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Antithrombotics for stable angina

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 Antithrombotics for stable angina.

Contents

0.1 Synthesis of the meta-analysis results

In all 15 randomised controlled trials (RCTs) were included. These included 1 studie of **aspirin** involving 2,035 patients, 2 studies of **clopidogrel** involving 20,186 patients, 10 studies of **dipyridamol** involving 401 patients, 1 studie of **oral platelet GP IIbIIIa receptor inhibitor** involving 120 patients and 1 studie of **ticlopidine** involving 38 patients. 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).

0.1.1 Aspirin

Only one trials including 2035 patients was found.
Among these comparisons, one trial are about aspirin.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with aspirin for all the endpoints with data in at least one trial are summarized table 1.

Table 1: *Results summary - Aspirin*

Benefit	Harmful	No evidence
	Aspirin versus placebo	
↓ cardiovascular events RR=0.71† [0.57;0.89] k=1 ↓ non fatal MI RR=0.67* [0.45;0.98] k=1		→ cardiovascular death RR=0.76^{NS} [0.54;1.07] k=1 → non vascular death RR=1.66^{NS} [0.79;3.51] k=1 → non fatal stroke RR=0.79^{NS} [0.45;1.39] k=1

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

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

0.1.2 Clopidogrel

Reports of 2 trials (including 20,186 patients) were identified .
Among these comparisons, two trials are about clopidogrel.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with clopidogrel for all the endpoints with data in at least one trial are summarized table 2.

Table 2: *Results summary - Clopidogrel*

Benefit	Harmful	No evidence
	Clopidogrel versus aspirin	

continued...

Benefit	Harmful	No evidence
↓ cardiovascular events RR=0.92* [0.85;1.00] k=2 ↓ non fatal MI RR=0.84* [0.70;1.00] k=1		→ cardiovascular death RR=0.92^{NS} [0.80;1.07] k=1 → all cause death RR=0.98^{NS} [0.87;1.10] k=1 → non fatal stroke RR=0.94^{NS} [0.82;1.07] k=1 → major bleeding RR=0.88^{NS} [0.70;1.12] k=1

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

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

0.1.3 Dipyridamol

Reports of 10 trials (including 401 patients) were identified .
Among these comparisons, 10 trials are about dipyridamol.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with dipyridamol for all the endpoints with data in at least one trial are summarized table 3.

Table 3: *Results summary - Dipyridamol*

Benefit	Harmful	No evidence
Dipyridamol versus control		
		→ cardiovascular events RR=1.28^{NS} [0.43;3.83] k=3 → cardiovascular death RR=1.61^{NS} [0.22;12.11] k=3 → non vascular death RR=0.98^{NS} [0.10;9.12] k=3 → non fatal MI RR=0.79^{NS} [0.23;2.77] k=3 → non fatal stroke RR=1.29^{NS} [0.15;10.73] k=3
Dipyridamol versus placebo		

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

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

0.1.4 Oral platelet GP IIbIIIa receptor inhibitor

Only one trials including 120 patients was found.
Among these comparisons, one trial are about roxifiban .
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with roxifiban for all the endpoints with data in at least one trial are summarized table 4.

Table 4: *Results summary - Roxifiban*

Benefit	Harmful	No evidence
	Roxifiban versus placebo	

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

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

0.1.5 Ticlopidine

Only one trials including 38 patients was found.
Among these comparisons, one trial are about ticlopidine.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.
Results obtained with ticlopidine for all the endpoints with data in at least one trial are summarized table 5.

Table 5: *Results summary - Ticlopidine*

Benefit	Harmful	No evidence
	Ticlopidine versus placebo	
		→ cardiovascular events RR=0.81^{NS} [0.02;38.71] k=1 → cardiovascular death RR=0.81^{NS} [0.02;38.71] k=1 → non vascular death RR=0.81^{NS} [0.02;38.71] k=1 → non fatal MI RR=0.81^{NS} [0.02;38.71] k=1 → non fatal stroke RR=0.81^{NS} [0.02;38.71] 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 antithrombotics for the treatment of stable angina. The following classes of treatment are considered:

1. aspirin
2. clopidogrel
3. dipyridamol
4. oral platelet GP IIbIIIa receptor inhibitor
5. ticlopidine

1.2 Search strategy

The search aimed to identify all randomized clinical trials relating to the clinical effectiveness of antithrombotics for the treatment of stable angina in all type of patient.

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

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 Non vascular death, Cardiovascular death, Non fatal MI, cardiovascular events, Non fatal stroke, .

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 I to **??**, listed by therapeutic class. The therapeutic classes included aspirin, clopidogrel, dipyridamol, oral platelet GP IIbIIIa receptor inhibitor, ticlopidine,
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.

Part I

Aspirin

2 Overview of aspirin

2.1 Included trials

Only one trial which randomized 2035 patients was identified. In all, 1 randomized comparison concerned aspirin.
The detailed descriptions of trials and meta-analysis results is given in section 3 (page 19) for aspirin.

This trial included 2035 patients and was published in 1992.
This trial was double blind in design.
It was reported in English language.
The table 2.1 (page 16) 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 aspirin provide the results listed in tables 2.2 to 2.2 (page 17) and in the following graphs.

2.2.1 Aspirin

Aspirin was superior to **placebo** in terms of cardiovascular events (RR=0.71, 95% CI 0.57 to 0.89, p=0.0030, 1 trial)and non fatal MI (RR=0.67, 95% CI 0.45 to 0.98, p=0.0412, 1 trial). However, no significant difference was found on cardiovascular death (RR=0.76, 95% CI 0.54 to 1.07, p=0.1173, 1 trial), non vascular death (RR=1.66, 95% CI 0.79 to 3.51, p=0.1804, 1 trial)and non fatal stroke (RR=0.79, 95% CI 0.45 to 1.39, p=0.4146, 1 trial).

Table 2.1: *Main study characteristics - aspirin*

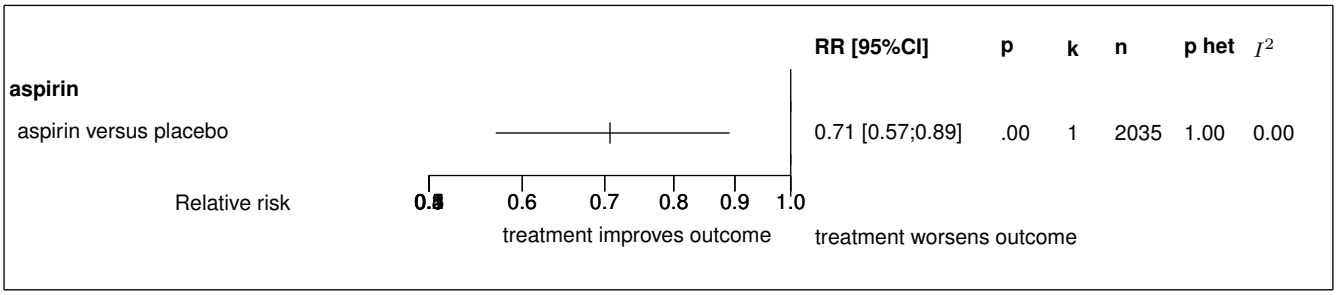
Trial	Patients	Treatments	Trial design and method
Aspirin			
Aspirin versus placebo			
SAPAT, 1992 [1] n = 1009 vs. 1026	patients with stable chronic angina pectoris	aspirin 75 mg daily **versus** placebo	double blind parallel groups Primary endpoint: myocardial infarction and sudden death Sweden

Table 2.2: *Summary of all results for aspirin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
aspirin versus placebo						
cardiovascular events	RR=0.71	0.57;0.89	0.0030	1.0000 (0.00)	1	2035
cardiovascular death	RR=0.76	0.54;1.07	0.1173	1.0000 (0.00)	1	2035
non vascular death	RR=1.66	0.79;3.51	0.1804	1.0000 (0.00)	1	2035
non fatal MI	RR=0.67	0.45;0.98	0.0412	1.0000 (0.00)	1	2035
non fatal stroke	RR=0.79	0.45;1.39	0.4146	1.0000 (0.00)	1	2035

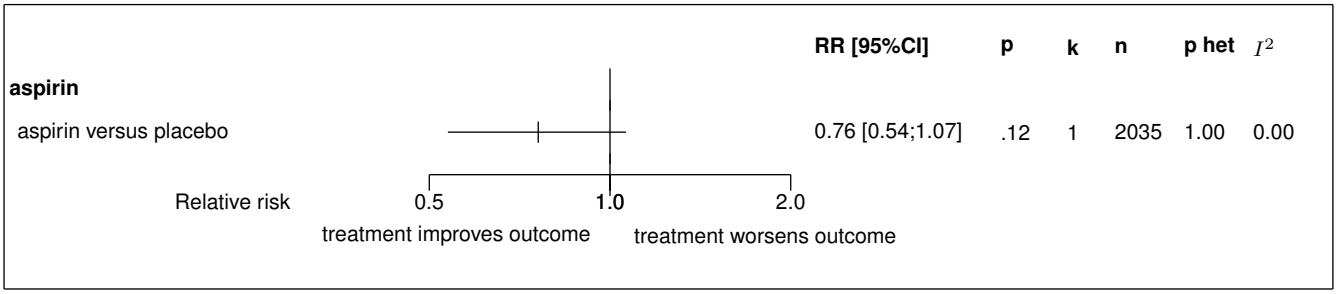
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 2.1: *Forest's plot for cardiovascular events*



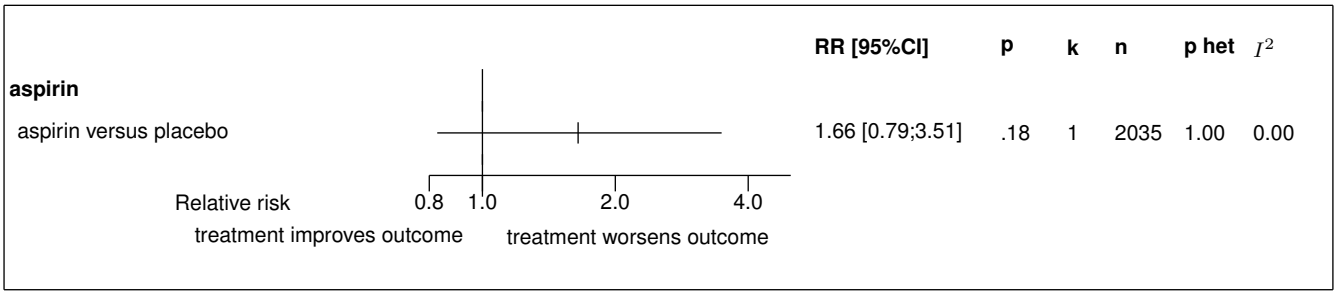
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

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



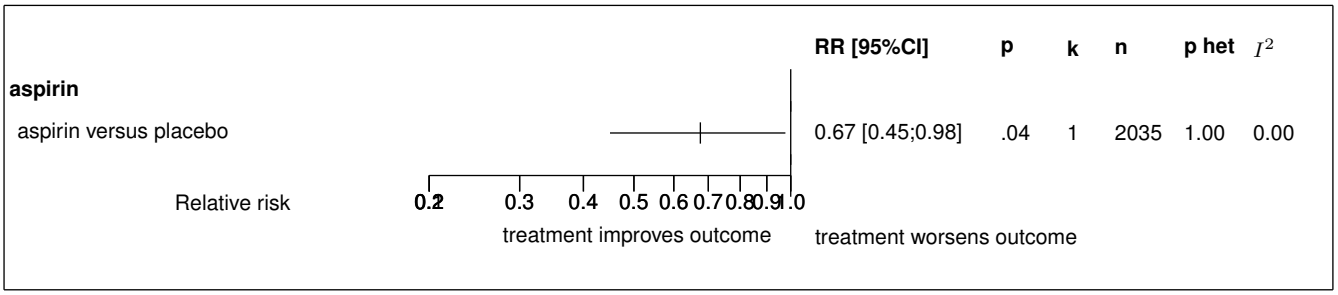
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 2.3: *Forest's plot for non vascular death*



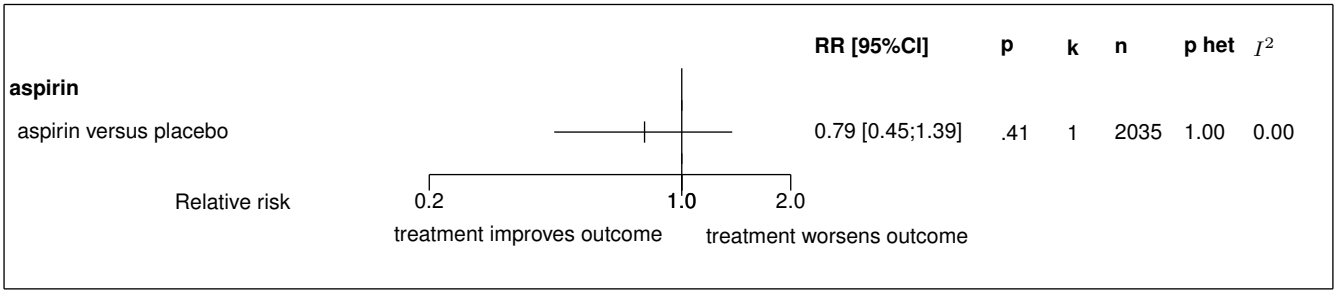
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 2.4: *Forest's plot for non fatal 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; ᶠ: random effect model used

Figure 2.5: *Forest's plot for non fatal stroke*



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; ᶠ: random effect model used

3 Details

3.1 Available trials

Only one trial which randomized 2035 patients was identified: it compared aspirin with placebo.
This trial included 2035 patients and was published in 1992.
This trial was double blind in design.
It was reported in English language.
Non vascular death data was reported in 1 trials; 1 trials reported data on cardiovascular death; 1 trials reported data on non fatal MI; 1 trials reported data on cardiovascular events; and 1 trials reported data on non fatal stroke.
Following tables 3.1 (page 19), 3.2 (page 19), 3.4 (page 21), and 3.3 (page 19) summarized the main characteristics of the trial including in this systematic review of randomized trials of aspirin.

Table 3.1: *Treatment description - aspirin - aspirin*

Trial	Studied treatment	Control treatment
Aspirin versus placebo		
SAPAT (1992) [1]	aspirin 75 mg daily	placebo
	Concomittant treatment: sotalol for control of symptoms	

Table 3.2: *Descriptions of participants - aspirin - aspirin*

Trial	Patients
Aspirin versus placebo	
SAPAT (1992) [1]	Patients with stable chronic angina pectoris

Table 3.3: *Design and methodological quality of trials - aspirin - aspirin*

Trial	Design	Duration	Centre	Primary end-point
Aspirin versus placebo				

continued...

Trial	Design	Duration	Centre	Primary endpoint
SAPAT, 1992 [1] n=2035	Parallel groups double blind confirmatory trial at low risk of bias	50 months	Sweden	myocardial infarction and sudden death

Table 3.4: *Trial characteristics - aspirin - aspirin*

Trial
Aspirin versus placebo
SAPAT, 1992 [1]

3.2 Meta-analysis results

The results are detailed in table 3.5 (page 22). This table is followed by the Forest's plot corresponding to each endpoint.

Aspirin versus placebo

The single study eligible for this comparison provided data on **cardiovascular events**. The analysis detected a statistically significant difference in favor of aspirin in cardiovascular events, with a RR of 0.71 (95% CI 0.57 to 0.89, p=0.0030).
The single study eligible for this comparison provided data on **cardiovascular death**. No statistically significant difference between the groups was found in cardiovascular death, with a RR of 0.76 (95% CI 0.54 to 1.07, p=0.1173).
The single study eligible for this comparison provided data on **non vascular death**. No statistically significant difference between the groups was found in non vascular death, with a RR of 1.66 (95% CI 0.79 to 3.51, p=0.1804).
The single study eligible for this comparison provided data on **non fatal MI**. The analysis detected a statistically significant difference in favor of aspirin in non fatal MI, with a RR of 0.67 (95% CI 0.45 to 0.98, p=0.0412).
The single study eligible for this comparison provided data on **non fatal stroke**. No statistically significant difference between the groups was found in non fatal stroke, with a RR of 0.79 (95% CI 0.45 to 1.39, p=0.4146).

Table 3.5: *Results details - aspirin - aspirin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
aspirin versus placebo						
cardiovascular events	RR=0.71	[0.57;0.89]	0.0030	1.0000 (I^2=0.00)	1	2035
cardiovascular death	RR=0.76	[0.54;1.07]	0.1173	1.0000 (I^2=0.00)	1	2035
non vascular death	RR=1.66	[0.79;3.51]	0.1804	1.0000 (I^2=0.00)	1	2035
non fatal MI	RR=0.67	[0.45;0.98]	0.0412	1.0000 (I^2=0.00)	1	2035
non fatal stroke	RR=0.79	[0.45;1.39]	0.4146	1.0000 (I^2=0.00)	1	2035

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 cardiovascular events*

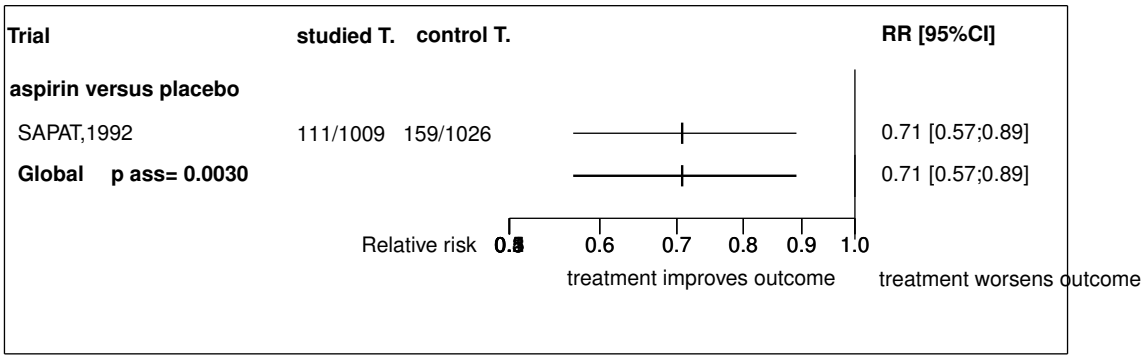


Figure 3.2: *Forest's plot for cardiovascular death*

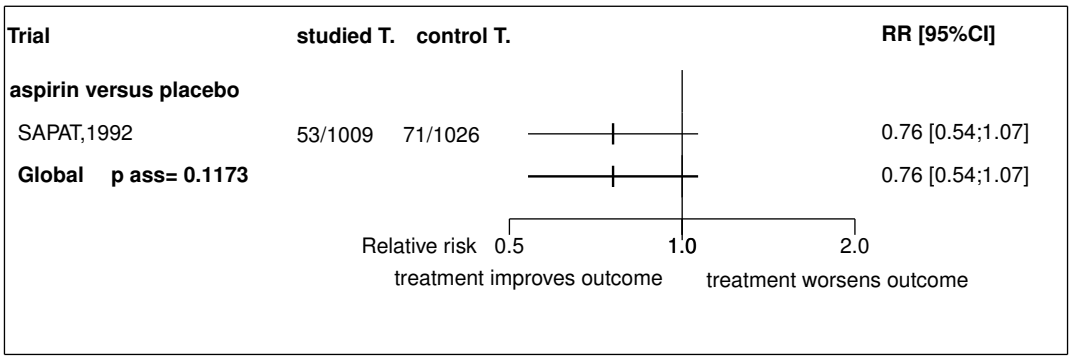


Figure 3.3: *Forest's plot for non vascular death*

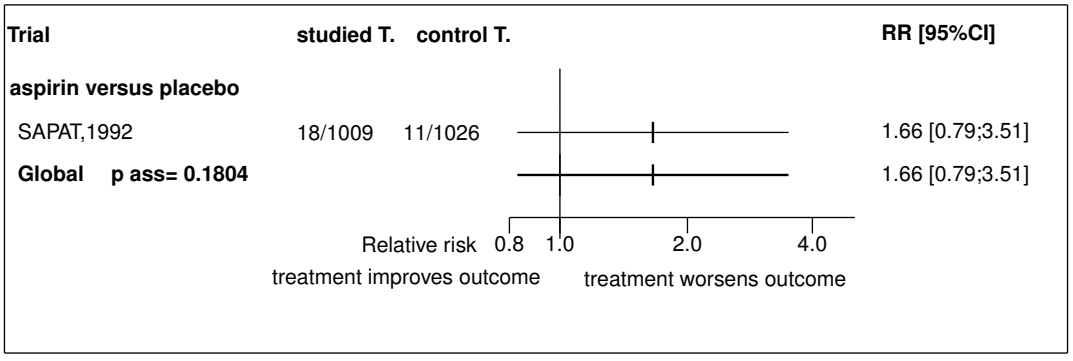


Figure 3.4: *Forest's plot for non fatal MI*

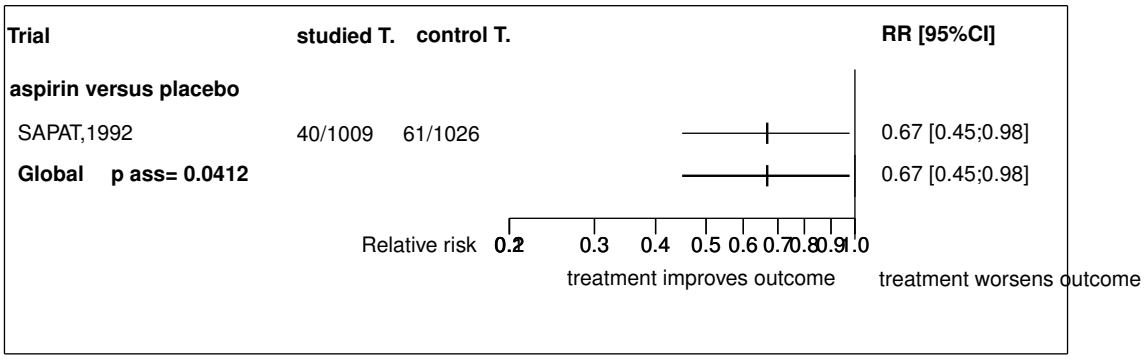
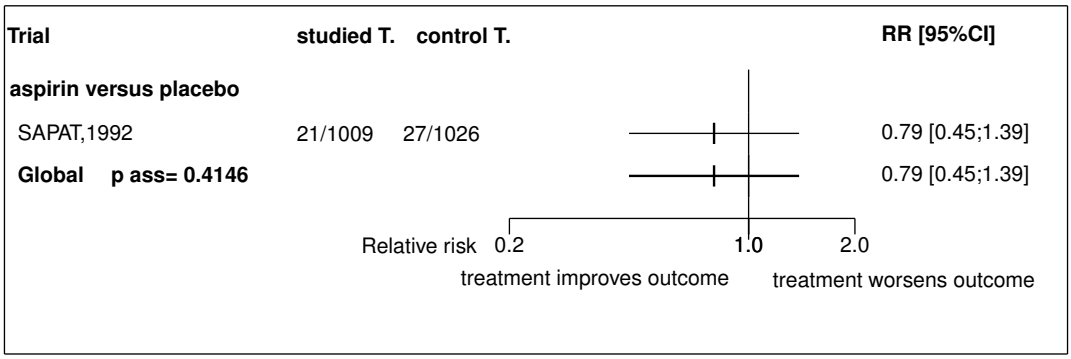


Figure 3.5: *Forest's plot for non fatal stroke*



References

[1] Juul-Möller S, Edvardsson N, Jahnmatz B, Rosn A, Srensen S, Omblus R. Double-blind trial of aspirin in primary prevention of myocardial infarction in patients with stable chronic angina pectoris. The Swedish Angina Pectoris Aspirin Trial (SAPAT) Group. Lancet 1992;340:1421-5. [PMID=1360557]

3.3 Individual trial summaries

Table 3.6: *SAPAT, 1992 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=2035 (1009 vs. 1026) **Follow-up duration:** 50 months **Study design:** Randomized controlled trial Parallel groups Double blind Confirmatory trial at low risk of bias Sweden	Patients with stable chronic angina pectoris	**Studied treatment:** aspirin 75 mg daily **Control treatment:** placebo **Concomittant treat.:**sotalol for control of symptoms	Cardiovascular events RR=0.71 [0.57;0.89] Cardiovascular death RR=0.76 [0.54;1.07] Non vascular death RR=1.66 [0.79;3.51] Non fatal MI RR=0.67 [0.45;0.98] Non fatal stroke RR=0.79 [0.45;1.39]

Reference

Juul-Möller S, Edvardsson N, Jahnmatz B, Rosn A, Srensen S, Omblus R. Double-blind trial of aspirin in primary prevention of myocardial infarction in patients with stable chronic angina pectoris. The Swedish Angina Pectoris Aspirin Trial (SAPAT) Group. Lancet 1992;340:1421-5 [PMID=1360557]

4 Global meta-analysis: all aspirin

4.1 Global meta-analysis: all aspirin versus placebo

Table 4.1: *All aspirinversus placebo*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
cardiovascular events	RR=0.71	0.57;0.89	0.0030	1.0000 (0.00)	1	2035
cardiovascular death	RR=0.76	0.54;1.07	0.1173	1.0000 (0.00)	1	2035
non vascular death	RR=1.66	0.79;3.51	0.1804	1.0000 (0.00)	1	2035
non fatal MI	RR=0.67	0.45;0.98	0.0412	1.0000 (0.00)	1	2035
non fatal stroke	RR=0.79	0.45;1.39	0.4146	1.0000 (0.00)	1	2035

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

5 Ongoing studies of aspirin

No ongoing trial was identified.

6 Excluded studies for aspirin

No trial was excluded.

References

Part II

Clopidogrel

7 Overview of clopidogrel

7.1 Included trials

A total of 2 randomized comparisons which enrolled 20186 patients were identified. In all, 2 randomized comparisons concerned clopidogrel.
The detailed descriptions of trials and meta-analysis results is given in section 8 (page 36) for clopidogrel.

The average study size was 10093 patients (range 1001 to 19185). The first study was published in 1996, and the last study was published in 1996.
A total of 1 trials were double blind and 1 were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
The table 7.1 (page 32) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

7.2 Summary of meta-analysis results

The meta-analysis of the available trials about clopidogrel provide the results listed in tables 7.2 to 7.2 (page 33) and in the following graphs.

7.2.1 Clopidogrel

Clopidogrel was superior to **aspirin** in terms of cardiovascular events (RR=0.92, 95% CI 0.85 to 1.00, p=0.0393, 2 trials)and non fatal MI (RR=0.84, 95% CI 0.70 to 1.00, p=0.0440, 1 trial). However, no significant difference was found on cardiovascular death (RR=0.92, 95% CI 0.80 to 1.07, p=0.2818, 1 trial), all cause death (RR=0.98, 95% CI 0.87 to 1.10, p=0.7184, 1 trial), non fatal stroke (RR=0.94, 95% CI 0.82 to 1.07, p=0.3657, 1 trial)and major bleeding (RR=0.88, 95% CI 0.70 to 1.12, p=0.3019, 1 trial).

Table 7.1: *Main study characteristics - clopidogrel*

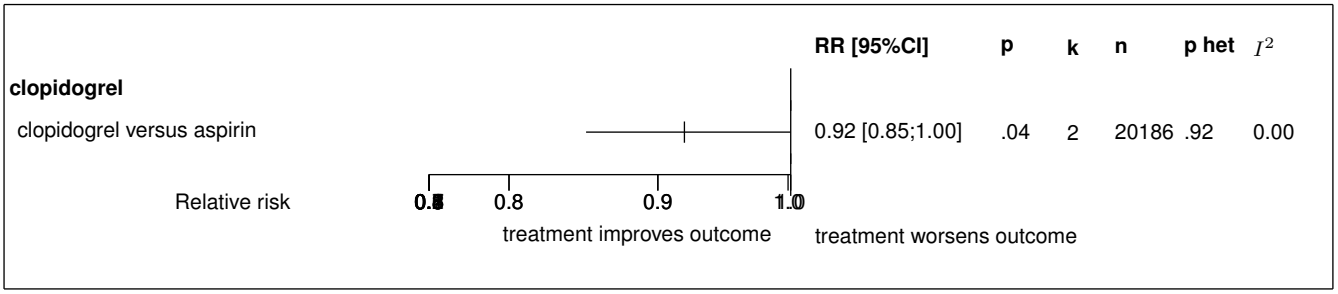
Trial	Patients	Treatments	Trial design and method
Clopidogrel			
Clopidogrel versus aspirin			
ASCET, n = 498 vs. 503	patients with documented coronary heart disease and treated with aspirin	clopidogrel 75 mg once daily for two years **versus** aspirin 160 mg once daily for two years	open parallel groups Primary endpoint: all-cause death, nonfatal MI, ischemic stroke, and unstable angina
CAPRIE, 1996 [1] n = 9599 vs. 9586	patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease	clopidogrel 75 mg once daily **versus** aspirin 325 mg once daily	double blind parallel groups Primary endpoint: ischaemic stroke, myocardial infarction, or vascular death 384 centres, 16 countries

Table 7.2: *Summary of all results for clopidogrel*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
clopidogrel versus aspirin						
cardiovascular events	RR=0.92	0.85;1.00	0.0393	0.9230 (0.00)	2	20186
cardiovascular death	RR=0.92	0.80;1.07	0.2818	1.0000 (0.00)	1	19185
non fatal MI	RR=0.84	0.70;1.00	0.0440	1.0000 (0.00)	1	19185
all cause death	RR=0.98	0.87;1.10	0.7184	1.0000 (0.00)	1	19185
non fatal stroke	RR=0.94	0.82;1.07	0.3657	1.0000 (0.00)	1	19185
major bleeding	RR=0.88	0.70;1.12	0.3019	1.0000 (0.00)	1	19185

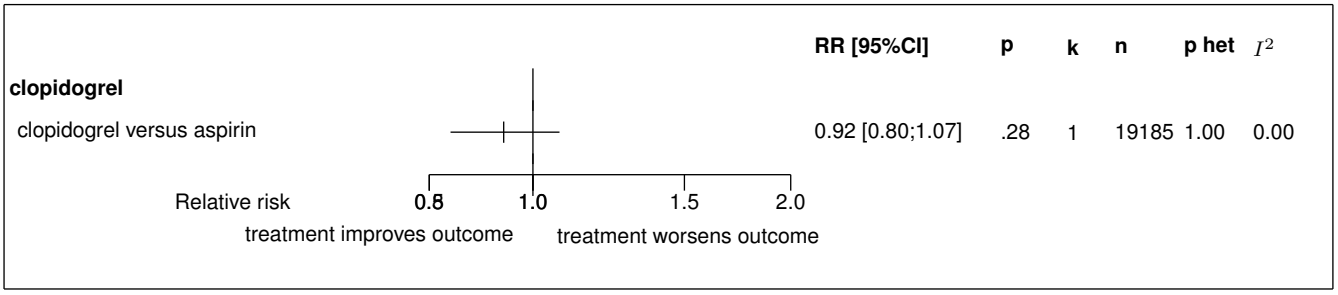
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 7.1: *Forest's plot for cardiovascular events*



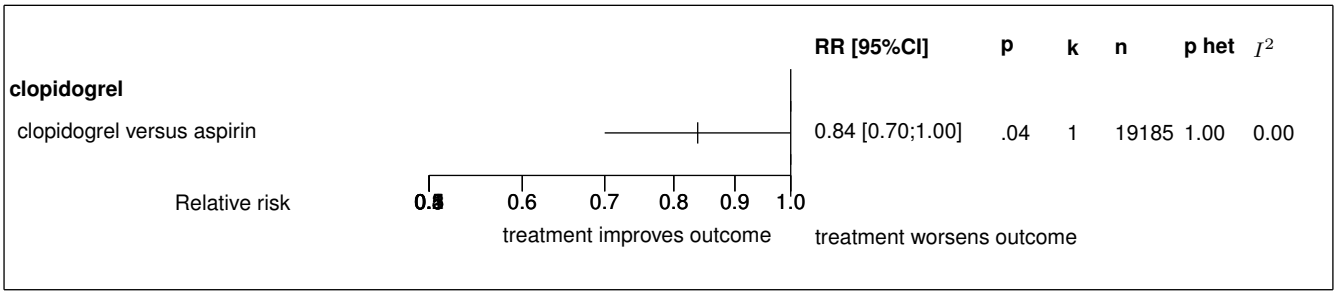
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 7.2: *Forest's plot for cardiovascular death*



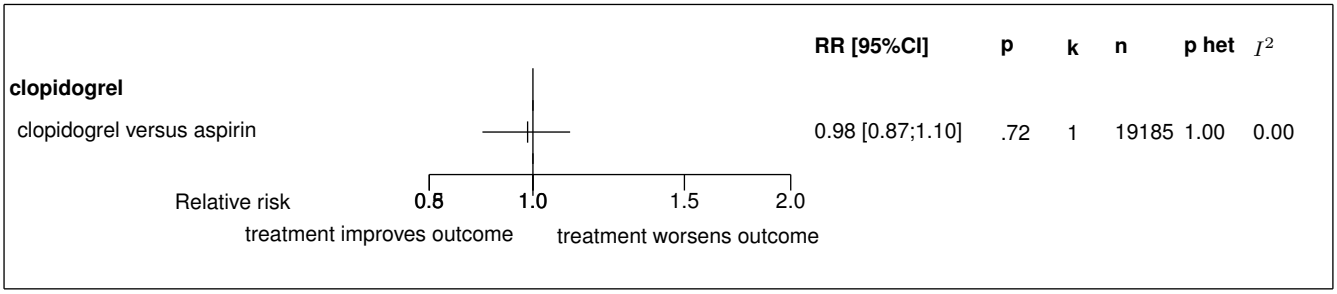
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 7.3: *Forest's plot for non fatal MI*



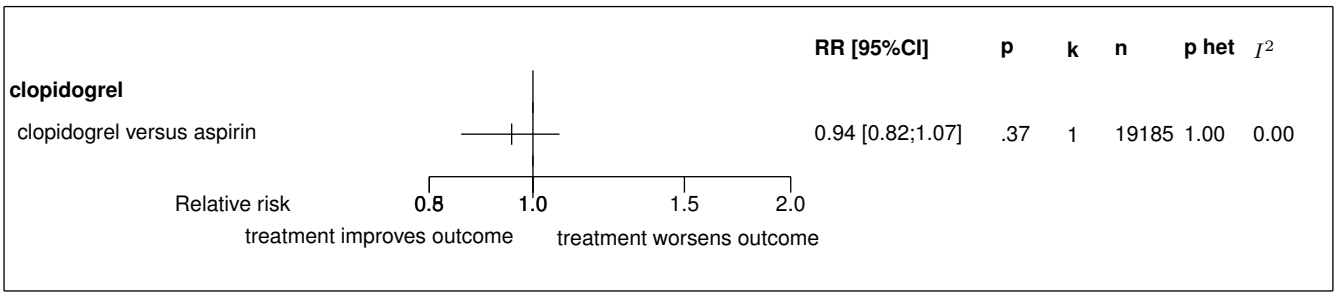
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 7.4: *Forest's plot for all cause death*



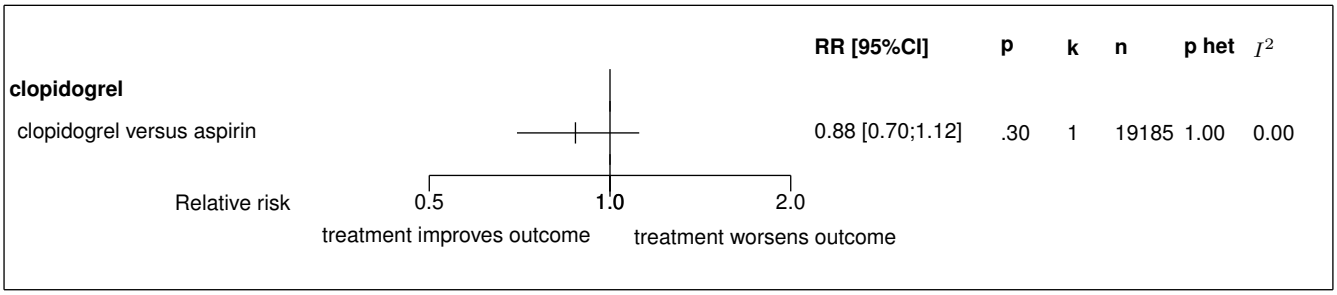
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 7.5: *Forest's plot for non fatal stroke*



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 7.6: *Forest's plot for major bleeding*



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

8 Details

8.1 Available trials

A total of 2 RCTs which randomized 20186 patients were identified: all compared clopidogrel with aspirin.
The average study size was 10093 patients (range 1001 to 19185). The first study was published in 1996, and the last study was published in 1996.
A total of 1 trials were double blind and 1 were open-label in design. All included studies were reported in English language. We did not found any unpublished trial.
Cardiovascular events data was reported in 2 trials; 1 trials reported data on major bleeding; 1 trials reported data on non fatal MI; 1 trials reported data on all cause death; 1 trials reported data on non fatal stroke; and 1 trials reported data on cardiovascular death.
Following tables 8.1 (page 36), 8.2 (page 36), 8.4 (page 38), and 8.3 (page 37) summarized the main characteristics of the trials including in this systematic review of randomized trials of clopidogrel.

Table 8.1: *Treatment description - clopidogrel - clopidogrel*

Trial	Studied treatment	Control treatment
Clopidogrel versus aspirin		
ASCET ()	clopidogrel 75 mg once daily for two years	Aspirin 160 mg once daily for two years
CAPRIE (1996) [1]	clopidogrel 75 mg once daily	aspirin 325 mg once daily

Table 8.2: *Descriptions of participants - clopidogrel - clopidogrel*

Trial	Patients
Clopidogrel versus aspirin	
ASCET ()[a]	Patients with documented coronary heart disease and treated with aspirin

continued...

Trial	Patients	
CAPRIE (1996) [1]	Patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease	
	Inclusion criteria: ischaemic stroke (including retinal origin and lacunar infarction): Focal neurological deficit likely to be of atherothrombotic; Onset >=1 week and <=6 months before randomisation; Neurological signs persisting >=1 week from stroke onset, CT or MRI ruling out haemorrhage or non-relevant disease-Myocardial infarction: Onset <=35 days before randomisation; Two of: Characteristic ischaemic pain for >=20 min, Elevation of CK, CK-MB, LDH, or AST to 2x upper limit of laboratory normal with no other explanation, Development of new >=40 Q waves in at least two adjacent ECG leads or new dominant R wave in V1 (R >=1 mm >S in V1)Atherosclerotic peripheral: Intermittent claudication (WHO: leg pain on walking, arterial disease disappearing in <10 min on standing) of presumed atherosclerotic origin; andankle/arm systolic BP ratio <=0.85 in either leg at rest (two assessments on separate days); or history of intermittent claudication with previous leg amputation, reconstructive surgery, or angioplasty with no persisting complications from intervention	**Exclusion criteria:** age <21 years; Severe cerebral deficit likely to lead to patient being bedridden or demented; Carotid endarterectomy after qualifying stroke; Qualifying stroke induced by carotid endarterectomy or angiography; Patient unlikely to be discharged aline after qualifying event; Severe co-morbidity likely to limit patients life expectancy to less than 3 y; Uncontrolled hypertension; Scheduled for major surgery; Contraindications to study drugs: Severe renal or hepatic insufficiency, Haemostatic disorder or systemic bleeding, History of haemostatic disorder or systemic bleeding, History of thrombocytopenia or neutropenia, History of drug-induced haematologic or hepatic abnormalities, Known to have abnormal WBC, differential, or platelet count, anticipated requirement for long-term anticoagulants, non-study antiplatelet drugsor NSAIDs affecting platelet function, History of aspirin sensitivity

a) platelet function was also assessed at randomization with the PFA100 method and platelet aggregometry

Table 8.3: *Design and methodological quality of trials - clopidogrel - clopidogrel*

Trial	Design	Duration	Centre	Primary endpoint
Clopidogrel versus aspirin				
ASCET, n=1001	Parallel groups open confirmatory trial at risk of bias			all-cause death, nonfatal MI, ischemic stroke, and unstable angina
CAPRIE, 1996 [1] n=19185	Parallel groups Double blind confirmatory trial at low risk of bias	mean 1.91 years inclusion period: Mar 1992 - Feb 1995	16 countries 384 centres	ischaemic stroke, myocardial infarction, or vascular death

Table 8.4: *Trial characteristics - clopidogrel - clopidogrel*

Trial
Clopidogrel versus aspirin
ASCET,
CAPRIE, 1996 [1]

8.2 Meta-analysis results

The results are detailed in table 8.5 (page 39). This table is followed by the Forest's plot corresponding to each endpoint.

Clopidogrel versus aspirin

All the 2 studies had extractable data about the number of participants with **cardiovascular events**. The analysis detected a statistically significant difference in favor of clopidogrel in cardiovascular events, with a RR of 0.92 (95% CI 0.85 to 1.00, p=0.0393). No heterogeneity was detected (p = 0.9230, I^2 = 0.00%).
Only one of the 2 studies eligible for this comparison provided data on **cardiovascular death**. No statistically significant difference between the groups was found in cardiovascular death, with a RR of 0.92 (95% CI 0.80 to 1.07, p=0.2818).
Only one of the 2 studies eligible for this comparison provided data on **non fatal MI**. The analysis detected a statistically significant difference in favor of clopidogrel in non fatal MI, with a RR of 0.84 (95% CI 0.70 to 1.00, p=0.0440).
Only one of the 2 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 0.98 (95% CI 0.87 to 1.10, p=0.7184).
Only one of the 2 studies eligible for this comparison provided data on **non fatal stroke**. No statistically significant difference between the groups was found in non fatal stroke, with a RR of 0.94 (95% CI 0.82 to 1.07, p=0.3657).
Only one of the 2 studies eligible for this comparison provided data on **major bleeding**. No statistically significant difference between the groups was found in major bleeding, with a RR of 0.88 (95% CI 0.70 to 1.12, p=0.3019).

Table 8.5: *Results details - clopidogrel - clopidogrel*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
clopidogrel versus aspirin						
cardiovascular events	RR=0.92	[0.85;1.00]	0.0393	0.9230 (I^2=0.00)	2	20186
cardiovascular death	RR=0.92	[0.80;1.07]	0.2818	1.0000 (I^2=0.00)	1	19185
non fatal MI	RR=0.84	[0.70;1.00]	0.0440	1.0000 (I^2=0.00)	1	19185
all cause death	RR=0.98	[0.87;1.10]	0.7184	1.0000 (I^2=0.00)	1	19185
non fatal stroke	RR=0.94	[0.82;1.07]	0.3657	1.0000 (I^2=0.00)	1	19185
major bleeding	RR=0.88	[0.70;1.12]	0.3019	1.0000 (I^2=0.00)	1	19185

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 8.1: *Forest's plot for cardiovascular events*

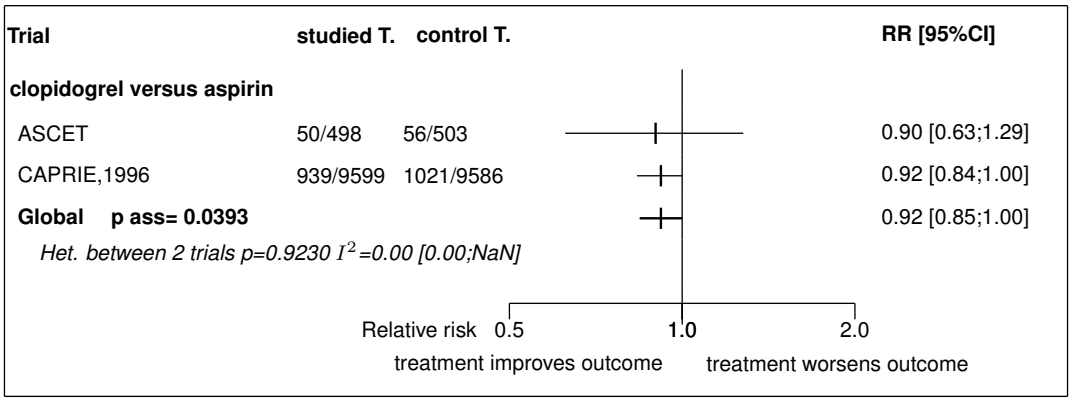


Figure 8.2: *Forest's plot for cardiovascular death*

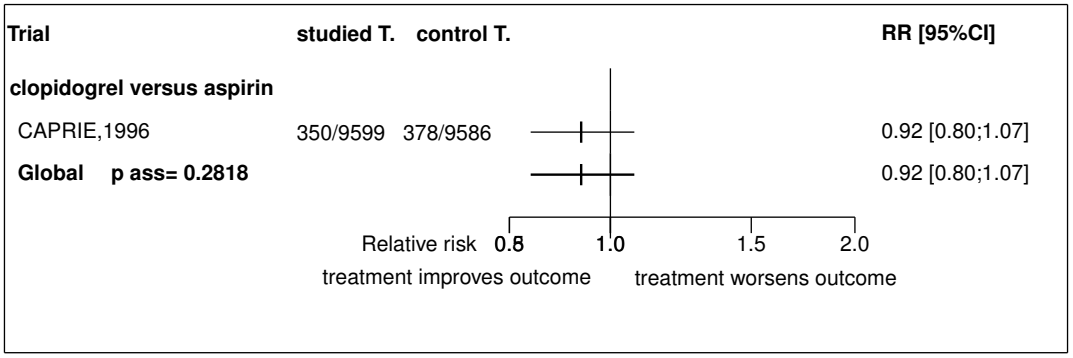


Figure 8.3: *Forest's plot for non fatal MI*

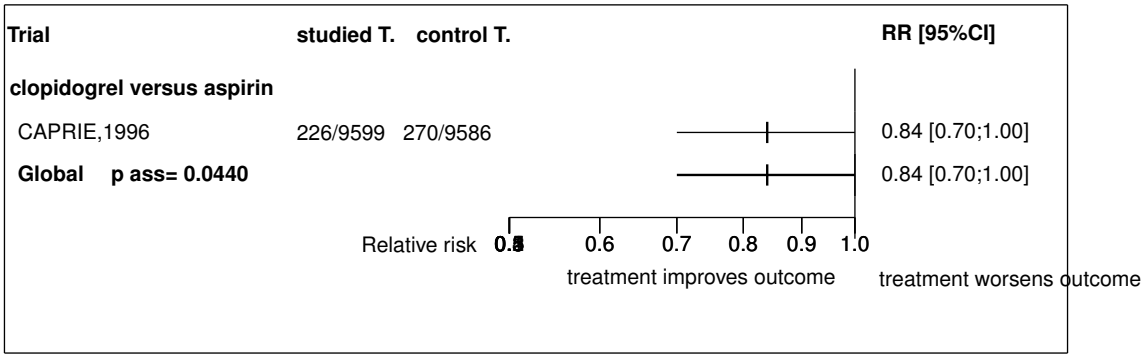


Figure 8.4: *Forest's plot for all cause death*

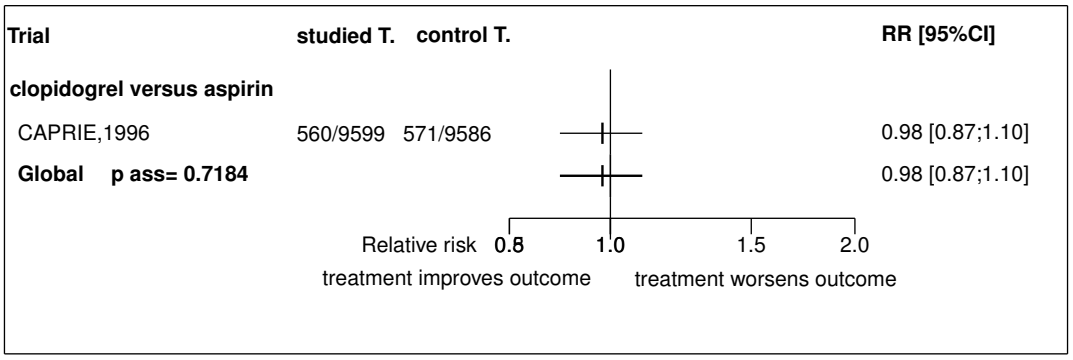


Figure 8.5: *Forest's plot for non fatal stroke*

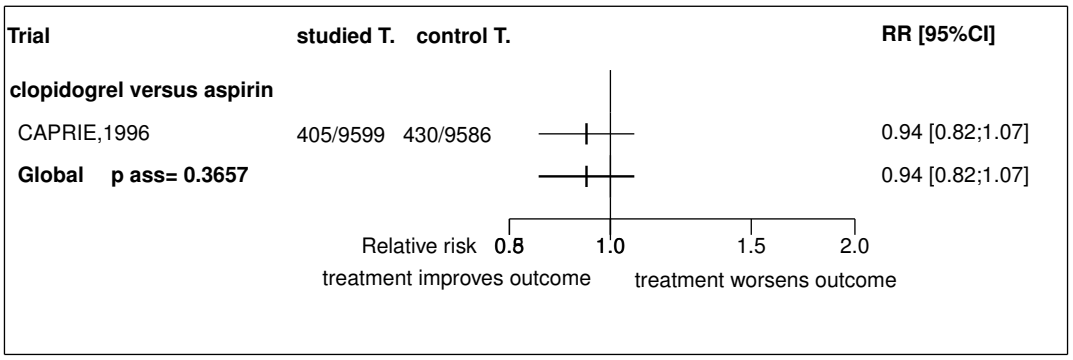
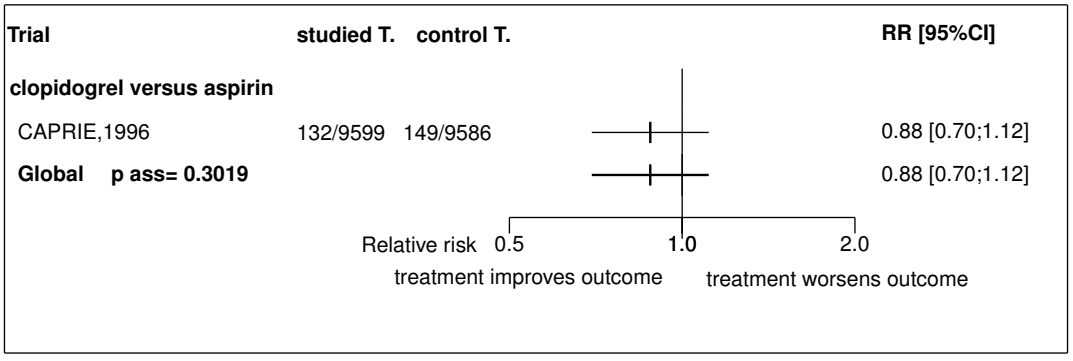


Figure 8.6: *Forest's plot for major bleeding*



References

[1] . A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996 Nov 16;348:1329-39. [PMID=8918275]

8.3 Individual trial summaries

Table 8.6: *ASCET, - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=1001 (498 vs. 503) **Follow-up duration:** **Study design:** Randomized controlled trial Parallel groups Open Confirmatory trial at risk of bias	Patients with documented coronary heart disease and treated with aspirin **note:** platelet function was also assessed at randomization with the PFA100 method and platelet aggregometry	**Studied treatment:** clopidogrel 75 mg once daily for two years **Control treatment:** Aspirin 160 mg once daily for two years	Cardiovascular events RR=0.90 [0.63;1.29] (all-cause death, nonfatal MI, ischemic stroke, and unstable angina)
Reference			

Table 8.7: *CAPRIE, 1996 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=19185 (9599 vs. 9586) **Follow-up duration:** mean 1.91 years **Study design:** Randomized controlled trial Parallel groups Double blind Confirmatory trial at low risk of bias 16 countries, 384 centres **Inclusion period:** Mar 1992 - Feb 1995	Patients with atherosclerotic vascular disease manifested as either recent ischaemic stroke, recent myocardial infarction, or symptomatic peripheral arterial disease **Inclusion criteria:** Ischaemic stroke (including retinal origin and lacunar infarction): Focal neurological deficit likely to be of atherothrombotic; Onset >=1 week and <=6 months before randomisation; Neurological signs persisting >=1 week from stroke onset, CT or MRI ruling out haemorrhage or non-relevant diseaseMyocardial infarction: Onset <=35 days before randomisation; Two of: Characteristic ischaemic pain for >=20 min, Elevation of CK, CK-MB, LDH, or AST to 2x upper limit of laboratory normal with no other explanation, Development of new **Exclusion criteria:** Age <21 years; Severe cerebral deficit likely to lead to patient being bedridden or demented; Carotid endarterectomy after qualifying stroke; Qualifying stroke induced by carotid endarterectomy or angiography; Patient unlikely to be discharged aline after qualifying event; Severe co-morbidity likely to limit patients life expectancy to less than 3 y; Uncontrolled hypertension; Scheduled for major surgery; Contraindications to study drugs: Severe renal or hepatic insufficiency, Haemostatic disorder or systemic bleeding, History of haemostatic disorder or systemic bleeding, History of	**Studied treatment:** clopidogrel 75 mg once daily **Control treatment:** aspirin 325 mg once daily	Cardiovascular events RR=0.92 [0.84;1.00] Cardiovascular death RR=0.92 [0.80;1.07] (vascular death) Non fatal MI RR=0.84 [0.70;1.00] All cause death RR=0.98 [0.87;1.10] Non fatal stroke RR=0.94 [0.82;1.07] Major bleeding RR=0.88 [0.70;1.12]

continued...

trial details	Patients	Treatments	Outcomes

Reference

. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. Lancet 1996 Nov 16;348:1329-39 [PMID=8918275]

9 Global meta-analysis: all clopidogrel

9.1 Global meta-analysis: all clopidogrel versus aspirin

Table 9.1: *All clopidogrelversus aspirin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
cardiovascular events	RR=0.92	0.85;1.00	0.0393	0.9230 (0.00)	2	20186
cardiovascular death	RR=0.92	0.80;1.07	0.2818	1.0000 (0.00)	1	19185
non fatal MI	RR=0.84	0.70;1.00	0.0440	1.0000 (0.00)	1	19185
all cause death	RR=0.98	0.87;1.10	0.7184	1.0000 (0.00)	1	19185
non fatal stroke	RR=0.94	0.82;1.07	0.3657	1.0000 (0.00)	1	19185
major bleeding	RR=0.88	0.70;1.12	0.3019	1.0000 (0.00)	1	19185

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

10 Ongoing studies of clopidogrel

No ongoing trial was identified.

11 Excluded studies for clopidogrel

No trial was excluded.

References

Part III

Dipyridamol

12 Overview of dipyridamol

12.1 Included trials

A total of 10 randomized comparisons which enrolled 401 patients were identified. In all, 10 randomized comparisons concerned dipyridamol.
The detailed descriptions of trials and meta-analysis results is given in section 13 (page 56) for dipyridamol.

The average study size was 40 patients (range 26 to 60). The first study was published in 1960, and the last study was published in 1970.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
The table 12.1 (page 52) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

12.2 Summary of meta-analysis results

The meta-analysis of the available trials about dipyridamol provide the results listed in tables 12.2 to 12.2 (page 54) and in the following graphs.

12.2.1 Dipyridamol

No significant difference was found between **dipyridamol** and **control** in terms of cardiovascular events (RR=1.28, 95% CI 0.43 to 3.83, p=0.6557, 3 trials), cardiovascular death (RR=1.61, 95% CI 0.22 to 12.11, p=0.6411, 3 trials), non vascular death (RR=0.98, 95% CI 0.10 to 9.12, p=0.9825, 3 trials), non fatal MI (RR=0.79, 95% CI 0.23 to 2.77, p=0.7128, 3 trials)and non fatal stroke (RR=1.29, 95% CI 0.15 to 10.73, p=0.8144, 3 trials).

Data were insufficient to compare **dipyridamol** to **placebo**. There were 7 eligible trials but none provided sufficient information about the endpoints considered by this meta-analysis.

Table 12.1: *Main study characteristics - dipyridamol*

Trial	Patients	Treatments	Trial design and method
Dipyridamol			
Dipyridamol versus control			
Atlanta (Sbar), 1967 [1] n = 30 vs. 30	patients with angina pectoris	dipyridamole 150mg daily **versus** placebo	double-blind parallel groups Primary endpoint: not defined
Wirecki, 1967 [2] n = 28 vs. 28	patients with angina pectoris	dipyridamole 150mg daily **versus** placebo	double blind parallel groups Primary endpoint: not defined
Becker, 1967 [3] n = 14 vs. 13		dipyridamole 225mg daily **versus** placebo	double-blind parallel groups Primary endpoint: not defined
Dipyridamol versus placebo			
Kinsella, 1962 [4] n = 13 vs. 13		dipyridamole 37.5 mg and 100mg daily **versus** placebo	double-blind parallel groups Primary endpoint: not defined
Leiberman, 1964 [5] n = 19 vs. 19		dipyridamole 100mg daily **versus** placebo	double blind parallel groups Primary endpoint: not defined
Zion, 1961 [6] n = 14 vs. 14	patients with angina pectoris	dipyridamole 37.5mg **versus** placebo	double-blind cross-over Primary endpoint: not defined
Dewar, 1961 [7] n = 17 vs. 17	patients with angina pectoris	dipyridamole 100mg daily **versus** placebo	double-blind parallel groups Primary endpoint: not defined
Neumann, 1964 [8] n = 20 vs. 16	elderly with precordial pain	dipyridamole 150mg daily **versus** placebo	double-blind parallel groups Primary endpoint: not defined

continued...

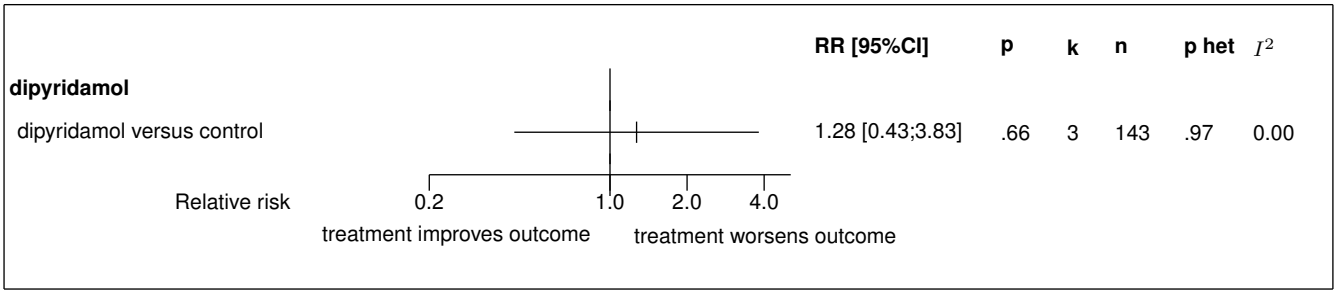
Trial	Patients	Treatments	Trial design and method
Foulds, 1960 [9] n = 24 vs. 24	patients with angina pectoris	dipyridamole 200mg daily **versus** placebo	double-blind parallel groups Primary endpoint: not defined
Igloe, 1970 [10] n = 26 vs. 22	patients with angina pectoris	dipyridamole 200mg daily **versus** placebo	double blind parallel groups Primary endpoint: not defined

Table 12.2: *Summary of all results for dipyridamol*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
dipyridamol versus control						
cardiovascular events	RR=1.28	0.43;3.83	0.6557	0.9678 (0.00)	3	143
cardiovascular death	RR=1.61	0.22;12.11	0.6411	0.9604 (0.00)	3	143
non vascular death	RR=0.98	0.10;9.12	0.9825	0.9995 (0.00)	3	143
non fatal MI	RR=0.79	0.23;2.77	0.7128	0.9870 (0.00)	3	143
non fatal stroke	RR=1.29	0.15;10.73	0.8144	0.9464 (0.00)	3	143
dipyridamol versus placebo						
No data were presented in the trial identified						

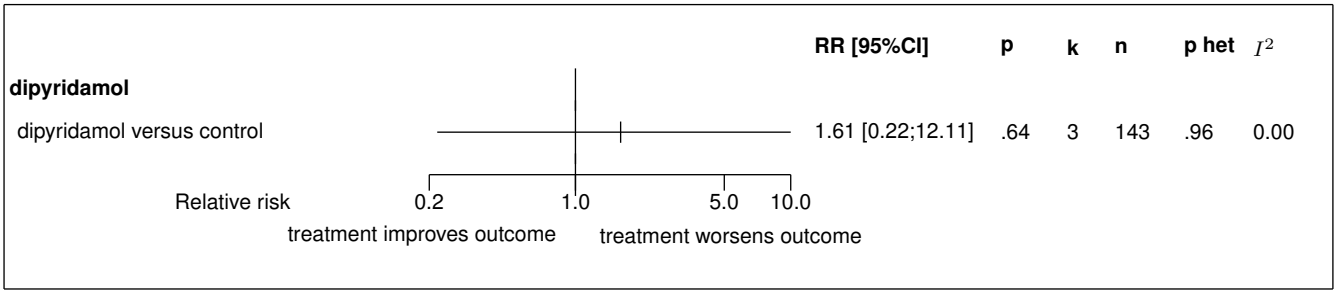
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 12.1: *Forest's plot for cardiovascular events*



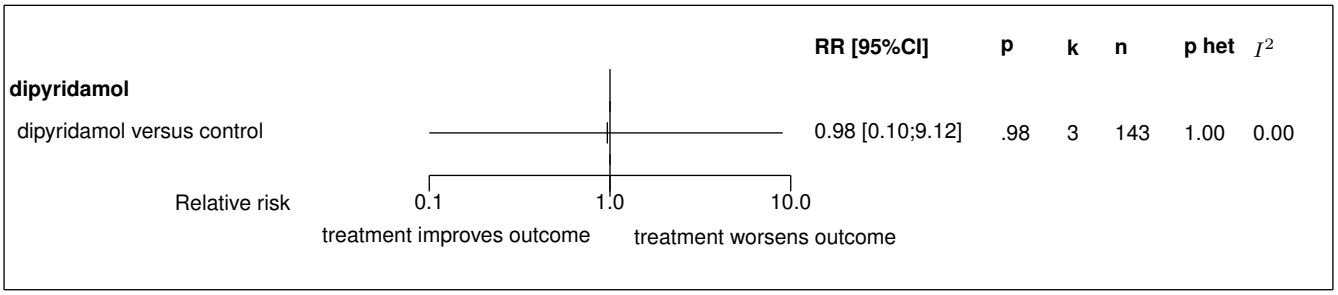
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 12.2: *Forest's plot for cardiovascular death*



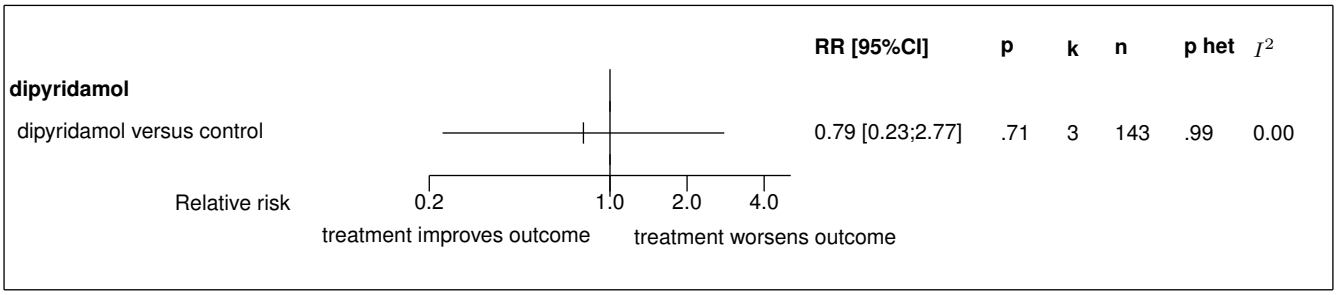
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 12.3: *Forest's plot for non vascular death*



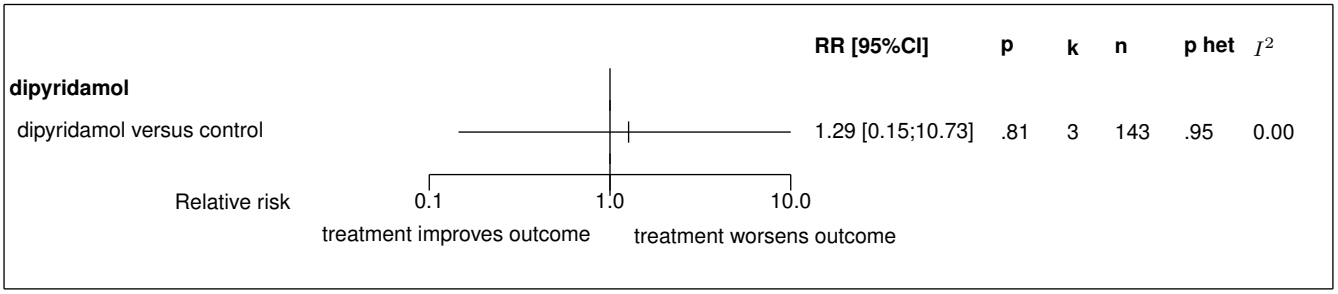
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 12.4: *Forest's plot for non fatal 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 12.5: *Forest's plot for non fatal stroke*



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

13 Details

13.1 Available trials

A total of 10 RCTs which randomized 401 patients were identified: 3 trials compared dipyridamol with control and 7 trials compared dipyridamol with placebo.
The average study size was 40 patients (range 26 to 60). The first study was published in 1960, and the last study was published in 1970.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
Non vascular death data was reported in 3 trials; 3 trials reported data on cardiovascular death; 3 trials reported data on non fatal MI; 3 trials reported data on cardiovascular events; and 3 trials reported data on non fatal stroke.
Following tables 13.1 (page 56), 13.2 (page 57), 13.4 (page 59), and 13.3 (page 57) summarized the main characteristics of the trials including in this systematic review of randomized trials of dipyridamol.

Table 13.1: *Treatment description - dipyridamol - dipyridamol*

Trial	Studied treatment	Control treatment
Dipyridamol versus control		
Atlanta (Sbar) (1967) [1]	dipyridamole 150mg daily	placebo
Wirecki (1967) [2]	dipyridamole 150mg daily	placebo
Becker (1967) [3]	dipyridamole 225mg daily	placebo
Dipyridamol versus placebo		
Kinsella (1962) [4]	dipyridamole 37.5 mg and 100mg daily	placebo
Leiberman (1964) [5]	dipyridamole 100mg daily	placebo
Zion (1961) [6]	Dipyridamole 37.5mg	placebo
Dewar (1961) [7]	Dipyridamole 100mg daily	placebo
Neumann (1964) [8]	dipyridamole 150mg daily	placebo
Foulds (1960) [9]	Dipyridamole 200mg daily	placebo
Igloe (1970) [10]	Dipyridamole 200mg daily	placebo

Table 13.2: *Descriptions of participants - dipyridamol - dipyridamol*

Trial	Patients
Dipyridamol versus control	
Atlanta (Sbar) (1967) [1]	Patients with angina pectoris
Wirecki (1967) [2]	Patients with angina pectoris
Becker (1967) [3]	
Dipyridamol versus placebo	
Kinsella (1962) [4]	
Leiberman (1964) [5]	
Zion (1961) [6]	Patients with angina pectoris
Dewar (1961) [7]	Patients with angina pectoris
Neumann (1964) [8]	Elderly with precordial pain
Foulds (1960) [9]	Patients with angina pectoris
Igloe (1970) [10]	Patients with angina pectoris

Table 13.3: *Design and methodological quality of trials - dipyridamol - dipyridamol*

Trial	Design	Duration	Centre	Primary end-point
Dipyridamol versus control				
Atlanta (Sbar), 1967 [1] n=60	parallel groups double-blind exploratory trial	6 months		not defined
Wirecki, 1967 [2] n=56	parallel groups double blind exploratory trial	7 months		not defined
Becker, 1967 [3] n=27	parallel groups double-blind exploratory trial	5 months		not defined

continued...

Trial	Design	Duration	Centre	Primary end-point
Dipyridamol versus placebo				
Kinsella, 1962 [4] n=26	parallel groups double-blind exploratory trial	0.5 months		not defined
Leiberman, 1964 [5] n=38	parallel groups double blind exploratory trial	>3 months		not defined
Zion, 1961 [6] n=28	cross-over double-blind exploratory trial	0.5 months		not defined
Dewar, 1961 [7] n=34	parallel groups double-blind exploratory trial	0.5 months		not defined
Neumann, 1964 [8] n=36	parallel groups double-blind exploratory trial	1.5 months		not defined
Foulds, 1960 [9] n=48	parallel groups double-blind exploratory trial	1 months		not defined
Igloe, 1970 [10] n=48	parallel groups double blind exploratory trial	2-7 months		not defined

Table 13.4: *Trial characteristics - dipyridamol - dipyridamol*

Trial
Dipyridamol versus control
Atlanta (Sbar), 1967 [1]
Wirecki, 1967 [2]
Becker, 1967 [3]
Dipyridamol versus placebo
Kinsella, 1962 [4]
Leiberman, 1964 [5]
Zion, 1961 [6]
Dewar, 1961 [7]
Neumann, 1964 [8]
Foulds, 1960 [9]
Igloe, 1970 [10]

13.2 Meta-analysis results

The results are detailed in table 13.5 (page 60). This table is followed by the Forest's plot corresponding to each endpoint.

Dipyridamol versus control

All the 3 studies had extractable data about the number of participants with **cardiovascular events**. There was no statistically significant difference in cardiovascular events between dipyridamol and control, with a RR of 1.28 (95%CI 0.43 to 3.83, p=0.6557) in favour of control. In other words, cardiovascular events was slightly lower in the control group , but this was not statistically significant. No heterogeneity was detected (p = 0.9678, I^2 = 0.00%).
All the 3 studies had extractable data about the number of participants with **cardiovascular death**. When pooled together, there was no statistically significant difference between the groups in cardiovascular death, with a RR of 1.61 (95% CI 0.22 to 12.11, p=0.6411). No heterogeneity was detected (p = 0.9604, I^2 = 0.00%).
All the 3 studies had extractable data about the number of participants with **non vascular death**. When pooled together, there was no statistically significant difference between the groups in non vascular death, with a RR of 0.98 (95% CI 0.10 to 9.12, p=0.9825). No heterogeneity was detected (p = 0.9995, 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 0.79 (95% CI 0.23 to 2.77, p=0.7128). No heterogeneity was detected (p = 0.9870, I^2 = 0.00%).
All the 3 studies had extractable data about the number of participants with **non fatal stroke**. When pooled together, there was no statistically significant difference between the groups in non fatal stroke, with a RR of 1.29 (95% CI 0.15 to 10.73, p=0.8144). No heterogeneity was detected (p = 0.9464, I^2 = 0.00%).

Dipyridamol versus placebo

No data were presented in the 7 trials identified

Table 13.5: *Results details - dipyridamol - dipyridamol*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
dipyridamol versus control						
cardiovascular events	RR=1.28	[0.43;3.83]	0.6557	0.9678 (I^2=0.00)	3	143
cardiovascular death	RR=1.61	[0.22;12.11]	0.6411	0.9604 (I^2=0.00)	3	143
non vascular death	RR=0.98	[0.10;9.12]	0.9825	0.9995 (I^2=0.00)	3	143
non fatal MI	RR=0.79	[0.23;2.77]	0.7128	0.9870 (I^2=0.00)	3	143
non fatal stroke	RR=1.29	[0.15;10.73]	0.8144	0.9464 (I^2=0.00)	3	143
dipyridamol versus placebo						
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

Figure 13.1: *Forest's plot for cardiovascular events*

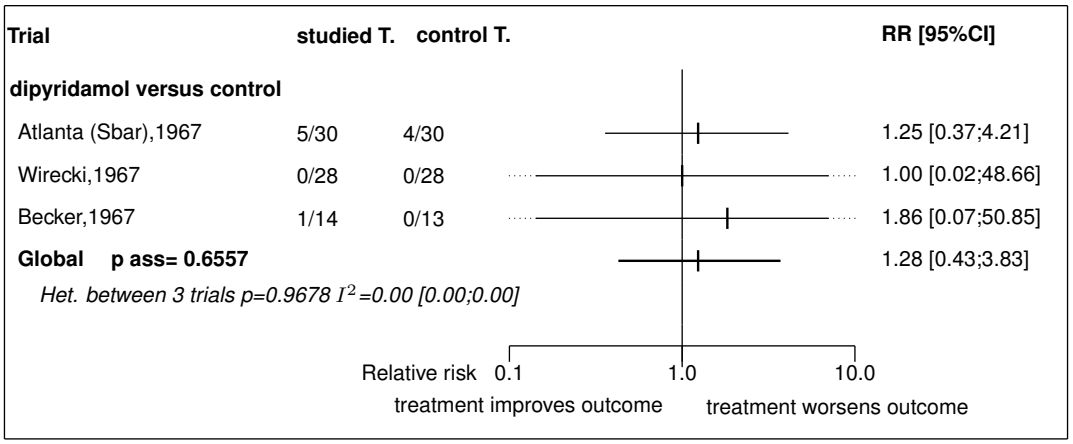


Figure 13.2: *Forest's plot for cardiovascular death*

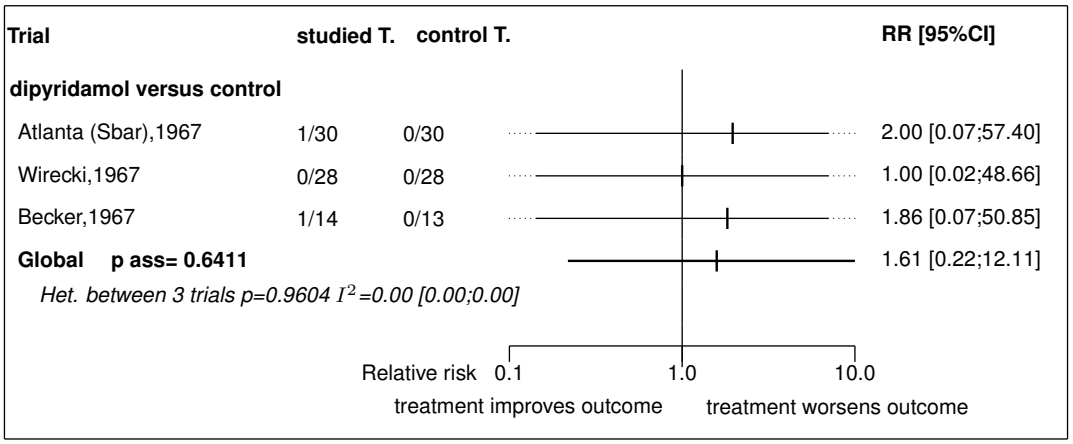


Figure 13.3: *Forest's plot for non vascular death*

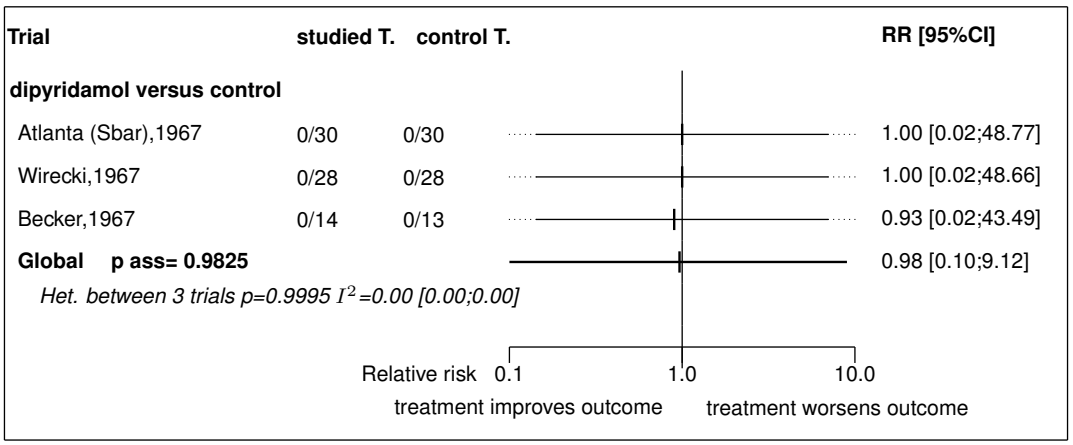


Figure 13.4: *Forest's plot for non fatal MI*

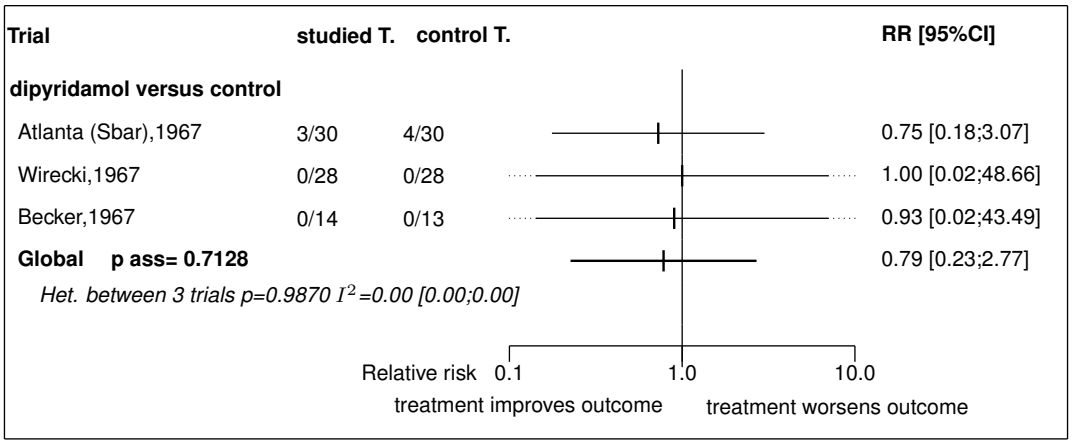
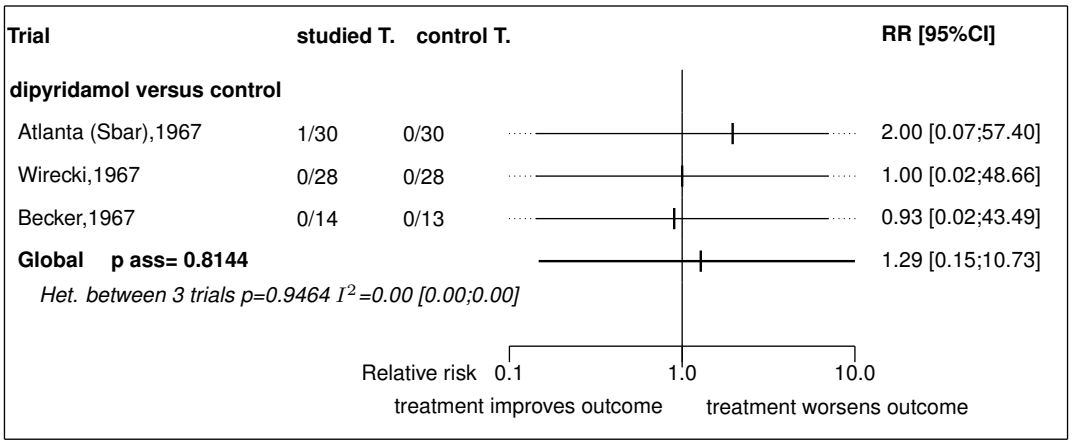


Figure 13.5: *Forest's plot for non fatal stroke*



References

[1] Sbar S, Schlant RC. Dipyridamole in the treatment of angina pectoris. A double-blind evaluation. JAMA 1967;201:865-7. [PMID=5340622]

[2] Wirecki M. Treatment of angina pectoris with dipyridamole: a long-term double blind study. J Chronic Dis 1967;20:139-45. [PMID=5336520]

[3] Becker MC. Angina pectoris: A double blind study with dipyridamole. Journal of the Newark Beth Israel Hospital 1967;18:88-94.

[4] KINSELLA D, TROUP W, McGREGOR M. Studies with a new coronary vasodilator drug: persantin. Am Heart J 1962;63:146-51. [PMID=14456202]

[5] LEIBERMAN A, GUGLIELMELLI S. PERSANTIN– A DOUBLE BLIND STUDY. Angiology 1964;15:290-2. [PMID=14170587]

[6] ZION MM, BRADLOW BA. A controlled clinical trial of 'persantin' (R A 8) in angina pectoris. S Afr Med J 1961;35:11-3. [PMID=13788617]

[7] DEWAR HA, HORLER AR. A clinical trial of Persantin and Crodimyl in the treatment of angina of effort. Scott Med J 1961;6:149-52. [PMID=13722387]

[8] NEUMANN M, LUISADA AA. EFFECT OF RAPID AND SLOW-ACTING "CORONARY" DRUGS ON PRECORDIAL PAIN OF THE AGED. Am J Med Sci 1964;247:156-63. [PMID=14124704]

[9] FOULDS T, MACKINNON J. Controlled double-blind trial of "persantin" in treatment of angina pectoris. Br Med J 1960;2:835. [PMID=13824151]

[10] Igloe MC. Treatment of angina pectoris with dipyridamole: a double-blind study. J Am Geriatr Soc 1970;18:233-41. [PMID=4984849]

13.3 Individual trial summaries

Table 13.6: *Atlanta (Sbar), 1967 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=60 (30 vs. 30) **Follow-up duration:** 6 months **Study design:** Randomized controlled trial parallel groups Double-blind Exploratory trial	Patients with angina pectoris	**Studied treatment:** dipyridamole 150mg daily **Control treatment:** placebo	Cardiovascular events RR=1.25 [0.37;4.21] Non fatal MI RR=0.75 [0.18;3.07]

Reference

Sbar S, Schlant RC. Dipyridamole in the treatment of angina pectoris. A double-blind evaluation. JAMA 1967;201:865-7 [PMID=5340622]

Table 13.7: *Wirecki, 1967 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=56 (28 vs. 28) **Follow-up duration:** 7 months **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	Patients with angina pectoris	**Studied treatment:** dipyridamole 150mg daily **Control treatment:** placebo	

Reference

Wirecki M. Treatment of angina pectoris with dipyridamole: a long-term double blind study. J Chronic Dis 1967;20:139-45 [PMID=5336520]

Table 13.8: *Becker, 1967 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=27 (14 vs. 13) **Follow-up duration:** 5 months **Study design:** Randomized controlled trial parallel groups Double-blind Exploratory trial		**Studied treatment:** dipyridamole 225mg daily **Control treatment:** placebo	

Reference

Becker MC. Angina pectoris: A double blind study with dipyridamole. Journal of the Newark Beth Israel Hospital 1967;18:88-94

Table 13.9: *Kinsella, 1962 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=26 (13 vs. 13) **Follow-up duration:** 0.5 months **Study design:** Randomized controlled trial parallel groups Double-blind Exploratory trial		**Studied treatment:** dipyridamole 37.5 mg and 100mg daily **Control treatment:** placebo	

Reference

KINSELLA D, TROUP W, McGREGOR M. Studies with a new coronary vasodilator drug: persantin. Am Heart J 1962;63:146-51 [PMID=14456202]

Table 13.10: *Leiberman, 1964 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=38 (19 vs. 19) **Follow-up duration:** >3 months **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial		**Studied treatment:** dipyridamole 100mg daily **Control treatment:** placebo	
Reference LEIBERMAN A, GUGLIELMELLI S. PERSANTIN– A DOUBLE BLIND STUDY. Angiology 1964;15:290-2 [PMID=14170587]			

Table 13.11: *Zion, 1961 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=28 (14 vs. 14) **Follow-up duration:** 0.5 months **Study design:** Randomized controlled trial cross-over Double-blind Exploratory trial	Patients with angina pectoris	**Studied treatment:** Dipyridamole 37.5mg **Control treatment:** placebo	

Reference

ZION MM, BRADLOW BA. A controlled clinical trial of 'persantin' (R A 8) in angina pectoris. S Afr Med J 1961;35:11-3 [PMID=13788617]

Table 13.12: *Dewar, 1961 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=34 (17 vs. 17) **Follow-up duration:** 0.5 months **Study design:** Randomized controlled trial parallel groups Double-blind Exploratory trial	Patients with angina pectoris	**Studied treatment:** Dipyridamole 100mg daily **Control treatment:** placebo	

Reference

DEWAR HA, HORLER AR. A clinical trial of Persantin and Crodimyl in the treatment of angina of effort. Scott Med J 1961;6:149-52 [PMID=13722387]

Table 13.13: *Neumann, 1964 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=36 (20 vs. 16) **Follow-up duration:** 1.5 months **Study design:** Randomized controlled trial parallel groups Double-blind Exploratory trial	Elderly with precordial pain	**Studied treatment:** dipyridamole 150mg daily **Control treatment:** placebo	

Reference

NEUMANN M, LUISADA AA. EFFECT OF RAPID AND SLOW-ACTING "CORONARY" DRUGS ON PRECORDIAL PAIN OF THE AGED. Am J Med Sci 1964;247:156-63 [PMID=14124704]

Table 13.14: *Foulds, 1960 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=48 (24 vs. 24) **Follow-up duration:** 1 months **Study design:** Randomized controlled trial parallel groups Double-blind Exploratory trial	Patients with angina pectoris	**Studied treatment:** Dipyridamole 200mg daily **Control treatment:** placebo	

Reference
FOULDS T, MACKINNON J. Controlled double-blind trial of ”persantin” in treatment of angina pectoris. Br Med J 1960;2:835 [PMID=13824151]

Table 13.15: *Igloe, 1970 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=48 (26 vs. 22) **Follow-up duration:** 2-7 months **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	Patients with angina pectoris	**Studied treatment:** Dipyridamole 200mg daily **Control treatment:** placebo	

Reference

Igloe MC. Treatment of angina pectoris with dipyridamole: a double-blind study. J Am Geriatr Soc 1970;18:233-41 [PMID=4984849]

14 Global meta-analysis: all dipyridamol

14.1 Global meta-analysis: all dipyridamol versus control

Table 14.1: *All dipyridamolversus control*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
cardiovascular events	RR=1.28	0.43;3.83	0.6557	0.9678 (0.00)	3	143
cardiovascular death	RR=1.61	0.22;12.11	0.6411	0.9604 (0.00)	3	143
non vascular death	RR=0.98	0.10;9.12	0.9825	0.9995 (0.00)	3	143
non fatal MI	RR=0.79	0.23;2.77	0.7128	0.9870 (0.00)	3	143
non fatal stroke	RR=1.29	0.15;10.73	0.8144	0.9464 (0.00)	3	143

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

14.2 Global meta-analysis: all dipyridamol versus placebo

Table 14.2: *All dipyridamolversus placebo*

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

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

15 Ongoing studies of dipyridamol

No ongoing trial was identified.

16 Excluded studies for dipyridamol

No trial was excluded.

References

Part IV

Oral platelet GP IIbIIIa receptor inhibitor

17 Overview of oral platelet GP IIbIIIa receptor inhibitor

17.1 Included trials

Only one trial which randomized 120 patients was identified. In all, 1 randomized comparison concerned roxifiban .
The detailed descriptions of trials and meta-analysis results is given in section 18 (page 82) for roxifiban .

This trial included 120 patients and was published in 2003.
This trial was double blind in design.
It was reported in English language.
The table 17.1 (page 80) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

17.2 Summary of meta-analysis results

The meta-analysis of the available trials about oral platelet GP IIbIIIa receptor inhibitor provide the results listed in tables 17.2 to 17.2 (page 81) and in the following graphs.

17.2.1 Roxifiban

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

Table 17.1: *Main study characteristics - oral platelet GP IIbIIIa receptor inhibitor*

Trial	Patients	Treatments	Trial design and method
Roxifiban			
Roxifiban versus placebo			
Murphy, 2003 [1] n= 120	patients with stable coronary artery disease	roxifiban 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2, or 2.5 mg/day for up to 30 days **versus** placebo	double blind parallel groups

Table 17.2: *Summary of all results for roxifiban*

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

18 Details

18.1 Available trials

Only one trial which randomized 120 patients was identified: it compared roxifiban with placebo.
This trial included 120 patients and was published in 2003.
This trial was double blind in design.
It was reported in English language.
data was reported in trials;
Following tables 18.1 (page 82), 18.2 (page 82), 18.4 (page 83), and 18.3 (page 82) summarized the main characteristics of the trial including in this systematic review of randomized trials of roxifiban .

Table 18.1: *Treatment description - oral platelet GP IIbIIIa receptor inhibitor - roxifiban*

Trial	Studied treatment	Control treatment
Roxifiban versus placebo		
Murphy (2003) [1]	roxifiban 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2, or 2.5 mg/day for up to 30 days	placebo

Table 18.2: *Descriptions of participants - oral platelet GP IIbIIIa receptor inhibitor - roxifiban*

Trial	Patients
Roxifiban versus placebo	
Murphy (2003) [1]	Patients with stable coronary artery disease

Table 18.3: *Design and methodological quality of trials - oral platelet GP IIbIIIa receptor inhibitor - roxifiban*

Trial	Design	Duration	Centre	Primary endpoint
Roxifiban versus placebo				
Murphy, 2003 [1] n=120	Parallel groups double blind exploratory trial	30 days		

Table 18.4: *Trial characteristics - oral platelet GP IIbIIIa receptor inhibitor - roxifiban*

Trial
Roxifiban versus placebo
Murphy, 2003 [1]

18.2 Meta-analysis results

The results are detailed in table 18.5 (page 84). This table is followed by the Forest's plot corresponding to each endpoint.

Roxifiban versus placebo

No data were presented in the 1 trial identified

Table 18.5: *Results details - oral platelet GP IIbIIIa receptor inhibitor - roxifiban*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
roxifiban versus placebo						
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] Murphy J, Wright RS, Gussak I, Williams B, Daly RN, Cain VA, Pieniaszek HJ, Sy SK, Ebling W, Simonson K, Wilcox RA, Kopecky SL. The use of roxifiban (DMP754), a novel oral platelet glycoprotein IIb/IIIa receptor inhibitor, in patients with stable coronary artery disease. Am J Cardiovasc Drugs 2003;3:101-12. [PMID=14727937]

18.3 Individual trial summaries

Table 18.6: *Murphy, 2003 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=0 (120 vs. 0) **Follow-up duration:** 30 days **Study design:** Randomized controlled trial Parallel groups Double blind Exploratory trial	Patients with stable coronary artery disease	**Studied treatment:** roxifiban 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2, or 2.5 mg/day for up to 30 days **Control treatment:** placebo	

Reference

Murphy J, Wright RS, Gussak I, Williams B, Daly RN, Cain VA, Pieniaszek HJ, Sy SK, Ebling W, Simonson K, Wilcox RA, Kopecky SL. The use of roxifiban (DMP754), a novel oral platelet glycoprotein IIb/IIIa receptor inhibitor, in patients with stable coronary artery disease. Am J Cardiovasc Drugs 2003;3:101-12 [PMID=14727937]

19 Global meta-analysis: all oral platelet GP IIbIIIa receptor inhibitor

19.1 Global meta-analysis: all oral platelet GP IIbIIIa receptor inhibitor versus placebo

Table 19.1: *All oral platelet GP IIbIIIa receptor inhibitorversus placebo*

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

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

20 Ongoing studies of oral platelet GP IIbIIIa receptor inhibitor

No ongoing trial was identified.

21 Excluded studies for oral platelet GP IIbIIIa receptor inhibitor

No trial was excluded.

References

Part V

Ticlopidine

22 Overview of ticlopidine

22.1 Included trials

Only one trial which randomized 38 patients was identified. In all, 1 randomized comparison concerned ticlopidine.
The detailed descriptions of trials and meta-analysis results is given in section 23 (page 95) for ticlopidine.

This trial included 38 patients and was published in 1985.
This trial was double blind in design.
It was reported in English language.
The table 22.1 (page 92) summmarizes the main characteristics of all the included trials. More detailed description is given in the following section.

22.2 Summary of meta-analysis results

The meta-analysis of the available trials about ticlopidine provide the results listed in tables 22.2 to 22.2 (page 93) and in the following graphs.

22.2.1 Ticlopidine

No significant difference was found between **ticlopidine** and **placebo** in terms of cardiovascular events (RR=0.81, 95% CI 0.02 to 38.71, p=0.9147, 1 trial), cardiovascular death (RR=0.81, 95% CI 0.02 to 38.71, p=0.9147, 1 trial), non vascular death (RR=0.81, 95% CI 0.02 to 38.71, p=0.9147, 1 trial), non fatal MI (RR=0.81, 95% CI 0.02 to 38.71, p=0.9147, 1 trial)and non fatal stroke (RR=0.81, 95% CI 0.02 to 38.71, p=0.9147, 1 trial).

Table 22.1: *Main study characteristics - ticlopidine*

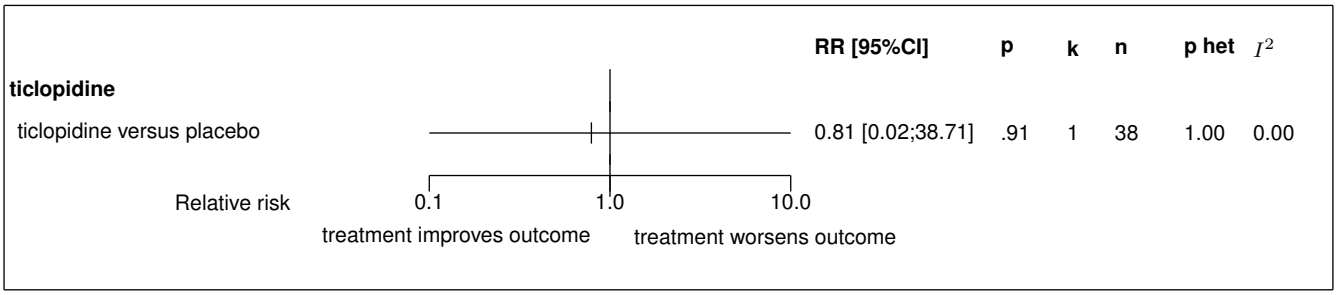
Trial	Patients	Treatments	Trial design and method
Ticlopidine			
Ticlopidine versus placebo			
Berglund, 1985 [1] n = 21 vs. 17	middle-aged men with stable incapacitating angina pectoris	ticlopidine 500 mg daily **versus** placebo	double blind parallel groups Primary endpoint: not defined

Table 22.2: *Summary of all results for ticlopidine*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
ticlopidine versus placebo						
cardiovascular events	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
cardiovascular death	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
non vascular death	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
non fatal MI	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
non fatal stroke	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38

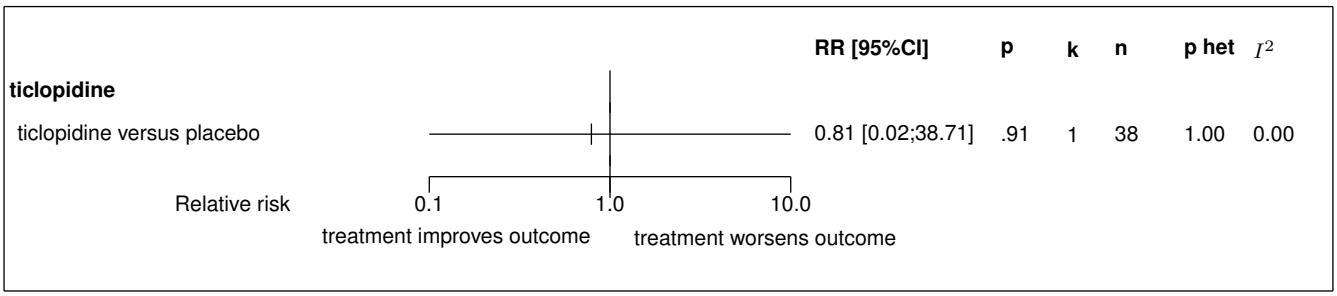
CI: confidence interval; p ass: p-value of association test; p het: p-value of the heterogeneity test; k: number of trials; n: total number of patients

Figure 22.1: *Forest's plot for cardiovascular events*



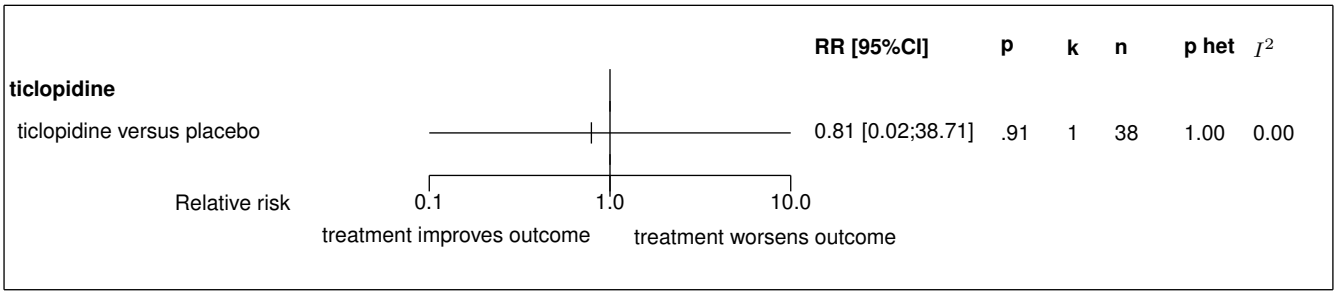
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 22.2: *Forest's plot for cardiovascular death*



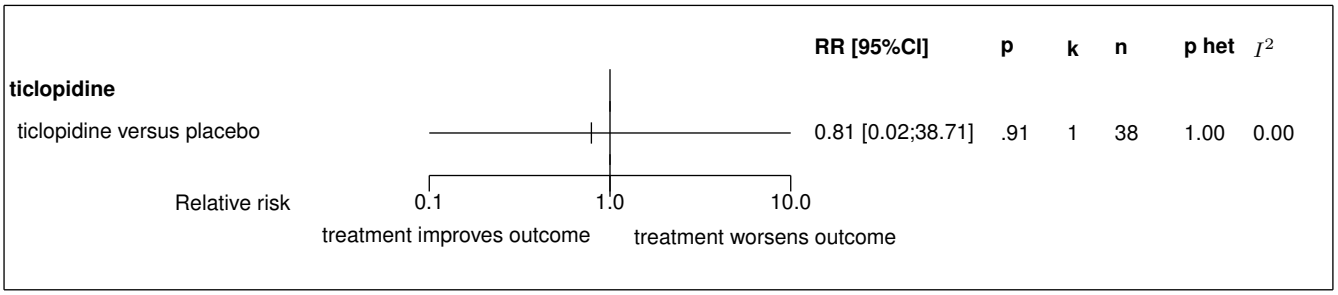
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 22.3: *Forest's plot for non vascular death*



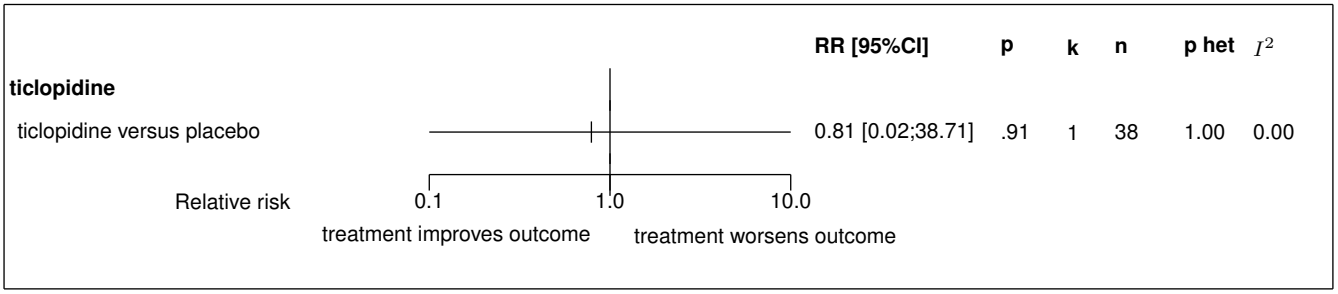
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 22.4: *Forest's plot for non fatal 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 22.5: *Forest's plot for non fatal stroke*



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

23 Details

23.1 Available trials

Only one trial which randomized 38 patients was identified: it compared ticlopidine with placebo.
This trial included 38 patients and was published in 1985.
This trial was double blind in design.
It was reported in English language.
Non vascular death data was reported in 1 trials; 1 trials reported data on cardiovascular death; 1 trials reported data on non fatal MI; 1 trials reported data on cardiovascular events; and 1 trials reported data on non fatal stroke.
Following tables 23.1 (page 95), 23.2 (page 95), 23.4 (page 96), and 23.3 (page 95) summarized the main characteristics of the trial including in this systematic review of randomized trials of ticlopidine.

Table 23.1: *Treatment description - ticlopidine - ticlopidine*

Trial	Studied treatment	Control treatment
Ticlopidine versus placebo		
Berglund (1985) [1]	ticlopidine 500 mg daily	placebo

Table 23.2: *Descriptions of participants - ticlopidine - ticlopidine*

Trial	Patients
Ticlopidine versus placebo	
Berglund (1985) [1]	Middle-aged men with stable incapacitating angina pectoris

Table 23.3: *Design and methodological quality of trials - ticlopidine - ticlopidine*

Trial	Design	Duration	Centre	Primary endpoint
Ticlopidine versus placebo				
Berglund, 1985 [1] n=38	parallel groups double blind exploratory trial	2m		not defined

Table 23.4: *Trial characteristics - ticlopidine - ticlopidine*

Trial
Ticlopidine versus placebo
Berglund, 1985 [1]

23.2 Meta-analysis results

The results are detailed in table 23.5 (page 97). This table is followed by the Forest's plot corresponding to each endpoint.

Ticlopidine versus placebo

The single study eligible for this comparison provided data on **cardiovascular events**. There was no statistically significant difference in cardiovascular events between ticlopidine and placebo, with a RR of 0.81 (95%CI 0.02 to 38.71, p=0.9147) in favour of ticlopidine. In other words, cardiovascular events was slightly lower in the ticlopidine group , but this was not statistically significant.
The single study eligible for this comparison provided data on **cardiovascular death**. No statistically significant difference between the groups was found in cardiovascular death, with a RR of 0.81 (95% CI 0.02 to 38.71, p=0.9147).
The single study eligible for this comparison provided data on **non vascular death**. No statistically significant difference between the groups was found in non vascular death, with a RR of 0.81 (95% CI 0.02 to 38.71, p=0.9147).
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 0.81 (95% CI 0.02 to 38.71, p=0.9147).
The single study eligible for this comparison provided data on **non fatal stroke**. No statistically significant difference between the groups was found in non fatal stroke, with a RR of 0.81 (95% CI 0.02 to 38.71, p=0.9147).

Table 23.5: *Results details - ticlopidine - ticlopidine*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
ticlopidine versus placebo						
cardiovascular events	RR=0.81	[0.02;38.71]	0.9147	1.0000 (I^2=0.00)	1	38
cardiovascular death	RR=0.81	[0.02;38.71]	0.9147	1.0000 (I^2=0.00)	1	38
non vascular death	RR=0.81	[0.02;38.71]	0.9147	1.0000 (I^2=0.00)	1	38
non fatal MI	RR=0.81	[0.02;38.71]	0.9147	1.0000 (I^2=0.00)	1	38
non fatal stroke	RR=0.81	[0.02;38.71]	0.9147	1.0000 (I^2=0.00)	1	38

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 23.1: *Forest's plot for cardiovascular events*

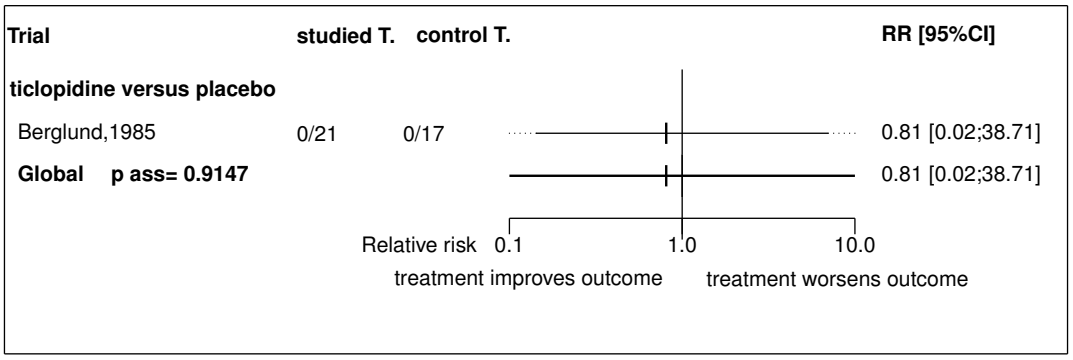


Figure 23.2: *Forest's plot for cardiovascular death*

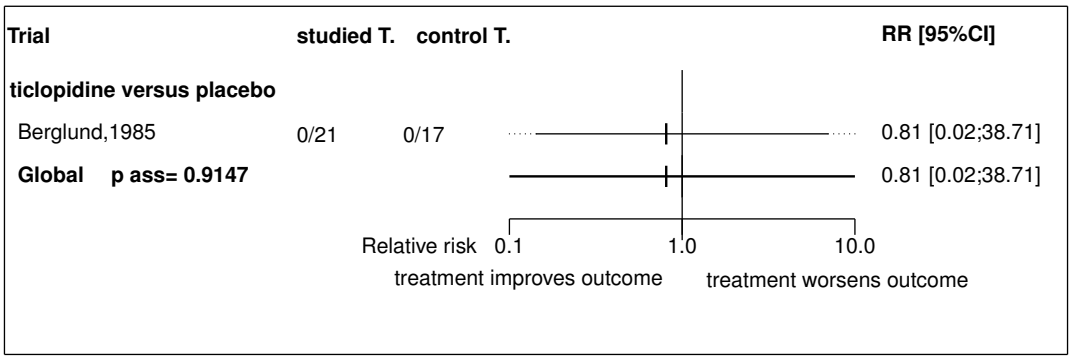


Figure 23.3: *Forest's plot for non vascular death*

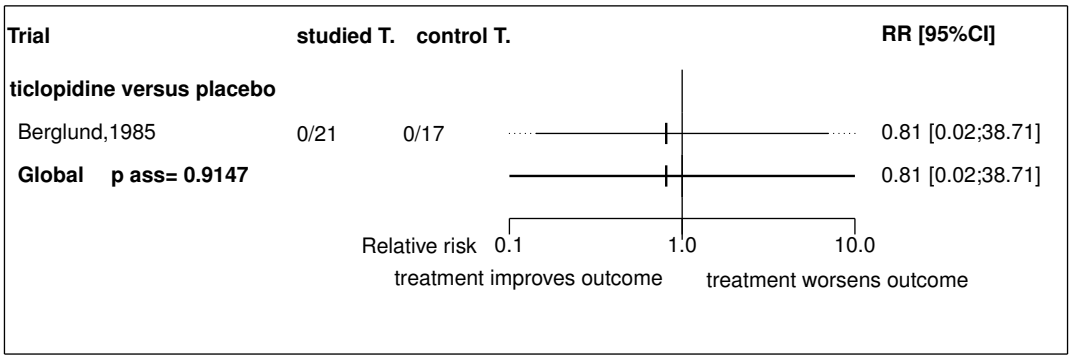


Figure 23.4: *Forest's plot for non fatal MI*

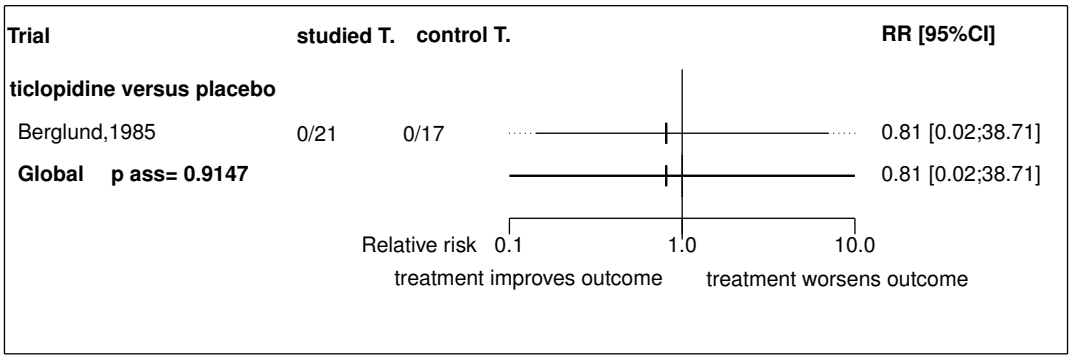
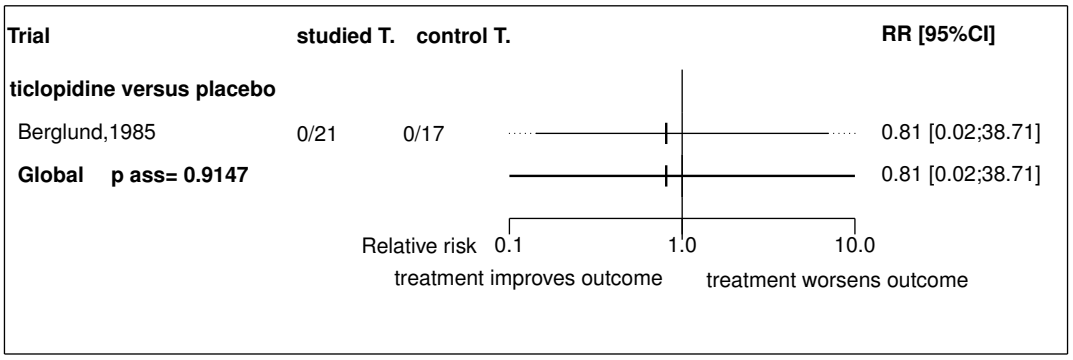


Figure 23.5: *Forest's plot for non fatal stroke*



References

[1] Berglund U, von Schenck H, Wallentin L. Effects of ticlopidine of platelet function in men with stable angina pectoris. Thromb Haemost 1985;54:808-12. [PMID=3911481]

23.3 Individual trial summaries

Table 23.6: *Berglund, 1985 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=38 (21 vs. 17) **Follow-up duration:** 2m **Study design:** Randomized controlled trial parallel groups Double blind Exploratory trial	Middle-aged men with stable incapacitating angina pectoris	**Studied treatment:** ticlopidine 500 mg daily **Control treatment:** placebo	

Reference

Berglund U, von Schenck H, Wallentin L. Effects of ticlopidine of platelet function in men with stable angina pectoris. Thromb Haemost 1985;54:808-12 [PMID=3911481]

24 Global meta-analysis: all ticlopidine

24.1 Global meta-analysis: all ticlopidine versus placebo

Table 24.1: *All ticlopidineversus placebo*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
cardiovascular events	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
cardiovascular death	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
non vascular death	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
non fatal MI	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38
non fatal stroke	RR=0.81	0.02;38.71	0.9147	1.0000 (0.00)	1	38

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

25 Ongoing studies of ticlopidine

No ongoing trial was identified.

26 Excluded studies for ticlopidine

No trial was excluded.

References