# Myocardial revascularization for coronary artery disease in multivessels disease

## A systematic review and meta-analysis of randomized clinical trials

2017 - 7 - 1

This report should be referenced as follows:
TrialResults-center.org; Results of all major randomized clinical trials about Myocardial revascularization for coronary artery disease in multivessels disease.

# Contents

## 0.1 Synthesis of the meta-analysis results

We found 16 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 wich a benefit effect was detected, endpoints revealing a harmful effect and the other for wich no statistically significant difference was obtained (no evidence).
Reports of 16 trials (including 11,163 patients) were identified .
Among these comparisons, 7 trials are about balloon angioplasty,one about PCI,one about PCI with drug-eluting stents and 7 about stent.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.

### Balloon angioplasty

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

***Table 1:*** *Results summary - Balloon angioplasty*

| Benefit | Harmful | No evidence |
|---|---|---|
| | *Balloon angioplasty versus CABG* | |
| | ↑ angina (grade 2 or worse) in first year<br>RR=1.56¶ [1.20;2.04] k=4<br>↑ CABG<br>RR=16.04¶ [9.73;26.43] k=6 | → cardiac death or MI<br>RR=0.96$^{NS}$ [0.72;1.29] k=6<br>→ angina<br>RR=1.31$^{NS}$ [0.90;1.93] k=2<br>→ all cause death<br>RR=1.12$^{NS}$ [0.93;1.36] k=7 |

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

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

### PCI

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

***Table 2:*** *Results summary - PCI*

| Benefit | Harmful | No evidence |
|---|---|---|
| | *PCI versus CABG* | |
| | | |

* $p < 0.05$; † $p < 0.01$; ¶ $p < 0.001$ 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 3.

***Table 3:*** *Results summary - PCI with drug-eluting stents*

| Benefit | Harmful | No evidence |
|---|---|---|
| | *PCI with drug-eluting stents versus CABG* | |
| | ↑ long term cardiovascular events<br>RR=1.39¶ [1.14;1.68] k=1<br>↑ long term death<br>RR=1.36* [1.05;1.77] k=1 | → 2 yr MACE<br>RR=1.11$^{NS}$ [0.87;1.42] 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)

## Stent

Results obtained with stent for all the endpoints with data in at least one trial are summarized table 4.

***Table 4:*** *Results summary - Stent*

| Benefit | Harmful | No evidence |
|---|---|---|
| | *Stent versus CABG* | |
| | ↑ 1 year event<br>RR=1.82¶ [1.42;2.34] k=3<br>↑<br>RR=2.01¶ [1.63;2.47] k=1<br>↑ 1 year revascularization<br>RR=4.88¶ [3.62;6.58] k=3<br>↑ 2 yr MACE<br>RR=2.01¶ [1.60;2.51] k=1 | → long term cardiovascular events<br>RR=1.13$^{NS}$ [0.81;1.56] H k=4<br>→ 1 year death from any cause<br>RR=0.94$^{NS}$ [0.32;2.75] H k=3<br>→ 1 year MI<br>RR=0.91$^{NS}$ [0.46;1.83] k=2<br>→ long term MI<br>RR=0.92$^{NS}$ [0.47;1.82] H k=2<br>→ long term death<br>RR=1.00$^{NS}$ [0.66;1.50] k=4<br>→ all cause death<br>RR=1.49$^{NS}$ [0.81;2.71] k=1 |
| | *Stent versus OPCAB* | |
| | ↑ 1 year revascularization<br>RR=3.60† [1.50;8.65] k=1 | → 1 year event<br>RR=1.71$^{NS}$ [0.87;3.37] k=1<br>→ 1 year death from any cause<br>RR=0.13$^{NS}$ [0.01;2.41] k=1<br>→ 1 year MI<br>RR=0.88$^{NS}$ [0.30;2.56] 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 coronary artery disease in multivessels 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 coronary artery disease in multivessels 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 coronary artery disease.

**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 All cause death, CABG, Cardiac death or MI, Long term death, 1 year death from any cause, long term cardiovascular events, Angina (grade 2 or worse) in first year, 1 year revascularization, 1 year MI, 1 year event, long term MI, 2 yr MACE, Angina, , .

## 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 16 randomized comparisons which enrolled 11163 patients were identified. In all, 7 randomized comparisons concerned balloon angioplasty , one PCI , one PCI with drug-eluting stents and 7 stent.
The detailed descriptions of trials and meta-analysis results is given in section 3 (page 25) for balloon angioplasty, in section 4 (page 40) for PCI, in section 5 (page 47) for PCI with drug-eluting stents and in section 6 (page 55) for stent.

The average study size was 697 patients (range 44 to 1900). The first study was published in 1992, and the last study was published in 2012.
All trials were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
The table 2.1 (page 13) summmarizes 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 2.5 (page 16) and in the following graphs.

### 2.2.1 Balloon angioplasty

**Balloon angioplasty** was inferior to **CABG** in terms of angina (grade 2 or worse) in first year (RR=1.56, 95% CI 1.20 to 2.04, p=0.0000, 4 trials)and CABG (RR=16.04, 95% CI 9.73 to 26.43, p=0.0000, 6 trials). No significant difference was found on cardiac death or MI (RR=0.96, 95% CI 0.72 to 1.29, p=0.7937, 6 trials), angina (RR=1.31, 95% CI 0.90 to 1.93, p=0.1630, 2 trials)and all cause death (RR=1.12, 95% CI 0.93 to 1.36, p=0.2386, 7 trials).

### 2.2.2 PCI

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

### 2.2.3 PCI with drug-eluting stents

**PCI with drug-eluting stents** was inferior to **CABG** in terms of long term cardiovascular events (RR=1.39, 95% CI 1.14 to 1.68, p=0.0000, 1 trial)and long term death (RR=1.36, 95% CI 1.05 to 1.77, p=0.0208, 1 trial). No significant difference was found on 2 yr MACE (RR=1.11, 95% CI 0.87 to 1.42, p=0.3873, 1 trial).

### 2.2.4 Stent

**Stent** was inferior to **CABG** in terms of 1 year event (RR=1.82, 95% CI 1.42 to 2.34, p=0.0000, 3 trials), (RR=2.01, 95% CI 1.63 to 2.47, p=0.0000, 1 trial), 1 year revascularization (RR=4.88, 95% CI 3.62 to 6.58, p=0.0000, 3 trials)and 2 yr MACE (RR=2.01, 95% CI 1.60 to 2.51, p=0.0000, 1 trial). No significant difference was found on long term cardiovascular events

(RR=1.13, 95% CI 0.81 to 1.56, p=0.4791, 4 trials)with a random effect model in reason of a heterogeneity (Het. p=0.0418)(RR=0.94, 95% CI 0.32 to 2.75, p=0.9155, 3 trials)with a random effect model in reason of a heterogeneity (Het. p=0.0136)(RR=0.91, 95% CI 0.46 to 1.83, p=0.7944, 2 trials), long term MI (RR=0.92, 95% CI 0.47 to 1.82, p=0.8166, 2 trials)with a random effect model in reason of a heterogeneity (Het. p=0.0386)(RR=1.00, 95% CI 0.66 to 1.50, p=0.9849, 4 trials)and all cause death (RR=1.49, 95% CI 0.81 to 2.71, p=0.1977, 1 trial).

**Stent** was inferior to **OPCAB** in terms of 1 year revascularization (RR=3.60, 95% CI 1.50 to 8.65, p=0.0042, 1 trial). No significant difference was found on 1 year event (RR=1.71, 95% CI 0.87 to 3.37, p=0.1180, 1 trial), 1 year death from any cause (RR=0.13, 95% CI 0.01 to 2.41, p=0.1702, 1 trial)and 1 year MI (RR=0.88, 95% CI 0.30 to 2.56, p=0.8172, 1 trial).

***Table 2.1:*** *Main study characteristics - PCI*

| Trial | Patients | Treatments | Trial design and method |
|---|---|---|---|
| **Balloon angioplasty** | | | |
| ***Balloon angioplasty versus CABG*** | | | |
| EAST, 1994 [1]<br>n = 198 vs. 194 | patients with multivessels coronary artery disease | transluminal coronary angioplasty<br>**versus**<br>coronary-artery bypass grafting | open<br>USA |
| GABI, 1994 [2]<br>n = 182 vs. 177 | patients with symptomatic multivessel coronary disease | percutaneous transluminal coronary angioplasty<br>**versus**<br>coronary-artery bypass grafting | open<br>8 centres, Germany |
| BARI, 1996 [3]<br>n = 915 vs. 914 | patients with multivessel disease | PTCA<br>**versus**<br>CABG | open<br>USA, Canada |
| RITA, 1993 [4]<br>n = 510 vs. 501 | patients with one, two, or three diseased coronary arteries | percutaneous transluminal coronary angioplasty<br>**versus**<br>coronary artery bypass surgery | open<br>UK |
| ERACI, 1992 [5]<br>n = 63 vs. 64 | patients with multivessel disease and lesions suitable for either form of therapy | percutaneous transluminal coronary angioplasty<br>**versus**<br>coronary artery bypass grafting | open<br>Argentina |
| Toulouse, 1992<br>n = 76 vs. 76 | patients with multivessels coronary artery disease | PTCA<br>**versus**<br>CABG | open<br>France |
| CABRI, 1995 [6, 7]<br>n = 541 vs. 513 | patients with symptomatic multivessel coronary disease | percutaneous transluminal coronary angioplasty<br>**versus**<br>coronary artery bypass grafting | open<br>Europe |
| **PCI** | | | |

continued...

| Trial | Patients | Treatments | Trial design and method |
|---|---|---|---|
| ***PCI versus CABG*** | | | |
| AWESOME, 2001 [1, 2, 3, 4, 5, 6, 7, 8] n = 222 vs. 232 | high-risk patients with medically refractory ischemia | percutaneous coronary intervention **versus** coronary artery bypass graft<br>arterial grafts: 76%<br>stent (%): 54% | open<br>parallel groups<br>16 centres, US (Veterans Affairs Medical Centers) |
| **PCI with drug-eluting stents** | | | |
| ***PCI with drug-eluting stents versus CABG*** | | | |
| FREEDOM, 2012 [1] n = 953 vs. 947 | patients with diabetes and multivessel coronary artery disease | percutaneous coronary stenting **versus** CABG | open<br>parallel groups<br>Primary endpoint: death, MI, stroke<br>140 centres, international |
| **Stent** | | | |
| ***Stent versus CABG*** | | | |
| ARTS, 2001 [1, 2, 3, 4, 5] n = 600 vs. 605 | multi vessel disease with 2 or more de novo lesion in different major arteries Total occlusion <1month | palmaz-Schatz Crown/Cross flex (Cordis) **versus** conventional CABG<br>arterial grafts: 93%<br>stent (%): 100% | open<br>parallel group<br>Primary endpoint: major adverse cardiac and cerebrovascular events at one year<br>Multicentre, International |
| CARDia (PCI), 2008 [6] n = 256 vs. 254 | patients with diabetes and symptomatic multivessel coronary artery disease or complex single-vessel disease. | PCI plus stenting (and routine abciximab) **versus** CABG<br>arterial grafts: 100%<br>stent (%): 100% | open<br>parallel groups<br>Primary endpoint: death, stroke, and MI<br>24 centres, UK, Ireland |
| ERACI II, 2003 [7, 8] n = 225 vs. 225 | multi vessel disease Angina CSS III-IV; no angina but large area of heart at risk; unstable =1 vessel to be treated Lesion >3.0mm | gianturco Robin II (Cook) Primary device **versus** conventional CABG<br>arterial grafts: 89%<br>stent (%): 100% | open<br>parallel group<br>Multicentre, Argentinad |

continued...

| Trial | Patients | Treatments | Trial design and method |
|---|---|---|---|
| MASS II, 2007 [9, 10]<br>n = 205 vs. 203 | patients with multivessel coronary artery disease with stable angina and preserved ventricular function | PCI (73% stent)<br>**versus**<br>CABG<br>arterial grafts: NA<br>stent (%): 68.3% | open<br>parallel groups<br>Primary endpoint: MACE<br>single-center, South America |
| Myoprotect, 2004 [11]<br>n = 23 vs. 21 | patients with symptomatic main-stem and main-stem-equivalent lesions with substantially increased risk for bypass surgery | percutaneous transluminal coronary angioplasty/stent<br>**versus**<br>CABG<br>arterial grafts: 100%<br>stent (%): 100% | open<br>parallel groups<br>Primary endpoint: not defined<br>single center, Europe |
| SOS, 2002<br>[12, 13, 14, 15, 16, 17]<br>n = 488 vs. 500 | multiple vessel disease Symptomatic 1 or more vessel suitable for stenting | stent<br>**versus**<br>CABG<br>arterial grafts: 93%<br>stent (%): 100% | open<br>parallel group<br>Primary endpoint: repeat revascularisation<br>Multicentre, Canada, United Kingdom, Europe |
| ***Stent versus OPCAB*** | | | |
| OCTOSTENT, 2003 [18, 19]<br>n = 138 vs. 142 | multi or single vessel disease Moderate LV function CABG or stenting to be considered feasible | stent type not reported<br>**versus**<br>off-pump coronary artery bypass<br>arterial grafts: 100%<br>stent (%): 100% | open<br>parallel groups<br>Primary endpoint: death, stroke,MI, revascularization<br>Multicentre, Europe |

***Table 2.2:*** *Summary of all results for balloon angioplasty*

| Endpoint | Effect | 95% CI | p ass | p het ($I^2$) | k | n |
|---|---|---|---|---|---|---|
| ***balloon angioplasty versus CABG*** | | | | | | |
| cardiac death or MI | RR=0.96 | 0.72;1.29 | 0.7937 | 0.2365 (0.26) | 6 | 3095 |
| angina (grade 2 or worse) in first year | RR=1.56 | 1.20;2.04 | 0.0000 | 0.1159 (0.49) | 4 | 2610 |
| CABG | RR=16.04 | 9.73;26.43 | 0.0000 | 0.8372 (0.00) | 6 | 3095 |
| angina | RR=1.31 | 0.90;1.93 | 0.1630 | 0.1638 (0.48) | 2 | 1349 |
| all cause death | RR=1.12 | 0.93;1.36 | 0.2386 | 0.5119 (0.00) | 7 | 4924 |

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 PCI*

| Endpoint | Effect | 95% CI | p ass | p het ($I^2$) | k | n |
|---|---|---|---|---|---|---|
| ***PCI 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 2.4:*** *Summary of all results for PCI with drug-eluting stents*

| Endpoint | Effect | 95% CI | p ass | p het ($I^2$) | k | n |
|---|---|---|---|---|---|---|
| ***PCI with drug-eluting stents versus CABG*** | | | | | | |
| long term cardiovascular events | RR=1.39 | 1.14;1.68 | 0.0000 | 1.0000 (0.00) | 1 | 1900 |
| long term death | RR=1.36 | 1.05;1.77 | 0.0208 | 1.0000 (1.00) | 1 | 1900 |
| 2 yr MACE | RR=1.11 | 0.87;1.42 | 0.3873 | 1.0000 (0.00) | 1 | 1900 |

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 stent*

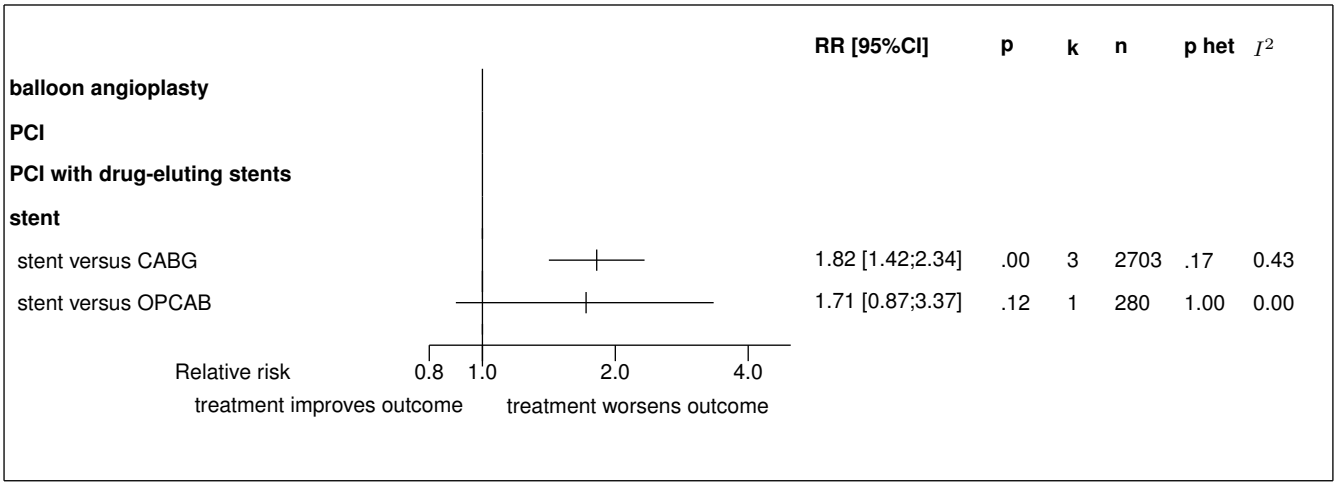
| Endpoint | Effect | 95% CI | p ass | p het ($I^2$) | k | n |
|---|---|---|---|---|---|---|
| ***stent versus CABG*** | | | | | | |
| 1 year event | RR=1.82 | 1.42;2.34 | 0.0000 | 0.1740 (0.43) | 3 | 2703 |
| | RR=2.01 | 1.63;2.47 | 0.0000 | 1.0000 (1.00) | 1 | 1205 |
| 1 year revascularization | RR=4.88 | 3.62;6.58 | 0.0000 | 0.6615 (0.00) | 3 | 2703 |

continued...

| Endpoint | Effect | 95% CI | p ass | p het | k | n |
|---|---|---|---|---|---|---|
| long term cardiovascular events | RR=1.13 [1] | 0.81;1.56 | 0.4791 | 0.0418 (0.63) † | 4 | 3051 |
| 1 year death from any cause | RR=0.94 [2] | 0.32;2.75 | 0.9155 | 0.0136 (0.77) † | 3 | 2643 |
| 1 year MI | RR=0.91 | 0.46;1.83 | 0.7944 | 0.0501 (0.74) | 2 | 2193 |
| long term MI | RR=0.92 [3] | 0.47;1.82 | 0.8166 | 0.0386 (0.77) † | 2 | 2193 |
| long term death | RR=1.00 | 0.66;1.50 | 0.9849 | 0.0507 (0.61) | 4 | 3051 |
| 2 yr MACE | RR=2.01 | 1.60;2.51 | 0.0000 | 1.0000 (0.00) | 1 | 1205 |
| all cause death | RR=1.49 | 0.81;2.71 | 0.1977 | 1.0000 (0.00) | 1 | 408 |
| ***stent versus OPCAB*** | | | | | | |
| 1 year event | RR=1.71 | 0.87;3.37 | 0.1180 | 1.0000 (0.00) | 1 | 280 |
| 1 year revascularization | RR=3.60 | 1.50;8.65 | 0.0042 | 1.0000 (0.00) | 1 | 280 |
| 1 year death from any cause | RR=0.13 | 0.01;2.41 | 0.1702 | 1.0000 (0.00) | 1 | 280 |
| 1 year MI | RR=0.88 | 0.30;2.56 | 0.8172 | 1.0000 (0.00) | 1 | 280 |

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

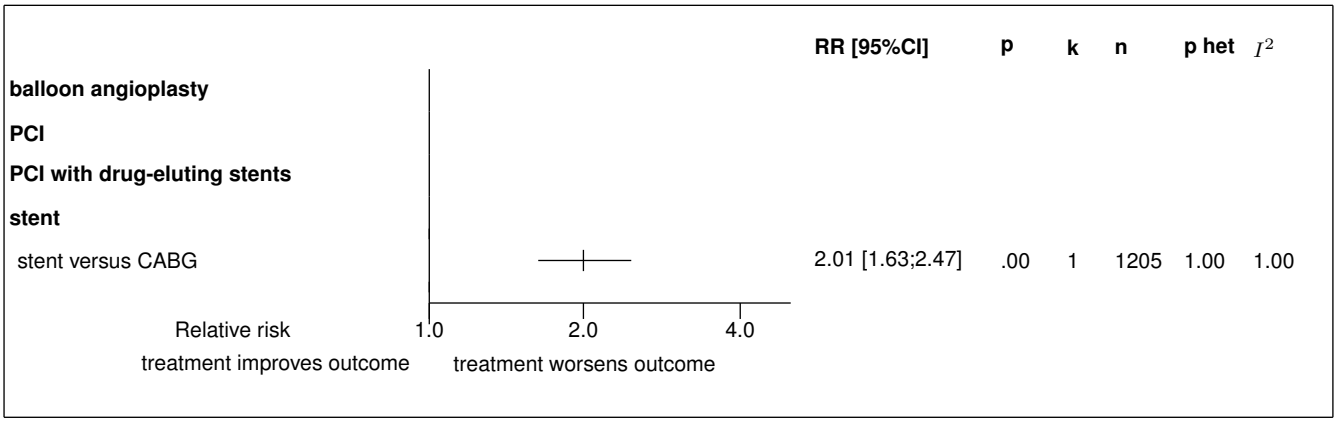
***Figure 2.1:*** *Forest's plot for 1 year event*




Results obtained with a fixed effect model except in case of heterogenity 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 hetereogenity test; [r]: random effect model used

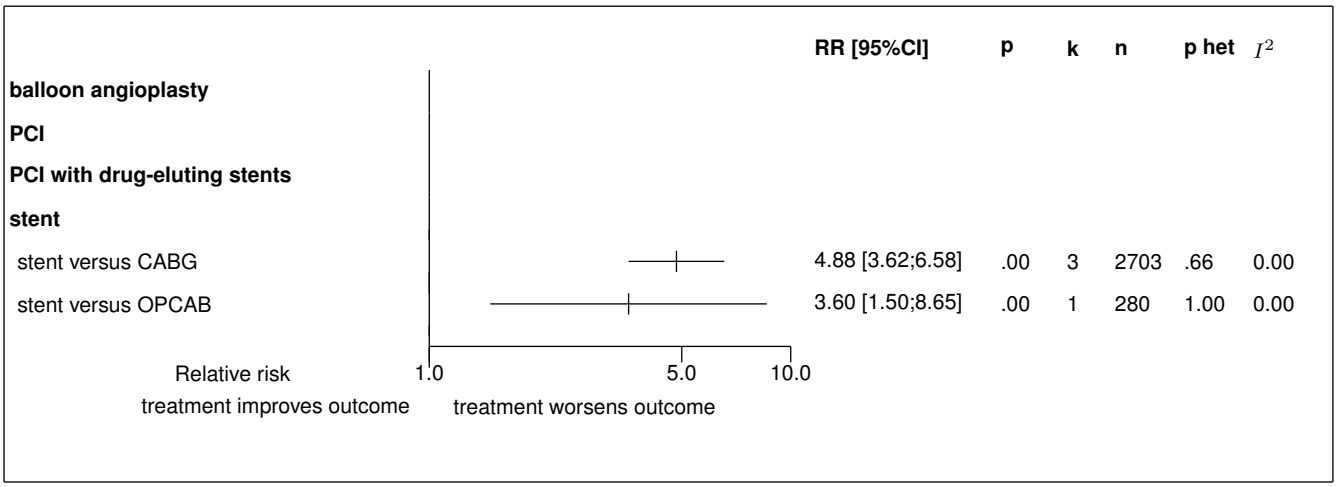
[1] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=1.04 95% CI 0.86;1.26
[2] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.86 95% CI 0.53;1.41
[3] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.93 95% CI 0.67;1.30

***Figure 2.2:*** *Forest's plot for*



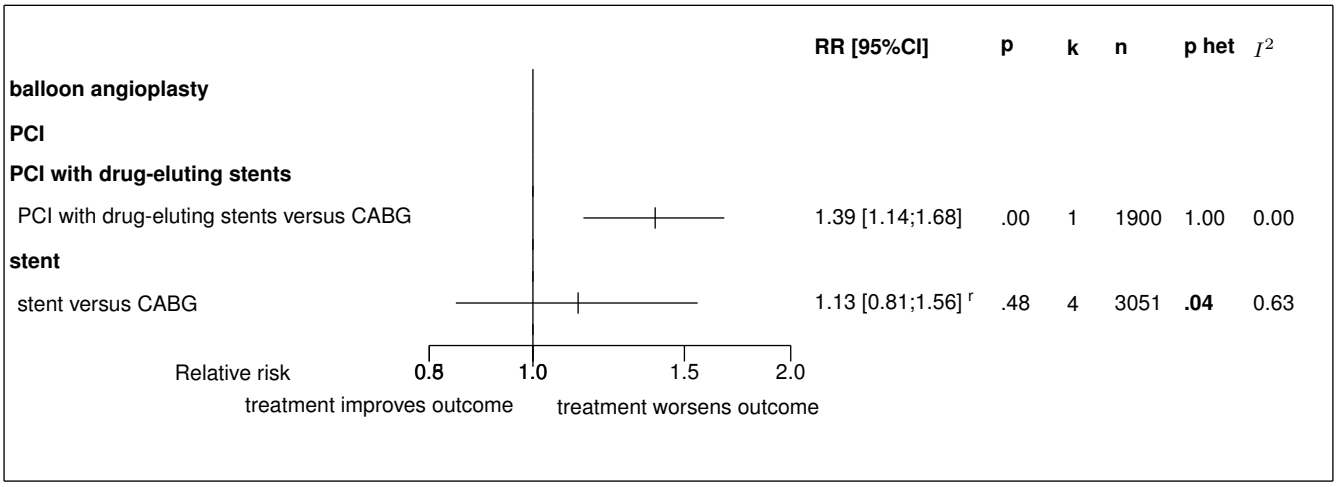

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.3:*** *Forest's plot for 1 year revascularization*



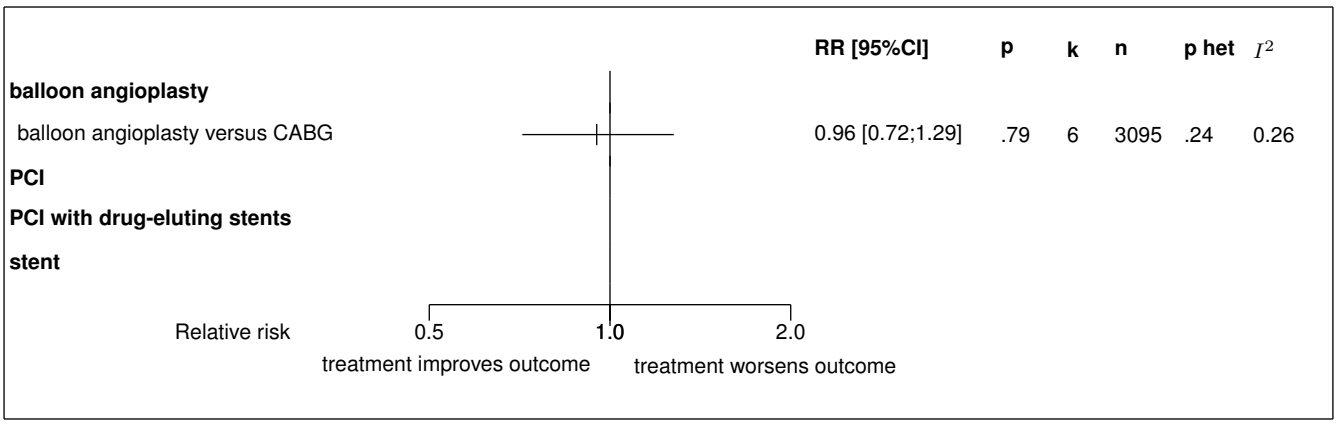

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.4:*** *Forest's plot for long term cardiovascular events*



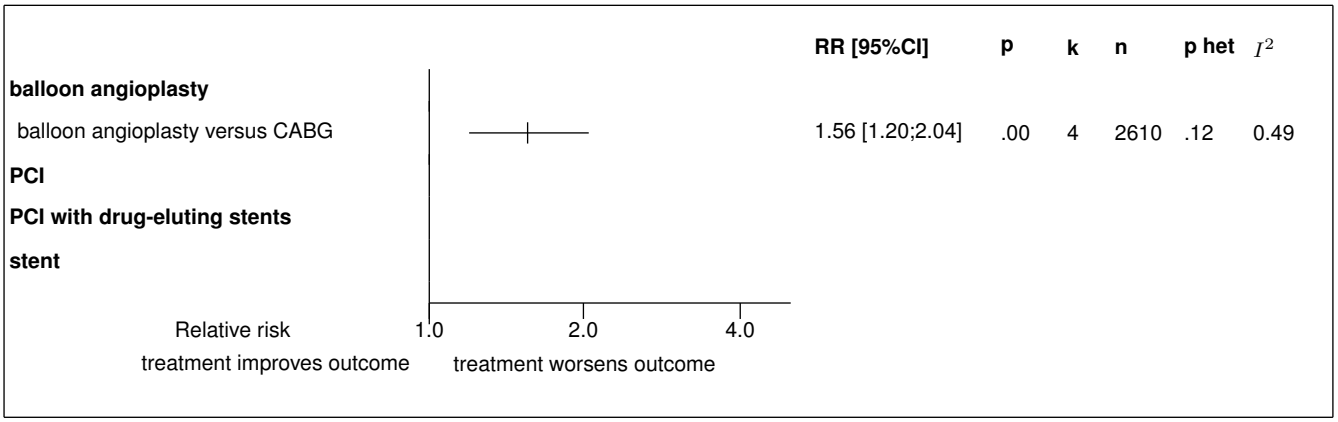

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.5:*** *Forest's plot for cardiac death or MI*



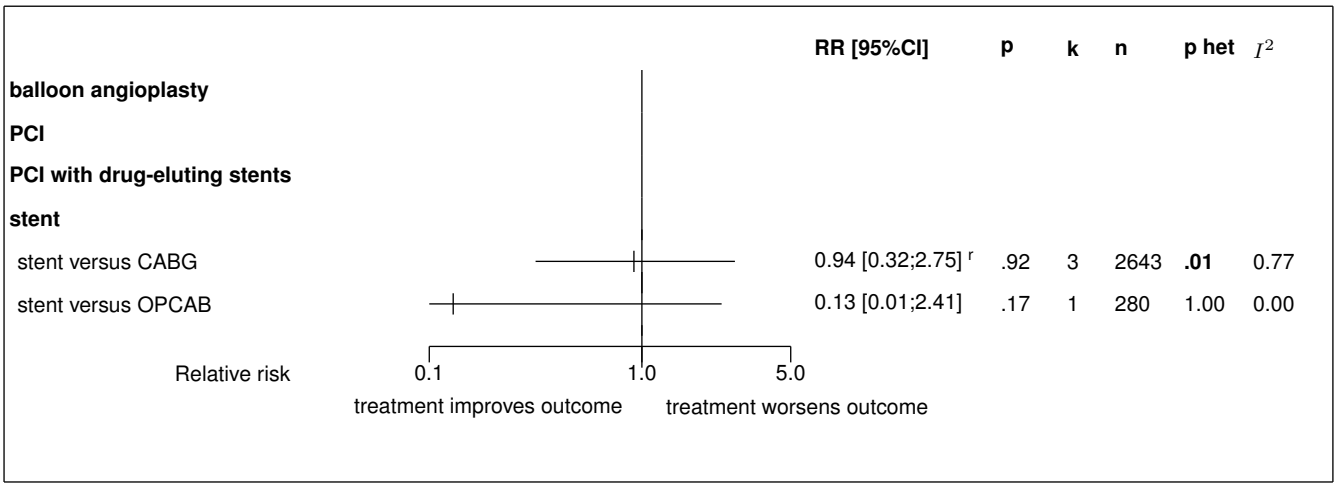

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.6:*** *Forest's plot for angina (grade 2 or worse) in first year*



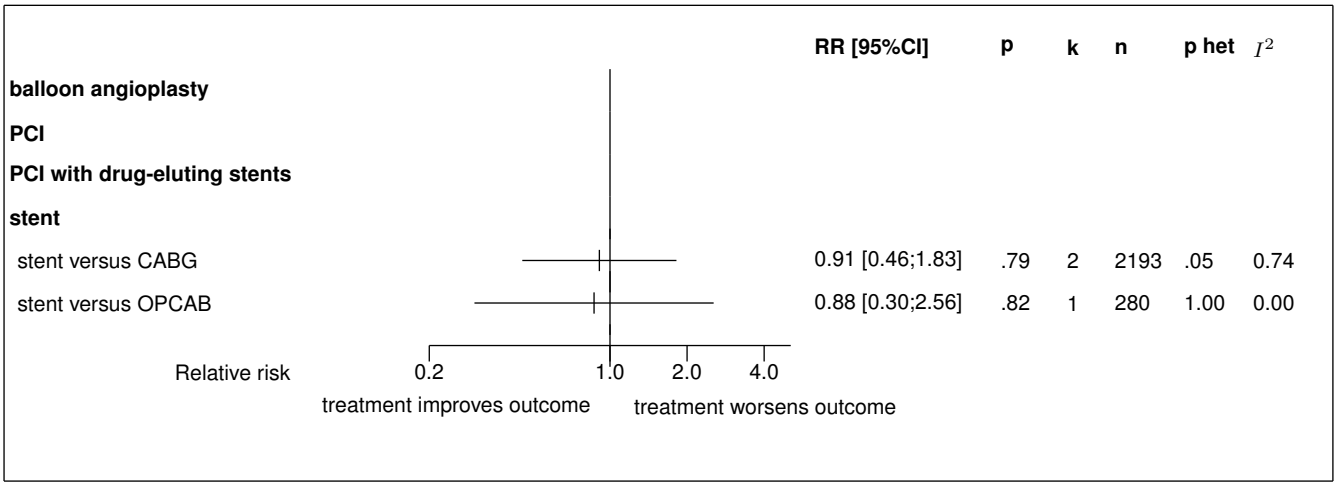

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.7:*** *Forest's plot for 1 year death from any cause*



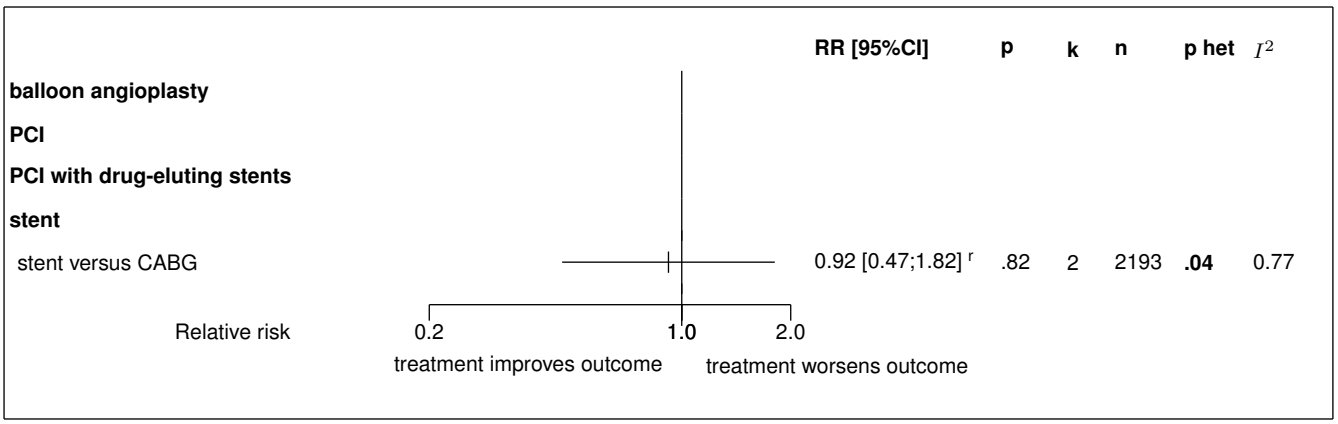

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.8:*** *Forest's plot for 1 year MI*



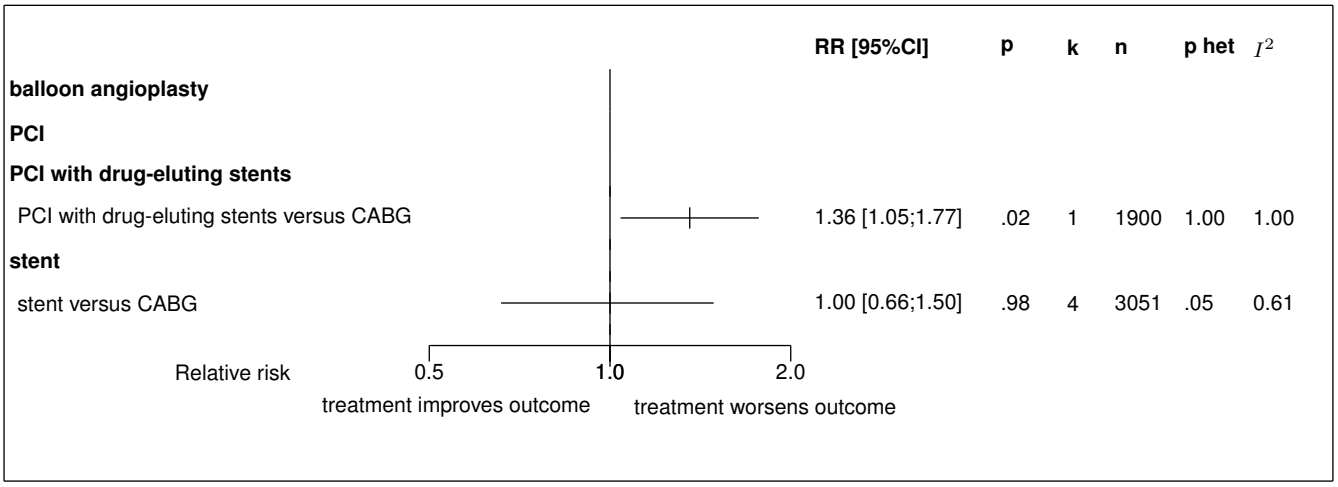

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.9:*** *Forest's plot for long term MI*



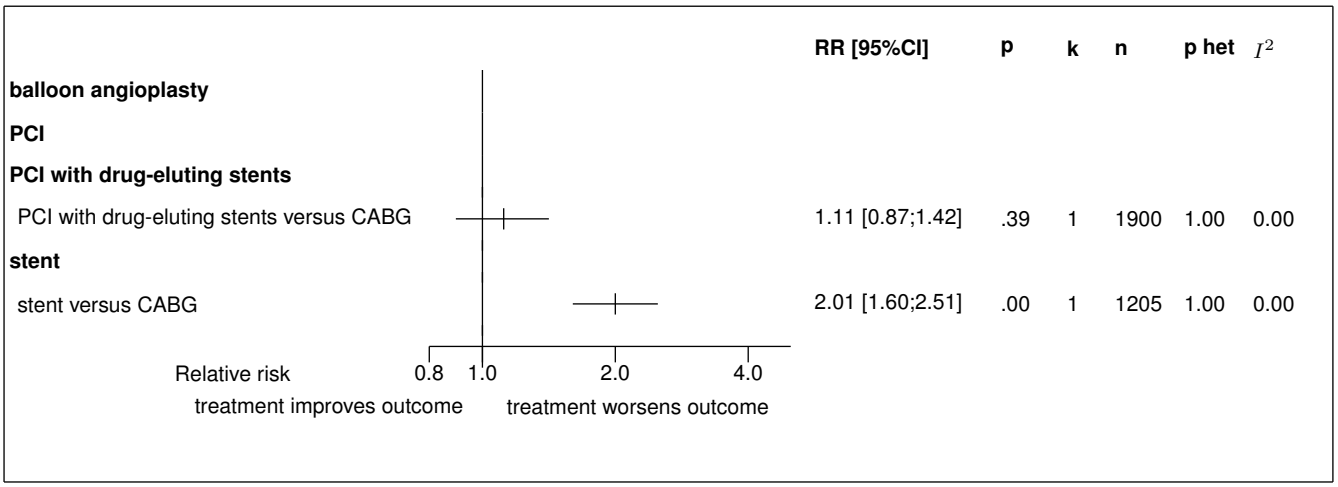

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.10:*** *Forest's plot for long term death*



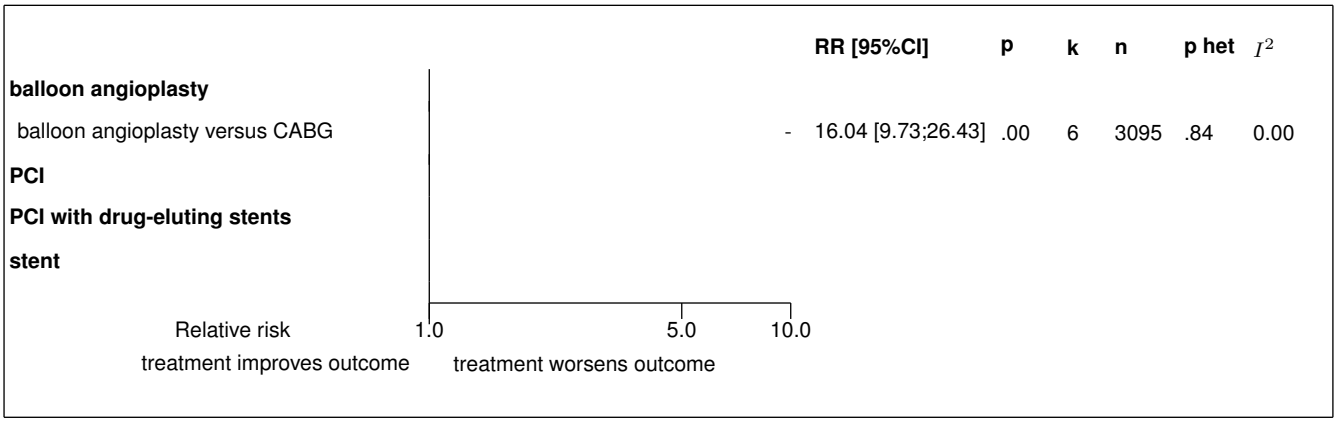

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.11:*** *Forest's plot for 2 yr MACE*



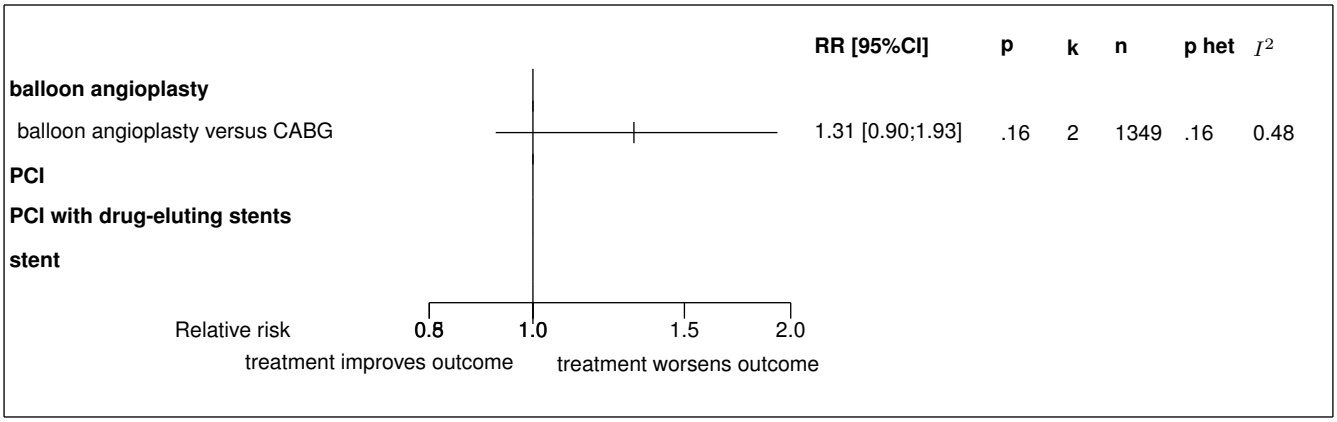

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.12:*** *Forest's plot for CABG*



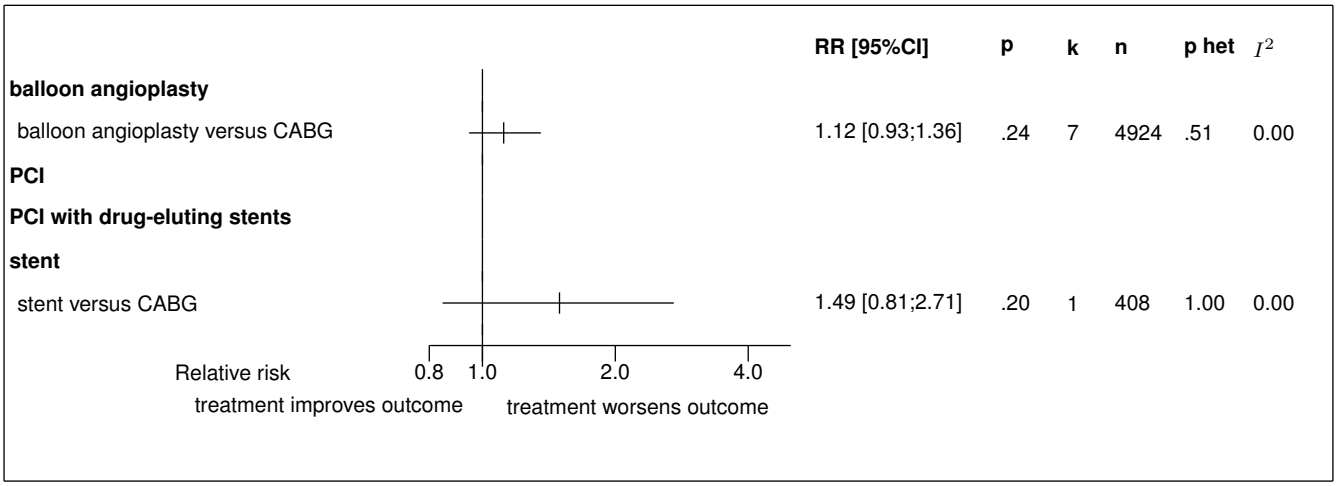

Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

***Figure 2.13:*** *Forest's plot for angina*




Results obtained with a fixed effect model except in case of heterogenity 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 hetereogenity test; ʳ: random effect model used

***Figure 2.14:*** *Forest's plot for all cause death*




Results obtained with a fixed effect model except in case of heterogenity 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 hetereogenity test; ʳ: random effect model used

# 3 Detailed results for balloon angioplasty

## 3.1 Available trials

A total of 7 RCTs which randomized 4924 patients were identified: all compared balloon angioplasty with CABG.
The average study size was 703 patients (range 127 to 1829). The first study was published in 1992, and the last study was published in 1996.
All trials were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
All cause death data was reported in 7 trials; 6 trials reported data on CABG; 6 trials reported data on cardiac death or MI; 4 trials reported data on angina (grade 2 or worse) in first year; and 2 trials reported data on angina.
Following tables 3.1 (page 25), 3.2 (page 25), 3.4 (page 27), and 3.3 (page 26) summarized the main characteristics of the trials including in this systematic review of randomized trials of balloon angioplasty.

***Table 3.1:*** *Treatment description - PCI - balloon angioplasty*

| Trial | Studied treatment | Control treatment |
|---|---|---|
| **Balloon angioplasty versus CABG** | | |
| EAST (1994) [1] | transluminal coronary angioplasty | coronary-artery bypass grafting |
| GABI (1994) [2] | Percutaneous transluminal coronary angioplasty | coronary-artery bypass grafting |
| BARI (1996) [3] | PTCA | CABG |
| RITA (1993) [4] | percutaneous transluminal coronary angioplasty | coronary artery bypass surgery |
| ERACI (1992) [5] | Percutaneous transluminal coronary angioplasty | coronary artery bypass grafting |
| Toulouse (1992) | PTCA | CABG |
| CABRI (1995) [6, 7] | percutaneous transluminal coronary angioplasty | coronary artery bypass grafting |

***Table 3.2:*** *Descriptions of participants - PCI - balloon angioplasty*

| Trial | Patients |
|---|---|
| **Balloon angioplasty versus CABG** | |

continued...

| Trial | Patients |
|---|---|
| EAST (1994) [1] | Patients with multivessels coronary artery disease |
| GABI (1994) [2] | Patients with symptomatic multivessel coronary disease |
| BARI (1996) [3] | Patients with multivessel disease |
| RITA (1993) [4] | Patients with one, two, or three diseased coronary arteries |
| ERACI (1992) [5] | Patients with multivessel disease and lesions suitable for either form of therapy |
| Toulouse (1992) | Patients with multivessels coronary artery disease |
| CABRI (1995) [6, 7] | Patients with symptomatic multivessel coronary disease |

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

| Trial | Design | Duration | Centre | Primary end-point |
|---|---|---|---|---|
| **Balloon angioplasty versus CABG** | | | | |
| EAST, 1994 [1] n=392 | open | 3 y | USA | |
| GABI, 1994 [2] n=359 | open | 1 y | Germany 8 centres | |
| BARI, 1996 [3] n=1829 | open | 5.4 y | USA, Canada | |
| RITA, 1993 [4] n=1011 | open | 2.5 y (6.5y) | UK | |
| ERACI, 1992 [5] n=127 | open | 3.8 y | Argentina | |
| Toulouse, 1992 n=152 | open | 2.8 y | France | |
| CABRI, 1995 [6, 7] n=1054 | open | 1 y | Europe | |

***Table 3.4:*** *Trial characteristics - PCI - balloon angioplasty*

| Trial |
|---|
| **Balloon angioplasty versus CABG** |
| EAST, 1994 [1] |
| GABI, 1994 [2] |
| BARI, 1996 [3] |
| RITA, 1993 [4] |
| ERACI, 1992 [5] |
| Toulouse, 1992 |
| CABRI, 1995 [6, 7] |

## 3.2 Meta-analysis results

The results are detailed in table 3.5 (page 28). This table is followed by the Forest's plot corresponding to each endpoint.

### Balloon angioplasty versus CABG

A total of 6 of the 7 studies eligible for this comparison provided data on **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 0.96 (95% CI 0.72 to 1.29, p=0.7937). No heterogeneity was detected (p = 0.2365, $I^2$ = 0.26%).
A total of 4 of the 7 studies eligible for this comparison provided data on **angina (grade 2 or worse) in first year**. The analysis detected a statistically significant difference in favor of CABG in angina (grade 2 or worse) in first year, with a RR of 1.56 (95% CI 1.20 to 2.04, p=0.0000). No heterogeneity was detected (p = 0.1159, $I^2$ = 0.49%).
A total of 6 of the 7 studies eligible for this comparison provided data on **CABG**. The analysis detected a statistically significant difference in favor of CABG in CABG, with a RR of 16.04 (95% CI 9.73 to 26.43, p=0.0000). No heterogeneity was detected (p = 0.8372, $I^2$ = 0.00%).
A total of 2 of the 7 studies eligible for this comparison provided data on **angina**. When pooled together, there was no statistically significant difference between the groups in angina, with a RR of 1.31 (95% CI 0.90 to 1.93, p=0.1630). No heterogeneity was detected (p = 0.1638, $I^2$ = 0.48%).
All the 7 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 1.12 (95% CI 0.93 to 1.36, p=0.2386). No heterogeneity was detected (p = 0.5119, $I^2$ = 0.00%).

***Table 3.5:*** *Results details - PCI - balloon angioplasty*

| Comparison Endpoint | Effect | 95% CI | p ass | p het | k | n |
|---|---|---|---|---|---|---|
| ***balloon angioplasty versus CABG*** | | | | | | |
| cardiac death or MI | RR=0.96 | [0.72;1.29] | 0.7937 | 0.2365 ($I^2$=0.26) | 6 | 3095 |
| angina (grade 2 or worse) in first year | RR=1.56 | [1.20;2.04] | 0.0000 | 0.1159 ($I^2$=0.49) | 4 | 2610 |
| CABG | RR=16.04 | [9.73;26.43] | 0.0000 | 0.8372 ($I^2$=0.00) | 6 | 3095 |
| angina | RR=1.31 | [0.90;1.93] | 0.1630 | 0.1638 ($I^2$=0.48) | 2 | 1349 |
| all cause death | RR=1.12 | [0.93;1.36] | 0.2386 | 0.5119 ($I^2$=0.00) | 7 | 4924 |

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; $I^2$: inconsistance degree

***Figure 3.1:*** *Forest's plot for cardiac death or MI*

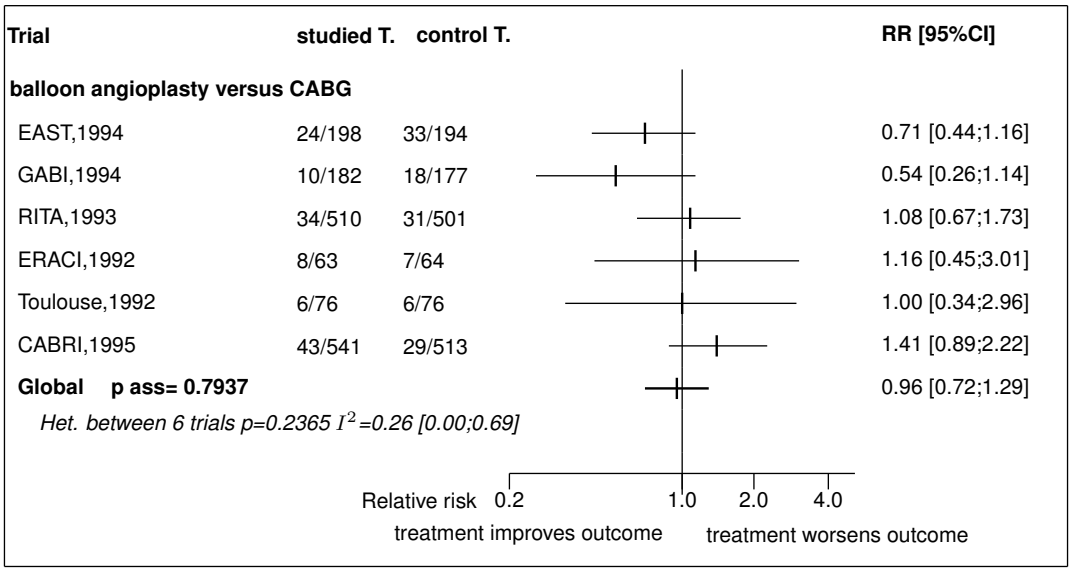



***Figure 3.2:*** *Forest's plot for angina (grade 2 or worse) in first year*

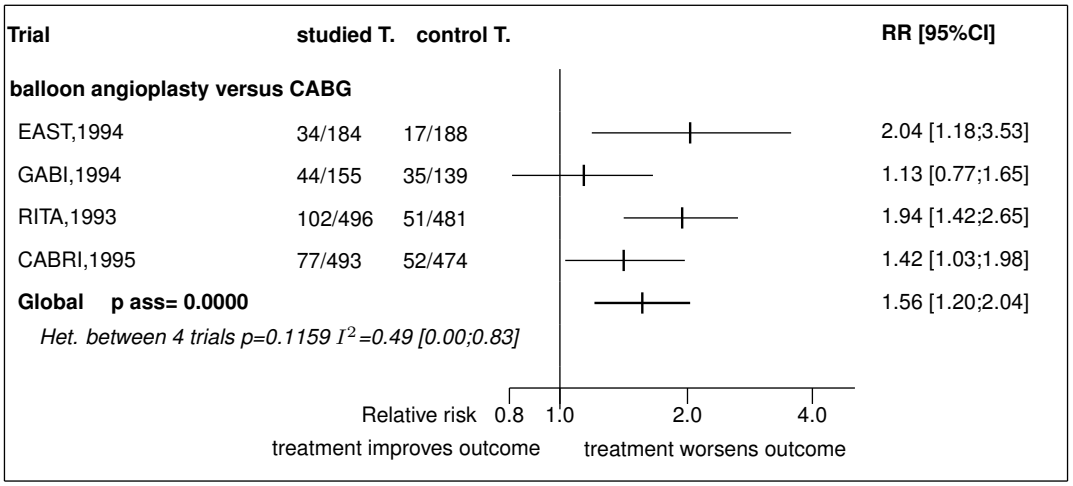


***Figure 3.3:*** *Forest's plot for CABG*

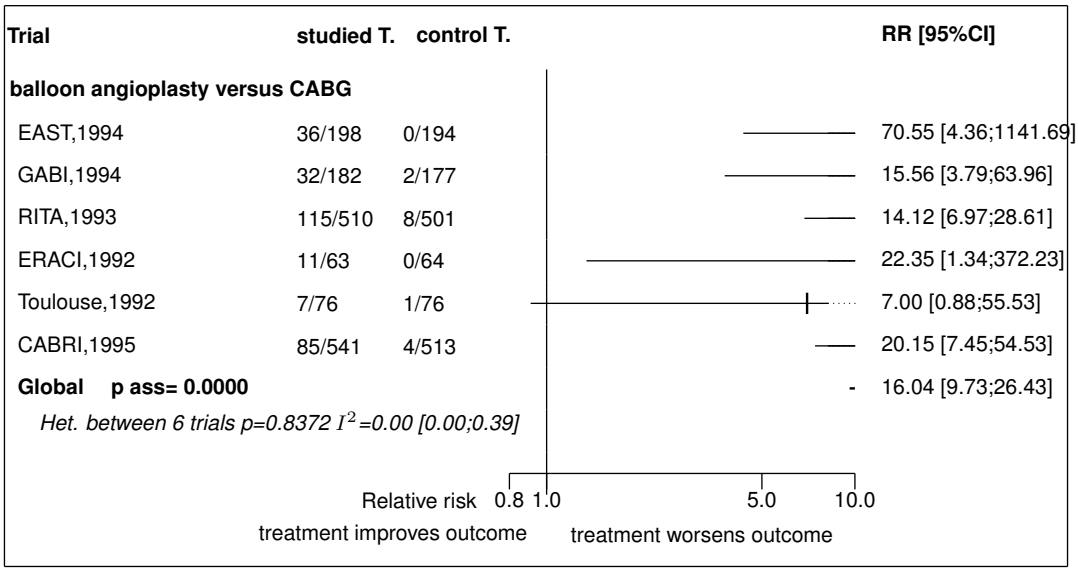



***Figure 3.4:*** *Forest's plot for angina*

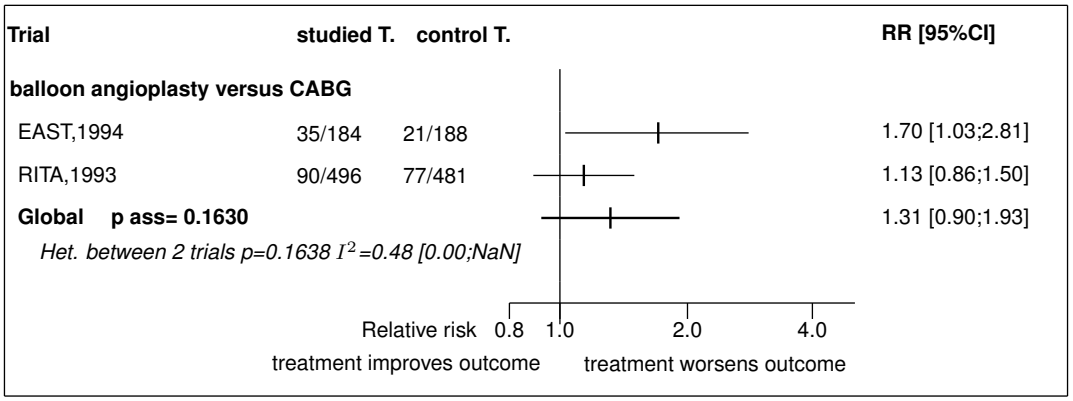
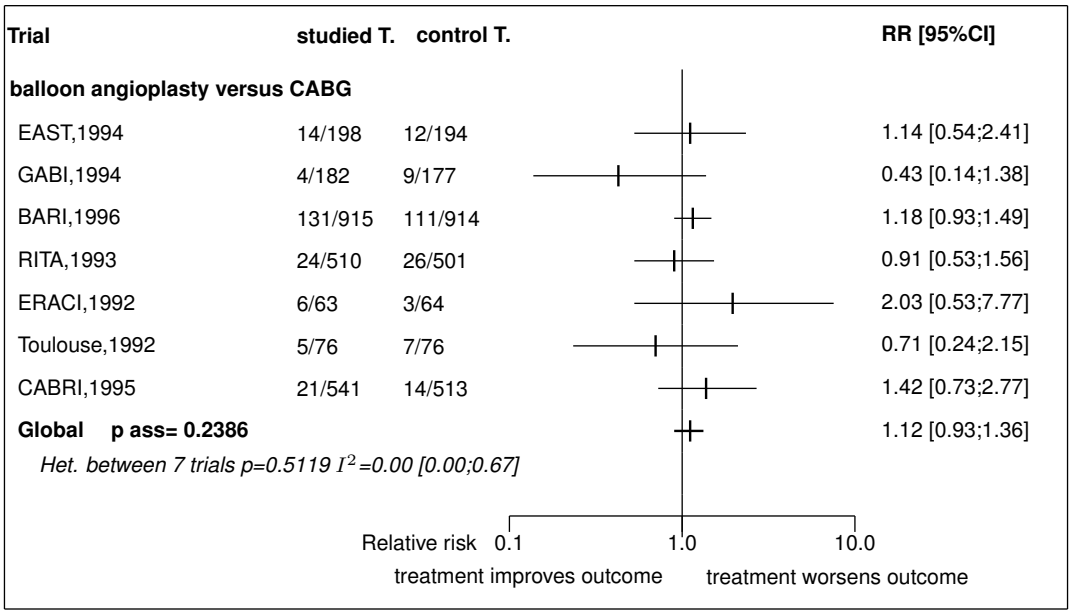


***Figure 3.5:*** *Forest's plot for all cause death*




# References

[1] King SB 3rd, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, Alazraki NP, Guyton RA, Zhao XQ. A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST). N Engl J Med 1994 Oct 20;331:1044-50. [PMID=8090163]

[2] Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI). N Engl J Med 1994 Oct 20;331:1037-43. [PMID=8090162]

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[4] . Coronary angioplasty versus coronary artery bypass surgery: the Randomized Intervention Treatment of Angina (RITA) trial. Lancet 1993 Mar 6;341:573-80. [PMID=8094826]

[5] Rodriguez A, Boullon F, Perez-Balino N, Paviotti C, Liprandi MI, Palacios IF. Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. ERACI Group. J Am Coll Cardiol 1993 Oct;22:1060-7. [PMID=8409041]

[6] . First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995 Nov 4;346:1179-84. [PMID=7475656]

[7] Martuscelli E, Clementi F, Gallagher MM, D'Eliseo A, Chiricolo G, Nigri A, Marino B, Romeo F. Revascularization strategy in patients with multivessel disease and a major vessel chronically occluded; data from the CABRI trial. Eur J Cardiothorac Surg 2008;33:4-8. [PMID=17988889]

## 3.3 Individual trial summaries

***Table 3.6:*** *EAST, 1994 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=392 (198 vs. 194)<br>**Follow-up duration:** 3 y<br>**Study design:** Randomized controlled trial<br>Open<br><br>USA | Patients with multivessels coronary artery disease | **Studied treatment:** transluminal coronary angioplasty<br>**Control treatment:** coronary-artery bypass grafting | Cardiac death or MI<br>RR=0.71 [0.44;1.16]<br>Angina (grade 2 or worse) in first year<br>RR=2.04 [1.18;3.53] |

**Reference**

King SB 3rd, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, Alazraki NP, Guyton RA, Zhao XQ. A randomized trial comparing coronary angioplasty with coronary bypass surgery. Emory Angioplasty versus Surgery Trial (EAST). N Engl J Med 1994 Oct 20;331:1044-50 [PMID=8090163]

***Table 3.7:*** *GABI, 1994 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=359 (182 vs. 177)<br>**Follow-up duration:** 1 y<br>**Study design:** Randomized controlled trial<br>Open<br><br>Germany, 8 centres | Patients with symptomatic multivessel coronary disease | **Studied treatment:** Percutaneous transluminal coronary angioplasty<br>**Control treatment:** coronary-artery bypass grafting | Cardiac death or MI<br>RR=0.54 [0.26;1.14]<br>Angina (grade 2 or worse) in first year<br>RR=1.13 [0.77;1.65] |

**Reference**

Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. German Angioplasty Bypass Surgery Investigation (GABI). N Engl J Med 1994 Oct 20;331:1037-43 [PMID=8090162]

***Table 3.8:*** *BARI, 1996 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=1829 (915 vs. 914)<br>**Follow-up duration:** 5.4 y<br>**Study design:** Randomized controlled trial<br>Open<br><br>USA, Canada | Patients with multivessel disease | **Studied treatment:** PTCA<br>**Control treatment:** CABG | |

**Reference**

. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. N Engl J Med 1996 Jul 25;335:217-25 [PMID=8657237]

***Table 3.9:*** *RITA, 1993 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=1011 (510 vs. 501)<br>**Follow-up duration:** 2.5 y (6.5y)<br>**Study design:** Randomized controlled trial<br>Open<br><br>UK | Patients with one, two, or three diseased coronary arteries | **Studied treatment:** percutaneous transluminal coronary angioplasty<br>**Control treatment:** coronary artery bypass surgery | Cardiac death or MI<br>RR=1.08 [0.67;1.73]<br>Angina (grade 2 or worse) in first year<br>RR=1.94 [1.42;2.65] |

**Reference**

. Coronary angioplasty versus coronary artery bypass surgery: the Randomized Intervention Treatment of Angina (RITA) trial. Lancet 1993 Mar 6;341:573-80 [PMID=8094826]

***Table 3.10:*** *ERACI, 1992 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=127 (63 vs. 64)<br>**Follow-up duration:** 3.8 y<br>**Study design:** Randomized controlled trial<br>Open<br><br>Argentina | Patients with multivessel disease and lesions suitable for either form of therapy | **Studied treatment:** Percutaneous transluminal coronary angioplasty<br>**Control treatment:** coronary artery bypass grafting | Cardiac death or MI<br>RR=1.16 [0.45;3.01] |

**Reference**

Rodriguez A, Boullon F, Perez-Balino N, Paviotti C, Liprandi MI, Palacios IF. Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. ERACI Group. J Am Coll Cardiol 1993 Oct;22:1060-7 [PMID=8409041]

***Table 3.11:*** *Toulouse, 1992 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=152 (76 vs. 76)<br>**Follow-up duration:** 2.8 y<br>**Study design:** Randomized controlled trial<br>Open<br><br>France | Patients with multivessels coronary artery disease | **Studied treatment:** PTCA<br>**Control treatment:** CABG | Cardiac death or MI<br>RR=1.00 [0.34;2.96] |
| **Reference** | | | |

***Table 3.12:*** *CABRI, 1995 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=1054 (541 vs. 513)<br>**Follow-up duration:** 1 y<br>**Study design:** Randomized controlled trial<br>Open<br><br>Europe | Patients with symptomatic multivessel coronary disease | **Studied treatment:** percutaneous transluminal coronary angioplasty<br>**Control treatment:** coronary artery bypass grafting | Cardiac death or MI<br>RR=1.41 [0.89;2.22]<br>Angina (grade 2 or worse) in first year<br>RR=1.42 [1.03;1.98] |

**References**

. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularisation Investigation). CABRI Trial Participants. Lancet 1995 Nov 4;346:1179-84 [PMID=7475656]
Martuscelli E, Clementi F, Gallagher MM, D'Eliseo A, Chiricolo G, Nigri A, Marino B, Romeo F. Revascularization strategy in patients with multivessel disease and a major vessel chronically occluded; data from the CABRI trial. Eur J Cardiothorac Surg 2008;33:4-8 [PMID=17988889]

# 4 Detailed results for PCI

## 4.1 Available trials

Only one trial which randomized 454 patients was identified: it compared PCI with CABG.
This trial included 454 patients and was published in 2001.
This trial was open-label in design.
It was reported in English language.
data was reported in trials;
Following tables 4.1 (page 40), 4.2 (page 40), 4.4 (page 41), and 4.3 (page 40) summarized the main characteristics of the trial including in this systematic review of randomized trials of PCI.

***Table 4.1:*** *Treatment description - PCI - PCI*

| Trial | Studied treatment | Control treatment |
|---|---|---|
| **PCI versus CABG** | | |
| AWESOME (2001) [1, 2, 3, 4, 5, 6, 7, 8] | percutaneous coronary intervention | coronary artery bypass graft |

***Table 4.2:*** *Descriptions of participants - PCI - PCI*

| Trial | Patients |
|---|---|
| **PCI versus CABG** | |
| AWESOME (2001) [1, 2, 3, 4, 5, 6, 7, 8] | High-risk patients with medically refractory ischemia |

***Table 4.3:*** *Design and methodological quality of trials - PCI - PCI*

| Trial | Design | Duration | Centre | Primary end-point |
|---|---|---|---|---|
| **PCI versus CABG** | | | | |
| AWESOME, 2001 [1, 2, 3, 4, 5, 6, 7, 8] n=454 | Parallel groups open confirmatory trial at risk of bias | 5 years | US (Veterans Affairs Medical Centers) 16 centres | |

***Table 4.4:*** *Trial characteristics - PCI - PCI*

| Trial | Age (mean, year) | Men (%) | Ejection fraction (%) | Extent of Disease | arterial grafts | stent (%) |
|---|---|---|---|---|---|---|
| **PCI versus CABG** | | | | | | |
| AWESOME, 2001 [1, 2, 3, 4, 5, 6, 7, 8] | | | | multiple vessels disease | 76% | 54% |

## 4.2 Meta-analysis results

The results are detailed in table 4.5 (page 42). This table is followed by the Forest's plot corresponding to each endpoint.

### PCI versus CABG

No data were presented in the 1 trial identified

***Table 4.5:*** *Results details - PCI - PCI*

| Comparison Endpoint | Effect | 95% CI | p ass | p het | k | n |
|---|---|---|---|---|---|---|
| ***PCI 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; $I^2$: inconsistance degree

# References

[1] Morrison DA, Sethi G, Sacks J, Henderson W, Grover F, Sedlis S, Esposito R, Ramanathan K, Weiman D, Saucedo J, Antakli T, Paramesh V, Pett S, Vernon S, Birjiniuk V, Welt F, Krucoff M, Wolfe W, Lucke JC, Mediratta S, Booth D, Barbiere C, Lewis D. Percutaneous coronary intervention versus coronary artery bypass graft surgery for patients with medically refractory myocardial ischemia and risk factors for adverse outcomes with bypass: a multicenter, randomized trial. Investigators of the Department of Veterans Affairs Cooperative Study #385, the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME). J Am Coll Cardiol 2001;38:143-9. [PMID=11451264]

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## 4.3 Individual trial summaries

***Table 4.6:*** *AWESOME, 2001 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=454 (222 vs. 232)<br>**Follow-up duration:** 5 years<br>**Study design:** Randomized controlled trial<br>Parallel groups<br>Open<br>Confirmatory trial at risk of bias<br>US (Veterans Affairs Medical Centers), 16 centres | High-risk patients with medically refractory ischemia | **Studied treatment:** percutaneous coronary intervention<br>**Control treatment:** coronary artery bypass graft | |

continued...

| trial details | Patients | Treatments | Outcomes |
|---|---|---|---|

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Sedlis SP, Morrison DA, Lorin JD, Esposito R, Sethi G, Sacks J, Henderson W, Grover F, Ramanathan KB, Weiman D, Saucedo J, Antakli T, Paramesh V, Pett S, Vernon S, Birjiniuk V, Welt F, Krucoff M, Wolfe W, Lucke JC, Mediratta S, Booth D, Murphy E, Ward H,. Percutaneous coronary intervention versus coronary bypass graft surgery for diabetic patients with unstable angina and risk factors for adverse outcomes with bypass: outcome of diabetic patients in the AWESOME randomized trial and registry. J Am Coll Cardiol 2002;40:1555-66 [PMID=12427406]

Sedlis SP, Ramanathan KB, Morrison DA, Sethi G, Sacks J, Henderson W. Outcome of percutaneous coronary intervention versus coronary bypass grafting for patients with low left ventricular ejection fractions, unstable angina pectoris, and risk factors for adverse outcomes with bypass (the AWESOME Randomized Trial and Registry). Am J Cardiol 2004;94:118-20 [PMID=15219521]

Stroupe KT, Morrison DA, Hlatky MA, Barnett PG, Cao L, Lyttle C, Hynes DM, Henderson WG. Cost-effectiveness of coronary artery bypass grafts versus percutaneous coronary intervention for revascularization of high-risk patients. Circulation 2006;114:1251-7 [PMID=16966588]

# 5 Detailed results for PCI with drug-eluting stents

## 5.1 Available trials

Only one trial which randomized 1900 patients was identified: it compared PCI with drug-eluting stents with CABG.
This trial included 1900 patients and was published in 2012.
This trial was open-label in design.
It was reported in English language.
Long term cardiovascular events data was reported in 1 trials; 1 trials reported data on 2 yr MACE; and 1 trials reported data on long term death.
Following tables 5.1 (page 47), 5.2 (page 47), 5.4 (page 49), and 5.3 (page 48) summarized the main characteristics of the trial including in this systematic review of randomized trials of PCI with drug-eluting stents.

***Table 5.1:*** *Treatment description - PCI - PCI with drug-eluting stents*

| Trial | Studied treatment | Control treatment |
|---|---|---|
| **PCI with drug-eluting stents versus CABG** | | |
| FREEDOM (2012) [1] | percutaneous coronary stenting | CABG |
| | **Concomittant treatment:** recommended medical therapies for the control oflow-density lipoprotein cholesterol, systolic blood pressure, and glycated hemoglobin | |

***Table 5.2:*** *Descriptions of participants - PCI - PCI with drug-eluting stents*

| Trial | Patients |
|---|---|
| **PCI with drug-eluting stents versus CABG** | |

continued...

| Trial | Patients | |
|---|---|---|
| FREEDOM (2012) [1] | Patients with diabetes and multivessel coronary artery disease | |
| | **Inclusion criteria:** diabetes mellitus (Type 1 or Type 2) (presence of classic symptoms of diabetes mellitus with unequivocal elevation of plasma glucose 2-hour post-prandial or random of greater than 200 mg/dL (11mmol/L) or fasting plasma glucose elevation on more than one occasion of at least 126 mg/dL (7mmol/L)); Currently undergoing pharmacological or non-pharmacological treatment for diabetes; Angiographically confirmed multivessel CAD [critical (greater than or equal to 70%) lesions in at least two major epicardial vessels and in at least two separate coronary artery territories (LAD, LCX, RCA)] amenable to either PCI or CABG; Angiographic characteristics amendable to both PCI/DES and CABG; Indication for revascularization based upon symptoms of angina and/or objective evidence of myocardial ischemia | **Exclusion criteria:** severe congestive heart failure (class III or IV according to New York Heart Association [NYHA] or pulmonary edema); Prior CABG surgeryPrior valve surgery; Prior PCI with stent implantation within 6 months of study entry; stroke within 6 months of study entry; if stroke occured more than 6 months prior to study entry, must have significant residual neurologic involvement, as reflected in a Rankin Score of greater than 1Prior history of significant bleeding (within 6 months of study entry) that may occur during CABG or PCI/DES related anticoagulationIn-stent restenosis of a target vessel; Two or more chronic total occlusions in major coronary territories; Left main stenosis (at least 50% diameter stenosis); Acute ST-elevation MI (Q-wave) within 72 hours of study entry requiring revascularization; Abnormal creatine kinase level (greater than twice the normal limit); or abnormal CK-MB level at study entry; Planned simultaneous surgical procedure unrelated to coronary revascularization (e.g., valve repair/replacement, aneurysmectomy, carotid endarterectomy, or carotid stent); Cannot undergo either CABG or PCI/DES because of a coexisting medical condition; Significant leukopenia, neutropenia, thrombocytopenia, anemia, or known bleeding diathesis; Intolerance to aspirin or both clopidogrel and ticlopidine; Dementia with a score of less than 20 on the Mini Mental Status Examination (MMSE); Extra-cardiac illness that is expected to limit survival to less than 5 years (e.g., oxygen-dependent chronic obstructive pulmonary disease, active hepatitis, significant hepatic failure, or severe kidney disease) |

***Table 5.3:*** *Design and methodological quality of trials - PCI - PCI with drug-eluting stents*

| Trial | Design | Duration | Centre | Primary endpoint |
|---|---|---|---|---|
| **PCI with drug-eluting stents versus CABG** | | | | |
| FREEDOM, 2012 [1] n=1900 | Parallel groups open confirmatory trial at risk of bias | 3.8 yrs (median) | international 140 centres | death, MI, stroke |

***Table 5.4:*** *Trial characteristics - PCI - PCI with drug-eluting stents*

| Trial | Age (mean, year) | Men (%) | Ejection fraction (%) | Extent of Disease | arterial grafts | stent (%) |
|---|---|---|---|---|---|---|
| **PCI with drug-eluting stents versus CABG** | | | | | | |
| FREEDOM, 2012 [1] | | | | | | |

## 5.2 Meta-analysis results

The results are detailed in table 5.5 (page 50). This table is followed by the Forest's plot corresponding to each endpoint.

### PCI with drug-eluting stents versus CABG

The single study eligible for this comparison provided data on **long term cardiovascular events**. The analysis detected a statistically significant difference in favor of CABG in long term cardiovascular events, with a RR of 1.39 (95% CI 1.14 to 1.68, p=0.0000).
The single study eligible for this comparison provided data on **long term death**. The analysis detected a statistically significant difference in favor of CABG in long term death, with a RR of 1.36 (95% CI 1.05 to 1.77, p=0.0208).
The single study eligible for this comparison provided data on **2 yr MACE**. No statistically significant difference between the groups was found in 2 yr MACE, with a RR of 1.11 (95% CI 0.87 to 1.42, p=0.3873).

***Table 5.5:*** *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*** | | | | | | |
| long term cardiovascular events | RR=1.39 | [1.14;1.68] | 0.0000 | 1.0000 ($I^2$=0.00) | 1 | 1900 |
| long term death | RR=1.36 | [1.05;1.77] | 0.0208 | 1.0000 ($I^2$=1.00) | 1 | 1900 |
| 2 yr MACE | RR=1.11 | [0.87;1.42] | 0.3873 | 1.0000 ($I^2$=0.00) | 1 | 1900 |

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; $I^2$: inconsistance degree

***Figure 5.1:*** *Forest's plot for long term cardiovascular events*

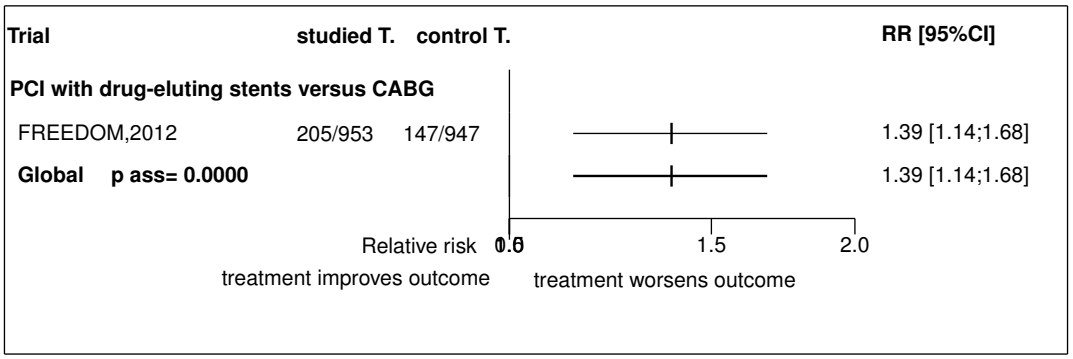


***Figure 5.2:*** *Forest's plot for long term death*

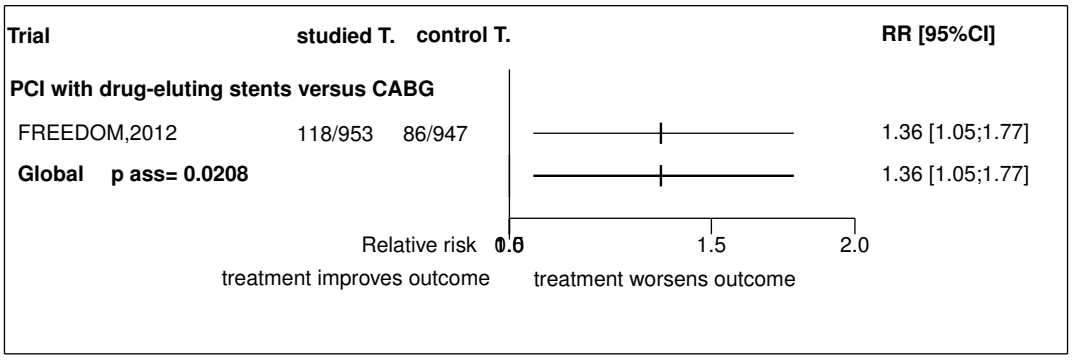
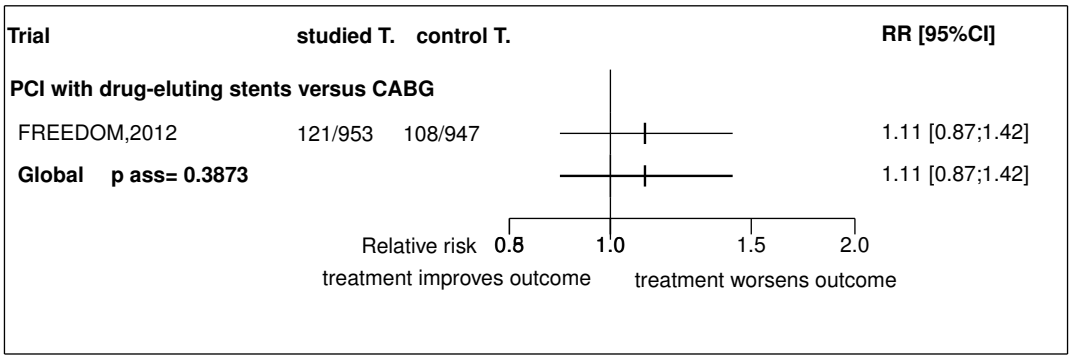



***Figure 5.3:*** *Forest's plot for 2 yr MACE*

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## 5.3 Individual trial summaries

***Table 5.6:*** *FREEDOM, 2012 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=1900 (953 vs. 947)<br>**Follow-up duration:** 3.8 yrs (median)<br>**Study design:** Randomized controlled trial<br>Parallel groups<br>Open<br>Confirmatory trial at risk of bias<br>international, 140 centres | Patients with diabetes and multivessel coronary artery disease<br>**Inclusion criteria:** Diabetes mellitus (Type 1 or Type 2) (presence of classic symptoms of diabetes mellitus with unequivocal elevation of plasma glucose 2-hour post-prandial or random of greater than 200 mg/dL (11mmol/L) or fasting plasma glucose elevation on more than one occasion of at least 126 mg/dL (7mmol/L)); Currently undergoing pharmacological or non-pharmacological treatment for diabetes; Angiographically confirmed multivessel CAD [critical (greater than or equal to 70%) lesions in at least two major epicardial vessels and in at least two separate coronary artery territories (LAD, LCX, RCA)] amenable to<br>**Exclusion criteria:** Severe congestive heart failure (class III or IV according to New York Heart Association [NYHA] or pulmonary edema); Prior CABG surgeryPrior valve surgery; Prior PCI with stent implantation within 6 months of study entry; stroke within 6 months of study entry; if stroke occured more than 6 months prior to study entry, must have significant residual neurologic involvement, as reflected in a Rankin Score of greater than 1Prior history of significant bleeding (within 6 months of study entry) that may occur during CABG or PCI/DES related anticoagulationIn-stent restenosis of a target vessel; Two o | **Studied treatment:** percutaneous coronary stenting<br>**Control treatment:** CABG<br>**Concomittant treat.:**recommended medical therapies for the control oflow-density lipoprotein cholesterol, systolic blood pressure, and glycated hemoglobin | Long term cardiovascular events RR=1.39 [1.14;1.68] |

continued...

| trial details | Patients | Treatments | Outcomes |
|---|---|---|---|

**Reference**

Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, Yang M, Cohen DJ, Rosenberg Y, Solomon SD, Desai AS, Gersh BJ, Magnuson EA, Lansky A, Boineau R, Weinberger J, Ramanathan K, Sousa JE, Rankin J, Bhargava B, Buse J, Hueb W, Smith CR, Muratov. Strategies for Multivessel Revascularization in Patients with Diabetes. N Engl J Med 2012 Nov 4;: [PMID=23121323]

# 6 Detailed results for stent

## 6.1 Available trials

A total of 7 RCTs which randomized 3885 patients were identified: 6 trials compared stent with CABG and it compared stent with OPCAB.
The average study size was 555 patients (range 44 to 1205). The first study was published in 2001, and the last study was published in 2008.
All trials were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
1 year death from any cause data was reported in 4 trials; 3 trials reported data on long term cardiovascular events; 3 trials reported data on 1 year revascularization; 3 trials reported data on 1 year MI; 3 trials reported data on 1 year event; 3 trials reported data on long term death; 2 trials reported data on long term MI; 1 trials reported data on ; 1 trials reported data on all cause death; and 1 trials reported data on 2 yr MACE.
Following tables 6.1 (page 55), 6.2 (page 56), 6.4 (page 58), and 6.3 (page 56) summarized the main characteristics of the trials including in this systematic review of randomized trials of stent.

***Table 6.1:*** *Treatment description - PCI - stent*

| Trial | Studied treatment | Control treatment |
|---|---|---|
| **Stent versus CABG** | | |
| ARTS (2001) [1, 2, 3, 4, 5] | Palmaz-Schatz Crown/Cross flex (Cordis) | Conventional CABG |
| CARDia (PCI) (2008) [6] [b] | PCI plus stenting (and routine abciximab) bare metal stent or sirolimus-coated stents (CYPHER) and abciximab | CABG |
| ERACI II (2003) [7, 8] | Gianturco Robin II (Cook) Primary device | Conventional CABG |
| MASS II (2007) [9, 10] [d] | PCI (73% stent) | CABG |
| Myoprotect (2004) [11] | percutaneous transluminal coronary angioplasty/stent | CABG |
| SOS (2002) [12, 13, 14, 15, 16, 17] | Stent No restriction on type of stent | CABG No restriction on type of surgical technique (3% of procedures OPCAB) |
| **Stent versus OPCAB** | | |
| OCTOSTENT (2003) [18, 19] | Stent type not reported | off-pump coronary artery bypass |

b) BMS n=72, CYPHER n=180 d) 3 arms: PCI, CABGand medical treatment

***Table 6.2:*** *Descriptions of participants - PCI - stent*

| Trial | Patients | |
|---|---|---|
| **Stent versus CABG** | | |
| ARTS (2001) [1, 2, 3, 4, 5] | Multi vessel disease with 2 or more de novo lesion in different major arteries Total occlusion <1month | |
| | **Inclusion criteria:** | **Exclusion criteria:** transmural MI 1 week |
| CARDia (PCI) (2008) [6] | Patients with diabetes and symptomatic multivessel coronary artery disease or complex single-vessel disease. | |
| | **Inclusion criteria:** multi-vessel disease or complex single-vessel disease (ostial or proximal left anterior descending artery); diabetes mellitus; anatomy suitable for both PCI and CABG | **Exclusion criteria:** previous PCI or CABG; age >80 years; left main disease; cardiogenic shock; recent ST-elevation MI (within 6 weeks); ejection fraction <20%; contraindications to abciximab, aspirin, and clopidogrel |
| ERACI II (2003) [7, 8] | Multi vessel disease Angina CSS III-IV; no angina but large area of heart at risk; unstable =1 vessel to be treated Lesion >3.0mm | |
| | **Inclusion criteria:** | **Exclusion criteria:** MI <=24h |
| MASS II (2007) [9, 10] | Patients with multivessel coronary artery disease with stable angina and preserved ventricular function | |
| | **Inclusion criteria:** | **Exclusion criteria:** MI/unstable angina requiring emergency revascularization |
| Myoprotect (2004) [11] | Patients with symptomatic main-stem and main-stem-equivalent lesions with substantially increased risk for bypass surgery | |
| SOS (2002) [12, 13, 14, 15, 16, 17] | Multiple vessel disease Symptomatic 1 or more vessel suitable for stenting | |
| | **Inclusion criteria:** | **Exclusion criteria:** MI <=48h |
| **Stent versus OPCAB** | | |
| OCTOSTENT (2003) [18, 19] | Multi or single vessel disease Moderate LV function CABG or stenting to be considered feasible | |
| | **Inclusion criteria:** stable or unstable angina (Braunwald class IIIB) and/ordocumented ischemia; irrespective of the extent of vessel disease;provided that both stenting and off-pump surgery were consideredtechnically feasible | **Exclusion criteria:** left main stem stenosis; totallyoccluded artery supplying an akinetic myocardial area; in-stentrestenosis; need of >1 graft for complete revascularization of theleft circumflex artery; poor ventricular function; emergency revascularization, Q-wave MI inthe previous 6 weeks, angioplasty in the previous 6 months; previous bypass surgery, hemorrhagic disorder, hypercoagulability, or intoleranceto acetylsalicylic acid or ticlopidine |

***Table 6.3:*** *Design and methodological quality of trials - PCI - stent*

| Trial | Design | Duration | Centre | Primary endpoint |
|---|---|---|---|---|
| **Stent versus CABG** | | | | |

continued...

| Trial | Design | Duration | Centre | Primary endpoint |
|---|---|---|---|---|
| ARTS, 2001 [1, 2, 3, 4, 5] n=1205 | parallel group open | 1 year | International Multicentre | major adverse cardiac and cerebrovascular events at one year |
| CARDia (PCI), 2008 [6] n=510 | Parallel groups open confirmatory trial at risk of bias | 1 y | UK, Ireland 24 centres | death, stroke, and MI |
| ERACI II, 2003 [7, 8] n=450 | parallel group open confirmatory trial at risk of bias | 30d, 1year | Argentinad Multicentre | |
| MASS II, 2007 [9, 10] n=408 | Parallel groups open confirmatory trial at risk of bias | 5y (1y) inclusion period: May 1995 - may 2000 | South America single-center | MACE |
| Myoprotect, 2004 [11] n=44 | Parallel groups open exploratory trial | 1 year | Europe single center | not defined |
| SOS, 2002 [12, 13, 14, 15, 16, 17] n=988 | parallel group open confirmatory trial at risk of bias | 3 years | Canada, United Kingdom, Europe Multicentre | repeat revascularisation |
| **Stent versus OPCAB** | | | | |
| OCTOSTENT, 2003 [18, 19] n=280 | Parallel groups open confirmatory trial at risk of bias | 1 year inclusion period: mar 1998 - aug 2000 | Europe Multicentre | death, stroke,MI, revascularization |

***Table 6.4:*** *Trial characteristics - PCI - stent*

| Trial | Age (mean, year) | Men (%) | Ejection fraction (%) | Extent of Disease | arterial grafts | stent (%) |
|---|---|---|---|---|---|---|
| **Stent versus CABG** | | | | | | |
| ARTS, 2001 [1, 2, 3, 4, 5] | 61 y | 76.5% | 61% | multiple vessels disease | 93% | 100% |
| CARDia (PCI), 2008 [6] | 64y | 74% | 13.6% | multi vessel disease | 100% | 100% |
| ERACI II, 2003 [7, 8] | 62 y | 79.35% | | multiple vessels disease | 89% | 100% |
| MASS II, 2007 [9, 10] | 60 y | 69.49% | 67% | multiple vessels disease | NA | 68.3% |
| Myoprotect, 2004 [11] | | | | multiple vessels disease | 100% | 100% |
| SOS, 2002 [12, 13, 14, 15, 16, 17] | 61.5 y | 78.99% | 57% | multiple vessels disease | 93% | 100% |
| **Stent versus OPCAB** | | | | | | |
| OCTOSTENT, 2003 [18, 19] | 59.6% | 71% | NA | multiple vessels disease | 100% | 100% |

## 6.2 Meta-analysis results

The results are detailed in table 6.5 (page 60). This table is followed by the Forest's plot corresponding to each endpoint.

### Stent versus CABG

A total of 3 of the 6 studies eligible for this comparison provided data on **1 year event**. The analysis detected a statistically significant difference in favor of CABG in 1 year event, with a RR of 1.82 (95% CI 1.42 to 2.34, p=0.0000). No heterogeneity was detected (p = 0.1740, $I^2$ = 0.43%).
Only one of the 6 studies eligible for this comparison provided data on . The analysis detected a statistically significant difference in favor of CABG in , with a RR of 2.01 (95% CI 1.63 to 2.47, p=0.0000).
A total of 3 of the 6 studies 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 4.88 (95% CI 3.62 to 6.58, p=0.0000). No heterogeneity was detected (p = 0.6615, $I^2$ = 0.00%).
A total of 4 of the 6 studies eligible for this comparison provided data on **long term cardiovascular events**. When pooled together, there was no statistically significant difference between the groups in long term cardiovascular events, with a RR of 1.13 (95% CI 0.81 to 1.56, p=0.4791). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies (p = 0.0418, $I^2$ = 0.63%).
A total of 3 of the 6 studies eligible for this comparison provided data on **1 year death from any cause**. When pooled together, there was no statistically significant difference between the groups in 1 year death from any cause, with a RR of 0.94 (95% CI 0.32 to 2.75, p=0.9155). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies (p = 0.0136, $I^2$ = 0.77%).
A total of 2 of the 6 studies eligible for this comparison provided data on **1 year MI**. When pooled together, there was no statistically significant difference between the groups in 1 year MI, with a RR of 0.91 (95% CI 0.46 to 1.83, p=0.7944). No heterogeneity was detected (p = 0.0501, $I^2$ = 0.74%).
A total of 2 of the 6 studies eligible for this comparison provided data on **long term MI**. When pooled together, there was no statistically significant difference between the groups in long term MI, with a RR of 0.92 (95% CI 0.47 to 1.82, p=0.8166). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies (p = 0.0386, $I^2$ = 0.77%).
A total of 4 of the 6 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 1.00 (95% CI 0.66 to 1.50, p=0.9849). No heterogeneity was detected (p = 0.0507, $I^2$ = 0.61%).
Only one of the 6 studies eligible for this comparison provided data on **2 yr MACE**. The analysis detected a statistically significant difference in favor of CABG in 2 yr MACE, with a RR of 2.01 (95% CI 1.60 to 2.51, p=0.0000).
Only one of the 6 studies eligible for this comparison provided data on **all cause death**. No statistically significant difference between the groups was found in all cause death, with a RR of 1.49 (95% CI 0.81 to 2.71, p=0.1977).

### Stent versus OPCAB

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 1.71 (95% CI 0.87 to 3.37, p=0.1180).

The single study eligible for this comparison provided data on **1 year revascularization**. The analysis detected a statistically significant difference in favor of OPCAB in 1 year revascularization, with a RR of 3.60 (95% CI 1.50 to 8.65, p=0.0042).
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 0.13 (95% CI 0.01 to 2.41, p=0.1702).
The single study eligible for this comparison provided data on **1 year MI**. No statistically significant difference between the groups was found in 1 year MI, with a RR of 0.88 (95% CI 0.30 to 2.56, p=0.8172).

***Table 6.5:*** *Results details - PCI - stent*

| Comparison Endpoint | Effect | 95% CI | p ass | p het | k | n |
|---|---|---|---|---|---|---|
| ***stent versus CABG*** | | | | | | |
| 1 year event | RR=1.82 | [1.42;2.34] | 0.0000 | 0.1740 ($I^2$=0.43) | 3 | 2703 |
| | RR=2.01 | [1.63;2.47] | 0.0000 | 1.0000 ($I^2$=1.00) | 1 | 1205 |
| 1 year revascularization | RR=4.88 | [3.62;6.58] | 0.0000 | 0.6615 ($I^2$=0.00) | 3 | 2703 |
| long term cardiovascular events | RR=1.13 | [0.81;1.56] | 0.4791 | 0.0418 ($I^2$=0.63) | 4 | 3051 |
| 1 year death from any cause | RR=0.94 | [0.32;2.75] | 0.9155 | 0.0136 ($I^2$=0.77) | 3 | 2643 |
| 1 year MI | RR=0.91 | [0.46;1.83] | 0.7944 | 0.0501 ($I^2$=0.74) | 2 | 2193 |
| long term MI | RR=0.92 | [0.47;1.82] | 0.8166 | 0.0386 ($I^2$=0.77) | 2 | 2193 |
| long term death | RR=1.00 | [0.66;1.50] | 0.9849 | 0.0507 ($I^2$=0.61) | 4 | 3051 |
| 2 yr MACE | RR=2.01 | [1.60;2.51] | 0.0000 | 1.0000 ($I^2$=0.00) | 1 | 1205 |
| all cause death | RR=1.49 | [0.81;2.71] | 0.1977 | 1.0000 ($I^2$=0.00) | 1 | 408 |
| ***stent versus OPCAB*** | | | | | | |
| 1 year event | RR=1.71 | [0.87;3.37] | 0.1180 | 1.0000 ($I^2$=0.00) | 1 | 280 |
| 1 year revascularization | RR=3.60 | [1.50;8.65] | 0.0042 | 1.0000 ($I^2$=0.00) | 1 | 280 |
| 1 year death from any cause | RR=0.13 | [0.01;2.41] | 0.1702 | 1.0000 ($I^2$=0.00) | 1 | 280 |
| 1 year MI | RR=0.88 | [0.30;2.56] | 0.8172 | 1.0000 ($I^2$=0.00) | 1 | 280 |

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; $I^2$: inconsistance degree

***Figure 6.1:*** *Forest's plot for 1 year event*

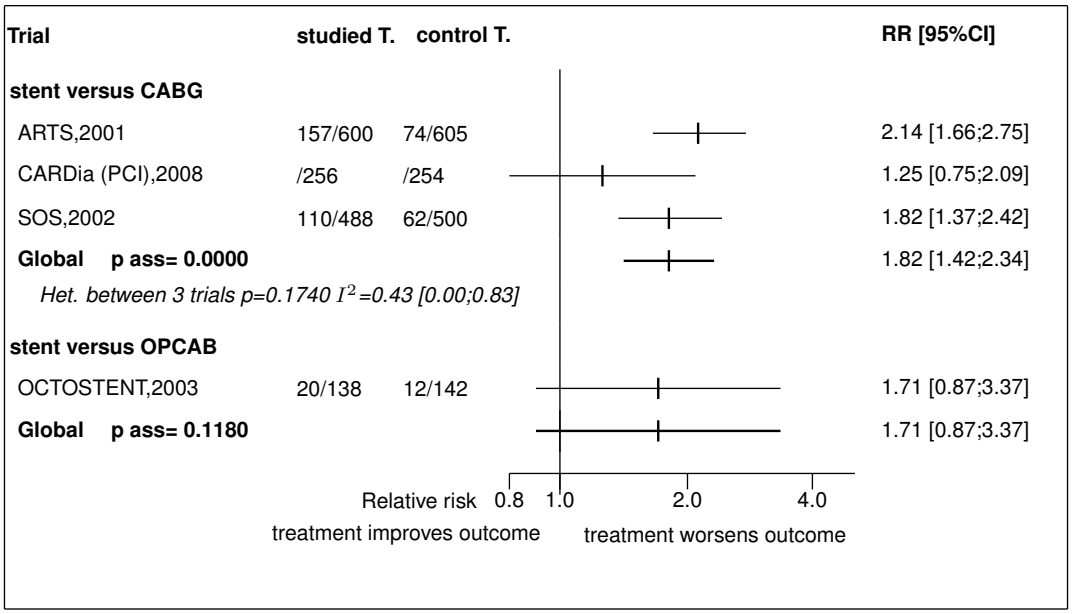



***Figure 6.2:*** *Forest's plot for*

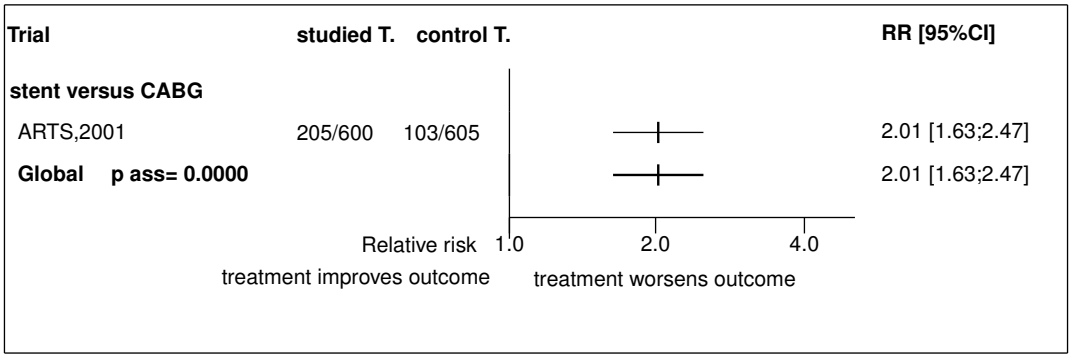


***Figure 6.3:*** *Forest's plot for 1 year revascularization*

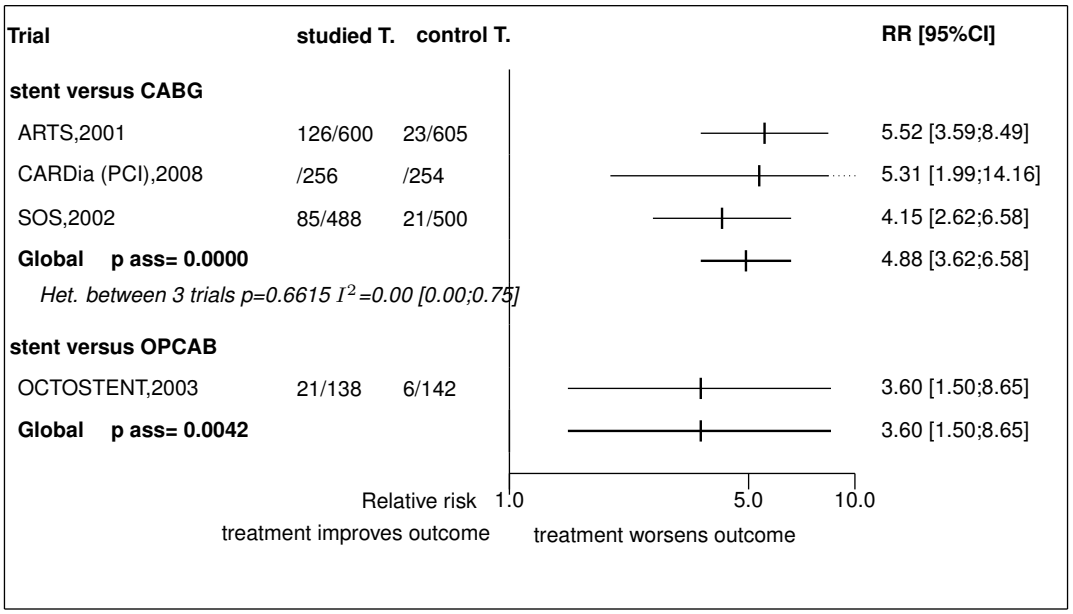



***Figure 6.4:*** *Forest's plot for long term cardiovascular events*

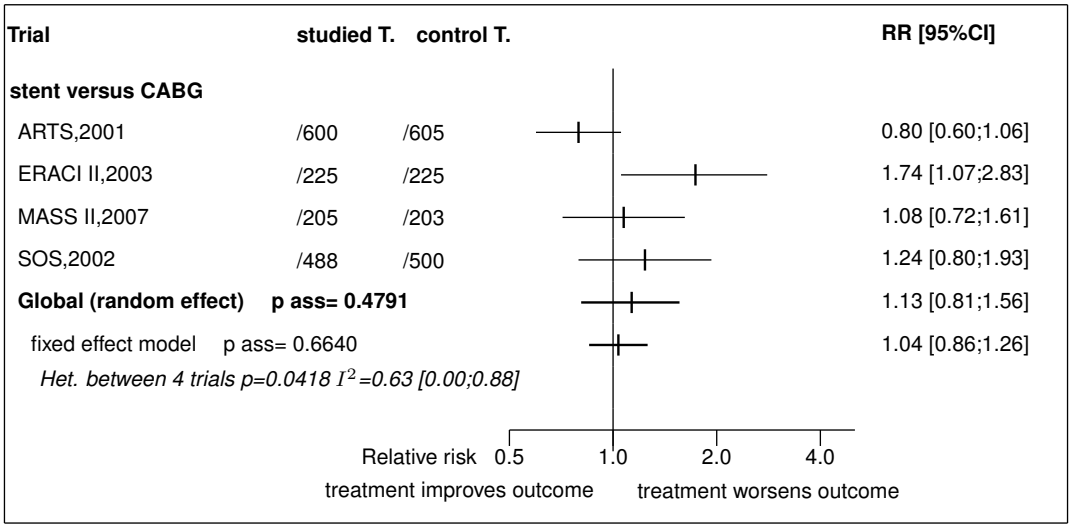


***Figure 6.5:*** *Forest's plot for 1 year death from any cause*

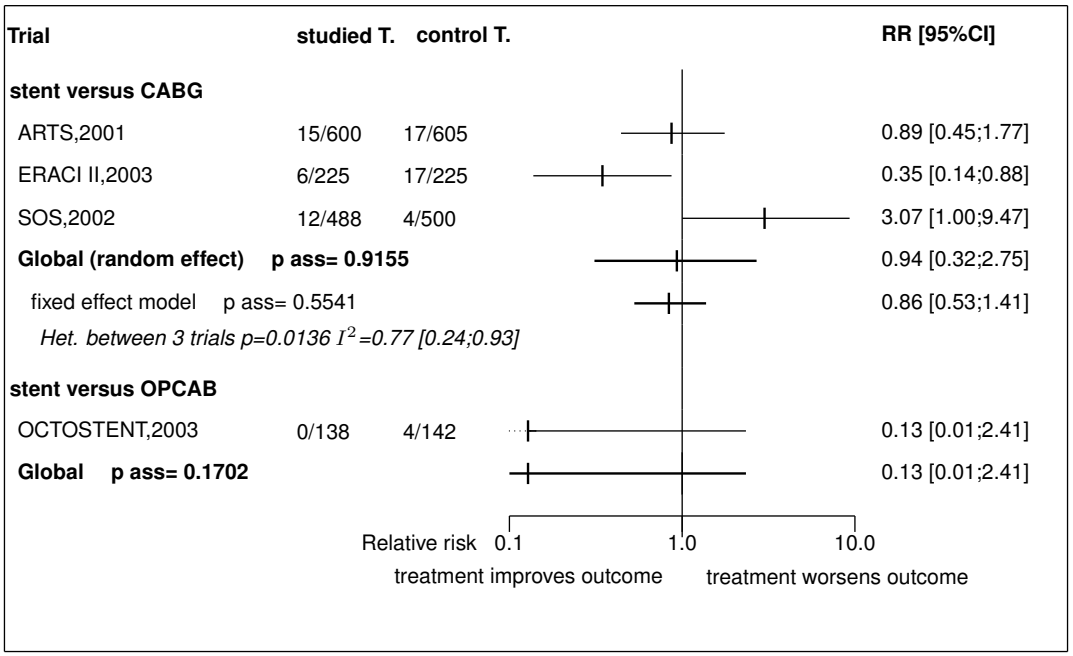



***Figure 6.6:*** *Forest's plot for 1 year MI*

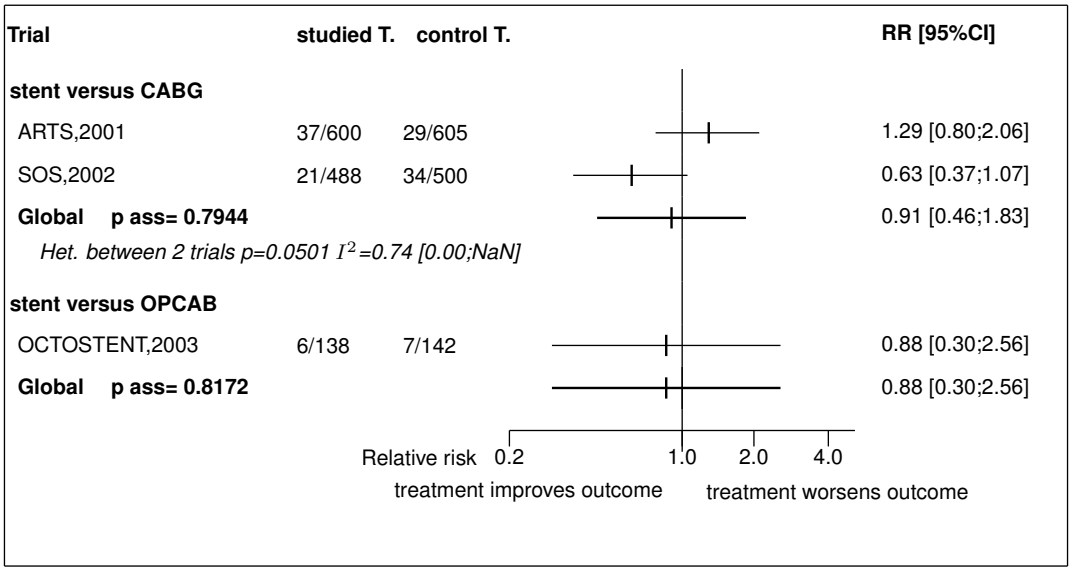


***Figure 6.7:*** *Forest's plot for long term MI*

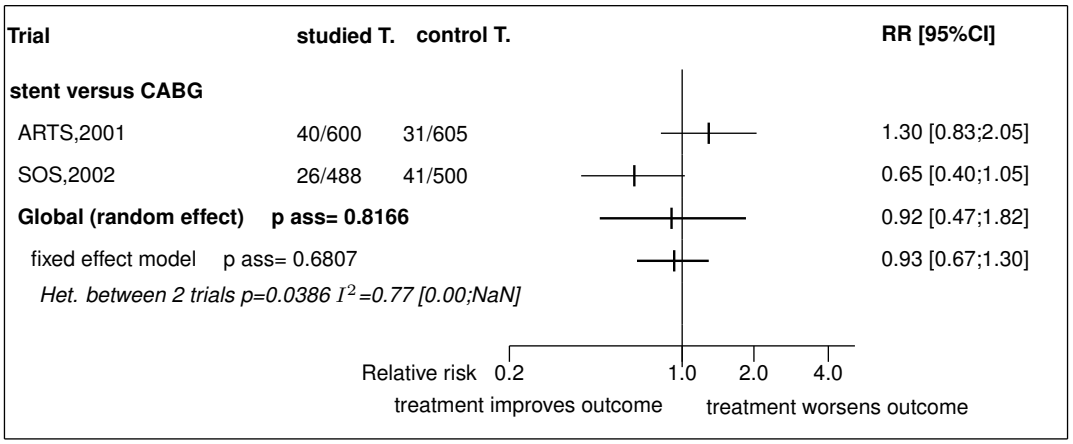



***Figure 6.8:*** *Forest's plot for long term death*

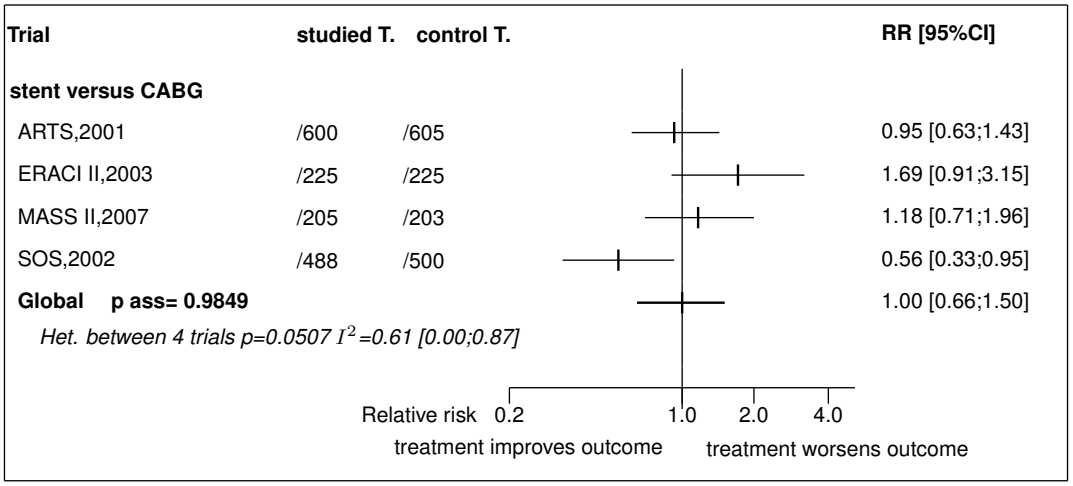



***Figure 6.9:*** *Forest's plot for 2 yr MACE*

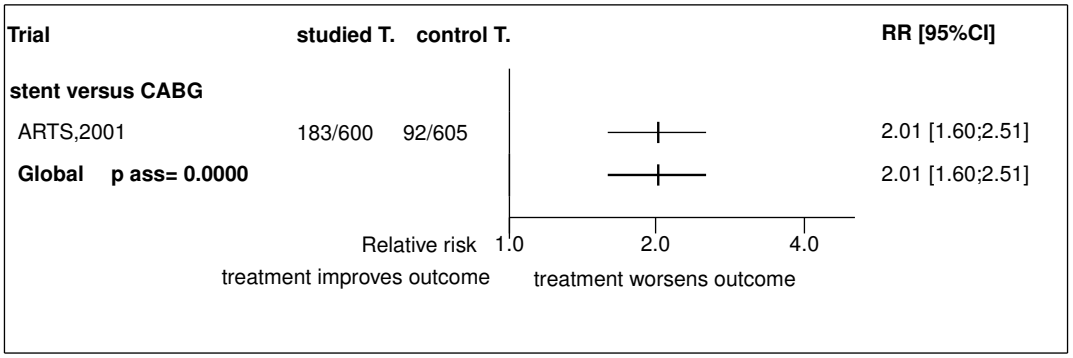
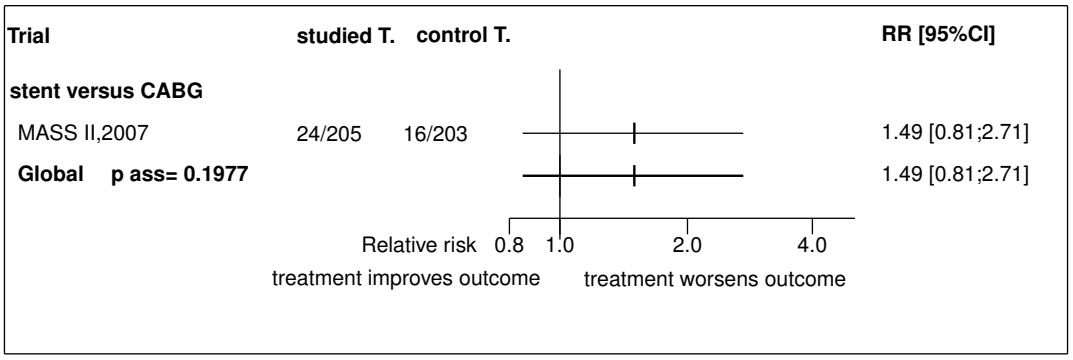


***Figure 6.10:*** *Forest's plot for all cause death*

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## 6.3 Individual trial summaries

***Table 6.6:*** *ARTS, 2001 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=1205 (600 vs. 605)<br>**Follow-up duration:** 1 year<br>**Study design:** Randomized controlled trial<br>parallel group<br>Open<br><br>International, Multicentre | Multi vessel disease with 2 or more de novo lesion in different major arteries Total occlusion <1month<br>**Exclusion criteria:** Transmural MI 1 week | **Studied treatment:** Palmaz-Schatz Crown/Cross flex (Cordis)<br>**Control treatment:** Conventional CABG | 1 year event<br>RR=2.14 [1.66;2.75]<br>RR=2.01 [1.63;2.47]<br>1 year revascularization<br>RR=5.52 [3.59;8.49]<br>1 year death from any cause<br>RR=0.89 [0.45;1.77]<br>1 year MI<br>RR=1.29 [0.80;2.06] |

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Legrand VM, Serruys PW, Unger F, van Hout BA, Vrolix MC, Fransen GM, Nielsen TT, Paulsen PK, Gomes RS, de Queiroz e Melo JM, Neves JP, Lindeboom W, Backx B. Three-year outcome after coronary stenting versus bypass surgery for the treatment of multivessel disease. Circulation 2004;109:1114-20 [PMID=14993134]

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***Table 6.7:*** *CARDia (PCI), 2008 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=510 (256 vs. 254)<br>**Follow-up duration:** 1 y<br>**Study design:** Randomized controlled trial<br>Parallel groups<br>Open<br>Confirmatory trial at risk of bias<br>UK, Ireland, 24 centres | Patients with diabetes and symptomatic multivessel coronary artery disease or complex single-vessel disease.<br>**Inclusion criteria:** multi-vessel disease or complex single-vessel disease (ostial or proximal left anterior descending artery); diabetes mellitus; anatomy suitable for both PCI and CABG<br>**Exclusion criteria:** previous PCI or CABG; age >80 years; left main disease; cardiogenic shock; recent ST-elevation MI (within 6 weeks); ejection fraction <20%; contraindications to abciximab, aspirin, and clopidogrel | **Studied treatment:** PCI plus stenting (and routine abciximab)<br>bare metal stent or sirolimus-coated stents (CYPHER) and abciximab<br>**Control treatment:** CABG<br>**note:** BMS n=72, CYPHER n=180 | |

**Reference**

Kapur A, Hall RJ, Malik IS, Qureshi AC, Butts J, de Belder M, Baumbach A, Angelini G, de Belder A, Oldroyd KG, Flather M, Roughton M, Nihoyannopoulos P, Bagger JP, Morgan K, Beatt KJ. Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients. 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial. J Am Coll Cardiol 2010 Feb 2;55:432-40 [PMID=20117456]

***Table 6.8:*** *ERACI II, 2003 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=450 (225 vs. 225)<br>**Follow-up duration:** 30d, 1year<br>**Study design:** Randomized controlled trial<br>parallel group<br>Open<br>Confirmatory trial at risk of bias<br>Argentinad, Multicentre | Multi vessel disease Angina CSS III-IV; no angina but large area of heart at risk; unstable =1 vessel to be treated Lesion >3.0mm<br>**Exclusion criteria:** MI <=24h | **Studied treatment:** Gianturco Robin II (Cook) Primary device<br>**Control treatment:** Conventional CABG | 1 year death from any cause<br>RR=0.35 [0.14;0.88] |

**References**

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***Table 6.9:*** *MASS II, 2007 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=408 (205 vs. 203)<br>**Follow-up duration:** 5y (1y)<br>**Study design:** Randomized controlled trial<br>Parallel groups<br>Open<br>Confirmatory trial at risk of bias<br>South America, single-center<br>**Inclusion period:** May 1995 - may 2000 | Patients with multivessel coronary artery disease with stable angina and preserved ventricular function<br>**Exclusion criteria:** MI/unstable angina requiring emergency revascularization | **Studied treatment:** PCI (73% stent)<br>**Control treatment:** CABG<br>**note:** 3 arms: PCI, CABGand medical treatment | |

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***Table 6.10:*** *Myoprotect, 2004 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=44 (23 vs. 21)<br>**Follow-up duration:** 1 year<br>**Study design:** Randomized controlled trial<br>Parallel groups<br>Open<br>Exploratory trial<br>Europe, single center | Patients with symptomatic main-stem and main-stem-equivalent lesions with substantially increased risk for bypass surgery | **Studied treatment:** percutaneous transluminal coronary angioplasty/stent<br>**Control treatment:** CABG | |

**Reference**

Pohl T, Giehrl W, Reichart B, Kupatt C, Raake P, Paul S, Reichenspurner H, Steinbeck G, Boekstegers P. Retroinfusion-supported stenting in high-risk patients for percutaneous intervention and bypass surgery: results of the prospective randomized myoprotect I study. Catheter Cardiovasc Interv 2004;62:323-30 [PMID=15224298]

***Table 6.11:*** *SOS, 2002 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=988 (488 vs. 500)<br>**Follow-up duration:** 3 years<br>**Study design:** Randomized controlled trial<br>parallel group<br>Open<br>Confirmatory trial at risk of bias<br>Canada, United Kingdom, Europe, Multicentre | Multiple vessel disease Symptomatic 1 or more vessel suitable for stenting<br>**Exclusion criteria:** MI <=48h | **Studied treatment:** Stent<br>No restriction on type of stent<br>**Control treatment:** CABG No restriction on type of surgical technique (3% of procedures OPCAB) | 1 year event<br>RR=1.82 [1.37;2.42]<br>1 year revascularization<br>RR=4.15 [2.62;6.58]<br>1 year death from any cause<br>RR=3.07 [1.00;9.47]<br>1 year MI<br>RR=0.63 [0.37;1.07] |

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***Table 6.12:*** *OCTOSTENT, 2003 - Trial synopsis*

| Trial details | Patients | Treatments | Outcomes |
|---|---|---|---|
| n=280 (138 vs. 142)<br>**Follow-up duration:** 1 year<br>**Study design:** Randomized controlled trial<br>Parallel groups<br>Open<br>Confirmatory trial at risk of bias<br>Europe, Multicentre<br>**Inclusion period:** mar 1998 - aug 2000 | Multi or single vessel disease Moderate LV function CABG or stenting to be considered feasible<br>**Inclusion criteria:** stable or unstable angina (Braunwald class IIIB) and/ordocumented ischemia; irrespective of the extent of vessel disease;provided that both stenting and off-pump surgery were consideredtechnically feasible<br>**Exclusion criteria:** left main stem stenosis; totallyoccluded artery supplying an akinetic myocardial area; in-stentrestenosis; need of >1 graft for complete revascularization of theleft circumflex artery; poor ventricular function; emergency revascularization, Q-wave MI inthe previous 6 weeks, angioplasty in the previous 6 months; previous bypass surgery, hemorrhagic disorder, hypercoagulability, or intoleranceto acetylsalicylic acid or ticlopidine | **Studied treatment:** Stent type not reported<br>**Control treatment:** off-pump coronary artery bypass | 1 year event<br>RR=1.71 [0.87;3.37]<br>1 year revascularization<br>RR=3.60 [1.50;8.65]<br>1 year MI<br>RR=0.88 [0.30;2.56] |

**References**

Eefting F, Nathoe H, van Dijk D, Jansen E, Lahpor J, Stella P, Suyker W, Diephuis J, Suryapranata H, Ernst S, Borst C, Buskens E, Grobbee D, de Jaegere P. Randomized comparison between stenting and off-pump bypass surgery in patients referred for angioplasty. Circulation 2003;108:2870-6 [PMID=14656913]
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# 7 Global meta-analysis: all PCI

## 7.1 Global meta-analysis: all PCI versus CABG

***Table 7.1:*** *All PCIversus CABG*

| Endpoint | Effect | 95% CI | p ass | p het ($I^2$) | k | n |
|---|---|---|---|---|---|---|
| 1 year event | RR=1.82 | 1.42;2.34 | 0.0000 | 0.1740 (0.43) | 3 | 2703 |
| | RR=2.01 | 1.63;2.47 | 0.0000 | 1.0000 (1.00) | 1 | 1205 |
| 1 year revascularization | RR=4.88 | 3.62;6.58 | 0.0000 | 0.6615 (0.00) | 3 | 2703 |
| long term cardiovascular events | RR=1.19 [1] | 0.91;1.55 | 0.2079 | 0.0141 (0.68) † | 5 | 4951 |
| cardiac death or MI | RR=0.96 | 0.72;1.29 | 0.7937 | 0.2365 (0.26) | 6 | 3095 |
| angina (grade 2 or worse) in first year | RR=1.56 | 1.20;2.04 | 0.0000 | 0.1159 (0.49) | 4 | 2610 |
| 1 year death from any cause | RR=0.94 [2] | 0.32;2.75 | 0.9155 | 0.0136 (0.77) † | 3 | 2643 |
| 1 year MI | RR=0.91 | 0.46;1.83 | 0.7944 | 0.0501 (0.74) | 2 | 2193 |
| long term MI | RR=0.92 [3] | 0.47;1.82 | 0.8166 | 0.0386 (0.77) † | 2 | 2193 |
| long term death | RR=1.08 [4] | 0.78;1.50 | 0.6358 | 0.0261 (0.64) † | 5 | 4951 |
| 2 yr MACE | RR=1.50 [5] | 0.84;2.67 | 0.1702 | 0.0000 (0.92) † | 2 | 3105 |
| CABG | RR=16.04 | 9.73;26.43 | 0.0000 | 0.8372 (0.00) | 6 | 3095 |
| angina | RR=1.31 | 0.90;1.93 | 0.1630 | 0.1638 (0.48) | 2 | 1349 |
| all cause death | RR=1.15 | 0.96;1.38 | 0.1306 | 0.5381 (0.00) | 8 | 5332 |

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; $I^2$: inconsistance degree

## 7.2 Global meta-analysis: all PCI versus OPCAB

[1] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=1.20 95% CI 1.05;1.37
[2] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.86 95% CI 0.53;1.41
[3] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.93 95% CI 0.67;1.30
[4] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=1.14 95% CI 0.95;1.37
[5] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=1.53 95% CI 1.30;1.81

***Table 7.2:*** *All PCIversus OPCAB*

| Endpoint | Effect | 95% CI | p ass | p het ($I^2$) | k | n |
|---|---|---|---|---|---|---|
| 1 year event | RR=1.71 | 0.87;3.37 | 0.1180 | 1.0000 (0.00) | 1 | 280 |
| 1 year revascularization | RR=3.60 | 1.50;8.65 | 0.0042 | 1.0000 (0.00) | 1 | 280 |
| 1 year death from any cause | RR=0.13 | 0.01;2.41 | 0.1702 | 1.0000 (0.00) | 1 | 280 |
| 1 year MI | RR=0.88 | 0.30;2.56 | 0.8172 | 1.0000 (0.00) | 1 | 280 |

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; $I^2$: inconsistance degree

# 8 Ongoing studies

No ongoing trial was identified.

# 9 Excluded studies

No trial was excluded.

# References