TrialResults-center.org

www.trialresultscenter.org

Antibiotics for stable angina

A systematic review and meta-analysis of randomized clinical trials

2017 - 7 - 1

Browse interactively these data at http://www.trialresultscenter.org/go-Q34

This report should be referenced as follows:
TrialResults-center.org; Results of all major randomized clinical trials about Antibiotics for stable angina.

Contents

0.1 Synthesis of the meta-analysis results

We found 12 trials concerning antibiotics.
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 12 trials (including 26,190 patients) were identified .
Among these comparisons, 6 trials are about Azithromycin,two about clarithromycin,one about Gatifloxacin and 3 about Roxithromycin.
No trial was excluded on grounds of potentially flawed methodology or incomplete presentation of results. No ongoing trial was found.

Azithromycin

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

Table 1: *Results summary - Azithromycin*

Benefit	Harmful	No evidence
	Azithromycin versus placebo	
		→ acute coronary syndrome RR=0.96^{NS} [0.85;1.08] k=5 → myocardial infarction (fatal and non fatal) RR=0.97^{NS} [0.83;1.13] k=4 → all cause death RR=1.01^{NS} [0.90;1.15] k=6

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

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

Clarithromycin

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

Table 2: *Results summary - Clarithromycin*

Benefit	Harmful	No evidence
	Clarithromycin versus placebo	
	↑ cardiovascular events RR=1.17* [1.02;1.35] k=1	→ acute coronary syndrome RR=0.70^{NS} [0.26;1.86] H k=2 → myocardial infarction (fatal and non fatal) RR=0.52^{NS} [0.19;1.37] k=1 → coronary event RR=1.14^{NS} [0.99;1.31] k=1 → all cause death RR=1.17^{NS} [0.95;1.43] k=2

continued...

Benefit	Harmful	No evidence

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

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

Gatifloxacin

Results obtained with gatifloxacin for all the endpoints with data in at least one trial are summarized table 3.

Table 3: *Results summary - Gatifloxacin*

Benefit	Harmful	No evidence
	Gatifloxacin versus placebo	
		→ acute coronary syndrome RR=0.94^{NS} [0.79;1.11] k=1 → myocardial infarction (fatal and non fatal) RR=0.89^{NS} [0.72;1.12] k=1 → all cause death RR=1.28^{NS} [0.89;1.84] 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)

Roxithromycin

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

Table 4: *Results summary - Roxithromycin*

Benefit	Harmful	No evidence
	Roxithromycin versus placebo	
		→ acute coronary syndrome RR=0.78^{NS} [0.34;1.77] k=3 → myocardial infarction (fatal and non fatal) RR=1.24^{NS} [0.20;7.56] H k=3 → coronary event RR=1.20^{NS} [0.96;1.51] k=1 → all cause death RR=1.08^{NS} [0.66;1.79] k=3

* 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 antibiotics for the treatment of stable angina in all type of patient.

1.2 Search strategy

The search aimed to identify all randomized clinical trials relating to the clinical effectiveness of antibiotics 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 antibiotics was used.

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

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, Acute coronary syndrome, myocardial infarction (fatal and non fatal), Coronary event, cardiovascular events, .

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 antibiotics,

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 antibiotics

2.1 Included trials

A total of 12 randomized comparisons which enrolled 26190 patients were identified. In all, 6 randomized comparisons concerned Azithromycin , two clarithromycin , one Gatifloxacin and 3 Roxithromycin.
The detailed descriptions of trials and meta-analysis results is given in section 3 (page 19) for Azithromycin, in section 4 (page 32) for clarithromycin, in section 5 (page 41) for Gatifloxacin and in section 6 (page 47) for Roxithromycin.

The average study size was 2182 patients (range 60 to 7747). The first study was published in 1997, and the last study was published in 2006.
All trials were double blind 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 antibiotics provide the results listed in tables 2.2 to 2.5 (page 15) and in the following graphs.

2.2.1 Azithromycin

No significant difference was found between **Azithromycin** and **placebo** in terms of acute coronary syndrome (RR=0.96, 95% CI 0.85 to 1.08, p=0.5253, 5 trials), myocardial infarction (fatal and non fatal) (RR=0.97, 95% CI 0.83 to 1.13, p=0.6964, 4 trials)and all cause death (RR=1.01, 95% CI 0.90 to 1.15, p=0.8144, 6 trials).

2.2.2 Clarithromycin

Clarithromycin was inferior to **placebo** in terms of cardiovascular events (RR=1.17, 95% CI 1.02 to 1.35, p=0.0267, 1 trial). No significant difference was found on acute coronary syndrome (RR=0.70, 95% CI 0.26 to 1.86, p=0.4696, 2 trials)with a random effect model in reason of a heterogeneity (Het. p=0.0044)(RR=0.52, 95% CI 0.19 to 1.37, p=0.1850, 1 trial), coronary event (RR=1.14, 95% CI 0.99 to 1.31, p=0.0795, 1 trial)and all cause death (RR=1.17, 95% CI 0.95 to 1.43, p=0.1309, 2 trials).

2.2.3 Gatifloxacin

No significant difference was found between **Gatifloxacin** and **placebo** in terms of acute coronary syndrome (RR=0.94, 95% CI 0.79 to 1.11, p=0.4694, 1 trial), myocardial infarction (fatal and non fatal) (RR=0.89, 95% CI 0.72 to 1.12, p=0.3221, 1 trial)and all cause death (RR=1.28, 95% CI 0.89 to 1.84, p=0.1849, 1 trial).

2.2.4 Roxithromycin

No significant difference was found between **Roxithromycin** and **placebo** in terms of acute coronary syndrome (RR=0.78, 95% CI 0.34 to 1.77, p=0.5478, 3 trials), myocardial infarction (fatal and non fatal) (RR=1.24, 95% CI 0.20 to 7.56, p=0.8174, 3 trials)with a random effect model in reason of a heterogeneity (Het. p=0.0036)(RR=1.20, 95% CI 0.96 to 1.51, p=0.1107, 1 trial)and all cause death (RR=1.08, 95% CI 0.66 to 1.79, p=0.7520, 3 trials).

Table 2.1: *Main study characteristics - antibiotics*

Trial	Patients	Treatments	Trial design and method
Azithromycin			
Azithromycin versus placebo			
Gupta et al, 1997 [1] n = 43 vs. 41	male patients at least 6 mo from documented MI and with titers to Chlamydia pneumoniae >=1:64	azithromycin 500 mg/d for 3 d (28 received 1 course, 12 received 2 courses 3 mo apart) **versus** placebo	double blind parallel groups Primary endpoint: not defined
ACADEMIC, 1999 [2] n = 150 vs. 152	patients with CAD and C pneumoniae titers of >=1:16. Patients were at least 5 d from an MI	azithromycin 500 mg/d for 3 d then 500 mg/wk for 3 mo **versus** placebo	double blind parallel groups Primary endpoint: CV death, MI, stroke, unstable angina, revascularization
STAMINA (Azithromycin), 2002 [3] n = 111 vs. 107	patients with ACS	azithromycin 500 mg/d for 3 d plus omeprazole 20 mg 2/d for 1 wk plus metronidazole 400 mg 2/d for 1 wk **versus** placebo	double blind parallel groups Primary endpoint: not defined 4 centres, England
AZACS, 2003 [4] n = 2004 vs. 2008	patients with ACS	azithromycin 500 mg on day 1 followed by 250 mg/d for 4d **versus** placebo	double blind parallel groups Primary endpoint: death, MI, revascularization
WIZARD, 2003 [5] n = 3879 vs. 3868	patients with a history of MI of more than 6 weeks before and with C pneumoniae titers of >=1:16	azithromycin 600 mg/d for 3 d then 1/wk for 11 wk **versus** placebo	double blind parallel groups Primary endpoint: coronary events 271 centres, North America, Europe, Argentina, India
ACES, 2005 [6] n = 2004 vs. 2008	patients with stable CAD	azithromycin 600 mg/wk for 1 y **versus** placebo	double blind parallel groups Primary endpoint: coronary events 28 centres, US

continued...

Trial	Patients	Treatments	Trial design and method
Clarithromycin			
Clarithromycin versus placebo			
CLARIFY, 2001 [1] n = 74 vs. 74	patients with ACS	clarithromycin 500 mg/d for 85 d **versus** placebo	double blind parallel groups Primary endpoint: death, MI, unstable angina
CLARICOR, 2006 [2] n = 2172 vs. 2201	patients with adischarge diagnosis of myocardial infarction or angina pectoris	clarithromycin 500 mg/day **versus** placebo	double blind parallel groups Primary endpoint: death, MI, unstable angina 5 centres, Denmark
Gatifloxacin			
Gatifloxacin versus placebo			
PROVE-IT, 2005 [1] n = 2076 vs. 2086	patients hospitalized with ACS in the preceding 10 d	gatifloxacin 400 mg/d for 10 d/mo for 2y **versus** placebo	double blind parallel groups Primary endpoint: coronary events
Roxithromycin			
Roxithromycin versus placebo			
ROXIS, 1999 [1] n = 102 vs. 100	patients with documented history of CAD and ACS	roxithromycin 150 mg 2/d for 30 d **versus** placebo	double blind parallel groups
Leowattana et al, 2001 [2] n = 40 vs. 20	patients with ACS	roxithromycin 150 mg/d for 30 d **versus** placebo	parallel groups
ANTIBIO, 2003 [3] n = 433 vs. 437	patients with unstable angina or MI	roxithromycin 300 mg/d for 6 wk **versus** placebo	double blind parallel groups Primary endpoint: all cause death

Table 2.2: *Summary of all results for Azithromycin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
Azithromycin versus placebo						
acute coronary syndrome	RR=0.96	0.85;1.08	0.5253	0.6916 (0.00)	5	12338
myocardial infarction (fatal and non fatal)	RR=0.97	0.83;1.13	0.6964	0.7549 (0.00)	4	13475
all cause death	RR=1.01	0.90;1.15	0.8144	0.9130 (0.00)	6	13754

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 clarithromycin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
clarithromycin versus placebo						
acute coronary syndrome	RR=0.70 [1]	0.26;1.86	0.4696	0.0044 (0.88) †	2	4521
cardiovascular events	RR=1.17	1.02;1.35	0.0267	1.0000 (0.00)	1	4373
myocardial infarction (fatal and non fatal)	RR=0.52	0.19;1.37	0.1850	1.0000 (1.00)	1	181
coronary event	RR=1.14	0.99;1.31	0.0795	1.0000 (0.00)	1	4373
all cause death	RR=1.17	0.95;1.43	0.1309	0.7971 (0.00)	2	4521

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 Gatifloxacin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
Gatifloxacin versus placebo						
acute coronary syndrome	RR=0.94	0.79;1.11	0.4694	1.0000 (0.00)	1	4162
myocardial infarction (fatal and non fatal)	RR=0.89	0.72;1.12	0.3221	1.0000 (0.00)	1	4162
all cause death	RR=1.28	0.89;1.84	0.1849	1.0000 (0.00)	1	4152

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

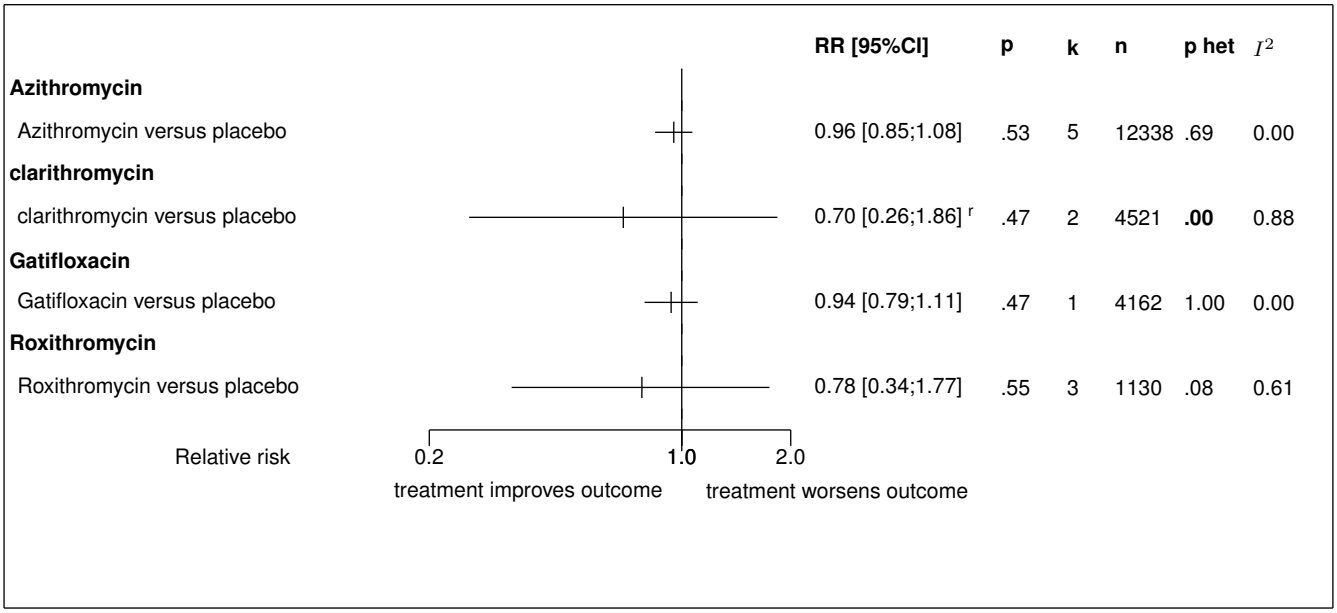
[1] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=0.99 95% CI 0.81;1.22

Table 2.5: *Summary of all results for Roxithromycin*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
Roxithromycin versus placebo						
acute coronary syndrome	RR=0.78	0.34;1.77	0.5478	0.0783 (0.61)	3	1130
myocardial infarction (fatal and non fatal)	RR=1.24 [2]	0.20;7.56	0.8174	0.0036 (0.82) †	3	1491
coronary event	RR=1.20	0.96;1.51	0.1107	1.0000 (0.00)	1	868
all cause death	RR=1.08	0.66;1.79	0.7520	0.9938 (0.00)	3	1156

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

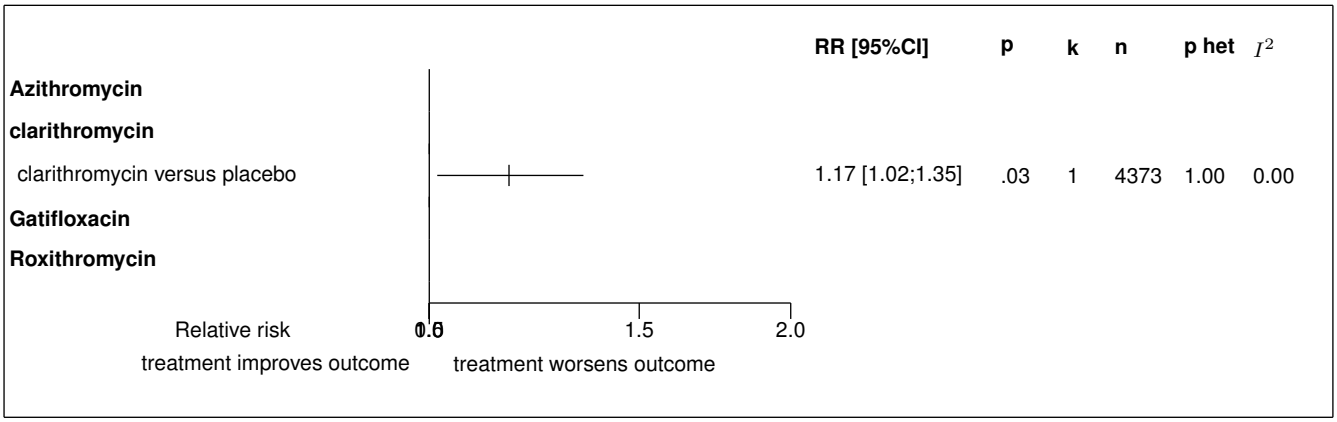
Figure 2.1: *Forest's plot for acute coronary syndrome*



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

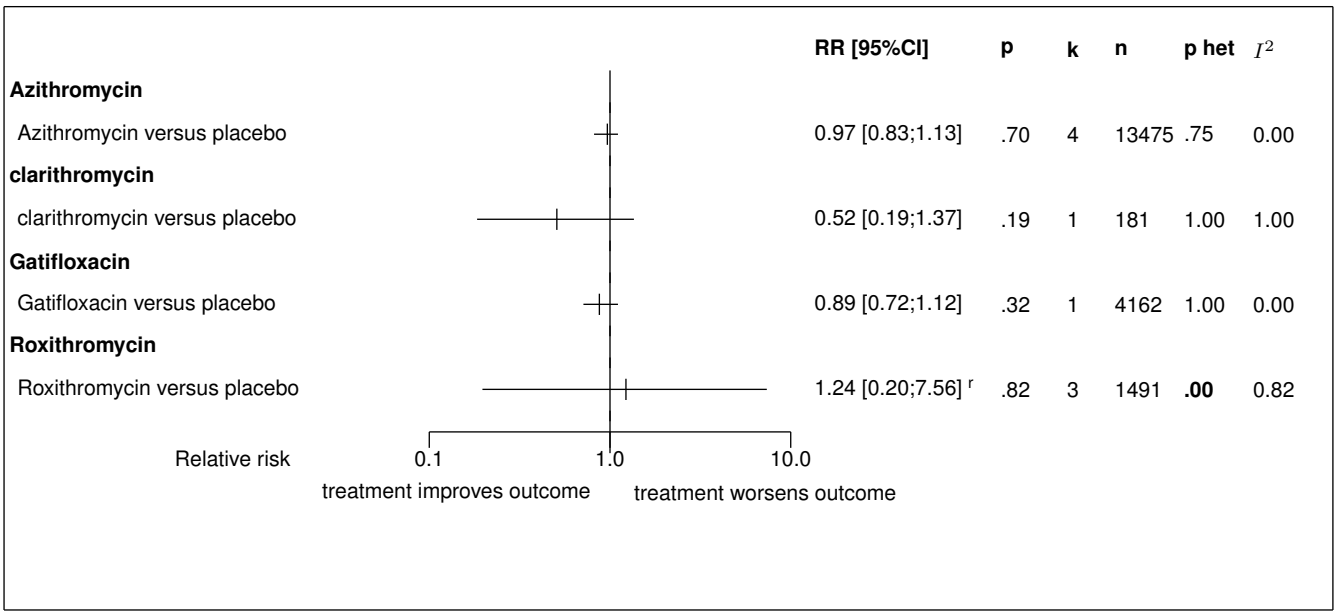
[2] with a random model ($\tau^2 = NaN$). The results with a fixed effect model was RRFE=1.19 95% CI 0.71;1.98

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



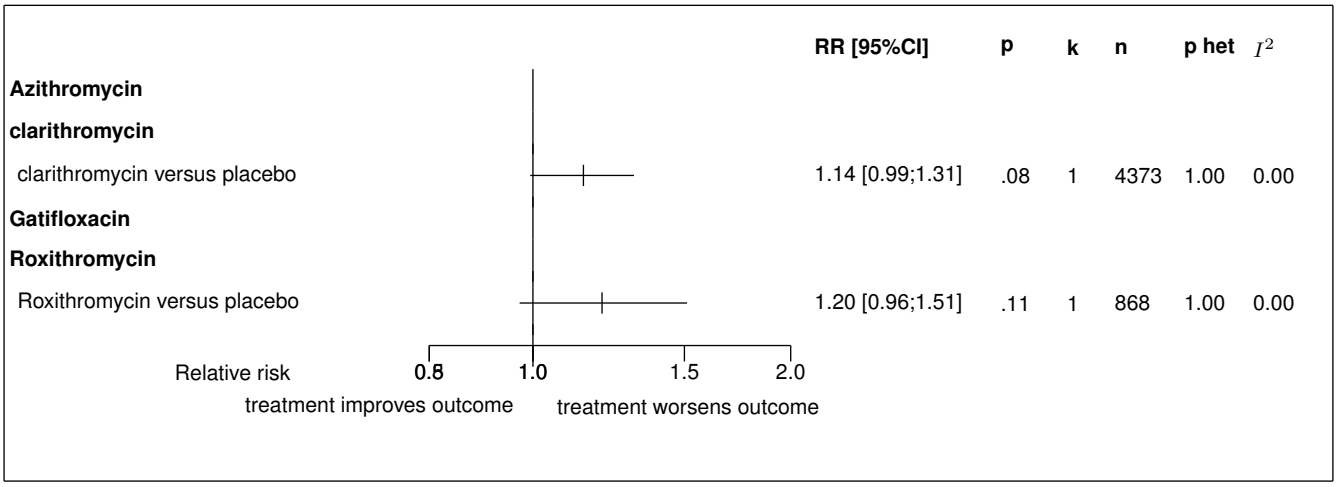
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 2.3: *Forest's plot for myocardial infarction (fatal and non fatal)*



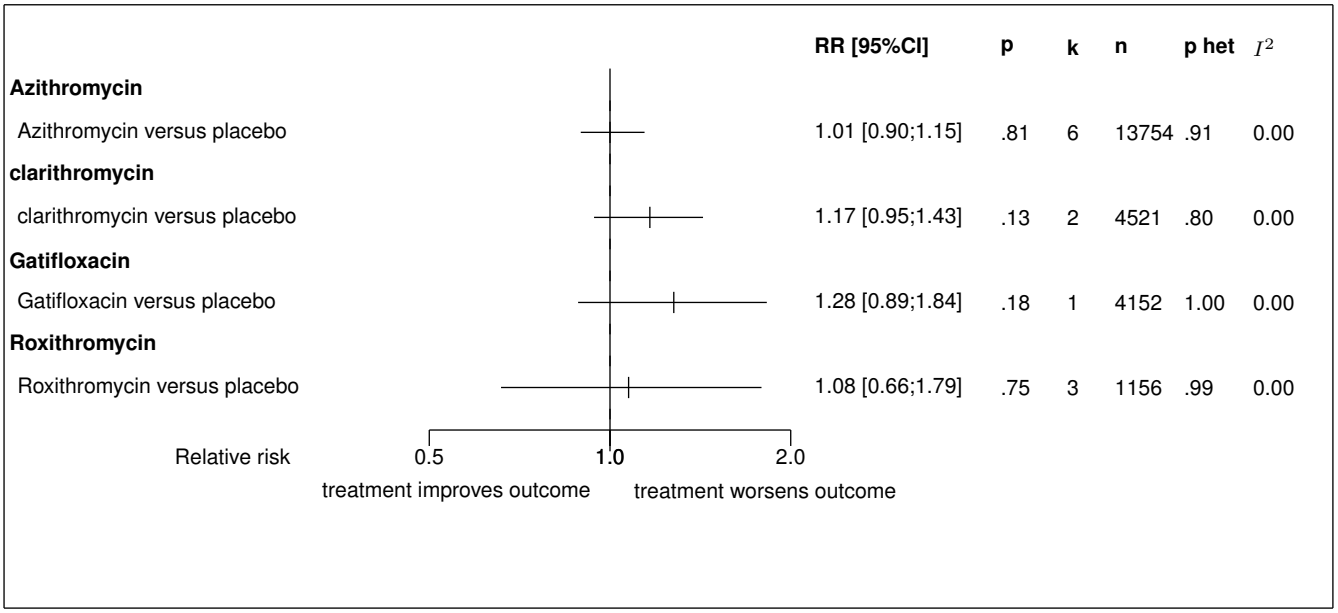
Results obtained with a fixed effect model except in case of heterogenity where a random model was used
RR: relative risk; 95% CI: 95% confidence interval; p: p-value of the association test; k: number of trials; n: total number of patients involving in the pooled trials; p het: p-value of the hetereogenity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

Figure 2.4: *Forest's plot for coronary 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

Figure 2.5: *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 Azithromycin

3.1 Available trials

A total of 6 RCTs which randomized 16375 patients were identified: all compared Azithromycin with placebo.
The average study size was 2729 patients (range 84 to 7747). The first study was published in 1997, and the last study was published in 2005.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
All cause death data was reported in 6 trials; 5 trials reported data on acute coronary syndrome; and 4 trials reported data on myocardial infarction (fatal and non fatal).
Following tables 3.1 (page 19), 3.2 (page 19), 3.4 (page 21), and 3.3 (page 20) summarized the main characteristics of the trials including in this systematic review of randomized trials of Azithromycin.

Table 3.1: *Treatment description - antibiotics - Azithromycin*

Trial	Studied treatment	Control treatment
Azithromycin versus placebo		
Gupta et al (1997) [1]	Azithromycin 500 mg/d for 3 d (28 received 1 course, 12 received 2 courses 3 mo apart)	placebo
ACADEMIC (1999) [2]	Azithromycin 500 mg/d for 3 d then 500 mg/wk for 3 mo	placebo
STAMINA (Azithromycin) (2002) [3]	Azithromycin 500 mg/d for 3 d plus omeprazole 20 mg 2/d for 1 wk plus metronidazole 400 mg 2/d for 1 wk	placebo
AZACS (2003) [4]	Azithromycin 500 mg on day 1 followed by 250 mg/d for 4d	placebo
WIZARD (2003) [5]	Azithromycin 600 mg/d for 3 d then 1/wk for 11 wk	placebo
ACES (2005) [6]	Azithromycin 600 mg/wk for 1 y	placebo

Table 3.2: *Descriptions of participants - antibiotics - Azithromycin*

Trial	Patients
Azithromycin versus placebo	
Gupta et al (1997) [1]	Male patients at least 6 mo from documented MI and with titers to Chlamydia pneumoniae >=1:64

continued...

Trial	Patients
ACADEMIC (1999) [2]	Patients with CAD and C pneumoniae titers of >=1:16. Patients were at least 5 d from an MI
STAMINA (Azithromycin) (2002) [3]	Patients with ACS
AZACS (2003) [4]	Patients with ACS
WIZARD (2003) [5]	Patients with a history of MI of more than 6 weeks before and with C pneumoniae titers of >=1:16
ACES (2005) [6]	Patients with stable CAD

Table 3.3: *Design and methodological quality of trials - antibiotics - Azithromycin*

Trial	Design	Duration	Centre	Primary endpoint
Azithromycin versus placebo				
Gupta et al, 1997 [1] n=84	Parallel groups double blind	18mo		not defined
ACADEMIC, 1999 [2] n=302	Parallel groups double blind	2y		CV death, MI, stroke, unstable angina, revascularization
STAMINA (Azithromycin), 2002 [3] n=218	Parallel groups double blind confirmatory trial at low risk of bias	1y	England 4 centres	not defined
AZACS, 2003 [4] n=4012	Parallel groups double blind	6mo		death, MI, revascularization
WIZARD, 2003 [5] n=7747	Parallel groups double blind	14mo	North America, Europe, Argentina, India 271 centres	coronary events
ACES, 2005 [6] n=4012	Parallel groups double blind	4y	US 28 centres	coronary events

Table 3.4: *Trial characteristics - antibiotics - Azithromycin*

Trial
Azithromycin versus placebo
Gupta et al, 1997 [1]
ACADEMIC, 1999 [2]
STAMINA (Azithromycin), 2002 [3]
AZACS, 2003 [4]
WIZARD, 2003 [5]
ACES, 2005 [6]

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.

Azithromycin versus placebo

A total of 5 of the 6 studies eligible for this comparison provided data on **acute coronary syndrome**. There was no statistically significant difference in acute coronary syndrome between azithromycin and placebo, with a RR of 0.96 (95%CI 0.85 to 1.08, p=0.5253) in favour of azithromycin. In other words, acute coronary syndrome was slightly lower in the azithromycin group , but this was not statistically significant. No heterogeneity was detected (p = 0.6916, I^2 = 0.00%).
A total of 4 of the 6 studies eligible for this comparison provided data on **myocardial infarction (fatal and non fatal)**. When pooled together, there was no statistically significant difference between the groups in myocardial infarction (fatal and non fatal), with a RR of 0.97 (95% CI 0.83 to 1.13, p=0.6964). No heterogeneity was detected (p = 0.7549, I^2 = 0.00%).
All the 6 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 1.01 (95% CI 0.90 to 1.15, p=0.8144). No heterogeneity was detected (p = 0.9130, I^2 = 0.00%).

Table 3.5: *Results details - antibiotics - Azithromycin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
Azithromycin versus placebo						
acute coronary syndrome	RR=0.96	[0.85;1.08]	0.5253	0.6916 (I^2=0.00)	5	12338
myocardial infarction (fatal and non fatal)	RR=0.97	[0.83;1.13]	0.6964	0.7549 (I^2=0.00)	4	13475
all cause death	RR=1.01	[0.90;1.15]	0.8144	0.9130 (I^2=0.00)	6	13754

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 acute coronary syndrome*

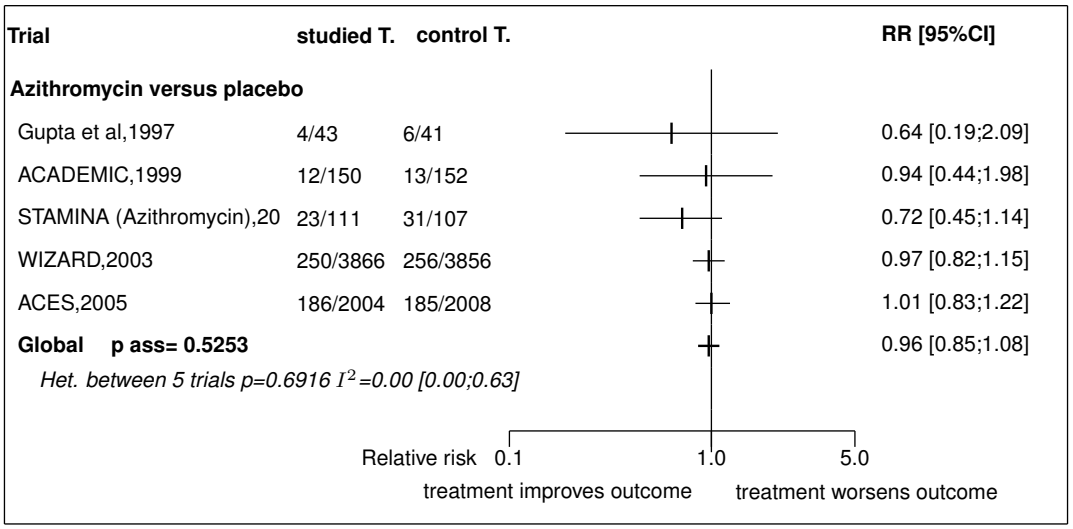


Figure 3.2: *Forest's plot for myocardial infarction (fatal and non fatal)*

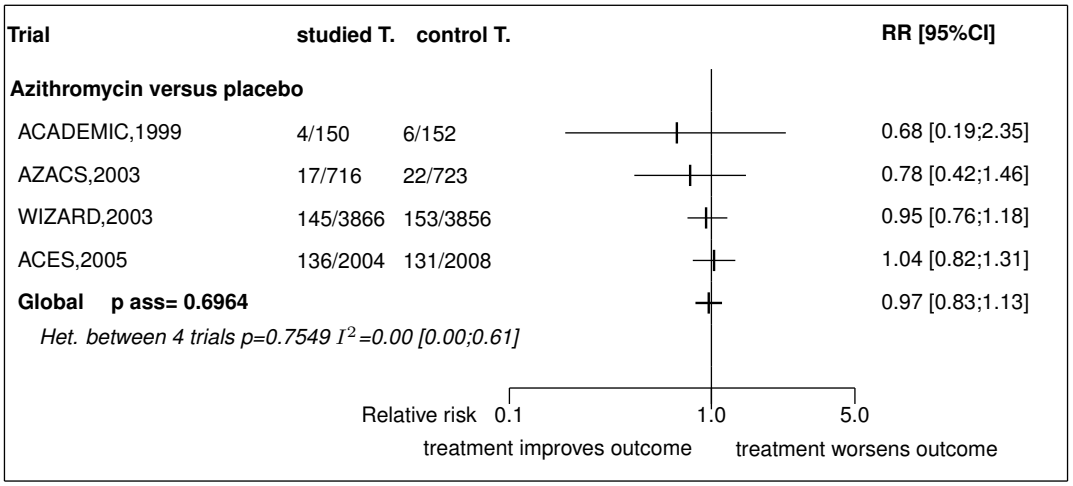
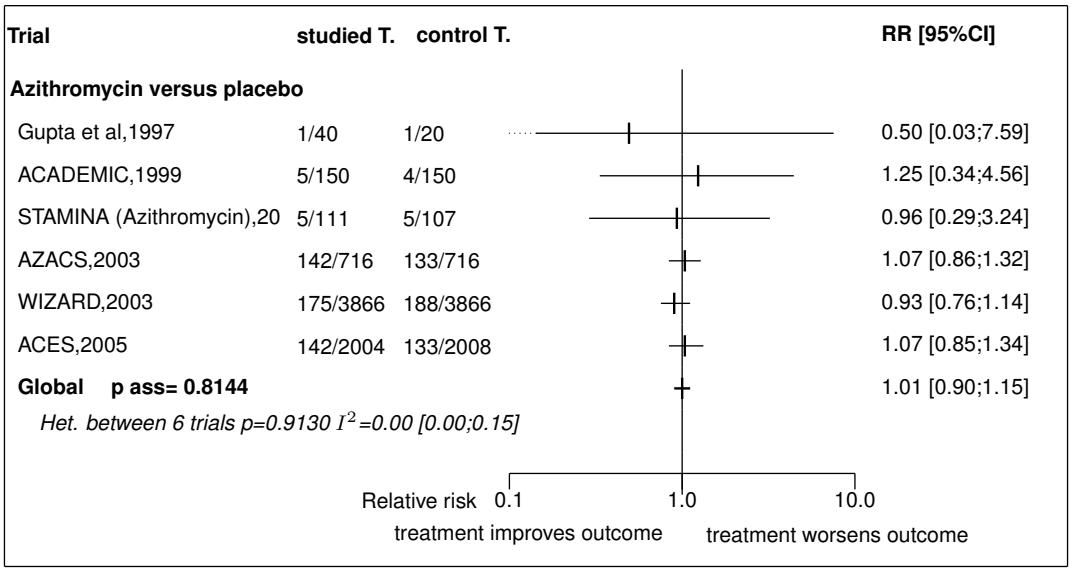


Figure 3.3: *Forest's plot for all cause death*



References

[1] Gupta S, Leatham EW, Carrington D, Mendall MA, Kaski JC, Camm AJ. Elevated Chlamydia pneumoniae antibodies, cardiovascular events, and azithromycin in male survivors of myocardial infarction. Circulation 1997 Jul 15;96:404-7. [PMID=9244203]

[2] Muhlestein JB, Anderson JL, Carlquist JF, Salunkhe K, Horne BD, Pearson RR, Bunch TJ, Allen A, Trehan S, Nielson C. Randomized secondary prevention trial of azithromycin in patients with coronary artery disease: primary clinical results of the ACADEMIC study. Circulation 2000 Oct 10;102:1755-60. [PMID=11023928]

[3] Stone AF, Mendall MA, Kaski JC, Edger TM, Risley P, Poloniecki J, Camm AJ, Northfield TC. Effect of treatment for Chlamydia pneumoniae and Helicobacter pylori on markers of inflammation and cardiac events in patients with acute coronary syndromes: South Thames Trial of Antibiotics in Myocardial Infarction and Unstable Angina (STAMINA). Circulation 2002 Sep 3;106:1219-23. [PMID=12208796]

[4] Cercek B, Shah PK, Noc M, Zahger D, Zeymer U, Matetzky S, Maurer G, Mahrer P. Effect of short-term treatment with azithromycin on recurrent ischaemic events in patients with acute coronary syndrome in the Azithromycin in Acute Coronary Syndrome (AZACS) trial: a randomised controlled trial. Lancet 2003 Mar 8;361:809-13. [PMID=12642046]

[5] O'Connor CM, Dunne MW, Pfeffer MA, Muhlestein JB, Yao L, Gupta S, Benner RJ, Fisher MR, Cook TD. Azithromycin for the secondary prevention of coronary heart disease events: the WIZARD study: a randomized controlled trial. JAMA 2003 Sep 17;290:1459-66. [PMID=13129985]

[6] Grayston JT, Kronmal RA, Jackson LA, Parisi AF, Muhlestein JB, Cohen JD, Rogers WJ, Crouse JR, Borrowdale SL, Schron E, Knirsch C. Azithromycin for the secondary prevention of coronary events. N Engl J Med 2005 Apr 21;352:1637-45. [PMID=15843666]

3.3 Individual trial summaries

Table 3.6: *Gupta et al, 1997 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=84 (43 vs. 41) **Follow-up duration:** 18mo **Study design:** Randomized controlled trial Parallel groups Double blind	Male patients at least 6 mo from documented MI and with titers to Chlamydia pneumoniae >=1:64	**Studied treatment:** Azithromycin 500 mg/d for 3 d (28 received 1 course, 12 received 2 courses 3 mo apart) **Control treatment:** placebo	Acute coronary syndrome RR=0.64 [0.19;2.09] All cause death RR=0.50 [0.03;7.59]

Reference

Gupta S, Leatham EW, Carrington D, Mendall MA, Kaski JC, Camm AJ. Elevated Chlamydia pneumoniae antibodies, cardiovascular events, and azithromycin in male survivors of myocardial infarction. Circulation 1997 Jul 15;96:404-7 [PMID=9244203]

Table 3.7: *ACADEMIC, 1999 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=302 (150 vs. 152) **Follow-up duration:** 2y **Study design:** Randomized controlled trial Parallel groups Double blind	Patients with CAD and C pneumoniae titers of >=1:16. Patients were at least 5 d from an MI	**Studied treatment:** Azithromycin 500 mg/d for 3 d then 500 mg/wk for 3 mo **Control treatment:** placebo	Acute coronary syndrome RR=0.94 [0.44;1.98] Myocardial infarction (fatal and non fatal) RR=0.68 [0.19;2.35] All cause death RR=1.25 [0.34;4.56]

Reference

Muhlestein JB, Anderson JL, Carlquist JF, Salunkhe K, Horne BD, Pearson RR, Bunch TJ, Allen A, Trehan S, Nielson C. Randomized secondary prevention trial of azithromycin in patients with coronary artery disease: primary clinical results of the ACADEMIC study. Circulation 2000 Oct 10;102:1755-60 [PMID=11023928]

Table 3.8: *STAMINA (Azithromycin), 2002 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=218 (111 vs. 107) **Follow-up duration:** 1y **Study design:** Randomized controlled trial Parallel groups Double blind Confirmatory trial at low risk of bias England, 4 centres	Patients with ACS	**Studied treatment:** Azithromycin 500 mg/d for 3 d plus omeprazole 20 mg 2/d for 1 wk plus metronidazole 400 mg 2/d for 1 wk **Control treatment:** placebo	Acute coronary syndrome RR=0.72 [0.45;1.14] All cause death RR=0.96 [0.29;3.24]

Reference

Stone AF, Mendall MA, Kaski JC, Edger TM, Risley P, Poloniecki J, Camm AJ, Northfield TC. Effect of treatment for Chlamydia pneumoniae and Helicobacter pylori on markers of inflammation and cardiac events in patients with acute coronary syndromes: South Thames Trial of Antibiotics in Myocardial Infarction and Unstable Angina (STAMINA). Circulation 2002 Sep 3;106:1219-23 [PMID=12208796]

Table 3.9: *AZACS, 2003 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=4012 (2004 vs. 2008) **Follow-up duration:** 6mo **Study design:** Randomized controlled trial Parallel groups Double blind	Patients with ACS	**Studied treatment:** Azithromycin 500 mg on day 1 followed by 250 mg/d for 4d **Control treatment:** placebo	Myocardial infarction (fatal and non fatal) RR=0.78 [0.42;1.46] All cause death RR=1.07 [0.86;1.32]

Reference

Cercek B, Shah PK, Noc M, Zahger D, Zeymer U, Matetzky S, Maurer G, Mahrer P. Effect of short-term treatment with azithromycin on recurrent ischaemic events in patients with acute coronary syndrome in the Azithromycin in Acute Coronary Syndrome (AZACS) trial: a randomised controlled trial. Lancet 2003 Mar 8;361:809-13 [PMID=12642046]

Table 3.10: *WIZARD, 2003 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=7747 (3879 vs. 3868) **Follow-up duration:** 14mo **Study design:** Randomized controlled trial Parallel groups Double blind North America, Europe, Argentina, India, 271 centres	Patients with a history of MI of more than 6 weeks before and with C pneumoniae titers of >=1:16	**Studied treatment:** Azithromycin 600 mg/d for 3 d then 1/wk for 11 wk **Control treatment:** placebo	Acute coronary syndrome RR=0.97 [0.82;1.15] Myocardial infarction (fatal and non fatal) RR=0.95 [0.76;1.18] All cause death RR=0.93 [0.76;1.14]

Reference

O'Connor CM, Dunne MW, Pfeffer MA, Muhlestein JB, Yao L, Gupta S, Benner RJ, Fisher MR, Cook TD. Azithromycin for the secondary prevention of coronary heart disease events: the WIZARD study: a randomized controlled trial. JAMA 2003 Sep 17;290:1459-66 [PMID=13129985]

Table 3.11: *ACES, 2005 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=4012 (2004 vs. 2008) **Follow-up duration:** 4y **Study design:** Randomized controlled trial Parallel groups Double blind US, 28 centres	Patients with stable CAD	**Studied treatment:** Azithromycin 600 mg/wk for 1 y **Control treatment:** placebo	Acute coronary syndrome RR=1.01 [0.83;1.22] Myocardial infarction (fatal and non fatal) RR=1.04 [0.82;1.31] All cause death RR=1.07 [0.85;1.34]

Reference

Grayston JT, Kronmal RA, Jackson LA, Parisi AF, Muhlestein JB, Cohen JD, Rogers WJ, Crouse JR, Borrowdale SL, Schron E, Knirsch C. Azithromycin for the secondary prevention of coronary events. N Engl J Med 2005 Apr 21;352:1637-45 [PMID=15843666]

4 Detailed results for clarithromycin

4.1 Available trials

A total of 2 RCTs which randomized 4521 patients were identified: all compared clarithromycin with placebo.
The average study size was 2260 patients (range 148 to 4373). The first study was published in 2001, and the last study was published in 2006.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
Acute coronary syndrome data was reported in 2 trials; 2 trials reported data on all cause death; 1 trials reported data on cardiovascular events; 1 trials reported data on coronary event; and 1 trials reported data on myocardial infarction (fatal and non fatal).
Following tables 4.1 (page 32), 4.2 (page 32), 4.4 (page 34), and 4.3 (page 33) summarized the main characteristics of the trials including in this systematic review of randomized trials of clarithromycin.

Table 4.1: *Treatment description - antibiotics - clarithromycin*

Trial	Studied treatment	Control treatment
Clarithromycin versus placebo		
CLARIFY (2001) [1]	Clarithromycin 500 mg/d for 85 d	placebo
CLARICOR (2006) [2]	clarithromycin 500 mg/day	placebo

Table 4.2: *Descriptions of participants - antibiotics - clarithromycin*

Trial	Patients
Clarithromycin versus placebo	
CLARIFY (2001) [1]	Patients with ACS
CLARICOR (2006) [2]	Patients with adischarge diagnosis of myocardial infarction or angina pectoris

Table 4.3: *Design and methodological quality of trials - antibiotics - clarithromycin*

Trial	Design	Duration	Centre	Primary endpoint
Clarithromycin versus placebo				
CLARIFY, 2001 [1] n=148	Parallel groups double blind	1y		death, MI, unstable angina
CLARICOR, 2006 [2] n=4373	Parallel groups double blind confirmatory trial at low risk of bias	3 years inclusion period: oct 1999 - apr 2000	Denmark 5 centres	death, MI, unstable angina

Table 4.4: *Trial characteristics - antibiotics - clarithromycin*

Trial
Clarithromycin versus placebo
CLARIFY, 2001 [1]
CLARICOR, 2006 [2]

4.2 Meta-analysis results

The results are detailed in table 4.5 (page 35). This table is followed by the Forest's plot corresponding to each endpoint.

Clarithromycin versus placebo

All the 2 studies had extractable data about the number of participants with **acute coronary syndrome**. There was no statistically significant difference in acute coronary syndrome between clarithromycin and placebo, with a RR of 0.70 (95%CI 0.26 to 1.86, p=0.4696) in favour of clarithromycin. In other words, acute coronary syndrome was slightly lower in the clarithromycin group , but this was not statistically significant. A random effect model was used because there was a substantial statistical heterogeneity detected between the studies (p = 0.0044, I^2 = 0.88%).
Only one of the 2 studies eligible for this comparison provided data on **cardiovascular events**. The analysis detected a statistically significant difference in favor of placebo in cardiovascular events, with a RR of 1.17 (95% CI 1.02 to 1.35, p=0.0267).
Only one of the 2 studies eligible for this comparison provided data on **myocardial infarction (fatal and non fatal)**. No statistically significant difference between the groups was found in myocardial infarction (fatal and non fatal), with a RR of 0.52 (95% CI 0.19 to 1.37, p=0.1850).
Only one of the 2 studies eligible for this comparison provided data on **coronary event**. No statistically significant difference between the groups was found in coronary event, with a RR of 1.14 (95% CI 0.99 to 1.31, p=0.0795).
All the 2 studies had extractable data about the number of participants with **all cause death**. When pooled together, there was no statistically significant difference between the groups in all cause death, with a RR of 1.17 (95% CI 0.95 to 1.43, p=0.1309). No heterogeneity was detected (p = 0.7971, I^2 = 0.00%).

Table 4.5: *Results details - antibiotics - clarithromycin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
clarithromycin versus placebo						
acute coronary syndrome	RR=0.70	[0.26;1.86]	0.4696	0.0044 (I^2=0.88)	2	4521
cardiovascular events	RR=1.17	[1.02;1.35]	0.0267	1.0000 (I^2=0.00)	1	4373
myocardial infarction (fatal and non fatal)	RR=0.52	[0.19;1.37]	0.1850	1.0000 (I^2=1.00)	1	181
coronary event	RR=1.14	[0.99;1.31]	0.0795	1.0000 (I^2=0.00)	1	4373
all cause death	RR=1.17	[0.95;1.43]	0.1309	0.7971 (I^2=0.00)	2	4521

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 4.1: *Forest's plot for acute coronary syndrome*

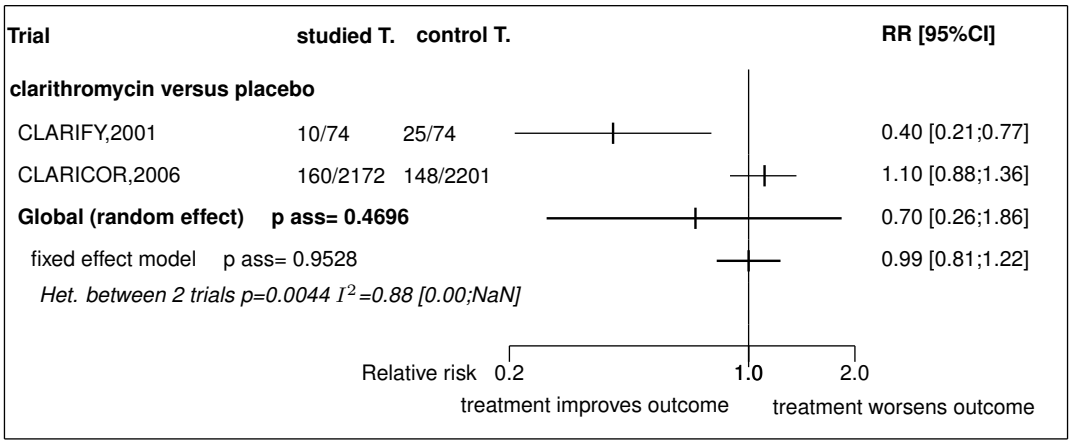


Figure 4.2: *Forest's plot for cardiovascular events*

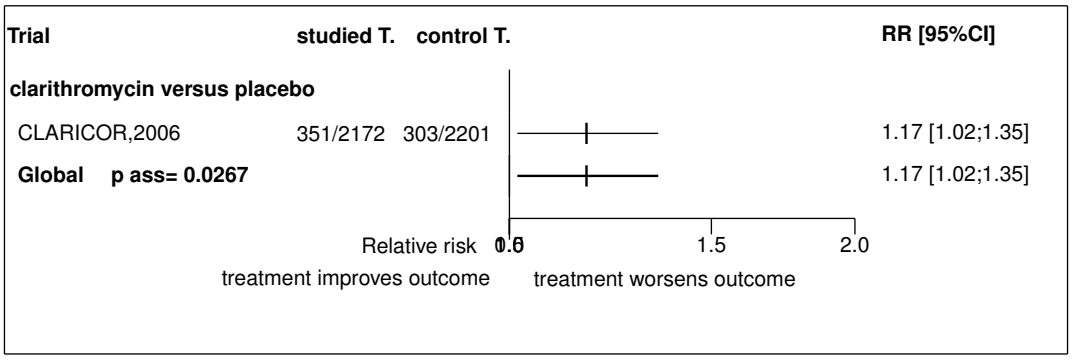


Figure 4.3: *Forest's plot for myocardial infarction (fatal and non fatal)*

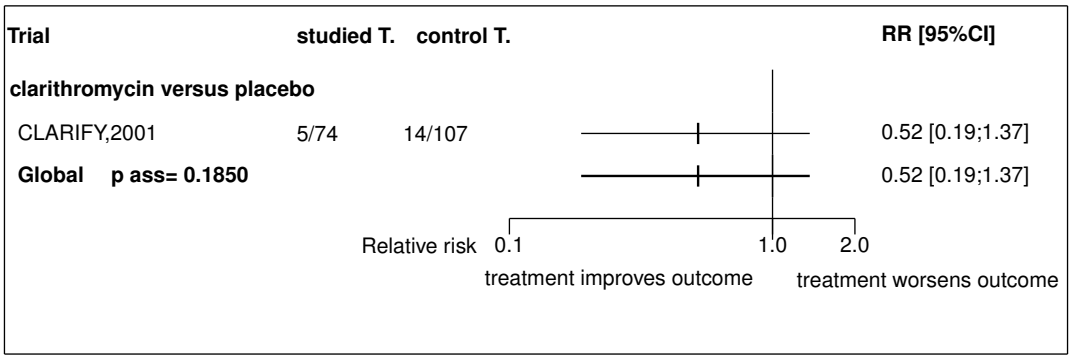


Figure 4.4: *Forest's plot for coronary event*

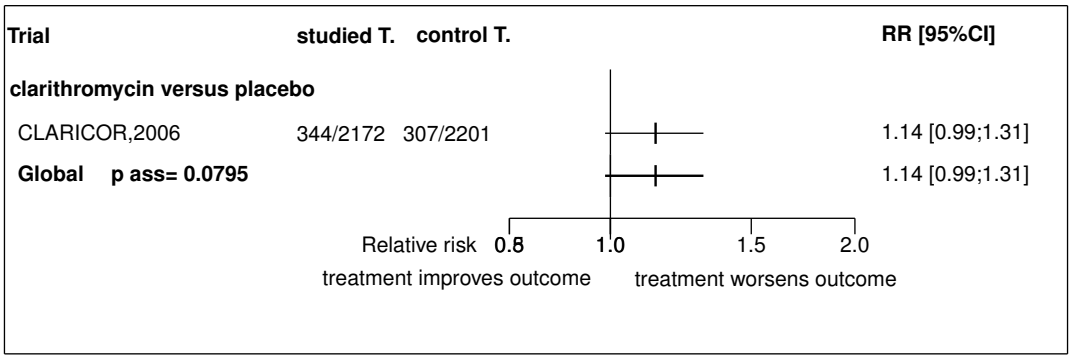
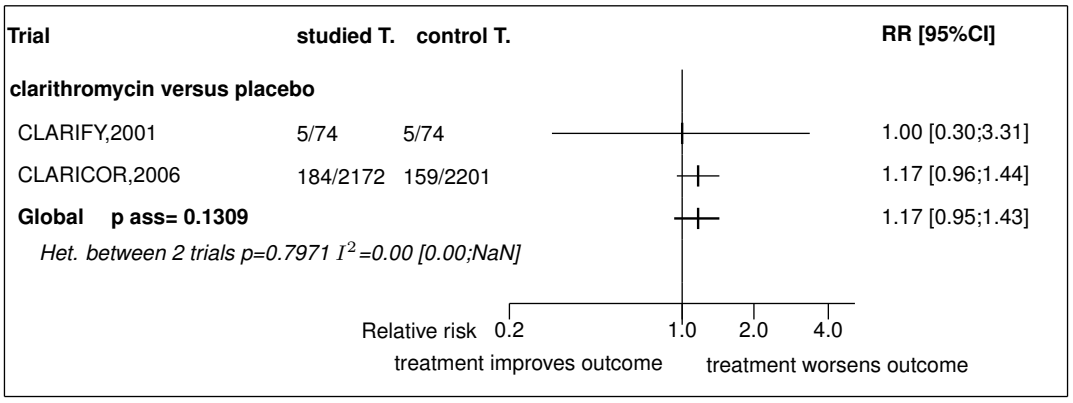


Figure 4.5: *Forest's plot for all cause death*



References

[1] Sinisalo J, Mattila K, Valtonen V, Anttonen O, Juvonen J, Melin J, Vuorinen-Markkola H, Nieminen MS. Effect of 3 months of antimicrobial treatment with clarithromycin in acute non-q-wave coronary syndrome. Circulation 2002 Apr 2;105:1555-60. [PMID=11927522]

[2] Jespersen CM, Als-Nielsen B, Damgaard M, Hansen JF, Hansen S, Hel OH, Hildebrandt P, Hilden J, Jensen GB, Kastrup J, Kolmos HJ, Kjller E, Lind I, Nielsen H, Petersen L, Gluud C. Randomised placebo controlled multicentre trial to assess short term clarithromycin for patients with stable coronary heart disease: CLARICOR trial. BMJ 2006 Jan 7;332:22-7. [PMID=16339220]

4.3 Individual trial summaries

Table 4.6: *CLARIFY, 2001 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=148 (74 vs. 74) **Follow-up duration:** 1y **Study design:** Randomized controlled trial Parallel groups Double blind	Patients with ACS	**Studied treatment:** Clarithromycin 500 mg/d for 85 d **Control treatment:** placebo	Acute coronary syndrome RR=0.40 [0.21;0.77] Myocardial infarction (fatal and non fatal) RR=0.52 [0.19;1.37] All cause death RR=1.00 [0.30;3.31]

Reference

Sinisalo J, Mattila K, Valtonen V, Anttonen O, Juvonen J, Melin J, Vuorinen-Markkola H, Nieminen MS. Effect of 3 months of antimicrobial treatment with clarithromycin in acute non-q-wave coronary syndrome. Circulation 2002 Apr 2;105:1555-60 [PMID=11927522]

Table 4.7: *CLARICOR, 2006 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=4373 (2172 vs. 2201) **Follow-up duration:** 3 years **Study design:** Randomized controlled trial Parallel groups Double blind Confirmatory trial at low risk of bias Denmark, 5 centres **Inclusion period:** oct 1999 - apr 2000	Patients with adischarge diagnosis of myocardial infarction or angina pectoris	**Studied treatment:** clarithromycin 500 mg/day **Control treatment:** placebo	Acute coronary syndrome RR=1.10 [0.88;1.36] Cardiovascular events RR=1.17 [1.02;1.35] (CV death, ACS, stroke, PVD) Coronary event RR=1.14 [0.99;1.31] All cause death RR=1.17 [0.96;1.44]

Reference

Jespersen CM, Als-Nielsen B, Damgaard M, Hansen JF, Hansen S, Hel OH, Hildebrandt P, Hilden J, Jensen GB, Kastrup J, Kolmos HJ, Kjller E, Lind I, Nielsen H, Petersen L, Gluud C. Randomised placebo controlled multicentre trial to assess short term clarithromycin for patients with stable coronary heart disease: CLARICOR trial. BMJ 2006 Jan 7;332:22-7 [PMID=16339220]

5 Detailed results for Gatifloxacin

5.1 Available trials

Only one trial which randomized 4162 patients was identified: it compared Gatifloxacin with placebo.
This trial included 4162 patients and was published in 2005.
This trial was double blind in design.
It was reported in English language.
Acute coronary syndrome data was reported in 1 trials; 1 trials reported data on all cause death; and 1 trials reported data on myocardial infarction (fatal and non fatal).
Following tables 5.1 (page 41), 5.2 (page 41), 5.4 (page 42), and 5.3 (page 41) summarized the main characteristics of the trial including in this systematic review of randomized trials of Gatifloxacin.

Table 5.1: *Treatment description - antibiotics - Gatifloxacin*

Trial	Studied treatment	Control treatment
Gatifloxacin versus placebo		
PROVE-IT (2005) [1]	Gatifloxacin 400 mg/d for 10 d/mo for 2y	placebo

Table 5.2: *Descriptions of participants - antibiotics - Gatifloxacin*

Trial	Patients
Gatifloxacin versus placebo	
PROVE-IT (2005) [1]	Patients hospitalized with ACS in the preceding 10 d

Table 5.3: *Design and methodological quality of trials - antibiotics - Gatifloxacin*

Trial	Design	Duration	Centre	Primary end-point
Gatifloxacin versus placebo				
PROVE-IT, 2005 [1] n=4162	Parallel groups double blind	24mo		coronary events

Table 5.4: *Trial characteristics - antibiotics - Gatifloxacin*

Trial
Gatifloxacin versus placebo
PROVE-IT, 2005 [1]

5.2 Meta-analysis results

The results are detailed in table 5.5 (page 43). This table is followed by the Forest's plot corresponding to each endpoint.

Gatifloxacin versus placebo

The single study eligible for this comparison provided data on **acute coronary syndrome**. There was no statistically significant difference in acute coronary syndrome between gatifloxacin and placebo, with a RR of 0.94 (95%CI 0.79 to 1.11, p=0.4694) in favour of gatifloxacin. In other words, acute coronary syndrome was slightly lower in the gatifloxacin group , but this was not statistically significant.
The single study eligible for this comparison provided data on **myocardial infarction (fatal and non fatal)**. No statistically significant difference between the groups was found in myocardial infarction (fatal and non fatal), with a RR of 0.89 (95% CI 0.72 to 1.12, p=0.3221).
The single study 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 1.28 (95% CI 0.89 to 1.84, p=0.1849).

Table 5.5: *Results details - antibiotics - Gatifloxacin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
Gatifloxacin versus placebo						
acute coronary syndrome	RR=0.94	[0.79;1.11]	0.4694	1.0000 (I^2=0.00)	1	4162
myocardial infarction (fatal and non fatal)	RR=0.89	[0.72;1.12]	0.3221	1.0000 (I^2=0.00)	1	4162
all cause death	RR=1.28	[0.89;1.84]	0.1849	1.0000 (I^2=0.00)	1	4152

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 acute coronary syndrome*

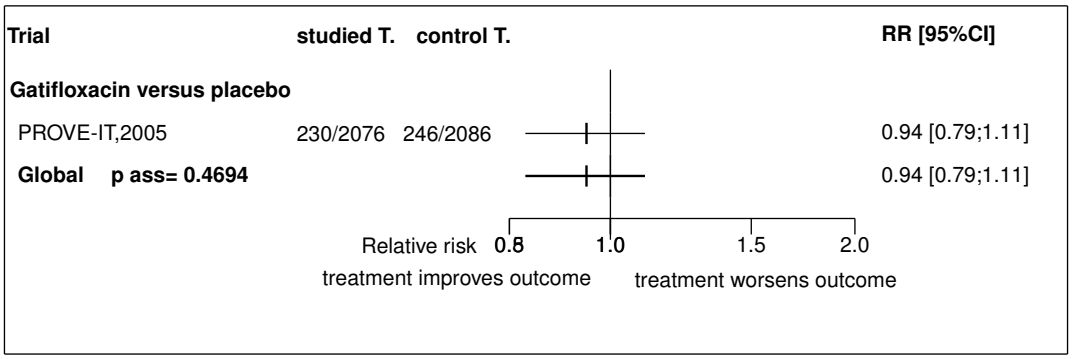


Figure 5.2: *Forest's plot for myocardial infarction (fatal and non fatal)*

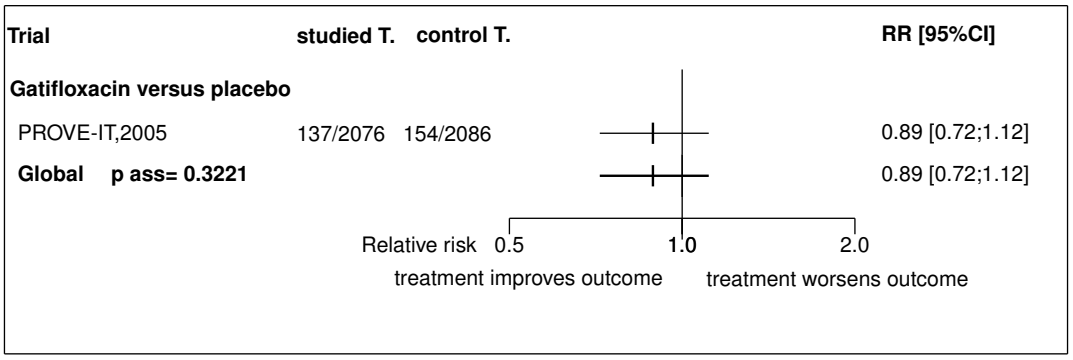
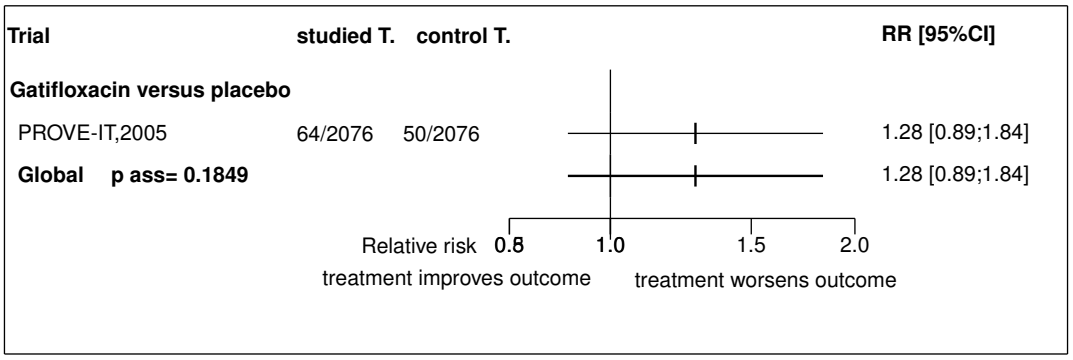


Figure 5.3: *Forest's plot for all cause death*



References

[1] Cannon CP, Braunwald E, McCabe CH, Grayston JT, Muhlestein B, Giugliano RP, Cairns R, Skene AM. Antibiotic treatment of Chlamydia pneumoniae after acute coronary syndrome. N Engl J Med 2005 Apr 21;352:1646-54. [PMID=15843667]

5.3 Individual trial summaries

Table 5.6: *PROVE-IT, 2005 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=4162 (2076 vs. 2086) **Follow-up duration:** 24mo **Study design:** Randomized controlled trial Parallel groups Double blind	Patients hospitalized with ACS in the preceding 10 d	**Studied treatment:** Gatifloxacin 400 mg/d for 10 d/mo for 2y **Control treatment:** placebo	Acute coronary syndrome RR=0.94 [0.79;1.11] Myocardial infarction (fatal and non fatal) RR=0.89 [0.72;1.12] All cause death RR=1.28 [0.89;1.84]

Reference

Cannon CP, Braunwald E, McCabe CH, Grayston JT, Muhlestein B, Giugliano RP, Cairns R, Skene AM. Antibiotic treatment of Chlamydia pneumoniae after acute coronary syndrome. N Engl J Med 2005 Apr 21;352:1646-54 [PMID=15843667]

6 Detailed results for Roxithromycin

6.1 Available trials

A total of 3 RCTs which randomized 1132 patients were identified: all compared Roxithromycin with placebo.
The average study size was 377 patients (range 60 to 870). The first study was published in 1999, and the last study was published in 2003.
All trials were double blind in design. All included studies were reported in English language. We did not found any unpublished trial.
Acute coronary syndrome data was reported in 3 trials; 3 trials reported data on all cause death; 3 trials reported data on myocardial infarction (fatal and non fatal); and 1 trials reported data on coronary event.
Following tables 6.1 (page 47), 6.2 (page 47), 6.4 (page 49), and 6.3 (page 48) summarized the main characteristics of the trials including in this systematic review of randomized trials of Roxithromycin.

Table 6.1: *Treatment description - antibiotics - Roxithromycin*

Trial	Studied treatment	Control treatment
Roxithromycin versus placebo		
ROXIS (1999) [1]	Roxithromycin 150 mg 2/d for 30 d	placebo
Leowattana et al (2001) [2]	Roxithromycin 150 mg/d for 30 d	placebo
ANTIBIO (2003) [3]	Roxithromycin 300 mg/d for 6 wk	placebo

Table 6.2: *Descriptions of participants - antibiotics - Roxithromycin*

Trial	Patients
Roxithromycin versus placebo	
ROXIS (1999) [1]	Patients with documented history of CAD and ACS
Leowattana et al (2001) [2]	Patients with ACS
ANTIBIO (2003) [3]	Patients with unstable angina or MI

Table 6.3: *Design and methodological quality of trials - antibiotics - Roxithromycin*

Trial	Design	Duration	Centre	Primary end-point
Roxithromycin versus placebo				
ROXIS, 1999 [1] n=202	Parallel groups double blind	6mo		
Leowattana et al, 2001 [2] n=60	Parallel groups	3mo		
ANTIBIO, 2003 [3] n=870	Parallel groups double blind	1y		all cause death

Table 6.4: *Trial characteristics - antibiotics - Roxithromycin*

Trial
Roxithromycin versus placebo
ROXIS, 1999 [1]
Leowattana et al, 2001 [2]
ANTIBIO, 2003 [3]

6.2 Meta-analysis results

The results are detailed in table 6.5 (page 50). This table is followed by the Forest's plot corresponding to each endpoint.

Roxithromycin versus placebo

All the 3 studies had extractable data about the number of participants with **acute coronary syndrome**. There was no statistically significant difference in acute coronary syndrome between roxithromycin and placebo, with a RR of 0.78 (95%CI 0.34 to 1.77, p=0.5478) in favour of roxithromycin. In other words, acute coronary syndrome was slightly lower in the roxithromycin group , but this was not statistically significant. No heterogeneity was detected (p = 0.0783, I^2 = 0.61%).
All the 3 studies had extractable data about the number of participants with **myocardial infarction (fatal and non fatal)**. When pooled together, there was no statistically significant difference between the groups in myocardial infarction (fatal and non fatal), with a RR of 1.24 (95% CI 0.20 to 7.56, p=0.8174). A random effect model was used because there was a substantial statistical heterogeneity detected between the studies (p = 0.0036, I^2 = 0.82%).
Only one of the 3 studies eligible for this comparison provided data on **coronary event**. No statistically significant difference between the groups was found in coronary event, with a RR of 1.20 (95% CI 0.96 to 1.51, p=0.1107).
All the 3 studies had extractable data about the number of participants with **all cause death**. When pooled together, there was no statistically significant difference between the groups in all cause death, with a RR of 1.08 (95% CI 0.66 to 1.79, p=0.7520). No heterogeneity was detected (p = 0.9938, I^2 = 0.00%).

Table 6.5: *Results details - antibiotics - Roxithromycin*

Comparison Endpoint	Effect	95% CI	p ass	p het	k	n
Roxithromycin versus placebo						
acute coronary syndrome	RR=0.78	[0.34;1.77]	0.5478	0.0783 (I^2=0.61)	3	1130
myocardial infarction (fatal and non fatal)	RR=1.24	[0.20;7.56]	0.8174	0.0036 (I^2=0.82)	3	1491
coronary event	RR=1.20	[0.96;1.51]	0.1107	1.0000 (I^2=0.00)	1	868
all cause death	RR=1.08	[0.66;1.79]	0.7520	0.9938 (I^2=0.00)	3	1156

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 acute coronary syndrome*

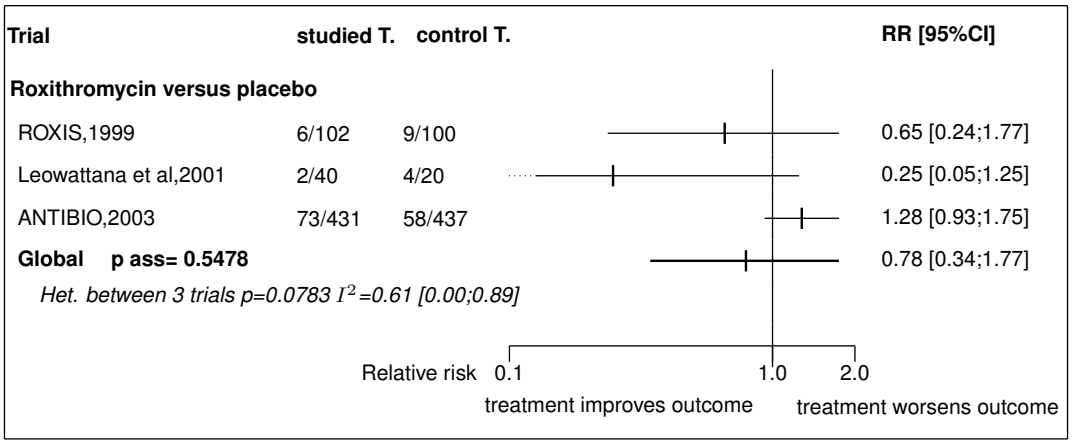


Figure 6.2: *Forest's plot for myocardial infarction (fatal and non fatal)*

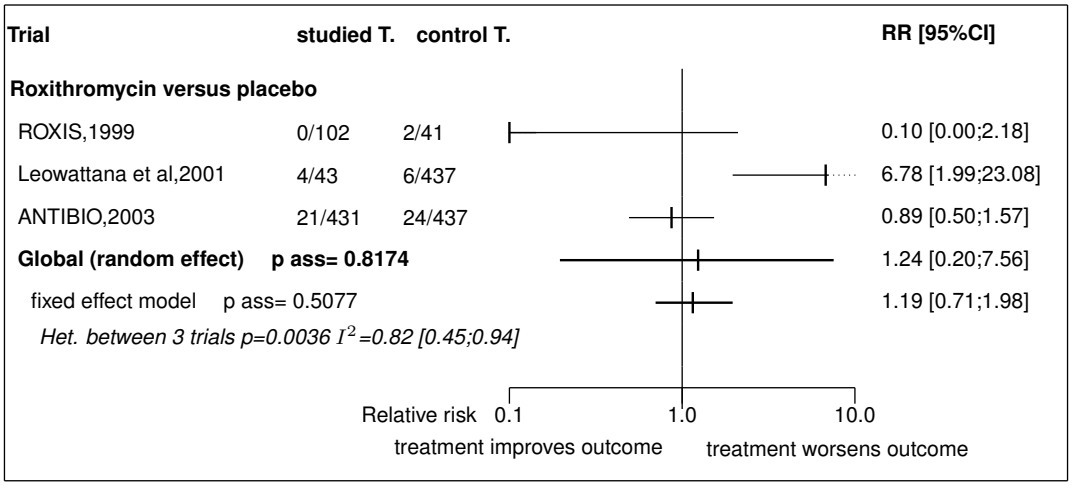


Figure 6.3: *Forest's plot for coronary event*

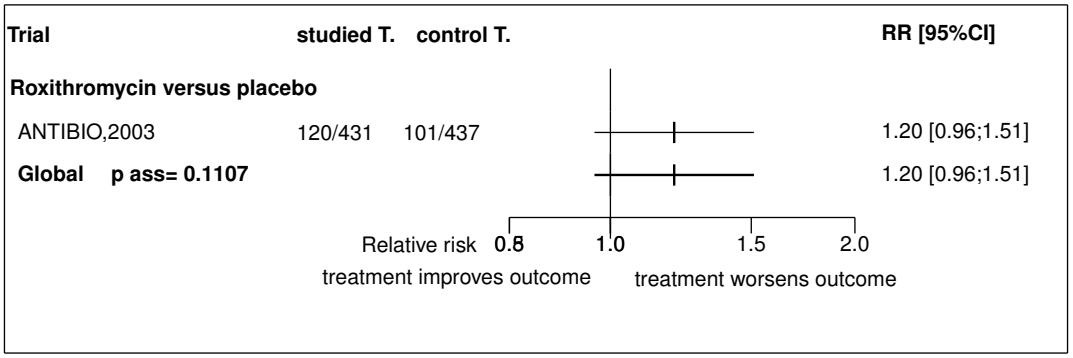
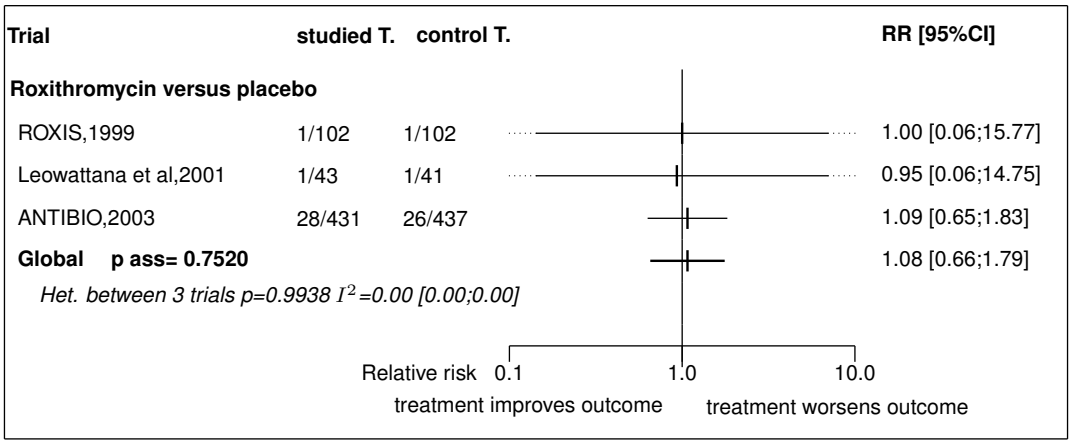


Figure 6.4: *Forest's plot for all cause death*



References

[1] Gurfinkel E, Bozovich G, Beck E, Testa E, Livellara B, Mautner B. Treatment with the antibiotic roxithromycin in patients with acute non-Q-wave coronary syndromes. The final report of the ROXIS Study. Eur Heart J 1999 Jan;20:121-7. [PMID=10099908]

[2] Leowattana W, Bhuripanyo K, Singhaviranon L,et al. . J Med Assoc Thai. 2001;84(suppl 3):S669-S675..

[3] Zahn R, Schneider S, Frilling B, Seidl K, Tebbe U, Weber M, Gottwik M, Altmann E, Seidel F, Rox J, Hoffler U, Neuhaus KL, Senges J. Antibiotic therapy after acute myocardial infarction: a prospective randomized study. Circulation 2003 Mar 11;107:1253-9. [PMID=12628944]

6.3 Individual trial summaries

Table 6.6: *ROXIS, 1999 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=202 (102 vs. 100) **Follow-up duration:** 6mo **Study design:** Randomized controlled trial Parallel groups Double blind	Patients with documented history of CAD and ACS	**Studied treatment:** Roxithromycin 150 mg 2/d for 30 d **Control treatment:** placebo	Acute coronary syndrome RR=0.65 [0.24;1.77] All cause death RR=1.00 [0.06;15.77]

Reference

Gurfinkel E, Bozovich G, Beck E, Testa E, Livellara B, Mautner B. Treatment with the antibiotic roxithromycin in patients with acute non-Q-wave coronary syndromes. The final report of the ROXIS Study. Eur Heart J 1999 Jan;20:121-7 [PMID=10099908]

Table 6.7: *Leowattana et al, 2001 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=60 (40 vs. 20) **Follow-up duration:** 3mo **Study design:** Randomized controlled trial Parallel groups	Patients with ACS	**Studied treatment:** Roxithromycin 150 mg/d for 30 d **Control treatment:** placebo	Acute coronary syndrome RR=0.25 [0.05;1.25] Myocardial infarction (fatal and non fatal) RR=6.78 [1.99;23.08] All cause death RR=0.95 [0.06;14.75]

Reference

Leowattana W, Bhuripanyo K, Singhaviranon L,et al. . J Med Assoc Thai. 2001;84(suppl 3):S669-S675.

Table 6.8: *ANTIBIO, 2003 - Trial synopsis*

Trial details	Patients	Treatments	Outcomes
n=870 (433 vs. 437) **Follow-up duration:** 1y **Study design:** Randomized controlled trial Parallel groups Double blind	Patients with unstable angina or MI	**Studied treatment:** Roxithromycin 300 mg/d for 6 wk **Control treatment:** placebo	Acute coronary syndrome RR=1.28 [0.93;1.75] Myocardial infarction (fatal and non fatal) RR=0.89 [0.50;1.57] Coronary event RR=1.20 [0.96;1.51] All cause death RR=1.09 [0.65;1.83]

Reference

Zahn R, Schneider S, Frilling B, Seidl K, Tebbe U, Weber M, Gottwik M, Altmann E, Seidel F, Rox J, Hoffler U, Neuhaus KL, Senges J. Antibiotic therapy after acute myocardial infarction: a prospective randomized study. Circulation 2003 Mar 11;107:1253-9 [PMID=12628944]

7 Global meta-analysis: all antibiotics

7.1 Global meta-analysis: all antibiotics versus placebo

Table 7.1: *All antibioticsversus placebo*

Endpoint	Effect	95% CI	p ass	p het (I^2)	k	n
acute coronary syndrome	RR=0.95	0.83;1.08	0.4462	0.0803 (0.40)	11	22151
cardiovascular events	RR=1.17	1.02;1.35	0.0267	1.0000 (0.00)	1	4373
myocardial infarction (fatal and non fatal)	RR=0.94	0.76;1.17	0.5817	0.0589 (0.47)	9	19309
coronary event	RR=1.15	1.02;1.30	0.0197	0.6669 (0.00)	2	5241
all cause death	RR=1.07	0.97;1.18	0.1783	0.9710 (0.00)	12	23583

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