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Myocardial revascularization for stable angina in single vessel disease

A systematic review and meta-analysis of randomized clinical trials

2017 - 7 - 1

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This report should be referenced as follows:

TrialResults-center.org; Results of all major randomized clinical trials about Myocardial revascularization for stable angina in single vessel disease.

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0.1 Synthesis of the meta-analysis results

We found 15 trials concerning PCI.

Results obtained by the meta-analysis are reported in the following tables, with the endpoints categorized according their results. Three classes are considered: endpoints for which a benefit effect was detected, endpoints revealing a harmful effect and the other for which no statistically significant difference was obtained (no evidence).

Reports of 14 trials (including 2,140 patients) were identified .

Among these comparisons, one trial are about angioplasty,5 about balloon angioplasty,one about PCI with or without stent,one about PCI with drug-eluting stents,one about PCI with sirolimus ES and 6 about stent.

No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.

Angioplasty

Results obtained with angioplasty for all the endpoints with data in at least one trial are summarized table 1.

Table 1: Results summary - Angioplasty

Benefit	Harmful	No evidence
<i>Angioplasty versus MIDCAB</i>		

* p <0.05; † p <0.01; ‡ p <0.001 RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test p <0.05)

Balloon angioplasty

Results obtained with balloon angioplasty for all the endpoints with data in at least one trial are summarized table 2.

Table 2: Results summary - Balloon angioplasty

Benefit	Harmful	No evidence
<i>Balloon angioplasty versus medical treatment</i>		

continued...

Benefit	Harmful	No evidence
		→ PTCA RR=1.46 ^{NS} [0.50;4.27] H k=3 → cardiac death or MI RR=1.66 ^{NS} [0.88;3.13] k=3 → myocardial infarction (fatal and non fatal) RR=1.51 ^{NS} [0.54;4.20] k=3 → cardiac death RR=1.52 ^{NS} [0.34;6.78] k=2 → CABG RR=1.06 ^{NS} [0.61;1.84] k=3 → non fatal MI RR=1.12 ^{NS} [0.49;2.54] k=3 → angina RR=0.59 ^{NS} [0.30;1.18] H k=3 → all cause death RR=1.04 ^{NS} [0.60;1.81] k=3
<i>Balloon angioplasty versus CABG</i>		
↑ CABG RR=10.67 [†] [2.03;56.04] k=2		→ cardiac death or MI RR=3.49 ^{NS} [0.99;12.28] k=2 → all cause death RR=2.29 ^{NS} [0.42;12.54] k=2

* p < 0.05; † p < 0.01; ¶ p < 0.001 RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test p < 0.05)

PCI with or without stent

Results obtained with PCI with or without stent for all the endpoints with data in at least one trial are summarized table 3.

Table 3: Results summary - PCI with or without stent

Benefit	Harmful	No evidence
<i>PCI with or without stent versus medical treatment</i>		
↓ PTCA RR=0.41* [0.18;0.89] k=1 ↓ cardiac death RR=0.29* [0.10;0.86] k=1 ↓ angina RR=0.30 [†] [0.13;0.74] k=1	↓ all cause death RR=0.36* [0.15;0.88] k=1	→ cardiac death or MI RR=0.55 ^{NS} [0.30;1.00] k=1 → CABG RR=0.25 ^{NS} [0.03;2.24] k=1 → non fatal MI RR=0.84 ^{NS} [0.38;1.89] k=1

* p < 0.05; † p < 0.01; ¶ p < 0.001 RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test p < 0.05)

PCI with drug-eluting stents

Results obtained with PCI with drug-eluting stents for all the endpoints with data in at least one trial are summarized table 4.

Table 4: Results summary - PCI with drug-eluting stents

Benefit	Harmful	No evidence
<i>PCI with drug-eluting stents versus CABG</i>		

* p < 0.05; † p < 0.01; ‡ p < 0.001 RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test p < 0.05)

PCI with sirolimus ES

Results obtained with PCI with sirolimus ES for all the endpoints with data in at least one trial are summarized table 5.

Table 5: Results summary - PCI with sirolimus ES

Benefit	Harmful	No evidence
<i>PCI with sirolimus ES versus MIDCAB</i>		

* p < 0.05; † p < 0.01; ‡ p < 0.001 RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test p < 0.05)

Stent

Results obtained with stent for all the endpoints with data in at least one trial are summarized table 6.

Table 6: Results summary - Stent

Benefit	Harmful	No evidence
<i>Stent versus CABG</i>		
	↑ 1 year revascularization RR=3.06* [1.20;7.80] k=1	→ 1 year event RR=1.25 ^{NS} [0.67;2.34] k=1 → 1 year death from any cause RR=0.25 ^{NS} [0.03;2.20] k=1
<i>Stent versus E-ACAB</i>		
	↑ 6 months events RR=22.00* [1.33;364.29] k=1	→ 6 months death RR=1.00 ^{NS} [0.02;49.42] k=1 → 6 months MI RR=1.00 ^{NS} [0.02;49.42] k=1
<i>Stent versus MIDCAB</i>		

continued...

Benefit	Harmful	No evidence
	↑ 6 months events RR=2.06 [†] [1.27;3.33] k=2	→ 6 months death RR=0.62 ^{NS} [0.14;2.72] k=3
	↑ 1 year event RR=3.00* [1.04;8.68] k=1	→ 6 months MI RR=1.21 ^{NS} [0.32;4.54] k=3
	↑ RR=3.24 [¶] [1.61;6.54] k=2	→ long term death RR=0.10 ^{NS} [0.00;8.53] H k=2
	↑ long term cardiovascular events RR=3.24 [¶] [1.61;6.54] k=2	
	↑ 1 year death from any cause RR=3.00* [1.04;8.68] k=1	

* p < 0.05; † p < 0.01; ¶ p < 0.001 RR: relative risk

H: heterogeneity with fixed effect model detected (heterogeneity test p < 0.05)

1 Introduction

1.1 Aim of the report

This report review all the randomized clinical trials of myocardial revascularization for the treatment of stable angina in single vessel disease.

1.2 Search strategy

The search aimed to identify all randomized clinical trials relating to the clinical effectiveness of myocardial revascularization for the treatment of stable angina in single vessel disease.

1.2.1 Sources searched

The following electronic databases were searched for relevant published literature for the period up to 2017 - 7 - 1:

- MEDLINE,
- EMBASE,
- Cochrane Database of Systematic Reviews (CDSR),
- Cochrane Central Register of Controlled Trials (CCTR),
- Health Technology Assessment (HTA) database,
- ISI Web of Science Proceedings (Index to Scientific and Technical Proceedings),
- ISI Web of Science Science Citation Index Expanded,

Each database was searched as far back as possible, with no language restrictions. Search strategies of relevant clinical keywords were developed through reference to published strategies, and by iterative searching, whereby keywords identified in references retrieved by initial scoping searches were used to extend the search strategy and so increase the sensitivity of retrieval.

In addition, the reference lists of relevant articles were handsearched.

Attempts to identify further studies were made by consulting health technology assessment and guideline producing agencies, and research and trials registers via the Internet.

Titles and, when available, abstracts of all studies identified in the searches were assessed by a single researcher for relevance to the review. In cases of doubt, the full article was obtained.

1.2.2 Search restrictions

No language, study/publication or date restrictions were applied to the main searches.

1.3 Inclusion criteria

Participants only those studies were included in which the participants had been diagnosed as having established stable angina.

Interventions studies in which myocardial revascularization was used.

Studies using other interventions in addition to myocardial revascularization therapy were included only if the treatment received by the intervention and control groups was identical in all respects other than the use of myocardial revascularization.

Methodology randomised controlled trials (RCTs). Trials were accepted as RCTs if the allocation of subjects to treatment groups was described by the authors as either randomised or double-blind.

1.4 Exclusion criteria

Studies considered methodologically unsound. The list of excluded studies with reason of their exclusion are given in a separate section for each treatment categories considered.

1.5 Meta-analysis strategy

Studies that met the reviews entry criteria were eligible for inclusion in the meta-analyses provided that they reported outcomes in terms of the number of subjects suffering clinical outcomes, as only this would allow calculation of the relative risk of subjects in the intervention group developing each outcome, compared with subjects in the control group.

Studies that only presented results in the form of relative risks, relative hazards or odds ratios, without the underlying numbers were also include in the meta-analyses.

Binary outcomes were analysed using the fixed-effect model. For continuous outcomes, weighted mean differences (WMDs) were analysed, using a fixed-effect model.

Heterogeneity was tested by the chi-2 test and the I2 statistic was obtained to describe the proportion of the variability.

Where quantitative heterogeneity was indicated, analysis using a random-effects model was conducted for comparison with results of fixed effect-based analysis. Results of the meta-analysis should be considered as being based on fixed-effect model unless stated otherwise.

Meta-analyses were conducted for data on Cardiac death or MI, All cause death, CABG, 6 months MI, Angina, 6 months death, PTCA, Non fatal MI, 6 months events, myocardial infarction (fatal and non fatal), cardiac death, Long term death, , long term cardiovascular events, 1 year death from any cause, 1 year event, 1 year revascularization, .

1.6 Structure of the report

Each of the eligible studies is summarised in part ???. A summary of the studies together with an evaluation of their quality is given in part ?? to ??, listed by therapeutic class. The therapeutic classes included PCI,

In these sections, studies in which an active intervention was compared with placebo or no treatment are discussed first, by intervention, followed by a discussion of those studies in which two or more active interventions were compared.

2 Overview of PCI

2.1 Included trials

A total of 15 randomized comparisons which enrolled 2140 patients were identified. In all, 1 randomized comparison concerned angioplasty, 5 balloon angioplasty, one PCI with or without stent, one PCI with drug-eluting stents, one PCI with sirolimus ES and 6 stent.

The detailed descriptions of trials and meta-analysis results is given in section 3 (page 30) for angioplasty, in section 4 (page 36) for balloon angioplasty, in section 5 (page 53) for PCI with or without stent, in section 6 (page 62) for PCI with drug-eluting stents, in section 7 (page 67) for PCI with sirolimus ES and in section 8 (page 73) for stent.

The average study size was 142 patients (range 53 to 300). The first study was published in 1992, and the last study was published in 2009.

All trials were open-label in design. All included studies were reported in English language. We did not find any unpublished trial.

The table 2.1 (page 15) summarizes the main characteristics of all the included trials. More detailed description is given in the following section.

2.2 Summary of meta-analysis results

The meta-analysis of the available trials about PCI provide the results listed in tables 2.2 to 2.7 (page 19) and in the following graphs.

2.2.1 Angioplasty

Data were insufficient to compare **angioplasty** to **MIDCAB**. There was an eligible trial but it did not provide sufficient information about the endpoints considered by this meta-analysis.

2.2.2 Balloon angioplasty

No significant difference was found between **balloon angioplasty** and **medical treatment** in terms of PTCA (RR=1.46, 95% CI 0.50 to 4.27, p=0.4913, 3 trials) with a random effect model in reason of a heterogeneity (Het. p=0.0057) (RR=1.66, 95% CI 0.88 to 3.13, p=0.1191, 3 trials), myocardial infarction (fatal and non fatal) (RR=1.51, 95% CI 0.54 to 4.20, p=0.4311, 3 trials), cardiac death (RR=1.52, 95% CI 0.34 to 6.78, p=0.5807, 2 trials), CABG (RR=1.06, 95% CI 0.61 to 1.84, p=0.8439, 3 trials), non fatal MI (RR=1.12, 95% CI 0.49 to 2.54, p=0.7951, 3 trials), angina (RR=0.59, 95% CI 0.30 to 1.18, p=0.1338, 3 trials) with a random effect model in reason of a heterogeneity (Het. p=0.0016) (RR=1.04, 95% CI 0.60 to 1.81, p=0.8835, 3 trials).

Balloon angioplasty was superior to **CABG** in terms of CABG (RR=10.67, 95% CI 2.03 to 56.04, p=0.0052, 2 trials). However, no significant difference was found on cardiac death or MI (RR=3.49, 95% CI 0.99 to 12.28, p=0.0518, 2 trials) and all cause death (RR=2.29, 95% CI 0.42 to 12.54, p=0.3407, 2 trials).

2.2.3 PCI with or without stent

PCI with or without stent was superior to **medical treatment** in terms of PTCA (RR=0.41, 95% CI 0.18 to 0.89, p=0.0247, 1 trial), cardiac death (RR=0.29, 95% CI 0.10 to 0.86, p=0.0256,

1 trial) and angina (RR=0.30, 95% CI 0.13 to 0.74, p=0.0083, 1 trial). But PCI with or without stent increased the risk of all cause death (RR=0.36, 95% CI 0.15 to 0.88, p=0.0256, 1 trial). However, no significant difference was found on cardiac death or MI (RR=0.55, 95% CI 0.30 to 1.00, p=0.0513, 1 trial), CABG (RR=0.25, 95% CI 0.03 to 2.24, p=0.2170, 1 trial) and non fatal MI (RR=0.84, 95% CI 0.38 to 1.89, p=0.6819, 1 trial).

2.2.4 PCI with drug-eluting stents

Data were insufficient to compare **PCI with drug-eluting stents** to **CABG**. There was an eligible trial but it did not provide sufficient information about the endpoints considered by this meta-analysis.

2.2.5 PCI with sirolimus ES

Data were insufficient to compare **PCI with sirolimus ES** to **MIDCAB**. There was an eligible trial but it did not provide sufficient information about the endpoints considered by this meta-analysis.

2.2.6 Stent

Stent was inferior to **CABG** in terms of 1 year revascularization (RR=3.06, 95% CI 1.20 to 7.80, p=0.0194, 1 trial). No significant difference was found on 1 year event (RR=1.25, 95% CI 0.67 to 2.34, p=0.4764, 1 trial) and 1 year death from any cause (RR=0.25, 95% CI 0.03 to 2.20, p=0.2142, 1 trial).

Stent was inferior to **E-ACAB** in terms of 6 months events (RR=22.00, 95% CI 1.33 to 364.29, p=0.0309, 1 trial). No significant difference was found on 6 months death (RR=1.00, 95% CI 0.02 to 49.42, p=1.0000, 1 trial) and 6 months MI (RR=1.00, 95% CI 0.02 to 49.42, p=1.0000, 1 trial).

Stent was inferior to **MIDCAB** in terms of 6 months events (RR=2.06, 95% CI 1.27 to 3.33, p=0.0035, 2 trials), 1 year event (RR=3.00, 95% CI 1.04 to 8.68, p=0.0428, 1 trial), (RR=3.24, 95% CI 1.61 to 6.54, p=0.0000, 2 trials), long term cardiovascular events (RR=3.24, 95% CI 1.61 to 6.54, p=0.0000, 2 trials) and 1 year death from any cause (RR=3.00, 95% CI 1.04 to 8.68, p=0.0428, 1 trial). No significant difference was found on 6 months death (RR=0.62, 95% CI 0.14 to 2.72, p=0.5279, 3 trials), 6 months MI (RR=1.21, 95% CI 0.32 to 4.54, p=0.7750, 3 trials) and long term death (RR=0.10, 95% CI 0.00 to 8.53, p=0.3072, 2 trials) with a random effect model in reason of a heterogeneity (Het. p=0.0216)

Table 2.1: Main study characteristics - PCI

Trial	Patients	Treatments	Trial design and method
Angioplasty			
Angioplasty versus MIDCAB			
AMIST (Reeves), 2004 [1] n = 50 vs. 50	single-vessel disease (at least 50% stenosis) of the left anterior descending coronary artery (LAD).	percutaneous transluminal coronary angioplasty (PTCA) with or without stenting versus minimally invasive direct coronary artery bypass grafting (MIDCAB)	open parallel groups Primary endpoint: cardiac-related events multicentre, England
Balloon angioplasty			
Balloon angioplasty versus medical treatment			
ACME, 1992 [1, 2] n = 105 vs. 107	stable angina, history of angina, MI within 3 months, exercise test with ST depression >3 mm, no previous PTCA; Single or serial stenosis within same artery 70% to 99% proximal two thirds	PTCA within 3 days of randomization versus medical treatment (nitrates, beta-blockers, calcium blockers)	open parallel groups US
MASS, 1995 [3] n = 72 vs. 72	stable angina, no Q wave MI, no left ventricular dysfunction	PTCA versus medical treatment (aspirin, nitrates, beta-blockers and calcium channel blocking)	open parallel groups Brazil
Sievers, 1993 [4] n = 44 vs. 44	previous nonQ wave MI, no angina in daily life, no previous Q wave MI	PTCA versus medical treatment	open parallel groups Germany
Balloon angioplasty versus CABG			

continued...

Trial	Patients	Treatments	Trial design and method
MASS, 1995 [5] n = 72 vs. 70	patients with stable angina, normal ventricular function and a proximal stenosis of the left anterior descending coronary artery >80%	percutaneous transluminal coronary angioplasty versus mammmary bypass surgery	open Brazil
Lausanne, 1994 [6] n = 68 vs. 66	patients with isolated proximal left anterior descending artery stenosis, conserved left ventricular function, and documented ischaemia	transluminal coronary angioplasty versus coronary artery bypass grafting	open Switzerland
PCI with or without stent			
PCI with or without stent versus medical treatment			
ALKK, 2003 [1] n = 149 vs. 151	patients with single vessel disease of the infarct vessel and no or minor angina pectoris in the subacute phase (1 to 6 weeks) after an acute myocardial infarction	angioplasty versus medical therapy	open parallel groups Primary endpoint: death, reMI, reintervention, CABG, severe AP multicenter, Germany
PCI with drug-eluting stents			
PCI with drug-eluting stents versus CABG			
Hong, 2005 [1] n = 119 vs. 70	proximal left anterior descending (LAD) coronary artery stenosis	drug-eluting stents versus invasive direct coronary artery bypass (MIDCAB) surgery	open parallel groups
PCI with sirolimus ES			
PCI with sirolimus ES versus MIDCAB			
Thiele, 2009 [1] n = 65 vs. 65	isolated LAD disease	sirolimus-eluting stent versus MIDCAB surgery	open parallel groups Primary endpoint: cardiac death, MI, and need for PCI single center, Germany

continued...

Trial	Patients	Treatments	Trial design and method
Stent			
Stent versus CABG			
LEMANS, 2002 [1] n = 52 vs. 53	patients with unprotected left main coronary artery stenosis	unprotected left main stenting versus coronary artery bypass grafting	open parallel groups Primary endpoint: change in left ventricular ejection fraction Poland
Stent versus E-ACAB			
Cisowski, 0 n = 50 vs. 50	single vessel disease ACC/AHA A or B lesion in proximal LAD Angina CCS II or higher Lesion diameter 3 mm or greater/length 20mm or greater	tristar, Tera, Penta (Guidant) (Cordis) versus endoscopic atraumatic coronary artery bypass grafting	open parallel group Single center, Poland
Stent versus MIDCAB			
Diegeler, 2002 [2, 3] n = 110 vs. 110	single vessel disease Lesion =75% stenosis in proximal LAD or between origin of left circumflex and 1st septal branch	various stents versus minimally invasive direct coronary artery bypass (off-pump procedure)	open parallel group Primary endpoint: major adverse cardiac events Multicentre, Germany
Drenth, 2002 [4, 5, 6] n = 51 vs. 51	single vessel disease Angina II Lesion (Grade B2 or C) of proximal LAD Suitable for CABG or stenting	stent type not reported versus minimally invasive direct coronary artery bypass (off-pump procedure)	open parallel group Primary endpoint: major Adverse Cardiac and Cerebrovascular Events Single centre, Netherlands
Grip, 2001 [7] n = 28 vs. 25	single vessel disease engaging LAD Stable or unstable angina	stent type not reported versus minimally invasive direct coronary artery bypass (off-pump procedure)	open parallel group Sweden

continued...

Trial	Patients	Treatments	Trial design and method
SIMA, 2000 [8] n = 62 vs. 59	single vessel disease silent ischaemia 1 LAD lesion Ejection fraction >45% Vessel >3.0mm	any CE marked, but Palmaz-Schatz recommended versus conventional CABG or minimally invasive direct coronary artery bypass (off-pump procedure) (10% of surgical procedures)	open parallel group Primary endpoint: death, myocardial infarction, revascularization Multicentre, Europe

Table 2.2: Summary of all results for angioplasty

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
angioplasty versus MIDCAB						
No data were presented in the trial identified						
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients						

Table 2.3: Summary of all results for balloon angioplasty

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
balloon angioplasty versus medical treatment						
PTCA	RR=1.46 ¹	0.50;4.27	0.4913	0.0057 (0.81) †	3	444
cardiac death or MI	RR=1.66	0.88;3.13	0.1191	0.9301 (0.00)	3	444
myocardial infarction (fatal and non fatal)	RR=1.51	0.54;4.20	0.4311	0.8799 (0.00)	3	444
cardiac death	RR=1.52	0.34;6.78	0.5807	0.4697 (0.00)	2	232
CABG	RR=1.06	0.61;1.84	0.8439	0.9849 (0.00)	3	444
non fatal MI	RR=1.12	0.49;2.54	0.7951	0.6289 (0.00)	3	444
angina	RR=0.59 ²	0.30;1.18	0.1338	0.0016 (0.85) †	3	444
all cause death	RR=1.04	0.60;1.81	0.8835	0.9029 (0.00)	3	444
balloon angioplasty versus CABG						
cardiac death or MI	RR=3.49	0.99;12.28	0.0518	0.7031 (0.00)	2	276
CABG	RR=10.67	2.03;56.04	0.0052	0.6060 (0.00)	2	276
all cause death	RR=2.29	0.42;12.54	0.3407	0.4383 (0.00)	2	276
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients						

Table 2.4: Summary of all results for PCI with or without stent

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
PCI with or without stent versus medical treatment						
PTCA	RR=0.41	0.18;0.89	0.0247	1.0000 (0.00)	1	300
cardiac death or MI	RR=0.55	0.30;1.00	0.0513	1.0000 (1.00)	1	300
cardiac death	RR=0.29	0.10;0.86	0.0256	1.0000 (0.00)	1	300

continued...

¹with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=1.11 95% CI 0.78;1.59²with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.63 95% CI 0.50;0.79

Endpoint	Effect	95% CI	p ass	p het	k	n
CABG	RR=0.25	0.03;2.24	0.2170	1.0000 (0.00)	1	300
non fatal MI	RR=0.84	0.38;1.89	0.6819	1.0000 (0.00)	1	300
angina	RR=0.30	0.13;0.74	0.0083	1.0000 (0.00)	1	300
all cause death	RR=0.36	0.15;0.88	0.0256	1.0000 (0.00)	1	300

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.5: Summary of all results for PCI with drug-eluting stents

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
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PCI with drug-eluting stents versus CABG

No data were presented in the trial identified

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.6: Summary of all results for PCI with sirolimus ES

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
----------	--------	--------	-------	-----------------	---	---

PCI with sirolimus ES versus MIDCAB

No data were presented in the trial identified

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Table 2.7: Summary of all results for stent

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
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stent versus CABG

1 year event RR=1.25 0.67;2.34 0.4764 1.0000 (0.00) 1 105

1 year revascularization RR=3.06 1.20;7.80 0.0194 1.0000 (0.00) 1 105

1 year death from any cause RR=0.25 0.03;2.20 0.2142 1.0000 (1.00) 1 105

stent versus E-ACAB

6 months events RR=22.00 1.33;364.29 0.0309 1.0000 (0.00) 1 100

6 months death RR=1.00 0.02;49.42 1.0000 1.0000 (0.00) 1 100

6 months MI RR=1.00 0.02;49.42 1.0000 1.0000 (0.00) 1 100

stent versus MIDCAB

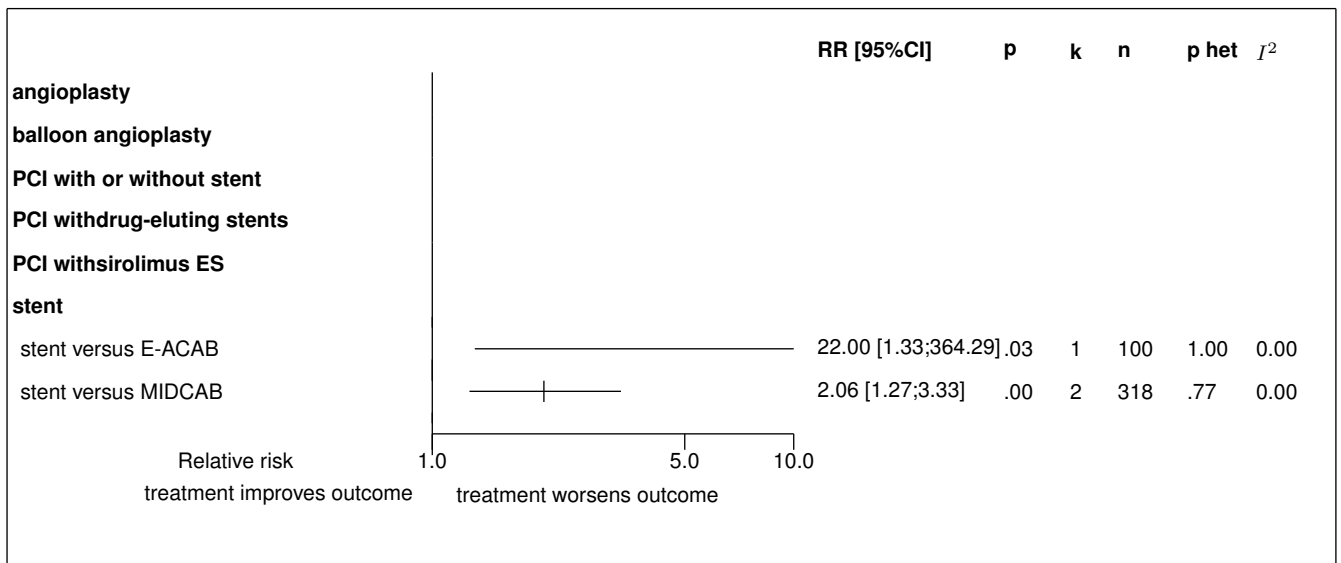
6 months events RR=2.06 1.27;3.33 0.0035 0.7664 (0.00) 2 318

continued...

Endpoint	Effect	95% CI	p ass	p het	k	n
1 year event	RR=3.00	1.04;8.68	0.0428	1.0000 (0.00)	1	102
	RR=3.24	1.61;6.54	0.0000	0.3771 (0.00)	2	223
6 months death	RR=0.62	0.14;2.72	0.5279	0.7390 (0.00)	3	371
6 months MI	RR=1.21	0.32;4.54	0.7750	0.2578 (0.26)	3	371
long term cardiovascular events	RR=3.24	1.61;6.54	0.0000	0.3771 (0.00)	2	223
1 year death from any cause	RR=3.00	1.04;8.68	0.0428	1.0000 (0.00)	1	102
long term death	RR=0.10 ³	0.00;8.53	0.3072	0.0216 (0.81) †	2	223

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

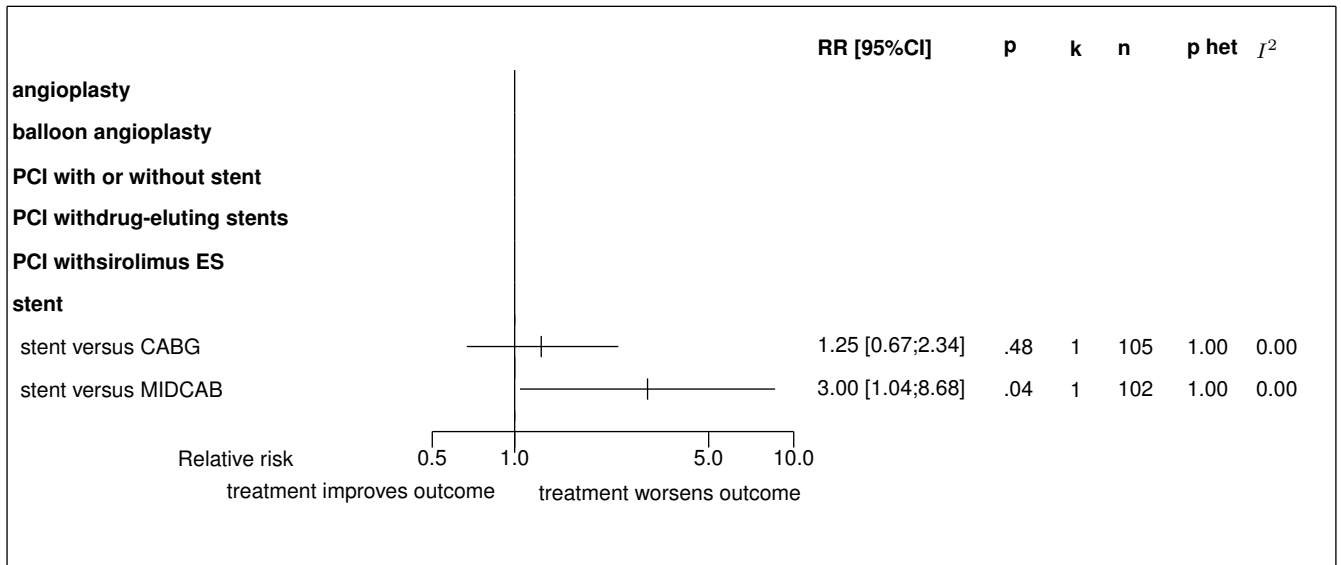
Figure 2.1: Forest's plot for 6 months events



Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; †: random effect model used

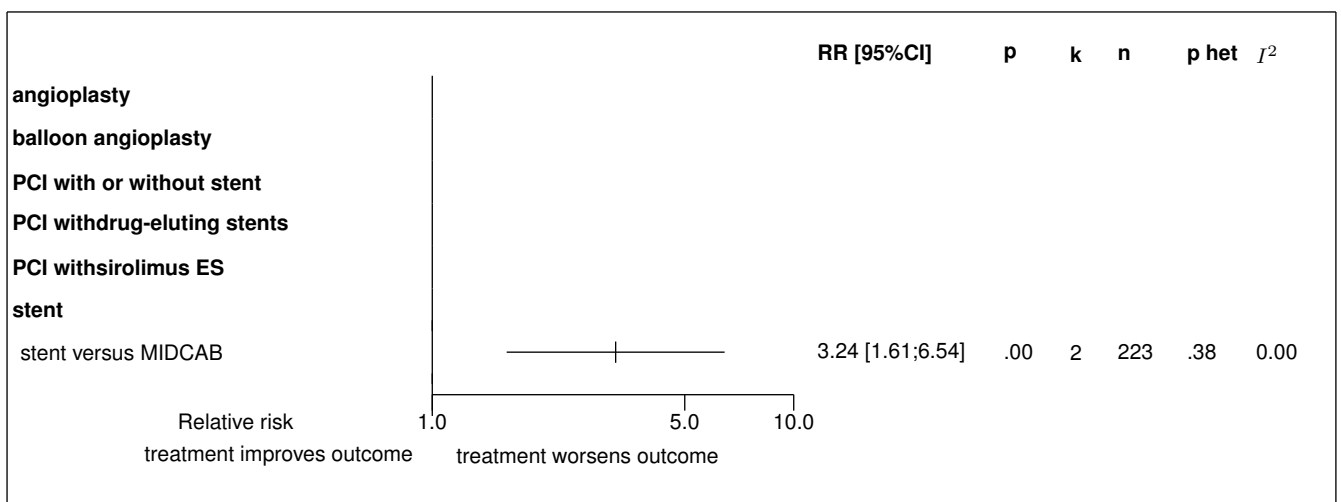
³with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.10 95% CI 0.01;0.69

Figure 2.2: Forest's plot for 1 year event



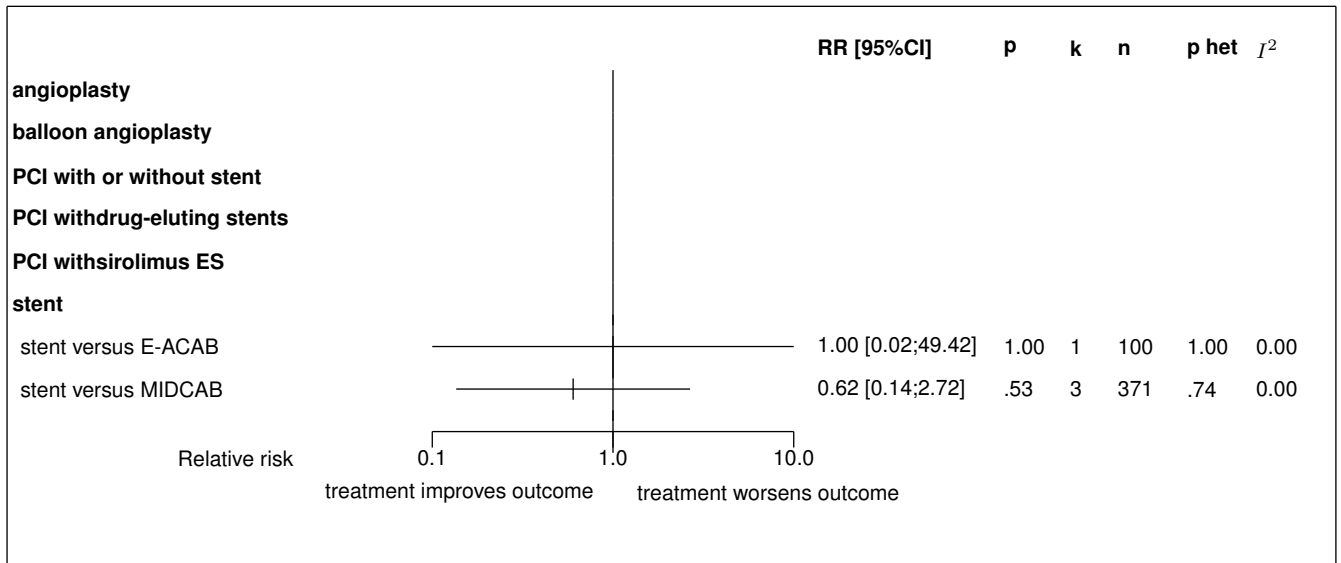
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.3: Forest's plot for



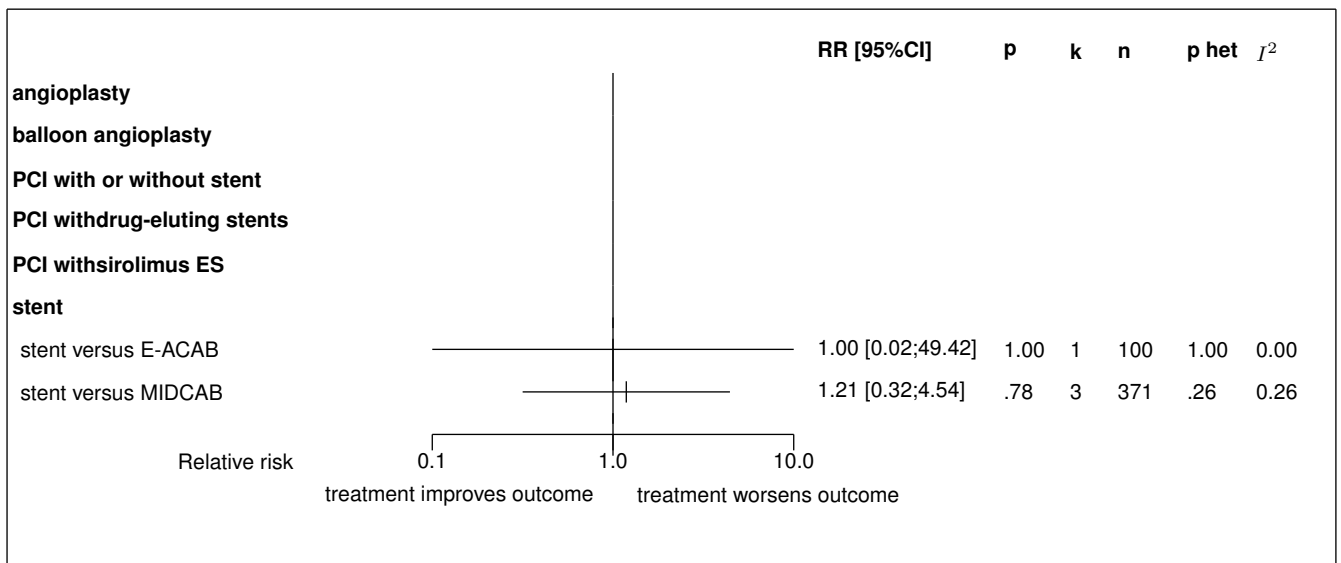
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.4: Forest's plot for 6 months death



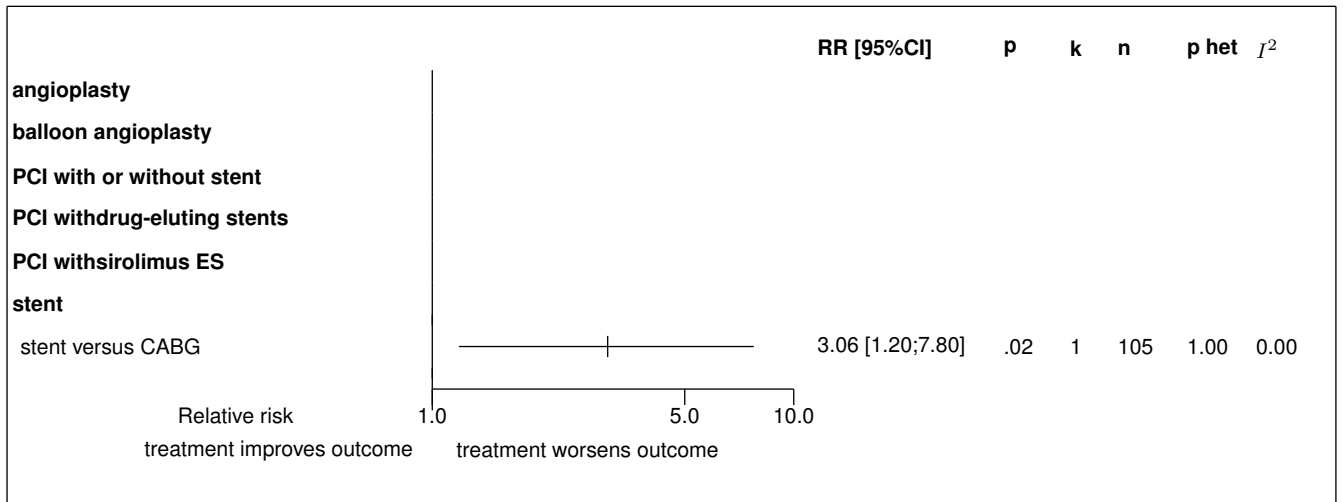
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.5: Forest's plot for 6 months MI



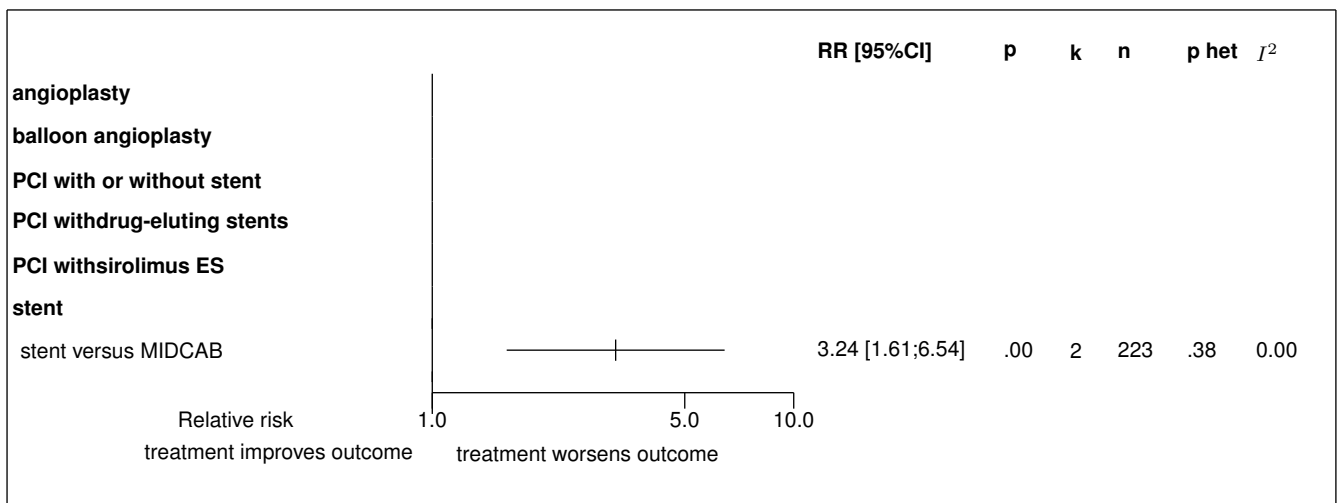
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.6: Forest's plot for 1 year revascularization



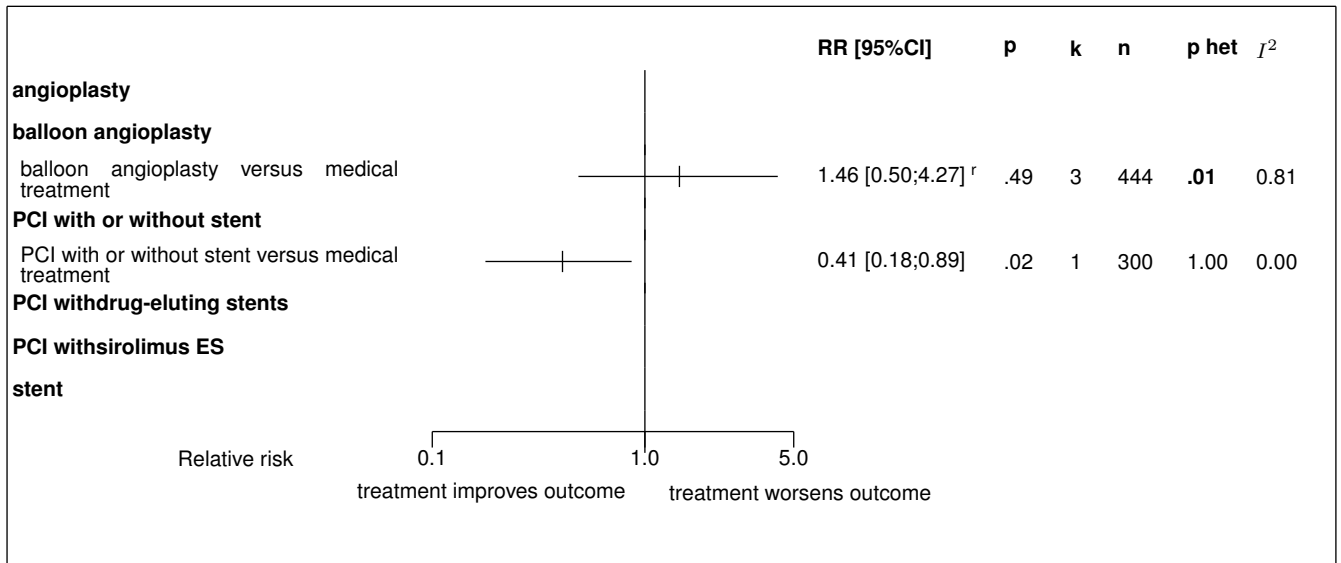
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.7: Forest's plot for long term cardiovascular events



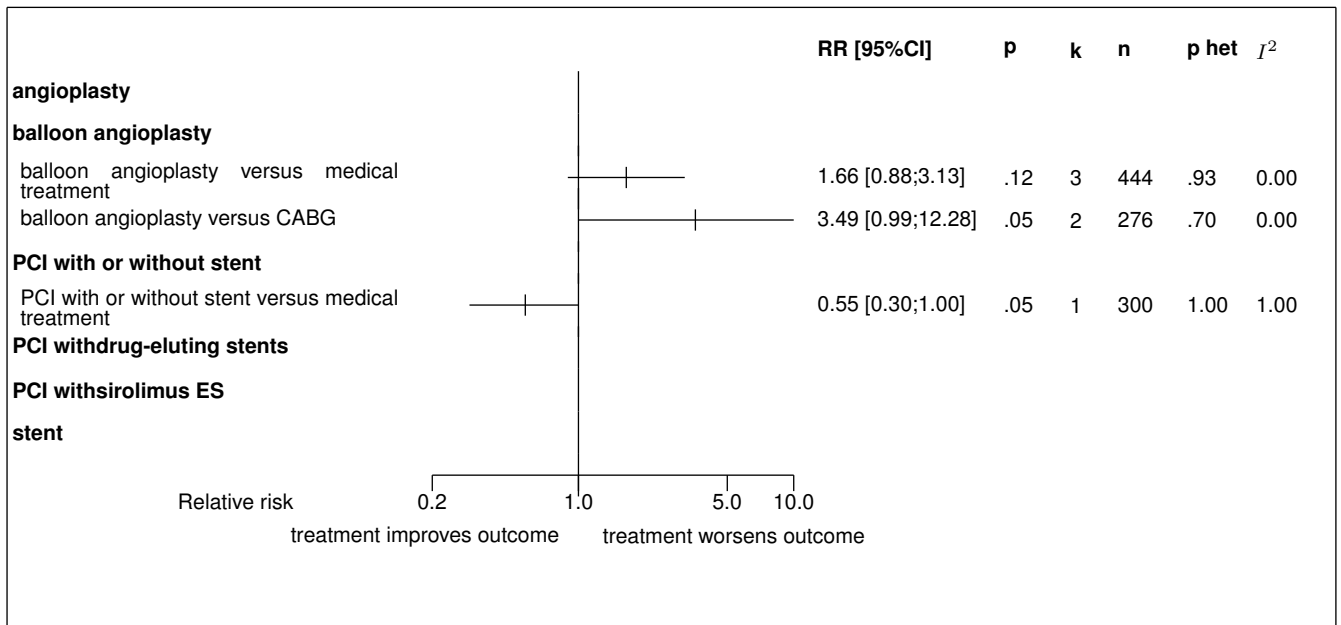
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.8: Forest's plot for PTCA



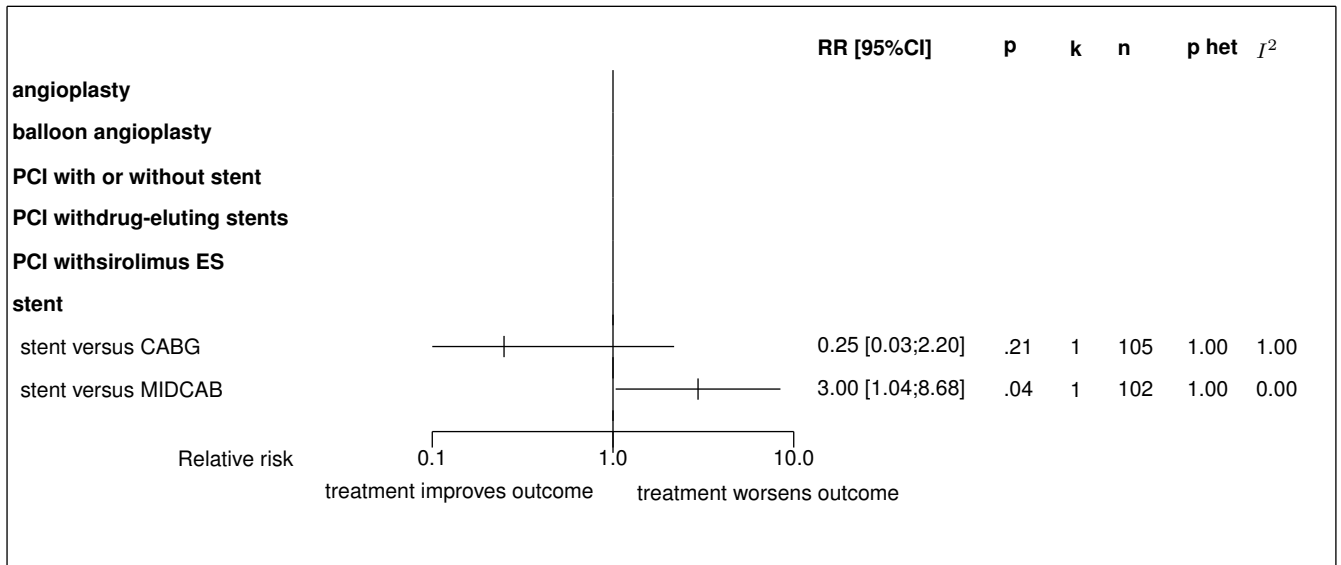
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; †: random effect model used

Figure 2.9: Forest's plot for cardiac death or MI



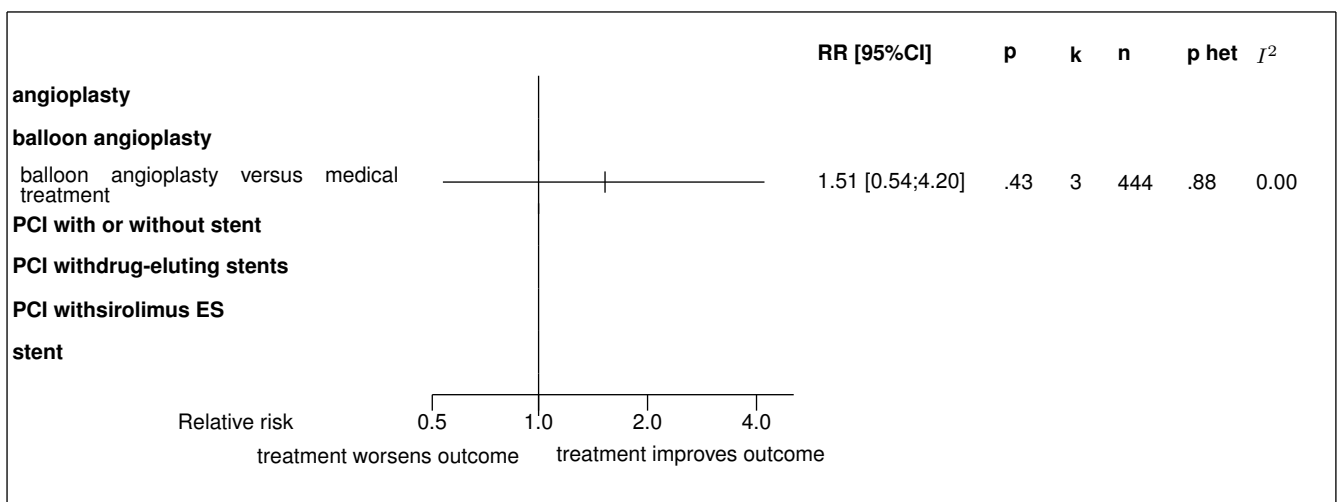
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; †: random effect model used

Figure 2.10: Forest's plot for 1 year death from any cause



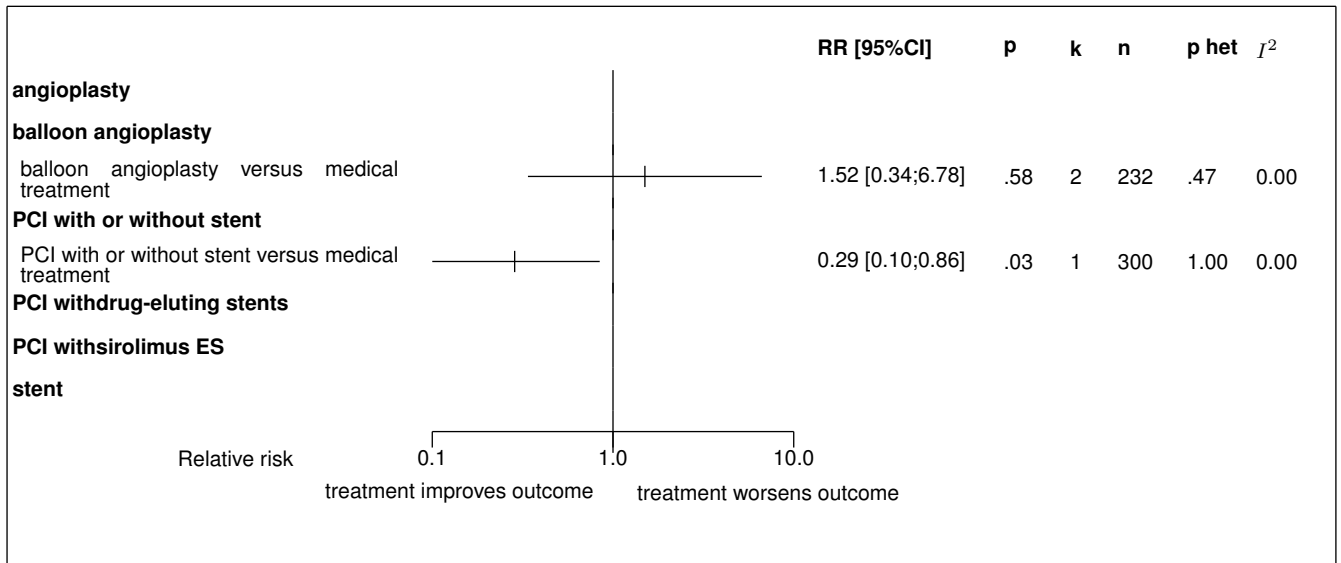
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.11: Forest's plot for myocardial infarction (fatal and non fatal)



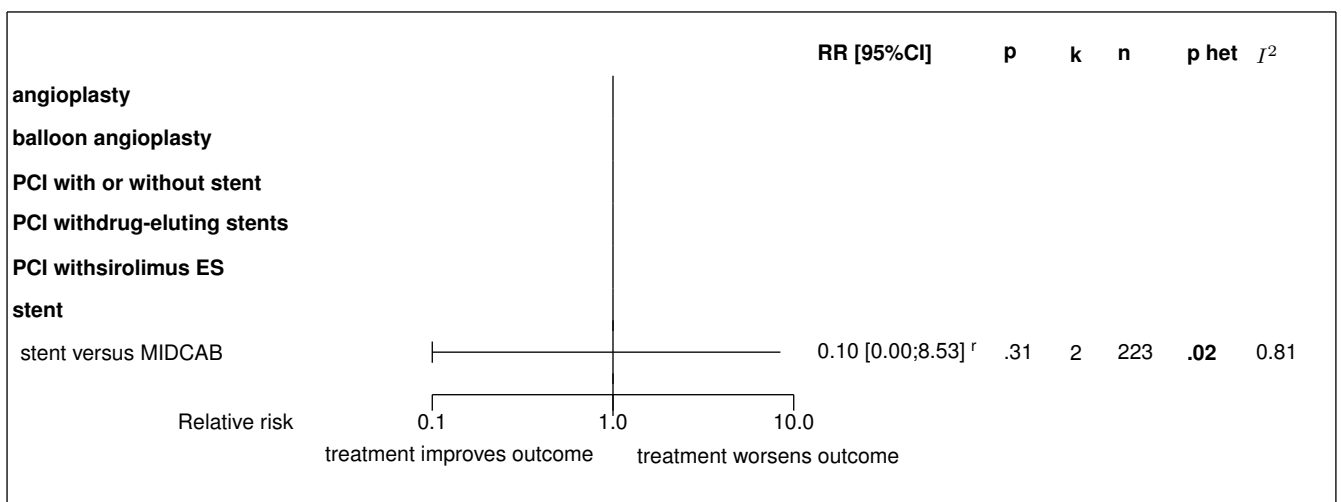
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.12: Forest's plot for cardiac death



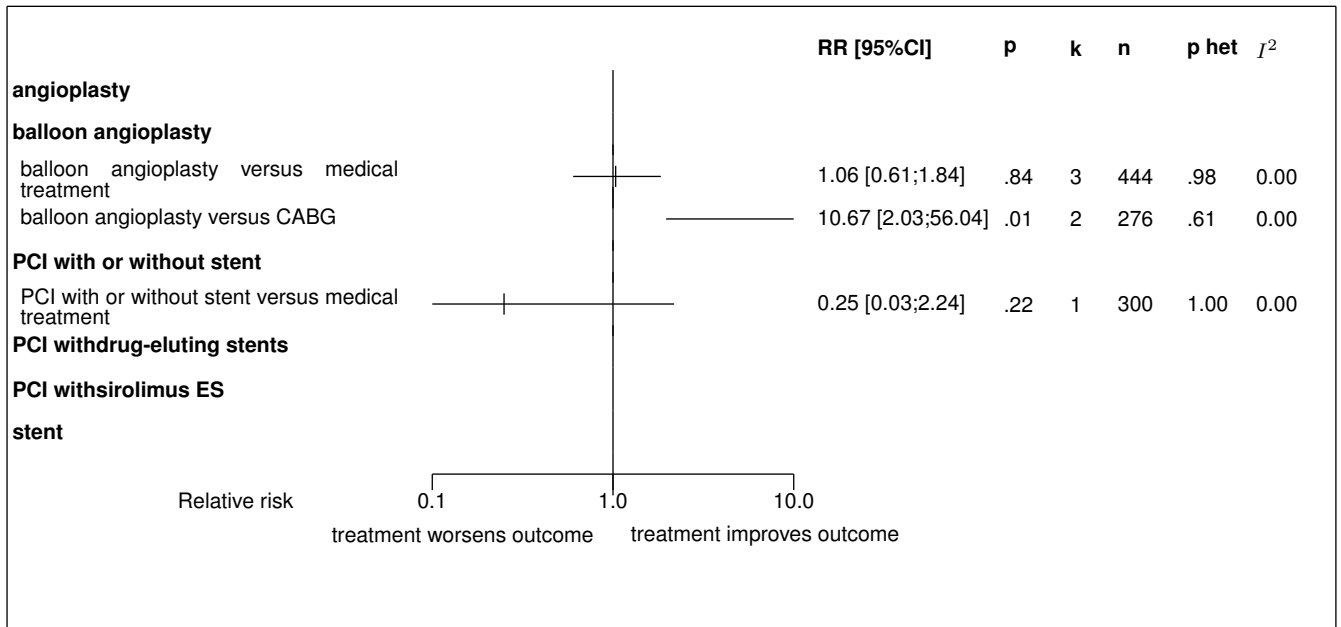
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; ^r: random effect model used

Figure 2.13: Forest's plot for long term death



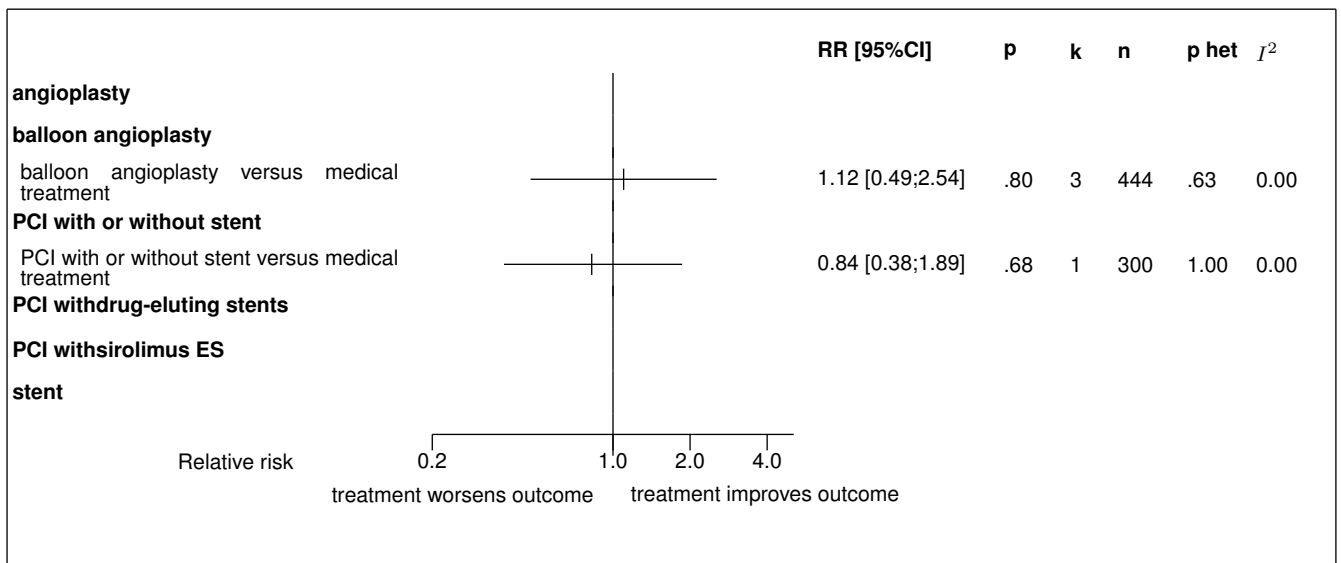
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; ^r: random effect model used

Figure 2.14: Forest's plot for CABG



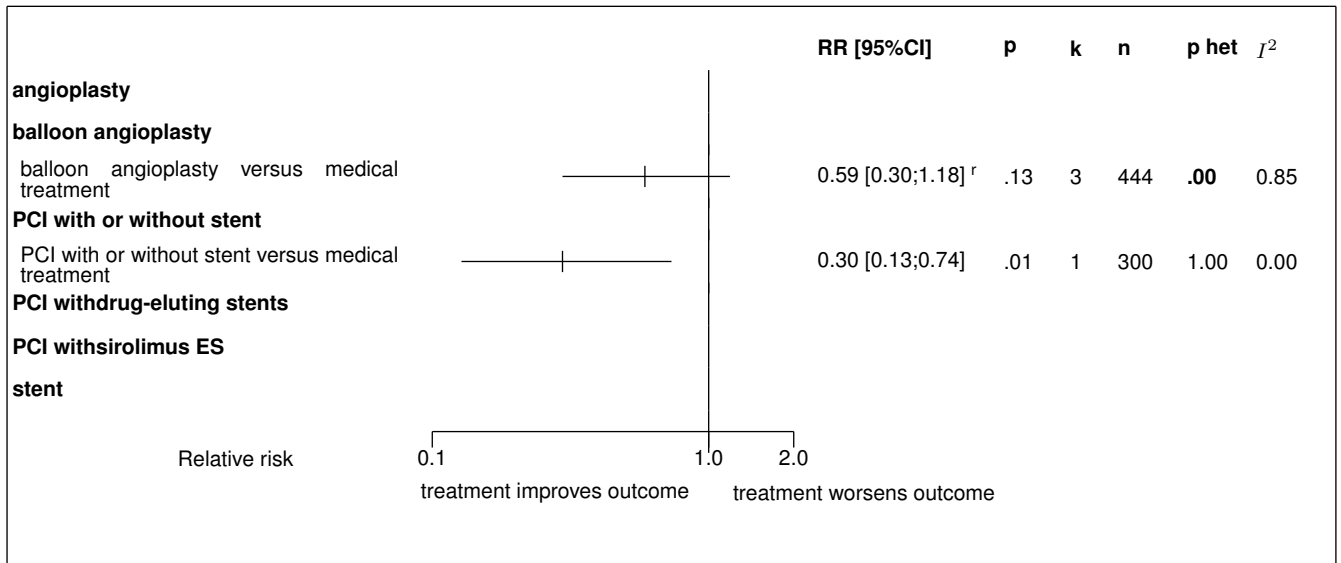
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.15: Forest's plot for non fatal MI



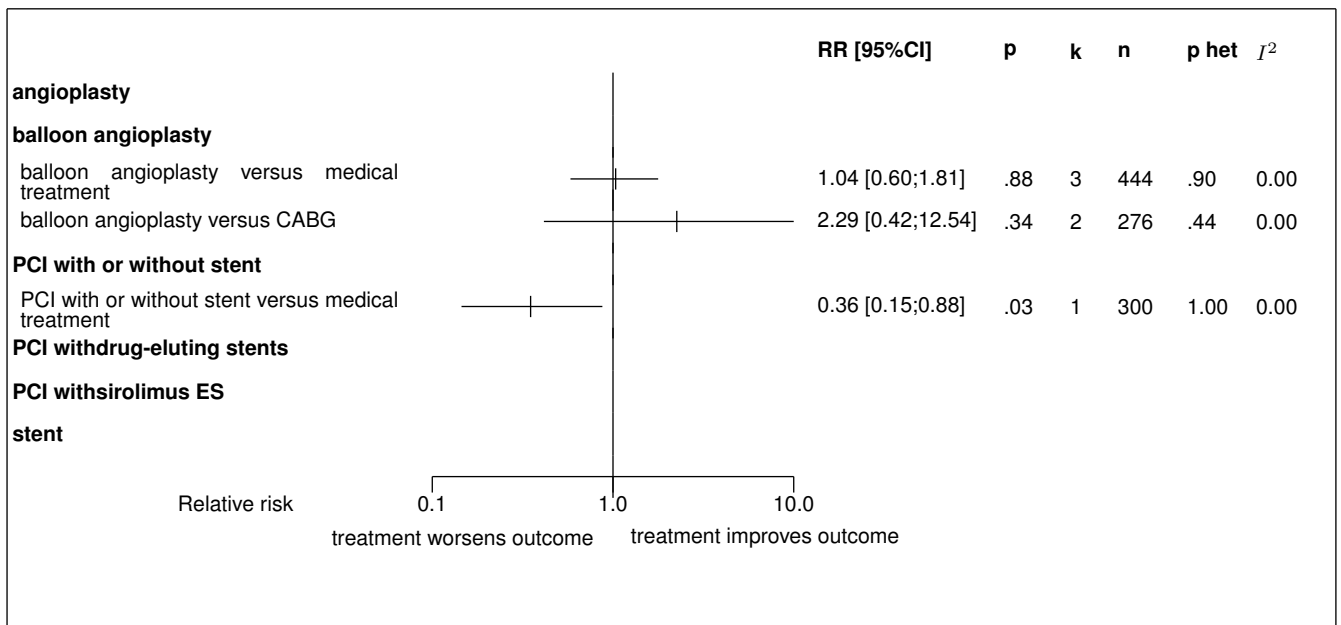
Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; I²: random effect model used

Figure 2.16: Forest's plot for angina



Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; †: random effect model used

Figure 2.17: Forest's plot for all cause death



Results obtained with a fixed effect model except in case of heterogeneity where a random model was used
 RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the heterogeneity test; †: random effect model used

3 Detailed results for angioplasty

3.1 Available trials

Only one trial which randomized 100 patients was identified: it compared angioplasty with MIDCAB.

This trial included 100 patients and was published in 2004.

This trial was open-label in design.

It was reported in English language.

data was reported in trials;

Following tables 3.1 (page 30), 3.2 (page 30), 3.4 (page 32), and 3.3 (page 30) summarized the main characteristics of the trial including in this systematic review of randomized trials of angioplasty.

Table 3.1: Treatment description - PCI - angioplasty

Trial	Studied treatment	Control treatment
Angioplasty versus MIDCAB		
AMIST (Reeves) (2004) [1]	percutaneous transluminal coronary angioplasty (PTCA) with or without stenting	minimally invasive direct coronary artery bypass grafting (MIDCAB)

Table 3.2: Descriptions of participants - PCI - angioplasty

Trial	Patients
Angioplasty versus MIDCAB	
AMIST (Reeves) (2004) [1]	Single-vessel disease (at least 50% stenosis) of the left anterior descending coronary artery (LAD).

Table 3.3: Design and methodological quality of trials - PCI - angioplasty

Trial	Design	Duration	Centre	Primary end-point
Angioplasty versus MIDCAB				
AMIST (Reeves), 2004 [1] n=100	Parallel groups open confirmatory trial at risk of bias	12 months	England multicentre	cardiac-related events

continued...

Trial	Design	Duration	Centre	Primary end-point
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Table 3.4: Trial characteristics - PCI - angioplasty

Trial	Age (mean, year)	Men (%)	Ejection fraction (%)	Extent of Disease	arterial grafts	stent (%)
Angioplasty versus MIDCAB						
AMIST (Reeves), 2004 [1]						

3.2 Meta-analysis results

The results are detailed in table 3.5 (page 33). This table is followed by the Forest's plot corresponding to each endpoint.

Angioplasty versus MIDCAB

No data were presented in the 1 trial identified

Table 3.5: Results details - PCI - angioplasty

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
angioplasty versus MIDCAB						
No data were presented in the trial identified						
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree						

References

- [1] Reeves BC, Angelini GD, Bryan AJ, Taylor FC, Cripps T, Spyt TJ, Samani NJ, Roberts JA, Jacklin P, Seehra HK, Culliford LA, Keenan DJ, Rowlands DJ, Clarke B, Stanbridge R, Foale R. A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery. *Health Technol Assess* 2004;8:1-43. [PMID=15080865]

3.3 Individual trial summaries

Table 3.6: AMIST (Reeves), 2004 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
<p>n=100 (50 vs. 50)</p> <p>Follow-up duration: 12 months</p> <p>Study design: Randomized controlled trial</p> <p>Parallel groups</p> <p>Open</p> <p>Confirmatory trial at risk of bias</p> <p>England, multicentre</p>	<p>Single-vessel disease (at least 50% stenosis) of the left anterior descending coronary artery (LAD).</p>	<p>Studied treatment: percutaneous transluminal coronary angioplasty (PTCA) with or without stenting</p> <p>Control treatment: minimally invasive direct coronary artery bypass grafting (MIDCAB)</p>	
<p>Reference</p> <p>Reeves BC, Angelini GD, Bryan AJ, Taylor FC, Cripps T, Spyt TJ, Samani NJ, Roberts JA, Jacklin P, Seehra HK, Culliford LA, Keenan DJ, Rowlands DJ, Clarke B, Stanbridge R, Foale R. A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery. <i>Health Technol Assess</i> 2004;8:1-43 [PMID=15080865]</p>			

4 Detailed results for balloon angioplasty

4.1 Available trials

A total of 5 RCTs which randomized 720 patients were identified: 3 trials compared balloon angioplasty with medical treatment and 2 trials compared balloon angioplasty with CABG. The average study size was 144 patients (range 88 to 212). The first study was published in 1992, and the last study was published in 1995.

All trials were open-label in design. All included studies were reported in English language. We did not find any unpublished trial.

Cardiac death or MI data was reported in 5 trials; 5 trials reported data on all cause death; 5 trials reported data on CABG; 3 trials reported data on angina; 3 trials reported data on myocardial infarction (fatal and non fatal); 3 trials reported data on PTCA; 3 trials reported data on non fatal MI; and 2 trials reported data on cardiac death.

Following tables 4.1 (page 36), 4.2 (page 37), 4.4 (page 39), and 4.3 (page 37) summarized the main characteristics of the trials including in this systematic review of randomized trials of balloon angioplasty.

Table 4.1: Treatment description - PCI - balloon angioplasty

Trial	Studied treatment	Control treatment
Balloon angioplasty versus medical treatment		
ACME (1992) [1, 2]	PTCA within 3 days of randomization	medical treatment (nitrates, beta-blockers, calcium blockers)
	Concomittant treatment: aspirin 325 mg/d	
MASS (1995) [3]	PTCA	medical treatment (aspirin, nitrates, beta-blockers and calcium channel blocking)
	Concomittant treatment: -	
Sievers (1993) [4]	PTCA	medical treatment
	Concomittant treatment: aspirin 100mg	
Balloon angioplasty versus CABG		
MASS (1995) [5]	percutaneous transluminal coronaryangioplasty	mammary bypass surgery
Lausanne (1994) [6]	transluminal coronary angioplasty	Coronary artery bypass grafting

Table 4.2: Descriptions of participants - PCI - balloon angioplasty

Trial	Patients
Balloon angioplasty versus medical treatment	
ACME (1992) [1, 2]	Stable angina, history of angina, MI within 3 months, exercise test with ST depression >3 mm, no previous PTCA; Single or serial stenosis within same artery 70% to 99% proximal two-thirds Inclusion criteria: stable angina pectoris or MI in the last 3 mo AND stenosis of 70 to 99% in one major vessel AND exercise-test with ST-segment depression Exclusion criteria: -
MASS (1995) [3]	Stable angina, no Q wave MI, no left ventricular dysfunction [^] Inclusion criteria: patient with stable angina and single proximal stenosis >80% of the left anterior descending artery Exclusion criteria: unstable angina, prior MI, valvular disease, cardiomyopathy, LV failure, total occlusion, lesion length >12mm, involvement of the ostium, calcification,
Sievers (1993) [4]	Previous nonQ wave MI, no angina in daily life, no previous Q wave MI Inclusion criteria: single vessel, no angina under medical therapy Exclusion criteria: previous MI, diabetes, positive stress test at 50W
Balloon angioplasty versus CABG	
MASS (1995) [5]	Patients with stable angina, normal ventricular function and a proximal stenosis of the left anterior descending coronary artery >80%
Lausanne (1994) [6]	Patients with isolated proximal left anterior descending artery stenosis, conserved left ventricular function, and documented ischaemia

Table 4.3: Design and methodological quality of trials - PCI - balloon angioplasty

Trial	Design	Duration	Centre	Primary endpoint
Balloon angioplasty versus medical treatment				
ACME, 1992 [1, 2] n=212	Parallel groups open confirmatory trial at risk of bias	5y inclusion period: 1987-1990	US	
MASS, 1995 [3] n=144	Parallel groups open confirmatory trial at risk of bias	5y inclusion period: 1988-1991	Brazil	
Sievers, 1993 [4] n=88	Parallel groups open confirmatory trial at risk of bias	2y inclusion period: ND	Germany	
Balloon angioplasty versus CABG				

continued...

Trial	Design	Duration	Centre	Primary end-point
MASS, 1995 [5] n=142	open	3.2 y	Brazil	
Lausanne, 1994 [6] n=134	open	3.2 y	Switzerland	

Table 4.4: Trial characteristics - PCI - balloon angioplasty

Trial
Balloon angioplasty versus medical treatment
ACME, 1992 [1, 2]
MASS, 1995 [3]
Sievers, 1993 [4]
Balloon angioplasty versus CABG
MASS, 1995 [5]
Lausanne, 1994 [6]

4.2 Meta-analysis results

The results are detailed in table 4.5 (page 41). This table is followed by the Forest's plot corresponding to each endpoint.

Balloon angioplasty versus medical treatment

All the 3 studies had extractable data about the number of participants with **PTCA**. When pooled together, there was no statistically significant difference between the groups in PTCA, with a RR of 1.46 (95% CI 0.50 to 4.27, $p=0.4913$). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies ($p = 0.0057$, $I^2 = 0.81\%$).

All the 3 studies had extractable data about the number of participants with **cardiac death or MI**. When pooled together, there was no statistically significant difference between the groups in cardiac death or MI, with a RR of 1.66 (95% CI 0.88 to 3.13, $p=0.1191$). No heterogeneity was detected ($p = 0.9301$, $I^2 = 0.00\%$).

All the 3 studies had extractable data about the number of participants with **myocardial infarction (fatal and non fatal)**. When pooled together, there was no statistically significant difference between the groups in myocardial infarction (fatal and non fatal), with a RR of 1.51 (95% CI 0.54 to 4.20, $p=0.4311$). No heterogeneity was detected ($p = 0.8799$, $I^2 = 0.00\%$).

A total of 2 of the 3 studies eligible for this comparison provided data on **cardiac death**. When pooled together, there was no statistically significant difference between the groups in cardiac death, with a RR of 1.52 (95% CI 0.34 to 6.78, $p=0.5807$). No heterogeneity was detected ($p = 0.4697$, $I^2 = 0.00\%$).

All the 3 studies had extractable data about the number of participants with **CABG**. When pooled together, there was no statistically significant difference between the groups in CABG, with a RR of 1.06 (95% CI 0.61 to 1.84, $p=0.8439$). No heterogeneity was detected ($p = 0.9849$, $I^2 = 0.00\%$).

All the 3 studies had extractable data about the number of participants with **non fatal MI**. When pooled together, there was no statistically significant difference between the groups in non fatal MI, with a RR of 1.12 (95% CI 0.49 to 2.54, $p=0.7951$). No heterogeneity was detected ($p = 0.6289$, $I^2 = 0.00\%$).

All the 3 studies had extractable data about the number of participants with **angina**. When pooled together, there was no statistically significant difference between the groups in angina, with a RR of 0.59 (95% CI 0.30 to 1.18, $p=0.1338$). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies ($p = 0.0016$, $I^2 = 0.85\%$).

All the 3 studies had extractable data about the number of participants with **all cause death**. When pooled together, there was no statistically significant difference between the groups in all cause death, with a RR of 1.04 (95% CI 0.60 to 1.81, $p=0.8835$). No heterogeneity was detected ($p = 0.9029$, $I^2 = 0.00\%$).

Balloon angioplasty versus CABG

All the 2 studies had extractable data about the number of participants with **cardiac death or MI**. When pooled together, there was no statistically significant difference between the groups in cardiac death or MI, with a RR of 3.49 (95% CI 0.99 to 12.28, $p=0.0518$). No heterogeneity was detected ($p = 0.7031$, $I^2 = 0.00\%$).

All the 2 studies had extractable data about the number of participants with **CABG**. The analysis detected a statistically significant difference in favor of balloon angioplasty in CABG, with a RR of 10.67 (95% CI 2.03 to 56.04, $p=0.0052$). No heterogeneity was detected ($p = 0.6060$, $I^2 = 0.00\%$).

All the 2 studies had extractable data about the number of participants with **all cause death**. When pooled together, there was no statistically significant difference between the groups in

all cause death, with a RR of 2.29 (95% CI 0.42 to 12.54, $p=0.3407$). No heterogeneity was detected ($p = 0.4383$, $I^2 = 0.00\%$).

Table 4.5: Results details - PCI - balloon angioplasty

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
balloon angioplasty versus medical treatment						
PTCA	RR=1.46	[0.50;4.27]	0.4913	0.0057 ($I^2=0.81$)	3	444
cardiac death or MI	RR=1.66	[0.88;3.13]	0.1191	0.9301 ($I^2=0.00$)	3	444
myocardial infarction (fatal and non fatal)	RR=1.51	[0.54;4.20]	0.4311	0.8799 ($I^2=0.00$)	3	444
cardiac death	RR=1.52	[0.34;6.78]	0.5807	0.4697 ($I^2=0.00$)	2	232
CABG	RR=1.06	[0.61;1.84]	0.8439	0.9849 ($I^2=0.00$)	3	444
non fatal MI	RR=1.12	[0.49;2.54]	0.7951	0.6289 ($I^2=0.00$)	3	444
angina	RR=0.59	[0.30;1.18]	0.1338	0.0016 ($I^2=0.85$)	3	444
all cause death	RR=1.04	[0.60;1.81]	0.8835	0.9029 ($I^2=0.00$)	3	444
balloon angioplasty versus CABG						
cardiac death or MI	RR=3.49	[0.99;12.28]	0.0518	0.7031 ($I^2=0.00$)	2	276
CABG	RR=10.67	[2.03;56.04]	0.0052	0.6060 ($I^2=0.00$)	2	276
all cause death	RR=2.29	[0.42;12.54]	0.3407	0.4383 ($I^2=0.00$)	2	276

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

Figure 4.1: Forest's plot for PTCA

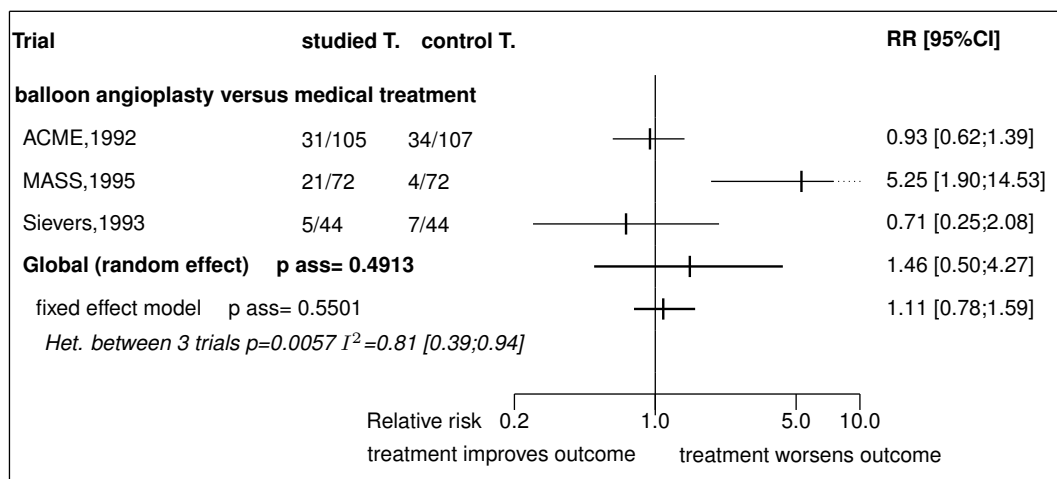


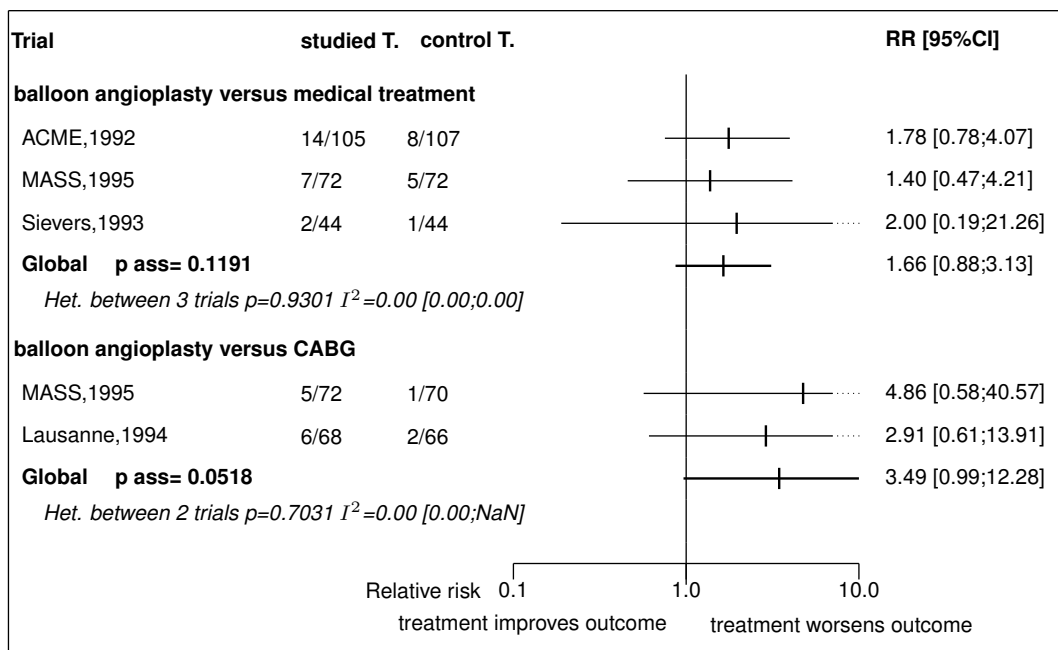
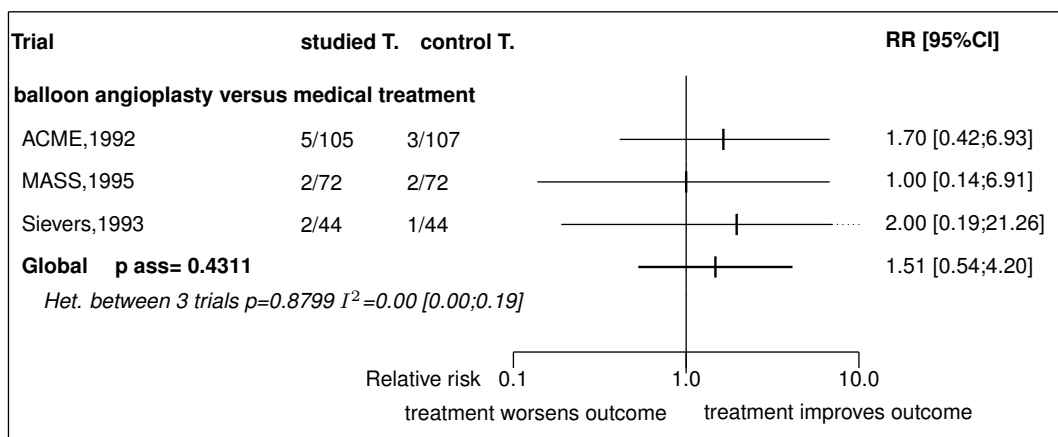
Figure 4.2: Forest's plot for cardiac death or MI**Figure 4.3:** Forest's plot for myocardial infarction (fatal and non fatal)

Figure 4.4: Forest's plot for cardiac death

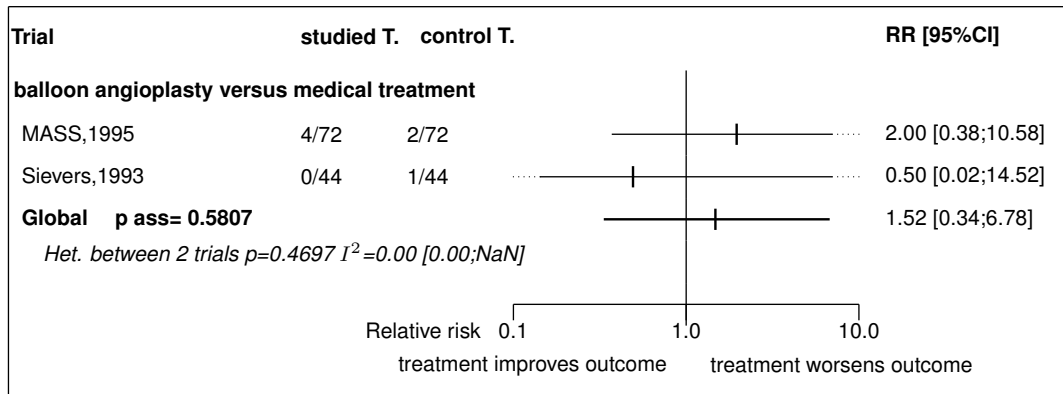


Figure 4.5: Forest's plot for CABG

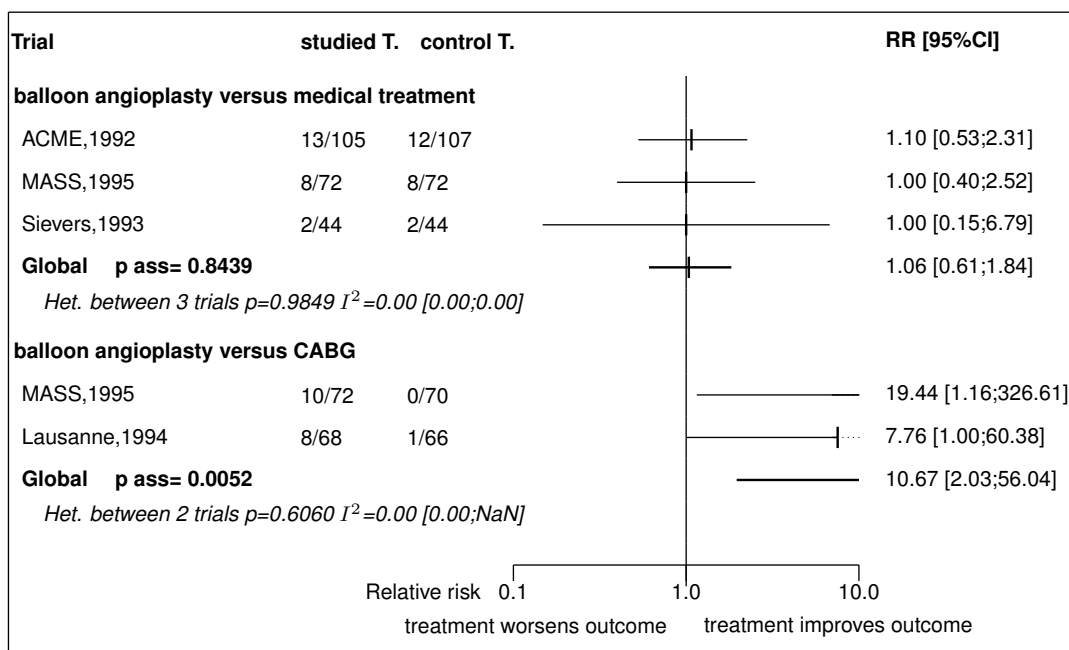


Figure 4.6: Forest's plot for non fatal MI

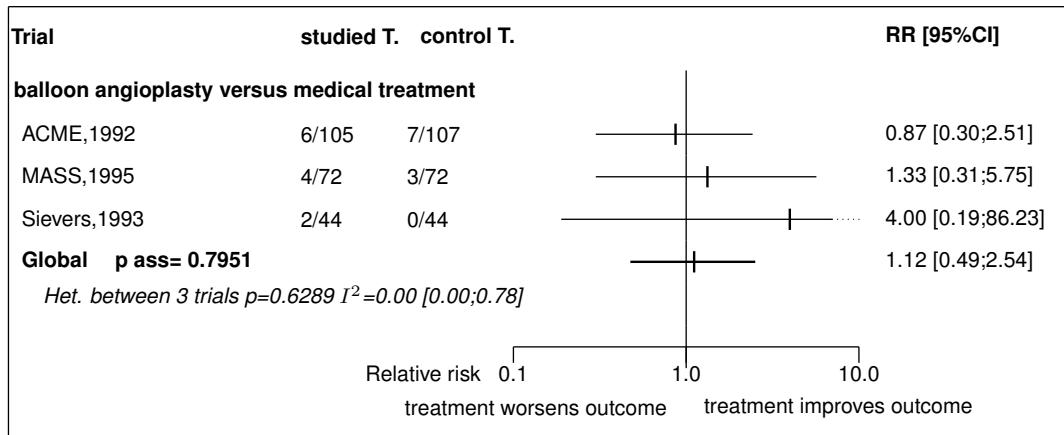


Figure 4.7: Forest's plot for angina

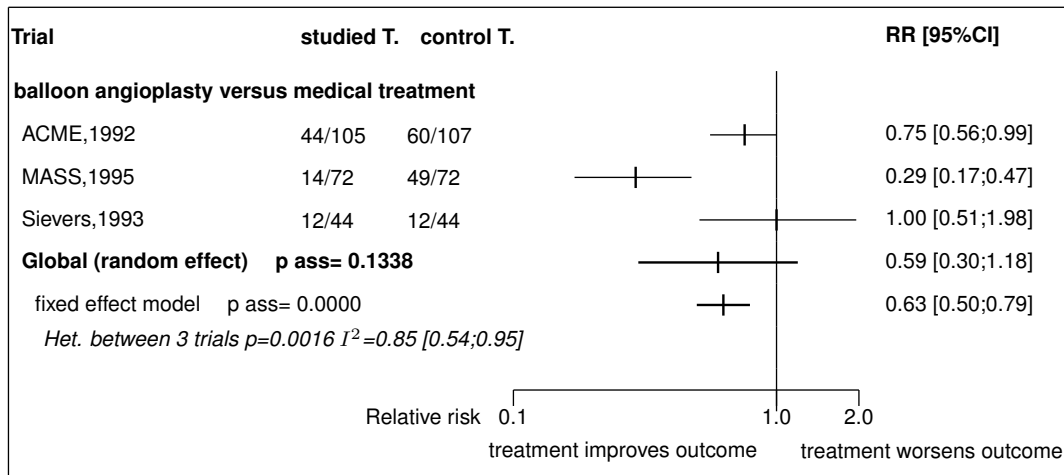
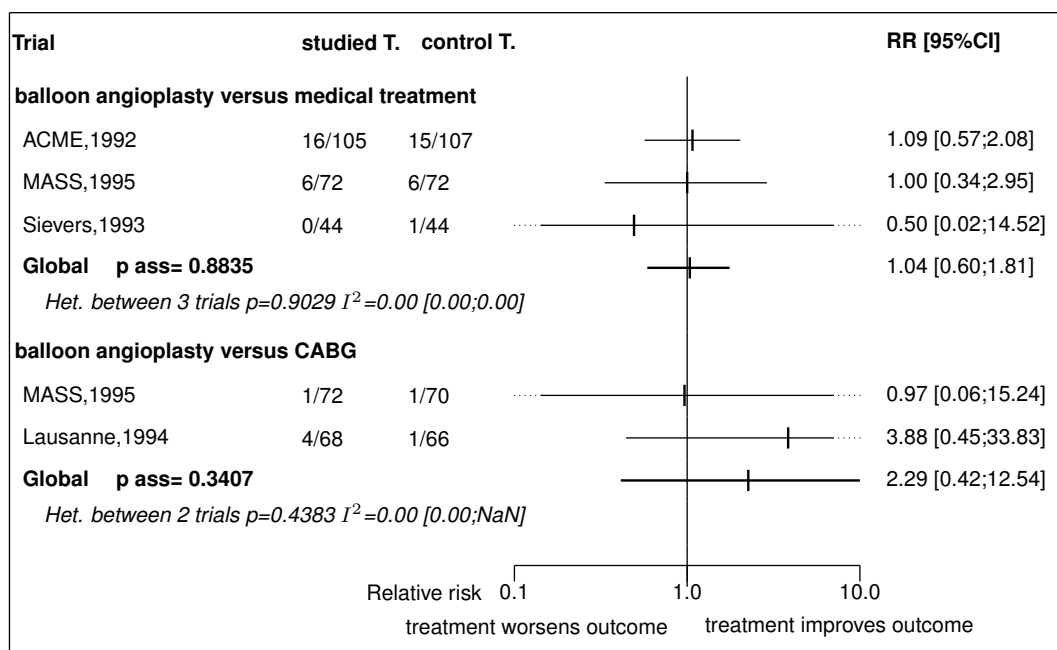


Figure 4.8: Forest's plot for all cause death

References

- [1] Parisi AF, Folland ED, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. Veterans Affairs ACME Investigators. N Engl J Med 1992;326:10-6. [PMID=1345754]
- [2] Hartigan PM, Giacomini JC, Folland ED, Parisi AF. Two- to three-year follow-up of patients with single-vessel coronary artery disease randomized to PTCA or medical therapy (results of a VA cooperative study). Veterans Affairs Cooperative Studies Program ACME Investigators. Angioplasty Compared to Medicine. Am J Cardiol 1998;82:1445-50. [PMID=9874045]
- [3] Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, Pileggi F. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995;26:1600-5. [PMID=7594092]
- [4] Sievers N, Hamm CW, Herzner A, Kuck KH. Medical therapy versus PTCA: a prospective, randomized trial in patients with asymptomatic coronary single-vessel disease. Abstract. Circulation. 1993;88(suppl 1):I-297. [PMID=0]
- [5] Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, Pileggi F. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995 Dec;26:1600-5. [PMID=7594092]

- [6] Goy JJ, Eeckhout E, Burnand B, Vogt P, Stauffer JC, Hurni M, Stumpe F, Ruchat P, Sadeghi H, Kappenberger L. Coronary angioplasty versus left internal mammary artery grafting for isolated proximal left anterior descending artery stenosis. *Lancet* 1994 Jun 11;343:1449-53. [PMID=7911175]

4.3 Individual trial summaries

Table 4.6: ACME, 1992 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=212 (105 vs. 107)	Stable angina, history of angina, MI within 3 months, exercise test with ST depression >3 mm, no previous PTCA; Single or serial stenosis within same artery 70% to 99% proximal two thirds	Studied treatment: PTCA within 3 days of randomization Control treatment: medical treatment (nitrates, beta-blockers, calcium blockers) Concomittant treat.: aspirin 325 mg/d	PTCA RR=0.93 [0.62;1.39] Cardiac death or MI RR=1.78 [0.78;4.07]
Follow-up duration: 5y	Inclusion criteria: Stable angina pectoris or MI in the last 3 mo AND stenosis of 70 to 99% in one major vessel AND exercise-test with ST-segment depression		
Study design: Randomized controlled trial	Exclusion criteria: -		
Parallel groups			
Open			
Confirmatory trial at risk of bias			
US			
Inclusion period: 1987-1990			
References	Parisi AF, Folland ED, Hartigan P. A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. Veterans Affairs ACME Investigators. N Engl J Med 1992;326:10-6 [PMID=1345754] Hartigan PM, Giacomini JC, Folland ED, Parisi AF. Two- to three-year follow-up of patients with single-vessel coronary artery disease randomized to PTCA or medical therapy (results of a VA cooperative study). Veterans Affairs Cooperative Studies Program ACME Investigators. Angioplasty Compared to Medicine. Am J Cardiol 1998;82:1445-50 [PMID=9874045]		

Table 4.7: MASS, 1995 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
<p>n=144 (72 vs. 72)</p> <p>Follow-up duration: 5y</p> <p>Study design: Randomized controlled trial</p> <p>Parallel groups</p> <p>Open</p> <p>Confirmatory trial at risk of bias</p> <p>Brazil</p> <p>Inclusion period: 1988-1991</p>	<p>Stable angina, no Q wave MI, no leftventricular dysfunction</p> <p>Inclusion criteria: patient with stable angina and single proximal stenosis >80% of the left anterior descending artery</p> <p>Exclusion criteria: unstable angina, prior MI, valvular disease, cardiomyopathy, LV failure, total occlusion, lesion length > 12mm, involvement of the ostium, calcification,</p>	<p>Studied treatment: PTCA</p> <p>Control treatment: medical treatment (aspirin, nitrates, beta-blockers and calcium channel blocking</p> <p>Concomittant treat:-</p>	<p>PTCA</p> <p>RR=5.25 [1.90;14.53]</p> <p>Cardiac death or MI</p> <p>RR=1.40 [0.47;4.21]</p>
<p>Reference</p>	<p>Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, Pileggi F. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995;26:1600-5 [PMID=7594092]</p>		

Table 4.8: Sievers, 1993 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=88 (44 vs. 44)	Previous nonQ wave MI, no angina indaily life, no previous Q wave MI	Studied treatment: PTCA	PTCA
Follow-up duration: 2y	Inclusion criteria: single vessel, no angina under medical therapy	Control treatment: medical treatment	RR=0.71 [0.25;2.08]
Study design: Randomized controlled trial	Exclusion criteria: previous MI, diabetes, positive stress test at 50W	Concomittant treat:. aspirin 100mg	Cardiac death or MI
Parallel groups			RR=2.00 [0.19;21.26]
Open			
Confirmatory trial at risk of bias			
Germany			
Inclusion period: ND			
Reference			
Sievers N, Hamm CW, Herzner A, Kuck KH. Medical therapy versusPTCA: a prospective, randomized trial in patients with asymptomaticcoronary single-vessel disease. Abstract. Circulation. 1993;88(suppl I):1-297 [PMID=0]			

Table 4.9: MASS, 1995 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=142 (72 vs. 70) Follow-up duration: 3.2 y Study design: Randomized controlled trial Open Brazil	Patients with stable angina, normal ventricular function and a proximal stenosis of the left anterior descending coronary artery >80%	Studied treatment: percutaneous transluminal coronary angioplasty Control treatment: mammary bypass surgery	Cardiac death or MI RR=4.86 [0.58;40.57]
Reference			
Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, Pileggi F. The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses. J Am Coll Cardiol 1995 Dec;26:1600-5 [PMID=7594092]			

Table 4.10: Lausanne, 1994 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=134 (68 vs. 66) Follow-up duration: 3.2 y Study design: Randomized controlled trial Open	Patients with isolated proximal left anterior descending artery stenosis, conserved left ventricular function, and documented ischaemia	Studied treatment: transluminal coronary angioplasty Control treatment: Coronary artery bypass grafting	Cardiac death or MI RR=2.91 [0.61;13.91]
Switzerland			
Reference			
Goy JJ, Eeckhout E, Burnand B, Vogt P, Stauffer JC, Hurni M, Stumpe F, Ruchat P, Sadeghi H, Kappenberger L. Coronary angioplasty versus left internal mammary artery grafting for isolated proximal left anterior descending artery stenosis. <i>Lancet</i> 1994 Jun 11;343:1449-53 [PMID=7911175]			

5 Detailed results for PCI with or without stent

5.1 Available trials

Only one trial which randomized 300 patients was identified: it compared PCI with or without stent with medical treatment.

This trial included 300 patients and was published in 2003.

This trial was open-label in design.

It was reported in English language.

Cardiac death data was reported in 1 trials; 1 trials reported data on angina; 1 trials reported data on non fatal MI; 1 trials reported data on cardiac death or MI; 1 trials reported data on PTCA; 1 trials reported data on CABG; and 1 trials reported data on all cause death.

Following tables 5.1 (page 53), 5.2 (page 53), 5.4 (page 55), and 5.3 (page 53) summarized the main characteristics of the trial including in this systematic review of randomized trials of PCI with or without stent.

Table 5.1: Treatment description - PCI - PCI with or without stent

Trial	Studied treatment	Control treatment
PCI with or without stent versus medical treatment		
ALKK (2003) [1]	angioplasty	medical therapy

Table 5.2: Descriptions of participants - PCI - PCI with or without stent

Trial	Patients
PCI with or without stent versus medical treatment	
ALKK (2003) [1]	Patients with single vessel disease of the infarct vessel and no or minor angina pectoris in the subacute phase (1 to 6 weeks) after an acute myocardial infarction

Table 5.3: Design and methodological quality of trials - PCI - PCI with or without stent

Trial	Design	Duration	Centre	Primary end-point
PCI with or without stent versus medical treatment				
ALKK, 2003 [1] n=300	Parallel groups open confirmatory trial at risk of bias	4.7y inclusion period: 1994-1997	Germany multicenter	death, reMI, reIntervention, CABG, severe AP

continued...

Trial	Design	Duration	Centre	Primary end-point
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Table 5.4: *Trial characteristics - PCI - PCI with or without stent*

Trial
PCI with or without stent versus medical treatment
ALKK, 2003 [1]

5.2 Meta-analysis results

The results are detailed in table 5.5 (page 56). This table is followed by the Forest's plot corresponding to each endpoint.

PCI with or without stent versus medical treatment

The single study eligible for this comparison provided data on **PTCA**. The analysis detected a statistically significant difference in favor of PCI with or without stent in PTCA, with a RR of 0.41 (95% CI 0.18 to 0.89, $p=0.0247$).

The single study eligible for this comparison provided data on **cardiac death or MI**. No statistically significant difference between the groups was found in cardiac death or MI, with a RR of 0.55 (95% CI 0.30 to 1.00, $p=0.0513$).

The single study eligible for this comparison provided data on **cardiac death**. The analysis detected a statistically significant difference in favor of PCI with or without stent in cardiac death, with a RR of 0.29 (95% CI 0.10 to 0.86, $p=0.0256$).

The single study eligible for this comparison provided data on **CABG**. No statistically significant difference between the groups was found in CABG, with a RR of 0.25 (95% CI 0.03 to 2.24, $p=0.2170$).

The single study eligible for this comparison provided data on **non fatal MI**. No statistically significant difference between the groups was found in non fatal MI, with a RR of 0.84 (95% CI 0.38 to 1.89, $p=0.6819$).

The single study eligible for this comparison provided data on **angina**. The analysis detected a statistically significant difference in favor of PCI with or without stent in angina, with a RR of 0.30 (95% CI 0.13 to 0.74, $p=0.0083$).

The single study eligible for this comparison provided data on **all cause death**. The analysis detected a statistically significant difference in favor of PCI with or without stent in all cause death, with a RR of 0.36 (95% CI 0.15 to 0.88, $p=0.0256$).

Table 5.5: Results details - PCI - PCI with or without stent

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
PCI with or without stent versus medical treatment						
PTCA	RR=0.41	[0.18;0.89]	0.0247	1.0000 ($I^2=0.00$)	1	300
cardiac death or MI	RR=0.55	[0.30;1.00]	0.0513	1.0000 ($I^2=1.00$)	1	300
cardiac death	RR=0.29	[0.10;0.86]	0.0256	1.0000 ($I^2=0.00$)	1	300
CABG	RR=0.25	[0.03;2.24]	0.2170	1.0000 ($I^2=0.00$)	1	300
non fatal MI	RR=0.84	[0.38;1.89]	0.6819	1.0000 ($I^2=0.00$)	1	300
angina	RR=0.30	[0.13;0.74]	0.0083	1.0000 ($I^2=0.00$)	1	300
all cause death	RR=0.36	[0.15;0.88]	0.0256	1.0000 ($I^2=0.00$)	1	300

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

Figure 5.1: Forest's plot for PTCA

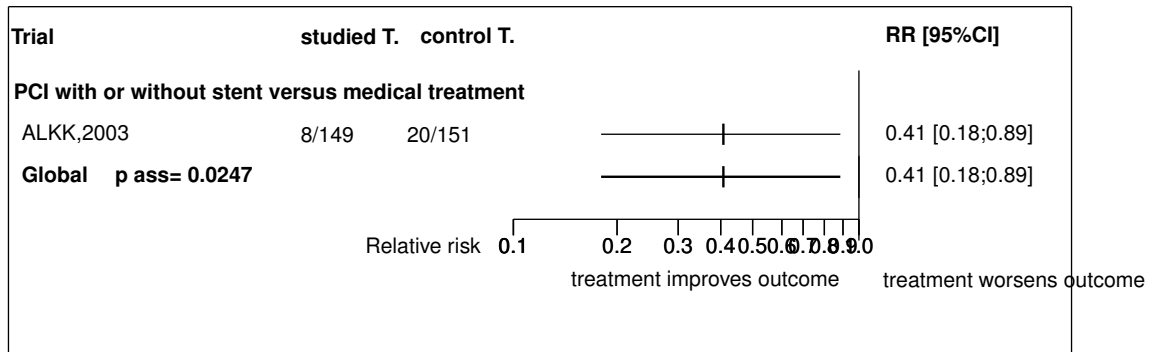


Figure 5.2: Forest's plot for cardiac death or MI

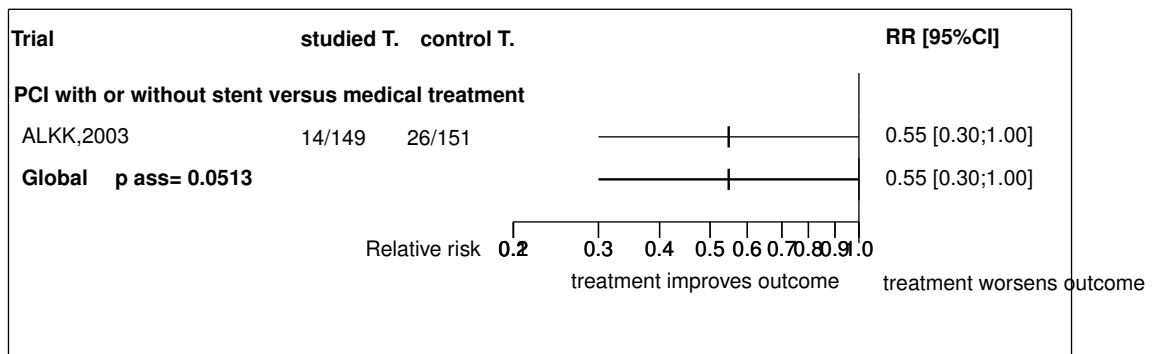


Figure 5.3: Forest's plot for cardiac death

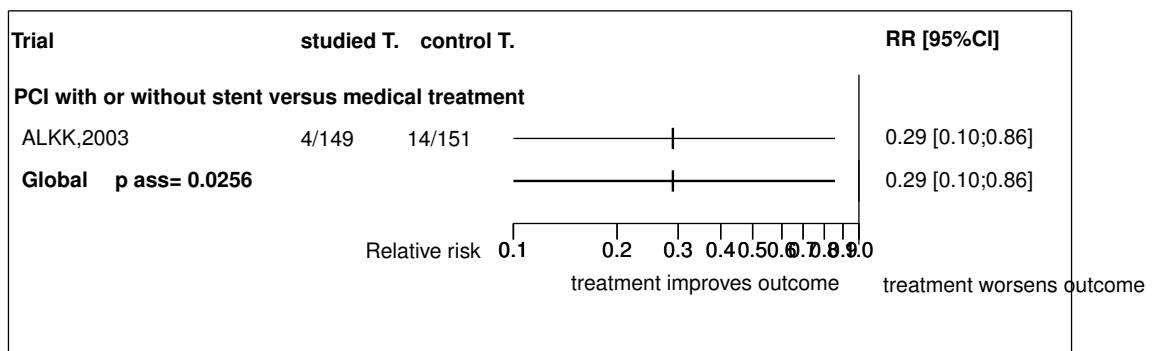


Figure 5.4: Forest's plot for CABG

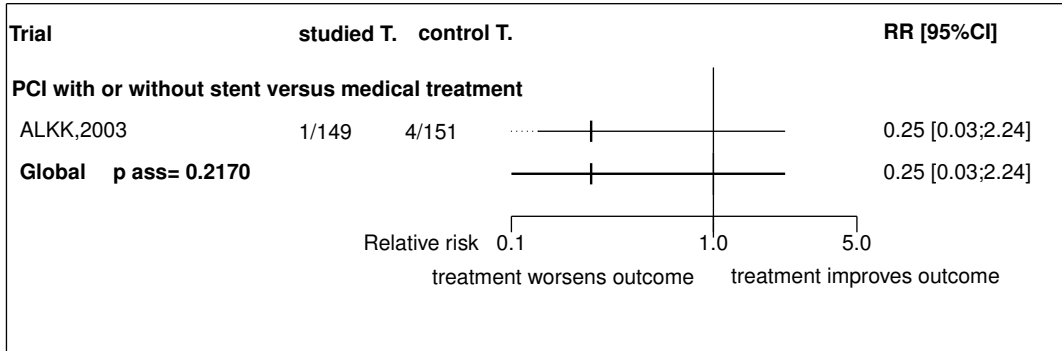


Figure 5.5: Forest's plot for non fatal MI

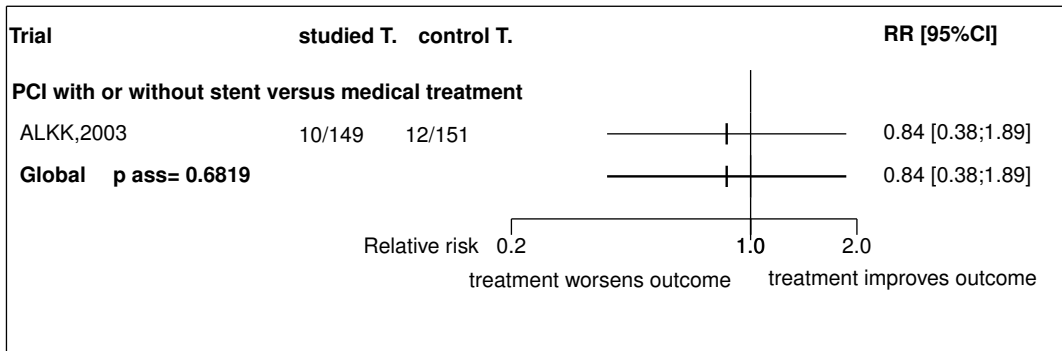


Figure 5.6: Forest's plot for angina

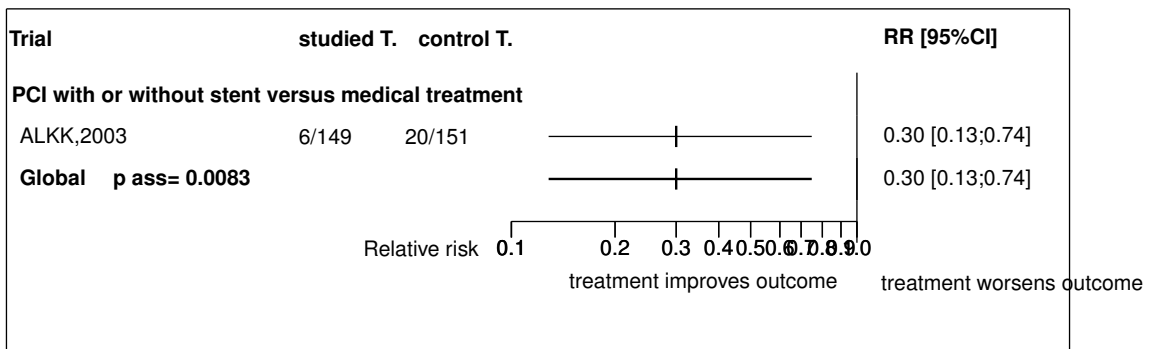
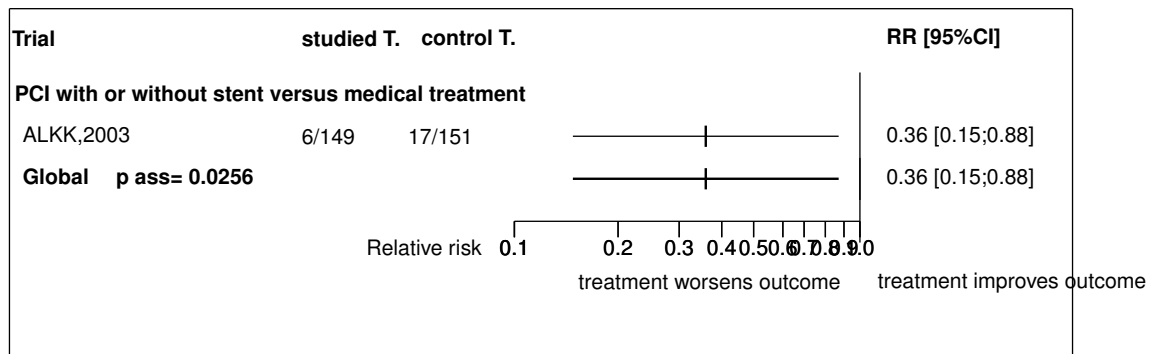


Figure 5.7: Forest's plot for all cause death



References

- [1] Zeymer U, Uebis R, Vogt A, Glunz HG, Vöhringer HF, Harmjanz D, Neuhaus KL. Randomized comparison of percutaneous transluminal coronary angioplasty and medical therapy in stable survivors of acute myocardial infarction with single vessel disease: a study of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte. *Circulation* 2003;108:1324-8. [PMID=12939210]

5.3 Individual trial summaries

Table 5.6: ALKK, 2003 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=300 (149 vs. 151)	Patients with single vessel disease of the infarct vessel and no or minor angina pectoris in the subacute phase (1 to 6 weeks) after an acute myocardial infarction	Studied treatment: angioplasty Control treatment: medical therapy	PTCA RR=0.41 [0.18;0.89] Cardiac death or MI RR=0.55 [0.30;1.00]
Follow-up duration: 4.7y			
Study design: Randomized controlled trial			
Parallel groups			
Open			
Confirmatory trial at risk of bias			
Germany, multicenter			
Inclusion period: 1994/1997			
Reference			
Zeymer U, Uebis R, Vogt A, Glunz HG, Vöhringer HF, Harmjanz D, Neuhaus KL. Randomized comparison of percutaneous transluminal coronary angioplasty and medical therapy in stable survivors of acute myocardial infarction with single vessel disease: a study of the Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte. <i>Circulation</i> 2003;108:1324-8 [PMID=12939210]			

6 Detailed results for PCI withdrug-eluting stents

6.1 Available trials

Only one trial which randomized 189 patients was identified: it compared PCI withdrug-eluting stents with CABG.

This trial included 189 patients and was published in 2005.

This trial was open-label in design.

It was reported in English language.

data was reported in trials;

Following tables 6.1 (page 62), 6.2 (page 62), 6.4 (page 63), and 6.3 (page 62) summarized the main characteristics of the trial including in this systematic review of randomized trials of PCI withdrug-eluting stents.

Table 6.1: Treatment description - PCI - PCI withdrug-eluting stents

Trial	Studied treatment	Control treatment
PCI withdrug-eluting stents versus CABG		
Hong (2005) [1]	drug-eluting stents	invasive direct coronary artery bypass (MIDCAB) surgery

Table 6.2: Descriptions of participants - PCI - PCI withdrug-eluting stents

Trial	Patients
PCI withdrug-eluting stents versus CABG	
Hong (2005) [1]	Proximal left anterior descending (LAD) coronary artery stenosis

Table 6.3: Design and methodological quality of trials - PCI - PCI withdrug-eluting stents

Trial	Design	Duration	Centre	Primary end-point
PCI withdrug-eluting stents versus CABG				
Hong, 2005 [1] n=189	Parallel groups open confirmatory trial at risk of bias	9 months		

Table 6.4: Trial characteristics - PCI - PCI withdrug-eluting stents

Trial	Age (mean, year)	Men (%)	Ejection fraction (%)	Extent of Disease	arterial grafts	stent (%)
PCI withdrug-eluting stents versus CABG						
Hong, 2005 [1]						

6.2 Meta-analysis results

The results are detailed in table 6.5 (page 64). This table is followed by the Forest's plot corresponding to each endpoint.

PCI with drug-eluting stents versus CABG

No data were presented in the 1 trial identified

Table 6.5: Results details - PCI - PCI with drug-eluting stents

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
PCI with drug-eluting stents versus CABG						
No data were presented in the trial identified						
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree						

References

- [1] Hong SJ, Lim DS, Seo HS, Kim YH, Shim WJ, Park CG, Oh DJ, Ro YM. Percutaneous coronary intervention with drug-eluting stent implantation vs. minimally invasive direct coronary artery bypass (MIDCAB) in patients with left anterior descending coronary artery stenosis. *Catheter Cardiovasc Interv* 2005;64:75-81. [PMID=15619278]

6.3 Individual trial summaries

Table 6.6: Hong, 2005 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
<p>n=189 (119 vs. 70)</p> <p>Follow-up duration: 9 months</p> <p>Study design: Randomized controlled trial</p> <p>Parallel groups</p> <p>Open</p> <p>Confirmatory trial at risk of bias</p>	<p>Proximal left anterior descending (LAD) coronary artery stenosis</p>	<p>Studied treatment: drug-eluting stents</p> <p>Control treatment: invasive direct coronary artery bypass (MIDCAB) surgery</p>	
Reference			
<p>Hong SJ, Lim DS, Seo HS, Kim YH, Shim WJ, Park CG, Oh DJ, Ro YM. Percutaneous coronary intervention with drug-eluting stent implantation vs. minimally invasive direct coronary artery bypass (MIDCAB) in patients with left anterior descending coronary artery stenosis. <i>Catheter Cardiovasc Interv</i> 2005;64:75-81 [PMID=15619278]</p>			

7 Detailed results for PCI withsirolimus ES

7.1 Available trials

Only one trial which randomized 130 patients was identified: it compared PCI withsirolimus ES with MIDCAB.

This trial included 130 patients and was published in 2009.

This trial was open-label in design.

It was reported in English language.

data was reported in trials;

Following tables 7.1 (page 67), 7.2 (page 67), 7.4 (page 69), and 7.3 (page 68) summarized the main characteristics of the trial including in this systematic review of randomized trials of PCI withsirolimus ES.

Table 7.1: Treatment description - PCI - PCI withsirolimus ES

Trial	Studied treatment	Control treatment
PCI withsirolimus ES versus MIDCAB		
Thiele (2009) [1]	sirolimus-eluting stent	MIDCAB surgery
	Concomittant treatment: fro PCI: aspirin (at least 100 mg/day, subsequently 100 mg/day indefinitely) and clopidogrel (600 mg orally, followed by 75 mg/day for at least 12 months); during the procedure heparin (60 U/kg body weight);for surgery : aspirin 100 mg/day indefinitely	

Table 7.2: Descriptions of participants - PCI - PCI withsirolimus ES

Trial	Patients
PCI withsirolimus ES versus MIDCAB	
Thiele (2009) [1]	<p>Isolated LAD disease</p> <p>Inclusion criteria: age >18 years; isolated proximal LAD stenosis >50% (between origin of left circumflex artery and first septal perforator); symptomatic; presence of myocardial ischemia</p> <p>Exclusion criteria: acute coronary syndrome; additional valvular heart disease requiring surgical intervention; previous interventional or surgical treatment for coronary artery disease or valvular heart disease; severe peripheral vascular disease; significant carotid disease needing treatment; end-stage renal disease on hemodialysis; overt congestive heart failure; upper gastrointestinal bleeding <4 weeks; contraindication to antiplatelet therapy; diseases with limited life expectancy; extreme obesity; total occlusions; involvement of left main trunk; stenosis of first diagonal branch; intramyocardial course of LAD; stenosis extending over a major diagonal branch; stenosis at any other location requiring treatment</p>

Table 7.3: Design and methodological quality of trials - PCI - PCI withsirolimus ES

Trial	Design	Duration	Centre	Primary end-point
PCI withsirolimus ES versus MIDCAB				
Thiele, 2009 [1] n=130	Parallel groups open confirmatory trial at risk of bias	12 months	Germany single center	cardiac death, MI, and need for PCI

Table 7.4: Trial characteristics - PCI - PCI withsirolimus ES

Trial	Age (mean, year)	Men (%)	Ejection fraction (%)	Extent of Disease	arterial grafts	stent (%)
PCI withsirolimus ES versus MIDCAB						
Thiele, 2009 [1]						

7.2 Meta-analysis results

The results are detailed in table 7.5 (page 70). This table is followed by the Forest's plot corresponding to each endpoint.

PCI withsirolimus ES versus MIDCAB

No data were presented in the 1 trial identified

Table 7.5: Results details - PCI - PCI withsirolimus ES

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
PCI withsirolimus ES versus MIDCAB						
No data were presented in the trial identified						
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree						

References

- [1] Thiele H, Neumann-Schriedewind P, Jacobs S, Boudriot E, Walther T, Mohr FW, Schuler G, Falk V. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. *J Am Coll Cardiol* 2009 Jun 23;53:2324-31. [PMID=19539141]

7.3 Individual trial summaries

Table 7.6: Thiele, 2009 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
<p>n=130 (65 vs. 65)</p> <p>Follow-up duration: 12 months</p> <p>Study design: Randomized controlled trial</p> <p>Parallel groups</p> <p>Open</p> <p>Confirmatory trial at risk of bias</p> <p>Germany, single center</p>	<p>Isolated LAD disease</p> <p>Inclusion criteria: age > 18 years; isolated proximal LAD stenosis > 50% (between origin of left circumflex artery and first septal perforator); symptomatic; presence of myocardial ischemia</p> <p>Exclusion criteria: acute coronary syndrome; additional valvular heart disease requiring surgical intervention; previous interventional or surgical treatment for coronary artery disease or valvular heart disease; severe peripheral vascular disease; significant carotid disease needing treatment; end-stage renal disease on hemodialysis; overt congestive heart failure; upper gastrointestinal bleeding < 4 weeks; contraindication to antiplatelet therapy; diseases with limited life expectancy; extreme obesity; total occlusions; involvement of left main trunk; stenosis of first diagonal branch; intramyocardial</p>	<p>Studied treatment: sirolimus-eluting stent</p> <p>Control treatment: MIDCAB surgery</p> <p>Concomittant treat.: fro PCI: aspirin (at least 100 mg/day, subsequently 100 mg/day indefinitely) and clopidogrel (600 mg orally, followed by 75 mg/day for at least 12 months); during the procedure heparin (60 U/kg body weight); for surgery : aspirin 100 mg/day indefinitely</p>	
Reference	<p>Thiele H, Neumann-Schiedewind P, Jacobs S, Boudriot E, Walther T, Mohr FW, Schuler G, Falk V. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. <i>J Am Coll Cardiol</i> 2009 Jun 23;53:2324-31 [PMID=19539141]</p>		

8 Detailed results for stent

8.1 Available trials

A total of 6 RCTs which randomized 701 patients were identified: it compared stent with CABG , it compared stent with E-ACAB and 4 trials compared stent with MIDCAB.

The average study size was 116 patients (range 53 to 220). The first study was published in 2000, and the last study was published in 2002.

All trials were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.

6 months MI data was reported in 4 trials; 4 trials reported data on 6 months death; 3 trials reported data on 6 months events; 2 trials reported data on long term death; 2 trials reported data on ; 2 trials reported data on long term cardiovascular events; 2 trials reported data on 1 year death from any cause; 2 trials reported data on 1 year event; and 1 trials reported data on 1 year revascularization.

Following tables 8.1 (page 73), 8.2 (page 74), 8.4 (page 76), and 8.3 (page 74) summarized the main characteristics of the trials including in this systematic review of randomized trials of stent.

Table 8.1: Treatment description - PCI - stent

Trial	Studied treatment	Control treatment
Stent versus CABG		
LEMANS (2002) [1]	unprotected left main stenting	coronary artery bypass grafting
Stent versus E-ACAB		
Cisowski (0)	Tristar, Tera, Penta (Guidant) (Cordis)	endoscopic atraumatic coronary artery bypass grafting
Stent versus MIDCAB		
Diegeler (2002) [2, 3]	Various stents	minimally invasive direct coronary artery bypass (off-pump procedure)
Drenth (2002) [4, 5, 6]	Stent type not reported	minimally invasive direct coronary artery bypass (off-pump procedure)
Grip (2001) [7]	Stent type not reported	minimally invasive direct coronary artery bypass (off-pump procedure)
SIMA (2000) [8]	Any CE marked, but Palmaz-Schatz recommended	Conventional CABG or minimally invasive direct coronary artery bypass (off-pump procedure) (10% of surgical procedures)

Table 8.2: Descriptions of participants - PCI - stent

Trial	Patients
Stent versus CABG	
LEMANS (2002) [1]	Patients with unprotected left main coronary artery stenosis
Stent versus E-ACAB	
Cisowski (0)	Single vessel disease ACC/AHA A or B lesion in proximal LAD Angina CCS II or higher Lesion diameter 3 mm or greater/length 20mm or greater
Stent versus MIDCAB	
Diegeler (2002) [2, 3]	Single vessel disease Lesion =75% stenosis in proximal LAD or between origin of left circumflex and 1st septal branch
Drenth (2002) [4, 5, 6]	Single vessel disease Angina II Lesion (Grade B2 or C) of proximal LAD Suitable for CABG or stenting
Grip (2001) [7]	Single vessel disease engaging LAD Stable or unstable angina
SIMA (2000) [8]	Single vessel disease Symptomatic or silent ischaemia 1 LAD lesion Ejection fraction >45% Vessel >3.0mm

Table 8.3: Design and methodological quality of trials - PCI - stent

Trial	Design	Duration	Centre	Primary end-point
Stent versus CABG				
LEMANS, 2002 [1] n=105	Parallel groups open exploratory trial	1y	Poland	change in left ventricular ejection fraction
Stent versus E-ACAB				
Cisowski, 0 n=100	parallel group open	2 years	Poland Single center	
Stent versus MIDCAB				
Diegeler, 2002 [2, 3] n=220	parallel group open confirmatory trial at risk of bias	5 years	Germany Multicentre	major adverse cardiac events
Drenth, 2002 [4, 5, 6] n=102	parallel group open confirmatory trial at risk of bias	6 months, 3 years	Netherlands Single centre	Major Adverse Cardiac and Cerebrovascular Events

continued...

Trial	Design	Duration	Centre	Primary end-point
Grip, 2001 [7] n=53	parallel group open		Sweden	
SIMA, 2000 [8] n=121	parallel group open	2.4 years	Europe Multicentre	death, myocardial infarction, revascularization

Table 8.4: Trial characteristics - PCI - stent

Trial	Age (mean, year)	Men (%)	Ejection fraction (%)	Extent of Disease	arterial grafts	stent (%)
Stent versus CABG						
LEMANS, 2002 [1]						
Stent versus E-ACAB						
Cisowski, 0						
Stent versus MIDCAB						
Diegeler, 2002 [2, 3]						
Drenth, 2002 [4, 5, 6]						
Grip, 2001 [7]						
SIMA, 2000 [8]						

8.2 Meta-analysis results

The results are detailed in table 8.5 (page 78). This table is followed by the Forest's plot corresponding to each endpoint.

Stent versus CABG

The single study eligible for this comparison provided data on **1 year event**. No statistically significant difference between the groups was found in 1 year event, with a RR of 1.25 (95% CI 0.67 to 2.34, $p=0.4764$).

The single study eligible for this comparison provided data on **1 year revascularization**. The analysis detected a statistically significant difference in favor of CABG in 1 year revascularization, with a RR of 3.06 (95% CI 1.20 to 7.80, $p=0.0194$).

The single study eligible for this comparison provided data on **1 year death from any cause**. No statistically significant difference between the groups was found in 1 year death from any cause, with a RR of 0.25 (95% CI 0.03 to 2.20, $p=0.2142$).

Stent versus E-ACAB

The single study eligible for this comparison provided data on **6 months events**. The analysis detected a statistically significant difference in favor of E-ACAB in 6 months events, with a RR of 22.00 (95% CI 1.33 to 364.29, $p=0.0309$).

The single study eligible for this comparison provided data on **6 months death**. No statistically significant difference between the groups was found in 6 months death, with a RR of 1.00 (95% CI 0.02 to 49.42, $p=1.0000$).

The single study eligible for this comparison provided data on **6 months MI**. No statistically significant difference between the groups was found in 6 months MI, with a RR of 1.00 (95% CI 0.02 to 49.42, $p=1.0000$).

Stent versus MIDCAB

A total of 2 of the 4 studies eligible for this comparison provided data on **6 months events**. The analysis detected a statistically significant difference in favor of MIDCAB in 6 months events, with a RR of 2.06 (95% CI 1.27 to 3.33, $p=0.0035$). No heterogeneity was detected ($p = 0.7664$, $I^2 = 0.00\%$).

Only one of the 4 studies eligible for this comparison provided data on **1 year event**. The analysis detected a statistically significant difference in favor of MIDCAB in 1 year event, with a RR of 3.00 (95% CI 1.04 to 8.68, $p=0.0428$).

A total of 2 of the 4 studies eligible for this comparison provided data on . The analysis detected a statistically significant difference in favor of MIDCAB in , with a RR of 3.24 (95% CI 1.61 to 6.54, $p=0.0000$). No heterogeneity was detected ($p = 0.3771$, $I^2 = 0.00\%$).

A total of 3 of the 4 studies eligible for this comparison provided data on **6 months death**. When pooled together, there was no statistically significant difference between the groups in 6 months death, with a RR of 0.62 (95% CI 0.14 to 2.72, $p=0.5279$). No heterogeneity was detected ($p = 0.7390$, $I^2 = 0.00\%$).

A total of 3 of the 4 studies eligible for this comparison provided data on **6 months MI**. When pooled together, there was no statistically significant difference between the groups in 6 months MI, with a RR of 1.21 (95% CI 0.32 to 4.54, $p=0.7750$). No heterogeneity was detected ($p = 0.2578$, $I^2 = 0.26\%$).

A total of 2 of the 4 studies eligible for this comparison provided data on **long term cardiovascular events**. The analysis detected a statistically significant difference in favor of MIDCAB in long term cardiovascular events, with a RR of 3.24 (95% CI 1.61 to 6.54, $p=0.0000$). No heterogeneity was detected ($p = 0.3771$, $I^2 = 0.00\%$).

Only one of the 4 studies eligible for this comparison provided data on **1 year death from any cause**. The analysis detected a statistically significant difference in favor of MIDCAB in 1 year death from any cause, with a RR of 3.00 (95% CI 1.04 to 8.68, $p=0.0428$).

A total of 2 of the 4 studies eligible for this comparison provided data on **long term death**. When pooled together, there was no statistically significant difference between the groups in long term death, with a RR of 0.10 (95% CI 0.00 to 8.53, $p=0.3072$). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies ($p = 0.0216$, $I^2 = 0.81\%$).

Table 8.5: Results details - PCI - stent

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
stent versus CABG						
1 year event	RR=1.25	[0.67;2.34]	0.4764	1.0000 ($I^2=0.00$)	1	105
1 year revascularization	RR=3.06	[1.20;7.80]	0.0194	1.0000 ($I^2=0.00$)	1	105
1 year death from any cause	RR=0.25	[0.03;2.20]	0.2142	1.0000 ($I^2=1.00$)	1	105
stent versus E-ACAB						
6 months events	RR=22.00	[1.33;364.29]	0.0309	1.0000 ($I^2=0.00$)	1	100
6 months death	RR=1.00	[0.02;49.42]	1.0000	1.0000 ($I^2=0.00$)	1	100
6 months MI	RR=1.00	[0.02;49.42]	1.0000	1.0000 ($I^2=0.00$)	1	100
stent versus MIDCAB						
6 months events	RR=2.06	[1.27;3.33]	0.0035	0.7664 ($I^2=0.00$)	2	318
1 year event	RR=3.00	[1.04;8.68]	0.0428	1.0000 ($I^2=0.00$)	1	102
	RR=3.24	[1.61;6.54]	0.0000	0.3771 ($I^2=0.00$)	2	223
6 months death	RR=0.62	[0.14;2.72]	0.5279	0.7390 ($I^2=0.00$)	3	371
6 months MI	RR=1.21	[0.32;4.54]	0.7750	0.2578 ($I^2=0.26$)	3	371
long term cardiovascular events	RR=3.24	[1.61;6.54]	0.0000	0.3771 ($I^2=0.00$)	2	223
1 year death from any cause	RR=3.00	[1.04;8.68]	0.0428	1.0000 ($I^2=0.00$)	1	102
long term death	RR=0.10	[0.00;8.53]	0.3072	0.0216 ($I^2=0.81$)	2	223

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

Figure 8.1: Forest's plot for 6 months events

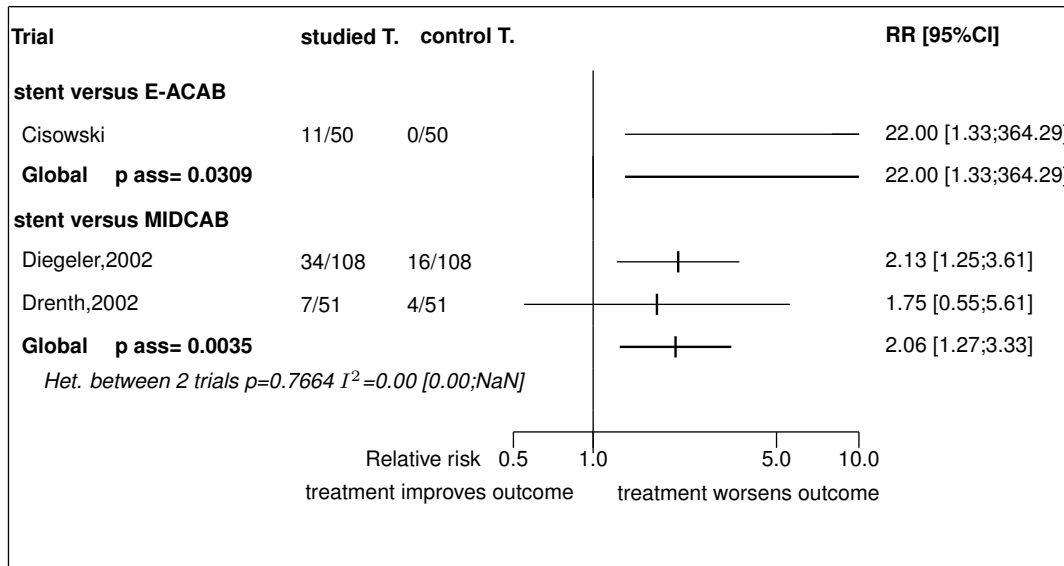


Figure 8.2: Forest's plot for 1 year event

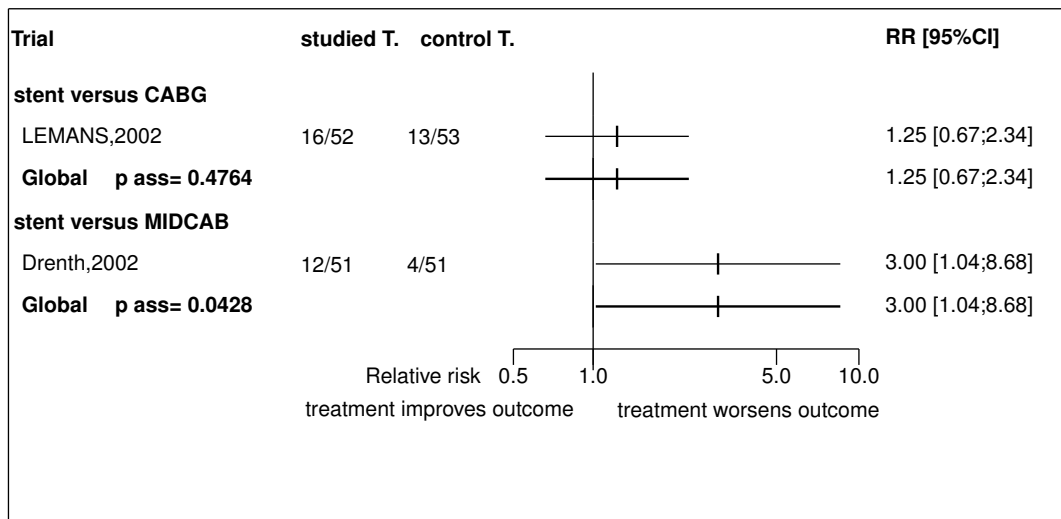


Figure 8.3: Forest's plot for

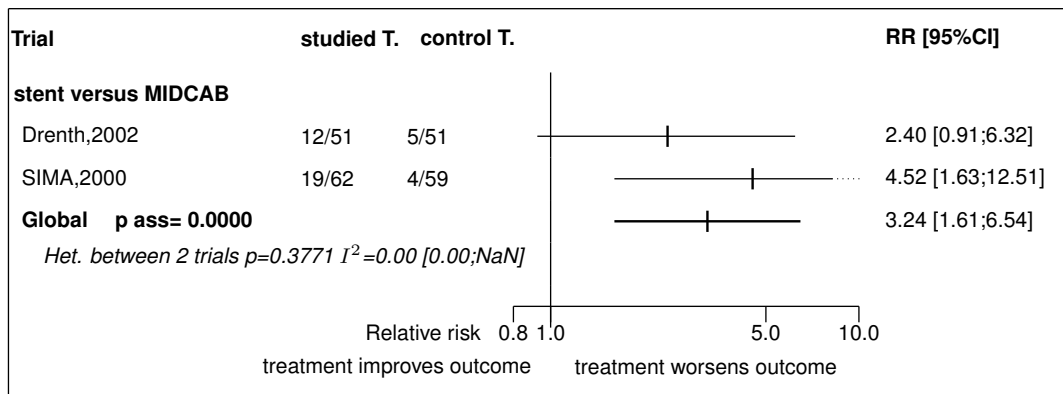


Figure 8.4: Forest's plot for 6 months death

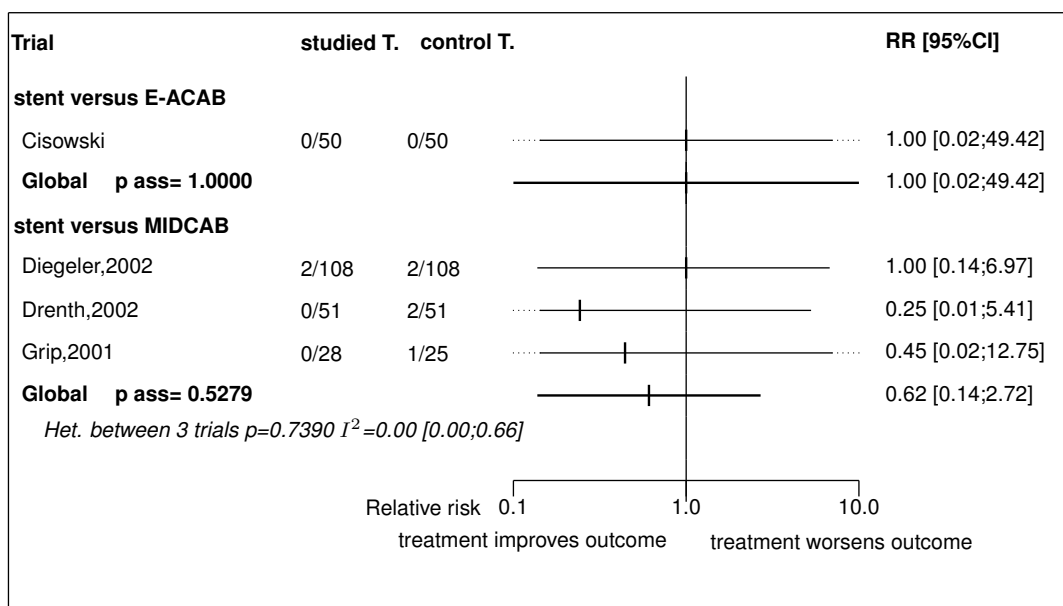


Figure 8.5: Forest's plot for 6 months MI

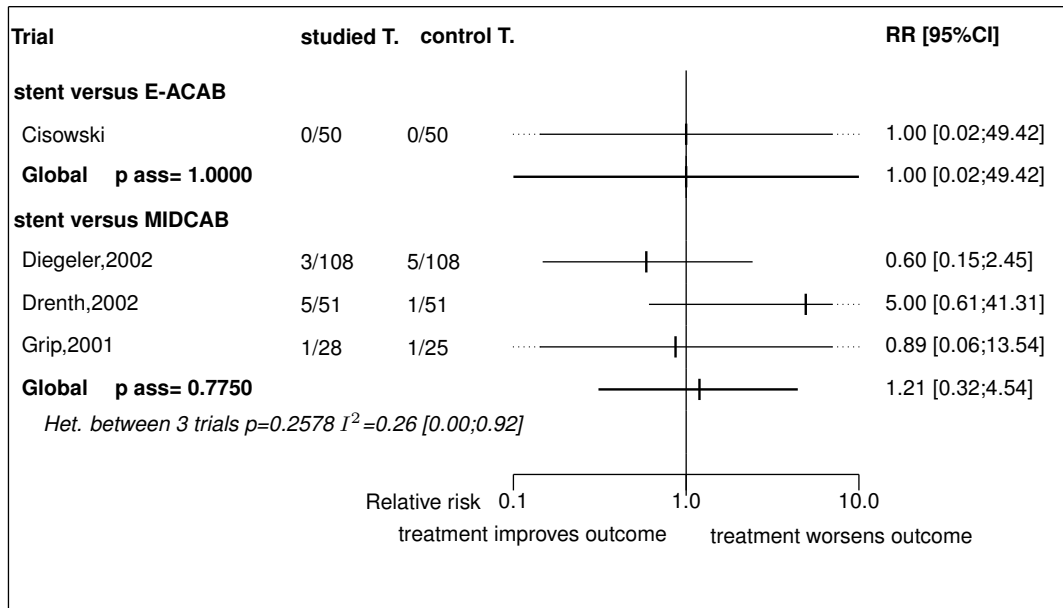


Figure 8.6: Forest's plot for 1 year revascularization

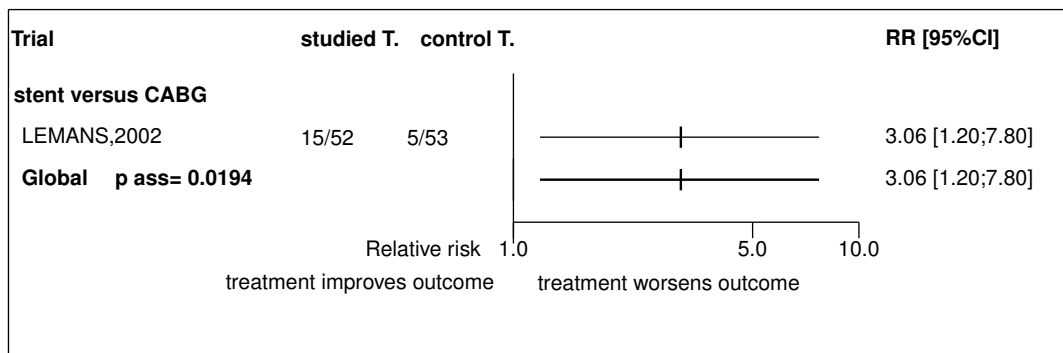


Figure 8.7: Forest's plot for long term cardiovascular events

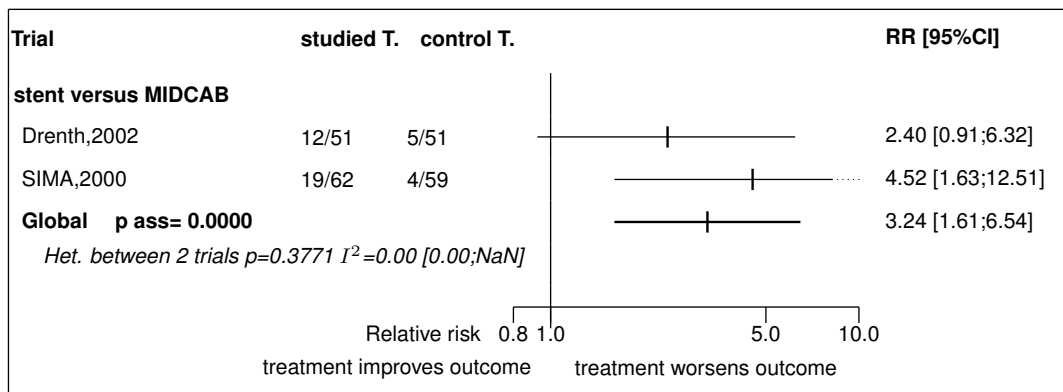


Figure 8.8: Forest's plot for 1 year death from any cause

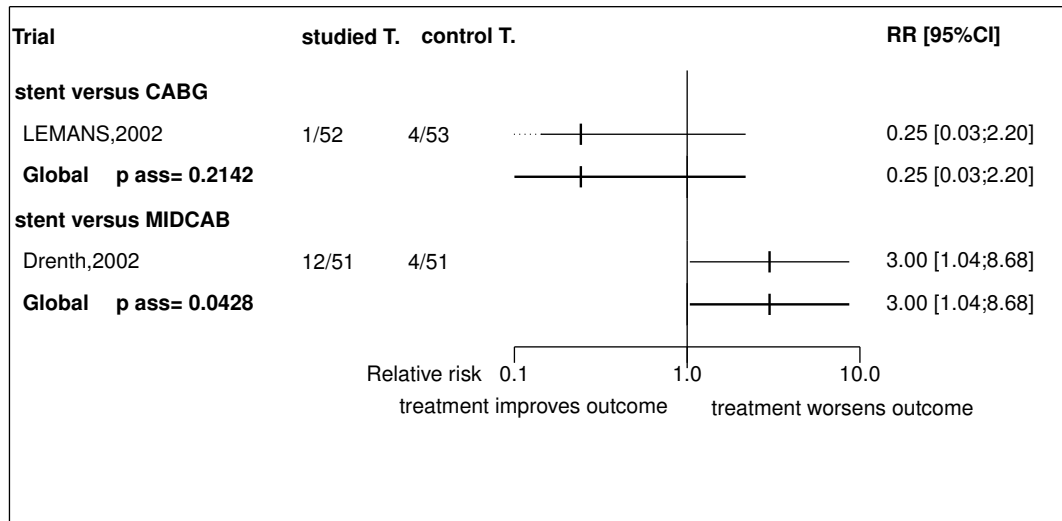
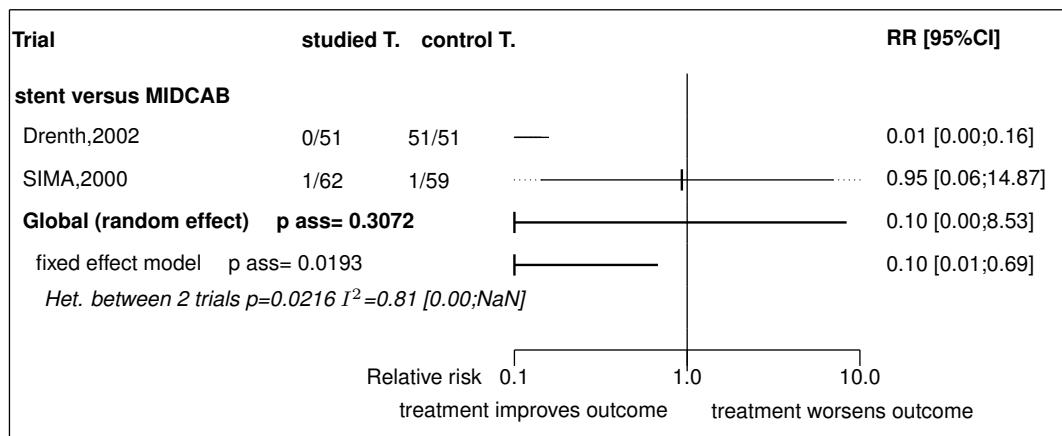


Figure 8.9: Forest's plot for long term death



References

- [1] Buszman PE, Kiesz SR, Bochenek A, Peszek-Przybyla E, Szkrobka I, Debinski M, Bialkowska B, Dudek D, Gruszka A, Zurakowski A, Milewski K, Wilczynski M, Rzeszutko L, Buszman P, Szymshal J, Martin JL, Tendra M. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. *J Am Coll Cardiol* 2008;51:538-45. [PMID=18237682]
- [2] Diegeler A, Thiele H, Falk V, Hambrecht R, Spyridis N, Sick P, Diederich KW, Mohr FW, Schuler G. Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. *N Engl J Med* 2002;347:561-6. [PMID=12192015]

- [3] Diegeler A, Spyranis N, Matin M, Falk V, Hambrecht R, Autschbach R, Mohr FW, Schuler G. The revival of surgical treatment for isolated proximal high grade LAD lesions by minimally invasive coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2000;17:501-4. [PMID=10814909]
- [4] Drenth DJ, Veeger NJ, Grandjean JG, Mariani MA, van Boven AJ, Boonstra PW. Isolated high-grade lesion of the proximal LAD: a stent or off-pump LIMA?. *Eur J Cardiothorac Surg* 2004;25:567-71. [PMID=15037273]
- [5] Drenth DJ, Veeger NJ, Winter JB, Grandjean JG, Mariani MA, Boven van AJ, Boonstra PW. A prospective randomized trial comparing stenting with off-pump coronary surgery for high-grade stenosis in the proximal left anterior descending coronary artery: three-year follow-up. *J Am Coll Cardiol* 2002;40:1955-60. [PMID=12475455]
- [6] Drenth DJ, Winter JB, Veeger NJ, Monnick SH, van Boven AJ, Grandjean JG, Mariani MA, Boonstra PW. Minimally invasive coronary artery bypass grafting versus percutaneous transluminal coronary angioplasty with stenting in isolated high-grade stenosis of the proximal left anterior descending coronary artery: six months' angiographic and clinical follow-up of a prospective randomized study. *J Thorac Cardiovasc Surg* 2002;124:130-5. [PMID=12091818]
- [7] Grip L, Wahrborg P, Odell A, Albertsson P, Berglin E, Brandrup-. Coronary artery bypass beating heart surgery with LIMA graft, versus coronary angioplasty with stent for patients with single left anterior descending artery - a pilot study. *European Heart Journal* 2001;22 (Suppl):597.
- [8] Goy JJ, Kaufmann U, Goy-Eggenberger D, Garachemani A, Hurni M, Carrel T, Gaspardone A, Burnand B, Meier B, Versaci F, Tomai F, Bertel O, Pieper M, de Benedictis M, Eeckhout E. A prospective randomized trial comparing stenting to internal mammary artery grafting for proximal, isolated de novo left anterior coronary artery stenosis: the SIMA trial. *Stenting vs Internal Mammary Artery*. *Mayo Clin Proc* 2000;75:1116-23. [PMID=11075740]

8.3 Individual trial summaries

Table 8.6: LEMANS, 2002 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=105 (52 vs. 53)	Patients with unprotected left main coronary artery stenosis	Studied treatment: unprotected left main stenting	1 year event RR=1.25 [0.67;2.34]
Follow-up duration: 1y		Control treatment: coronary artery bypass grafting	(cardiac and cerebrovascular events)
Study design: Randomized controlled trial			1 year revascularization
Parallel groups			RR=3.06 [1.20;7.80]
Open			
Exploratory trial			
Poland			
Reference			
Buszman PE, Kiesz SR, Bochenek A, Peszek-Przybyla E, Szkrobka I, Debinski M, Bialkowska B, Dudek D, Gruszka A, Zurakowski A, Milewski K, Wilczynski M, Rzeszutko L, Buszman P, Szymaszal J, Martin JL, Tendera M. Acute and late outcomes of unprotected left main stenting in comparison with surgical revascularization. J Am Coll Cardiol 2008;51:538-45 [PMID=18237682]			

Table 8.7: Cisowski, 0 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
<p>n=100 (50 vs. 50)</p> <p>Follow-up duration: 2 years</p> <p>Study design: Randomized controlled trial parallel group Open</p>	<p>Single vessel disease ACC/AHA A or B lesion in proximal LAD Angina CCS II or higher Lesion diameter 3 mm or greater/length 20mm or greater</p>	<p>Studied treatment: Tristar, Tera, Penta (Guidant) (Cordis)</p> <p>Control treatment: endoscopic atraumatic coronary artery bypass grafting</p>	
<p>Poland, Single center</p>			
<p>Reference</p>			

Table 8.8: Diegeler, 2002 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=220 (110 vs. 110)	Single vessel disease Lesion =75% stenosis in proximal LAD or between origin of left circumflex and 1st septal branch	Studied treatment: Various stents Control treatment: minimally invasive direct coronary artery bypass (off-pump procedure)	6 months events RR=2.13 [1.25;3.61] 6 months death RR=1.00 [0.14;6.97] 6 months MI RR=0.60 [0.15;2.45]
Follow-up duration: 5 years Study design: Randomized controlled trial parallel group Open			
Confirmatory trial at risk of bias Germany, Multicentre			
References			
Diegeler A, Thiele H, Falk V, Hambrecht R, Spyranitis N, Sick P, Diederich KW, Mohr FW, Schuler G. Comparison of stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery. N Engl J Med 2002;347:561-6 [PMID=12192015] Diegeler A, Spyranitis N, Matin M, Falk V, Hambrecht R, Autschbach R, Mohr FW, Schuler G. The revival of surgical treatment for isolated proximal high grade LAD lesions by minimally invasive coronary artery bypass grafting. Eur J Cardiothorac Surg 2000;17:501-4 [PMID=10814909]			

Table 8.9: Drenth, 2002 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=102 (51 vs. 51) Follow-up duration: 6 months, 3 years Study design: Randomized controlled trial parallel group Open Confirmatory trial at risk of bias Netherlands, Single centre	Single vessel disease Angina II Lesion (Grade B2 or C) of proximal LAD Suitable for CABG or stenting	Studied treatment: Stent type not reported Control treatment: minimally invasive direct coronary artery bypass (off-pump procedure)	6 months events RR=1.75 [0.55;5.61] 1 year event RR=3.00 [1.04;8.68] RR=2.40 [0.91;6.32] 6 months MI RR=5.00 [0.61;41.31] Long term cardiovascular events RR=2.40 [0.91;6.32]
References			
Drenth DJ, Veeger NJ, Grandjean JG, Mariani MA, van Boven AJ, Boonstra PW. Isolated high-grade lesion of the proximal LAD: a stent or off-pump LIMA?. Eur J Cardiothorac Surg 2004;25:567-71 [PMID=15037273]			
Drenth DJ, Veeger NJ, Winter JB, Grandjean JG, Mariani MA, Boven van AJ, Boonstra PW. A prospective randomized trial comparing stenting with off-pump coronary surgery for high-grade stenosis in the proximal left anterior descending coronary artery: three-year follow-up. J Am Coll Cardiol 2002;40:1955-60 [PMID=12475455]			
Drenth DJ, Winter JB, Veeger NJ, Monnick SH, van Boven AJ, Grandjean JG, Mariani MA, Boonstra PW. Minimally invasive coronary artery bypass grafting versus percutaneous transluminal coronary angioplasty with stenting in isolated high-grade stenosis of the proximal left anterior descending coronary artery: six months' angiographic and clinical follow-up of a prospective randomized study. J Thorac Cardiovasc Surg 2002;124:130-5 [PMID=12091818]			

Table 8.10: Grip, 2001 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=53 (28 vs. 25) Follow-up duration: Study design: Randomized controlled trial parallel group Open	Single vessel disease engaging LAD Stable or unstable angina	Studied treatment: Stent type not reported Control treatment: minimally invasive direct coronary artery bypass (off-pump procedure)	6 months MI RR=0.89 [0.06;13.54]
Sweden			
Reference			
Grip L, Wahrborg P, Odell A, Albertsson P, Berglin E, Brandrup-. Coronary artery bypass beating heart surgery withLIMA graft, versus coronary angioplasty with stent for patients withsingle left anterior descending artery - a pilot study. European HeartJournal 2001;22 (Suppl):597			

Table 8.11: SIMA, 2000 - Trial synopsis

Trial details	Patients	Treatments	Outcomes
n=121 (62 vs. 59) Follow-up duration: 2.4 years Study design: Randomized controlled trial parallel group Open	Single vessel disease Symptomatic or silent ischaemia 1 LAD lesion Ejection fraction >45% Vessel >3.0mm	Studied treatment: Any CE marked, but Palmaz-Schatz recommended Control treatment: Conventional CABG or minimally invasive direct coronary artery bypass (off-pump procedure) (10% of surgical procedures)	RR=4.52 [1.63;12.51] Long term cardiovascular events RR=4.52 [1.63;12.51]
Europe, Multicentre			
Reference			
Goy JJ, Kaufmann U, Goy-Eggenberger D, Garachemani A, Humi M, Carrel T, Gasparone A, Burnand B, Meier B, Versaci F, Tomai F, Bertel O, Pieper M, de Benedictis M, Eeckhout E. A prospective randomized trial comparing stenting to internal mammary artery grafting for proximal, isolated de novo left anterior coronary artery stenosis: the SIMA trial. <i>Stenting vs Internal Mammary Artery</i> . <i>Mayo Clin Proc</i> 2000;75:1116-23 [PMID=11075740]			

9 Global meta-analysis: all PCI

9.1 Global meta-analysis: all PCI versus CABG

Table 9.1: All PCI versus CABG

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
1 year event	RR=1.25	0.67;2.34	0.4764	1.0000 (0.00)	1	105
1 year revascularization	RR=3.06	1.20;7.80	0.0194	1.0000 (0.00)	1	105
cardiac death or MI	RR=3.49	0.99;12.28	0.0518	0.7031 (0.00)	2	276
1 year death from any cause	RR=0.25	0.03;2.20	0.2142	1.0000 (1.00)	1	105
CABG	RR=10.67	2.03;56.04	0.0052	0.6060 (0.00)	2	276
all cause death	RR=2.29	0.42;12.54	0.3407	0.4383 (0.00)	2	276

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

9.2 Global meta-analysis: all PCI versus E-ACAB

Table 9.2: All PCI versus E-ACAB

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
6 months events	RR=22.00	1.33;364.29	0.0309	1.0000 (0.00)	1	100
6 months death	RR=1.00	0.02;49.42	1.0000	1.0000 (0.00)	1	100
6 months MI	RR=1.00	0.02;49.42	1.0000	1.0000 (0.00)	1	100

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

9.3 Global meta-analysis: all PCI versus medical treatment

Table 9.3: All PCI versus medical treatment

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
PTCA	RR=1.05 ¹	0.43;2.53	0.9175	0.0014 (0.81) †	4	744
cardiac death or MI	RR=1.09	0.53;2.24	0.8203	0.0994 (0.52)	4	744

continued...

¹with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.94 95% CI 0.68;1.30

Endpoint	Effect	95% CI	p ass	p het	k	n
myocardial infarction (fatal and non fatal)	RR=1.51	0.54;4.20	0.4311	0.8799 (0.00)	3	444
cardiac death	RR=0.62	0.16;2.46	0.4977	0.1632 (0.45)	3	532
CABG	RR=0.97	0.57;1.66	0.9108	0.6637 (0.00)	4	744
non fatal MI	RR=0.97	0.54;1.72	0.9116	0.7649 (0.00)	4	744
angina	RR=0.52 ²	0.28;0.95	0.0337	0.0015 (0.80) †	4	744
all cause death	RR=0.75	0.41;1.37	0.3432	0.2475 (0.27)	4	744

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

9.4 Global meta-analysis: all PCI versus MIDCAB

Table 9.4: All PCI versus MIDCAB

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
6 months events	RR=2.06	1.27;3.33	0.0035	0.7664 (0.00)	2	318
1 year event	RR=3.00	1.04;8.68	0.0428	1.0000 (0.00)	1	102
	RR=3.24	1.61;6.54	0.0000	0.3771 (0.00)	2	223
6 months death	RR=0.62	0.14;2.72	0.5279	0.7390 (0.00)	3	371
6 months MI	RR=1.21	0.32;4.54	0.7750	0.2578 (0.26)	3	371
long term cardiovascular events	RR=3.24	1.61;6.54	0.0000	0.3771 (0.00)	2	223
1 year death from any cause	RR=3.00	1.04;8.68	0.0428	1.0000 (0.00)	1	102
long term death	RR=0.10 ³	0.00;8.53	0.3072	0.0216 (0.81) †	2	223

CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients; ES: effect size; I^2 : inconsistency degree

10 Ongoing studies

No ongoing trial was identified.

²with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.60 95% CI 0.48;0.75

³with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.10 95% CI 0.01;0.69

11 Excluded studies

No trial was excluded.

References

