: BMS = bare-metal stent; DES = drug-eluting stent; ERG = evidence review group; ICER = incremental cost-effectiveness ratio; PCI = percutaneous coronary intervention; PES = paclitaxel-eluting stent; QALY = quality-adjusted life years; RCT = randomised controlled trial; SES = sirolimus-eluting stent; STEMI = ST segment elevation myocardial infarction; TLR = target lesion revascularisation; TVR = target vessel revascularisation

(a) 2007 French healthcare perspective may not reflect current UK context. Some methods used to derive quality of life weights are not in line with NICE reference case and where EQ5D has been used it is unclear if with the UK tariff.

(b) Within-trial analysis based on a French subgroup of a single trial (TYPHOON RCT) and so does not reflect full body of available evidence for this area and may not reflect real world UK context.. Time horizon of 1 year may not fully capture differences in costs and health outcomes as NGC review suggests effects continue beyond 1 year. It is unclear what is driving lower QALYs in the DES group as most outcomes favour DES; the only outcomes that are numerically worse in the DES group are 'Other cardiac events' which authors' state includes things such as such as hospitalizations for chest pain without proof of ischaemia, acute pulmonary oedema or heart failure and stroke where 1 event occurred with DES and 0 with BMS. Utility scores are reported for the following events suggesting they were incorporated: angioplasty, CABG, MI, congestive heart failure, severe chest pain, stroke, implantable cardioverter defibrillator, carotid thromboendarterectomy, infrainguinal surgery, insulin-dependent diabetes mellitus, medulloblastoma tumour – non-metastatic, stomach ulcer, hip fracture, catheter ablation in patients with ventricular tachycardia.

(c) Utility scores are reported for angioplasty, CABG, MI, congestive heart failure, severe chest pain, stroke, implantable cardioverter defibrillator, carotid thromboendarterectomy, infrainguinal surgery, insulin dependent diabetes mellitus, medulloblastoma tumour – non-metastatic, stomach ulcer, hip fracture, catheter ablation in patients with ventricular tachycardia.

(d) 2007 French Euros converted to UK pounds.[83] Cost components included: index admission costs (stent costs, procedure cost, drug costs, ICU cost, ward costs, rehabilitation) and follow-up including medication and all repeat hospitalisation costs. (Cost of stents included in analysis (mean, median): BMS = £544, £439; DES = £1,587, £1,237).

(e) Resource use from 2000-2002 and 2004/05 UK unit costs may not reflect current UK practice. The analysis does not include the variety of drug-eluting stents currently available in the NHS as it only focuses on two types of stents (CYPHER and TAXUS) which dominated the market at the time.

(f) Analysis based on 7 RCTS (TAXUS I, TAXUS II, TAXUS IV, E-SIRIUS, RAVEL, SIRIUS and Pache) and so does not reflect full body of available evidence for this area and also includes studies stable patients that have been excluded from the clinical review for this guideline. Time horizon of 1 year may not fully capture differences in costs and health outcomes as NGC review suggests effects continue beyond 1 year and there may be benefits other than revascularisation that are not captured in the analysis..

(g) Different relative risks were applied based on 'broad' and 'narrow' estimates. 'Broad' estimates are based on cases involved any TLR/TVR irrespective of any other lesions/vessels revascularised (0.369) and 'narrow' estimates are based on cases involving TLR/TVR only (0.492).

(h) Cost components: stent costs, cost of angiography, follow-up appointments and repeat revascularisation cost. Stent costs: BMS = £291.95; DES effective list price Taxus = £997.50, Cypher = £1044.75; DES actual cost Taxus = £855.43, Cypher = £983.51.

(i) Spanish healthcare perspective and international resource use may not reflect current UK context. STEMI only. Discounting at 3% and use of Spanish EQ5D tariff not fully in line with NICE reference case.

(j) Within-trial analysis of a single RCT and so does not reflect full body of available evidence for this area. Baseline risks based on multinational RCT (Spain, Italy, Netherlands) and so may not be reflective of real world UK risk; although authors note that "The EXAMINATION trial had broad inclusion and few exclusion criteria to ensure an all-comers population of adult STEMI patients which is representative of routine clinical practice".

(k) 2016 Spanish Euros converted to UK pounds.[83] Cost components included: type and number of stents; clinical events up to 5 years: MIs, stent thrombosis events, revascularisation procedures (PCI and CABG); annual CV outpatient treatment and drug costs during first 5 years (when clinical events accounted for explicitly); long-term annual CV treatment costs after year 5; 12 months antiplatelet therapy after revascularisation events. Cost of stents: BMS = £466; DES = £897.

(l) 2008 Norwegian healthcare perspective may not reflect current UK context. Analysis includes patients with stable coronary artery disease as well as ACS. 4% discount rate and measure of effect (life years) not in line with NICE reference case methods.

(m) Baseline risks are based on the overall CAD population in Scandinavia and so may differ from a UK ACS population. Treatment effects were based on both ACS and stable patients and so studies excluded from our review have been incorporated; additional studies have also been identified by the review undertaken for this guideline. The price of stents used in the model was not official prices and were obtained through personal communication with a cardiologist.

(n) 2008 Norwegian Kroner converted to UK pounds.[83] Cost components included: stent costs, costs of procedures and cost of medication. Cost of stents: BMS = £107; SES = £515; PES = £419.

(o) 2013 Swiss healthcare payer perspective and international resource use from 2007-2008 may not reflect the current UK context. Analysis includes patients with stable coronary artery disease as well as ACS (proportion not reported for analysis subgroups but for overall BASKET-PROVE RCT was 64% ACS). QALYs were derived using EQ-5D German population utility value set instead of the UK population value set.

(p) Within-trial analysis of subgroup of one RCT (BASKET-PROVE subgroup with stents >3mm and <15mm lesion length) and so does not reflect full body of available evidence for this area. Analysis was conducted on a retrospective subgroup. Incremental cost data is not numerically reported. Time horizon of 2 years may not fully capture differences in costs and health outcomes as NGC review suggests effects on revascularisations for ACS overall maintained at 1-3 year time point and approach to modelling may not fully capture benefits to patients e.g. if QALY losses are generally short-term following revascularisation. Unclear if survival incorporated when calculating QALYs per patient.

(q) Incremental cost data not reported numerically, but was calculated using reported incremental QALYs and ICER. 2013 Swiss Francs converted to UK pounds.[83] Cost components: stent costs, inpatient and outpatient procedures, only included costs of follow-up if it involved revascularisation. Cost of stents: BMS = £610; DES = £761.

The tables below show additional cost effectiveness results from Hill 2007 (this analysis informed NICE TA152).[48]

Table 6: Hill 2007 cost-effectiveness results for non-elective PCI patients

Prices	Effectiveness	Brand	Incremental cost	Incremental QALYs	ICER
Overall					
Effective list	Narrow	Taxus	£852	0.002444	£348,700
		Cypher	£919	0.002444	£376,100
	Broad	Taxus	£795	0.003251	£244,400
		Cypher	£861	0.003251	£264,800
Actual	Narrow	Taxus	£651	0.002444	£266,200
		Cypher	£832	0.002444	£340,500
	Broad	Taxus	£595	0.003251	£182,900
		Cypher	£775	0.003251	£238,300
No risk factors					
Effective list	Narrow	Taxus	£844	0.002155	£391,600
		Cypher	£909	0.002155	£421,900
	Broad	Taxus	£793	0.002867	£276,600
		Cypher	£858	0.002867	£299,200
Actual	Narrow	Taxus	£648	0.002155	£300,500
		Cypher	£825	0.002155	£382,600
	Broad	Taxus	£598	0.002867	£208,700
		Cypher	£774	0.002867	£269,900
1 risk factor					
Effective list	Narrow	Taxus	£947	0.005332	£177,500
		Cypher	£1,032	0.005332	£193,500
	Broad	Taxus	£821	0.007095	£115,700
		Cypher	£905	0.007095	£127,600
Actual	Narrow	Taxus	£691	0.005332	£129,500
		Cypher	£921	0.005332	£172,800
	Broad	Taxus	£569	0.007095	£80,200
		Cypher	£796	0.007095	£112,200
2 risk factors					
Effective list	Narrow	Taxus	£627	0.009716	£64.600
		Cypher	£709	0.009716	£73,000
	Broad	Taxus	£399	0.012928	£30,800
		Cypher	£478	0.012928	£37,000
Actual	Narrow	Taxus	£382	0.009716	£39,300
		Cypher	£603	0.009716	£62,100
	Broad	Taxus	£160	0.012928	**£12,400**
		Cypher	£375	0.012928	£29,000

(a) ICERs in bold indicate where drug-eluting stents are cost-effective at a threshold of £20,000.

Table 7: Hill 2007 cost –effectiveness results for all non-elective patients (using mean number of stents implanted, 1.46 stents) by absolute risk of TVR and level of price premium for DES

Absolute risk (%)	Incremental cost per QALY by levels of price premium							
	£100	**£200**	**£300**	**£400**	**£500**	**£600**	**£700**	**£800**
6	**£18,000**	£87,400	£156,800	£226,100	£295,500	£364,900	£434,200	£503,600
8	**£2,100**	£57,500	£112,800	£168,200	£223,600	£279,000	£334,300	£389,700
10	**DES dominant**	£37,400	£83,400	£129,400	£175,400	£221,400	£267,400	£313,400
10.04	**DES dominant**	£37,100	£83,000	£128,800	£174,700	£220,500	£266,400	£312,200
12	**DES dominant**	£23,000	£62,300	£101,600	£140,800	£180,100	£219,400	£258,600
14	**DES dominant**	**£12,200**	£46,400	£80,700	£114,900	£149,100	£183,300	£217,500
16	**DES dominant**	**£3,800**	£34,100	£64,300	£94,600	£124,900	£155,200	£185,400
18	**DES dominant**	**DES dominant**	£24,200	£51,300	£78,400	£105,500	£132,600	£159,700
20	**DES dominant**	**DES dominant**	**£16,100**	£40,600	£65,100	£89,600	£114,200	£138,700
22	**DES dominant**	**DES dominant**	**£9,300**	£31,700	£54,000	£76,400	£98,800	£121,100
24	**DES dominant**	**DES dominant**	**£3,500**	£24,100	£44,600	£65,200	£85,700	£106,300
26	**DES dominant**	**DES dominant**	**DES dominant**	**£17,600**	£36,600	£55,600	£74,500	£93,500
28	**DES dominant**	**DES dominant**	**DES dominant**	**£12,000**	£29,600	£47,200	£64,800	£82,400
30	**DES dominant**	**DES dominant**	**DES dominant**	**£7,100**	£23,500	£39,900	£56,300	£72,800
32	**DES dominant**	**DES dominant**	**DES dominant**	**£2,700**	**£18,100**	£33,500	£48,800	£64,200
34	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**£13,300**	£27,700	£42,200	£56,600
36	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**£9,000**	£22,600	£36,200	£49,800
38	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**£5,100**	**£18,000**	£30,800	£43,700
40	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**£1,600**	**£13,800**	£26,000	£38,100
42	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**-£1,600**	**£10,000**	£21,500	£33,100
44	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**-£4,500**	**£6,500**	**£17,500**	£28,500
46	**DES dominant**	**DES dominant**	**DES dominant**	**DES dominant**	**-£7,100**	**£3,300**	**£13,800**	£24,300

(b) ICERs in bold indicate where drug-eluting stents are cost-effective at a threshold of £20,000

Table 8 summarises the stent prices used in the health economic studies. Current UK stent costs are provided in Table 10.

Table 8: Stent costs used in studies

Study	BMS cost	DES cost	Difference
Canoui-Poitrine 2009[24] (France)	£439	£1,237	£798
Hill 2007[48] (UK)	£292	Taxus = £997, Cypher = £1,045	£705 (Taxus), £753 (Cypher)
Schur 2018[106] (Spain)	£466	£897	£431
Wisloff 2013[135] (Norway)	£107	SES = £515, PES = £419	£408 (SES), £312 (PES)
Zbinden 2017[137] (Switzerland)	£610	£761	£151

Table 9 summarises the treatment effects from the NGC systematic review and meta analyses reports in section 1.5 and the relevant treatment effects in the included economic analyses to aid interpretation. For models these are the reported treatment effects applied in the models. For within trial analyses these are the relative treatment effects from the relevant RCT or RCT subgroup. Specific details are provided under the table.

Table 9: Comparison of NGC meta-analysis results and treatment effects in economic studies

	NGC meta-analysis				Canoui-Poitrine 2009 (Typhoon trial - French subgroup)[a]		Schur 2018 (Examination trial)[b]				Zbinden 2017 (Basket prove trial)[c]		Hill 2007(model)[d]		Wisloff 2013 (model)[e]			
	</= 12 months		1-3 years		1yr		2 year		5 year		1-3 yrs		1 year		6 month probabilities		Applied for 5 years	
	BMS	RR DES	BMS	RR DES	BR BMS	RR DES	BR BMS	RR DES	BR BMS	HR DES	BR BMS	RR DES	BR BMS	RR DES	BR BMS first 6 months	BR BMS after 6 months	RR PES	RR SES
All-cause mortality	5%	0.95	6%	0.87	4%	0.69	5%	0.86	12%	0.72	4%	0.77			unclear	1%	0.89	1.05
TVR	10%	0.51	13%	0.52	22%	0.30	8%	0.61	10%	0.62	10%	0.39		0.43				
Stent thrombosis	3%	0.71	3%	0.81	5%	0.90	3%	0.47	3%	0.64	1%	0.60						
MI	5%	0.60	4%	0.66	2%	1.03	2%	0.77	4%	1.27	3%	0.49			6%	2%	1.05	0.81
All revasc					29%	0.39			16%	0.77			7% 11%	0.59 0.45	2%	2%	0.46	0.29

(a) Economic analysis was a within-trial analysis; data here is as reported in paper for the French subgroup of the Typhoon RCT used for the economic analysis
(b) Economic analysis was a within-trial analysis; 2 year data here is as reported in NGC met- analysis (to facilitate comparison with estimate from same timepoint); 5 year data is as reported in economic paper
(c) Economic analysis was a within-trial analysis of a subgroup of the Basket Prove RCT with >15mm lesion (a people in Basket prove had stent >3mm diameter); data for these outcomes was not reported for the subgroup and the results for the overall population are presented here.

(d) Economic analysis was a model. The all revascularisation data is what is reported as the model inputs; the TVR RR was used to estimate the all revasc effect by combining with real world data about repeat revascularisations. The first figures were what were calculated for the basecase initially; the second figures were the agreed best estimates following TA committee discussion.

(e) Economic analysis was a model; data here is as reported in the paper

1.6.4 Health economic modelling

This area was not prioritised for new cost-effectiveness analysis.

1.6.5 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 10 shows coronary stent costs from the NHS Supply Chain and local hospital estimates. Data about the usage of different types of drug eluting stents in the NHS was obtained the British Cardiovascular Intervention Society (BCIS) from 1st April 2017 to 31st March 2018 for people undergoing PCI for ACS. This was to inform calculation of a weighted average to reflect what types of stents are often used in practice. Data was not available on the different types of bare metal stents that are used in the NHS. In addition, committee members highlighted that their local costs were considerably lower than those in the NHS supply chain catalogue. As a result, average local costs and average NHS supply chain costs are provided based on weighted averages for drug-eluting stents.

Table 10: UK unit costs of coronary stents: local costs and equivalent NHS supply chain costs

	Using local costs	Using NHS supply chain costs 1[(a)]	Using NHS supply chain costs 2[(b)]
Average DES cost (weighted by stent type usage)	£250[(c)]	£348	£380
Typical BMS cost[(d)]	£75	£87	£87
Difference	£175	£261	£293

Source: Stent type usage from BCIS audit for 1st April 2017 to 31st March 2018 on people undergoing PCI for ACS; local stent costs provided by committee members; NHS Supply Chain 2018[82]

(a) Where there were two costs listed for one stent in the NHS Supply Chain Catalogue, this estimate uses the lower cost that was listed.

(b) Where there were two costs listed for one stent in the NHS Supply Chain Catalogue, this estimate uses the higher cost that was listed.

(c) Two types of drug-eluting stents did not have local costs available therefore the cost listed in the NHS supply chain catalogue was used. These two types of stents had low usage and it is not thought to impact estimates significantly.

(d) Audit data does not report a breakdown of bare metal stent use as their use is low. Therefore, the cost of bare metal stents was based on the cost of the Integrity bare metal stent which was the last available BMS at one of the committee member's local hospital. Please note that this was the cheapest BMS listed on the NHS Supply Chain catalogue and therefore estimates are considered conservative towards drug-eluting stents.

1.7 Evidence statements

1.7.1 Clinical evidence statements

- There was a clinically important benefit of drug eluting stents (DES) compared to bare metal stents (BMS) for all-cause mortality at 1 year (14049 participants in 22 studies, moderate quality evidence) and at 1-3 years (12999 participants in 12 studies, low quality evidence)

- There was a clinically important benefit of DES compared to BMS for cardiac mortality at 1 year (12117 participants in 14 studies, moderate quality evidence) and at 1-3 years (12416 participants in 10 studies, low quality evidence)

- There was a clinically important benefit of DES compared to BMS for target vessel failure up to 1 year (2041 participants in 4 studies, very low quality evidence) and at 1-3 years (703 participants in 3 studies, moderate quality evidence)

- There was a clinically important benefit of DES compared to BMS for target vessel revascularisation up to 1 year (12858 participants in 18 studies, moderate quality evidence) and at 1-3 years (15141 participants in 3 studies, moderate quality evidence)

- There was no clinically important difference of DES compared to BMS for definite or probable stent thrombosis up to 1 year (11405 participants in 12 studies, low quality evidence) and at 1-3 years (14390 participants in 12 studies, low quality evidence)

- There was a clinically important benefit of DES compared to BMS for myocardial infarction (MI) up to 1 year (10780 participants in 20 studies, moderate quality evidence) and at 1-3 years (9456 participants in 10 studies, low quality evidence)

- At 1 year, there was no clinically important difference of DES compared to BMS for bleeding (unspecified, 1467 participants in 2 studies, very low quality evidence), major bleeding (7395 participants in 6 studies, low quality evidence), minor bleeding (6595 participants in 5 studies, low quality evidence).

- There was no clinically important difference of DES compared to BMS for major bleeding (5104 participants in 2 studies, very low quality evidence) or for minor bleeding (2314 participants in 1 study, very low quality evidence) at 1-3 years.

- At 1 year, there was no clinically important difference of DES compared to BMS for in segment minimal luminal diameter (MLD; 346 participants in 2 studies, moderate quality evidence), for in stent MLD (1103 participants in 5 studies, moderate quality evidence), in lesion MLD (695 participants in 2 studies, low quality evidence), MLD proximal edge (37 participants in 1 study, low quality evidence), MLD distal edge (40 participants in 1 study, very low quality evidence) and MLD unspecified (5273 participants in 7 studies, very low quality evidence).

1.7.2 Health economic evidence statements

- One cost-utility analysis found that in people with STEMI undergoing PCI bare metal stents was dominant (less costly and more effective) compared to drug-eluting stents. This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that in people with ACS undergoing PCI drug-eluting stents was not cost effective compared to bare metal stents (ICER: £244,400 - £376,100 per QALY gained). This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that in people with STEMI undergoing PCI drug-eluting stents was cost effective compared to bare metal stents (ICER: £4,180 per QALY gained. This analysis was assessed as partially applicable with potentially serious limitations.
- One cost effectiveness analysis found that in people with STEMI, NSTEMI, unstable or stable angina undergoing PCI drug eluting stents was dominant (less costly and more effective) compared to bare metal stents. This analysis was assessed as partially applicable with potentially serious limitations.
- One cost-utility analysis found that in people with stable coronary artery disease or ACS undergoing PCI with at least one stent with a diameter ≥3mm and ≤15 mm lesion, drug eluting stents was cost effective compared to bare metal stents (ICER: £15,105 per QALY

gained). This analysis was assessed as partially applicable with potentially serious limitations.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

1.8.1.1 The outcomes that matter most

The committee agreed that the following outcomes were critical for decision-making: all-cause mortality, cardiac mortality, target vessel failure, target lesion revascularisation (TLR), target vessel revascularisation (TVR), stent thrombosis, myocardial infarction and health-related quality of life. In the analyses, TLR outcome data was combined with TVR outcome data as the committee noted that by definition TVR encompasses TLR. The committee acknowledged that outcomes such as TLR and TVR were surrogate indicators of clinical effectiveness, but felt that they represent an important sense check for the clinical outcome measures.

The committee also agreed that the outcomes major bleeding, minor bleeding and minimal lumen diameter, were important for decision-making.

Outcome data was meta-analysed according to the pre-specified time-points agreed by the committee. These were 'early' (before one year or at one year) and 'late' (more than one year, until 3 years) reporting of the outcomes of interest.

Outcome data was identified for the majority of the outcomes. There was outcome data for all of the important and critical outcomes, except for health-related quality of life (a critical outcome).

1.8.1.2 The quality of the evidence

Twenty-nine randomised controlled trials were included in this review. One relevant Cochrane review was identified for this evidence review. The search strategy and search dates were updated. Papers included in the Cochrane review were assessed and included if they satisfied the PICO criteria for this review.

Overall, the evidence was graded from very low to moderate quality. There was serious risk of bias for a majority of the outcomes due to inadequate information reported in the studies about the process of randomisation. There were also concerns about the presence of imprecision for a majority of the evidence that was graded as very low or low quality.

There are many different types of DES containing a variety of pharmacological agents and polymer coatings. The committee elected to consider these as a single class as this would otherwise involve assessment of highly fragmented data. Differences in effectiveness between the various agents/stents cannot be excluded by this review, but the committee believe that any such variation would be small.

1.8.1.3 Benefits and harms

The evidence suggested benefits of using drug-eluting stents (DES) in terms of all-cause mortality, cardiac mortality, myocardial infarction, target vessel failure, target vessel revascularisation and MI up to 1 year and 1-3 years. However, the committee noted uncertainty in the evidence for several of these outcomes including those for all-cause and cardiac mortality, and this uncertainty was taken into account during decision-making. The data for bleeding risk, both major and minor, showed no difference between drug-eluting and bare metal stents.

The committee had not anticipated seeing any major difference in mortality, and although there was no definitive evidence of a mortality benefit some members felt there was a signal favouring DES in terms of mortality in the longer term.

The committee agreed there was no evidence of harm with DES and evidence of benefit, albeit with less certainty for some outcomes than others. They also noted the cost-effectiveness data described below and recommended the use of DES in people with acute STEMI undergoing revascularisation by primary PCI and people with unstable angina and NSTEMI undergoing revascularisation by PCI.

1.8.2 Cost effectiveness and resource use

Five economic evaluations were included for this review. These weren't consistent in their conclusions regarding the cost-effectiveness of DES compared to BMS in people with ACS but they also varied in terms of their methods. The committee considered the methods in detail in the context of the clinical review above in order to come to a conclusion regarding the cost effectiveness of DES compared to BMS.

The analysis that informed NICE technology appraisal 152 which this review is partially updating found that DES were not cost-effective for non-elective patients overall (which was assumed to equate to ACS). Drug-eluting stents were found to be cost effective under some limited circumstances where cost differences between DES and BMS were reduced to £300 and the risk of revascularisation was high. The committee highlighted that DES have evolved since the time of this analysis and much more evidence is available now about the benefits of DES than at the time of the technology appraisal. The analysis only included treatment effects of target-vessel revascularisation whereas the clinical review found other effects, such as a reduction in MI and potentially a mortality benefit. The clinical review also found evidence of effects beyond 1 year but this analysis only employed a 1 year time horizon. The committee agreed that both these things may mean that health effects have not been fully captured. It was noted that the treatment effect for target-vessel revascularisation applied in this analysis was greater than that estimated in the clinical review for this update; however the longer term treatment effects and effects on other outcomes could outweigh this. The cost of DES has considerably reduced since the publication of this technology appraisal, which used costs ranging from £997 to £1,045 and a difference with BMS of around £700. Our estimates of current average costs for DES ranged from £250 to £380, with a difference of £170 to £300. It was agreed it was therefore likely that this analysis would under estimate the benefits of DES as understood from the current clinical evidence base and may overestimate the costs.

One other included analysis also suggested DES might not be cost effective for people with STEMI. This was based on an analysis of patient-level data from the TYPHOON RCT that was included in the clinical evidence review. In this analysis DES had higher costs and slightly lower QALYs. However, it was noted that the QALY loss with DES in this study appeared potentially inconsistent with the key clinical endpoints from the TYPHOON trial which suggested that DES had lower mortality, target-vessel revascularisation and stent thrombosis and it was unclear what was driving the slight QALY loss. In addition, methods appear to indicate that other cardiac and non-cardiac adverse events were also incorporated in the analysis and the committee agreed that many of these would not be related to the choice of stent and it was unclear if this was appropriate and how inclusion of these events were effecting QALYs. As noted above, the clinical review found evidence of effects beyond 1 year, and this analysis only employed a 1 year time horizon, which means health effects such as mortality may not have been fully captured. Given these issues the committee were concerned the conclusions of this analysis were not reliable.

The remaining 3 included analyses suggested that DES are cost effective compared to BMS.

A model comparing two types of DES (paclitaxel and sirolimus stents) with each other and with BMS in people with ACS or stable angina undergoing PCI found DES dominated BMS with lower costs and an increase in life years. This analysis from a 2008 Norwegian perspective incorporated revascularisation, MI and mortality, used a lifetime horizon and applied treatment effects for 5 years. This was deemed appropriate by the committee as the clinical evidence review showed longer-term treatment effects and also a small mortality benefit, which indicates that people should be modelled over a lifetime to capture the difference in life years gained. Treatment effects were derived from a meta-analysis of 35 RCTs that included studies that were excluded from our clinical evidence review and it was somewhat difficult to assess the impact of this as the time points and outcomes used in the model did not exactly match those used in our review. However, relative treatment effects generally seemed similar or less favourable and the committee agreed that it didn't seem likely that the benefits were being overestimated. In addition the baseline risks were also derived from the overall coronary artery disease population and were lower than seen in the clinical evidence review which is also unlikely to favour DES. In addition, the cost difference was higher than the current UK estimates, with the difference ranging from £312 to £408 for the two types of DES. QALYs were not estimated but given the life years are higher with DES this was not considered likely to impact conclusions.

A study comparing DES with BMS in a subgroup of people with stable disease or ACS undergoing PCI with at least one stent with a diameter >3mm and ≤15 mm lesion at baseline from the BASKET-PROVE RCT found that DES were cost-effective with an ICER of £15,105 per QALY gained. The within-trial analysis from a 2013 Swiss perspective used EQ-5D data collected over a 2 year follow-up period to estimate QALY gains. It was noted that QALY gains were quite small in this study. One limitation was that the analysis included people with stable disease and did not report the proportion that was ACS, however the BASKET-PROVE RCT reported that 64% had an ACS. Also, the time horizon of 2 years may not fully capture differences in costs and health outcomes, as the clinical evidence review showed differences in effects at 3 years. It was also unclear if survival was incorporated when calculating QALYs. One benefit was that this analysis showed that DES were cost-effective in a lower risk group, a group of people that the previous TA excluded from their recommendation. Therefore, this may indicate that DES are more cost-effective for a wider population. The difference in costs between DES and BMS was quite low, at £151. This is slightly less than current UK estimates.

An analysis based on the EXAMINATION RCT which was included in the clinical review also found that DES were cost effective in people with STEMI with an ICER of £4,180 per QALY gained. This analysis took a 2016 Spanish perspective and used 5-year patient level data from the RCT and a modelled extrapolation to a lifetime perspective. It incorporated mortality, MI, stent thrombosis and revascularisation. The committee noted that the NICE technology appraisal assumed a 1 month reduction in quality of life after having PCI, whereas this Spanish analysis applied a 1 year reduction. The committee noted that it is hard to determine how long quality of life would be impacted, however they agreed that the impact would be closer to 1 year and that 1 month was likely to be too short. The committee agreed that the QALY loss applied for 1 year for having repeat MI or stent thrombosis was appropriate. The committee noted that relative treatment effects in EXAMINATION trial were similar to those seen in our clinical review and the study was conducted in three European countries similar to the UK. It was agreed that this analysis was the most applicable and had the least methodological limitations of all the included analyses. They highlighted that the EXAMINATION trial had a broad inclusion criterion to ensure it was an all-comers population and so baseline risk and treatment effects were likely to most accurately reflect the real world. The committee agreed it was likely to be reasonable to generalise the conclusions from this analysis to the UA/NSTEMI population undergoing PCI.

In summary, although NICE technology appraisal 152 only found DES to be cost-effective under certain circumstances, newer analyses that incorporated other treatment effects and adopted longer time horizon generally found DES to be cost-effective. The committee

concluded that there was sufficient evidence that DES are cost effective to support a recommendation for use of DES in people with ACS.

The committee noted that the use of DES is common practice. Audit data obtained from BCIS showed that from April 2017 to March 2018 91% of all PCIs used a stent during the procedure. Of these procedures that used stents, 97% used DES. Therefore, the committee concluded that a recommendation for DES would not be a change in practice and would not result in a substantial resource impact to the NHS in the England.

1.8.3 Other factors the committee took into account

The committee noted that design of DES has changed, and by implication improved, since they were first introduced whereas bare-metal stents have not changed appreciably. Some of the studies considered in this review used older versions of DES and it was therefore considered that the benefits of currently used DES might be greater than indicated by the results presented here.

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126. Valgimigli M, Tebaldi M, Borghesi M, Vranckx P, Campo G, Tumscitz C et al. Two-year outcomes after first- or second-generation drug-eluting or bare-metal stent implantation in all-comer patients undergoing percutaneous coronary intervention: A pre-specified analysis from the PRODIGY study (PROlonging Dual Antiplatelet Treatment After Grading stent-induced Intimal hyperplasia studY). JACC: Cardiovascular Interventions. 2014; 7(1):20-8

127. Van den Branden BJ, Rahel BM, Laarman GJ, Slagboom T, Kelder JC, Ten Berg JM et al. Five-year clinical outcome after primary stenting of totally occluded native coronary arteries: A randomised comparison of bare metal stent implantation with sirolimus-eluting stent implantation for the treatment of total coronary occlusions (PRISON II study). EuroIntervention. 2012; 7(10):1189-96

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129. van Hout BA, Serruys PW, Lemos PA, van den Brand MJ, van Es G, Lindeboom WK et al. One year cost effectiveness of sirolimus eluting stents compared with bare metal stents in the treatment of single native de novo coronary lesions: An analysis from the RAVEL trial. Heart. 2005; 91(4):507-512

130. Vink MA, Dirksen MT, Suttorp MJ, Tijssen JG, van Etten J, Patterson MS et al. 5-year follow-up after primary percutaneous coronary intervention with a paclitaxel-eluting stent versus a bare-metal stent in acute ST-segment elevation myocardial infarction: A follow-up study of the PASSION (Paclitaxel-Eluting Versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation) trial. JACC: Cardiovascular Interventions. 2011; 4(1):24-9

131. Violini R, Musto C, De Felice F, Nazzaro MS, Cifarelli A, Petitti T et al. Maintenance of long-term clinical benefit with sirolimus-eluting stents in patients with ST-segment elevation myocardial infarction 3-year results of the SESAMI (sirolimus-eluting stent versus bare-metal stent in acute myocardial infarction) trial. Journal of the American College of Cardiology. 2010; 55(8):810-4

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133. Wijnbergen I, Helmes H, Tijssen J, Brueren G, Peels K, van Dantzig JM et al. Comparison of drug-eluting and bare-metal stents for primary percutaneous coronary intervention with or without abciximab in ST-segment elevation myocardial infarction: DEBATER: The Eindhoven reperfusion study. JACC: Cardiovascular Interventions. 2012; 5(3):313-22

134. Wijnbergen I, Tijssen J, Brueren G, Peels K, van Dantzig JM, Veer MV et al. Long-term comparison of sirolimus-eluting and bare-metal stents in ST-segment elevation myocardial infarction. Coronary Artery Disease. 2014; 25(5):378-83

135. Wisloff T, Atar D, Sonbo Kristiansen I. Cost effectiveness of drug-eluting stents as compared with bare metal stents in patients with coronary artery disease. American Journal of Therapeutics. 2013; 20(6):596-601

136. Witzenbichler B, Wohrle J, Guagliumi G, Peruga JZ, Brodie BR, Dudek D et al. Paclitaxel-eluting stents compared with bare metal stents in diabetic patients with acute myocardial infarction: the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial. Circulation: Cardiovascular Interventions. 2011; 4(2):130-8

137. Zbinden R, von Felten S, Wein B, Tueller D, Kurz DJ, Reho I et al. Impact of stent diameter and length on in-stent restenosis after DES vs BMS implantation in patients needing large coronary stents-A clinical and health-economic evaluation. Cardiovascular Therapeutics. 2017; 35(1):19-25

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Appendices

Appendix A: Review protocols

Table 11: Review protocol: Clinical and cost-effectiveness of drug-eluting stents

ID	Field	Content
I	Review question	5.1 What is the clinical and cost effectiveness of drug-eluting stents in adults with acute coronary syndromes, including those with unstable angina or NSTEMI undergoing percutaneous coronary intervention and those with STEMI undergoing primary percutaneous coronary intervention?
II	Type of review question	Intervention A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
III	Objective of the review	To determine the comparative effectiveness of bare metal stents and drug eluting stents. Rationale for including this question: CG167 does not make any recommendations on the use of PPCI using drug-eluting stents in patients with STEMI. It refers to the general recommendation in TA 152 (see section XIV below). New evidence on the efficacy and safety of drug eluting stents has been identified and warrants a review as it may provide enough evidence to make a recommendation. It would also be useful to extrapolate this question to the UA/NSTEMI population
IV	Eligibility criteria – population / disease / condition / issue / domain	Patients with UA/NSTEMI and those with STEMI intended for treatment with a stent Include PCI for various indications only if reports populations separately Populations: Can include global ACS population and can include papers specifically looking at NSTEMI and STEMI, - pathophysiology is the same and the long term mechanistic results shouldn't be different. Main benefit is a reduction in repeat revascularisation For studies including stable and unstable disease, include only if majority is ACS - >50% - For studies that have stable and ACS and have reported ACS separately use ACS data only
V	Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Drug eluting stents including: • Sirolimus • Everolimus • Paclitaxel • Rapamycin • Paclitaxel & Cilostazol

		• Ridaforolimus • Novolimus • Zotarolimus Include stents with or without bioabsorbable poylmers Not comparing DES to DES and BMS to BMS
VI	Eligibility criteria – comparator(s) / control or reference (gold) standard	Bare metal stents including: • Cobalt Chronium • Platinium Chronium • Stainless Steel
VII	Outcomes and prioritisation	**CRITICAL** Time points: early ≤1 and later >1-3 year • All-cause mortality • Cardiac mortality • TVF- target vessel failure • TLR and TVR – target lesion and target vessel revascularisation • Stent thrombosis(definite and/or probable) (record if assessed using optical coherence tomography (OCT), Intravascular ultrasound (IVUS) or angio) • Myocardial infarction • Health-related quality of life including EQ5D and SF-36. All data for the stated quality of life measures will be collected. Only overall scores will be reported for meta-analysis and GRADE. **IMPORTANT** • Bleeding- Where possible, bleeding outcomes will be categorised into: o Major bleeding (including BARC 3-5 and as reported by author) o Minor bleeding (including BARC 2, TIMI and as reported by author). • The following hierarchy of bleeding scales will be used: o BARC o Author's definition o TIMI o GUSTO • MLD - Minimal lumen diameter (measuring how much restenosis there is)- surrogate marker for TLR and TVR
VIII	Eligibility criteria – study design	• Randomised Controlled Trials (RCT) • Systematic Reviews (SR) of RCTs
IX	Other inclusion exclusion criteria	• Exclude endothelial progenitor cell (EPC) capture • Bioabsorbable scaffolds – these are not stents – include DES with bioabsorbable polymer but exclude any that are re-absorbed
X	Proposed sensitivity /	If there is heterogeneity (P-value is <0.1 or I^2 is >50%), the following subgroups will be investigated:

	subgroup analysis, or meta-regression	• diameter and number of stents if possible (length and width)- > = 3mm width and length 15 • STEMI and NSTEMI • duration of antiplatelet therapy • differential usage of antiplatelet therapy • renal disease/renal insufficiency • older patients (>75) • Diabetes • Mixed Stable and ACS • restenosis A statement will be included about subgroup analyses that have been conducted. However, only those analyses that explain heterogeneity will be reported.
XI	Selection process – duplicate screening / selection / analysis	Studies will be sifted by title and abstract. Potentially relevant publications obtained in full text and assessed against the inclusion criteria specified in this protocol. A sample of a minimum of 10% of the abstract lists will be double-sifted by a senior research fellow and any discrepancies discussed and rectified.
XII	Data management (software)	• EndNote will be used for reference management, sifting, citations and bibliographies. • EviBASE will be used for data extraction and quality assessment for clinical studies. • MS Excel will be used for data extraction and critical appraisal for health economic studies. • Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). • GRADEpro will be used to assess the quality of evidence for each outcome.
XIII	Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library Language: Restrict to English only Supplementary search techniques: backward citation searching
XIV	Identify if an update	This question is an update of TA 152 Recommendation in TA 152 states the following: Drug-eluting stents are recommended for use in percutaneous coronary intervention for the treatment of coronary artery disease, within their instructions for use, only if: • the target artery to be treated has less than a 3-mm calibre or the lesion is longer than 15 mm, and • the price difference between drug-eluting stents and bare-metal stents is no more than £300.
XV	Author contacts	ACS@nice.org.uk
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
XVII	Search	For details please see appendix B

	strategy – for one database	
XVIII	Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix/ces [X] of the evidence report.
XIX	Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
XX	Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ [Please document any deviations/alternative approach when GRADE isn't used or if a modified GRADE approach has been used for non-intervention or non-comparative studies.]
XXI	Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
XXII	Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. [Consider exploring publication bias for review questions where it may be more common, such as pharmacological questions, certain disease areas, etc. Describe any steps taken to mitigate publication bias, such as examining trial registries.]
XXIV	Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
XXV	Rationale / context – what is known	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee [www.nice.org.uk/guidance/ng185/history] developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Margaret Lally in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
XXVII	Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
XXVIII	Name of	NGC is funded by NICE and hosted by the Royal College of

	sponsor	Physicians.
XXIX	Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
XXX	PROSPERO registration number	Not registered

Table 12: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2003, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published after 2003 that were included in the previous guidelines will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[80] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS

	setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2003 or later (including any such studies included in the previous guideline(s)) but that depend on unit costs and resource data entirely or predominantly from before 2003 will be rated as 'Not applicable'. • Studies published before 2003 (including any such studies included in the previous guidelines) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. • The following will be rated as 'Very serious limitations' and excluded: economic analyses undertaken as part of clinical studies that are excluded from the clinical review; economic models where relative treatment effects are based entirely on studies that are excluded from the clinical review.

Appendix B: Literature search strategies

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[80]

For more information, please see the Methods report published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 13: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 24 June 2019	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 24 June 2019	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2019 Issue 6 of 12 CENTRAL to 2019 Issue 6 of 12	None

Medline (Ovid) search terms

1.	Acute Coronary Syndrome/ or Angina Pectoris/ or Angina, Unstable/ or Coronary Thrombosis/ or exp Myocardial Infarction/
2.	Heart Arrest/
3.	(acute coronary adj2 syndrome*).ti,ab.
4.	((myocardial or heart) adj infarct*).ti,ab.
5.	(heart adj (attack* or event*)).ti,ab.
6.	((heart or cardiac) adj arrest*).ti,ab.
7.	(coronary adj2 thrombos*).ti,ab.
8.	(stemi or st-segment or st segment or st-elevation or st elevation).ti,ab.
9.	"non-ST-segment elevation".ti,ab.
10.	(non-STEMI or NSTEMI or nonSTEMI).ti,ab.
11.	"Q wave myocardial infarction".ti,ab.
12.	"non Q wave MI".ti,ab.
13.	(NSTE-ACS or STE-ACS).ti,ab.
14.	(subendocardial adj3 infarct*).ti,ab.
15.	((unstable or variant) adj2 angina*).ti,ab.
16.	(unstable adj2 coronary).ti,ab.
17.	or/1-16
18.	letter/
19.	editorial/
20.	news/
21.	exp historical article/
22.	Anecdotes as Topic/
23.	comment/
24.	case report/

25.	(letter or comment*).ti.
26.	or/18-25
27.	randomized controlled trial/ or random*.ti,ab.
28.	26 not 27
29.	animals/ not humans/
30.	exp Animals, Laboratory/
31.	exp Animal Experimentation/
32.	exp Models, Animal/
33.	exp Rodentia/
34.	(rat or rats or mouse or mice).ti.
35.	or/28-34
36.	17 not 35
37.	limit 36 to English language
38.	randomized controlled trial.pt.
39.	controlled clinical trial.pt.
40.	randomi#ed.ti,ab.
41.	placebo.ab.
42.	randomly.ti,ab.
43.	Clinical Trials as topic.sh.
44.	trial.ti.
45.	or/38-44
46.	Meta-Analysis/
47.	exp Meta-Analysis as Topic/
48.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
49.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
50.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
51.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
52.	(search* adj4 literature).ab.
53.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
54.	cochrane.jw.
55.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
56.	or/46-55
57.	Percutaneous Coronary Intervention/
58.	Percutaneous coronary intervention*.ti,ab.
59.	(PPCI or PCI).ti,ab.
60.	Percutaneous Transluminal Coronary Angioplasty.ti,ab.
61.	PTCA.ti,ab.
62.	Angioplasty, Balloon, Coronary/
63.	exp Angioplasty/
64.	(Balloon adj3 coronary).ti,ab.
65.	((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
66.	Coronary artery dilat*.ti,ab.
67.	or/57-66

68.	exp *Stents/
69.	drug eluting stent*.ti,ab.
70.	(eluting adj3 stent*).ti,ab.
71.	((paclitaxel or sirolimus or everolimus or biolimus or ridaforolimus or zotarolimus or novolimus) adj3 stent*).ti,ab.
72.	or/68-71
73.	37 and 67 and 72
74.	73 and (45 or 56)

Embase (Ovid) search terms

1.	acute coronary syndrome/ or angina pectoris/ or unstable angina pectoris/ or coronary artery thrombosis/ or exp heart infarction/
2.	heart arrest/
3.	(acute coronary adj2 syndrome*).ti,ab.
4.	((myocardial or heart) adj infarct*).ti,ab.
5.	(heart adj (attack* or event*)).ti,ab.
6.	((heart or cardiac) adj arrest*).ti,ab.
7.	(coronary adj2 thrombos*).ti,ab.
8.	(stemi or st-segment or st segment or st-elevation or st elevation).ti,ab.
9.	"non-ST-segment elevation".ti,ab.
10.	(non-STEMI or NSTEMI or nonSTEMI).ti,ab.
11.	"Q wave myocardial infarction".ti,ab.
12.	"non Q wave MI".ti,ab.
13.	(NSTE-ACS or STE-ACS).ti,ab.
14.	(subendocardial adj3 infarct*).ti,ab.
15.	((unstable or variant) adj2 angina*).ti,ab.
16.	(unstable adj2 coronary).ti,ab.
17.	or/1-16
18.	letter.pt. or letter/
19.	note.pt.
20.	editorial.pt.
21.	Case report/ or Case study/
22.	(letter or comment*).ti.
23.	or/18-22
24.	randomized controlled trial/ or random*.ti,ab.
25.	23 not 24
26.	animal/ not human/
27.	Nonhuman/
28.	exp Animal Experiment/
29.	exp Experimental animal/
30.	Animal model/
31.	exp Rodent/
32.	(rat or rats or mouse or mice).ti.
33.	or/25-32
34.	17 not 33
35.	limit 34 to English language

36.	random*.ti,ab.
37.	factorial*.ti,ab.
38.	(crossover* or cross over*).ti,ab.
39.	((doubl* or singl*) adj blind*).ti,ab.
40.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
41.	crossover procedure/
42.	single blind procedure/
43.	randomized controlled trial/
44.	double blind procedure/
45.	or/36-44
46.	systematic review/
47.	meta-analysis/
48.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
49.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
50.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
51.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
52.	(search* adj4 literature).ab.
53.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
54.	((pool* or combined) adj2 (data or trials or studies or results)).ab.
55.	cochrane.jw.
56.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
57.	or/46-56
58.	transluminal coronary angioplasty/ or percutaneous coronary intervention/
59.	Percutaneous coronary intervention*.ti,ab.
60.	(PPCI or PCI).ti,ab.
61.	Percutaneous Transluminal Coronary Angioplasty.ti,ab.
62.	PTCA.ti,ab.
63.	transluminal coronary angioplasty/ or percutaneous transluminal angioplasty/ or angioplasty/ or percutaneous transluminal angioplasty balloon/
64.	(Balloon adj3 coronary).ti,ab.
65.	((primary or coronary or transluminal or balloon) adj3 angioplasty).ti,ab.
66.	Coronary artery dilat*.ti,ab.
67.	or/58-66
68.	*stent/ or exp *cardiovascular stent/ or exp *drug eluting stent/ or exp *metal stent/
69.	drug eluting stent*.ti,ab.
70.	(eluting adj3 stent*).ti,ab.
71.	((paclitaxel or sirolimus or everolimus or biolimus or ridaforolimus or zotarolimus or novolimus) adj3 stent*).ti,ab.
72.	or/68-71
73.	35 and 67 and 72
74.	73 and (45 or 57)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Acute Coronary Syndrome] this term only

#2.	MeSH descriptor: [Angina Pectoris] this term only
#3.	MeSH descriptor: [Angina, Unstable] this term only
#4.	MeSH descriptor: [Coronary Thrombosis] this term only
#5.	MeSH descriptor: [Myocardial Infarction] explode all trees
#6.	(or #1-#5)
#7.	MeSH descriptor: [Heart Arrest] this term only
#8.	(acute coronary near/2 syndrome*):ti,ab
#9.	((myocardial or heart) next infarct*):ti,ab
#10.	(heart next (attack* or event*)):ti,ab
#11.	((heart or cardiac) next arrest*):ti,ab
#12.	(coronary near/2 thrombos*):ti,ab
#13.	(stemi or st-segment or st segment or st-elevation or st elevation):ti,ab
#14.	non-ST-segment elevation:ti,ab
#15.	(non-STEMI or NSTEMI or nonSTEMI):ti,ab
#16.	Q wave myocardial infarction:ti,ab
#17.	non Q wave MI:ti,ab
#18.	NSTE-ACS:ti,ab
#19.	(subendocardial near/3 infarct*):ti,ab
#20.	((unstable or variant) near/2 angina*):ti,ab
#21.	(unstable near/2 coronary):ti,ab
#22.	(or #6-#21)
#23.	MeSH descriptor: [Percutaneous Coronary Intervention] explode all trees
#24.	Percutaneous coronary intervention*:ti,ab
#25.	(PPCI or PCI):ti,ab
#26.	MeSH descriptor: [Angioplasty, Balloon, Coronary] explode all trees
#27.	Percutaneous Transluminal Coronary Angioplasty:ti,ab
#28.	PTCA:ti,ab
#29.	MeSH descriptor: [Angioplasty] explode all trees
#30.	(Balloon near/3 coronary):ti,ab
#31.	((primary or coronary or transluminal or balloon) near/3 angioplasty):ti,ab
#32.	Coronary artery dilat*:ti,ab
#33.	(or #23-#32)
#34.	MeSH descriptor: [Stents] explode all trees
#35.	(drug next eluting next stent*):ti,ab
#36.	(eluting near/3 stent*):ti,ab
#37.	((paclitaxel or sirolimus) near/3 stent*):ti,ab
#38.	(or #34-#37)
#39.	#22 and #33 and #38

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a search relating to acute coronary syndromes population combined with terms for interventions in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase using a filter for health economics studies.

Table 14: Database date parameters and filters used

base	s searched	ch filter used
ine	nuary 2014 – 18 June 2019	sions h economics studies
ase	nuary 2014 – 18 June 2019	sions h economics studies
e for Research and Dissemination (CRD)	- 2003 – 31 March 2018 EED - 2003 to 31 March 2015	

Medline (Ovid) search terms

1.	Acute Coronary Syndrome/ or Angina Pectoris/ or Angina, Unstable/ or Coronary Thrombosis/ or exp Myocardial Infarction/
2.	Heart Arrest/
3.	(acute coronary adj2 syndrome*).ti,ab.
4.	((myocardial or heart) adj infarct*).ti,ab.
5.	(heart adj (attack* or event*)).ti,ab.
6.	((heart or cardiac) adj arrest*).ti,ab.
7.	(coronary adj2 thrombos*).ti,ab.
8.	(stemi or st-segment or st segment or st-elevation or st elevation).ti,ab.
9.	"non-ST-segment elevation".ti,ab.
10.	(non-STEMI or NSTEMI or nonSTEMI).ti,ab.
11.	"Q wave myocardial infarction".ti,ab.
12.	"non Q wave MI".ti,ab.
13.	NSTE-ACS.ti,ab.
14.	(subendocardial adj3 infarct*).ti,ab.
15.	((unstable or variant) adj2 angina*).ti,ab.
16.	(unstable adj2 coronary).ti,ab.
17.	or/1-16
18.	letter/
19.	editorial/
20.	news/
21.	exp historical article/
22.	Anecdotes as Topic/
23.	comment/

24.	case report/
25.	(letter or comment*).ti.
26.	or/18-25
27.	randomized controlled trial/ or random*.ti,ab.
28.	26 not 27
29.	animals/ not humans/
30.	exp Animals, Laboratory/
31.	exp Animal Experimentation/
32.	exp Models, Animal/
33.	exp Rodentia/
34.	(rat or rats or mouse or mice).ti.
35.	or/28-34
36.	17 not 35
37.	limit 36 to English language
38.	Economics/
39.	Value of life/
40.	exp "Costs and Cost Analysis"/
41.	exp Economics, Hospital/
42.	exp Economics, Medical/
43.	Economics, Nursing/
44.	Economics, Pharmaceutical/
45.	exp "Fees and Charges"/
46.	exp Budgets/
47.	budget*.ti,ab.
48.	cost*.ti.
49.	(economic* or pharmaco?economic*).ti.
50.	(price* or pricing*).ti,ab.
51.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
52.	(financ* or fee or fees).ti,ab.
53.	(value adj2 (money or monetary)).ti,ab.
54.	or/38-53
55.	37 and 54
56.	*Angiography/
57.	Angiocardiography/
58.	Coronary Angiography/
59.	Angiograph*.ti.
60.	Arteriograph*.ti.
61.	Angiocardiograph*.ti,ab.
62.	Coronary Angiograph*.ti,ab.
63.	Angiogram*.ti,ab.
64.	Cardioangiograph*.ti,ab.

65.	Angiocardiogram.ti,ab.
66.	Angio Cardiograph*.ti,ab.
67.	Coronary Arteriogra*.ti,ab.
68.	Coronarograph*.ti,ab.
69.	*Myocardial Revascularization/
70.	Angioplasty, Balloon, Coronary/
71.	(Myocardial adj revasculari?ation).ti,ab.
72.	PCI.ti,ab.
73.	Percutaneous coronary intervention.ti,ab.
74.	Percutaneous Transluminal Coronary Angioplasty.ti,ab.
75.	PTCA.ti,ab.
76.	exp Angioplasty/
77.	Blunt microdissection.ti,ab.
78.	((laser or patch) adj angioplasty).ti,ab.
79.	Percutaneous Transluminal Angioplasty.ti,ab.
80.	Transluminal Coronary Angioplasty.ti,ab.
81.	(Balloon adj3 coronary).ti,ab.
82.	(Balloon adj3 angioplasty).ti,ab.
83.	exp STENTS/
84.	stent*.ti,ab.
85.	Or/56-84
86.	aspirin/
87.	(aspirin or acetylsalicylic acid).ti,ab.
88.	(clopidogrel or plavix).ti,ab.
89.	(ticagrelor or brilique).ti,ab.
90.	(prasugrel or efient or effient or prasita).ti,ab.
91.	Prasugrel Hydrochloride/
92.	platelet aggregation inhibitors/
93.	(Glycoproteins IIb-IIIa or GPIIb-IIIa Receptors or Integrin alpha-IIb beta-3 or Integrin alphaIIbbeta3 or GPIIB IIIA).ti,ab.
94.	exp Platelet Glycoprotein GPIIb-IIIa Complex/
95.	exp Receptors, Fibrinogen/
96.	(Abciximab or Reopro or Eptifibatide or Integrelin or Integrilin or Intrifiban or Tirofiban or Aggrastat).ti,ab.
97.	exp adrenergic beta-antagonists/
98.	(propranolol or angilol or inderal-la or half-inderal or inderal or bedranol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or esmolol or brevibloc or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or sotalol or beta-cardone or sotacor or timolol or betim).ti,ab.
99.	propranolol/ or acebutolol/ or atenolol/ or bisoprolol/ or celiprolol/ or labetalol/ or metoprolol/ or nadolol/ or nebivolol/ or oxprenolol/ or pindolol/ or sotalol/ or timolol/
100.	(beta adj3 block*).ti,ab.
101.	(b adj3 block*).ti,ab.
102.	(beta adj2 antagonist*).ti,ab.
103.	Antithrombins/

104.	Antithrombin*.ti,ab.
105.	(thrombin adj3 inhibitor*).ti,ab.
106.	Hirudins/
107.	Hirudin*.ti,ab.
108.	Hirulog.ti,ab.
109.	Bivalirudin.ti,ab.
110.	Or/86-109
111.	55 and (85 or 110)

Embase (Ovid) search terms

1.	acute coronary syndrome/ or angina pectoris/ or unstable angina pectoris/ or coronary artery thrombosis/ or exp heart infarction/
2.	heart arrest/
3.	(acute coronary adj2 syndrome*).ti,ab.
4.	((myocardial or heart) adj infarct*).ti,ab.
5.	(heart adj (attack* or event*)).ti,ab.
6.	((heart or cardiac) adj arrest*).ti,ab.
7.	(coronary adj2 thrombos*).ti,ab.
8.	(stemi or st-segment or st segment or st-elevation or st elevation).ti,ab.
9.	"non-ST-segment elevation".ti,ab.
10.	(non-STEMI or NSTEMI or nonSTEMI).ti,ab.
11.	"Q wave myocardial infarction".ti,ab.
12.	"non Q wave MI".ti,ab.
13.	NSTE-ACS.ti,ab.
14.	(subendocardial adj3 infarct*).ti,ab.
15.	((unstable or variant) adj2 angina*).ti,ab.
16.	(unstable adj2 coronary).ti,ab.
17.	or/1-16
18.	letter.pt. or letter/
19.	note.pt.
20.	editorial.pt.
21.	Case report/ or Case study/
22.	(letter or comment*).ti.
23.	or/18-22
24.	randomized controlled trial/ or random*.ti,ab.
25.	23 not 24
26.	animal/ not human/
27.	Nonhuman/
28.	exp Animal Experiment/
29.	exp Experimental animal/
30.	Animal model/
31.	exp Rodent/

32.	(rat or rats or mouse or mice).ti.
33.	or/25-32
34.	17 not 33
35.	limit 34 to English language
36.	health economics/
37.	exp economic evaluation/
38.	exp health care cost/
39.	exp fee/
40.	budget/
41.	funding/
42.	budget*.ti,ab.
43.	cost*.ti.
44.	(economic* or pharmaco?economic*).ti.
45.	(price* or pricing*).ti,ab.
46.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
47.	(financ* or fee or fees).ti,ab.
48.	(value adj2 (money or monetary)).ti,ab.
49.	or/36-48
50.	35 and 49
51.	angiography/
52.	angiocardiography/
53.	coronary angiography/
54.	Angiograph*.ti.
55.	Arteriograph*.ti.
56.	Angiocardiograph*.ti,ab.
57.	Coronary Angiograph*.ti,ab.
58.	Angiogram*.ti,ab.
59.	Cardioangiograph*.ti,ab.
60.	Angiocardiogram.ti,ab.
61.	Angio Cardiograph*.ti,ab.
62.	Coronary Arteriogra*.ti,ab.
63.	Coronarograph*.ti,ab.
64.	*heart muscle revascularization/
65.	transluminal coronary angioplasty/
66.	(Myocardial adj revasculari?ation).ti,ab.
67.	PCI.ti,ab.
68.	Percutaneous coronary intervention.ti,ab.
69.	Percutaneous Transluminal Coronary Angioplasty.ti,ab.
70.	PTCA.ti,ab.
71.	*angioplasty/

72.	Blunt microdissection.ti,ab.
73.	((laser or patch) adj angioplasty).ti,ab.
74.	Percutaneous Transluminal Angioplasty.ti,ab.
75.	Transluminal Coronary Angioplasty.ti,ab.
76.	(Balloon adj3 coronary).ti,ab.
77.	(Balloon adj3 angioplasty).ti,ab.
78.	exp STENTS/
79.	stent*.ti,ab.
80.	Or/51-79
81.	acetylsalicylic acid/
82.	(aspirin or acetylsalicylic acid).ti,ab.
83.	(clopidogrel or plavix).ti,ab.
84.	(ticagrelor or brilique).ti,ab.
85.	(prasugrel or efient or effient or prasita).ti,ab.
86.	prasugrel/
87.	antithrombocytic agent/
88.	(Glycoproteins IIb-IIIa or GPIIb-IIIa Receptors or Integrin alpha-IIb beta-3 or Integrin alphaIIbbeta3 or GPIIB IIIA).ti,ab.
89.	exp fibrinogen receptor/
90.	(Abciximab or Reopro or Eptifibatide or Integrelin or Integrilin or Intrifiban or Tirofiban or Aggrastat).ti,ab.
91.	abciximab/ or eptifibatide/ or tirofiban/
92.	exp beta adrenergic receptor blocking agent/
93.	(propranolol or angilol or inderal-la or half-inderal or inderal or bedranol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or esmolol or brevibloc or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or sotalol or beta-cardone or sotacor or timolol or betim).ti,ab.
94.	propranolol/ or acebutolol/ or atenolol/ or bisoprolol/ or bisoprolol fumarate/ or carvedilol/ or celiprolol/ or esmolol/ or labetalol/ or metoprolol/ or nadolol/ or nebivolol/ or oxprenolol/ or pindolol/ or sotalol/ or timolol/ or timolol maleate/
95.	(beta adj3 block*).ti,ab.
96.	(b adj3 block*).ti,ab.
97.	(beta adj2 antagonist*).ti,ab.
98.	antithrombin/
99.	Antithrombin*.ti,ab.
100.	(thrombin adj3 inhibitor*).ti,ab.
101.	hirudin derivative/
102.	Hirudin*.ti,ab.
103.	Hirulog.ti,ab.
104.	Bivalirudin.ti,ab.
105.	Or/81-104

106.	50 and (80 or 105)

NHS EED and HTA (CRD) search terms

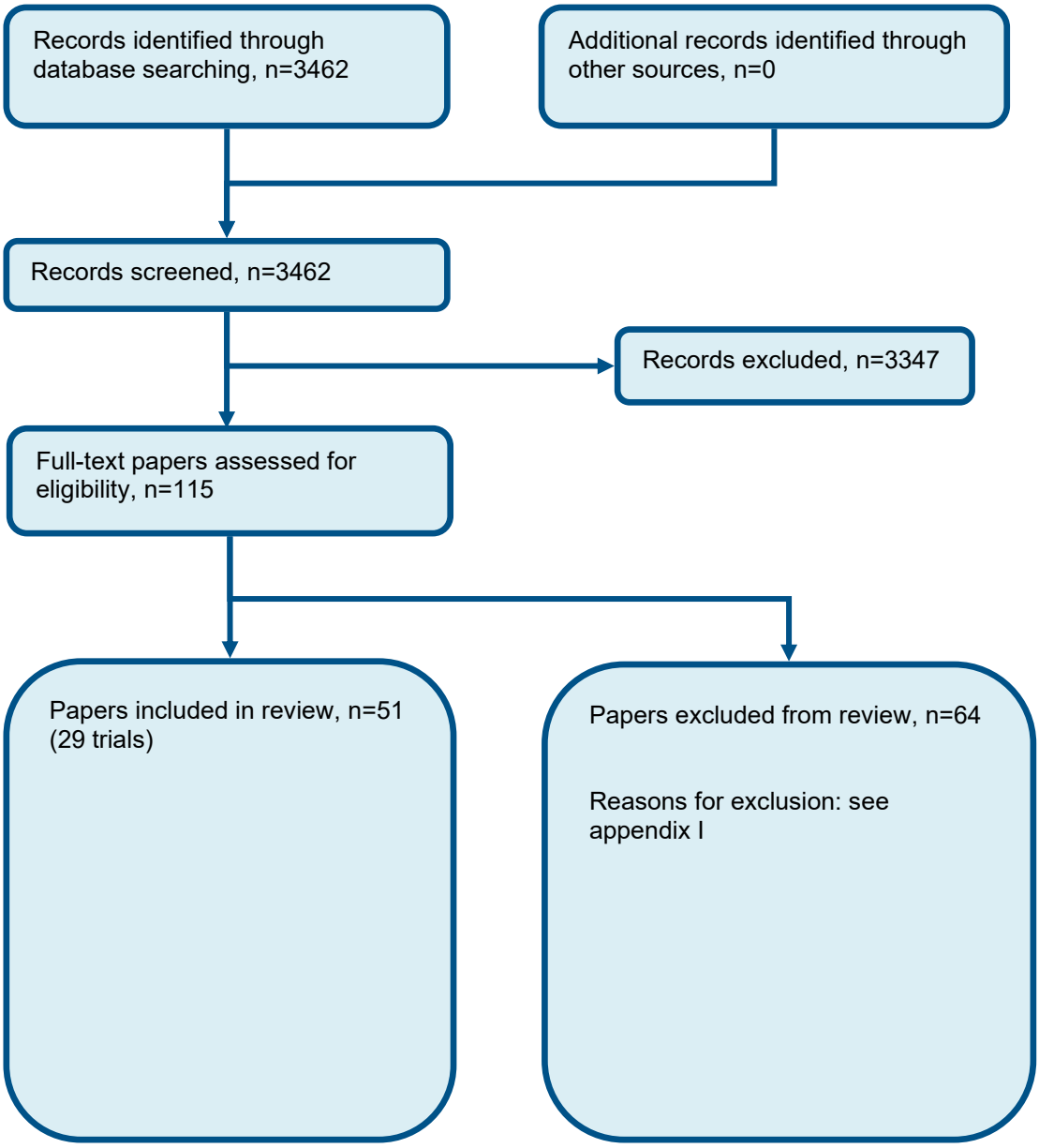
#1.	MeSH DESCRIPTOR Acute Coronary Syndrome
#2.	(MeSH DESCRIPTOR angina pectoris)
#3.	(MeSH DESCRIPTOR Angina, Unstable)
#4.	(MeSH DESCRIPTOR Coronary Thrombosis)
#5.	MeSH DESCRIPTOR Myocardial Infarction EXPLODE ALL TREES
#6.	#1 OR #2 OR #3 OR #4 OR #5
#7.	(MeSH DESCRIPTOR Heart Arrest)
#8.	((acute coronary adj2 syndrome*))
#9.	(((myocardial or heart) adj infarct*))
#10.	((heart adj (attack* or event*)))
#11.	(((heart or cardiac) adj arrest*))
#12.	((coronary adj2 thrombos*))
#13.	((stemi or st-segment or st segment or st-elevation or st elevation))
#14.	("non-ST-segment elevation")
#15.	((non-STEMI or NSTEMI or nonSTEMI))
#16.	("Q wave myocardial infarction")
#17.	("non Q wave MI")
#18.	(NSTE-ACS)
#19.	(STE-ACS)
#20.	(((subendocardial adj3 infarct*)))
#21.	(((((unstable or variant) adj2 angina*)))
#22.	(((unstable adj2 coronary)))
#23.	(#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22)
#24.	(MeSH DESCRIPTOR Angiography)
#25.	(MeSH DESCRIPTOR Angiocardiography)
#26.	((MeSH DESCRIPTOR Coronary Angiography))
#27.	((Angiograph*))
#28.	((Arteriograph*))
#29.	((Angiocardiograph*))
#30.	((Coronary Angiograph*))
#31.	((Angiogram*))
#32.	((Cardioangiograph*))
#33.	((Angiocardiogram))
#34.	((Angio Cardiograph*))
#35.	((Coronary Arteriogra*))
#36.	((Coronarograph*))
#37.	(MeSH DESCRIPTOR Myocardial Revascularization)
#38.	(MeSH DESCRIPTOR Angioplasty, Balloon, Coronary)
#39.	(((Myocardial adj revasculari?ation)))
#40.	((PCI))
#41.	((Percutaneous coronary intervention))
#42.	((Percutaneous Transluminal Coronary Angioplasty))

#43.	((PTCA))
#44.	(MeSH DESCRIPTOR Angioplasty EXPLODE ALL TREES)
#45.	((Blunt microdissection))
#46.	(((((laser or patch) adj angioplasty)))
#47.	((Percutaneous Transluminal Angioplasty))
#48.	((Transluminal Coronary Angioplasty))
#49.	(((Balloon adj3 coronary)))
#50.	((Balloon adj3 angioplasty))
#51.	(MeSH DESCRIPTOR Stents EXPLODE ALL TREES)
#52.	((stent*))
#53.	(#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52)
#54.	(MeSH DESCRIPTOR Aspirin)
#55.	((aspirin or acetylsalicylic acid))
#56.	((clopidogrel or plavix))
#57.	((ticagrelor or brilique))
#58.	((prasugrel or efient or effient or prasita))
#59.	MeSH DESCRIPTOR Prasugrel Hydrochloride
#60.	MeSH DESCRIPTOR Platelet Aggregation Inhibitors
#61.	((Glycoproteins IIb-IIIa or GPIIb-IIIa Receptors or Integrin alpha-IIb beta-3 or Integrin alphaIIbbeta3 or GPIIB IIIA))
#62.	MeSH DESCRIPTOR Platelet Glycoprotein GPIIb-IIIa Complex EXPLODE ALL TREES
#63.	MeSH DESCRIPTOR Receptors, Fibrinogen EXPLODE ALL TREES
#64.	((Abciximab or Reopro or Eptifibatide or Integrelin or Integrilin or Intrifiban or Tirofiban or Aggrastat))
#65.	MeSH DESCRIPTOR Adrenergic beta-Antagonists EXPLODE ALL TREES
#66.	((propranolol or angilol or inderal-la or half-inderal or inderal or bedranol or prograne or slo-pro or acebutolol or sectral or atenolol or tenormin or bisoprolol or cardicor or emcor or carvedilol or eucardic or celiprolol or celectol or co-tenidone or tenoret or tenoretic or esmolol or brevibloc or labetalol or trandate or metoprolol or betaloc or lopresor or nadolol or corgard or nebivolol or nebilet or hypoloc or oxprenolol or trasicor or slow-trasicor or pindolol or visken or sotalol or beta-cardone or sotacor or timolol or betim))
#67.	(MeSH DESCRIPTOR propranolol)
#68.	(MeSH DESCRIPTOR acebutolol)
#69.	(MeSH DESCRIPTOR atenolol)
#70.	(MeSH DESCRIPTOR bisoprolol)
#71.	(MeSH DESCRIPTOR celiprolol)
#72.	(MeSH DESCRIPTOR labetalol)
#73.	(MeSH DESCRIPTOR metoprolol)
#74.	(MeSH DESCRIPTOR nadolol)
#75.	(MeSH DESCRIPTOR nebivolol)
#76.	(MeSH DESCRIPTOR oxprenolol)
#77.	(MeSH DESCRIPTOR pindolol)
#78.	(MeSH DESCRIPTOR sotalol)
#79.	(MeSH DESCRIPTOR timolol)
#80.	((beta adj3 block*))

#81.	((b adj3 block*))
#82.	((beta adj2 antagonist*))
#83.	MeSH DESCRIPTOR Antithrombins
#84.	(Antithrombin*)
#85.	((thrombin adj3 inhibitor*))
#86.	MeSH DESCRIPTOR Hirudins
#87.	(Hirudin*)
#88.	(Hirulog)
#89.	(Bivalirudin)
#90.	#54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89
#91.	(#23 AND (#53 OR #90))

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of drug-eluting stents in adults with acute coronary syndromes, including those with unstable angina or NSTEMI undergoing percutaneous coronary intervention and those with STEMI undergoing primary percutaneous coronary intervention



Appendix D: Clinical evidence tables

Study	BASKET-PROVE I trial: Kaiser 2010[55]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=2314)
Countries and setting	Conducted in Austria, Botswana, Denmark, Italy, Switzerland
Line of therapy	Mixed line
Duration of study	Follow up (post intervention):
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who presented with chronic or acute coronary disease, who underwent angioplasty with stenting, and who required only stents that were 3.0 mm or more in diameter. No restrictions were placed on the number of treated lesions or vessels, the length of treated lesions, or the number of stents placed.
Exclusion criteria	Cardiogenic shock; in-stent restenosis or thrombosis of stents placed before the study; unprotected left main coronary artery (i.e. with no functioning bypass graft) or substantial stenosis in a bypass graft; plans for any surgery within 12 months; a need for oral anticoagulation, an increased risk of bleeding, or known intolerance to or suspected noncompliance with long-term antiplatelet therapy; or circumstances that would have made follow-up impossible. In addition, patients requiring stents larger than 4.0mm in diameter were excluded because no sirolimus eluting stents of this size were available
Age, gender and ethnicity	Age - Mean (SD): 66.3 (NS). Gender (M:F): 1749:565. Ethnicity: Not stated
Further population details	1. ACS population: Not stated / Unclear 2. Diabetes: Not stated / Unclear 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Extra comments	Stable angina 822 (35.5 %) Unstable angina 754 (32.5%)

Study	BASKET-PROVE I trial: Kaiser 2010[55]
	STEMI 738 (32%)
Indirectness of population	No indirectness
Interventions	(n=775) Intervention 1: Drug eluting stents - DES- Sirolimus. 3 armed trial. Participants randomised to first-generation SES . Duration 2 years. Concurrent medication/care: All participants were prescribed aspirin at a daily dose of 75 to 100 mg indefinitely and clopidogrel at a daily dose of 75 mg for 1 year, after a loading dose of 300 mg or 600 mg, regardless of stent type. Therapeutic agents for secondary prevention, such as statins, were prescribed according to current guidelines. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (number of stents per patient (SD): SES 1.6 (0.9), BMS 1.7 (1.1)). 2. Use of antiplatelet therapy: with antiplatelet therapy (clopidogrel loading dose of 300 mg or 600 mg then a daily dose of 75 mg for 1 year). (n=774) Intervention 2: Drug eluting stents - DES- Everolimus. 3 armed trial. Participants randomised to second-generation EES . Concurrent medication/care: All participants were prescribed aspirin at a daily dose of 75 to 100 mg indefinitely and clopidogrel at a daily dose of 75 mg for 1 year, after a loading dose of 300 mg or 600 mg, regardless of stent type. Therapeutic agents for secondary prevention, such as statins, were prescribed according to current guidelines. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (number of stents per patient (SD): EES 1.7 (1.1), BMS 1.7 (1.1)). 2. Use of antiplatelet therapy: without antiplatelet therapy (clopidogrel loading dose of 300 mg or 600 mg then a daily dose of 75 mg for 1 year). (n=765) Intervention 3: Bare metal stents - BMS - Cobalt Chronium. BMS colbalt chronium. Duration 2 years. Concurrent medication/care: All participants were prescribed aspirin at a daily dose of 75 to 100 mg indefinitely and clopidogrel at a daily dose of 75 mg for 1 year, after a loading dose of 300 mg or 600 mg, regardless of stent type. Therapeutic agents for secondary prevention, such as statins, were prescribed according to current guidelines. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (1.7 (1.1) per patient). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Academic or government funding (Supported by the Basel Cardiovascular Research Foundation and a grant from the Swiss National Foundation for Research.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES (EVEROLIMUS + SIROLIMUS) versus BMS - COBALT CHRONIUM

Protocol outcome 1: All-cause mortality at later >1-3 year
- Actual outcome: Death at 2 years; Group 1: 53/1549, Group 2: 34/765
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No

Study	BASKET-PROVE I trial: Kaiser 2010[55]
indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Cardiac mortality at later >1-3 year - Actual outcome: Cardiac death at 2 years; Group 1: 26/1549, Group 2: 22/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TVR at 2 years; Group 1: 62/1549, Group 2: 79/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Myocardial infarction at later >1-3 year - Actual outcome: Non-fatal myocardial infarction at 2 years; Group 1: 20/1549, Group 2: 20/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Stent thrombosis at later >1-3 year - Actual outcome: Definite or probable stent thrombosis at 2 years; Group 1: 11/1549, Group 2: 9/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: Minor bleeding - Actual outcome: Minor bleeding at 2 years; Group 1: 24/1549, Group 2: 13/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Minor bleeding at 1 year; Group 1: 15/1549, Group 2: 8/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: Major bleeding

Study	BASKET-PROVE I trial: Kaiser 2010[55]
- Actual outcome: Major bleeding at 1 year; Group 1: 26/1549, Group 2: 16/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Major bleeding at 2 years; Group 1: 33/1549, Group 2: 22/765 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Comments - the critical-events committee adjudicated the final one third of events without blinding; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; Cardiac mortality at early ≤1 ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; Myocardial infarction at early ≤1 ; Quality of life; Stent thrombosis at early ≤1 ; Bleeding; MLD - Minimal lumen diameter ;

Study	BASKET PROVE II trial: Kaiser 2015[56]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=2291)
Countries and setting	Conducted in Switzerland; Setting: Eight centers in Switzerland, Denmark, Germany, and Austria contributed patients
Line of therapy	1st line
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with chronic or acute coronary artery disease requiring angioplasty and stenting with stents ≥3.0 mm in diameter by visual assessment
Exclusion criteria	Patients with cardiogenic shock, in-stent restenosis or thrombosis, unprotected left main coronary artery or bypass-graft disease, planned surgery within 12 months, need for oral anticoagulation, increased bleeding risk, known intolerance to or suspected noncompliance with long term antiplatelet drug therapy, history of transient ischemic attack or stroke, or circumstances that would have made follow-up impossible
Recruitment/selection of patients	Not reported

Study	BASKET PROVE II trial: Kaiser 2015[56]
Age, gender and ethnicity	Age - Mean (SD): biodegradable-polymer DES group: 62 (11); durable-polymer DES group: 62 (11); BMS group: 63 (11). Gender (M:F): 1780/511. Ethnicity: Not reported
Further population details	1. ACS population: Not stated / Unclear (28.7% STEMI, 34.4% NSTEMI). 2. Diabetes: Not stated / Unclear (18.7% diabetes). 3. Mixed ACS and stable population: Not stated / Unclear (36.9% stable angina). 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=1530) Intervention 1: Drug eluting stents - DES- other . a second-generation biolimus-A9–eluting biodegradable-polymer stainless-steel DES or a second generation everolimus-eluting durable-polymer cobalt-chromium DES. Duration N/A. Concurrent medication/care: All patients were prescribed acetylsalicylic acid 75 to 100 mg daily long term. All patients received a loading dose of 60 mg prasugrel with a maintenance dose of 10 mg daily, risk-adjusted to 5 mg in patients aged >75 years or body weight <60 kg. Prasugrel was prescribed for 12 months after stenting with DES and for patients with acute coronary syndrome and for 4 weeks after elective stenting with BMS. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (stents per patient: 1.5±0.8). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=761) Intervention 2: Bare metal stents - BMS- unspecified. a newest-generation thin-strut BMS coated with a biocompatible silicone-carbide layer. Duration N/A. Concurrent medication/care: All patients were prescribed acetylsalicylic acid 75 to 100 mg daily long term. All patients received a loading dose of 60 mg prasugrel with a maintenance dose of 10 mg daily, risk-adjusted to 5 mg in patients aged >75 years or body weight <60 kg. Prasugrel was prescribed for 12 months after stenting with DES and for patients with acute coronary syndrome and for 4 weeks after elective stenting with BMS. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (Stents per patient: 1.5 (0.8)). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Academic or government funding (Basel Cardiac Research Foundation, Basel, Switzerland, and the University Hospital, Basel, Switzerland. Prasugrel was provided free of charge by Daiichy Sankyo and Eli Lilly)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- OTHER versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at later >1-3 year
- Actual outcome: Death at 2 years; Group 1: 37/1530, Group 2: 26/761
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Study	BASKET PROVE II trial: Kaiser 2015[56]
Protocol outcome 2: Cardiac mortality at later >1-3 year - Actual outcome: Cardiac death at 2 years; Group 1: 17/1530, Group 2: 14/761 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TVR at 2 years; Group 1: 74/1530, Group 2: 79/761 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Myocardial infarction at later >1-3 year - Actual outcome: Non-fatal MI at 2 years; Group 1: 39/1530, Group 2: 24/761 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Stent thrombosis at later >1-3 year - Actual outcome: Definite or probable stent thrombosis at 2 years; Group 1: 8/1530, Group 2: 6/761 Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; Cardiac mortality at early ≤1 ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; Myocardial infarction at early ≤1 ; Quality of life; Stent thrombosis at early ≤1 ; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding

Study	DIVA trial: Brilakis 2018[17]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=597)
Countries and setting	Conducted in USA; Setting: Multicentre (25 centres)
Line of therapy	1st line
Duration of study	Intervention + follow up: Follow up median 2.7 years
Method of assessment of guideline condition	Method of assessment /diagnosis not stated

Study	DIVA trial: Brilakis 2018[17]
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with previous CABG undergoing cardiac catheterisation at participating sites were evaluated for enrolment. Eligible patients were aged at least 18 years, had at least one significant de-novo SVG lesion (50–99% stenosis of a 2·25–4·5 mm diameter SVG) requiring PCI with intent to use embolic protection devices, and agreed to participate and take medication as prescribed
Exclusion criteria	Patients were excluded if they had planned non-cardiac surgery within 12 months of screening; presented with ST-segment elevation acute myocardial infarction; had a target SVG that was the last remaining vessel or was a left main equivalent; had any previous percutaneous treatment of the target vessel within the previous 12 months; had haemorrhagic diatheses, or refused to receive blood transfusions; required warfarin administration for the following 12 months and were considered to be at high risk of bleeding with triple anticoagulation/antiplatelet therapy; had recent positive pregnancy test, breastfeeding, or possibility of a future pregnancy; had coexisting conditions that limited life expectancy to less than 12 months; had a history of allergic reaction or significant sensitivity to any drug or metal included in DES; were allergic to clopidogrel and did not present with acute coronary syndrome at sites that use blinded study medication; or were already participating in another interventional randomised trial
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 69 (7.4); BMS group: 68.2 (7.7). Gender (M:F): 595/2. Ethnicity: White 88.5%, Black 8.5%, Hispanic 5.5%
Further population details	1. ACS population: Not stated / Unclear (23.5% NSTEMI). 2. Diabetes: Not stated / Unclear (60% had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear (37.5% stable angina, 31% unstable angina). 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=292) Intervention 1: Drug eluting stents - DES - unspecified. DES of the operators choice. . Duration N/A. Concurrent medication/care: All patients were prescribed aspirin as per standard of care. Each patient received as many stents as clinically indicated on the basis of operator judgment. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (1.3 (0.6) per patient). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=305) Intervention 2: Bare metal stents - BMS- unspecified. BMS of the operators choice. Duration N/A. Concurrent medication/care: All patients were prescribed aspirin as per standard of care. Each patient received as many stents as clinically indicated on the basis of operator judgment. Indirectness: No

Study	DIVA trial: Brilakis 2018[17]
	indirectness Further details: 1. Number of stents: Multiple stents (1.4 (0.8) per patient). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Academic or government funding (US Department of Veterans Affairs Cooperative Studies Program)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES - UNSPECIFIED versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 23/292, Group 2: 21/305
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Cardiac mortality at early ≤1
- Actual outcome: Cardiac death at 1 year; Group 1: 15/292, Group 2: 11/305
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: TVF- target vessel failure at early ≤1
- Actual outcome: TVF at 1 year; Group 1: 51/292, Group 2: 58/305
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: TLR at 1 year; Group 1: 26/292, Group 2: 25/305
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: TVR at 1 year; Group 1: 34/292, Group 2: 34/305
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Myocardial infarction at early ≤1
- Actual outcome: Myocardial infarction at 1 year; Group 1: 28/292, Group 2: 31/305
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 6: Stent thrombosis at early ≤1

Study	DIVA trial: Brilakis 2018[17]
- Actual outcome: Definite and probable stent thrombosis at 1 year; Group 1: 14/292, Group 2: 17/305 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: Bleeding - Actual outcome: Post procedural bleeding at 1 year; Group 1: 0/292, Group 2: 2/305 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year ; Minor bleeding; MLD - Minimal lumen diameter ; Major bleeding;

Study	CEREA-DES trial: Ribichini 2011[96]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=250)
Countries and setting	Conducted in Italy; Setting: Five tertiary Italian hospitals
Line of therapy	Not applicable
Duration of study	Intervention time: 1 year
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Consecutive patients undergoing coronary angiography were considered suitable for inclusion in the study when showing significant coronary artery disease (either single or multi-vessel involvement), with signs or symptoms of myocardial ischemia, amenable for PCI.
Exclusion criteria	Diabetes, age ≥80 years, recent Q-wave myocardial infarction (<2 weeks), uncontrolled hypertension; gastric ulcer, neoplasia, renal failure (creatinine >2.5 mg/dL), left main disease, contraindications to high doses of steroids, known contraindications to dual antiplatelet therapy for at least 6 months, and the lack of signed informed consent.
Recruitment/selection of patients	Consecutive patients undergoing coronary angiography between September 2006 and September 2008

Study	CEREA-DES trial: Ribichini 2011[96]
Age, gender and ethnicity	Age - Mean (SD): 63.99 years: 63.89 (9.6) DES group; 64.08 (9.67) BMS group. Gender (M:F): 210/40. Ethnicity: Not reported
Further population details	1. ACS population : UA/STEMI (Unstable angina: 30.8%; NSTEMI: 26.8%). 2. Diabetes: Without diabetes (Diabetic patients excluded from trial). 3. Mixed ACS and stable population: Not applicable 4. Older patients: < 75 years (Mean age: 63.99 years). 5. Renal disease/renal insufficiency: Not applicable 6. Size of stenosis: < > = 3mm width and length 15 (Mean in DES group: 15.70 mm, 3.07 mm; Mean in BMS group: 15.64 mm, 3.15 mm).
Indirectness of population	No indirectness
Interventions	(n=125) Intervention 1: Drug eluting stents - DES - unspecified. Drug-eluting stents were implanted (paclitaxel-eluting stents or the sirolimus-eluting stents). Duration 1 year. Concurrent medication/care: All patients were pretreated with a loading dose of either ticlopidine 500 mg or clopidogrel 300 mg per day, and conventional doses of aspirin (325 mg to 500 mg in patients with acute coronary syndromes). After successful stent implantation, all patients received standard medications including aspirin 100 mg to 160 mg, ticlopidine 250 mg twice daily or clopidogrel 75 mg per day for 1 month. Patients receiving DES were under double antiplatelet treatment for a minimum of 6 months, but ideally for 1 year, independently of clinical presentation.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (Mean number in DES group: 1.57). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin and clopidogrel used). (n=125) Intervention 2: Bare metal stents - BMS- unspecified. Bare metal stents were implanted (no details about type of BMS reported). Duration 1 year. Concurrent medication/care: All patients were pretreated with a loading dose of either ticlopidine 500 mg or clopidogrel 300 mg per day, and conventional doses of aspirin (325 mg to 500 mg in patients with acute coronary syndromes). After successful stent implantation, all patients received standard medications including aspirin 100 mg to 160 mg, ticlopidine 250 mg twice daily or clopidogrel 75 mg per day for 1 month. Patients receiving BMS were under double antiplatelet treatment for a minimum of 6 months, but ideally for 1 year, independently of clinical presentation.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (Mean number in BMS group: 1.53). 2. Use of antiplatelet therapy: with antiplatelet (Aspirin and clopidogrel).
Funding	Academic or government funding (Research grant of the Regione Piemonte, Torino, Italy)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES - UNSPECIFIED versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: All-cause mortality at 1 year; Group 1: 0/125, Group 2: 1/125

Study	CEREA-DES trial: Ribichini 2011[96]
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Cardiac mortality at early ≤1 - Actual outcome: Cardiac mortality at 1 year; Group 1: 0/125, Group 2: 1/125 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: Target lesion revascularisation at 1 year; Group 1: 4/125, Group 2: 15/125 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Target vessel revascularisation at 1 year; Group 1: 14/125, Group 2: 22/125 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction (QWMI + NQWMI) at 1 year; Group 1: 1/125, Group 2: 4/125; Comments: Results for Q-wave myocardial infarction (QWMI) and non-Q-wave myocardial infarction (NQWMI) were combined. 2 QWMI and NQWMI events in BMS group. One NQWMI event in the DES group Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1 ; Stent thrombosis at later >1-3 year; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study	SELECTION trial: Chechi 2007[27]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in Italy

Study	SELECTION trial: Chechi 2007[27]
Line of therapy	1st line
Duration of study	Follow up (post intervention): 7 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ECG
Stratum	Overall:
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients < 75 years, chest pain persisting for ≥30 mins associated with ST elevation by ECG.
Exclusion criteria	Cardiogenic shock, thrombolytic therapy, oral anticoagulant therapy, prolonged cardiopulmonary resuscitation, previous CABG, PCI or stroke within 6 months and haemorrhagic diabetes.
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): DES 59.7 (8.9), BMS 61.7 (8.7). Gender (M:F): 66/14. Ethnicity: Not stated
Further population details	1. ACS population : STEMI 2. Diabetes: With diabetes (DES 7.5%, BMS 17.5%). 3. Mixed ACS and stable population: ACS 4. Older patients: < 75 years 5. Renal disease/renal insufficiency: Patients with renal disease/insufficiency 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=40) Intervention 1: Drug eluting stents - DES- Paclitaxel. PES. Duration 7 months. Concurrent medication/care: Abciximab bolus, unfractionated heparin bolus, routine aspirin indefinitely and clopidogrel for 9 months. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy (n=40) Intervention 2: Bare metal stents - BMS- unspecified. Duration 7 months. Concurrent medication/care: Abciximab bolus, unfractionated heparin bolus, routine aspirin indefinitely and clopidogrel for 9 months. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- PACLITAXEL versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: All-cause mortality at 7 months; Group 1: 1/40, Group 2: 3/40
Risk of bias: All domain – High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study	SELECTION trial: Chechi 2007[27]
Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 28% vs 28%, Hypertension 38% vs 55%, Previous MI 5% vs 1%, Multivessel disease 40% vs 50%; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: Target lesion revascularisation at 7 months; Group 1: 2/40, Group 2: 13/40 Risk of bias: All domain - Low, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 28% vs 28%, Hypertension 38% vs 55%, Previous MI 5% vs 1%, Multivessel disease 40% vs 50%; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: Target vessel revascularisation at 7 months; Group 1: 7/40, Group 2: 17/40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 28% vs 28%, Hypertension 38% vs 55%, Previous MI 5% vs 1%, Multivessel disease 40% vs 50%; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 7 months; Group 1: 0/40, Group 2: 1/40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 28% vs 28%, Hypertension 38% vs 55%, Previous MI 5% vs 1%, Multivessel disease 40% vs 50%; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: MLD - Minimal lumen diameter - Actual outcome: Minimal luminal diameter at 7 months; Group 1: mean 2.92 mm (SD 0.4); n=40, Group 2: mean 2.99 mm (SD 0.39); n=40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 28% vs 28%, Hypertension 38% vs 55%, Previous MI 5% vs 1%, Multivessel disease 40% vs 50%; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year ; Minor bleeding; Bleeding; Major bleeding;

Study (subsidiary papers)	COMFORTABLE trial: Raber 2012[90] (Magro 2014[73], Raber 2016[88], Raber 2012[89], Raber 2014[91])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1161)

Study (subsidiary papers)	COMFORTABLE trial: Raber 2012[90] (Magro 2014[73], Raber 2016[88], Raber 2012[89], Raber 2014[91])
Countries and setting	Conducted in Denmark, Israel, Multiple countries, Netherlands, Serbia, Switzerland, United Kingdom; Setting: 11 centres throughout Europe and Israel
Line of therapy	1st line
Duration of study	Follow up (post intervention): 2 years
Method of assessment of guideline condition	Unclear method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients aged 18 years or older with symptom onset within 24 hours and STsegment elevation of at least 1 mm in 2 or more contiguous leads, true posterior MI, or new left bundle branch block were eligible in the presence of at least 1 culprit lesion within the infarct vessel. There was no limit regarding the number of treated lesions, vessels, or complexity.
Exclusion criteria	Presence of mechanical complications of acute MI, known allergy to any study medication, use of vitamin K antagonists, planned surgery unless dual antiplatelet therapy could be maintained throughout the perisurgical period, history of bleeding diathesis or known coagulopathy, pregnancy, female of child-bearing potential (age <50 years and last menstruation within 12 months) who had not undergone tubal ligation, ovariectomy or hysterectomy, participation in another trial before reaching the primary end point, inability to provide informed consent, and non-cardiac comorbid conditions with life expectancy of less than 1 year.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 60.7 (11.6); BMS group 60.4 (11.9). Gender (M:F): 918/243. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: Not stated / Unclear (Mixed (15.05%)). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear (Mixed). 5. Renal disease/renal insufficiency: Not stated / Unclear (Mixed (14.6%)). 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=578) Intervention 1: Drug eluting stents - DES- other. Stents eluting biolimus from a biodegradable polylactic acid polymer (Bio-Matrix, Biosensors Europe SA).Both stent types were available in diameters of 2.25, 2.50, 2.75, 3.00, 3.50, and 4.00 mm and in lengths of 8, 11, 18, 24, and 28 mm. . Duration N/A. Concurrent medication/care: Acetylsalicylic acid (250 mg) was administered before the procedure. In centers where prasugrel was available, an initial dose of 60 mg (including patients preloaded with clopidogrel) was administered followed up with a daily dose of 10 mg. If prasugrel was not available or contraindicated, clopidogrel was administered at a loading dose of 600 mg, followed up with a dose of 75 mg

Study (subsidiary papers)	COMFORTABLE trial: Raber 2012[90] (Magro 2014[73], Raber 2016[88], Raber 2012[89], Raber 2014[91])
	twice daily for 7 days, followed up with a maintenance dose of 75 mg once daily. Dual antiplatelet therapy was prescribed for the duration of at least 1 year in all patients. Unfractionated heparin was routinely administered with a minimal dose of 5000 IE or a dose of 70 to 100 IU/kg to maintain an activated clotting time of 250 seconds. Bivalirudin was administered at a dose of 0.75 mg/kg intravenously followed up with an infusion of 1.75 mg/kg per hour during the duration of the procedure. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the operator.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents per lesion 1.32 (0.61)). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin). (n=583) Intervention 2: Bare metal stents - BMS- unspecified. Baremetal stents of otherwise identical design (Gazelle, Biosensors Europe SA). Both stent types were available in diameters of 2.25, 2.50, 2.75, 3.00, 3.50, and 4.00 mm and in lengths of 8, 11, 18, 24, and 28 mm. . Duration N/A. Concurrent medication/care: Acetylsalicylic acid (250 mg) was administered before the procedure. In centers where prasugrel was available, an initial dose of 60 mg (including patients preloaded with clopidogrel) was administered followed up with a daily dose of 10 mg. If prasugrel was not available or contraindicated, clopidogrel was administered at a loading dose of 600 mg, followed up with a dose of 75 mg twice daily for 7 days, followed up with a maintenance dose of 75 mg once daily. Dual antiplatelet therapy was prescribed for the duration of at least 1 year in all patients. Unfractionated heparin was routinely administered with a minimal dose of 5000 IE or a dose of 70 to 100 IU/kg to maintain an activated clotting time of 250 seconds. Bivalirudin was administered at a dose of 0.75 mg/kg intravenously followed up with an infusion of 1.75 mg/kg per hour during the duration of the procedure. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the operator. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Mixed - number of stents per lesion 1.26 (0.60)). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin).
Funding	Academic or government funding (Supported by the Swiss National Science Foundation (grant 33CM30-124112), and an unrestricted research grant from Biosensors Europe SA, Morges, Switzerland (Drs Juni and Windecker). Dr Raber is the recipient of a research fellowship (SPUM) funded by the Swiss NationalScience Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- OTHER versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1 year
- Actual outcome: Death at 1 year; Group 1: 18/575, Group 2: 23/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation

Study (subsidiary papers)	COMFORTABLE trial: Raber 2012[90] (Magro 2014[73], Raber 2016[88], Raber 2012[89], Raber 2014[91])

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 2 years; Group 1: 28/575, Group 2: 32/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation

Protocol outcome 3: Cardiac mortality at early ≤1 year
- Actual outcome: Cardiac death at 1 year; Group 1: 16/575, Group 2: 20/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation

Protocol outcome 4: Cardiac mortality at later >1-3 year
- Actual outcome: Cardiac death at 2 years; Group 1: 17/575, Group 2: 25/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation

Protocol outcome 5: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: Any TLR at 1 year; Group 1: 9/575, Group 2: 34/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation
- Actual outcome: Any TVR at 1 year; Group 1: 11/575, Group 2: 37/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation

Protocol outcome 6: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year
- Actual outcome: Any TLR at 2 years; Group 1: 19/575, Group 2: 53/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation
- Actual outcome: Any TVR at 2 years; Group 1: 26/575, Group 2: 58/582
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number

Study (subsidiary papers)	COMFORTABLE trial: Raber 2012[90] (Magro 2014[73], Raber 2016[88], Raber 2012[89], Raber 2014[91])
missing: 1, Reason: Refused consent after randomisation Protocol outcome 7: Stent thrombosis at early ≤1 year - Actual outcome: Stent thrombosis (definite or probable) at 1 year; Group 1: 14/575, Group 2: 21/582 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomisation Protocol outcome 8: Stent thrombosis at later >1-3 years - Actual outcome: Stent thrombosis (definite or probable) at 2 years; Group 1: 18/575, Group 2: 25/582 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomization Protocol outcome 9: Myocardial infarction at early ≤1 year - Actual outcome: Myocardial infarction at 1 year; Group 1: 11/575, Group 2: 21/582 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomization Protocol outcome 9: Myocardial infarction at early >1-3 years - Actual outcome: Myocardial infarction at 1 year; Group 1: 18/575, Group 2: 28/582 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Refused consent after randomisation; Group 2 Number missing: 1, Reason: Refused consent after randomization Protocol outcome 11: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter (in stent) at 13 months; Group 1: mean 2.73 mm (SD 0.57); n=46, Group 2: mean 1.79 mm (SD 0.83); n=45; Comments: DES group: 53 patients, 62 lesions; BMS group: 50 patients, 59 lesions Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 525, Reason: Subgroup which were given a angiography at 13 months; Group 2 Number missing: 533, Reason: Subgroup which were given a angiography at 13 months - Actual outcome: Minimal lumen diameter (in segment) at 13 months; Group 1: mean 2.37 mm (SD 0.47); n=53, Group 2: mean 1.75 mm (SD 0.8); n=50; Comments: DES group: 53 patients, 62 lesions; BMS group: 50 patient, 59 lesions Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 525, Reason: Subgroup which were given a angiography at 13	

Study (subsidiary papers)	COMFORTABLE trial: Raber 2012[90] (Magro 2014[73], Raber 2016[88], Raber 2012[89], Raber 2014[91])
months; Group 2 Number missing: 533, Reason: Subgroup which were given a angiography at 13 months	
Protocol outcomes not reported by the study	TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ;; Myocardial infarction at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; Major bleeding;

Study (subsidiary papers)	DEBATER trial: Wijnbergen 2012[133]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=907)
Countries and setting	Conducted in Netherlands; Setting: 10 regional referring centers
Line of therapy	1st line
Duration of study	Follow up (post intervention): 5 years
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients 18 years of age or older with STEMI, who resented within 12 h of onset of symptoms
Exclusion criteria	Patients who were on oral anticoagulation and patients who had received thrombolytic therapy or treatment with a glycoprotein IIb/IIIa inhibitor in the previous 24 h, contraindications for DES, contraindications for clopidogrel or glycoprotein IIb/IIIa inhibitors, comorbid conditions with a predictable fatal outcome in the short run, cardiogenic shock, and inability to give informed consent
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 60 (11); BMS group: 61 (11). Gender (M:F): 668/202. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: Not stated / Unclear (Mixed (10%)). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear (Mixed). 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=441) Intervention 1: Drug eluting stents - DES- Sirolimus. Sirolimus eluting stent (CYPHER, Cordis Corporation, Bridgewater, New Jersey) and participants were also randomised to treatment with abciximab or no abciximab (DES alone or DES + abciximab). Duration N/A. Concurrent medication/care: All patients received aspirin (300 mg chewed or 500 mg intravenously), clopidogrel (600 mg) and a fixed bolus of intravenous unfractionated heparin (5,000 IU) in the ambulance. Before angiography, all patients received an

Study (subsidiary papers)	DEBATER trial: Wijnbergen 2012[133]
	additional intravenous bolus of heparin (5,000 IU). After primary PCI, aspirin 80 mg per day was given indefinitely, and clopidogrel was prescribed (75 mg/day) for at least 1 month after BMS and 6 to 12 months after SES. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin). (n=466) Intervention 2: Bare metal stents - BMS- unspecified. The choice of the BMS was left to the discretion of the operator. Patients were also randomised to abciximab (BMS + abciximab or BMS alone). Duration N/A. Concurrent medication/care: All patients received aspirin (300 mg chewed or 500 mg intravenously), clopidogrel (600 mg) and a fixed bolus of intravenous unfractionated heparin (5,000 IU) in the ambulance. Before angiography, all patients received an additional intravenous bolus of heparin (5,000 IU). After primary PCI, aspirin 80 mg per day was given indefinitely, and clopidogrel was prescribed (75 mg/day) for at least 1 month after BMS and 6 to 12 months after SES. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin).
Funding	Academic or government funding (Supported by unrestricted research grants from Johnson & Johnson (Cordis), Guidant, Abbott, and the Friends of the Heart Foundation in Eindhoven, the Netherlands)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 11/424, Group 2: 10/446
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17; Group 2 Number missing: 20

Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: Target vessel revascularisation at 1 year; Group 1: 28/424, Group 2: 49/446
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17; Group 2 Number missing: 20

Protocol outcome 4: Stent thrombosis at early ≤1
- Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: 14/424, Group 2: 16/446
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17; Group 2 Number missing: 20
- Actual outcome: Stent thrombosis (probable) at 1 year; Group 1: 3/424, Group 2: 2/446
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study (subsidiary papers)	DEBATER trial: Wijnbergen 2012[133]
Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17; Group 2 Number missing: 20 Protocol outcome 5: Bleeding - Actual outcome: Bleeding at 1 year; Group 1: 18/424, Group 2: 24/446 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 17; Group 2 Number missing: 20	
Protocol outcomes not reported by the study	Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Stent thrombosis at later >1-3 year; Myocardial infarction at early ≤1 ; Myocardial infarction at later >1-3 year ; Quality of life; Minor bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study (subsidiary papers)	DEDICATION trial: Kelbaek 2008[61] (Kaltoft 2010[57])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=626)
Countries and setting	Conducted in Denmark; Setting: Two high-volume invasive cardiology centers in Denmark
Line of therapy	1st line
Duration of study	Follow up (post intervention): 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ECG
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with chest pain of >30-minute duration who had a cumulated ST-segment elevation of >4 mm in at least 2 contiguous leads of the ECG, provided that they were >18 years of age and had a high-grade stenosis or occlusion of a coronary artery without excessive tortuosity or calcification prohibiting advancement of a filter wire to the distal vascular bed of the vessel. Patients who were admitted directly to the tertiary unit with laboratory facilities or via a referring hospital as long as they presented to the catheterization laboratory within 12 hours from symptom onset were not distinguished between
Exclusion criteria	Previous myocardial infarction in the target vessel area, development of cardiogenic shock before enrollment, culprit lesions in an unprotected left main coronary artery, gastrointestinal bleeding within 1 month, pregnancy, known renal failure, life expectancy <1 year, and linguistic problems

Study (subsidiary papers)	DEDICATION trial: Kelbaek 2008[61] (Kaltoft 2010[57])
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 61.8 (SD not reported); BMS group: 62.3 (SD not reported). Gender (M:F): 458/168. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: (Mixed (10.4%)). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=313) Intervention 1: Drug eluting stents - DES - unspecified. Mixed (47% were sirolimus-eluting (Cordis, NJ), 40% were paclitaxeleluting (Boston Scientific, Natick, Mass), and 13% were zotarolimus-eluting stents (Medtronic, Calif). All stents were implanted under high pressure (>12 atm). Implantation of >1 stent of the same kind was allowed to cover the entire lesion.. Duration N/A. Concurrent medication/care: Patients were pretreated with 300 to 500 mg aspirin, 300 to 600 mg clopidogrel, and 10 000 IU unfractionated heparin as soon as transportation to the catheterization laboratory was arranged. A beta-blocker was administered at the discretion of the transportation team according to blood pressure and heart rate. If there was no contraindication, patients were treated with a glycoprotein IIb/IIIa receptor blocker on arrival at the catheterization laboratory. Patients were examined during and after the index procedure with ST-segment monitoring, cardiac markers, and echocardiography. At discharge, patients received a daily dose of a statin, clopidogrel (for 12 months), and aspirin (indefinitely). A beta-blocker was administered in the absence of contraindications, and an angiotensin-converting enzyme inhibitor was given in case of reduced (<45%) left ventricular ejection fraction.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Mixed (number of stents per lesion: 1.3 (0.62)). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin). (n=313) Intervention 2: Bare metal stents - BMS- unspecified. Mixed (38% were made of cobalt alloy (Vision, Abbott, Ill, and Driver, Medtronic), 39% were stainless steel stents from Boston Scientific, and 23% were miscellaneous stainless steel stents from Biotronik (Seoul, South Korea), Cordis, Guidant, Diegem (Belgium), Jomed (Helsingborg, Sweden), and Terumo (Tokyo, Japan)). All stents were implanted under high pressure (12 atm). Implantation of 1 stent of the same kind was allowed to cover the entire lesion.. Duration N/A. Concurrent medication/care: Patients were pretreated with 300 to 500 mg aspirin, 300 to 600 mg clopidogrel, and 10 000 IU unfractionated heparin as soon as transportation to the catheterization laboratory was arranged. A beta-blocker was administered at the discretion of the transportation team according to blood pressure and heart rate. If there was no contraindication, patients were treated with a glycoprotein IIb/IIIa receptor blocker on arrival at the catheterization laboratory. Patients were examined during and after the index procedure with ST-segment monitoring, cardiac markers, and echocardiography. At discharge, patients received a daily dose of a statin, clopidogrel (for 12 months), and aspirin (indefinitely). A beta-blocker was administered in the absence of contraindications, and an angiotensin-converting enzyme

Study (subsidiary papers)	DEDICATION trial: Kelbaek 2008[61] (Kaltoft 2010[57])
	inhibitor was given in case of reduced (<45%) left ventricular ejection fraction.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Mixed (stents per lesion: 1.3 (0.62))). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin).
Funding	Study funded by industry (Supported by unrestricted grants from the Cordis/ Johnson & Johnson, Medtronic, Abbott, and Boston Scientific companies.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES - UNSPECIFIED versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 16/313, Group 2: 8/313
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 3 years; Group 1: 33/313, Group 2: 20/313
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Cardiac mortality at early ≤1
- Actual outcome: Cardiac death at 1 year; Group 1: 13/313, Group 2: 5/313
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Cardiac mortality at later >1-3 year
- Actual outcome: Cardiac death at 3 years; Group 1: 19/313, Group 2: 6/313
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: TLR at 1 year; Group 1: 16/313, Group 2: 41/313
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: TLR only; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: TVR at 1 year; Group 1: 20/313, Group 2: 50/313
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: TLR only; Group 1 Number missing: ; Group 2 Number missing:

Study (subsidiary papers)	DEDICATION trial: Kelbaek 2008[61] (Kaltoft 2010[57])
Protocol outcome 6: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TLR at 3 years; Group 1: 16/313, Group 2: 41/313 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: TVR at 3 years; Group 1: 28/313, Group 2: 62/313 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 1 year; Group 1: 5/313, Group 2: 8/313 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 8: Myocardial infarction at later >1-3 year - Actual outcome: Myocardial infarction at 3 years; Group 1: 9/313, Group 2: 15/313 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 9: Stent thrombosis at later >1-3 year - Actual outcome: Stent thrombosis (definite) at 3 years; Group 1: 5/313, Group 2: 10/313 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Stent thrombosis (probable) at 3 years; Group 1: 4/313, Group 2: 0/313 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 10: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter (in-lesion zone) at 8 months; Group 1: mean 2.36 mm (SD 0.77); n=258, Group 2: mean 1.91 mm (SD 0.77); n=267 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: TLR only; Group 1 Number missing: 55; Group 2 Number missing: 46 - Actual outcome: Minimal lumen diameter (in-stent zone) at 8 months; Group 1: mean 2.61 mm (SD 0.88); n=257, Group 2: mean 2 mm (SD 0.8); n=264 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: TLR only; Group 1 Number missing: 56; Group 2 Number missing: 49	
Protocol outcomes not reported by the study	TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; Major bleeding;

Study	Diaz de la Llera 2007[35]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in Spain; Setting: Hospital
Line of therapy	Mixed line
Duration of study	Intervention + follow up: 1 year
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall:
Subgroup analysis within study	Not applicable:
Inclusion criteria	Participants with STEMI over the age of 18 years who were candidates for primary angioplasty and who met the following criteria were included: (1) chest pain lasting for > 30 minutes with elevation of the ST-segment by 1 mm or more on 2 or more contiguous electrocardiographic leads or recent-onset left branch blocking, and (2) admitted to the hospital centre within the first 12 hours after the onset of symptoms
Exclusion criteria	Patients in a state of cardiogenic shock and/or Killip IV before randomisation; the partial or total administration of prior fibrinolytic treatment or administration of any glycoprotein IIb/IIIa inhibitors during the previous 30 days; chronic kidney failure requiring dialysis; pregnant women; history of haemorrhagic diathesis or allergy to aspirin, clopidogrel, and/or abciximab; major surgery in the last 15 days; active bleeding or previous stroke in the last 6 months; and a life expectancy of less than 6 months. Patients with a reference diameter < 2.25mmand > 4.0mmby visual estimation in the infarction-related artery were excluded from the study
Recruitment/selection of patients	Consecutive patients
Age, gender and ethnicity	Age - Mean (SD): BMS: 65 (13) ; SES: 64 (12). Gender (M:F): 95:19. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: Not stated / Unclear (27.5% had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Extra comments	.
Indirectness of population	No indirectness
Interventions	(n=60) Intervention 1: Drug eluting stents - DES- Sirolimus. DES (sirolimus). Duration N/A. Concurrent medication/care: Before the procedure, all patients received aspirin (300-500 mg by mouth as the loading dose and then 100 mg a day indefinitely) plus clopidogrel (300 or 600 mg as the loading dose and then 75 mg a day for at least 1 or 9 months depending on whether the type of stent used was BMS or SES). Abciximab was administered to all patients as a bolus at a dose of 0.25 Ag/ kg, followed by an infusion at a

Study	Diaz de la Llera 2007[35]
	dose of 0.125 Ag/kg per minute for 12 hours. Heparin was administered as a bolus in relation to the patient's body weight at a dose of 70 U/kg (maximum 7 000 U), with additional doses to maintain an activated clotting time (ACT) of between 200 and 250 seconds. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy (n=60) Intervention 2: Bare metal stents - BMS- unspecified. BMS . Duration N/A. Concurrent medication/care: Before the procedure, all patients received aspirin (300-500 mg by mouth as the loading dose and then 100 mg a day indefinitely) plus clopidogrel (300 or 600 mg as the loading dose and then 75 mg a day for at least 1 or 9 months depending on whether the type of stent used was BMS or SES). Abciximab was administered to all patients as a bolus at a dose of 0.25 Ag/ kg, followed by an infusion at a dose of 0.125 Ag/kg per minute for 12 hours. Heparin was administered as a bolus in relation to the patient's body weight at a dose of 70 U/kg (maximum 7 000 U), with additional doses to maintain an activated clotting time (ACT) of between 200 and 250 seconds. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED Protocol outcome 1: All-cause mortality at early ≤1 - Actual outcome: Death at 1 year; Group 1: 3/60, Group 2: 2/54 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 4 Protocol outcome 2: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: Target vessel revascularisation at 1 year; Group 1: 0/60, Group 2: 3/54 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 4	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at early ≤1 ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1; Stent thrombosis at later >1-3 year; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study	ELISA 3 trial: Remkes 2016[94]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=474)
Countries and setting	Conducted in Netherlands; Setting: multicentre
Line of therapy	1st line
Duration of study	Follow up (post intervention): 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ECG
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients were eligible if they were hospitalised with ischaemic chest pain or dyspnoea at rest, with the last episode occurring 24hours or less before randomisation, and had at least two of three of the following high-risk characteristics: (1) evidence of extensive myocardial ischaemia on ECG (shown by new cumulative ST depression >5mm or temporary ST segment elevation in two contiguous leads <30min), (2) elevated biomarkers (troponin T >0.10 µg/L or myoglobin >150 µg/L) or elevated CKMB fraction (>6% of total CK), (3) age above 65years.
Exclusion criteria	Persistent STsegment elevation, symptoms of ongoing myocardial ischaemia despite optimal medical therapy, contraindication for diagnostic angiography, active bleeding, cardiogenic shock, acute posterior infarction and life expectancy<1year
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 65.91 (11.69); BMS group: 64.63 (12.24). Gender (M:F): 351/123. Ethnicity: Not reported
Further population details	1. ACS population: UA/STEMI (NSTEMI). 2. Diabetes: Not stated / Unclear (17.9% had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: > = 3mm width and length 15
Extra comments	Patients with NSTEMI who did not want to participate in, or who did not meet the inclusion criteria for, high-risk NSTEMI of the ELISA-3 study, were recruited in the ELISA prospective registry.
Indirectness of population	No indirectness
Interventions	(n=234) Intervention 1: Drug eluting stents - DES- Everolimus. everolimus-eluting stents (EES). Duration N/A. Concurrent medication/care: Patients received dual antiplatelet therapy (acetylsalicic acid and clopidogrel) for the duration of 1 year. Indirectness: No indirectness

Study	ELISA 3 trial: Remkes 2016[94]
	Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.22±0.48). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=240) Intervention 2: Bare metal stents - BMS- unspecified. bare-metal stents (BMS). Duration N/A. Concurrent medication/care: Patients received dual antiplatelet therapy (acetylsalicic acid and clopidogrel) for the duration of 1 year. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.18±0.42). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Study funded by industry (Abbott (unrestricted research grant).)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- EVEROLIMUS versus BMS- UNSPECIFIED Protocol outcome 1: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TVR at 2 years; Group 1: 9/234, Group 2: 25/240 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter at 9 months; Group 1: mean 2.37 mm (SD 0.63); n=85, Group 2: mean 1.84 mm (SD 0.62); n=87 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 149; Group 2 Number missing: 153	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1; Myocardial infarction at early ≤1 ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1; Stent thrombosis at later >1-3 years ; Minor bleeding; Bleeding; Major bleeding;

Study	EUCATAX trial: Rodriguez 2011[100]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=422)
Countries and setting	Conducted in Argentina; Setting: Multicentre - seven sites in Argentina
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 12 months

Study	EUCATAX trial: Rodriguez 2011[100]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: De novo stenosis (≥70% stenosis on visual assessment)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with a de novo stenosis (≥70% stenosis on visual assessment) in a major coronary artery, suitable for stent deployment and clinical indication to revascularisation were eligible for inclusion.
Exclusion criteria	Age <18 years, acute myocardial infarction (MI) in the preceding 72 hours, venous graft as the target vessel, anticipated noncompliance to dual anti-platelet treatment, previous percutaneous coronary intervention (PCI) with drug-eluting stents, in-stent restonosis, severe left ventricular dysfunction (left ventricular ejection fraction <30%), severe comorbidities with decreased life expectancy, and participation in another study.
Recruitment/selection of patients	Between August 2007 and August 2009 patients were screened and selected based on inclusion criteria and exclusion criteria.
Age, gender and ethnicity	Age - Mean (SD): 64.3 year; PES group 63.8 (10.2); BMS group 64.7 (12.2). Gender (M:F): 343/79. Ethnicity: Not reported
Further population details	1. ACS population: Unstable angina: PES group 59.7%; BMS group 66.8%. 2. Diabetes: Without diabetes (PES group 23.2%; BMS group 16.1%). 3. Mixed ACS and stable population: Not applicable 4. Older patients: < 75 years (Mean age: 64.3 years). 5. Renal disease/renal insufficiency: Patients without renal disease/insufficiency (Chronic renal failure - PES group 5.2%; BMS group 3.8%). 6. Size of stenosis: Not applicable
Indirectness of population	No indirectness
Interventions	(n=211) Intervention 1: Drug eluting stents - DES- Paclitaxel. Paciltaxel-eluting stents with a double coating including a bioadsorable polymer as the platform for paclitaxel elution and glycocalyx to increase hemocompatability. . Duration 6 months. Concurrent medication/care: PCI was performed using standard techniques. Patients received 325 mg/day of aspirin indefinitely and clopidogrel as a loading dose of 300 mg in the day of the procedure and 75 mg/day thereafter for 6 months. . Indirectness: No indirectness Further details: 1. Number of stents: Single stent (Mean number (SD): 1.36 (0.55)). 2. Use of antiplatelet therapy: with antiplatelet (Aspirin and clopidogrel administered). (n=211) Intervention 2: Bare metal stents - BMS- unspecified. Bare metal stent used, type of bare metal stent not specified.. Duration 6 months. Concurrent medication/care: PCI was performed using standard techniques. Patients received 325 mg/day of aspirin indefinitely and clopidogrel as a loading dose of 300 mg

Study	EUCATAX trial: Rodriguez 2011[100]
	in the day of the procedure and 75 mg/day thereafter for 6 months.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (Mean number (SD): 1.29 (0.54)). 2. Use of antiplatelet therapy: with antiplatelet (Aspirin and clopidogrel administered).
Funding	Study funded by industry (Study grant from Eucatech AG, Reinhelfeden, Germany)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- PACLITAXEL versus BMS- UNSPECIFIED Protocol outcome 1: All-cause mortality at early ≤1 - Actual outcome: All-cause mortality at 1 year; Group 1: 5/211, Group 2: 8/211 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 2: Cardiac mortality at early ≤1 - Actual outcome: Cardiac mortality at 1 year; Group 1: 4/211, Group 2: 4/211 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: TVF- target vessel failure at early ≤1 - Actual outcome: Target vessel failure at 1 year; Group 1: 20/211, Group 2: 36/211 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction (acute) at 1 year; Group 1: 6/211, Group 2: 5/211 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1 ; Stent thrombosis at later >1-3 year ; Minor bleeding; Bleeding; MLD - Minimal lumen diameter ; Major bleeding;

Study	GRACIA-3 trial: Sanchez 2010[105]
Study type	RCT (Patient randomised; Parallel)

Study	GRACIA-3 trial: Sanchez 2010[105]
Number of studies (number of participants)	1 (n=433)
Countries and setting	Conducted in Spain; Setting: 20 Spanish hospitals
Line of therapy	1st line
Duration of study	Follow up (post intervention): 12 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Age 18 years or older; symptom onset within 12 hours before random assignment; chest pain lasting more than 30 minutes; ST-segment elevation of at least 0.1 mV in at least 2 limb leads, ST-segment elevation of at least 0.2 mV in 2 or more contiguous precordial leads, or left bundle-branch block or paced rhythm; and no severe heart failure (Killip class <3)
Exclusion criteria	Cardiogenic shock, defined as a systolic blood pressure <90 mm Hg with no response to fluid administration or <100 mm Hg in patients with supportive treatment and no bradycardia; suspected mechanical complications of acute myocardial infarction; previous coronary artery bypass graft; noncardiac disease that is likely to jeopardize the planned termination of the study; women of childbearing potential unless they had a negative pregnancy test result; active bleeding and recent surgery (within 2 weeks) that contraindicate the use of heparin, tirofiban, or platelet aggregation inhibitors; contraindications for thrombolysis (previous hemorrhagic stroke at any time, history of nonhemorrhagic cerebrovascular accident within the previous 12 months, intracerebral neoplasm, active internal bleeding, suspected aortic dissection, uncontrolled hypertension >180/110 in several measurements, any other known intracerebral condition not covered in contraindications, current use of anticoagulants or heparin use within 8 hours, known bleeding diathesis, recent trauma [<4 weeks] including head trauma or traumatic or prolonged [>10 minutes] cardiopulmonary resuscitation or recent major surgery or biopsy [<8 weeks], noncompressible vascular punctures, recent [<4 weeks] internal bleeding, pregnancy, and active peptic ulcer); history of hypersensitivity to aspirin, ticlopidine, clopidogrel, heparin, tirofiban, or stainless steel; known renal failure, creatinine 2.5 mg/dL; known impaired hepatic function that contraindicates the use of clopidogrel; known thrombocytopenia (<100 000); participation in other trials; known multivessel disease identified as not suitable for revascularization; and known peripheral vascular disease that makes cardiac catheterization difficult.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): BMS group: 60.9 (1.3); DES group: 61.1 (1.26). Gender (M:F): 358/75. Ethnicity: Not reported
Further population details	1. ACS population : STEMI 2. Diabetes: Not stated / Unclear (Mixed (18.4%)). 3. Mixed ACS and stable

Study	GRACIA-3 trial: Sanchez 2010[105]
	population: Not stated / Unclear 4. Older patients: < 75 years (Age range 59-64). 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=217) Intervention 1: Drug eluting stents - DES- Paclitaxel. Paclitaxel-eluting stent with or without tirofiban. The stenting procedure was carried out using Express stents (Boston Scientific, Natick, Mass) or TAXUS stents (Boston Scientific). When a large amount of myocardium was threatened by severe stenosis (90% reduction in lumen diameter by visual estimation in a coronary segment with a reference diameter larger than 2.75 mm), stenting of nonculprit lesions was also performed.. Duration N/A. Concurrent medication/care: All patients received fibrinolysis and aspirin. Immediately after stenting, patients received a loading dose of 300 mg of clopidogrel and 75 mg daily for 1 year. Maintenance aspirin therapy was administered indefinitely at 80 to 325 mg once daily (coated or uncoated), unless contraindicated. The tirofiban infusion was stopped 24 hours after initiation. Finally, beta-blockers, angiotensin-converting enzyme inhibitors, statins, and any additional postinfarction therapy were administered, as outlined in international guidelines.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin). (n=216) Intervention 2: Bare metal stents - BMS- unspecified. Bare metal stent with or without tirofiban. The stenting procedure was carried out using Express stents (Boston Scientific, Natick, Mass) or TAXUS stents (Boston Scientific). When a large amount of myocardium was threatened by severe stenosis (90% reduction in lumen diameter by visual estimation in a coronary segment with a reference diameter larger than 2.75 mm), stenting of nonculprit lesions was also performed.. Duration N/A. Concurrent medication/care: All patients received fibrinolysis and aspirin. Immediately after stenting, patients received a loading dose of 300 mg of clopidogrel and 75 mg daily for 1 year. Maintenance aspirin therapy was administered indefinitely at 80 to 325 mg once daily (coated or uncoated), unless contraindicated. The tirofiban infusion was stopped 24 hours after initiation. Finally, beta-blockers, angiotensin-converting enzyme inhibitors, statins, and any additional postinfarction therapy were administered, as outlined in international guidelines.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin).
Funding	Academic or government funding (Unrestricted grants to fund the study were obtained from Red Tematica de Enfermedades Cardiovasculares (RECAVA) of the Instituto de Salud Carlos III (Spanish Ministry of Science and Innovation), from the Fondo de Investigacion Sanitaria of the Instituto de Salud Carlos III (Spanish Ministry of Science and Innovation), and from the Junta de Castilla y Leon.)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- PACLITAXEL versus BMS- UNSPECIFIED	

Study	GRACIA-3 trial: Sanchez 2010[105]
Protocol outcome 1: Cardiac mortality at early ≤1 - Actual outcome: Cardiovascular death at 1 year; Group 1: 21/217, Group 2: 15/216 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Myocardial infarction at early ≤1 - Actual outcome: Non-fatal myocardial infarction at 1 year; Group 1: 5/217, Group 2: 3/216 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Stent thrombosis at early ≤1 - Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: 2/217, Group 2: 3/216 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Stent thrombosis (probable) at 1 year; Group 1: 2/217, Group 2: 2/216 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Minor bleeding - Actual outcome: Minor bleeding at 1 year; Group 1: 27/217, Group 2: 24/216 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter at 1 year; Group 1: mean 2.26 mm (SD 0.9); n=209, Group 2: mean 2.17 mm (SD 0.84); n=210 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7; Group 2 Number missing: 7 Protocol outcome 7: Major bleeding - Actual outcome: Major bleeding at 1 year; Group 1: 8/217, Group 2: 11/216 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year ; Bleeding;

Study	Han 2007[47]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=200)
Countries and setting	Conducted in Chile; Setting: Not reported
Line of therapy	1st line
Duration of study	Follow up (post intervention): Mean 8 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	People with symptomatic or documented myocardial ischemia, including acute myocardial infarction (AMI) fit for coronary stent implantation; to be treated exclusively with one kind of stent, no more than 3 stents for one target vessel (or total length of stents ≤ 85 mm), and providing written informed consent
Exclusion criteria	In-stent restenosis lesion, graft lesion, not eligible for DES implantation, such as intolerant of anti-platelet treatment or planned to undergo surgery, and administration of IIb/IIIa antagonist
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): BMS group 58.79 (11.26); DES group 57.94 (11.52). Gender (M:F): 153/47. Ethnicity: Not reported
Further population details	1. ACS population: Not stated / Unclear (3.5% had NSTEMI). 2. Diabetes: Not stated / Unclear (22% had diabetes). 3. Mixed ACS and stable population: ACS (76% had ACS). 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=100) Intervention 1: Drug eluting stents - DES- other . Tacrolimus-eluting (Janus) stent. A 300-600 mg loading dose clopidogrel were given for all patients at admission. Duration N/A. Concurrent medication/care: After stent implantation, all patients received dual antiplatelet therapy: aspirin 300 mg per day for the initial one month continued with 100 mg per day for life-long and clopidogrel 75 mg per day for 4 months. In patients with AMI, the antiplatelet regimen was mostly the same except clopidogrel 150 mg per day for the initial one week.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents per person: 1.22 (0.82)). 2. Use of antiplatelet therapy: with antiplatelet therapy

Study	Han 2007[47]
	(n=100) Intervention 2: Bare metal stents - BMS- unspecified. Bare metal stent. A 300-600 mg loading dose clopidogrel were given for all patients at admission. Duration N/A. Concurrent medication/care: After stent implantation, all patients received dual antiplatelet therapy: aspirin 300 mg per day for the initial one month continued with 100 mg per day for life-long and clopidogrel 75 mg per day for 4 months. In patients with AMI, the antiplatelet regimen was mostly the same except clopidogrel 150 mg per day for the initial one week. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents per person: 1.35 (1.08)). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- OTHER versus BMS- UNSPECIFIED Protocol outcome 1: Cardiac mortality at early ≤1 - Actual outcome: Cardiac death at 8 months; Group 1: 0/100, Group 2: 1/100 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Myocardial infarction at early ≤1 - Actual outcome: Acute myocardial infarction at 8 months; Group 1: 0/100, Group 2: 2/100 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year ; Minor bleeding; Bleeding; MLD - Minimal lumen diameter ; Major bleeding;

Study (subsidiary papers)	HORIZONS-AMI trial: Stone 2009[112] (Mehran 2008[75], Stone 2010[113])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=3006)
Countries and setting	Conducted in Argentina, Austria, Germany, Israel, Italy, Multiple countries, Netherlands, Norway, Poland, Spain, United Kingdom, USA; Setting: Multicentre
Line of therapy	1st line

Study (subsidiary papers)	HORIZONS-AMI trial: Stone 2009[112] (Mehran 2008[75], Stone 2010[113])
Duration of study	Follow up (post intervention): 3 years
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants 18 years of age or older who presented within 12 hours after the onset of symptoms and who had ST-segment elevation of 1 mm or more in two or more contiguous leads, new left bundle-branch block, or true posterior myocardial infarction. Participants were considered to be eligible for random assignment to paclitaxel-eluting stents or baremetal stents if an acute-infarct–related artery was present in which all lesions requiring PCI had a visually estimated reference-vessel diameter between 2.25 mm and 4.0 mm, without excessive tortuosity or severe calcification
Exclusion criteria	Hypersensitivity or contraindication to heparin, both abciximab and eptifibatide, aspirin, both clopidogrel and ticlopidine, bivalirudin, paclitaxel or taxol, the polymer components of the TAXUS stent, stainless steel, or contrast media (refractory to medications or history of anaphylaxis); prior administration of thrombolytic therapy, bivalirudin, GP IIb/IIIa inhibitors, low molecular weight heparin, or fondaparinux for this admission; current use of Coumadin; systemic (IV) paclitaxel or taxol use within 12 m; female of childbearing potential, unless a recent pregnancy test is negative, who possibly plans to become pregnant any time after enrollment into this study; history of bleeding diathesis or known coagulopathy (including heparin-induced thrombocytopenia) or refusal of blood transfusions; history of intracerebral mass, aneurysm, arteriovenous malformation, or hemorrhagic stroke; stroke or transient ischemic attack within the past 6 m or any permanent residual neurologic defect; gastrointestinal or genitourinary bleeding within the last 2 m or major surgery within 6 wk; recent history or known current platelet count b100000 cells/mm3 or hemoglobin b10 g/dL; extensive peripheral vascular disease, such that emergent angiography and intervention in the opinion of the investigator is likely to be difficult or complicated; an elective surgical procedure is planned that would necessitate interruption of thienopyridines during the first 6 m postenrollment; noncardiac comorbid conditions are present with life expectancy b1 y or that may result in protocol noncompliance; patients who are actively participating in another drug or device investigational study, which have not completed the primary end point follow-up period; previous enrollment in this trial; patients who underwent coronary stent implantation within the past 30 days; one or more hemodynamically significant lesion(s) is present in the infarct vessel (or side branches), which can only undergo balloon angioplasty or cannot be stented with a study stent, (ie, do not meet the angiographic inclusion criteria for a study stent); the presence of a bifurcation lesion in the infarct vessel, which will definitely require the implantation of 2 stents for treatment; anticipated need for greater than 100 mm of study stent length; the infarct related artery is an unprotected left main segment; patients with significant multivessel disease or anatomical features otherwise unfavorable for angioplasty such that the patient will have a high likelihood of requiring bypass surgery before 30 days;

Study (subsidiary papers)	HORIZONS-AMI trial: Stone 2009[112] (Mehran 2008[75], Stone 2010[113])
	the culprit vessel or lesion cannot be identified; patient presenting with possible/probable stent thrombosis; any patient in whom angiography demonstrates the infarct lesion to be at the site of a previously implanted stent (bare metal or drug eluting).
Recruitment/selection of patients	Consecutive patients
Age, gender and ethnicity	Age - Median (range): DES group: 59.9 (30.9–92.3); BMS group: 59.3 (26.0–89.0). Gender (M:F): 2307/699. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: Not stated / Unclear (Mixed (15.65%)). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear (Mixed). 5. Renal disease/renal insufficiency: Not stated / Unclear (Mixed (15.5%)). 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=2257) Intervention 1: Drug eluting stents - DES- Paclitaxel & Cilostazol. Paclitaxel-eluting stents. Stents with a diameter between 100 and 110% of the distal reference-vessel diameter were implanted, and implantation was performed with a minimum pressure of 14 atm. Direct stenting (i.e., without balloon predilation) was permitted according to the discretion of the physician if the infarct-related vessel was patent (i.e, had a Thrombolysis in Myocardial Infarction [TIMI] flow grade of 2 or 3) at baseline. Study stents were available in diameters ranging from 2.25 to 4.0 mm and in lengths ranging from 8 to 32 mm.. Duration N/A. Concurrent medication/care: Aspirin (324 mg administered in chewable form or 500 mg administered intravenously) was given in the emergency room, after which 300 to 325 mg was given orally every day during the hospitalization and 75 to 81 mg every day thereafter indefinitely. A loading dose of clopidogrel (either 300 mg or 600 mg, at the discretion of the investigator) was administered before catheterization, followed by 75 mg orally every day for at least 6 months (with a recommendation of 1 year or longer).. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Average of 1.5±0.9 in the DES group and 1.4±0.7 in the BMS group). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin given as concomitant therapy). (n=749) Intervention 2: Bare metal stents - BMS- unspecified. Bare-metal stents. Stents with a diameter between 100 and 110% of the distal reference-vessel diameter were implanted, and implantation was performed with a minimum pressure of 14 atm. Direct stenting (i.e., without balloon predilation) was permitted according to the discretion of the physician if the infarct-related vessel was patent (i.e, had a Thrombolysis in Myocardial Infarction [TIMI] flow grade of 2 or 3) at baseline. Study stents were available in diameters ranging from 2.25 to 4.0 mm and in lengths ranging from 8 to 32 mm.. Duration N/A. Concurrent medication/care: Aspirin (324 mg administered in chewable form or 500 mg administered intravenously) was given in the emergency room, after which 300 to 325 mg was given orally every day during the hospitalization and 75 to 81 mg every day thereafter indefinitely. A loading dose of clopidogrel (either 300

Study (subsidiary papers)	HORIZONS-AMI trial: Stone 2009[112] (Mehran 2008[75], Stone 2010[113])
	mg or 600 mg, at the discretion of the investigator) was administered before catheterization, followed by 75 mg orally every day for at least 6 months (with a recommendation of 1 year or longer).. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Average of 1.5±0.9 in the DES group and 1.4±0.7 in the BMS group). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin was used as concomitant therapy).
Funding	Study funded by industry (Sponsored by the Cardiovascular Research Foundation, with grant support from Boston Scientific Corporation and the Medicines Company)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- PACLITAXEL & CILOSTAZOL versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 78/2186, Group 2: 26/715
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported)

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 3 years; Group 1: 123/2103, Group 2: 48/687
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported)
- Actual outcome: Death at 2 years; Group 1: 96/2257, Group 2: 39/749
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Cardiac mortality at early ≤1
- Actual outcome: Cardiac death at 1 year; Group 1: 54/2186, Group 2: 20/715
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported)

Protocol outcome 4: Cardiac mortality at later >1-3 year
- Actual outcome: Cardiac death at 3 years; Group 1: 71/2103, Group 2: 28/687
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not

Study (subsidiary papers)	HORIZONS-AMI trial: Stone 2009[112] (Mehran 2008[75], Stone 2010[113])

reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported)
- Actual outcome: Cardiac death at 2 years; Group 1: 60/2257, Group 2: 24/749
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: Ischemia-driven TLR at 1 year; Group 1: 98/2186, Group 2: 54/715
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported)
- Actual outcome: Ischemia-driven TVR at 1 year; Group 1: 126/2186, Group 2: 63/715
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported)

Protocol outcome 6: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year
- Actual outcome: Ischemia-driven TLR at 3 years; Group 1: 202/2103, Group 2: 107/687
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported)
- Actual outcome: Ischemia-driven TVR at 3 years; Group 1: 265/2103, Group 2: 125/687
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported)
- Actual outcome: Ischemia-driven TLR at 2 years; Group 1: 178/2257, Group 2: 101/749
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: Ischemia-driven TVR at 2 years; Group 1: 236/2257, Group 2: 118/749
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 7: Stent thrombosis at early ≤1
- Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: 58/2186, Group 2: 22/715
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported)
- Actual outcome: Stent thrombosis (probable) at 1 year; Group 1: 12/2257, Group 2: 3/749

Study (subsidiary papers)	HORIZONS-AMI trial: Stone 2009[112] (Mehran 2008[75], Stone 2010[113])
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported) Protocol outcome 8: Stent thrombosis at later >1-3 year - Actual outcome: Stent thrombosis (definite) at 3 years; Group 1: 91/2103, Group 2: 27/687 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported) - Actual outcome: Stent thrombosis (definite) at 2 years; Group 1: 79/2257, Group 2: 26/749 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Stent thrombosis (probable) at 2 years; Group 1: 11/2257, Group 2: 4/749 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Stent thrombosis (probable) at 3 years; Group 1: 12/2103, Group 2: 4/687 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported) Protocol outcome 9: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter at 1 year; Group 1: mean 2.36 mm (SD 0.55); n=2186, Group 2: mean 2.37 mm (SD 0.52); n=715 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 71, Reason: 18 withdrew, 53 lost to follow up (reason not reported); Group 2 Number missing: 34, Reason: 7 withdrew, 27 lost to follow up (reason not reported) Protocol outcome 10: Major bleeding - Actual outcome: Major bleeding (including CABG) at 3 years; Group 1: 205/2103, Group 2: 56/687 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 154, Reason: 41 withdrew, 113 lost to follow up (reason not reported); Group 2 Number missing: 62, Reason: 15 withdrew, 47 lost to follow up (reason not reported)	
Protocol outcomes not reported by the study	TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Myocardial infarction at early ≤1 ; Myocardial infarction at later >1-3 year ; Quality of life; Minor bleeding; Bleeding;

Study (subsidiary papers)	MISSION trial: Van der Hoeven 2008[128] (Atary 2010[7], Boden 2011[13], Boden 2012[14])

Study (subsidiary papers)	MISSION trial: Van der Hoeven 2008[128] (Atary 2010[7], Boden 2011[13], Boden 2012[14])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	(n=310)
Countries and setting	Conducted in Netherlands; Setting: Hospital (single-centre)
Line of therapy	1st line
Duration of study	Intervention + follow up: 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Participants with STEMI symptoms started 9 h before the procedure and the ECG demonstrated STEMI (ST-segment elevation 0.2 mV in 2 contiguous leads in V 1 through V 3 or 0.1 mV in other leads, or (presumed) new left bundle branch block). The target lesion length should be equal to or less than 24 mm
Exclusion criteria	1) age 18 years or 80 years; 2) left main stenosis of 50%; 3) triplevessel disease, defined as 50% stenosis in 3 major epicardial branches; 4) previous PCI or coronary artery bypass grafting of the infarct-related artery; 5) thrombolytic therapy for the index infarction; 5) target vessel reference diameter 2.25mmor 3.75mm; 6) need for mechanical ventilation; 7) contraindication to the use of aspirin, clopidogrel, heparin, or abciximab; 8) known renal failure; or 9) a life expectancy 12 months
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): SES: 59.2 (11.2); BMS: 59.1 (11.6) . Gender (M:F): 241:69. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: 3. Mixed ACS and stable population: 4. Older patients: 5. Renal disease/renal insufficiency: 6. Size of stenosis:
Indirectness of population	No indirectness
Interventions	(n=158) Intervention 1: Drug eluting stents - DES- Sirolimus.. Duration 12 months follow up. Concurrent medication/care: During the study period, all participants were treated according to the institutional STEMI protocol,which included standardised outpatient follow-up. Before the procedure all participants received 300 mg of aspirin, 300 to 600 mg of clopidogrel, and an intravenous bolus of abciximab (25 g/kg), followed by a continuous infusion of 10g/kg/min for 12 h. Aspirin (80 to 100 mg/day) was prescribed indefinitely and clopidogrel (75 mg/day) for 12 months. Participants were treated with beta-blocking agents, statins, and angiotensin-converting enzyme inhibitors or angiotensin II blockers . Indirectness: No indirectness

Study (subsidiary papers)	MISSION trial: Van der Hoeven 2008[128] (Atary 2010[7], Boden 2011[13], Boden 2012[14])
	Further details: 1. Number of stents: 2. Use of antiplatelet therapy: with antiplatelet (300 to 600 mg of clopidogrel before the procedure and 75 mg/day for 12 months). (n=152) Intervention 2: Bare metal stents - BMS- unspecified. Duration 12 months follow up. Concurrent medication/care: During the study period, all participants were treated according to the institutional STEMI protocol, which included standardised outpatient follow-up. Before the procedure all participants received 300 mg of aspirin, 300 to 600 mg of clopidogrel, and an intravenous bolus of abciximab (25 g/kg), followed by a continuous infusion of 10g/kg/min for 12 h. Aspirin (80 to 100 mg/day) was prescribed indefinitely and clopidogrel (75 mg/day) for 12 months. Participants were treated with beta-blocking agents, statins, and angiotensin-converting enzyme inhibitors or angiotensin II blockers. Indirectness: No indirectness Further details: 1. Number of stents: 2. Use of antiplatelet therapy: with antiplatelet (300 to 600 mg of clopidogrel before the procedure and 75 mg/day for 12 months).
Funding	Study funded by industry (Supported by the Netherlands Heart Foundation and by an unrestricted research grant from Guidant Inc.,Nieuwegein, the Netherlands.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death (cardiac and non-cardiac) at 1 year; Group 1: 2/158, Group 2: 4/152; Comments: 1 participant crossed over from the DES group to the BMS group
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death (cardiac and non-cardiac) at 3 years; Group 1: 7/158, Group 2: 10/152
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Cardiac mortality at early ≤1
- Actual outcome: Cardiac mortality at 1 year; Group 1: 2/158, Group 2: 2/152
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Cardiac mortality at later >1-3 year
- Actual outcome: Cardiac mortality at 3 years; Group 1: 3/158, Group 2: 5/152
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Study (subsidiary papers)	MISSION trial: Van der Hoeven 2008[128] (Atary 2010[7], Boden 2011[13], Boden 2012[14])
Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: TVF- target vessel failure at early ≤1 - Actual outcome: Target vessel failure at 1 year; Group 1: 11/158, Group 2: 23/158 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: TVF- target vessel failure at later >1-3 year - Actual outcome: Target vessel failure at 3 years; Group 1: 19/158, Group 2: 30/152 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: TVR at 1 year; Group 1: 8/158, Group 2: 20/152 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: TLR at 1 year; Group 1: 5/158, Group 2: 17/152 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 8: Myocardial infarction at early ≤1 - Actual outcome: MI (Recurrent MI spontaneous and procedure related) at 1 year; Group 1: 9/158, Group 2: 14/152 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 9: Myocardial infarction at later >1-3 year - Actual outcome: MI (Recurrent MI spontaneous and procedure related) at 3 years; Group 1: 12/158, Group 2: 17/152 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 10: Stent thrombosis at early ≤1 - Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: 1/158, Group 2: 1/152 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 11: Stent thrombosis at later >1-3 year - Actual outcome: Stent thrombosis (definite) at 3 years; Group 1: 4/158, Group 2: 1/152	

Study (subsidiary papers)	MISSION trial: Van der Hoeven 2008[128] (Atary 2010[7], Boden 2011[13], Boden 2012[14])
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 12: MLD - Minimal lumen diameter - Actual outcome: MLD- in segment at 1 year; Group 1: mean 2.24 mm (SD 0.55); n=131, Group 2: mean 1.74 mm (SD 0.59); n=124 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 27; Group 2 Number missing: 28 - Actual outcome: MLD- in stent at 1 year; Group 1: mean 2.48 mm (SD 0.52); n=131, Group 2: mean 1.77 mm (SD 0.59); n=124 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 27; Group 2 Number missing: 28	
Protocol outcomes not reported by the study	TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; Major bleeding;

Study (subsidiary papers)	MULTISTRATEGY trial: Valgimigli 2008[122] (Valgimigli 2013[121])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=744)
Countries and setting	Conducted in Italy; Setting: 16 centers in Italy, Argentina, and Spain
Line of therapy	1st line
Duration of study	Follow up (post intervention): 8 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Define
Exclusion criteria	Define
Recruitment/selection of patients	Between October 2004 and April 2007
Age, gender and ethnicity	Age - Mean (SD): BMS group: 64.6 (11.9); DES group: 63.1 (11.6). Gender (M:F): 565:179. Ethnicity: Not reported
Further population details	1. ACS population: STEMI 2. Diabetes: Not stated / Unclear (27% had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear

Study (subsidiary papers)	MULTISTRATEGY trial: Valgimigli 2008[122] (Valgimigli 2013[121])
Indirectness of population	No indirectness
Interventions	(n=372) Intervention 1: Drug eluting stents - DES- Sirolimus. Sirolimus-Eluting Stent. . Duration N/A. Concurrent medication/care: Either tirofiban or abciximab was administered at first medical contact, before arterial sheath insertion during the angiography procedure. Tirofiban was given as a bolus of 25 µg/kg, followed by an 18- to 24-hour infusion at 0.15 µg/kg/min. Abciximab was administered as a bolus of 0.25 mg/kg, followed by a 12-hour infusion at 0.125 µg/kg/min. Heparin was given at 40 to 70 U/kg, targeting an activated clotting time of at least 200 seconds. Patients received aspirin (160-325 mg orally or 250 mg intravenously, followed by 80-125 mg/d orally indefinitely) and clopidogrel (300 mg orally and then 75 mg/d for at least 3 months).. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents inserted: median 1; range 1-4). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=372) Intervention 2: Bare metal stents - BMS- unspecified. Uncoated bare metal stent. Duration N/A. Concurrent medication/care: Either tirofiban or abciximab was administered at first medical contact, before arterial sheath insertion during the angiography procedure. Tirofiban was given as a bolus of 25 µg/kg, followed by an 18- to 24-hour infusion at 0.15 µg/kg/min. Abciximab was administered as a bolus of 0.25 mg/kg, followed by a 12-hour infusion at 0.125 µg/kg/min. Heparin was given at 40 to 70 U/kg, targeting an activated clotting time of at least 200 seconds. Patients received aspirin (160-325 mg orally or 250 mg intravenously, followed by 80-125 mg/d orally indefinitely) and clopidogrel (300 mg orally and then 75 mg/d for at least 3 months).. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents inserted: median 1, range 1-4). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Academic or government funding (Partially supported by a medical school grant from Merck)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 8 months; Group 1: 11/372, Group 2: 15/372
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: Death at 30 days; Group 1: 5/372, Group 2: 8/372
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 3 years; Group 1: 26/372, Group 2: 28/372

Study (subsidiary papers)	MULTISTRATEGY trial: Valgimigli 2008[122] (Valgimigli 2013[121])
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Cardiac mortality at later >1-3 year - Actual outcome: Cardiovascular death at 3 years; Group 1: 21/372, Group 2: 21/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: Clinically driven TVR at 8 months; Group 1: 12/372, Group 2: 38/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TVR at 3 years; Group 1: 23/372, Group 2: 51/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: Myocardial infarction at early ≤1 - Actual outcome: Reinfarction at 8 months; Group 1: 12/372, Group 2: 17/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: Reinfarction at 30 days; Group 1: 5/372, Group 2: 10/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: Stent thrombosis at early ≤1 - Actual outcome: Definite or probable stent thrombosis at 8 months; Group 1: 10/372, Group 2: 15/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 8: Stent thrombosis at later >1-3 year - Actual outcome: Definite or probable stent thrombosis at 3 years; Group 1: 15/372, Group 2: 17/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 9: Minor bleeding	

Study (subsidiary papers)	MULTISTRATEGY trial: Valgimigli 2008[122] (Valgimigli 2013[121])
- Actual outcome: Minor bleeding at 30 days; Group 1: 15/372, Group 2: 26/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 10: Major bleeding - Actual outcome: Major bleeding at 30 days; Group 1: 7/372, Group 2: 8/372 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Cardiac mortality at early ≤1 ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Bleeding; MLD - Minimal lumen diameter;

Study	OCTAMI trial: Guagliumi 2010[46]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=44)
Countries and setting	Conducted in Italy, USA; Setting: Single centre
Line of therapy	1st line
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Eligible patients presented with STEMI <12 h after symptom onset (prolonged chest pain for more than 20 min, unresponsive to nitroglycerin, and ST-segment elevation of at least 1 mm in 2 or more contiguous leads, or true posterior myocardial infarction), an infarct artery in a native coronary vessel with >70% diameter stenosis, a reference vessel diameter of 2.5 to 3.75 mm, and underwent primary PCI with stent implantation
Exclusion criteria	Patients with left main disease, infarct lesions in bypass grafts, cardiogenic shock, renal failure, recent major bleeding, allergy to aspirin or clopidogrel, on anticoagulant therapy, or with no suitable anatomy for OCT (ostial lesions, extreme tortuosity, and large vessels >3.75 mm in diameter)
Recruitment/selection of patients	Consecutive
Age, gender and ethnicity	Age - Mean (SD): DES group: 61.1 (11.4); BMS group: 61.1 (12.4). Gender (M:F): 34/10. Ethnicity: Not

Study	OCTAMI trial: Guagliumi 2010[46]
	reported
Further population details	1. ACS population: STEMI 2. Diabetes: Not stated / Unclear (Mixed (13.6%)). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Drug eluting stents - DES- Zotarolimus. Drug eluting stents (zotarolimus). Duration N/A. Concurrent medication/care: All patients were pre-treated with aspirin 250 mg intravenously and clopidogrel 300 mg orally before PCI, followed by daily administration of clopidogrel 75 mg for at least 6 months after discharge and aspirin indefinitely. During PCI, patients received unfractionated heparin to maintain an activated clotting time of 300 s or more. Patients were readmitted for planned imaging follow-up at 6 months.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin). (n=11) Intervention 2: Bare metal stents - BMS- unspecified. BMS (not specified). Duration N/A. Concurrent medication/care: All patients were pre-treated with aspirin 250 mg intravenously and clopidogrel 300 mg orally before PCI, followed by daily administration of clopidogrel 75 mg for at least 6 months after discharge and aspirin indefinitely. During PCI, patients received unfractionated heparin to maintain an activated clotting time of 300 s or more. Patients were readmitted for planned imaging follow-up at 6 months.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin).
Funding	Study funded by industry (Grant/research support from Boston Scientific Corporation, Medtronic Vascular, LightLab Imaging)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- ZOTAROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 0/33, Group 2: 0/11
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Hyperlipidemia (30.3% vs 63.6%); Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: TLR at 1 year; Group 1: 2/33, Group 2: 1/11

Study	OCTAMI trial: Guagliumi 2010[46]
Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Hyperlipidemia (30.3% vs 63.6%); Group 1 Number missing: ; Group 2 Number missing: - Actual outcome: TVR at 1 year; Group 1: 2/33, Group 2: 0/11 Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Hyperlipidemia (30.3% vs 63.6%); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 1 year; Group 1: 0/33, Group 2: 0/11 Risk of bias: All domain - Very high, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: Hyperlipidemia (30.3% vs 63.6%); Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study (subsidiary papers)	PASEO trial: Di Lorenzo 2009[33] (Di Lorenzo 2009[34])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=270)
Countries and setting	Conducted in Italy; Setting: Single centre trial, Italy.
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 2 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ST-segment elevation of 1 mm or more in 2 or more contiguous electrocardiograph leads or with presumably new left bundle branch block
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	1) chest pain for more than 30 min; 2) ST-segment elevation of 1 mm or more in 2 or more contiguous electrocardiograph leads or with presumably new left bundle branch block; 3) hospital admission within 12 hours from symptoms onset.

Study (subsidiary papers)	PASEO trial: Di Lorenzo 2009[33] (Di Lorenzo 2009[34])
Exclusion criteria	1) active internal bleeding or a history of bleeding diathesis within the previous 30 days; 2) history of intracranial hemorrhage, intracranial neoplasm, arteriovenous malformation or aneurysm; 3) known allergy to sirolimus, paclitaxel, heparin, aspirin, or clopidogrel; 4) history of stroke within 30 days or any history of hemorrhagic stroke; 5) major surgical procedure or severe physical trauma within the previous month; 6) history, symptoms, or findings suggestive of aortic dissection; 7)thrombolytic/fibrinolytic therapy within 24 h; 8) history of thrombocytopenia;9) haemorrhagic retinopathy; 10) patients on warfarin or acenocoumarol within ternational normalised ratio >2; and 11) pregnancy.
Recruitment/selection of patients	From 1st October 2003 to 31st December 2005
Age, gender and ethnicity	Age - Mean (SD): 62.5 years. Gender (M:F): 190/80. Ethnicity: Not reported
Further population details	1. ACS population: STEMI (Patients had acute STEMI). 2. Diabetes: Without diabetes (PES group: 23.3%, SES group: 27.8%, BMS group: 25.6%). 3. Mixed ACS and stable population: ACS 4. Older patients: < 75 years (Mean age: 62.5 years). 5. Renal disease/renal insufficiency: Not applicable 6. Size of stenosis: Not applicable
Indirectness of population	No indirectness
Interventions	(n=90) Intervention 1: Drug eluting stents - DES- Paclitaxel. Participants were randomised to paclitaxel-eluting stents.. Duration 2 years. Concurrent medication/care: All patients received 70 U/kg intravenous bolus of unfractionated heparin plus 1000 U/h infusion (to maintain an activated clotting time of at least 200 s), aspirin intravenously (500 mg), and clopidogrel (300-mg loading dose). All patients received upstream glycoproteinIIb/IIIa inhibitors as a routine adjunctive therapy before primary PCI. Post-interventional antiplatelet therapy for all patients included in the study groups consisted of aspirin (100 mg) indefinitely and clopidogrel (75 mg for 6 months).. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (>1 stent: PES group - 15.6%). 2. Use of antiplatelet therapy: with antiplatelet therapy (Clopidogrel (75 mg for 6 months) and aspirin (100 mg)). (n=90) Intervention 2: Drug eluting stents - DES- Sirolimus. Participants were randomised to sirolimus-eluting stents.. Duration 2 years. Concurrent medication/care: All patients received 70 U/kg intravenous bolus of unfractionated heparin plus 1000 U/h infusion (to maintain an activated clotting time of at least 200 s), aspirin intravenously (500 mg), and clopidogrel (300-mg loading dose). All patients received upstream glycoproteinIIb/IIIa inhibitors as a routine adjunctive therapy before primary PCI. Post-interventional antiplatelet therapy for all patients included in the study groups consisted of aspirin (100 mg) indefinitely and clopidogrel (75 mg for 6 months).. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (>1 stent: SES group -22.2%). 2. Use of antiplatelet therapy: with antiplatelet therapy (Clopidogrel (75 mg for 6 months) and aspirin (100 mg)). (n=90) Intervention 3: Bare metal stents - BMS- unspecified. Participants were randomised to bare-metal

Study (subsidiary papers)	PASEO trial: Di Lorenzo 2009[33] (Di Lorenzo 2009[34])
	stents.2 years. Duration 2 years. Concurrent medication/care: All patients received 70 U/kg intravenous bolus of unfractionated heparin plus 1000 U/h infusion (to maintain an activated clotting time of at least 200 s), aspirin intravenously (500 mg), and clopidogrel (300-mg loading dose). All patients received upstream glycoproteinIIb/IIIa inhibitors as a routine adjunctive therapy before primary PCI. Post-interventional antiplatelet therapy for all patients included in the study groups consisted of aspirin (100 mg) indefinitely and clopidogrel (75 mg for 6 months).. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (>1 stent: BMS group - 10%). 2. Use of antiplatelet therapy: with antiplatelet therapy (Clopidogrel (75 mg for 6 months) and aspirin (100 mg)).
Funding	Academic or government funding (San Giuseppe Moscati Hospital funded the study)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES (SIROLIMUS +PACLITAXEL) versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: Observed events 7 n=180 ; Group 2: Observed events 6 n=90; HR 0.66; Lower CI 0.19 to Upper CI 2.34 (PES vs BMS); HR 0.49; Lower CI 0.12 to Upper CI 1.96 (SES vs BMS)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 2 years; Group 1: Observed events 11 n=180 ; Group 2: Observed events 9 n=90; HR 0.66; Lower CI 0.23 to Upper CI 1.85 (PES vs BMS); HR 0.54; Lower CI 0.18 to Upper CI 1.61 (SES vs BMS)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: Target lesion vascularisation at 1 year; Group 1: Observed events 7 n=180 ; Group 2: Observed events 13 n=90; HR 0.29; Lower CI 0.095 to Upper CI 0.89 (PES vs BMS); HR 0.21; Lower CI 0.06 to Upper CI 0.75 (SES vs BMS)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 4: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year
- Actual outcome: Target lesion vascularisation at 2 years; Group 1: Observed events 9 n=180 ; Group 2: Observed events 16 n=90; HR 0.29; Lower CI 0.11 to Upper CI 0.8 (PES vs BMS); HR 0.23; Lower CI 0.08 to Upper CI 0.68 (SES vs BMS)
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Study (subsidiary papers)	PASEO trial: Di Lorenzo 2009[33] (Di Lorenzo 2009[34])
Protocol outcome 5: Myocardial infarction at early ≤1 - Actual outcome: Re-infarction at 1 year; Group 1: Observed events 7 n=180 ; Group 2: Observed events 6 n=90; HR 0.49; Lower CI 0.12 to Upper CI 1.96 (PES vs BMS); HR 0.65; Lower CI 0.18 to Upper CI 2.23 (SES vs BMS) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 6: Myocardial infarction at later >1-3 year - Actual outcome: Re-infarction at 2 years; Group 1: Observed events 11 n=180 ; Group 2: Observed events 10 n=90; HR 0.8; Lower CI 0.16 to Upper CI 1.42 (PES vs BMS); HR 0.58; Lower CI 0.21 to Upper CI 1.59 (SES vs BMS) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 7: Stent thrombosis at early ≤1 - Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: Observed events 1 n=180 ; Group 2: Observed events 1 n=90; HR 0.5; Lower CI 0.045 to Upper CI 5.47 (PES vs BMS); HR 0.0015; Lower CI 0 to Upper CI 147346 (SES vs BMS) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 8: Stent thrombosis at later >1-3 year - Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: Observed events 1 n=180 ; Group 2: Observed events 1 n=90; HR 0.5; Lower CI 0.045 to Upper CI 5.47 (PES vs BMS); HR 0.0015; Lower CI 0 to Upper CI 147346 (SES vs BMS) Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study (subsidiary papers)	PASSION trial: Laarman 2006[67] (Dirksen 2008[36])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=619)
Countries and setting	Conducted in Netherlands; Setting: Onze Lieve Vrouwe Gasthuis in Amsterdam and St. Antonius Hospitalin Nieuwegein
Line of therapy	Not applicable

Study (subsidiary papers)	PASSION trial: Laarman 2006[67] (Dirksen 2008[36])
Duration of study	Intervention time: 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Acute myocardial infarction with ST-segment elevation (>20minutes of chest pain and at least 1 mm of ST-segment elevation in at least two contiguous leads or a new left bundle-branch block)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Between the ages of 18 and 80 years if they had had an acute myocardial infarction with ST-segment elevation (>20 minutes of chest pain and at least 1 mm of ST-segment elevation in at least two contiguous leads or anew left bundle-branch block), reperfusion was expected to be achieved within 6hours after the onset of symptoms, and the native coronary artery was considered to be suitable for primary PCI with stent implantation.
Exclusion criteria	Patients were excluded if they had received thrombolytic therapy; the infarction was caused by in-stent thrombosis or restenosis; there was a contraindication to aspirin, clopidogrel, or both; patients were participating in another clinical trial; cardiogenic shock was evident before randomisation; the neurologic outcome after resuscitation was uncertain; they had undergone intubation, ventilation, or both; there was known intracranial disease; or the estimated life expectancy was less than 6 months.
Recruitment/selection of patients	Based on inclusion criteria for trial, between 28th March 2003 and 12st December 2004.
Age, gender and ethnicity	Age - Mean (SD): 61 years. Gender (M:F): 470/149. Ethnicity: Not reported
Further population details	1. ACS population : STEMI (100% patients who had myocardial infarction with ST-segment elevation). 2. Diabetes: Without diabetes (PES group - 10%; Uncoated stent group - 12%). 3. Mixed ACS and stable population: Not applicable 4. Older patients: < 75 years (Mean age = 61 years). 5. Renal disease/renal insufficiency: Not applicable 6. Size of stenosis: Not applicable
Indirectness of population	No indirectness
Interventions	(n=310) Intervention 1: Drug eluting stents - DES- Paclitaxel. Following randomisation, participants were randomised to paclitaxel-eluting stent.. Duration 1 year. Concurrent medication/care: Aspirin (at a dose of 100 to 500 mg) and clopidogrel (300mg) when patients first arrived at the hospital. A glycoprotein IIb/IIIa receptor blocker was administered at the discretion of the operator. A bolus of 10,000IU of unfractionated heparin was administered before the procedure. 80 to 100 mg of aspirin prescribed daily for life and 75 mg of clopidogrel daily for at least 6 months. . Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (If dissection or incomplete coverage of the lesion occurred, additional stents of the same type as the assigned stent were used.). 2. Use of antiplatelet therapy: with antiplatelet therapy (Clopidogrel daily for 6 months.).

Study (subsidiary papers)	PASSION trial: Laarman 2006[67] (Dirksen 2008[36])
	(n=309) Intervention 2: Bare metal stents - BMS- unspecified. Following randomisation, participants were randomised to uncoated stent.. Duration 1 year. Concurrent medication/care: Aspirin (at a dose of 100 to 500 mg) and clopidogrel (300mg) when patients first arrived at the hospital. A glycoprotein IIb/IIIa receptor blocker was administered at the discretion of the operator. A bolus of 10,000IU of unfractionated heparin was administered before the procedure. 80 to 100 mg of aspirin prescribed daily for life and 75 mg of clopidogrel daily for at least 6 months.. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (If dissection or incomplete coverage of the lesion occurred, additional stents of the same type as the assigned stent were used.). 2. Use of antiplatelet therapy: with antiplatelet therapy (Clopidogrel daily for 6 months.).
Funding	Academic or government funding (Johnson & Johnson, and Medtronic; Dr. Dirksen, lecture fees from Boston Scientific; Dr. Kiemeneij, lecture fees from Terumo Medical andCordis, Johnson & Johnson, and royalties from Boston Scientific; and Dr.Slagboom, consulting fees from Biotronik and lecture fees from Cordis, Johnson& Johnson. No other potential conflict of interest relevant to this article was reported.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- PACLITAXEL versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: All-cause mortality at 1 year; Group 1: 14/302, Group 2: 20/303
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 8, Reason: Not reported; Group 2 Number missing: 6, Reason: Not reported

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: All-cause mortality at 2 years; Group 1: 21/303, Group 2: 27/303
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7, Reason: Not reported; Group 2 Number missing: 4, Reason: Not reported

Protocol outcome 3: Cardiac mortality at early ≤1
- Actual outcome: Cardiac mortality at 1 year; Group 1: 12/302, Group 2: 19/303
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 8, Reason: Not reported; Group 2 Number missing: 6, Reason: Not reported

Protocol outcome 4: Cardiac mortality at later >1-3 year
- Actual outcome: Cardiac mortality at 2 years; Group 1: 17/303, Group 2: 22/303

Study (subsidiary papers)	PASSION trial: Laarman 2006[67] (Dirksen 2008[36])
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 7, Reason: Not reported; Group 2 Number missing: 4, Reason: Not reported Protocol outcome 5: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: Target lesion revascularisation at 1 year; Group 1: 16/302, Group 2: 23/303 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 8, Reason: Not reported; Group 2 Number missing: 6, Reason: Not reported Protocol outcome 6: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: Target lesion revascularisation (PCI + CABG) at 2 years; Group 1: 18/298, Group 2: 29/299 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: Not reported; Group 2 Number missing: 10, Reason: Not reported Protocol outcome 7: Myocardial infarction at early ≤1 - Actual outcome: Recurrent MI at 1 year; Group 1: 5/302, Group 2: 6/303 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 8, Reason: Not reported; Group 2 Number missing: 6, Reason: Not reported - Actual outcome: Recurrent MI at 30 days; Group 1: 2/308, Group 2: 5/306 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 3, Reason: Not reported Protocol outcome 8: Myocardial infarction at later >1-3 year - Actual outcome: Recurrent MI at 2 years; Group 1: 9/298, Group 2: 7/299 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12, Reason: Not reported; Group 2 Number missing: 10, Reason: Not reported	
Protocol outcomes not reported by the study	TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study	Ribamar Costa 2012[95]

Study	Ribamar Costa 2012[95]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Brazil; Setting: Single centre
Line of therapy	1st line
Duration of study	Follow up (post intervention): 12 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients who initially presented with acute coronary syndrome and the culprit lesion had to be located in a native coronary artery of 2.5 to 3.5 mm in diameter and had to be treated with a single stent implantation (up to 33 mm in length)
Exclusion criteria	Patients with ST-segment elevation myocardial infarction (MI) treated in the very early phase (primary or rescue percutaneous coronary intervention [PCI]), restenotic lesions, lesions located at grafts and at the left main stem. Patients with planned surgery within one year of the intervention or those with previous history of major bleeding or allergy to aspirin or thienopyridine were excluded as well. From the angiographic point of view, major exclusion criteria were the lack of edge segments (ostial lesions and presence of major side branches within the 5 mm proximal or distal to the stent) and pre-PCI TIMI flow ≤1.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): BMS group: 55.6 (6.4); DES group: 57 (7.1). Gender (M:F): 28/12. Ethnicity: Not reported
Further population details	1. ACS population: Not stated / Unclear 2. Diabetes: Not stated / Unclear (15/40 had diabetes). 3. Mixed ACS and stable population: ACS 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Drug eluting stents - DES - unspecified. DES (Cypher Select™; Cordis, Miami Lakes, FL, USA).. Duration N/A. Concurrent medication/care: After the procedure, aspirin (100 mg/day) was prescribed indefinitely and clopidogrel (75 mg/day) for at least 12 months. Unless in the presence of a formal contraindication, beta-blockers, angiotensin-converting-enzyme (ACE) inhibitors and statins were prescribed to all patients, according to current guidelines. . Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: with antiplatelet therapy

Study	Ribamar Costa 2012[95]
	(n=20) Intervention 2: Bare metal stents - BMS- unspecified. BMS (Driver™; Medtronic, Santa Clara, CA, USA). Duration N/A. Concurrent medication/care: After the procedure, aspirin (100 mg/day) was prescribed indefinitely and clopidogrel (75 mg/day) for at least 12 months. Unless in the presence of a formal contraindication, beta-blockers, angiotensin-converting-enzyme (ACE) inhibitors and statins were prescribed to all patients, according to current guidelines.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Equipment / drugs provided by industry (The stents used in this study were donated by Cordis Corporation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES - UNSPECIFIED versus BMS- UNSPECIFIED Protocol outcome 1: All-cause mortality at early ≤1 - Actual outcome: Death at 1 year; Group 1: 0/20, Group 2: 0/20 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 1 year; Group 1: 0/20, Group 2: 0/20 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Stent thrombosis at early ≤1 - Actual outcome: Stent thrombosis at 1 year; Group 1: 0/20, Group 2: 0/20 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter (proximal edge) at 1 year; Group 1: mean 2.74 mm (SD 0.3); n=19, Group 2: mean 2.86 mm (SD 0.66); n=18 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 2; Group 2 Number missing: 1 - Actual outcome: Minimal lumen diameter (distal edge) at 1 year; Group 1: mean 2.8 mm (SD 0.29); n=20, Group 2: mean 2.85 mm (SD 0.71); n=20 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent

Study	Ribamar Costa 2012[95]
	thrombosis at later >1-3 year ; Minor bleeding; Bleeding; Major bleeding;

Study (subsidiary papers)	EXAMINATION trial: Sabate 2012[104] (Brugaletta 2012[22], Sabate 2014[102])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1498)
Countries and setting	Conducted in Spain, Italy, Netherlands; Setting: Multicentre
Line of therapy	1st line
Duration of study	Intervention + follow up: 1 year
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Any patient presenting with STEMI with the following electrocardiogram criteria: at least 1 mm in two or more standard leads or at least 2 mm in two or more contiguous precordial leads or left bundle-branch block that was not known to be old, within the first 48 h after the symptoms onset requiring emergent percutaneous coronary intervention with a vessel size ranging between 2·25 mm and 4·0 mm without other anatomical restrictions could be included
Exclusion criteria	age younger than 18 years, pregnancy, patients with known intolerance to aspirin, clopidogrel, heparin, stainless steel, everolimus or contrast material, patients on chronic treatment with anti-vitamin K agents, and STEMI secondary to stent thrombosis
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 60·8 (12); BMS group: 61·6 (13). Gender (M:F): 1244/254. Ethnicity: Not reported
Further population details	1. ACS population : STEMI 2. Diabetes: Not stated / Unclear (17% with diabetes). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear (Mixed). 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=751) Intervention 1: Drug eluting stents - DES- Everolimus. second generation everolimus-eluting stent (Xience™ V stent; Abbott Vascular, Santa Clara, CA, USA). Duration N/A. Concurrent medication/care: At the index procedure, patients received appropriate anticoagulation and other therapy according to standard hospital practice. Either unfractionated heparin or bivalirudin might be used for procedural anticoagulation.

Study (subsidiary papers)	EXAMINATION trial: Sabate 2012[104] (Brugaletta 2012[22], Sabate 2014[102])
	The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the investigator. Aspirin (loading dose 250–500 mg) and clopidogrel (loading dose of at least 300 mg) had to be given before percutaneous coronary intervention for those patients not on chronic antiplatelet treatment. Neither prasugrel nor ticagrelor were approved during the recruitment period. Clopidogrel was prescribed for at least 1 year (75 mg per day) and aspirin (100 mg) indefinitely.. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (Number of stents per patient 1·4 (0·7)). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=747) Intervention 2: Bare metal stents - BMS - Cobalt Chronium. a cobalt-chromium BMS (Multilink-Vision® stent; Abbott Vascular, Santa Clara, CA, USA). Duration N/A. Concurrent medication/care: At the index procedure, patients received appropriate anticoagulation and other therapy according to standard hospital practice. Either unfractionated heparin or bivalirudin might be used for procedural anticoagu lation. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the investigator. Aspirin (loading dose 250–500 mg) and clopidogrel (loading dose of at least 300 mg) had to be given before percutaneous coronary intervention for those patients not on chronic antiplatelet treatment. Neither prasugrel nor ticagrelor were approved during the recruitment period. Clopid ogrel was prescribed for at least 1 year (75 mg per day) and aspirin (100 mg) indefi nitely.. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (1·4 (0·6)). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Academic or government funding (partially funded by an unrestricted grant from Abbott Vascular to the Spanish Heart Foundation (promoter))

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- EVEROLIMUS versus BMS - COBALT CHRONIUM

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 26/751, Group 2: 26/747
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 2 years; Group 1: 32/751, Group 2: 37/747
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0

Protocol outcome 3: Cardiac mortality at early ≤1
- Actual outcome: Cardiac death at 1 year; Group 1: 24/751, Group 2: 21/747

Study (subsidiary papers)	EXAMINATION trial: Sabate 2012[104] (Brugaletta 2012[22], Sabate 2014[102])
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 4: Cardiac mortality at later >1-3 year - Actual outcome: Cardiac death at 2 years; Group 1: 28/751, Group 2: 28/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 5: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: TLR at 1 year; Group 1: 16/751, Group 2: 37/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 - Actual outcome: TVR at 1 year; Group 1: 28/751, Group 2: 51/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 6: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TVR at 2 years; Group 1: 36/751, Group 2: 59/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 7: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 1 year; Group 1: 10/751, Group 2: 15/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 8: Myocardial infarction at later >1-3 year - Actual outcome: Myocardial infarction at 2 years; Group 1: 14/751, Group 2: 18/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 9: Stent thrombosis at early ≤1 - Actual outcome: Definite stent thrombosis at 1 year; Group 1: 4/751, Group 2: 14/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 - Actual outcome: Probable stent thrombosis at 1 year; Group 1: 3/751, Group 2: 5/747 Risk of bias: All domain - ; Indirectness of outcome: No indirectness	

Study (subsidiary papers)	EXAMINATION trial: Sabate 2012[104] (Brugaletta 2012[22], Sabate 2014[102])
Protocol outcome 10: Stent thrombosis at later >1-3 year - Actual outcome: Stent thrombosis (definite or probable) at 2 years; Group 1: 10/751, Group 2: 21/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 11: Minor bleeding - Actual outcome: Minor bleeding at 1 year; Group 1: 21/751, Group 2: 30/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0 Protocol outcome 12: Major bleeding - Actual outcome: Major bleeding at 1 year; Group 1: 9/751, Group 2: 12/747 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0 ; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Quality of life; Bleeding; MLD - Minimal lumen diameter;

Study (subsidiary papers)	SESAMI trial: Menichelli 2007[76] (Violini 2010[131])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=320)
Countries and setting	Conducted in Italy; Setting: San Camillo Hospital, Rome, Italy (single center trial)
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 12 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Standard morphologic criteria were used to characterise the complexity of the lesions at baseline and to identify angiographic complications
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients were included if they were >18 years of age, had symptoms of acute MI for ≥30 minutes but ≤12 hours, and had ≥1 mm ST-segment elevation in at least 2 contiguous leads or left bundle-branch block.
Exclusion criteria	Cardiogenic shock (systolic blood pressure <80 mm Hg for >30 minutes or need for intravenous pressors or intra-aortic balloon counterpulsation); a history of bleeding diathesis, leukopenia, thrombocytopenia, or

Study (subsidiary papers)	SESAMI trial: Menichelli 2007[76] (Violini 2010[131])
	severe hepatic or renal dysfunction; non-cardiac illness associated with a life expectancy of <1 year; left main coronary artery or graft disease; participation in another study; or inability to give informed consent owing to prolonged cardiopulmonary resuscitation. Excluded patients received clinically appropriate treatment.
Recruitment/selection of patients	Patients with suspected acute MI who were admitted directly to the cardiac catheterisation laboratory. Once blood flow was established (spontaneously or by balloon inflation), the operator determined if the patient qualified for randomisation. The infarct-related vessel had to be a native coronary artery with a visually estimated reference diameter >2.5 and ≤4.0 mm.
Age, gender and ethnicity	Age - Median (range): 63 years (sirolimus-eluting stent); 62 years (bare-metal stent). Gender (M:F): 128/32. Ethnicity: Not reported
Further population details	1. ACS population: STEMI (Mean % of study population - 98.4%). 2. Diabetes: Without diabetes (SES group: 17.5%; BMS group: 23.7%). 3. Mixed ACS and stable population: Not applicable 4. Older patients: < 75 years (Median values (IQR) years: SES group - 63 (54-70); BMS group - 62 (52-72)). 5. Renal disease/renal insufficiency: Not applicable 6. Size of stenosis: Not applicable
Indirectness of population	No indirectness
Interventions	(n=160) Intervention 1: Drug eluting stents - DES- Sirolimus. Following randomisation, sirolimus-eluting stent of the same diameter as the reference vessel was used. Clopidogrel was given as a bolus of 4 tablets immediately after the procedure and was continued for 1 year. . Duration 12 months (1 year). Concurrent medication/care: The study protocol recommended that aspirin (500 mg intravenously) and beta-blockers (in the absence of contraindications) be administered in the emergency room. Patients were then taken immediately to the cardiac catheterisation laboratory to undergo coronary angiography. Dilation after stent placement was at the operator's discretion. Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: with antiplatelet therapy (Clopidogrel was given as a bolus of 4 tablets immediaty after the procedure and was continued for 1 year). (n=160) Intervention 2: Bare metal stents - BMS- unspecified. Following randomisation, bare-metal stent of the same diameter as the reference vessel was used. Clopidogrel was given as a bolus of 4 tablets immediately after the procedure and was continued for 1 year. . Duration 12 months (1 year). Concurrent medication/care: The study protocol recommended that aspirin (500 mg intravenously) and beta-blockers (in the absence of contraindications) be administered in the emergency room. Patients were then taken immediately to the cardiac catheterisation laboratory to undergo coronary angiography. Dilation after stent placement was at the operator's discretion.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: (Clopidogrel was given as a bolus of 4 tablets immediaty after the procedure and was continued for 1 year).
Funding	Funding not stated

Study (subsidiary papers)	SESAMI trial: Menichelli 2007[76] (Violini 2010[131])

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 3/154, Group 2: 7/153
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: Not clearly reported; Group 2 Number missing: 7, Reason: Not clearly reported

Protocol outcome 2: All-cause mortality at later >1-3 year
- Actual outcome: Death at 3 years; Group 1: 5/157, Group 2: 8/156
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Not clearly reported; Group 2 Number missing: 4, Reason: Not clearly reported

Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at early ≤1
- Actual outcome: Target lesion revascularisation at 1 year; Group 1: 7/154, Group 2: 18/153
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: Not clearly reported; Group 2 Number missing: 7, Reason: Not clearly reported
- Actual outcome: Target vessel revascularisation at 1 year; Group 1: 8/154, Group 2: 22/153
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: Not clearly reported; Group 2 Number missing: 7, Reason: Not clearly reported

Protocol outcome 4: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year
- Actual outcome: Target lesion revascularisation at 3 years; Group 1: 11/157, Group 2: 21/156
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Not clearly reported; Group 2 Number missing: 4, Reason: Not clearly reported
- Actual outcome: Target vessel revascularisation at 3 years; Group 1: 13/157, Group 2: 25/156
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Not clearly reported; Group 2 Number missing: 4, Reason: Not clearly reported

Protocol outcome 5: Myocardial infarction at early ≤1
- Actual outcome: Reinfarction at 1 year; Group 1: 3/154, Group 2: 3/153

Study (subsidiary papers)	SESAMI trial: Menichelli 2007[76] (Violini 2010[131])
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: Not clearly reported; Group 2 Number missing: 7, Reason: Not clearly reported Protocol outcome 6: Myocardial infarction at later >1-3 year - Actual outcome: Reinfarction at 3 years; Group 1: 4/157, Group 2: 4/156 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Not clearly reported; Group 2 Number missing: 4, Reason: Not clearly reported Protocol outcome 7: Stent thrombosis at early ≤1 - Actual outcome: Stent thrombosis (definite) at 1 year; Group 1: 2/154, Group 2: 1/153 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: Not clearly reported; Group 2 Number missing: 7, Reason: Not clearly reported - Actual outcome: Stent thrombosis (probable/possible) at 1 year; Group 1: 5/154, Group 2: 6/153 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 6, Reason: Not clearly reported; Group 2 Number missing: 7, Reason: Not clearly reported Protocol outcome 8: Stent thrombosis at later >1-3 year - Actual outcome: Stent thrombosis (definite) at 3 years; Group 1: 3/157, Group 2: 2/156 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 3, Reason: Not clearly reported; Group 2 Number missing: 4, Reason: Not clearly reported	
Protocol outcomes not reported by the study	Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study (subsidiary papers)	SOS trial: Brilakis 2009[19] (Brilakis 2011[18])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in USA; Setting: Multicentre (5 clinical sites)
Line of therapy	1st line

Study (subsidiary papers)	SOS trial: Brilakis 2009[19] (Brilakis 2011[18])
Duration of study	Intervention + follow up: Median follow up 35 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	The inclusion criteria for the study were: 1) age ≥18 years; 2) 1 or more 50% to 99% de novo or restenotic lesions in an SVG that were between 2.5 and 4.0 mm in diameter; 3) need for percutaneous coronary intervention (PCI) in the opinion of the attending cardiologist; and 4) willingness to return for repeat graft angiography at 12 months and be contacted after 1, 6, 12, and 24 months for clinical follow-up.
Exclusion criteria	1) prior brachytherapy in the target vessel; 2) left ventricular ejection fraction <25%; 3) hemorrhagic diatheses; 4) contraindications or allergy to aspirin, thienopyridines, paclitaxel, or stainless steel; 5) history of anaphylaxis to iodinated contrast medium; 6) use of paclitaxel within 12 months before study entry or current use of colchicine; 7) serum creatinine level >2.0 mg/dl; 8) leukocyte count <3,500/mm3; 9) platelet count <100,000/mm3; 10) recent positive pregnancy test, breast-feeding, or possibility of a future pregnancy; and 11) coexisting conditions limiting life expectancy to <24 months or that could affect a patient's compliance with the protocol.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): BMS group: 67 (9); DES group 66 (9). Gender (M:F): Define. Ethnicity: 93.75% white, 2.5% black, 3.75% hispanic
Further population details	1. ACS population: Not stated / Unclear (Mixed: 22.5% NSTEMI). 2. Diabetes: Not stated / Unclear (Mixed: 44% diabetes). 3. Mixed ACS and stable population: Not stated / Unclear (Mixed: 31% stable angina, 37.5% unstable angina). 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: Drug eluting stents - DES- Paclitaxel. Paclitaxel-eluting stent. Duration N/A. Concurrent medication/care: Before stenting, all patients received oral aspirin (325 mg daily) and oral clopidogrel (a loading dose of 300 to 600 mg) as soon as possible but within 24 h of the procedure. Patients receiving daily clopidogrel for 72 h before stenting were not required to receive a clopidogrel loading dose. Aspirin was administered indefinitely after stenting. Clopidogrel was initially recommended for 6 months after PES placement and for at least 1 month after BMS placement. Since December 2006, a minimum of 1 year of clopidogrel was recommended after PES placement.. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (1.54 (0.84) per patient). 2. Use of antiplatelet therapy: with antiplatelet therapy

Study (subsidiary papers)	SOS trial: Brilakis 2009[19] (Brilakis 2011[18])
	(n=39) Intervention 2: Bare metal stents - BMS- unspecified. Bare metal stent, type unspecified. Duration N/A. Concurrent medication/care: Before stenting, all patients received oral aspirin (325 mg daily) and oral clopidogrel (a loading dose of 300 to 600 mg) as soon as possible but within 24 h of the procedure. Patients receiving daily clopidogrel for ≥72 h before stenting were not required to receive a clopidogrel loading dose. Aspirin was administered indefinitely after stenting. Clopidogrel was initially recommended for 6 months after PES placement and for at least 1 month after BMS placement. Since December 2006, a minimum of 1 year of clopidogrel was recommended after PES placement.. Indirectness: No indirectness Further details: 1. Number of stents: Multiple stents (1.56 (0.72) per patient). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Academic or government funding (a Veterans Affairs VISN-17 Startup Award, and the Clark R. Gregg fund of the Harris Methodist Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- PACLITAXEL versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at later >1-3 year
- Actual outcome: Death at Median 35 months; Group 1: 10/41, Group 2: 5/39
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Cardiac mortality at later >1-3 year
- Actual outcome: Cardiac death at Median 35 months; Group 1: 3/41, Group 2: 5/39
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: TVF- target vessel failure at later >1-3 year
- Actual outcome: TVF at Median 35 months; Group 1: 14/41, Group 2: 28/39
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year
- Actual outcome: TLR at Median 35 months; Group 1: 4/41, Group 2: 16/39
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome: TVR at Median 35 months; Group 1: 9/41, Group 2: 19/39

Study (subsidiary papers)	SOS trial: Brilakis 2009[19] (Brilakis 2011[18])
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Myocardial infarction at later >1-3 year - Actual outcome: Myocardial infarction at Median 35 months; Group 1: 7/41, Group 2: 18/39 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 6: Stent thrombosis at later >1-3 year - Actual outcome: Definite or probable stent thrombosis at Median 35 months; Group 1: 1/41, Group 2: 6/39 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 7: MLD - Minimal lumen diameter - Actual outcome: MLD (in stent) at 1 year; Group 1: mean 2.31 mm (SD 0.8); n=33, Group 2: mean 1.39 mm (SD 1.03); n=33 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 8; Group 2 Number missing: 6	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; Cardiac mortality at early ≤1 ; TVF- target vessel failure at early ≤1 ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; Myocardial infarction at early ≤1 ; Quality of life; Stent thrombosis at early ≤1 ; Minor bleeding; Bleeding; Major bleeding;

Study	Steinwender 2008[111]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=16)
Countries and setting	Conducted in Austria; Setting: Not reported
Line of therapy	1st line
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with a first ST-elevation anterior myocardial infarction who were eligible for primary percutaneous

Study	Steinwender 2008[111]
	coronary intervention
Exclusion criteria	Not reported
Recruitment/selection of patients	Consecutive patients
Age, gender and ethnicity	Age - Mean (SD): BMS group: 58 (10); DMS group 53 (9). Gender (M:F): 12/4. Ethnicity: Not reported
Further population details	1. ACS population : STEMI 2. Diabetes: Not stated / Unclear (7/16 had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=8) Intervention 1: Drug eluting stents - DES- Sirolimus. Sirolimus eluting stents - cypher stents . Duration N/A. Concurrent medication/care: On top of standard antiplatelet treatment, all patients received a weight-adjusted abciximab bolus immediately before the intervention. Post-interventional therapy consisted of aspirin (100mg/d), clopidogrel (75mg/d for 3mo), ß-blockers, angiotensin-converting enzyme or receptor blockers, and a statin, if indicated. The second day after stent implantation, G-CSF therapy (Neupogen, Amgen, Thousand Oaks, Calif., USA) at a daily dose of 10 µg/kg body weight divided into 2 subcutaneous injections, was initiated.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (2 overlapping stents were used). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=8) Intervention 2: Bare metal stents - BMS- unspecified. Bare-metal stents - driver stents. Duration N/A. Concurrent medication/care: On top of standard antiplatelet treatment, all patients received a weight-adjusted abciximab bolus immediately before the intervention. Post-interventional therapy consisted of aspirin (100mg/d), clopidogrel (75mg/d for 3mo), ß-blockers, angiotensin-converting enzyme or –receptor blockers, and a statin, if indicated. The second day after stent implantation, G-CSF therapy (Neupogen, Amgen, Thousand Oaks, Calif., USA) at a daily dose of 10 µg/kg body weight divided into 2 subcutaneous injections, was initiated.. Indirectness: No indirectness Further details: 1. Number of stents: Single stent 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 6 months; Group 1: 0/8, Group 2: 0/8
Risk of bias: All domain - High, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: TIIMI flow grade before PCI: Grade 2 (25% vs 12%); Group 1 Number

Study	Steinwender 2008[111]
missing: ; Group 2 Number missing: Protocol outcome 2: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter at 6 months; Group 1: mean 2.6 mm (SD 0.2); n=8, Group 2: mean 1.3 mm (SD 0.7); n=8 Risk of bias: All domain - High, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: TIIMI flow grade before PCI: Grade 2 (25% vs 12%); Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at early ≤1 ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year ; Minor bleeding; Bleeding; Major bleeding;

Study	Strozzi 2007[116]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=119)
Countries and setting	Conducted in Croatia; Setting: Not reported.
Line of therapy	Not applicable
Duration of study	Follow up (post intervention): 6 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Diagnosis of acute coronary syndrome included acute myocardial infarction with ST elevation, prolonged angina for more than 20 minutes, or recurrent episodes at rest with indicators of cardiac ischemia or injury (cardiac enzyme elevation and ST segment denivelation)
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Diagnosis of acute coronary syndrome included acute myocardial infarction with ST elevation, prolonged angina for more than 20 minutes, or recurrent episodes at rest with indicators of cardiac ischemia or injury (cardiac enzyme elevation and ST segment denivelation)
Exclusion criteria	Patients with previous percutaneous coronary intervention or coronary artery bypass graft surgery, multivessel, diffuse disease, tortuous vessel, arteries less than 3 mm in diameter, distal stenosis location, and left main and bifurcation lesions were excluded from the study.
Recruitment/selection of patients	The study included patients who underwent stent implantation in acute coronary syndrome from January

Study	Strozzi 2007[116]
	2003 to May 2004.
Age, gender and ethnicity	Age - Mean (SD): 57.8 years. Gender (M:F): 95/24. Ethnicity: Not reported
Further population details	1. ACS population: Not stated / Unclear 2. Diabetes: Without diabetes (Mean: 31.5% in study population). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: < 75 years (Mean age: 57.8 years). 5. Renal disease/renal insufficiency: Not applicable 6. Size of stenosis: Not applicable
Indirectness of population	No indirectness
Interventions	(n=39) Intervention 1: Drug eluting stents - DES- Sirolimus. Participants were randomised to sirolimus eluting stent.. Duration 6 months. Concurrent medication/care: All procedures were performed using standard transfemoral approach with seven-French guiding catheters. All patients received aspirin (300mg), heparin (10 000 IU or more in longer procedures), and eptifibatide 180µg/kg bolus in angiographic evidence of thrombus, followed by 6-12 hours infusion (2 µg kg-1 min-1). Standard percutaneous coronary intervention was performed with balloon predilation, stent placement, and post-dilation if needed. Post procedural medications included aspirin 100 mg/d and ticlopidine 500 mg/d (clopidogrel was not available). Ticlopidine was stopped 6 weeks after the procedure.. Indirectness: No indirectness Further details: 1. Number of stents: Not applicable 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin 100 mg/d and ticlopidine 500 mg/d). (n=40) Intervention 2: Bare metal stents - BMS- unspecified. Participants were randomised to bare metal stent.. Duration 6 months. Concurrent medication/care: All procedures were performed using standard transfemoral approach with seven-French guiding catheters. All patients received aspirin (300mg), heparin (10 000 IU or more in longer procedures), and eptifibatide 180µg/kg bolus in angiographic evidence of thrombus, followed by 6-12 hours infusion (2 µg kg-1 min-1). Standard percutaneous coronary intervention was performed with balloon predilation, stent placement, and post-dilation if needed. Post procedural medications included aspirin 100 mg/d and ticlopidine 500 mg/d (clopidogrel was not available). Ticlopidine was stopped 6 weeks after the procedure.. Indirectness: No indirectness Further details: 1. Number of stents: Not applicable 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin 100 mg/d and ticlopidine 500 mg/d).
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 6 months; Group 1: 0/39, Group 2: 0/40
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0

Study	Strozzi 2007[116]
Protocol outcome 2: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: Target lesion revascularisation at 6 months; Group 1: 2/39, Group 2: 9/40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 3: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 6 months; Group 1: 2/39, Group 2: 3/40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0 Protocol outcome 4: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter (MLD) at 6 months; Group 1: mean 2.7 (SD 0.6); n=39, Group 2: mean 2.4 (SD 0.9); n=40 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1 ; Stent thrombosis at later >1-3 year ; Minor bleeding; Bleeding; Major bleeding;

Study (subsidiary papers)	TYPHOON trial: Spaulding 2006[109]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=715)
Countries and setting	Conducted in Australia, Czech Republic, Denmark, France, Germany, Hungary, Israel, Italy, Latvia, Multiple countries, Netherlands, Poland, Portugal, Spain, Switzerland, United Kingdom; Setting: Multicentre
Line of therapy	1st line
Duration of study	Follow up (post intervention): 4 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Electrocargiogram
Stratum	Overall
Subgroup analysis within study	Not applicable

Study (subsidiary papers)	TYPHOON trial: Spaulding 2006[109]
Inclusion criteria	Patients were eligible for the trial if their symptoms began less than 12 hours before catheterization and if the electrocardiogram showed STsegment elevation (at least 1 mm in two or more standard leads or at least 2 mm in two or more contiguous precordial leads)
Exclusion criteria	Clinical criteria for exclusion included the administration of fibrinolytic agents for the index infarction, overt acute heart failure, a previously documented left ventricular ejection fraction of less than 30%, previous myocardial infarction, and an estimated life expectancy of less than 12 months
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): DES group: 58.0 (11.8); BMS group: 60.5 (12.4). Gender (M:F): 558/157. Ethnicity: Not reported
Further population details	1. ACS population : STEMI 2. Diabetes: (16% had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=356) Intervention 1: Drug eluting stents - DES- Sirolimus. Sirolimus-eluting stent. If more than one stent was implanted, the same type of stent (sirolimus-eluting or uncoated) was recommended. Duration N/A. Concurrent medication/care: Patients were premedicated with aspirin (at least 100 mg) and unfractionated heparin (5000 to 10,000 IU). A loading dose of 300 mg of clopidogrel was administered either before or immediately after PCI. Coronary angiography was performed through the femoral or radial artery with the use of standard techniques. Heparin was administered throughout the procedure in order to maintain an activated clotting time of 250 seconds or longer. Administration of platelet glycoprotein IIb/IIIa–receptor inhibitors was left to the investigator's discretion. Combined antiplatelet therapy included daily administration of aspirin (100 mg) and either clopidogrel (75 mg) or ticlopidine (250 mg). Dual antiplatelet therapy was recommended for at least 6 months, and aspirin therapy was recommended indefinitely. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.1 (0.4)). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=359) Intervention 2: Bare metal stents - BMS- unspecified. Duration N/A. Concurrent medication/care: Patients were premedicated with aspirin (at least 100 mg) and unfractionated heparin (5000 to 10,000 IU). A loading dose of 300 mg of clopidogrel was administered either before or immediately after PCI. Coronary angiography was performed through the femoral or radial artery with the use of standard techniques. Heparin was administered throughout the procedure in order to maintain an activated clotting time of 250 seconds or longer. Administration of platelet glycoprotein IIb/IIIa–receptor inhibitors was left to the investigator's discretion. Combined antiplatelet therapy included daily administration of aspirin (100 mg) and either clopidogrel (75 mg) or ticlopidine (250 mg). Dual antiplatelet therapy was recommended for at least 6

Study (subsidiary papers)	TYPHOON trial: Spaulding 2006[109]
	months, and aspirin therapy was recommended indefinitely.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.1 (0.4)). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Study funded by industry (Supported by Cordis, Johnson & Johnson)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- SIROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death at 1 year; Group 1: 8/355, Group 2: 8/357
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 3: Cardiac mortality at early ≤1
- Actual outcome: Cardiac death at 1 year; Group 1: 7/355, Group 2: 5/357
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 5: TVF- target vessel failure at early ≤1
- Actual outcome: Target vessel failure at 1 year; Group 1: 26/355, Group 2: 51/357
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 6: Myocardial infarction at early ≤1
- Actual outcome: Recurrent myocardial infarction at 1 year; Group 1: 4/355, Group 2: 5/357
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 7: Stent thrombosis at early ≤1
- Actual outcome: Angiographically proven stent thrombosis at 1 year; Group 1: 7/355, Group 2: 12/357
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 2

Protocol outcome 9: MLD - Minimal lumen diameter
- Actual outcome: Minimal lumen diameter (in stent) at 8 months; Group 1: mean 2.42 mm (SD 0.59); n=87, Group 2: mean 1.78 mm (SD 0.61); n=83
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 269; Group 2 Number missing: 276

Study (subsidiary papers)	TYPHOON trial: Spaulding 2006[109]
- Actual outcome: Minimal lumen diameter (in lesion) at 8 months; Group 1: mean 2.14 mm (SD 0.61); n=87, Group 2: mean 1.76 mm (SD 0.61); n=83 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 269; Group 2 Number missing: 276	
Protocol outcomes not reported by the study	TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Minor bleeding; Bleeding; Major bleeding;

Study (subsidiary papers)	PRODIGY trial: Valgimigli 2014[126] (Valgimigli 2010[123])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=2013)
Countries and setting	Conducted in Italy; Setting: Multicentre
Line of therapy	1st line
Duration of study	Follow up (post intervention): 2 years
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients 18 years of age or older with chronic stable coronary artery disease or acute coronary syndromes, including non–ST-segment elevation myocardial infarction (MI) and ST-segment elevation MI. They were eligible if they had at least 1 lesion with a stenosis diameter of ≥50% that was suitable for coronary stent implantation in a vessel with a reference vessel diameter of at least 2.25 mm. Selection criteria were broad, reflecting routine clinical practice. There was no set limit for the number of treated lesions, vessels, or lesion length and no patients were excluded on the basis of comorbid disorders or age
Exclusion criteria	Known allergy to acetylsalicylic acid or clopidogrel; planned surgery within 24 months of percutaneous coronary intervention unless the dual antiplatelet therapy could be maintained throughout the perisurgical period; history of bleeding diathesis; major surgery within 15 days; active bleeding or previous stroke in the past 6 months; concomitant or foreseeable need for oral anticoagulation therapy; pregnancy; life expectancy <24 months; participation in another trial; and inability to provide informed consent.
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): BMS group: 69 (11); ZES group: 68 (11); PES group: 68 (11); EES group: 68 (11). Gender (M:F): 1538/465. Ethnicity: Not reported

Study (subsidiary papers)	PRODIGY trial: Valgimigli 2014[126] (Valgimigli 2010[123])
Further population details	1. ACS population: Not stated / Unclear (Mixed: 22.5% had NSTEMI; 32.25% had STEMI). 2. Diabetes: Not stated / Unclear (24.8% had diabetes). 3. Mixed ACS and stable population: Not stated / Unclear (Mixed: 73.25% had ACS; 18.5% had unstable angina). 4. Older patients: Not stated / Unclear 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=1508) Intervention 1: Drug eluting stents - DES- other . DES (Everolimus-eluting stents or paclitaxel-eluting stent or zotarolimus eluting stent). Duration N/A. Concurrent medication/care: All patients received aspirin (160 to 325 mg orally or 500 mg intravenously as a loading dose and then 80 to 160 mg orally indefinitely) and clopidogrel (300 or 600 mg orally as a loading dose) and then 75 mg/day for the treatment duration according to the randomization scheme. At 30 days, patients in each stent group were randomized in a balanced fashion to either 6 or 24 months of dual antiplatelet treatment.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.83 ± 1.2). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=505) Intervention 2: Drug eluting stents - DES- Paclitaxel. Paclitaxel-eluting stents (PES). Duration N/A. Concurrent medication/care: All patients received aspirin (160 to 325 mg orally or 500 mg intravenously as a loading dose and then 80 to 160 mg orally indefinitely) and clopidogrel (300 or 600 mg orally as a loading dose) and then 75 mg/day for the treatment duration according to the randomization scheme. At 30 days, patients in each stent group were randomized in a balanced fashion to either 6 or 24 months of dual antiplatelet treatment.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.81 ± 1.3). 2. Use of antiplatelet therapy: Not stated / Unclear (Mixed). (n=502) Intervention 3: Drug eluting stents - DES- Zotarolimus. Zotarolimus-eluting Endeavor Sprint stents (ZES-S). Duration N/A. Concurrent medication/care: All patients received aspirin (160 to 325 mg orally or 500 mg intravenously as a loading dose and then 80 to 160 mg orally indefinitely) and clopidogrel (300 or 600 mg orally as a loading dose) and then 75 mg/day for the treatment duration according to the randomization scheme. At 30 days, patients in each stent group were randomized in a balanced fashion to either 6 or 24 months of dual antiplatelet treatment.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.91 ± 1.3). 2. Use of antiplatelet therapy: Not stated / Unclear (Mixed). (n=505) Intervention 4: Bare metal stents - BMS- unspecified. Third-generation thin-strut BMS. Duration N/A. Concurrent medication/care: All patients received aspirin (160 to 325 mg orally or 500 mg intravenously as a loading dose and then 80 to 160 mg orally indefinitely) and clopidogrel (300 or 600 mg orally as a loading dose) and then 75 mg/day for the treatment duration according to the randomization scheme. At 30 days,

Study (subsidiary papers)	PRODIGY trial: Valgimigli 2014[126] (Valgimigli 2010[123])
	patients in each stent group were randomized in a balanced fashion to either 6 or 24 months of dual antiplatelet treatment.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Number of stents: 1.82 ± 1.2). 2. Use of antiplatelet therapy: Not stated / Unclear (Mixed).
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- OTHER versus BMS- UNSPECIFIED Protocol outcome 1: TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year - Actual outcome: TLR at 2 years; Group 1: 118/1499, Group 2: 85/498 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12; Group 2 Number missing: 7 - Actual outcome: TVR at 2 years; Group 1: 131/1499, Group 2: 86/498 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12; Group 2 Number missing: 7 Protocol outcome 2: Stent thrombosis at later >1-3 year - Actual outcome: Definite or probable stent thrombosis at 2 years; Group 1: 35/1499, Group 2: 18/498 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 12; Group 2 Number missing: 7	
Protocol outcomes not reported by the study	All-cause mortality at early ≤1 ; All-cause mortality at later >1-3 year ; Cardiac mortality at early ≤1 ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at early ≤1 ; Myocardial infarction at early ≤1 ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1 ; Minor bleeding; Bleeding; MLD - Minimal lumen diameter ; Major bleeding;

Study	XIMA trial: De Belder 2014[32]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=800)
Countries and setting	Conducted in Multiple countries (United Kingdom and Spain); Setting: Hospital and primary care
Line of therapy	1st line
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline	Adequate method of assessment/diagnosis: Physical examination, angina status measurement of creatine

Study	XIMA trial: De Belder 2014[32]
condition	kinase and troponin
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Non–ST-segment elevation myocardial, infarction, unstable angina, and stable angina
Exclusion criteria	Acute ST-segment elevation myocardial infarction, cardiogenic shock, thrombocytopenia, poor life expectancy, GI haemorrhage in previous 3 months or intracerebral bleeding
Age, gender and ethnicity	Age - Mean (SD): DES 83.6 (3.2) BMS 83.4 (3.1) years. Gender (M:F): 480/320. Ethnicity: Not stated
Further population details	1. ACS population : UA/STEMI (Angina 32%). 2. Diabetes: With diabetes (DES 25.6%, BMS 24.2%). 3. Mixed ACS and stable population: ACS (Angina 32%). 4. Older patients: >= 75 years (Aded 80 years or older). 5. Renal disease/renal insufficiency: Not stated / Unclear 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=399) Intervention 1: Drug eluting stents - DES- Everolimus. Xience, Abbott Vascular, Santa Clara, California. Duration 1 year. Concurrent medication/care: Loading doses of aspirin 300 mg and clopidogrel 600 mg. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (2% in each arm had multiple stents). 2. Use of antiplatelet therapy: with antiplatelet therapy (n=401) Intervention 2: Bare metal stents - BMS- unspecified. Vision stents (Abbott Vascular). Duration 1 year. Concurrent medication/care: Loading doses of aspirin 300 mg and clopidogrel 600 mg. Indirectness: No indirectness Further details: 1. Number of stents: Single stent (2% in each arm had multiple stents). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DES- EVEROLIMUS versus BMS- UNSPECIFIED

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: All-cause mortality at 1 year; Group 1: 34/399, Group 2: 29/401
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 25.6 vs 24.2, Hypertension 75.1 vs 77.6, Previous MI 29.8 vs 21.5, Previous CABG 7.0 vs 4.2, Previous PCI 12.8 vs 10.2; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Cardiac mortality at early ≤1
- Actual outcome: Cardiac mortality at 1 year; Group 1: 13/399, Group 2: 19/401

Study	XIMA trial: De Belder 2014[32]
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 25.6 vs 24.2, Hypertension 75.1 vs 77.6, Previous MI 29.8 vs 21.5, Previous CABG 7.0 vs 4.2, Previous PCI 12.8 vs 10.2; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: TVR at 1 year; Group 1: 8/399, Group 2: 28/401 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 25.6 vs 24.2, Hypertension 75.1 vs 77.6, Previous MI 29.8 vs 21.5, Previous CABG 7.0 vs 4.2, Previous PCI 12.8 vs 10.2; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 1 year; Group 1: 17/399, Group 2: 35/401 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 25.6 vs 24.2, Hypertension 75.1 vs 77.6, Previous MI 29.8 vs 21.5, Previous CABG 7.0 vs 4.2, Previous PCI 12.8 vs 10.2; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Major bleeding - Actual outcome: Major haemorrhage at 1 year; Group 1: 9/399, Group 2: 7/401 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: DES vs BMS (%) Diabetes 25.6 vs 24.2, Hypertension 75.1 vs 77.6, Previous MI 29.8 vs 21.5, Previous CABG 7.0 vs 4.2, Previous PCI 12.8 vs 10.2; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at early ≤1 ; Stent thrombosis at later >1-3 year ; Minor bleeding; MLD - Minimal lumen diameter; Major bleeding;

Study (subsidiary papers)	ZEUS trial: Valgimigli 2015[125] (Valgimigli 2013[124])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1606)
Countries and setting	Conducted in Hungary, Italy, Multiple countries, Portugal, Switzerland; Setting: 20 site in 4 countries
Line of therapy	1st line

Study (subsidiary papers)	ZEUS trial: Valgimigli 2015[125] (Valgimigli 2013[124])
Duration of study	Follow up (post intervention): 1 year
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Those aged 18 years or older who had at least 1 qualifying criterion among the pre-specified uncertain DES recipients. High-bleeding risk status was defined as the following: a clinical indication for treatment with oral anticoagulant agents; recent bleeding episode(s) that required medical attention; previous bleeding episode(s) that required hospitalization if the bleeding diathesis has not been completely resolved (that is, surgical removal of the bleeding source); age older than 80 years; systemic conditions associated with increased bleeding risk (e.g., hematological disorders or any known coagulopathy-determining bleeding diathesis, including history of or current thrombocytopenia, which was defined as platelet count <100,000/mm3 [<100 × 109/l]; known anemia, defined as repeatedly documented hemoglobin <10 g/dl; and need for long-term treatment with steroids or nonsteroidal anti-inflammatory drugs. High-risk thrombotic criteria were defined as the following: allergy and/or intolerance to aspirin; allergy and/or intolerance to available P2Y12 inhibitors; planned surgery (other than skin) within 12 months of percutaneous coronary intervention; patient with cancer (other than skin) and life expectancy >1 year; and patients with systemic conditions associated with thrombosis diathesis (e.g., hematological disorders and any known systemic conditions determining a prothrombotic state, including immunological disorders). Finally, low restenosis risk was fulfilled if no planned stent <3.0-mm diameter was intended to be implanted, regardless of lesion length, apart from left main coronary artery or saphenous graft intervention
Exclusion criteria	Women who are pregnant. Women of childbearing potential must have a negative pregnancy test (urine or serum HCG) within 7 days prior to randomization; as close to randomization as possible, within 24 hours preferred; those who are unable to give informed consent and assurance for complete contact through 12 months; PCI with stenting in the previous 6 months
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): BMS group 71.8 (12); DES group 71.8 (11). Gender (M:F): 1133/473. Ethnicity: Not reported
Further population details	1. ACS population : Not stated / Unclear 2. Diabetes: Not stated / Unclear (Mixed (26.15%)). 3. Mixed ACS and stable population: Not stated / Unclear (Mixed 'patients with both stable and unstable symptoms'). 4. Older patients: Not stated / Unclear (Mixed). 5. Renal disease/renal insufficiency: Not stated / Unclear (Patients with creatinine clearance <30 ml/min: BMS group 66 (8.4); DES group 64 (8.3)). 6. Size of stenosis: Not stated / Unclear
Indirectness of population	No indirectness

Study (subsidiary papers)	ZEUS trial: Valgimigli 2015[125] (Valgimigli 2013[124])
Interventions	(n=804) Intervention 1: Bare metal stents - BMS- unspecified. Thin-strut BMS (strut thickness <100 µm) were allowed to be used in the study, the Tsunami, (Terumo, Leuven, Belgium), Skylor (Medtronic, Minneapolis, Minneapolis), Integrity (Medtronic), Vision (Abbott, Santa Clara, California), and Avant-Garde (CID Vascular, Saluggia, Italy) were the 5 most commonly utilized devices. Duration N/A. Concurrent medication/care: All eligible patients received aspirin (160 to 325 mg orally or 500 mg intravenously as a loading dose and then 80 to 160 mg orally per day) and clopidogrel (300 or 600 mg orally as a loading dose followed by 75 mg/day), or prasugrel (60 mg loading dose followed by 10 or 5 mg/day) or ticagrelor (180 mg loading dose followed by 90 mg twice daily). Patients who were not eligible for DAPT were treated with either aspirin or clopidogrel (or prasugrel or ticagrelor) monotherapy.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Mean number of stents: 1.69 (1.10) (199 participants received 2 or more stents)). 2. Use of antiplatelet therapy: with antiplatelet therapy (Aspirin). (n=802) Intervention 2: Drug eluting stents - DES- Zotarolimus. The Endeavor stent (Medtronic Vascular, Minneapolis, Minnesota) is a cobalt-based alloy stent (91-µm strut thickness) with a phosphorylcholine polymer (4.8 µm) loaded with zotarolimus at a dose concentration of 10 µg/mm stent length. Approximately 95% of the zotarolimus is eluted from the stent within 15 days of implantation, although drug concentrations within surrounding vascular tissue may be detected as late as 30 days after stent deployment.. Duration N/A. Concurrent medication/care: All eligible patients received aspirin (160 to 325 mg orally or 500 mg intravenously as a loading dose and then 80 to 160 mg orally per day) and clopidogrel (300 or 600 mg orally as a loading dose followed by 75 mg/day), or prasugrel (60 mg loading dose followed by 10 or 5 mg/day) or ticagrelor (180 mg loading dose followed by 90 mg twice daily). Patients who were not eligible for DAPT were treated with either aspirin or clopidogrel (or prasugrel or ticagrelor) monotherapy.. Indirectness: No indirectness Further details: 1. Number of stents: Not stated / Unclear (Mean number of stents: 1.70 (1.11) (201 participants received 2 or more stents)). 2. Use of antiplatelet therapy: with antiplatelet therapy
Funding	Study funded by industry (Funding from Medtronic through an unrestricted grant)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: BMS- UNSPECIFIED versus DES- ZOTAROLIMUS

Protocol outcome 1: All-cause mortality at early ≤1
- Actual outcome: Death from any cause at 1 year; Group 1: 92/804, Group 2: 89/802
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1

Protocol outcome 2: Cardiac mortality at early ≤1
- Actual outcome: Death from cardiovascular cause at 1 year; Group 1: 67/804, Group 2: 61/802

Study (subsidiary papers)	ZEUS trial: Valgimigli 2015[125] (Valgimigli 2013[124])
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1 Protocol outcome 3: TLR and TVR – target lesion and target vessel revascularisation at early ≤1 - Actual outcome: TVR at 1 year; Group 1: 86/804, Group 2: 47/802 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1 - Actual outcome: TLR at 1 year; Group 1: 84/804, Group 2: 42/802 Risk of bias: All domain - ; Indirectness of outcome: No indirectness Protocol outcome 4: Myocardial infarction at early ≤1 - Actual outcome: Myocardial infarction at 1 year; Group 1: 65/804, Group 2: 23/802 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1 Protocol outcome 5: Stent thrombosis at early ≤1 - Actual outcome: Definite or probable stent thrombosis at 1 year; Group 1: 33/804, Group 2: 16/802 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1 Protocol outcome 6: Minor bleeding - Actual outcome: Minor bleeding at 1 year; Group 1: 4/804, Group 2: 7/802 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1 Protocol outcome 7: MLD - Minimal lumen diameter - Actual outcome: Minimal lumen diameter at 1 year; Group 1: mean 2.7 mm (SD 0.5); n=804, Group 2: mean 2.73 mm (SD 0.52); n=802 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1 Protocol outcome 8: Major bleeding - Actual outcome: Major bleeding at 1 year; Group 1: 13/804, Group 2: 7/802 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 1; Group 2 Number missing: 1	
Protocol outcomes not reported by the study	All-cause mortality at later >1-3 year ; Cardiac mortality at later >1-3 year ; TVF- target vessel failure at early ≤1 ; TVF- target vessel failure at later >1-3 year ; TLR and TVR – target lesion and target vessel revascularisation at later >1-3 year ; Myocardial infarction at later >1-3 year ; Quality of life; Stent thrombosis at later >1-3 year;

Appendix E: Forest plots

E.1 Drug-eluting stents (DES) versus bare metal stents (BMS)

Figure 2: All-cause mortality (≤1 year)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Difference M-H, Fixed, 95% CI
Brikalis 2018 (DIVA)	23	292	21	305	4.5%	0.01 [-0.03, 0.05]
Chechi 2007 (SELECTION)	1	40	3	40	0.6%	-0.05 [-0.14, 0.04]
De Belder 2014 (XIMA)	34	399	29	401	6.0%	0.01 [-0.02, 0.05]
Di Lorenzo 2009 (PASEO)	7	180	6	90	1.8%	-0.03 [-0.09, 0.03]
Diaz de la Llera 2007	3	60	2	54	0.9%	0.01 [-0.06, 0.09]
Guagliumi 2010 (OCTAMI)	0	33	0	11	0.2%	0.00 [-0.12, 0.12]
Kelbaek 2008 (DEDICATION)	16	313	8	313	4.7%	0.03 [-0.00, 0.06]
Laarman 2006 (PASSION)	14	302	20	303	4.6%	-0.02 [-0.06, 0.02]
Menichelli 2007 (SESAMI)	3	154	7	153	2.3%	-0.03 [-0.07, 0.01]
Raber 2012 (COMFORTABLE)	18	575	23	582	8.7%	-0.01 [-0.03, 0.01]
Ribamar Costa 2012	0	20	0	20	0.3%	0.00 [-0.09, 0.09]
Ribibhini 2011 (CEREA-DES)	0	125	1	125	1.9%	-0.01 [-0.03, 0.01]
Rodriquez 2011 (EUCATAX)	5	211	8	211	3.2%	-0.01 [-0.05, 0.02]
Sabate 2012 (EXAMINATION)	26	751	26	747	11.3%	-0.00 [-0.02, 0.02]
Spaulding 2006 (TYPHOON)	8	355	8	357	5.4%	0.00 [-0.02, 0.02]
Steinwender 2008	0	8	0	8	0.1%	0.00 [-0.21, 0.21]
Stone 2009 (HORIZONS-AMI)	78	2186	26	715	16.3%	-0.00 [-0.02, 0.02]
Strozzi 2007	0	40	0	40	0.6%	0.00 [-0.05, 0.05]
Valgimigli 2008 (MULTISTRATEGY)	11	372	15	372	5.6%	-0.01 [-0.04, 0.02]
Valgimigli 2015 (ZEUS)	89	802	92	804	12.1%	-0.00 [-0.03, 0.03]
van der Hoeven 2008 (MISSION)	2	158	4	152	2.3%	-0.01 [-0.04, 0.02]
Wijinbergen 2012 (DEBATER)	11	424	10	446	6.6%	0.00 [-0.02, 0.02]
Total (95% CI)		**7800**		**6249**	**100.0%**	**-0.00 [-0.01, 0.00]**
Total events	349		309			

Heterogeneity: Chi² = 10.83, df = 21 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.63 (P = 0.53)

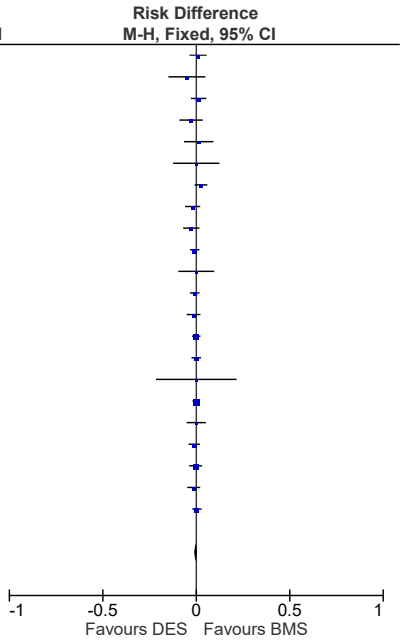


Figure 3: All-cause mortality (>1-3 years)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brilakis 2009 (SOS)	10	41	5	39	1.5%	1.90 [0.71, 5.07]
Di Lorenzo 2009 (PASEO)	11	180	9	90	3.6%	0.61 [0.26, 1.42]
Kaiser 2010	53	1549	34	765	13.7%	0.77 [0.50, 1.17]
Kaiser 2015 (BASKET PROVE II)	37	1530	26	761	10.5%	0.71 [0.43, 1.16]
Kelbaek 2008 (DEDICATION)	33	313	20	313	6.0%	1.65 [0.97, 2.81]
Laarman 2006 (PASSION)	21	303	27	303	8.1%	0.78 [0.45, 1.34]
Menichelli 2007 (SESAMI)	5	157	8	156	2.4%	0.62 [0.21, 1.86]
Raber 2012 (COMFORTABLE)	28	575	32	582	9.6%	0.89 [0.54, 1.45]
Sabate 2014 (EXAMINATION)	32	751	37	747	11.2%	0.86 [0.54, 1.37]
Stone 2009 (HORIZONS-AMI)	123	2103	48	687	21.8%	0.84 [0.61, 1.16]
Valgimigli 2008 (MULTISTRATEGY)	26	372	28	372	8.4%	0.93 [0.56, 1.55]
van der Hoeven 2008 (MISSION)	7	158	10	152	3.1%	0.67 [0.26, 1.72]
Total (95% CI)		**8032**		**4967**	**100.0%**	**0.87 [0.75, 1.01]**
Total events	386		284			

Heterogeneity: Chi² = 10.59, df = 11 (P = 0.48); I² = 0%
Test for overall effect: Z = 1.78 (P = 0.07)

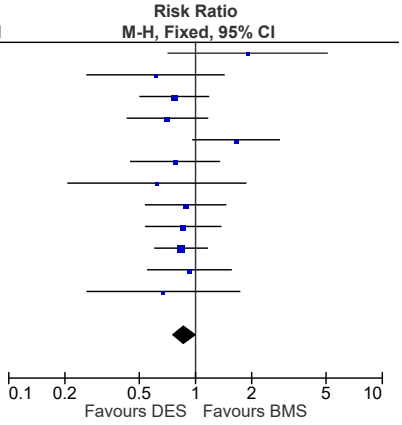


Figure 4: Cardiac mortality (≤1 year)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brikalis 2018 (DIVA)	15	292	11	305	4.9%	1.42 [0.67, 3.05]
De Belder 2014 (XIMA)	13	399	19	401	8.6%	0.69 [0.34, 1.37]
Han 2007	0	100	1	100	0.7%	0.33 [0.01, 8.09]
Kelbaek 2008 (DEDICATION)	13	313	5	313	2.3%	2.60 [0.94, 7.21]
Laarman 2006 (PASSION)	12	302	19	303	8.6%	0.63 [0.31, 1.28]
Raber 2012 (COMFORTABLE)	16	575	20	582	9.0%	0.81 [0.42, 1.55]
Ribibhini 2011 (CEREA-DES)	0	125	1	125	0.7%	0.33 [0.01, 8.10]
Rodriquez 2011 (EUCATAX)	4	211	4	211	1.8%	1.00 [0.25, 3.95]
Sabate 2012 (EXAMINATION)	24	751	21	747	9.5%	1.14 [0.64, 2.02]
Sanchez 2010 (GRACIAS-3)	21	217	15	216	6.8%	1.39 [0.74, 2.63]
Spaulding 2006 (TYPHOON)	7	355	5	357	2.3%	1.41 [0.45, 4.39]
Stone 2009 (HORIZONS-AMI)	54	2186	20	715	13.7%	0.88 [0.53, 1.46]
Valgimigli 2015 (ZEUS)	61	802	67	804	30.3%	0.91 [0.65, 1.27]
van der Hoeven 2008 (MISSION)	2	158	2	152	0.9%	0.96 [0.14, 6.74]
Total (95% CI)		**6786**		**5331**	**100.0%**	**0.98 [0.82, 1.17]**
Total events	242		210			

Heterogeneity: Chi² = 10.30, df = 13 (P = 0.67); I² = 0%
Test for overall effect: Z = 0.23 (P = 0.82)

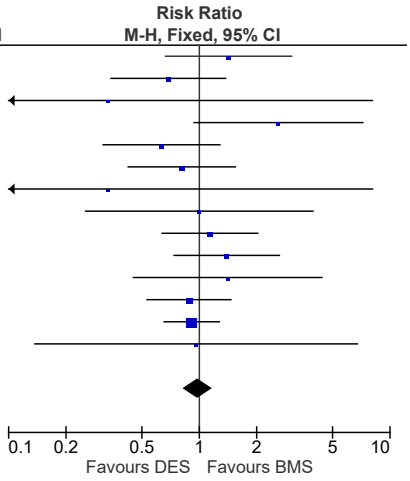


Figure 5: Cardiac mortality (>1-3 years)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brilakis 2009 (SOS)	3	41	5	39	2.5%	0.57 [0.15, 2.23]
Kaiser 2010	26	1549	22	765	14.5%	0.58 [0.33, 1.02]
Kaiser 2015 (BASKET PROVE II)	17	1530	14	761	9.2%	0.60 [0.30, 1.22]
Kelbaek 2008 (DEDICATION)	19	313	6	313	3.0%	3.17 [1.28, 7.82]
Laarman 2006 (PASSION)	17	303	22	303	10.9%	0.77 [0.42, 1.43]
Raber 2012 (COMFORTABLE)	17	575	25	582	12.3%	0.69 [0.38, 1.26]
Sabate 2014 (EXAMINATION)	28	751	28	747	13.9%	0.99 [0.59, 1.66]
Stone 2009 (HORIZONS-AMI)	71	2103	28	687	20.8%	0.83 [0.54, 1.27]
Valgimigli 2008 (MULTISTRATEGY)	21	372	21	372	10.4%	1.00 [0.56, 1.80]
van der Hoeven 2008 (MISSION)	3	158	5	152	2.5%	0.58 [0.14, 2.37]
Total (95% CI)		**7695**		**4721**	**100.0%**	**0.85 [0.70, 1.03]**
Total events	222		176			

Heterogeneity: Chi² = 12.58, df = 9 (P = 0.18); I² = 28%
Test for overall effect: Z = 1.67 (P = 0.10)

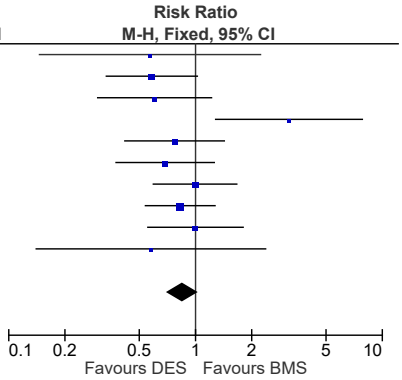


Figure 6: Target vessel failure (≤1 year)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Random, 95% CI
Brikalis 2018 (DIVA)	51	292	58	305	33.0%	0.92 [0.65, 1.29]
Rodriquez 2011 (EUCATAX)	20	211	36	211	23.5%	0.56 [0.33, 0.93]
Spaulding 2006 (TYPHOON)	26	355	51	357	26.7%	0.51 [0.33, 0.80]
van der Hoeven 2008 (MISSION)	11	158	23	152	16.8%	0.46 [0.23, 0.91]
Total (95% CI)		**1016**		**1025**	**100.0%**	**0.62 [0.44, 0.88]**
Total events	108		168			

Heterogeneity: Tau² = 0.06; Chi² = 6.37, df = 3 (P = 0.09); I² = 53%
Test for overall effect: Z = 2.68 (P = 0.007)

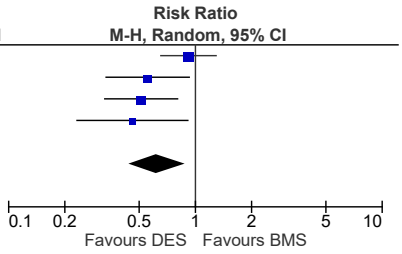


Figure 7: Target vessel failure (>1-3 years)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brilakis 2009 (SOS)	14	41	28	39	31.4%	0.48 [0.30, 0.76]
Menichelli 2007 (SESAMI)	18	157	32	156	35.1%	0.56 [0.33, 0.95]
van der Hoeven 2008 (MISSION)	19	158	30	152	33.5%	0.61 [0.36, 1.03]
Total (95% CI)		**356**		**347**	**100.0%**	**0.55 [0.41, 0.74]**
Total events	51		90			

Heterogeneity: Chi² = 0.52, df = 2 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.93 (P < 0.0001)

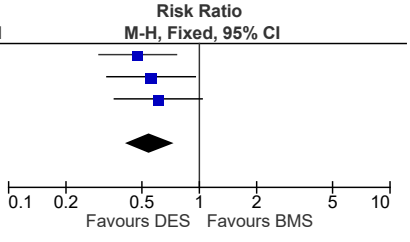
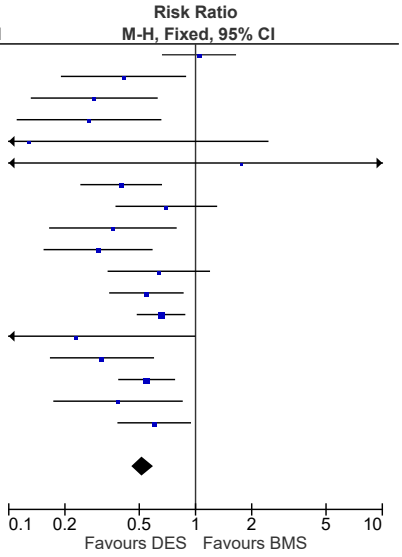


Figure 8: Target vessel revascularisation (≤1 year)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brikalis 2018 (DIVA)	34	292	34	305	5.5%	1.04 [0.67, 1.63]
Chechi 2007 (SELECTION)	7	40	17	40	2.8%	0.41 [0.19, 0.88]
De Belder 2014 (XIMA)	8	399	28	401	4.6%	0.29 [0.13, 0.62]
Di Lorenzo 2009 (PASEO)	7	180	13	90	2.9%	0.27 [0.11, 0.65]
Diaz de la Llera 2007	0	60	3	54	0.6%	0.13 [0.01, 2.44]
Guagliumi 2010 (OCTAMI)	2	33	0	11	0.1%	1.76 [0.09, 34.20]
Kelbaek 2008 (DEDICATION)	20	313	50	313	8.3%	0.40 [0.24, 0.66]
Laarman 2006 (PASSION)	16	302	23	303	3.8%	0.70 [0.38, 1.29]
Menichelli 2007 (SESAMI)	8	154	22	153	3.7%	0.36 [0.17, 0.79]
Raber 2012 (COMFORTABLE)	11	575	37	582	6.1%	0.30 [0.16, 0.58]
Ribibhini 2011 (CEREA-DES)	14	125	22	125	3.7%	0.64 [0.34, 1.19]
Sabate 2012 (EXAMINATION)	28	751	51	747	8.5%	0.55 [0.35, 0.86]
Stone 2009 (HORIZONS-AMI)	126	2186	63	715	15.8%	0.65 [0.49, 0.87]
Strozzi 2007	2	39	9	40	1.5%	0.23 [0.05, 0.99]
Valgimigli 2008 (MULTISTRATEGY)	12	372	38	372	6.3%	0.32 [0.17, 0.59]
Valgimigli 2015 (ZEUS)	47	802	86	804	14.3%	0.55 [0.39, 0.77]
van der Hoeven 2008 (MISSION)	8	158	20	152	3.4%	0.38 [0.17, 0.85]
Wijinbergen 2012 (DEBATER)	28	424	49	446	8.0%	0.60 [0.39, 0.94]
Total (95% CI)		**7205**		**5653**	**100.0%**	**0.52 [0.46, 0.59]**
Total events	378		565			

Heterogeneity: Chi² = 28.50, df = 17 (P = 0.04); I² = 40%
Test for overall effect: Z = 9.86 (P < 0.00001)

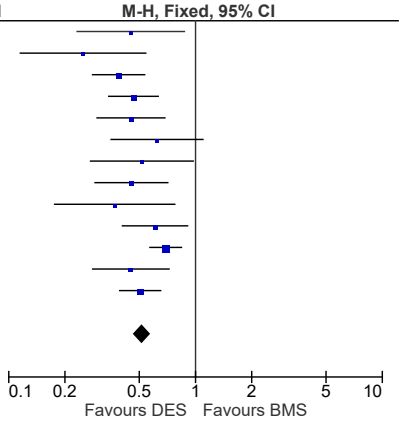


Di Lorenzo - data is TLR
Laarman 2006 - data is TLR
Bonna - data is TLR
Strozzi - data is TLR

Figure 9: Target vessel revascularisation (>1-3 years)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brilakis 2009 (SOS)	9	41	19	39	2.2%	0.45 [0.23, 0.87]
Di Lorenzo 2009 (PASEO)	9	180	16	80	2.5%	0.25 [0.12, 0.54]
Kaiser 2010	62	1549	79	765	12.0%	0.39 [0.28, 0.53]
Kaiser 2015 (BASKET PROVE II)	74	1530	79	761	12.0%	0.47 [0.34, 0.63]
Kelbaek 2008 (DEDICATION)	28	313	62	313	7.1%	0.45 [0.30, 0.69]
Laarman 2006 (PASSION)	18	298	29	299	3.3%	0.62 [0.35, 1.10]
Menichelli 2007 (SESAMI)	13	157	25	156	2.9%	0.52 [0.27, 0.97]
Raber 2012 (COMFORTABLE)	26	575	58	582	6.6%	0.45 [0.29, 0.71]
Remkes 2016 (ELISA 3)	9	234	25	240	2.8%	0.37 [0.18, 0.77]
Sabate 2014 (EXAMINATION)	36	751	59	747	6.7%	0.61 [0.41, 0.91]
Stone 2009 (HORIZONS-AMI)	265	2103	125	687	21.4%	0.69 [0.57, 0.84]
Valgimigli 2008 (MULTISTRATEGY)	23	372	51	372	5.8%	0.45 [0.28, 0.72]
Valgimigli 2014 (PRODIGY)	131	1499	86	498	14.7%	0.51 [0.39, 0.65]
Total (95% CI)		**9602**		**5539**	**100.0%**	**0.52 [0.47, 0.57]**
Total events	703		713			

Heterogeneity: Chi² = 18.70, df = 12 (P = 0.10); I² = 36%
Test for overall effect: Z = 12.68 (P < 0.00001)



Di Lorenzo - data is TLR
Laarman 2006 - data is TLR

Figure 10: Stent thrombosis – definite or probable (≤1 year)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brikalis 2018 (DIVA)	14	292	17	305	9.2%	0.86 [0.43, 1.71]
Di Lorenzo 2009 (PASEO)	1	180	1	90	0.7%	0.50 [0.03, 7.90]
Menichelli 2007 (SESAMI)	2	154	1	153	0.6%	1.99 [0.18, 21.69]
Raber 2012 (COMFORTABLE)	14	575	21	582	11.6%	0.67 [0.35, 1.31]
Sabate 2012 (EXAMINATION)	7	751	19	747	10.6%	0.37 [0.15, 0.87]
Sanchez 2010 (GRACIAS-3)	4	217	5	216	2.8%	0.80 [0.22, 2.93]
Spaulding 2006 (TYPHOON)	7	355	12	357	6.6%	0.59 [0.23, 1.47]
Stone 2009 (HORIZONS-AMI)	70	2186	25	715	20.9%	0.92 [0.58, 1.43]
Valgimigli 2008 (MULTISTRATEGY)	10	372	15	372	8.3%	0.67 [0.30, 1.46]
Valgimigli 2015 (ZEUS)	16	802	33	804	18.3%	0.49 [0.27, 0.88]
van der Hoeven 2008 (MISSION)	1	158	1	152	0.6%	0.96 [0.06, 15.24]
Wijinbergen 2012 (DEBATER)	17	424	18	446	9.7%	0.99 [0.52, 1.90]
Total (95% CI)		**6466**		**4939**	**100.0%**	**0.71 [0.57, 0.89]**
Total events	163		168			

Heterogeneity: Chi² = 7.48, df = 11 (P = 0.76); I² = 0%
Test for overall effect: Z = 3.01 (P = 0.003)

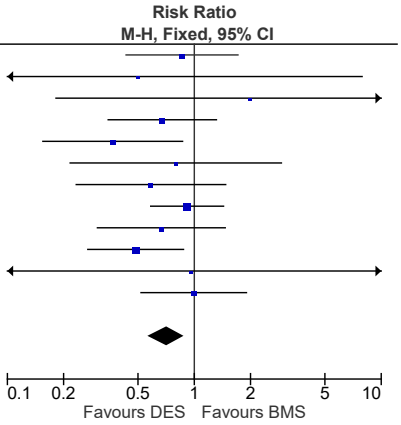


Figure 11: Stent thrombosis – definite or probable (>1-3 years)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Brilakis 2009 (SOS)	1	41	6	39	3.5%	0.16 [0.02, 1.26]
Di Lorenzo 2009 (PASEO)	1	180	1	90	0.8%	0.50 [0.03, 7.90]
Kaiser 2010	11	1549	9	765	6.8%	0.60 [0.25, 1.45]
Kaiser 2015 (BASKET PROVE II)	8	1530	6	761	4.5%	0.66 [0.23, 1.90]
Kelbaek 2008 (DEDICATION)	9	313	10	313	5.6%	0.90 [0.37, 2.18]
Menichelli 2007 (SESAMI)	3	157	2	156	1.1%	1.49 [0.25, 8.80]
Raber 2012 (COMFORTABLE)	18	575	25	582	14.0%	0.73 [0.40, 1.32]
Sabate 2014 (EXAMINATION)	10	751	21	747	11.9%	0.47 [0.22, 1.00]
Stone 2009 (HORIZONS-AMI)	103	2103	31	687	26.4%	1.09 [0.73, 1.61]
Valgimigli 2008 (MULTISTRATEGY)	15	372	17	372	9.6%	0.88 [0.45, 1.74]
Valgimigli 2014 (PRODIGY)	35	1499	18	498	15.2%	0.65 [0.37, 1.13]
van der Hoeven 2008 (MISSION)	4	158	1	152	0.6%	3.85 [0.44, 34.04]
Total (95% CI)		**9228**		**5162**	**100.0%**	**0.80 [0.64, 0.99]**
Total events	218		147			

Heterogeneity: Chi² = 10.47, df = 11 (P = 0.49); I² = 0%
Test for overall effect: Z = 2.06 (P = 0.04)

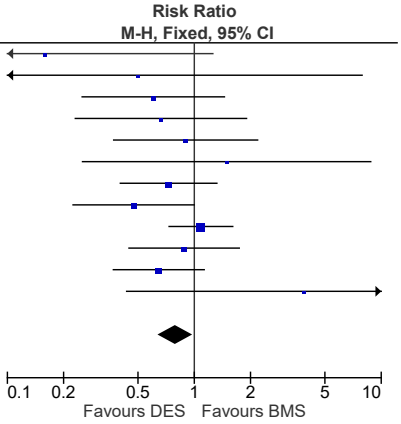


Figure 12: Myocardial infarction (≤1 year)

Study or Subgroup	DES Events	DES Total	BMS Events	BMS Total	Weight	Risk Difference M-H, Fixed, 95% CI
Brikalis 2018 (DIVA)	28	292	31	305	5.6%	-0.01 [-0.05, 0.04]
Chechi 2007 (SELECTION)	0	40	1	40	0.7%	-0.03 [-0.09, 0.04]
De Belder 2014 (XIMA)	17	399	35	401	7.4%	-0.04 [-0.08, -0.01]
Di Lorenzo 2009 (PASEO)	7	180	6	90	2.2%	-0.03 [-0.09, 0.03]
Guagliumi 2010 (OCTAMI)	0	33	0	11	0.3%	0.00 [-0.12, 0.12]
Han 2007	0	100	2	100	1.9%	-0.02 [-0.05, 0.01]
Kelbaek 2008 (DEDICATION)	5	313	8	313	5.8%	-0.01 [-0.03, 0.01]
Laarman 2006 (PASSION)	5	302	6	303	5.6%	-0.00 [-0.02, 0.02]
Menichelli 2007 (SESAMI)	3	154	3	153	2.9%	-0.00 [-0.03, 0.03]
Raber 2012 (COMFORTABLE)	11	575	21	582	10.8%	-0.02 [-0.04, 0.00]
Ribamar Costa 2012	0	20	0	20	0.4%	0.00 [-0.09, 0.09]
Ribibhini 2011 (CEREA-DES)	1	125	4	125	2.3%	-0.02 [-0.06, 0.01]
Rodriquez 2011 (EUCATAX)	6	211	5	211	3.9%	0.00 [-0.03, 0.04]
Sabate 2012 (EXAMINATION)	10	751	15	747	13.9%	-0.01 [-0.02, 0.01]
Sanchez 2010 (GRACIAS-3)	5	217	3	216	4.0%	0.01 [-0.02, 0.03]
Spaulding 2006 (TYPHOON)	4	355	5	357	6.6%	-0.00 [-0.02, 0.01]
Strozzi 2007	2	39	3	40	0.7%	-0.02 [-0.13, 0.08]
Valgimigli 2008 (MULTISTRATEGY)	12	372	17	372	6.9%	-0.01 [-0.04, 0.01]
Valgimigli 2015 (ZEUS)	23	802	65	804	15.0%	-0.05 [-0.07, -0.03]
van der Hoeven 2008 (MISSION)	9	158	14	152	2.9%	-0.04 [-0.09, 0.02]
Total (95% CI)		**5438**		**5342**	**100.0%**	**-0.02 [-0.03, -0.01]**
Total events	148		244			

Heterogeneity: Chi² = 29.79, df = 19 (P = 0.05); I² = 36%
Test for overall effect: Z = 5.12 (P < 0.00001)

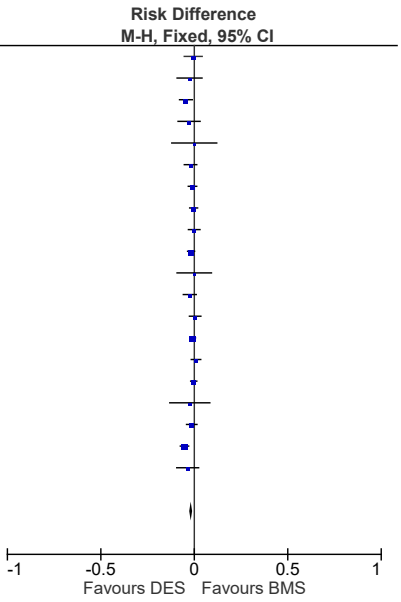


Figure 13: Myocardial infarction (>1-3 years)

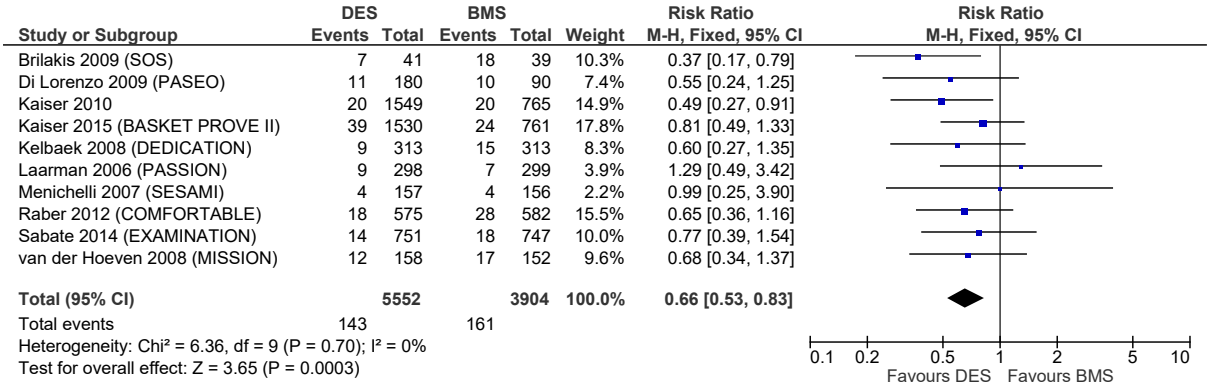


Figure 14: Bleeding(≤1 year)

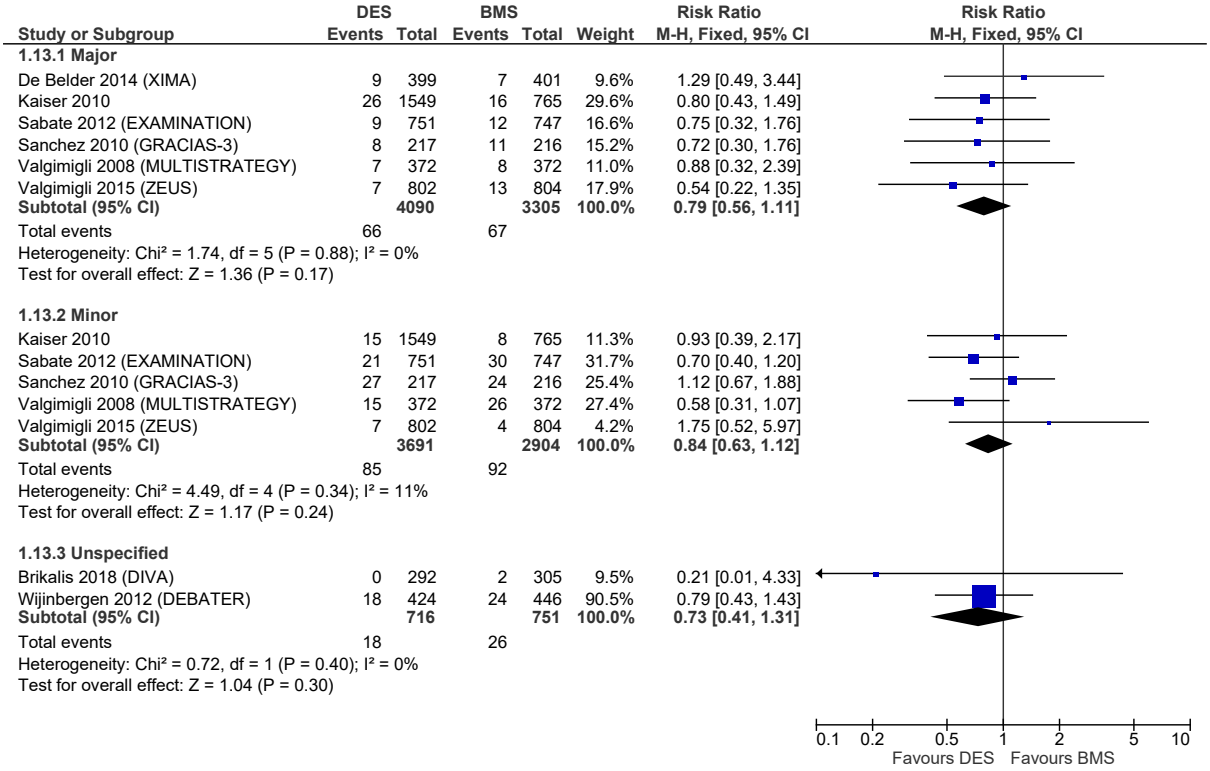


Figure 15: Bleeding (major) (>1-3 years)

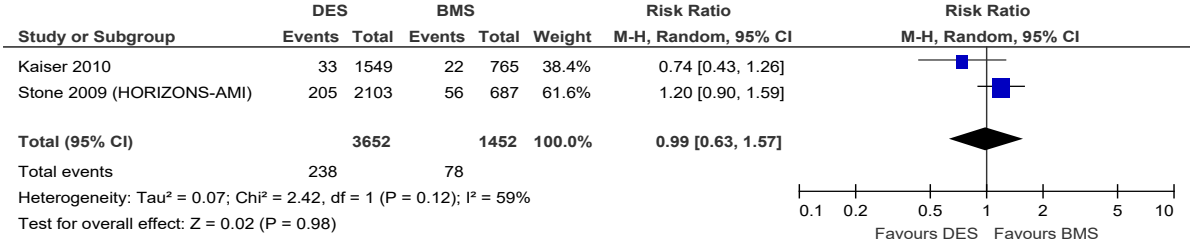


Figure 16: Bleeding (minor) (>1-3 years)

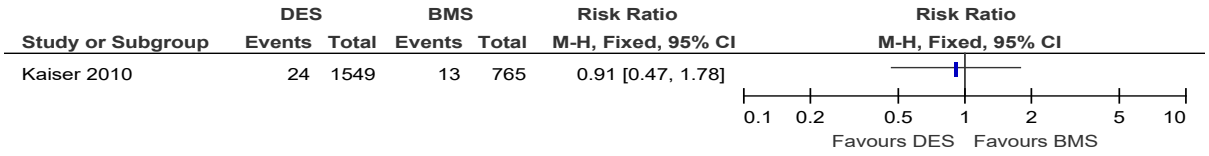


Figure 17: Minimal luminal diameter (≤1 year)

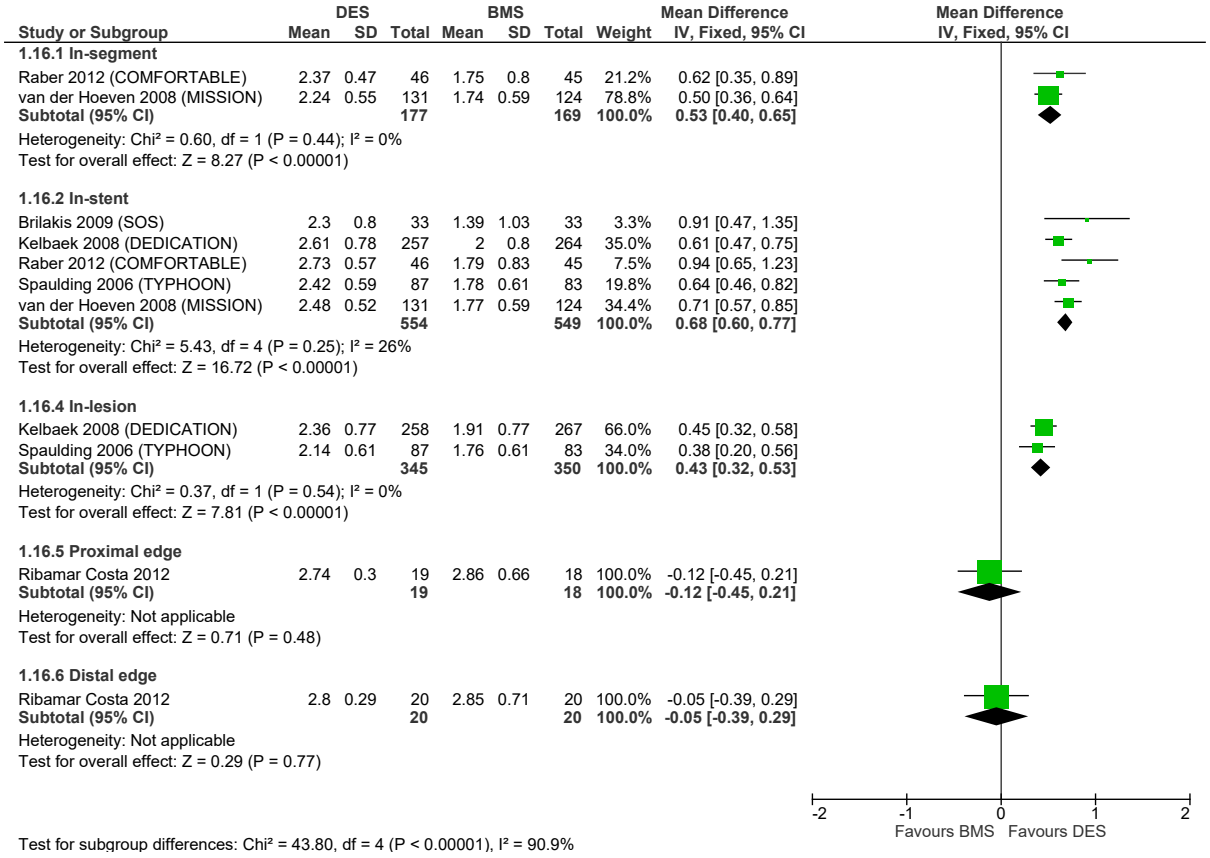
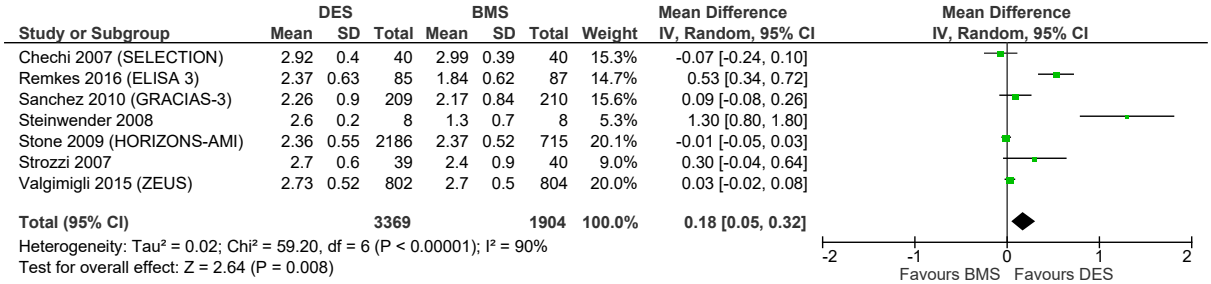


Figure 18: Minimal luminal diameter – unspecified (≤1 year)



E.1.1 Minimal important differences for continuous outcomes

The MID values reported in Table 15 were used to assess imprecision for the various continuous outcomes included in this evidence review.

Table 15: Minimal important difference: DES versus BMS

Outcomes	Minimal important difference (MID)
Minimal luminal diameter (≤1 year) (in-segment)	0.35
Minimal luminal diameter (≤1 year) (in-stent)	0.40
Minimal luminal diameter (≤1 year) (in-lesion)	0.35
Minimal luminal diameter (≤1 year) (proximal edge)	0.33
Minimal luminal diameter (≤1 year) (distal edge)	0.36
Minimal luminal diameter - unspecified (≤1 year)	0.33

Appendix F: GRADE tables

Table 16: Clinical evidence profile: Drug eluting stents (DES) versus bare metal stents (BMS)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DES	BMS	Relative (95% CI)	Absolute		
All-cause mortality (follow-up up to1 year)												
22	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	349/7800 (4.5%)	309/6249 (4.9%)	see comment[5]	2 fewer per 1000 (from 9 fewer to 5 more)	⊕⊕OO LOW	CRITICAL
All-cause mortality (follow-up 1-3 years)												
12	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	386/8032 (4.8%)	284/4967 (5.7%)	RR 0.87 (0.75 to 1.01)	7 fewer per 1000 (from 14 fewer to 1 more)	⊕⊕OO LOW	CRITICAL
Cardiac mortality (follow-up up to 1 year)												
14	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	242/6786 (3.6%)	210/5331 (3.9%)	RR 0.98 (0.82 to 1.17)	1 fewer per 1000 (from 7 fewer to 7 more)	⊕⊕⊕O MODERATE	CRITICAL
Cardiac mortality (follow-up 1-3 years)												
10	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	222/7695 (2.9%)	176/4721 (3.7%)	RR 0.85 (0.70 to 1.03)	6 fewer per 1000 (from 11 fewer to 1 more)	⊕⊕OO LOW	CRITICAL
Target vessel failure (follow-up up to 1 year)												
4	randomised trials	serious[1]	serious[4]	no serious indirectness	serious[2]	none	108/1016 (10.6%)	168/1025 (16.4%)	RR 0.62 (0.44 to 0.88)	62 fewer per 1000 (from 20 fewer to 92 fewer)	⊕OOO VERY LOW	CRITICAL

Target vessel failure (follow-up 1-3 years)												
3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	51/356 (14.3%)	90/347 (25.9%)	RR 0.55 (0.41 to 0.74)	117 fewer per 1000 (from 67 fewer to 153 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Target vessel revascularisation (follow-up up to 1 year)												
18	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	378/7205 (5.2%)	565/5653 (10%)	RR 0.52 (0.46 to 0.59)	48 fewer per 1000 (from 41 fewer to 54 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Target vessel revascularisation (follow-up 1-3 years)												
13	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	703/9602 (7.3%)	713/5539 (12.9%)	RR 0.52 (0.47 to 0.57)	62 fewer per 1000 (from 55 fewer to 68 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Stent thrombosis – Definite or probable (follow-up up to 1 year)												
12	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	163/6466 (2.5%)	168/4939 (3.4%)	RR 0.71 (0.57 to 0.89)	10 fewer per 1000 (from 4 fewer to 15 fewer)	⊕⊕OO LOW	CRITICAL
Stent thrombosis - Definite or probable (follow-up 1-3 years)												
12	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	218/9228 (2.4%)	147/5162 (2.8%)	RR 0.80 (0.64 to 0.99)	6 fewer per 1000 (from 0 fewer to 10 fewer)	⊕⊕OO LOW	CRITICAL
Myocardial infarction (follow-up up to 1 year)												
20	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	148/5438 (2.7%)	244/5342 (4.6%)	see comment[5]	18 fewer per 1000 (from 12 fewer to 23 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Myocardial infarction (follow-up 1-3 years)												
10	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	143/5552 (2.6%)	161/3904 (4.1%)	RR 0.66 (0.53 to 0.83)	14 fewer per 1000 (from 7 fewer to 19 fewer)	⊕⊕OO LOW	CRITICAL
Bleeding - Unspecified (follow-up up to 1 year)												

2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18/716 (2.5%)	26/751 (3.5%)	RR 0.73 (0.41 to 1.31)	9 fewer per 1000 (from 20 fewer to 11 more)	⊕OOO VERY LOW	IMPORTANT
Bleeding - Major (follow-up up to 1 year)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	66/4090 (1.6%)	67/3305 (2%)	RR 0.79 (0.56 to 1.11)	4 fewer per 1000 (from 9 fewer to 2 more)	⊕⊕OO LOW	IMPORTANT
Bleeding - Minor (follow-up up to 1 year)												
5	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	85/3691 (2.3%)	92/2904 (3.2%)	RR 0.84 (0.63 to 1.12)	5 fewer per 1000 (from 12 fewer to 4 more)	⊕⊕OO LOW	IMPORTANT
Bleeding - Major (follow-up 1-3 years)												
2	randomised trials	serious[1]	serious[4]	no serious indirectness	very serious[2]	none	238/3652 (6.5%)	78/1452 (5.4%)	RR 0.99 (0.63 to 1.57)	1 fewer per 1000 (from 20 fewer to 31 more)	⊕OOO VERY LOW	CRITICAL
Bleeding - Minor (follow-up 1-3 years)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24/1549 (1.5%)	13/765 (1.7%)	RR 0.91 (0.47 to 1.78)	2 fewer per 1000 (from 9 fewer to 13 more)	⊕OOO VERY LOW	IMPORTANT
Minimal luminal diameter - In-segment (follow-up up to 1 year; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	177	169	-	MD 0.53 higher (0.4 to 0.65 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Minimal luminal diameter - In-stent (follow-up up to 1 year; Better indicated by lower values)												
5	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	554	549	-	MD 0.68 higher (0.6 to 0.77 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Minimal luminal diameter - In-lesion (follow-up up to 1 year; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	345	350	-	MD 0.43 higher (0.32 to 0.53 higher)	⊕⊕OO LOW	IMPORTANT

Minimal luminal diameter - Proximal edge (follow-up up to 1 year; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	19	18	-	MD 0.12 lower (0.21 lower to 0.45 higher)	⊕⊕OO LOW	IMPORTANT
Minimal luminal diameter - Distal edge (follow-up up to 1 year; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	20	20	-	MD 0.05 lower (0.39 lower to 0.29 higher)	⊕OOO VERY LOW	IMPORTANT
Minimal luminal diameter - Unspecified (follow-up up to 1 year; Better indicated by lower values)												
7	randomised trials	serious[1]	very serious[4]	no serious indirectness	serious[2]	none	3369	1904	-	MD 0.18 higher (0.05 to 0.32 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

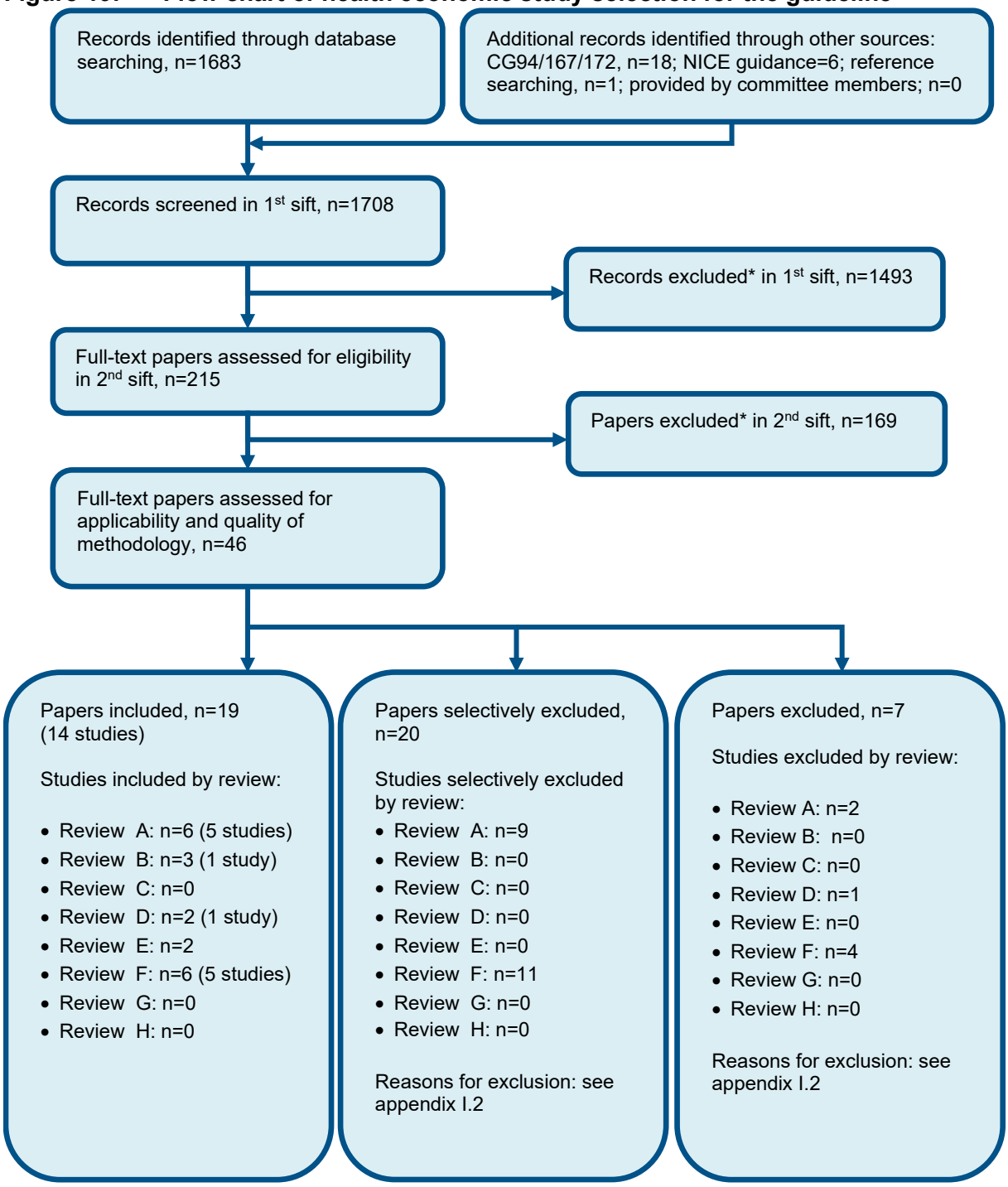
[3] Imprecision was assessed by calculating the optimal information size and graded as follows: <80% - very serious imprecision, 80-90%- serious imprecision, >90%– no imprecision

[4] Downgraded by 1 or 2 increments because heterogeneity, I2= > 50%, p= > 0.04, unexplained by subgroup analysis

No relative effect due to 0 events. Risk difference calculated in Review Manager

Appendix G: Health economic evidence selection

Figure 19: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Review A = dual-antiplatelet therapy; Review B = early invasive investigation for UA/NSTEMI; Review C = antithrombins in UA/NSTEMI; Review D = bivalirudin in STEMI; Review E = multi-vessel PCI; Review F = drug-eluting stents; Review G = combination of antiplatelets and anticoagulants; Review H = beta-blocker therapy.

Appendix H: Health economic evidence tables

Study	Canoui-Poitrine 2009[24]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA (health outcome: target vessel revascularisation) **Study design:** Within-trial analysis (RCT) with probabilistic analysis **Approach to analysis:** Within-trial analysis of French subgroup of the TYPHOON RCT. Analysis focused on Analysis of individual level data for clinical events and resource use. Unit costs applied. Quality of life weights applied to adverse events for QALY analysis (1 month for acute events (e.g. MI), lifetime for persistent states e.g. stroke, death). **Perspective:** French healthcare perspective **Follow-up:** 1 year	**Population:** Patients presenting with STEMI less than 12 hours after the onset of chest pain, undergoing PCI. **Patient characteristics:** N = 337 Mean age: 58.0 (SD: 12.3) Male: 78.9% **Intervention 1:** Bare-metal stent **Intervention 2:** Drug-eluting stent (sirolimus-eluting stent)	**Total costs (mean per patient):** Intervention 1: £9,325 Intervention 2: £10,236 Incremental (2−1): £911 (95% CI: -£236, £2,109) NR; p=0.10) **Currency & cost year:** 2007 euros (presented here as 2007 UK pounds[(b)]) **Cost components incorporated:** Index admission costs (stent costs, procedure cost, drug costs, intensive care unit cost, ward costs, rehabilitation) and follow-up costs (including medication and all repeat hospitalisations). Cost of stents: BMS = £439 DES = £1,237	**QALYs** Intervention 1: 0.8165 Intervention 2: 0.8159 Incremental (2−1): -0.0006 (95% CI: NR; p=0.36) **TVRs:** Intervention 1: 22.2% Intervention 2: 6.6% Incremental (2−1): -15.6% (95% CI: NR; p<0.001)	**ICER (Intervention 2 versus Intervention 1):** QALYs BMS dominant (lower costs and higher QALYs) Probability Intervention 2 cost effective (£20K/30K threshold): NR/NR TVRs £5,840 per repeat TVR avoided (pa) 95% CI: -£1,283, £27,643 54.9% of ICERs estimated remain under the authors' threshold of £7,980 per repeat TVR avoided. **Analysis of uncertainty:** Analysis did not conduct deterministic sensitivity analysis. One person in the DES arm had a heart transplant which considerably increased costs of the DES arm. Removing this incident resulted in an ICER of £4,635 per TVR avoided.

Treatment effect duration:[(a)] 1 year **Discounting:** Costs: n/a; Outcomes: n/a				

Data sources

Health outcomes: Baseline event rates for the BMS arm and relative treatment effects with DES were derived from analysis of individual-level data from a subgroup of French patients in the TYPHOON RCT. The TYPHOON RCT was based on patients with STEMI. This French subgroup made up 47.3% of the total population of the TYPHOON RCT. **Quality-of-life weights:** utility weights were from a mix of sources including EQ5D, QWB, HUI and SF36. Tariffs used for EQ-5D are not clear. Utility scores are reported for angioplasty, CABG, MI, congestive heart failure, severe chest pain, stroke, implantable cardioverter defibrillator, carotid thromboendarterectomy, infrainguinal surgery, insulin dependent diabetes mellitus, medulloblastoma tumor – non-metastetic, stomach ulcer, hip fracture, catherter ablation in patients with ventricular tachycardia. **Cost sources:** French National Hospital Cost Study and French National Price Schedule.

Comments

Source of funding: NR. **Limitations:** 2007 French healthcare perspective may not reflect current UK context. Some methods used to derive quality of life weights are not in line with NICE reference case and where EQ5D has been used it is unclear if with the UK tariff. Within-trial analysis based on a French subgroup of a single trial (TYPHOON RCT) and so does not reflect full body of available evidence for this area and may not reflect real world UK context. Time horizon of 1 year may not fully capture differences in costs and health outcomes as NGC review suggests effects continue beyond 1 year. It is unclear what is driving lower QALYs in the DES group as most outcomes favour DES; the only outcomes that are numerically worse in the DES group are 'Other cardiac events' which authors' state includes things such as such as hospitalizations for chest pain without proof of ischaemia, acute pulmonary oedema or heart failure and stroke where 1 event occurred with DES and 0 with BMS. Utility scores are reported for the following events suggesting they were incorporated: angioplasty, CABG, MI, congestive heart failure, severe chest pain, stroke, implantable cardioverter defibrillator, carotid thromboendarterectomy, infrainguinal surgery, insulin-dependent diabetes mellitus, medulloblastoma tumour – non-metastatic, stomach ulcer, hip fracture, catheter ablation in patients with ventricular tachycardia.

Overall applicability:[(c)] Partially applicable **Overall quality:**[(d)] Potentially serious limitations

Abbreviations: BMS= bare-metal stent; CEA= cost-effectiveness analysis; 95% CI= 95% confidence interval; DES= drug-eluting stent; ICER= incremental cost-effectiveness ratio; n/a= not applicable; NR= not reported; pa= probabilistic analysis; PCI= percutaneous coronary intervention; QALYs= quality-adjusted life years; RCT= randomised controlled trial; STEMI= ST segment elevation myocardial infarction; TVR= target vessel revascularisation

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2007 purchasing power parities[83]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Hill 2007[48]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Deterministic decision analytic model **Approach to analysis:** A decision analytic model was developed incorporating the reduced rate of repeat revascularisation within 12 months. Due to the absence of long-term outcomes affecting mortality or morbidity, simple equations were used to estimate the additional costs and additional benefits accrued at 12 months following index procedure. Differences in QALYs were estimated by attributing a short-term QALY loss to revascularisation events. This was based on QALY loss due to severe angina whilst waiting for revascularisation and QALY loss from the procedure (PCI or CABG itself).	**Population:** Patients with coronary artery disease revascularised in NHS hospitals; non-elective index PCI Note that analyses were also reported for elective PCI and a mix but the non-elective results are considered most relevant to an ACS population, **Cohort settings:** Start age: NR Male: NR **Intervention 1:** Bare metal stents **Intervention 2:** Drug eluting stents (CYPHER, TAXUS)	**Total costs (mean per patient):** Incremental (Intvn 2 – Intvn 1): *Narrow effectiveness:* Taxus = £852 Cypher = £919 *Broad effectiveness:* Taxus = £795 Cypher = £861 **Currency & cost year:** 2004-05 UK pounds **Cost components incorporated:** Stent costs, cost of angiography, follow-up appointments, repeat revascularisation cost Cost of stents: BMS = £291.95 DES Effective list price:[(b)] Taxus = £997.50 Cypher = £1044.75 DES actual cost:[(b)] Taxus = £855.43 Cypher = £983.51	**QALYs (mean per patient):** *Narrow effectiveness:* 0.002444 *Broad effectiveness:* 0.003251	**ICER (Intervention 2 versus Intervention 1):** *Narrow effectiveness:* Taxus = £348,700 Cypher = £376,100 *Broad effectiveness:* Taxus = £244,400 Cypher = £264,800 No probabilistic analysis. **Analysis of uncertainty:** A wide range of sensitivity analyses around baseline risks, relative risks, costs, utilities and other inputs were undertaken. The ICERs all remained too high ranging from £185,300 to £702,200 per QALY gained. Further results are shown in Table 6. A scenario exploring the absolute risk and difference in the costs of BMS and DES was undertaken. This showed that for elective patients with an absolute risk of 20% or more and with a price difference of £300 the ICER ranged from £900 to £26,000. For non-elective patients with an absolute risk of 18% or more and a price difference of £300 the ICER ranged from -£28,100 to £24,000. This led to the previous recommendation in NICE TA152. A breakdown of these results is demonstrated in Table 7.

Perspective: UK NHS **Time horizon:** 12 months **Treatment effect duration:**(a) 12 months **Discounting:** Costs: n/a; Outcomes: n/a				

Data sources

Health outcomes: Baseline risks were derived from the CTC Liverpool audit data. Treatment effects were obtained from a meta-analysis of RCTs (7 trials) and was combined with data from the CTC Liverpool audit data to obtain estimates that were more representative of UK. Different relative risks were applied based on 'broad' and 'narrow' estimates. 'Broad' estimates were based on cases involving any TLR/TVR irrespective of any other lesions/vessels revascularised (RR 0.369) and 'narrow' estimates were based on cases involving TLR/TVR only (0.492). Patients were split in to elective and non-elective and based on the number of risk factors they had (1 to 4). Non-elective PCI was 94% ACS (this analysis is presented here). Baseline risks varied by risk group. **Quality-of-life weights:** Utilities from published literature; patient survey data from the Health outcomes Data Repository (HODaR) database; EQ-5D UK tariff. Quality of life was independent of intervention used but varied by event experienced (requiring revascularisation and post-PCI). **Cost sources:** NHS reference costs. Stent prices were obtained from NHS Purchasing and Supply Agency survey.

Comments

Source of funding: NIHR. **Limitations:** Resource use from 2000-2002 and 2004/05 UK unit costs may not reflect current UK practice. Although the analysis for real world non-elective PCI risks of revascularisation with BMS was mostly ACS, relative treatment effects were based on data from a mix of stable and ACS patients. The analysis does not include the variety of drug-eluting stents currently available in the NHS as it only focuses on two types of stents (CYPHER and TAXUS) which dominated the market at the time. Analysis based on 7 RCTS (TAXUS I, TAXUS II, TAXUS IV, E-SIRIUS, RAVEL, SIRIUS and Pache) and so does not reflect full body of available evidence for this area. Time horizon of 1 year may not fully capture differences in costs and health outcomes as NGC review suggests benefits continue beyond 1 year and there may be benefits other than revascularisation that are not captured in the analysis. .

Overall applicability:(c) Partially applicable **Overall quality:**(d) Potentially serious limitations

Abbreviations: BMS= bare-mental stent; 95% CI= 95% confidence interval; CUA= cost–utility analysis; da= deterministic analysis; DES= drug-eluting stent; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NR= not reported; PCI= percutaneous coronary intervention; QALYs= quality-adjusted life years; RCT= randomised controlled trial

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Effective list price is the maximum price charged without discounts and actual costs were obtained from a survey conducted in by the NHS Purchasing and Supply Agency survey of prices which included discounts. Base case analysis uses effective list price, see Table 6 for actual prices.

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	Schur 2018[106]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Within-trial (EXAMINATION RCT[104]) analysis with modelled post-trial extrapolation; with probabilistic analysis. **Approach to analysis:** Analysis of individual-level mortality and clinical events (MI, stent thrombosis, revascularisation [PCI and CABG]) up to 5 years. Unit costs applied. EQ-5D weights applied. Long-term survival was calculated by applying average life expectancy estimates to those who survived at 5 years – these were independent of initial treatment strategy. CV events after five years were not explicitly modelled. **Perspective:** Spanish health service **Time horizon:** lifetime	**Population:** People with STEMI within the first 48 hours after symptom onset, requiring emergent PCI (with vessel sizes of 2.25 to 4.00mm to allow for the implantation of stents); 85% PPCI. **Patient characteristics:** N = 1498 Mean age = 61 Male = 83% **Intervention 1:** BMS **Intervention 2:** DES (everolimus)	**Total costs (mean per patient – 5 years):** Intervention 1: £2,978 Intervention 2: £3,345 Incremental (2−1): (95% CI: £114 to £619; p=NR) **Total costs (mean per patient – lifetime):** Intervention 1: £8,336 Intervention 2: £8,792 Incremental (2−1): £455 (95% CI: £61 to £844; p=NR) **Cost breakdown – incremental costs undiscounted** • Stents: £617 • Repeat MI: £37 • Stent thrombosis: -£17 • Revascularisation: -£285 • Outpatient CV costs: £18 • Lifetime CV costs: £96 **Currency & cost year:** 2016 Spanish Euros (presented here as 2016 UK pounds[(b)])] **Cost components incorporated:** Type and number of stents;	**QALYs (mean per patient – 5 years):** Intervention 1: 3.00 Intervention 2: 3.05 Incremental (2−1): 0.05 (95% CI: -0.02 to 0.12; p=NR) **QALYs (mean per patient – lifetime):** Intervention 1: 5.12 Intervention 2: 5.22 Incremental (2−1): 0.10 (95% CI: -0.06 to 0.26; p=NR)	**ICER (Intervention 2 versus Intervention 1):** 5 years: £7,294 per QALY gained (pa) 95% CI: BMS dominant (lower cost and higher QALYs) to £46,746 Probability Intervention 2 cost effective (£20K/30K threshold): NR Lifetime: £4,180 per QALY gained (pa) 95% CI: BMS dominant (lower cost and higher QALYs) to £26,022 Probability Intervention 2 cost effective (£20K/30K threshold): NR 86.9% were below a threshold of £26,467 per QALY gained. **Analysis of uncertainty:** A number of sensitivity analyses were undertaken around analysis inputs in addition to the bootstrapping/probabilistic analysis including: difference in stent costs, discount rate, unit costs and utilities; using on Spanish trial data. • In analyses varying unit costs and utilities the ICER ranged from around £3000 to £8000 per QALY gained. • Analyses varying the different in stent costs found that if this was £116 there was no difference in lifetime costs.

Treatment effect duration:[(a)] 5 years (based on available trial follow-up) **Discounting:** Costs: 3%; Outcomes: 3%		clinical events up to 5 years: MIs, stent thrombosis events, revascularisation procedures (PCI and CABG); annual CV outpatient treatment and drug costs during first 5 years (when clinical events accounted for explicitly); long-term annual CV treatment costs after year 5; 12 months antiplatelet therapy after revascularisation events. Cost of stents: BMS = £466; DES = £897.		• When only Spanish trial data was used the ICER increased to £5,005 with 83% of simulations below the £26,467 threshold used in the analysis.

Data sources

Health outcomes: Up to 5 years within-trial analysis for mortality and clinical events (for BMS and DES). Long-term survival beyond five years of follow-up was based on the average life expectancy by age group using World Life Expectancy estimates for Spain. It was reduced by estimates of the amount of years of potential life lost after acute MI from the published literature, adjusted to fit the age range of the EXAMINATION trial population. **Quality-of-life weights:** EQ-5D population norms for Spain, using country-specific time trade-off values were used. Decreases in utility due to the initial STEMI event were based on a published study in an English MI population using EQ-5D (tariff not stated but assumed to be UK); a larger decrement was applied in the first year. For repeat MI or stent thrombosis events during the 5 year follow-up it was assumed there was an additional decrease in utility that was half as much as the initial MI decrease. It was assumed that the full impact of a repeat event lasts for a year and that a reduced impact occurred in the subsequent years. Revascularisation, CABG and/or PCI were assumed to have the same impact on utility as repeat MI or stent thrombosis events for a year. **Cost sources:** Spanish DRG-based hospital reimbursement unit costs were used for stent costs and clinical events. Long-term annual cardiovascular treatment costs were estimated from a published UK model of thrombolysis versus primary PCI in MI patients adapted for Spain based on current health expenditure, PPPs and inflation rates; this included clinical events. Annual cardiovascular treatment costs during the first 5 years (where clinical events are modelled explicitly) were assumed to be half the long term costs. It was assumed that anti-platelet therapy after a revascularisation event would cost around €20 per month for twelve months.

Comments

Source of funding: The EXAMINATION trial was funded by the Spanish Heart Foundation. **Limitations:** Spanish healthcare perspective and international resource use may not reflect current UK context. STEMI only. Discounting at 3% and use of Spanish EQ5D tariff not fully in line with NICE reference case. Within-trial analysis of a single RCT and so does not reflect full body of available evidence for this area. Baseline risks based on multinational RCT (Spain, Italy, Netherlands) and so may not be reflective of real world UK risk; although authors note that “The EXAMINATION trial had broad inclusion and few exclusion criteria to ensure an all-comers population of adult STEMI patients which is representative of routine clinical practice”. **Other:**

Overall applicability:[(c)] Partially applicable **Overall quality:**[(d)] Potentially serious limitations

Abbreviations: 95% CI= 95% confidence interval; CUA= cost–utility analysis; da= deterministic analysis; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NR= not reported; pa= probabilistic analysis; QALYs= quality-adjusted life years

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2016 purchasing power parities[83]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Wisloff 2013[135]**			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA (health outcome: life years) **Study design:** Probabilistic decision analytic model **Approach to analysis:** Markov cohort state transition model with half year cycles. Health states were alive and dead with the possibility of events while alive including acute MI and revascularisation (treated with a second PCI or CABG). Efficacy data was based on a separate published network-meta analysis of RCTs. **Perspective:** Norwegian healthcare	**Population:** People with ACS or stable angina undergoing PCI with a stent. **Cohort settings:** Start age: 60 years Male: NR **Intervention 1:** Bare-metal stent **Intervention 2:** Drug-eluting stent(sirolimus) **Intervention 3:** Drug-eluting stent (paclitaxel)	**Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Intervention 3: NR Incremental (2−1): -£1,473 (95% CI: -£3,616, £134; p=NR) Incremental (3-1): -£223 (95% CI: NR; p=NR) Incremental (3−2): £1,250 (95% CI: -£536, £4,062; p=NR) **Currency & cost year:** 2008 Norwegian kroner (presented here as 2008 UK pounds[(b)])	**Life years (mean per patient):** Intervention 1: 12.090 Intervention 2: 12.093 Intervention 3: 12.241 Incremental (2−1): 0.003 (95% CI: -0.675, 0.448; p=NR) Incremental (3-1): 0.151 (95% CI: NR; p=NR) Incremental (3−2): 0.148 (95% CI: -0.422, 0.906; p=NR)	**ICER:** Intervention 1 dominated (higher costs and lower life-years) by intervention 2 Intervention 3 vs 2: £9,553 per life year gained (pa) 95% CI: NR Probability Intervention 2 cost effective (£20K/30K threshold): NR With a cost-effectiveness threshold of <£8,571 per life year gained SES had highest probability of being cost-effective. With a willingness to pay of >£8,571 per life year gained PES had the highest probability of being cost-effective. **Analysis of uncertainty:** An analysis was conducted where the relative treatment effect with DES was applied for a lifetime (rather than 5 years) and this found that PES was the most cost-effective option at the willingness to pay threshold of £8,571.

perspective **Time horizon:** Lifetime **Treatment effect duration:**(a) 5 years **Discounting:** Costs: 4%; Outcomes: 4%		**Cost components incorporated:** Stent costs, costs of procedures and cost of medication. Cost of stents: BMS = £107 SES = £515 PES = £419		

Data sources

Health outcomes: Baseline outcomes were obtained from registry data including the Swedish Coronary Angiography and Angioplasty Registry and Western Denmark Heart Registry. Although they were not obtained in Norway the authors stated that Swedish and Danish registry data reflects similar epidemiology to Norway. Relative treatment effects were obtained from a network meta-analysis of 35 RCTs comparing BMS, PES and SES. **Quality-of-life weights:** n/a **Cost sources:** Norwegian Medicines Agency and Norwegian DRGs. Stent prices were not official list prices and were obtained through personal communication with a cardiologist.

Comments

Source of funding: NR. **Limitations:** 2008 Norwegian healthcare perspective may not reflect current UK context. Analysis includes patients with stable coronary artery disease as well as ACS; baseline risk data and treatment effect data used reflect this. 4% discount rate and measure of effect (life years) not in line with NICE reference case methods. Baseline risks are based on the overall CAD population in Scandinavia and so may differ from a UK ACS population. Treatment effects were based on both ACS and stable patients and so studies excluded from our review have been incorporated; additional studies have also been identified by the review undertaken for this guideline. The price of stents used in the model was not official prices and were obtained through personal communication with a cardiologist.

Overall applicability:(c) Partially applicable **Overall quality:**(d) Potentially serious limitations

Abbreviations: BMS= bare-metal stent; CABG= coronary artery bypass graft; CAD= coronary artery disease; CEA= cost-effectiveness analysis; 95% CI= 95% confidence interval; DES= drug-eluting stent; DRG= diagnostic related grouping; ICER= incremental cost-effectiveness ratio; MI= myocardial infarction; NR= not reported; pa= probabilistic analysis; PCI= percutaneous coronary intervention; PES= paclitaxel-eluting stent; QALYs= quality-adjusted life years; SES= sirolimus-eluting stent

(a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(b) Converted using 2008 purchasing power parities[83]; the analysis was undertaken using Norwegian Kronor but some results are presented in Euros and dollars and these were first converted back to Norwegian Kronor using the conversion rates stated in the paper or provided by the author.

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

Study	**Zbinden 2017[137]**

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CUA (health outcome: QALYs) alternative analysis looked at TLRs avoided **Study design**: Within-trial analysis (RCT) with bootstrapping and probabilistic analysis to quantify uncertainty. **Approach to analysis:** Within trial analysis of a subgroup of the BASKET-PROVE RCT. Analysis of individual level data for target lesion revascularisation, EQ-5D and resource use. Unit costs applied. For the QALY analysis a subgroup that had at least some EQ-5D data was used. QALYs were calculated per patient based on baseline, 1 year and 2 year EQ-5D data with missing EQ-5D data was imputed. It is not stated if mortality was incorporated. For the TLR analysis a subgroup that had TLR and cost data was used.	**Population:** People with stable CAD or ACS undergoing PCI with at least one stent with a diameter >3mm and ≤15 mm lesion at baseline (this is a subgroup of the BASKET-PROVE trial) **Patient characteristics:** N (QALY analysis) = 1,286 (DES 861, BMS 425) N (TLR analysis) = 1647 (DES 1123, BMS 524) Mean age: 63.7 (SD: 10.9) Male: 75.8% % ACS: NR for economic analysis subgroups but for BASKET-PROVE overall 64% **Intervention 1:** Bare metal stent **Intervention 2:** Drug eluting stent (Cypher, Xience)	**QALY analysis** **Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): £75 (95% CI: NR; p=NR) **TLR analysis** **Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): £75 (95% CI: NR; p=NR) **Currency & cost year:** 2013 Swiss Francs (presented here as 2013 UK pounds[c]) **Cost components incorporated:** Stent costs, inpatient and outpatient procedures, only included costs of follow-up if it involved revascularisation. Cost of stents: BMS = £610 DES = £761	**QALYs (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.005 (95% CI: −0.059, 0.066; p=NR) **TLRs avoided (mean per patient):** Intervention 1: NR Intervention 2: NR Incremental (2−1): 0.083 (95% CI: 0.036, 0.124; p=NR)	**QALY analysis** **ICER (Intervention 2 versus Intervention 1):** £15,105 per QALY gained 95% CI: dominant to £100,256 per QALY gained Probability Intervention 2 cost effective (£26,486 threshold): 52.0% **TLR analysis** **ICER (Intervention 2 versus Intervention 1):** £1,986 per TLR avoided 95% CI: dominant to £5,451 per QALY gained Probability Intervention 2 cost effective (£5,297 threshold): 88.2% **Analysis of uncertainty:** No deterministic sensitivity analysis.

Perspective: Swiss healthcare payer (price-gap model reported here[a]) **Follow-up:** 2 years **Treatment effect duration:**[b] 2 years **Discounting:** Costs: None; Outcomes: None				

Data sources

Health outcomes: Baseline rates for TLR were based on patient level analysis from the BMS arm of the subgroup analysis in the BASKET-PROVE RCT. Treatment effects on target lesion revascularisation were obtained from the subgroup analysis of the BASKET-PROVE RCT and applied hazard ratios to the baseline rates. **Quality-of-life weights:** Within-RCT analysis: EQ-5D-3L (from patients); German population valuation tariff.. **Cost sources:** Swiss-DRG 2013 system for inpatient and the Swiss TARMED-tariff for outpatient procedures. Swiss stent list prices from 2007 discounted by 12.5%/10% per year DES/BMS respectively.

Comments

Source of funding: Authors declared no conflicts. **Limitations:** 2013 Swiss healthcare payer perspective and international resource use from 2007-2008 may not reflect the current UK context. Analysis includes patients with stable coronary artery disease as well as ACS (proportion not reported for analysis subgroups but for overall BASKET-PROVE RCT was 64% ACS). QALYs were derived using EQ-5D German population utility value set instead of the UK population value set. Within-trial analysis of subgroup of one RCT (BASKET-PROVE subgroup with stents >3mm and <15mm lesion length) and so does not reflect full body of available evidence for this area. Analysis was conducted on a retrospective subgroup. Incremental cost data is not reported. Time horizon of 2 years may not fully capture differences in costs and health outcomes as NGC review suggests effects on revascularisations for ACS overall maintained at 1-3 year time point and approach to modelling may not fully capture benefits to patients e.g. if QALY losses are generally short-term following revascularisation. Unclear if survival incorporated when calculating QALYs per patient. Unit costs are not reported (apart from stent costs).

Overall applicability:[c] Partially applicable **Overall quality:**[d] Potentially serious limitations

Abbreviations: BMS= bare-metal stent; 95% CI= 95% confidence interval; CUA= cost–utility analysis; DES= drug-eluting stent; DRG= diagnostic related grouping; EQ-5D= Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER= incremental cost-effectiveness ratio; NR= not reported; QALYs= quality-adjusted life years; RCT= randomised controlled trial; TLR= target lesion revascularisation

(a) The authors note that "As a peculiarity of the Swiss-DRG system, there is no difference in hospital reimbursement between the use of a DES or BMS, so we decided to generate two cost models, the "swiss- specific model" and the "price- gap model". In the latter, the price gap of 285 CHF per DES implanted directly affected healthcare costs in all procedures." The price-gap model is considered more consistent with the NICE reference case where a health service perspective is appropriate that considers overall costs to the NHS rather than hospital reimbursement rates.

(b) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

(c) Converted using 2013 purchasing power parities[83]

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 17: Studies excluded from the clinical review

Study	Exclusion reason
Ardissino 2004[4]	Incorrect population (<50% ACS)
Ahmed 2012[1]	Incorrect study design
Alfonso 2008[2]	Incorrect study design (pooled analysis)
Aoki 2009[3]	Incorrect comparison
Ariotti 2016[5]	Incorrect study design (subgroup analysis)
Arroyo 2014[6]	Study protocol
Belkacemi 2012[11]	Incorrect intervention
Belkacemi 2012[12]	Incorrect intervention
Bonaa 2016[15]	No extractable outcome data
Brener 2015[16]	Incorrect comparison
Brugaletta 2013[23]	No extractable outcome data
Carrier 2017[25]	Incorrect study design (subgroup analysis)
Chacko 2009[26]	No relevant extractable outcome data
Costa 2015[29]	Incorrect comparison
Crimi 2016[30]	Incorrect study design (subgroup analysis)
Darkahian 2014[31]	Incorrect intervention
Dominguez Franco 2008[37]	Incorrect study design
Dudek 2013[38]	Incorrect study design (subgroup analysis)
Ellis 2009[40]	No relevant extractable outcome data
Erglis 2007[41]	Incorrect population
Garg 2011[43]	Incorrect study design (subgroup analysis)
Garot 2017[44]	Incorrect population
Holmvang 2013[49]	No relevant extractable outcome data
Ielasi 2015[50]	Incorrect comparison (subgroup analysis for age)
Ischinger 2006[51]	No relevant extractable outcome data
Jimenez-Quevedo, 2013[53]	No relevant extractable outcome data
Kaiser 2005[54]	Incorrect population
Kandzari 2013[58]	Incorrect study design (pooled analysis)
Kaul 2015[59]	Incorrect comparison
Kelbaek 2008[60]	Incorrect population
Kim 2010[62]	Incorrect intervention
Konig 2007[63]	Incorrect intervention
Kurz 2015[64]	Incorrect study design (subgroup analysis)
La Manna 2011[66]	Incorrect comparison
Ledwoch 2017[68]	Incorrect study design
Lemos 2012[70]	Incorrect population
Lemos 2009[71]	Incorrect population
Li 2004[72]	Abstract only
Mehilli 2011[74]	Incorrect population

Study	Exclusion reason
Menozzi 2009[77]	Incorrect population
Morice 2017[78]	Incorrect study design (subgroup analysis)
Musto 2013[79]	No relevant extractable outcome data
Park 2013[84]	Study protocol
Pedersen 2014[85]	Incorrect study design (subgroup analysis)
Pitt 2007[86]	Abstract only
Raber 2016 [88]	Abstract only
Rebeiz 2009[92]	No relevant extractable outcome data
Ribichini 2009[97]	Study protocol
Ribichini, 2013[98]	No relevant extractable outcome data
Rodriguez 2009[99]	Incorrect intervention
Rubartelli 2010[101]	Incorrect population
Silber 2011[107]	Incorrect population
Sinning 2012[108]	No relevant extractable outcome data
Spaulding 2011[110]	No relevant extractable outcome data
Storger 2004[115]	Incorrect population
Tierala 2006[119]	Abstract only
Tomai 2014[120]	No relevant extractable outcome data
Van den Branden 2012[127]	No relevant extractable outcome data
Vink 2011[130]	No relevant extractable outcome data
Wiemer, 2010[132]	No relevant extractable outcome data
Wijnbergen 2014[134]	No relevant extractable outcome data
Witzenbichler 2011[136]	Incorrect study design (subgroup analysis)
Zellweger 2012[139]	Incorrect comparison
Zellweger 2008[138]	Incorrect comparison

I.2 Excluded health economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2003 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 18: Studies excluded from the health economic review

Reference	Reason for exclusion
Bagust 2006[8]	This study was assessed as partially applicable with potentially serious limitations. However, a more applicable UK analysis[48] was available that updated this analysis with more evidence therefore this study was selectively excluded.
Baschet 2006[9]	This study was rated as partially applicable with potentially serious limitations. However, given that a more applicable analysis[135] comparing drug-eluting with bare metal stents that included the same RCTs was available this study was selectively excluded.
Baumler 2012[10]	Excluded as rated very serious limitations due to being a model where treatment effects are based on a study that does not meet clinical review inclusion criteria. Also partially applicable, reasons include: German setting may not reflect current NHS context.

Reference	Reason for exclusion
Brophy 2004[20]	This study was assessed as partially applicable with potentially serious limitations. However, given that a more applicable UK analysis[48] comparing drug-eluting stents with bare-metal stents based on the same RCTs was available, this study was selectively excluded.
Brophy 2005[21]	This study was assessed as partially applicable with potentially serious limitations. However, given that a more applicable UK analysis[48] comparing drug-eluting stents with bare-metal stents based on the same RCTs was available, this study was selectively excluded.
Ekman 2006[39]	This study was assessed as partially applicable with potentially serious limitations. However, a more applicable UK analysis[48] was available that included the same RCT; therefore this study was selectively excluded.
Goeree 2009[45]	Excluded as rated very serious limitations due to being a model where treatment effects are based on a study that does not meet clinical review inclusion criteria. Also partially applicable, reasons include: Canadian setting may not reflect current NHS context.
Jahn 2010[52]	Excluded as rated very serious limitations due to being a model where treatment effects are based on studies that do not meet clinical review inclusion criteria. Also partially applicable, reasons include: Austrian perspective may not reflect current NHS context.
Kaiser 2005[54]	This study was assessed as partially applicable with potentially serious limitations. However, a more applicable UK analysis was available that incorporated the same RCT;[48] therefore this study was selectively excluded.
Kuukasjarvi 2007[65]	This study was assessed as partially applicable with potentially serious limitations. However, given that a more applicable UK analysis comparing drug-eluting stents with bare-metal stents based on the same RCTs[48] was available, this study was selectively excluded.
Lee 2014[69]	Excluded as rated very serious limitations due to being a model where treatment effects are based on a study that does not meet clinical review inclusion criteria. Also partially applicable, reasons include: Korean setting may not reflect current NHS context.
Poder 2017[87]	This study was assessed as partially applicable with potentially serious limitations. However, given there were more applicable analyses comparing drug-eluting stents with bare-metal stents with the relevant health outcomes this study was selectively excluded. The analysis was a cost-benefit analysis and did not use QALYs as the health outcome.
Suh 2013[117]	This study was assessed as partially applicable with potentially serious limitations. However, given there were more applicable analyses comparing drug-eluting stents with bare-metal stents with the relevant health outcomes this study was selectively excluded. The analysis was a cost-comparison and did not use QALYs as the health outcome.
Tarricone 2004[118]	This study was assessed as partially applicable with potentially serious limitations. However, given that a more applicable UK analysis comparing drug-eluting stents with bare-metal stents based on the same RCTs[48] was available, this study was selectively excluded.
Van Hout 2005[129]	This study was assessed as partially applicable with potentially serious limitations. However, a more applicable UK analysis was available that incorporated the same RCT;[48] therefore this study was selectively excluded.