實證醫學
Evidence Based Medicine (EBM)

Critical Appraisal for Systematic Review

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實證醫學組

實證醫學的五個步驟

1) Ask an answerable question〔問可以回答的問題〕
2) Search for the best evidences〔搜尋最佳證據〕
3) Critically appraise those evidences〔嚴格的文獻評讀〕
4) Apply to the patient〔臨床應用〕
5) Evaluate our performance〔評估與稽核以上步驟〕

CASP
Critical Appraisal Skills Programme

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CASP Checklist: 10 questions to help you make sense of a **Systematic Review**

How to use this appraisal tool: Three broad issues need to be considered when appraising a systematic review study:

- Are the results of the study valid? (Section A)
- What are the results? (Section B)
- Will the results help locally? (Section C)

The 10 questions on the following pages are designed to help you think about these issues systematically. The first two questions are screening questions and can be answered quickly. If the answer to both is "yes", it is worth proceeding with the remaining questions. There is some degree of overlap between the questions, you are asked to record a "yes", "no" or "can't tell" to most of the questions. A number of italicised prompts are given after each question. These are designed to remind you why the question is important. Record your reasons for your answers in the spaces provided.

About: These checklists were designed to be used as educational pedagogic tools, as part of a

1. Did the review address a clearly focused question?

Yes	
Can't Tell	
No	

- 此回顧是否問了一個清楚明確的問題？

  是否文有對題？

從文章標題、摘要 (Abstract)中的研究目的(objective)、前言or背景 (background)最後一、二段的地方找答案，以PICO (patient, intervention, comparison, outcome)的方式思考。

[Intervention Review]

Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Rachel Bedenis[1], Anne Lethaby[2], Heather Maxwell[3], Stefan Acosta[4], Martin H Prins[5]

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Citation: Bedenis R, Lethaby A, Maxwell H, Acosta S, Prins MH. Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery. *Cochrane Database of Systematic Reviews* 2015, Issue 2. Art. No.: CD000535. DOI: 10.1002/14651858.CD000535.pub3.

ABSTRACT

Background

Peripheral arterial disease (PAD) may cause occlusions (blockages) in the main arteries of lower limbs. One treatment option is bypass surgery using autologous (the patient's own tissue) vein graft or prosthetic (artificial) graft. A number of factors influence occlusion rates in these patients, including the material used. To prevent graft occlusion patients are usually treated with antiplatelet, antithrombotic drugs, or a combination of both.

Objectives

To determine the effects of antiplatelet agents for the prevention of thrombosis in people with lower limb atherosclerosis who were undergoing femoropopliteal or femorodistal bypass grafting. Outcomes included the overall success of therapy (graft patency and limb salvage rates) and complications of treatment.

Search methods

For this update the Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator searched the Specialised Register (last searched June 2014) and the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 5). We sought additional trials through screening the reference lists of relevant papers.

Selection criteria

Two review authors, RB and AL, independently reviewed studies found in the search and evaluated them based on the inclusion and exclusion criteria, resolving disagreements through discussion.

Data collection and analysis

RB and AL independently extracted details of the selected studies for the update. We compared the treatment and control groups for

OBJECTIVES

To determine the effects of antiplatelet agents for the prevention of thrombosis in patients with lower limb atherosclerosis who were undergoing femoropopliteal or femorodistal bypass grafting. Outcomes include the overall success of therapy (graft patency and limb salvage rates) and complications of treatment.

2. Did the authors look for the right type of papers?

Yes	
Can't Tell	
No	

- 作者是否收納適當的研究類型？
- 可以在 Methods 中的 inclusion and exclusion criteria 中找到答案。
- The inclusion or exclusion of studies in a systematic review should be clearly defined. Randomized controlled trial is preferred for papers evaluating interventions.

METHODS

Criteria for considering studies for this review

Types of studies

Trials in which participants were randomly allocated to receive either antiplatelet therapy versus placebo, one antiplatelet regimen versus another or antiplatelet therapy versus an alternative treatment. We include trials using alternation (allocation of treatment alternating between two interventions) and consider them as quasi-randomised clinical trials (qRCTs).

Types of participants

All people undergoing femoropopliteal or femorodistal bypass grafting for the treatment of intermittent claudication and critical limb ischaemia. We excluded people undergoing bypass surgery for trauma.

Types of interventions

Antiplatelet therapy versus placebo, one antiplatelet regimen versus another, or antiplatelet therapy versus an alternative treatment. We excluded studies that included the same antiplatelet agent in both treatment groups, unless another antiplatelet was also used, but in only one treatment arm. We recorded the type of therapy, dosage, time of starting compared to surgery (pre- or postoperatively) and duration of the therapy.

Types of outcome measures

Primary outcomes

(1) Primary graft patency: patency rates after surgery with no further intervention, as determined by clinical examination, measurement of the ankle-brachial pressure index (ABPI), duplex ultrasonography, angiography.
(2) Assisted primary patency: patency rates after intervention to improve blood flow in a graft which has not occluded.
We analysed primary patency and primary assisted patency for all grafts and for venous or prosthetic (artificial) grafts separately.

Secondary outcomes

1. Secondary graft patency: patency rates following secondary intervention to restore blood flow to the graft
2. Objective assessment of lower limb blood flow: ABPI, exercise tolerance test
3. Side effects of treatment and complications
4. Limb salvage rate: survival rates with limb intact (or limb amputation)
5. Incidence of other cardiovascular events and mortality
6. Participants' quality of life

3. Do you think all the important, relevant studies were included?

Yes ☐

Can't Tell ☐

No ☐

HINT: Look for

- which bibliographic databases were used
- follow up from reference lists
- personal contact with experts
- unpublished as well as published studies
- non-English language studies

- 作者有沒有收錄所有重要、相關的研究？
- 要找Methods中文獻搜尋的部分，看搜尋的資料庫(database)是否足夠？搜尋的關鍵字是否適當、無遺漏？作者是否無所不用其極的去尋找所有可能的文獻 (包括發表的、未發表的、只發表在學會的、從別人 review文章 reference 挖的、非英文的、寫信去找作者要資料的等等)？
- 在Results中可看到作者收錄與排除多少文章，並說明其理由。

Search methods for identification of studies

Electronic searches

For this update the Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator (TSC) searched the Specialised Register (last searched June 2014) and the Cochrane Central Register of Controlled Trials (CENTRAL) 2014, Issue 5, part of *The Cochrane Library* (www.thecochranelibrary.com). See Appendix 1 for details of the search strategy used to search CENTRAL. The Specialised Register is maintained by the TSC and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL, AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings which have been searched, as well as the search strategies used, are described in the Specialised Register section of the Cochrane Peripheral Vascular Diseases Group module in *The Cochrane Library*.

Searching other resources

We scanned reference lists of studies and reviews identified by the search for relevant studies.

Appendix 1. CENTRAL search strategy

#1	MeSH descriptor: [Arteriosclerosis] this term only	895
#2	MeSH descriptor: [Arteriolosclerosis] this term only	0
#3	MeSH descriptor: [Arteriosclerosis Obliterans] this term only	73
#4	MeSH descriptor: [Atherosclerosis] this term only	513
#5	MeSH descriptor: [Arterial Occlusive Diseases] this term only	810
#6	MeSH descriptor: [Intermittent Claudication] this term only	768
#7	MeSH descriptor: [Ischemia] this term only	814
#8	MeSH descriptor: [Peripheral Vascular Diseases] explode all trees	2293
#9	MeSH descriptor: [Vascular Diseases] this term only	424
#10	MeSH descriptor: [Leg] explode all trees and with qualifier(s) : [Blood supply - BS]	1145

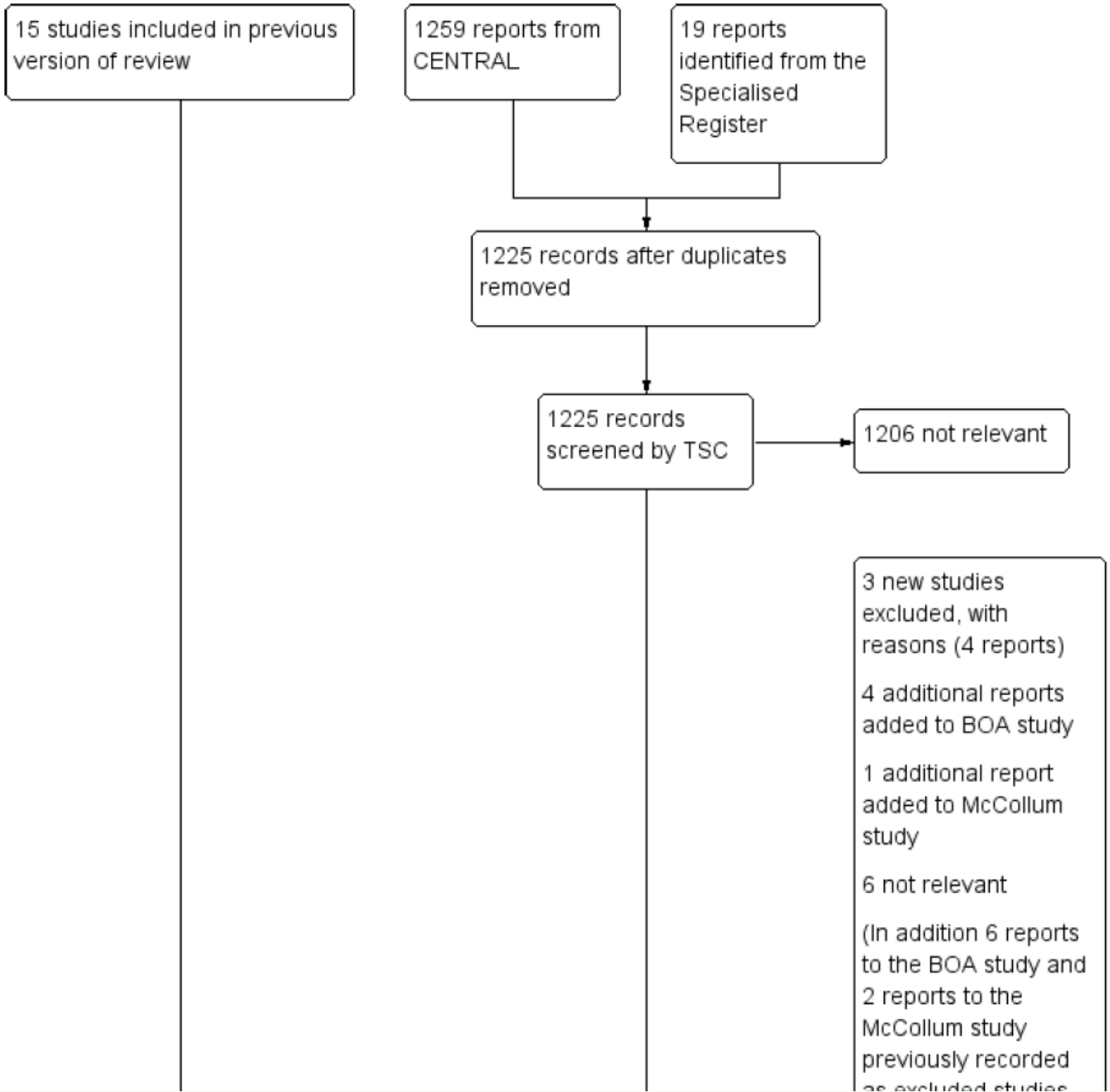
Methods

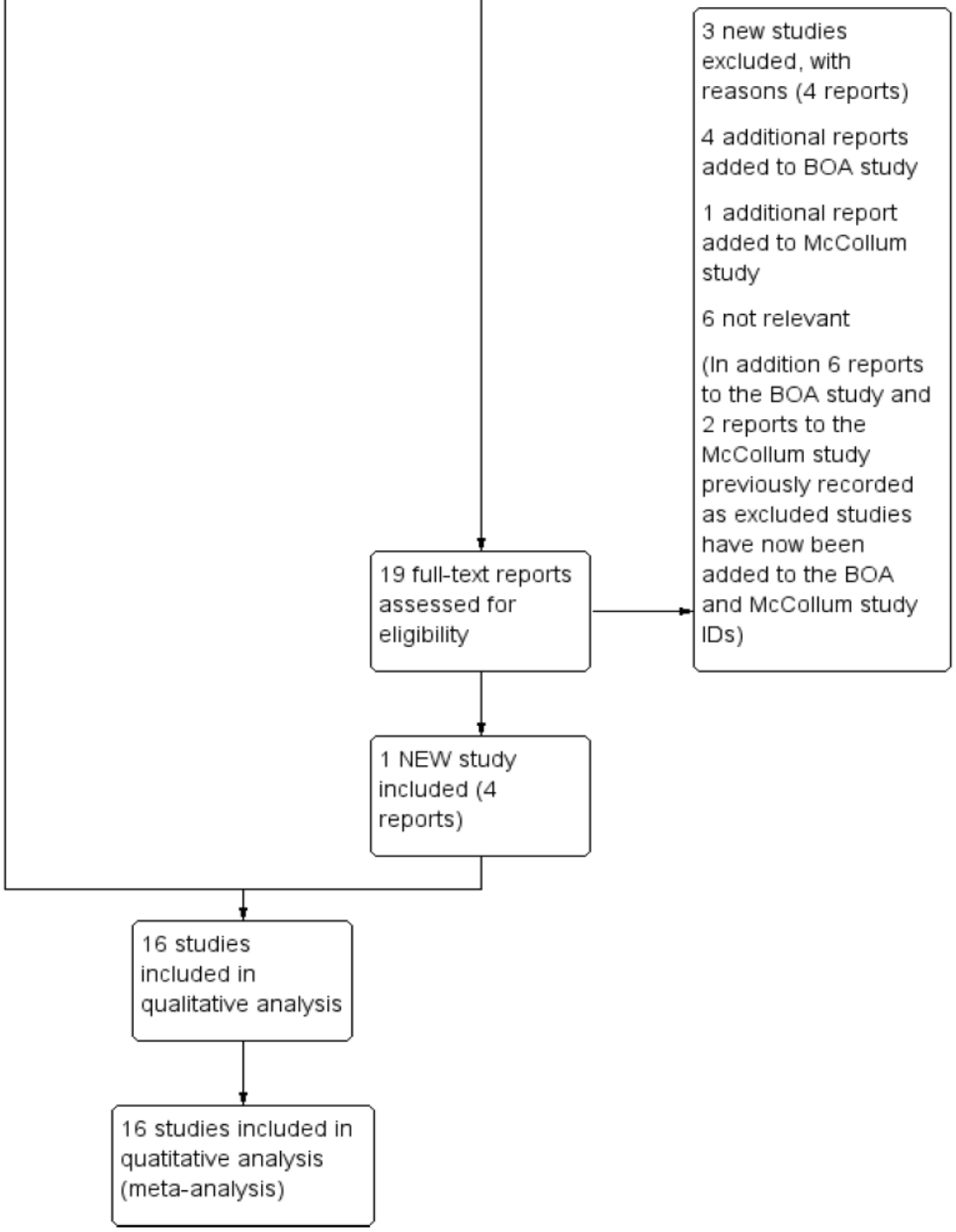
Search strategy

We systematically searched MEDLINE (1966–March 2008), EMBASE (1977–March 2008) and the Cochrane Central Register of Controlled Trials (CENTRAL) (1948–March 2008) for randomized trials examining the effect of intensive insulin therapy on mortality among critically ill patients. In addition, we conducted a manual search of abstracts from selected conferences held from 2000 to 2008, including conferences of the Society of Critical Care Medicine, the European Society of Intensive Care Medicine, the American Thoracic Society and the American College of Chest Physicians. We also searched by hand the bibliographies of all relevant trials. We obtained a confidential prepublication copy of the NICE-SUGAR report from the study's management committee. We included the NICE-SUGAR data subject to publication of the primary report and with the agreement of the journal publishing the trial.

For the bibliographic review, we constructed search filters for each of the concepts of critical care, intensive insulin therapy and clinical trials using a combination of exploded Medical Subject Heading (MeSH) terms and text words, all combined with the Boolean OR operator. The critical care filter contained the following MeSH terms: "critical care," "intensive care," "intensive care units," "cardiac care facilities," "critical illness," "postoperative care" with text words "intensive care," "ICU," "critical care," "CCU," "coronary care," "recovery room," "PAR," "critical illness," "burn unit," "critically ill" or "cardiac care." The intensive insulin filter contained the MeSH terms "insulin," "blood glucose," "hypoglycemic agents" with text words "intensive insulin," "glycemic control," "blood glucose" or "insulin." The clinical trials filter included the MeSH terms "clinical trials [publication type]," "clinical trials as topic," "placebos" with text words "trial*," "random*" or "placebo." We then combined all 3 filters using the Boolean operator AND. We used a similar search strategy to identify relevant articles in the EMBASE and CENTRAL databases (Appendix 1, available at www.cmaj.ca/cgi/content/full/cmaj.090206/DC1).

Figure 1. Study flow diagram.




3 new studies excluded, with reasons (4 reports)
4 additional reports added to BOA study
1 additional report added to McCollum study
6 not relevant
(In addition 6 reports to the BOA study and 2 reports to the McCollum study previously recorded as excluded studies have now been added to the BOA and McCollum study IDs)
19 full-text reports assessed for eligibility
1 NEW study included (4 reports)
16 studies included in qualitative analysis
16 studies included in quatitative analysis (meta-analysis)

4. Did the review's authors do enough to assess quality of the included studies?

Yes	
Can't Tell	
No	

- 作者是否有評估收納研究的品質？

可以在方法 (Methods)中品質評估 (quality assessment)的部分找到答案。

常用的文獻品質評比工具包括Cochrane Risk of Bias (RoB) Tool、Jadad scale等，並且需要至少兩個獨立作業的評讀者來執行這項工作。

Assessment of risk of bias in included studies

RB and AL independently assessed the methodological quality of included trials, using the 'Risk of bias' tool from The Cochrane Collaboration (Higgins 2011). We assessed the following five domains: selection bias (random sequence generation, allocation concealment), performance bias (blinding of participants and personnel and blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting) and other potential sources of bias. We classified the domains as being at low risk of bias, high risk of bias or unclear risk of bias according to the guidelines in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The two review authors assessing bias resolved disagreements by discussion.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

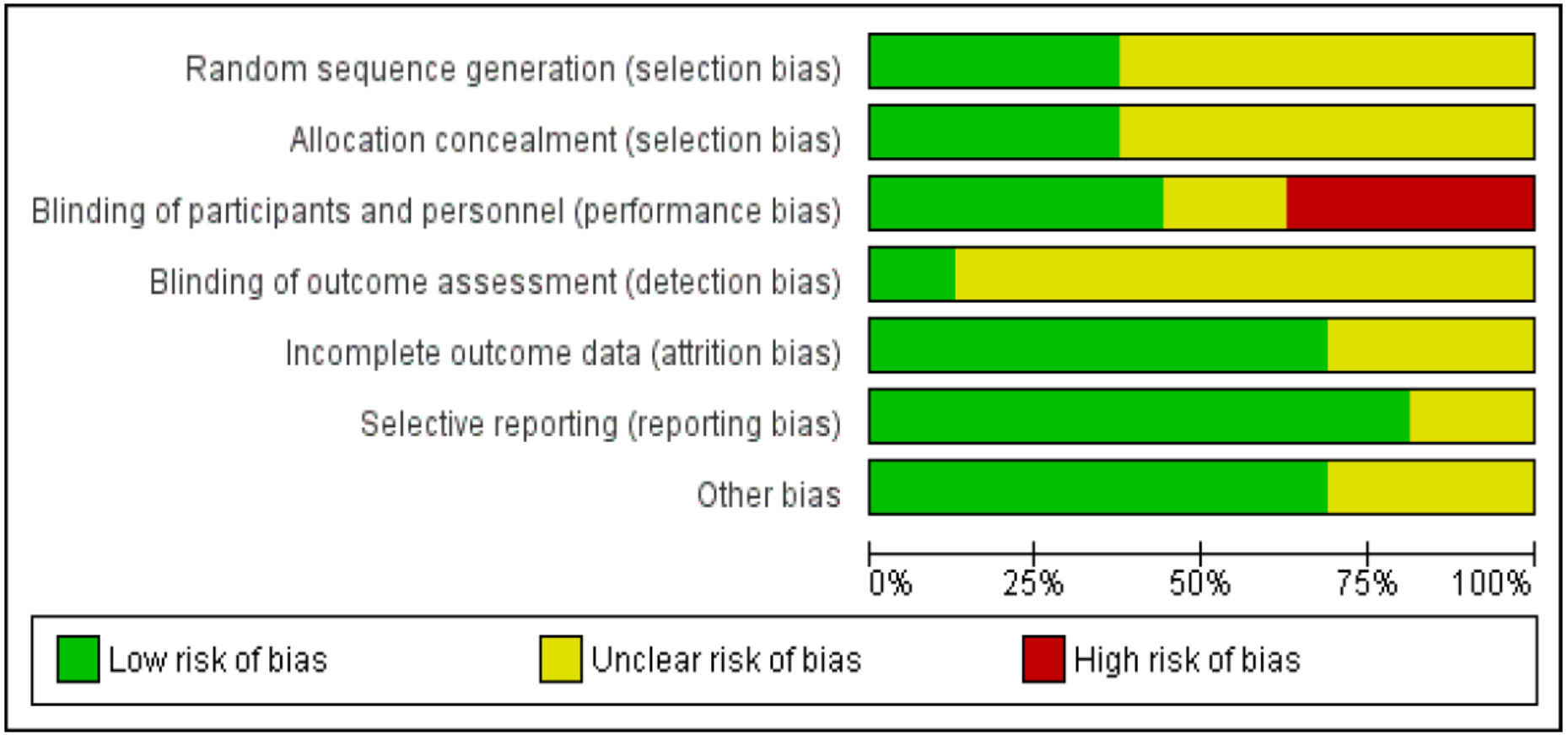
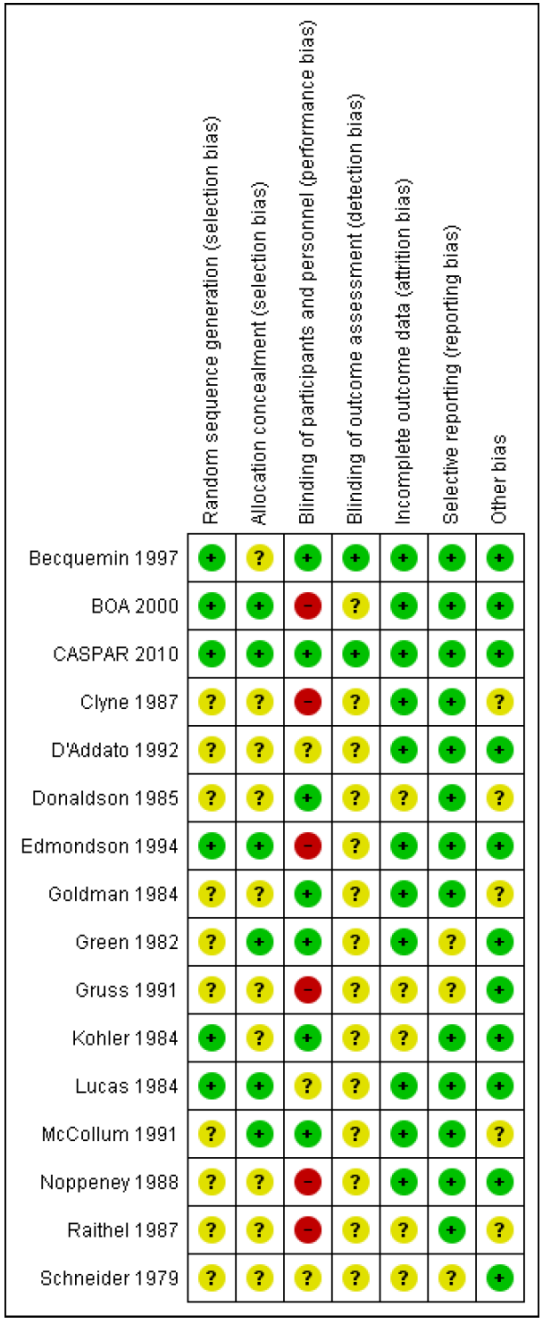


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Appendix 2: Jadad scores assigned to randomized trials included in this meta-analysis.

First Author, Year	Randomized	Randomization Appropriate	Blinded	Double Blinding Appropriate	Description of Withdrawals & Dropouts	Total Jadad Score
Arabi 2008[10]	Yes	Yes	No	No	Yes	3
Azevedo[a] 2007[22]	Yes	No	No	No	Yes	2
Bilotta 2007[24]	Yes	Yes	No	No	Yes	3
Bilotta 2008[23]	Yes	Yes	No	No	Yes	3
Bland 2005[25]	Yes	No	No	No	Yes	2
Brunkhorst 2008[11]	Yes	Yes	No	No	Yes	3
Bruno 2008[26]	Yes	Yes	No	No	Yes	3
De La Rosa 2008[12]	Yes	Yes	No	No	Yes	3
Devos[a] 2007[13]	Yes	No	No	No	Yes	2
Farah 2007[27]	Yes	No	No	No	Yes	2
Grey 2004[28]	Yes	No	No	No	Yes	2
He, W 2007[29]	Yes	Yes	No	No	Yes	2
He, Z 2008[30]	Yes	No	No	No	Yes	2
Henderson[a] 2005[31]	Yes	Yes	No	No	Yes	3
Iapichino 2008[32]	Yes	Yes	No	No	Yes	3
Mackenzie 2008[33]	Yes	Yes	No	No	Yes	3
McMullin 2007[34]	Yes	Yes	No	No	Yes	3
Mitchell 2006[35]	Yes	Yes	No	No	Yes	3
NICE-SUGAR 2009[18]	Yes	Yes	No	No	Yes	3
Oksanen 2007[36]	Yes	Yes	No	No	Yes	3
Van den Berghe 2001[8]	Yes	Yes	No	No	Yes	3
Van den Berghe 2006[9]	Yes	Yes	No	No	Yes	3
Walters 2006[37]	Yes	Yes	No	No	Yes	3
Wang, L 2006[38]	Yes	No	No	No	Yes	2
Yu 2005[39]	Yes	No	No	No	Yes	2
Zhang 2008[40]	Yes	Yes	No	No	Yes	2

Jadad Score Calculation	
Item	**Score**
Was the study described as randomized (this includes words such as randomly, random, and randomization)?	0/1
Was the method used to generate the sequence of randomization described and appropriate (table of random numbers, computer-generated, etc)?	0/1
Was the study described as double blind?	0/1
Was the method of double blinding described and appropriate (identical placebo, active placebo, dummy, etc)?	0/1
Was there a description of withdrawals and dropouts?	0/1
Deduct one point if the method used to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, or according to date of birth, hospital number, etc).	0/-1
Deduct one point if the study was described as double blind but the method of blinding was inappropriate (e.g., comparison of tablet vs. injection with no double dummy).	0/-1

5. If the results of the review have been combined, was it reasonable to do so?

Yes

Can't Tell

No

- 作者若把各個研究的結果合併起來，這樣的合併是合理的嗎？ (從 methods 及 results 中去找。)
- Are the results similar from study to study ? Any **heterogeneity(異質性)?**
- **Fixed-effect model** or **random-effects model** ?
- If heterogeneity exist, discuss the reason.

Heterogeneity(異質性)

- 不是所有的系統性回顧都適合把結果合併成一個值，變成統合分析 (meta-analysis)。如果這些收納的研究彼此間研究設計差異太大(不同病患族群、不同治療藥物、不同結果評估等)，就不適合揉在一起做meta-analysis，而應該到系統性回顧就止步。

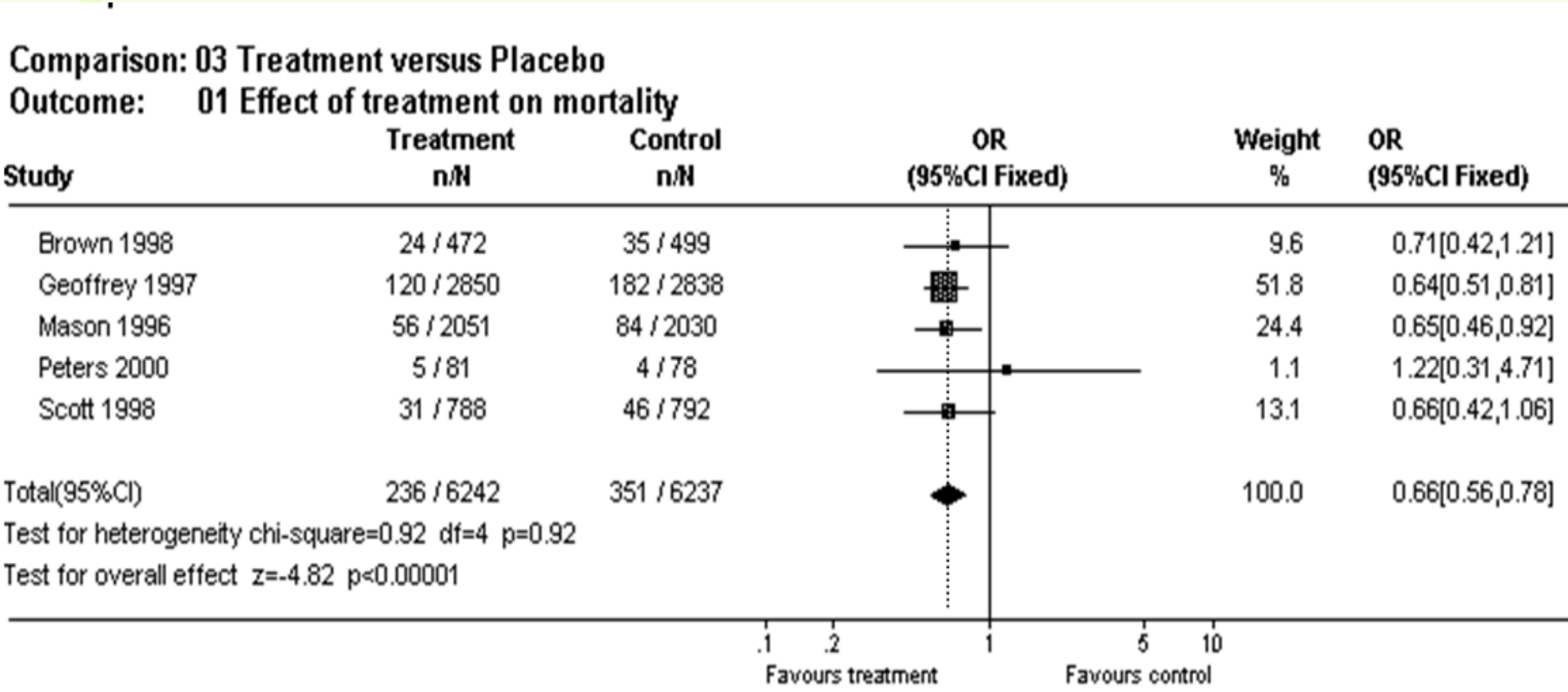
- 異質性(heterogeneity)太大時，應該先找出可能的原因，找出哪些不適合的研究，重新評估，選擇分開分析，做次群組分析 (subgroup-analysis)，或分析時予以刪除，或闡述各自研究結果即可，不須合併。

Heterogeneity(異質性)

- Methods use to define heterogeneity:

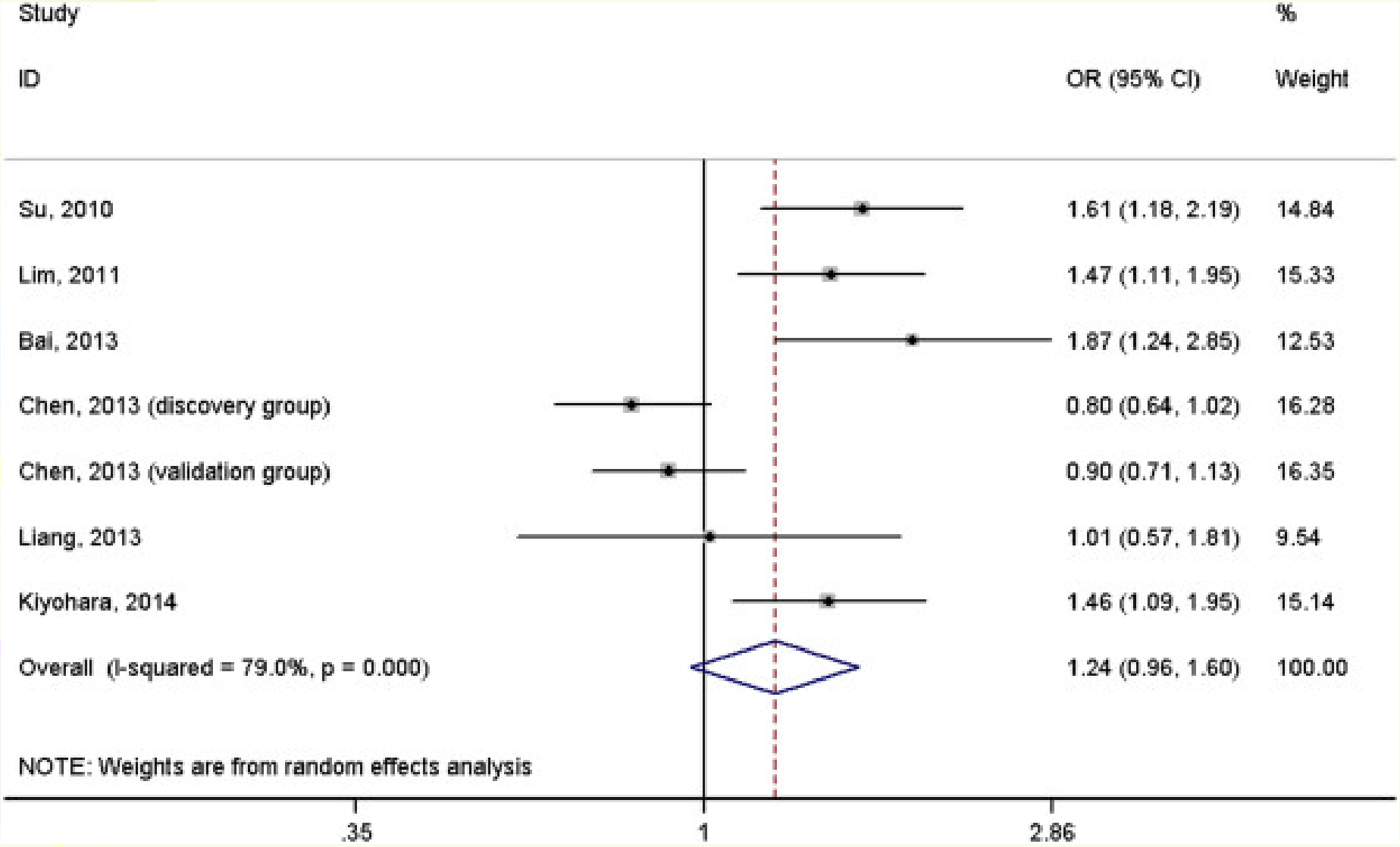
1) Eyeball test
2) Cochran's Q test (Cochran Chi-squared test)(X^2)
3) I^2 test
4) Tau^2 test (for random-effects model)

Eyeball test for Heterogeneity



Forest Plot (森林圖)

Eyeball test for Heterogeneity



Cochran's Q test (Cochran Chi-squared test)

- P > 0.1 --- no heterogeneity
- P < 0.1 --- heterogeneity exist
- P near 0.1:

  Cochran Q/df > 1 --- possible heterogeneity

  Cochran Q/df < 1 --- heterogeneity unlikely

(df: degrees of freedom)

Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

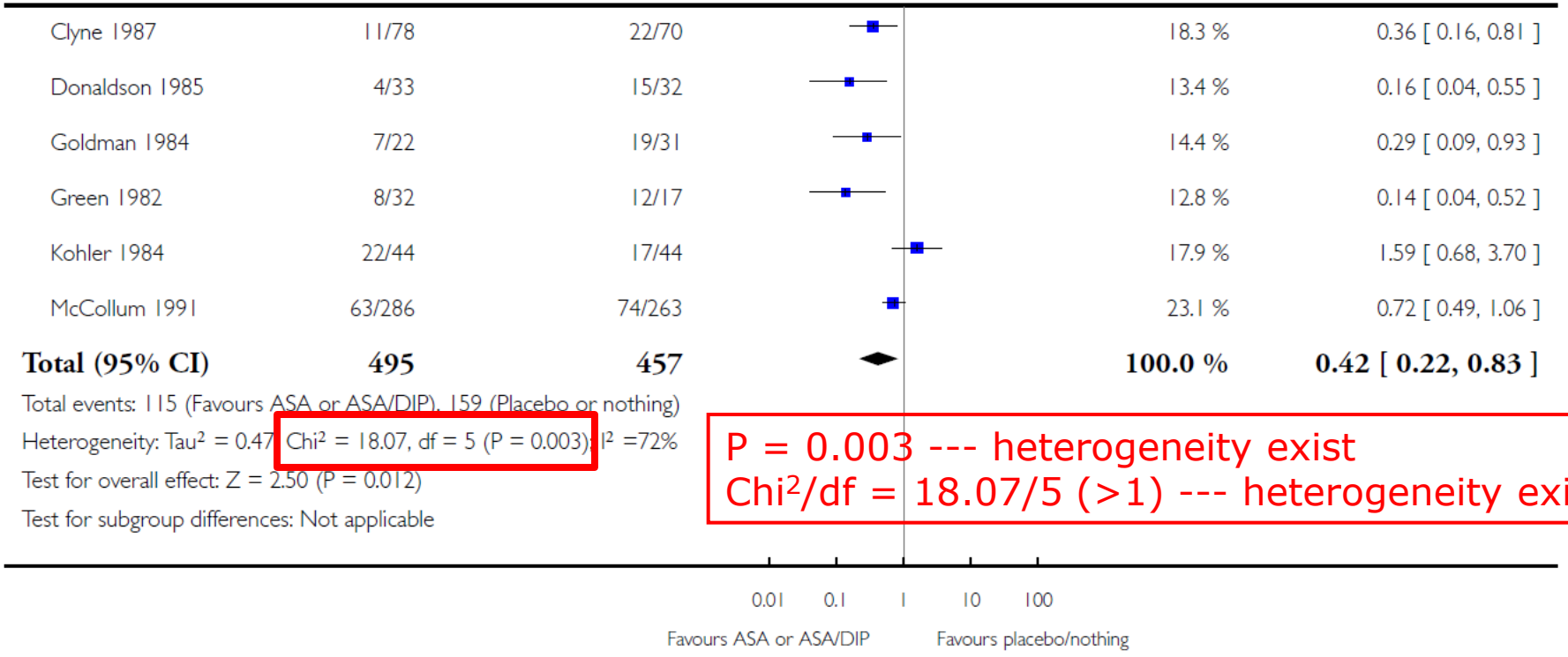
Study or subgroup	Favours ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	11/78	22/70		18.3 %	0.36 [0.16, 0.81]
Donaldson 1985	4/33	15/32		13.4 %	0.16 [0.04, 0.55]
Goldman 1984	7/22	19/31		14.4 %	0.29 [0.09, 0.93]
Green 1982	8/32	12/17		12.8 %	0.14 [0.04, 0.52]
Kohler 1984	22/44	17/44		17.9 %	1.59 [0.68, 3.70]
McCollum 1991	63/286	74/263		23.1 %	0.72 [0.49, 1.06]
Total (95% CI)	**495**	**457**		**100.0 %**	**0.42 [0.22, 0.83]**

Total events: 115 (Favours ASA or ASA/DIP), 159 (Placebo or nothing)

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 18.07$, df = 5 (P = 0.003); $I^2 = 72\%$

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



P = 0.003 --- heterogeneity exist

$Chi^2/df = 18.07/5$ (>1) --- heterogeneity exist

Cochran's Q test (Cochran Chi-squared test)

- P > 0.1 --- no heterogeneity
- P < 0.1 --- heterogeneity exist
- P near 0.1:

  Cochran Q/df > 1 --- possible heterogeneity

  Cochran Q/df < 1 --- heterogeneity unlikely

(df: degrees of freedom)

Analysis 1.5. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 5 Mortality.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 5 Mortality

Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Clyne 1987	11/78	8/70		14.2 %	1.27 [0.48, 3.37]
Goldman 1984	0/22	2/31		4.0 %	0.26 [0.01, 5.74]
Green 1982	2/32	0/17		1.2 %	2.87 [0.13, 63.22]
McCollum 1991	40/286	46/263		80.7 %	0.77 [0.48, 1.22]
Total (95% CI)	**418**	**381**		**100.0 %**	**0.84 [0.56, 1.26]**

Total events: 53 (ASA or ASA/DIP), 56 (Placebo or nothing)

Heterogeneity: $Chi^2 = 2.00$, df = 3 (P = 0.57); I^2 =0.0%

Test for overall effect: Z = 0.83 (P = 0.41)

Test for subgroup differences: Not applicable

P = 0.57 --- No heterogeneity

$Chi^2/df = 2/3 = 0.67$ --- No heterogeneity

0.005 0.1 1 10 200

Favours ASA or ASA/DIP Favours placebo/nothing

I^2 Test

- I^2 < 25% --- No heterogeneity
- I^2 > 50% --- Moderate heterogeneity
- I^2 > 75% --- Severe heterogeneity

Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

Study or subgroup	Favours ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	11/78	22/70		18.3 %	0.36 [0.16, 0.81]
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Goldman 1984	7/22	19/31		14.4 %	0.29 [0.09, 0.93]
Green 1982	8/32	12/17		12.8 %	0.14 [0.04, 0.52]
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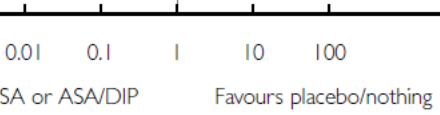
Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



I^2 = 72% --- Heterogeneity exist

Analysis 1.5. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 5 Mortality.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 5 Mortality

Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Clyne 1987	11/78	8/70		14.2 %	1.27 [0.48, 3.37]
Goldman 1984	0/22	2/31		4.0 %	0.26 [0.01, 5.74]
Green 1982	2/32	0/17		1.2 %	2.87 [0.13, 63.22]
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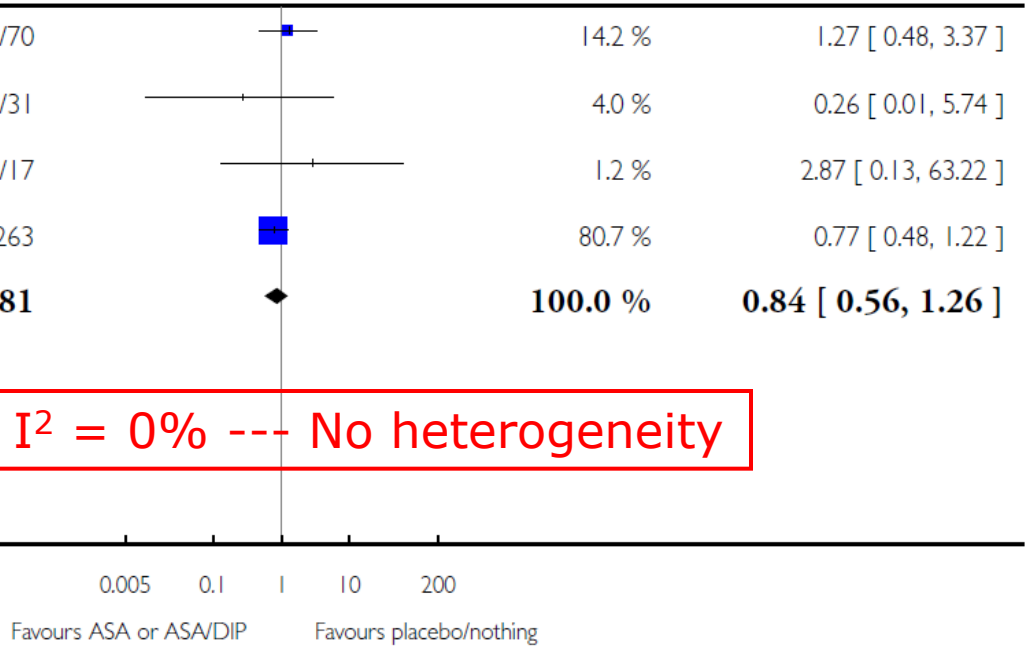
Total (95% CI)	**418**	**381**		**100.0 %**	**0.84 [0.56, 1.26]**

Total events: 53 (ASA or ASA/DIP), 56 (Placebo or nothing)

Heterogeneity: $Chi^2 = 2.00$, df = 3 (P = 0.57); $I^2 = 0.0\%$

Test for overall effect: Z = 0.83 (P = 0.41)

Test for subgroup differences: Not applicable



I^2 = 0% --- No heterogeneity

Tau^2 Test

For random effects model.

- $Tau^2 = 0$ --- no heterogeneity
- $Tau^2 > 0.1$ --- heterogeneity exist

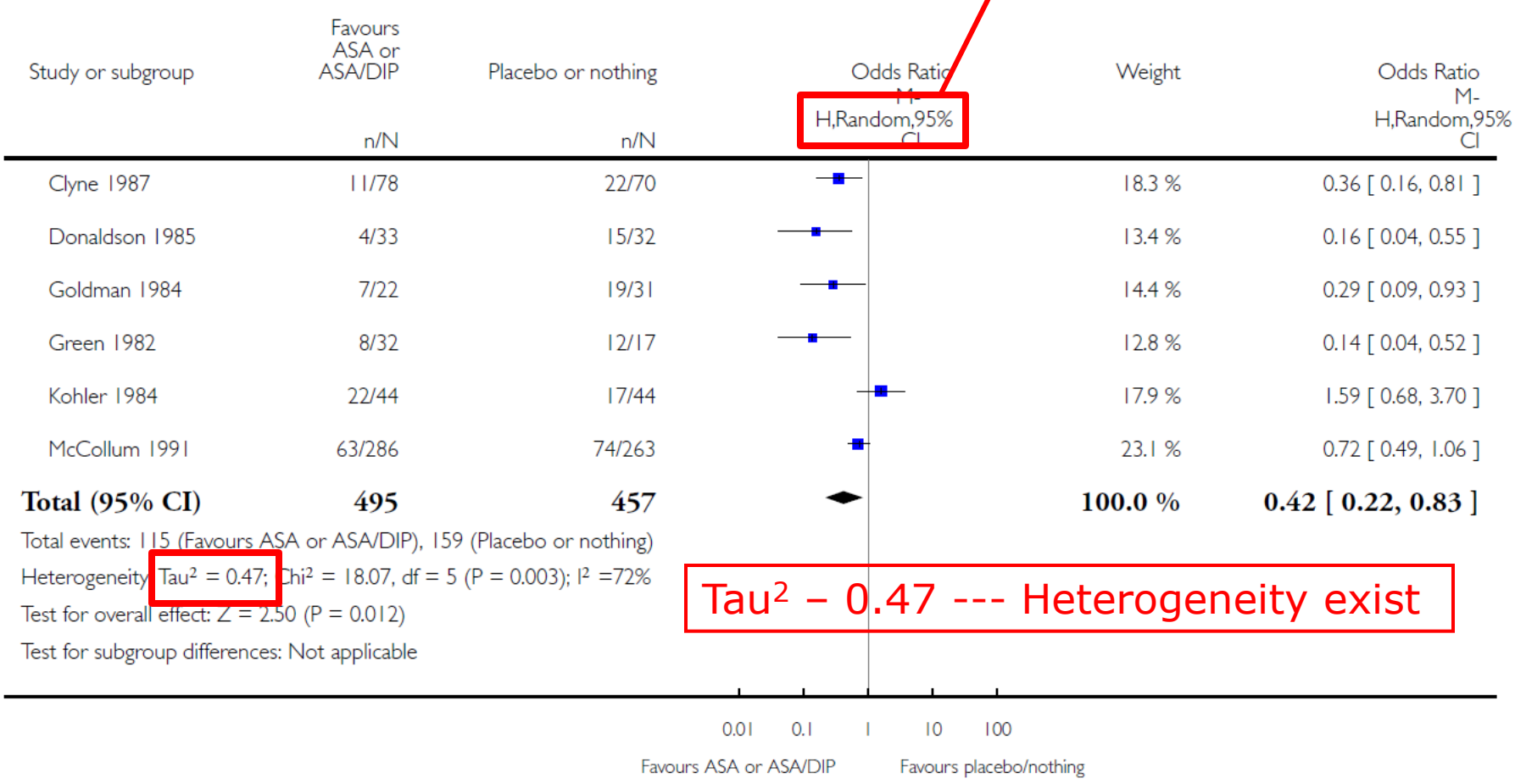
Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

Random-effects model



Tau² – 0.47 --- Heterogeneity exist

Two data pooling models in meta-analysis

- **Fixed-effect model**
- **Random-effects model**

Fixed-effect model

- Under the fixed-effect model we assume that there is one true effect size that underlies all the studies in the analysis, and that all differences in observed effects are due to sampling error.

- 假設你預估分析的研究皆有一個共同的真值，就用 fixed-effect model。

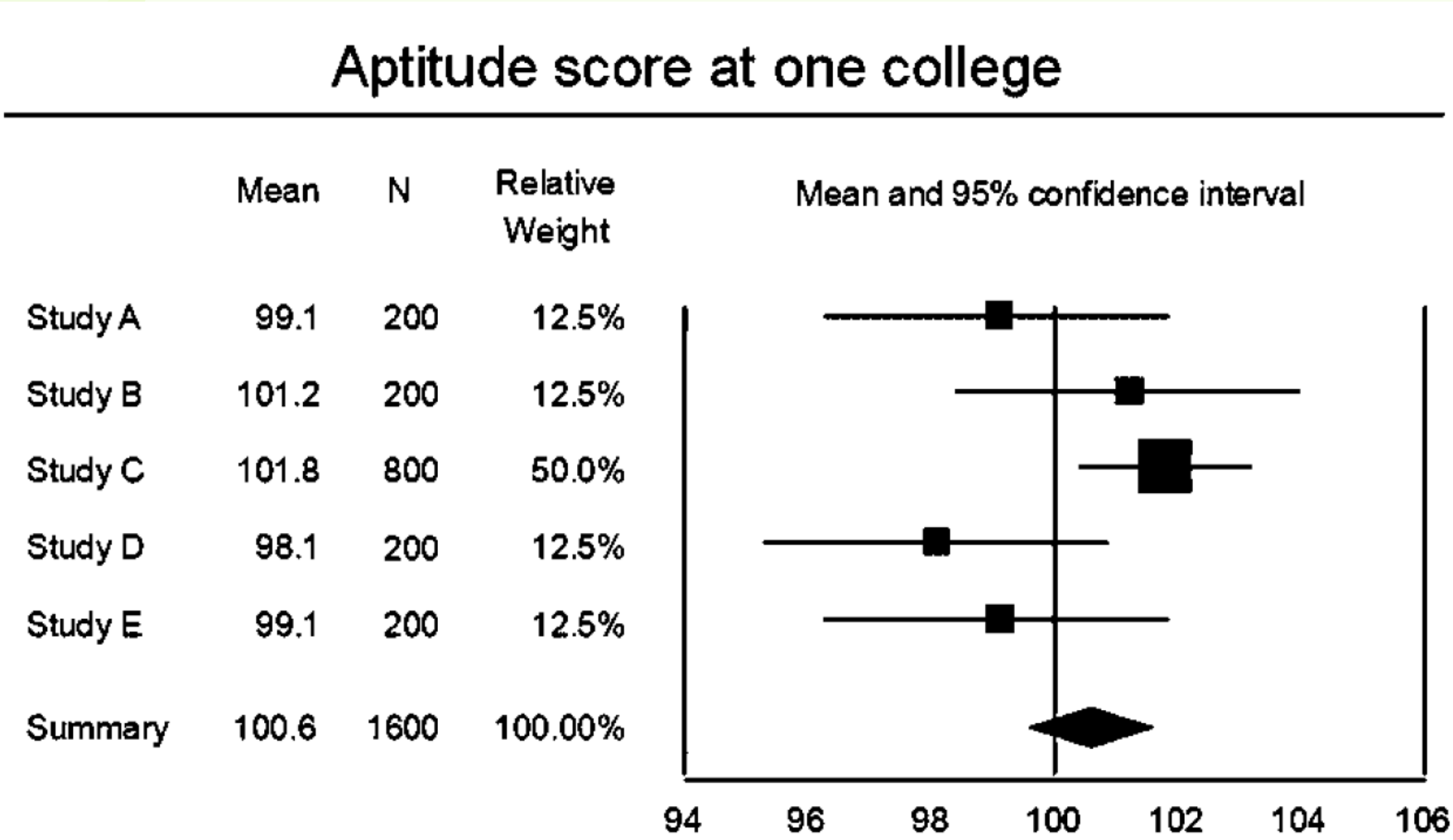
- 現實世界裡，符合條件能用 fixed-effect model 的統合分析是非常少的。

Random-effects model

- Under the random-effects model we allow the true effect sizes to differ. For example, the effect size might be higher (or lower) in studies where the participants are older, or more educated, or healthier than in other studies.

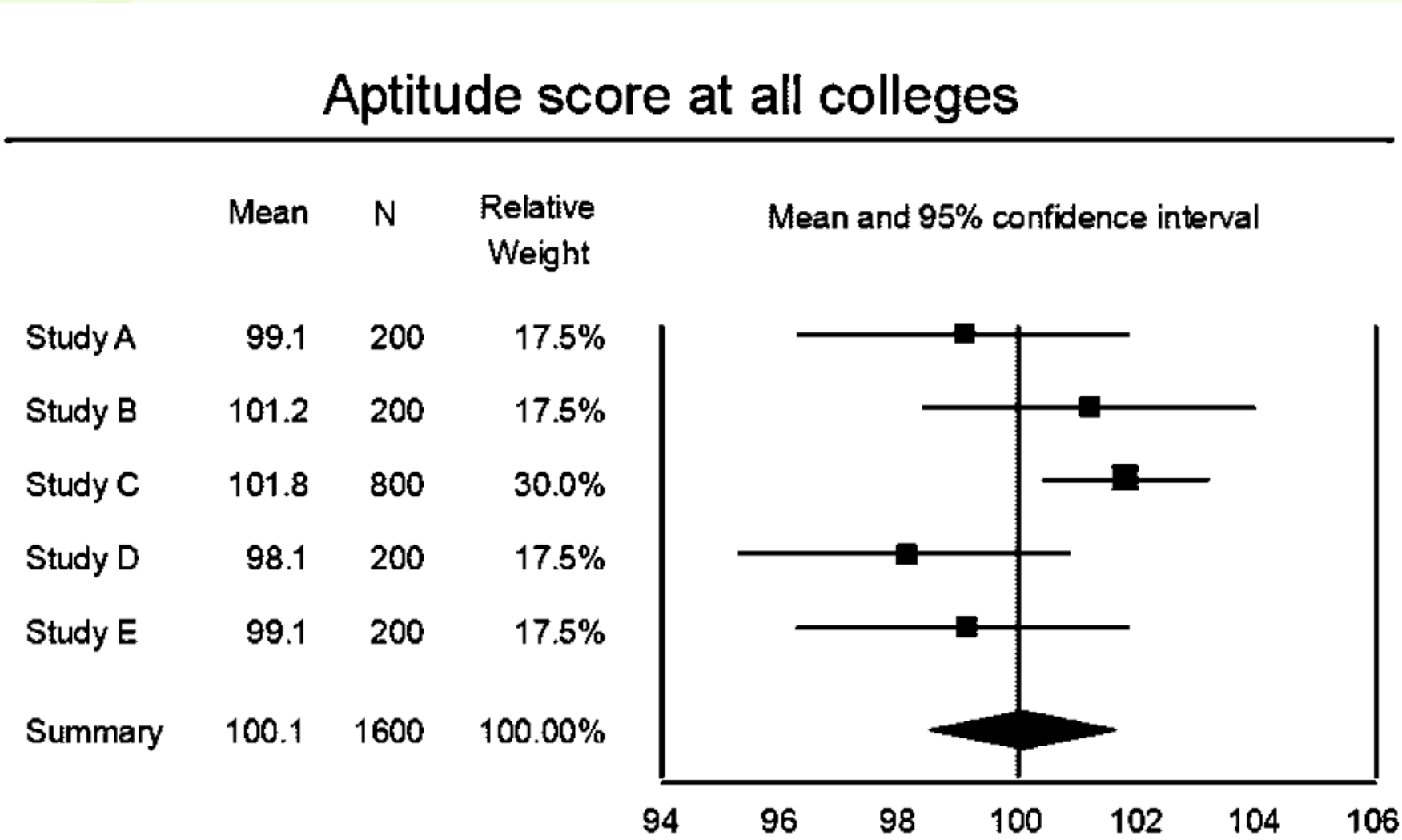
- 若你預估分析的研究會有各種不同的效值，就用 random-effects model 來做統合分析。

Fixed-effect model



Borenstein M et al. Res Synth Methods. 2010 Apr;1(2):97-111.

Random-effects model

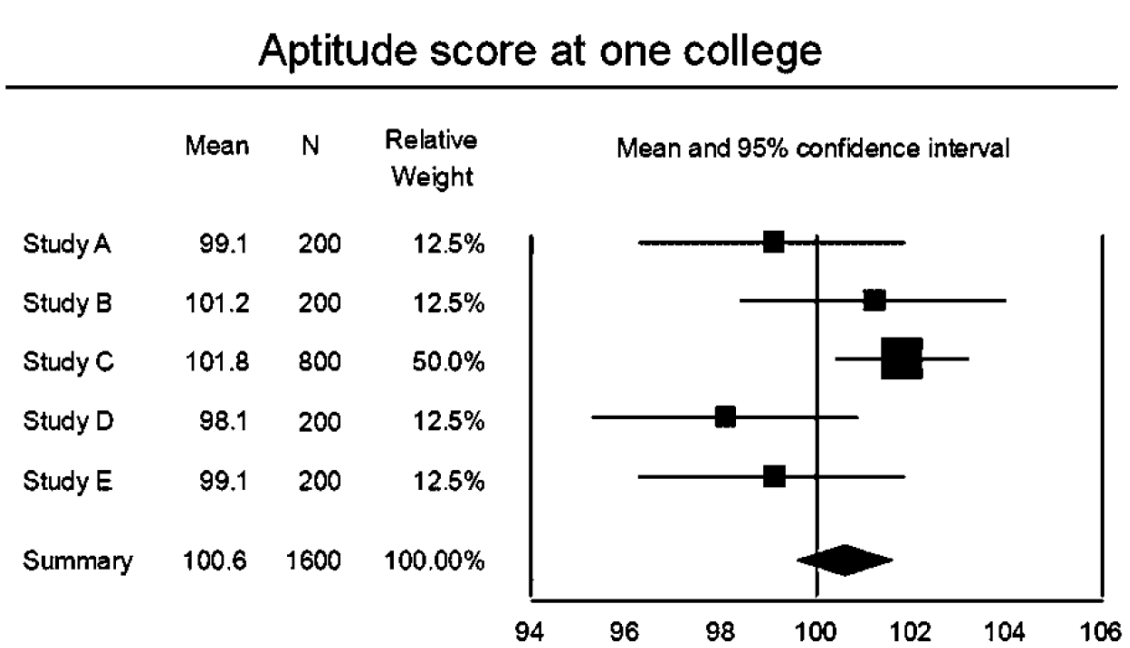


Borenstein M et al. Res Synth Methods. 2010 Apr;1(2):97-111.

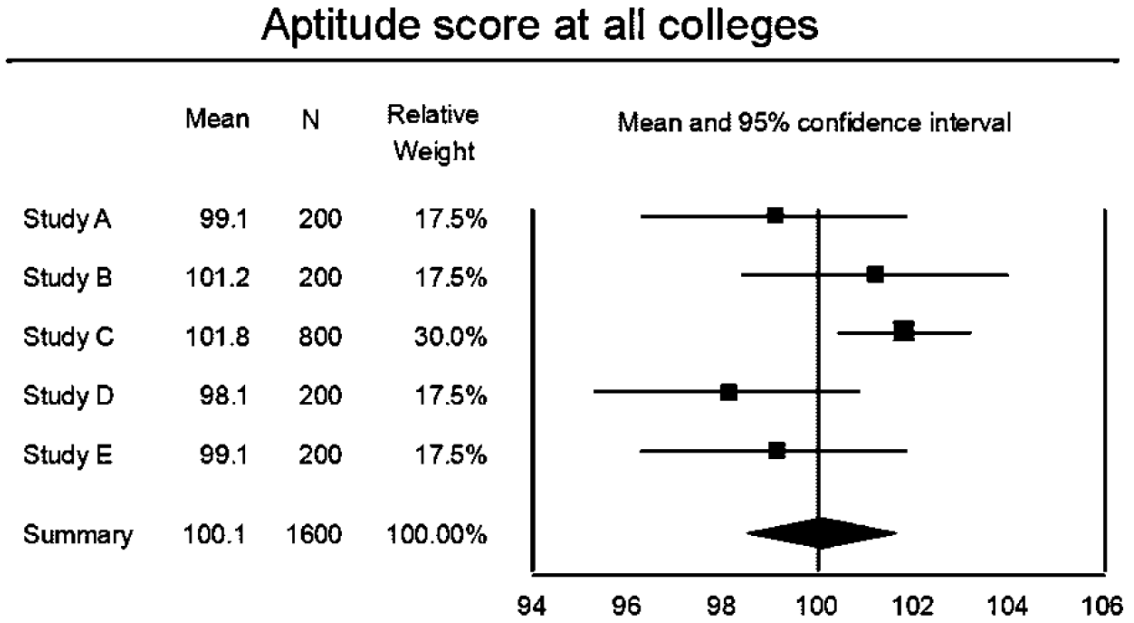
Random-effects model

- Almost identical to fixed-effect model when there is no heterogeneity.
- With wider confidence intervals than fixed effect model when there is heterogeneity.
- Gives relatively more weight to smaller studies.

Fixed-effect model



Random-effects models



Assessment of heterogeneity

To test for heterogeneity, we used the I^2 statistic (Higgins 2003). Where heterogeneity was high ($I^2 > 50\%$), we used a random-effects model for data synthesis.

Data synthesis

Where possible, we calculated the number of events occurring within the sample for each of the outcomes. We generated ORs with 95% CIs to evaluate the effect of treatment, using a fixed-effect model. Where heterogeneity was high ($I^2 > 50\%$) we used a random-effects model for data synthesis.

Data synthesis

Where possible, we calculated the number of events occurring within the sample for each of the outcomes. We generated ORs with 95% CIs to evaluate the effect of treatment, using a fixed-effect model. Where heterogeneity was high ($I^2 > 50\%$) we used a random-effects model for data synthesis.

不完全對！

- We should choose the model based on our understanding of how the studies were sampled, and not the results of a statistical test. If we are working with studies that assess the impact of an intervention in different populations then logic tells us that the random-effects model is the model that fits the data, and it's the model that we should choose.

Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

Random-effects model

Study or subgroup	Favours ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	11/78	22/70		18.3 %	0.36 [0.16, 0.81]
Donaldson 1985	4/33	15/32		13.4 %	0.16 [0.04, 0.55]
Goldman 1984	7/22	19/31		14.4 %	0.29 [0.09, 0.93]
Green 1982	8/32	12/17		12.8 %	0.14 [0.04, 0.52]
Kohler 1984	22/44	17/44		17.9 %	1.59 [0.68, 3.70]
McCollum 1991	63/286	74/263		23.1 %	0.72 [0.49, 1.06]
Total (95% CI)	**495**	**457**		**100.0 %**	**0.42 [0.22, 0.83]**

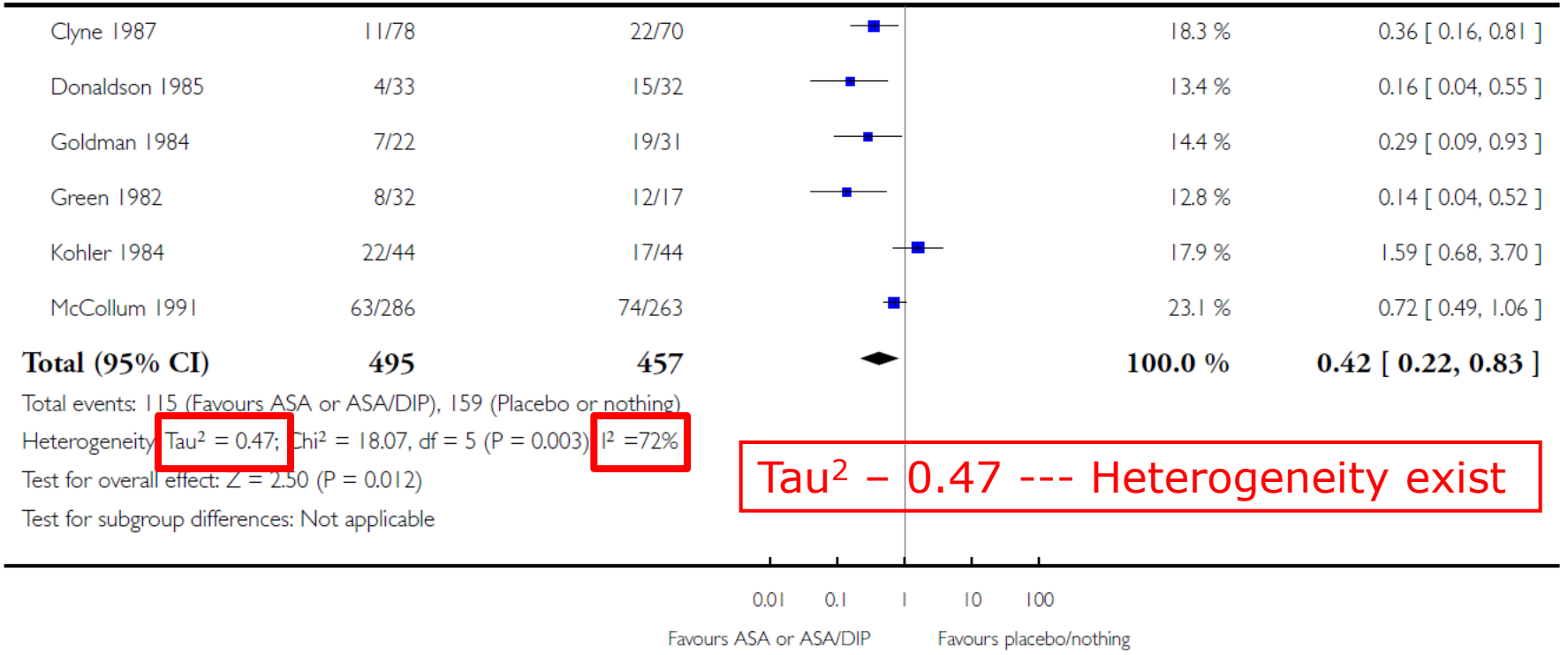
Total events: 115 (Favours ASA or ASA/DIP), 159 (Placebo or nothing)

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 18.07$, df = 5 (P = 0.003) $I^2 = 72\%$

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable

Tau^2 – 0.47 --- Heterogeneity exist



Analysis 1.5. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 5 Mortality.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 5 Mortality

Fixed-effect model

Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Clyne 1987	11/78	8/70		14.2 %	1.27 [0.48, 3.37]
Goldman 1984	0/22	2/31		4.0 %	0.26 [0.01, 5.74]
Green 1982	2/32	0/17		1.2 %	2.87 [0.13, 63.22]
McCollum 1991	40/286	46/263		80.7 %	0.77 [0.48, 1.22]
Total (95% CI)	**418**	**381**		**100.0 %**	**0.84 [0.56, 1.26]**

Total events: 53 (ASA or ASA/DIP), 56 (Placebo or nothing)

Heterogeneity: $Chi^2 = 2.00$, $df = 3$ ($P = 0.57$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.83$ ($P = 0.41$)

Test for subgroup differences: Not applicable

No heterogeneity

Tau^2 不會出現在 fixed-effect model 內

0.005 0.1 1 10 200

Favours ASA or ASA/DIP Favours placebo/nothing

- 用 fixed-effect model 是否恰當 ?
- 是不是 no heterogeneity 的 meta-analysis 就得用 fixed–effect model ?

Analysis 1.2. Comparison 1 Insulin analogues versus regular human insulin, Outcome 2 Severe hypoglycaemic episodes without cross-over trials.

Review: Short-acting insulin analogues versus regular human insulin for adults with type 1 diabetes mellitus

Comparison: 1 Insulin analogues versus regular human insulin

Outcome: 2 Severe hypoglycaemic episodes without cross-over trials

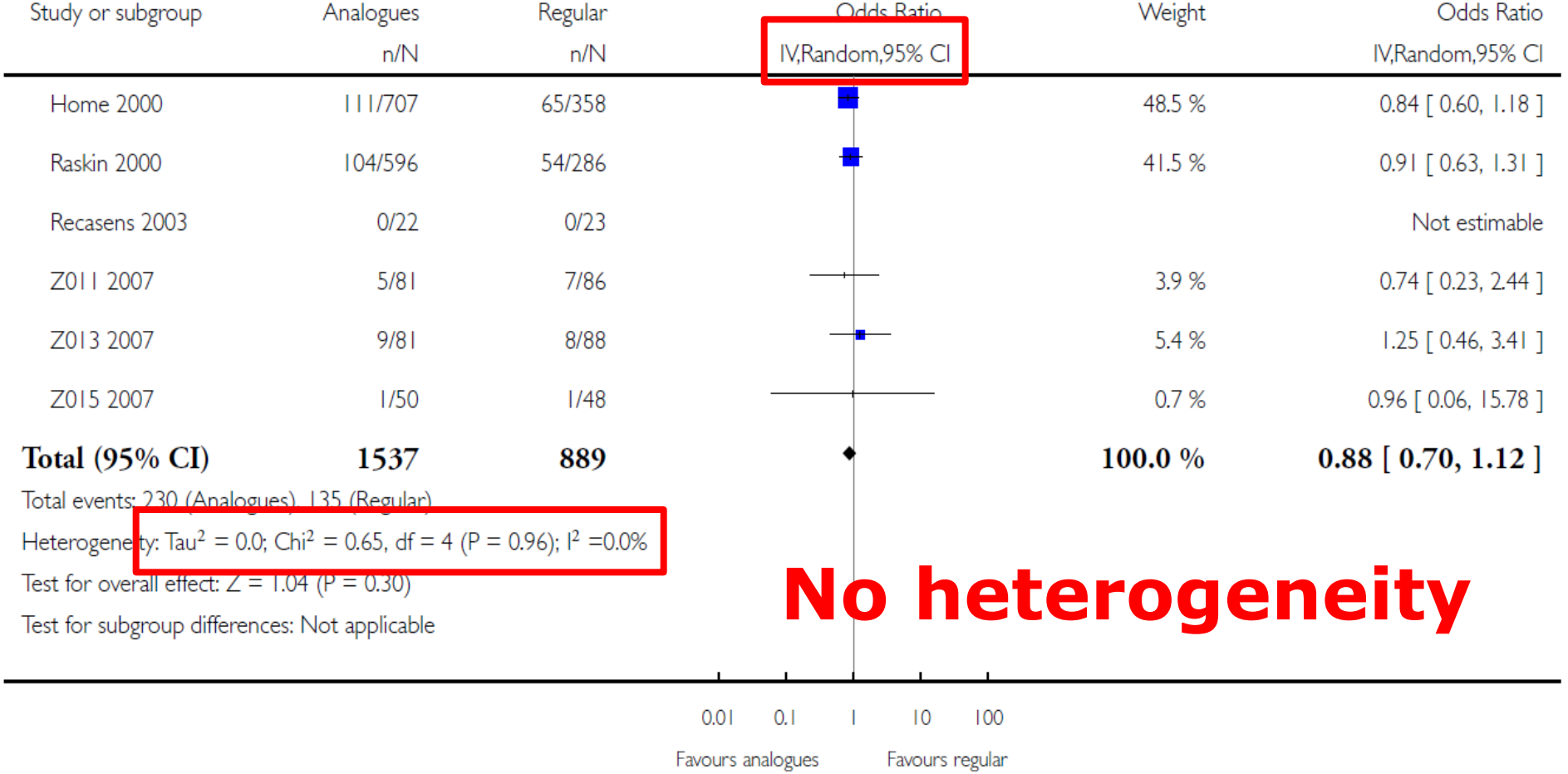
Study or subgroup	Analogues n/N	Regular n/N	Odds Ratio IV,Random,95% CI	Weight	Odds Ratio IV,Random,95% CI
Home 2000	111/707	65/358		48.5 %	0.84 [0.60, 1.18]
Raskin 2000	104/596	54/286		41.5 %	0.91 [0.63, 1.31]
Recasens 2003	0/22	0/23			Not estimable
Z011 2007	5/81	7/86		3.9 %	0.74 [0.23, 2.44]
Z013 2007	9/81	8/88		5.4 %	1.25 [0.46, 3.41]
Z015 2007	1/50	1/48		0.7 %	0.96 [0.06, 15.78]
Total (95% CI)	**1537**	**889**		**100.0 %**	**0.88 [0.70, 1.12]**

Total events: 230 (Analogues), 135 (Regular)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.65$, df = 4 (P = 0.96); $I^2 = 0.0\%$

Test for overall effect: Z = 1.04 (P = 0.30)

Test for subgroup differences: Not applicable



No heterogeneity

6. What are the overall results of the review?

- 這篇回顧呈現了什麼結果？

- What are the results ?
- How were the results expressed. Odds ratio ? Risk ratio ? Mean difference ? NNT ?

Risk Ratio & Odds Ratio

- Risk Ratio = Relative Risk = RR (風險比)

= risk of event in experiment group /risk of event in control group

- Odds Ratio = Relative Odds = OR (勝算比)

= odds of event in experiment group /odds of event in control group

- Odds = number of positive event/number of negative event

Example

- Control group: 100 death:20
- Experiment group: 100 death:10

- RR = (10/100)/(20/100)
  = 0.1/0.2 = 0.5

- OR = (10/90)/(20/80)
  = 0.11/0.25 = 0.44

Risk Ratio & Odds Ratio

- Odds ratio can be used in prospective & retrospective study (randomized controlled trial or case controlled study)

- Risk ratio can only be used in prospective study (cohort study)

Number needed to treat(NNT)

- For systematic review:

Method II: To calculate the NNT or NNH from any OR and PEER:

For OR < 1:

$$NNT = \frac{1 - \{PEER \times (1 - OR)\}}{(1 - PEER) \times PEER \times (1 - OR)}$$

For OR > 1:

$$NNH = \frac{1 + \{PEER \times (OR - 1)\}}{(1 - PEER) \times PEER \times (OR - 1)}$$

Convert relative risk (RR) to NNT：

For RR < 1 : $\rightarrow$NNT = $\frac{1}{[(1 - RR) \times PEER]}$

For RR > 1 : $\rightarrow$NNT = $\frac{1}{[(RR - 1) \times PEER]}$

OR: Odds Ratio or Relative Odds
RR: Risk Ratio or Relative Risk
PEER: Patient's Expected Event Rate
在文章中， PEER = CER (control event rate)

Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

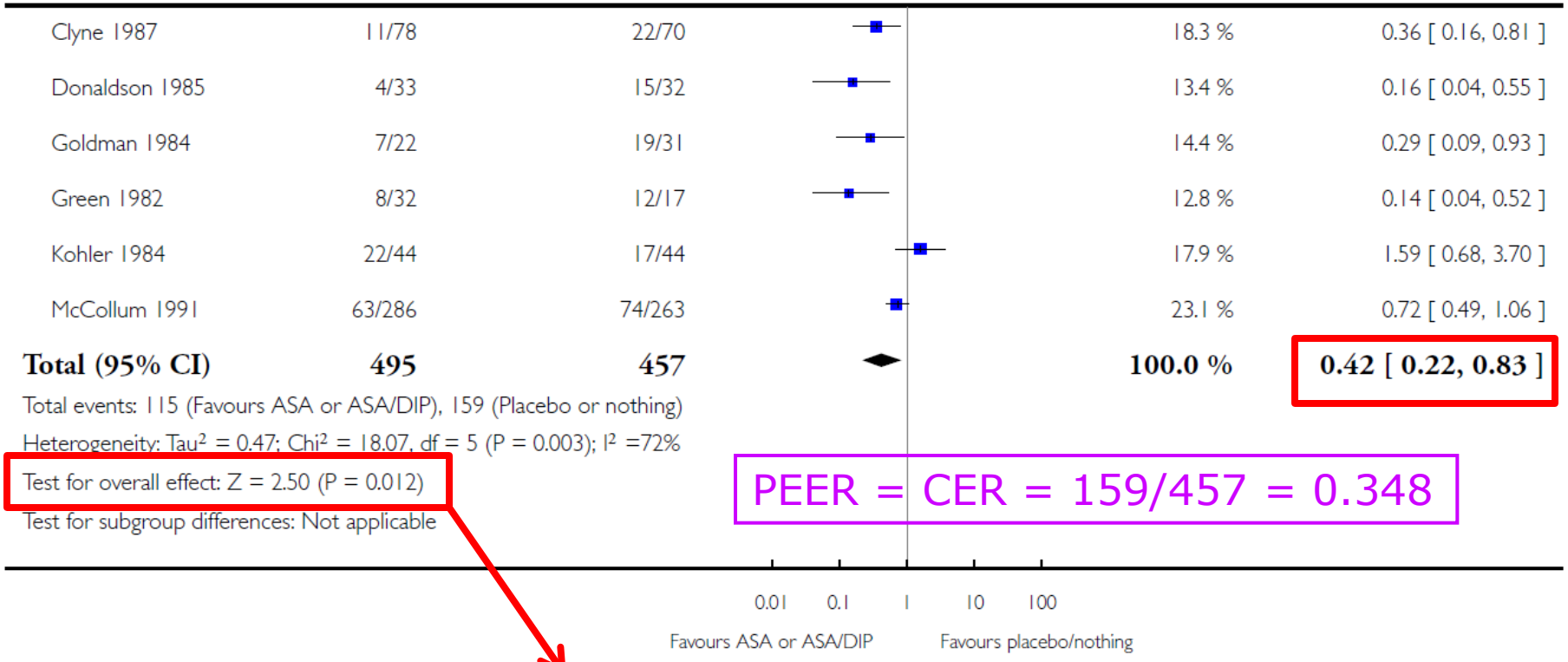
Study or subgroup	Favours ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	11/78	22/70		18.3 %	0.36 [0.16, 0.81]
Donaldson 1985	4/33	15/32		13.4 %	0.16 [0.04, 0.55]
Goldman 1984	7/22	19/31		14.4 %	0.29 [0.09, 0.93]
Green 1982	8/32	12/17		12.8 %	0.14 [0.04, 0.52]
Kohler 1984	22/44	17/44		17.9 %	1.59 [0.68, 3.70]
McCollum 1991	63/286	74/263		23.1 %	0.72 [0.49, 1.06]
Total (95% CI)	**495**	**457**		**100.0 %**	**0.42 [0.22, 0.83]**

Total events: 115 (Favours ASA or ASA/DIP), 159 (Placebo or nothing)

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 18.07$, df = 5 (P = 0.003); $I^2 = 72\%$

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



PEER = CER = 159/457 = 0.348

P = 0.012 (<0.05) --- statistically significant

Method II: To calculate the NNT or NNH from any OR and PEER:

For OR < 1:

$$NNT = \frac{1 - \{PEER \times (1 - OR)\}}{(1 - PEER) \times PEER \times (1 - OR)}$$

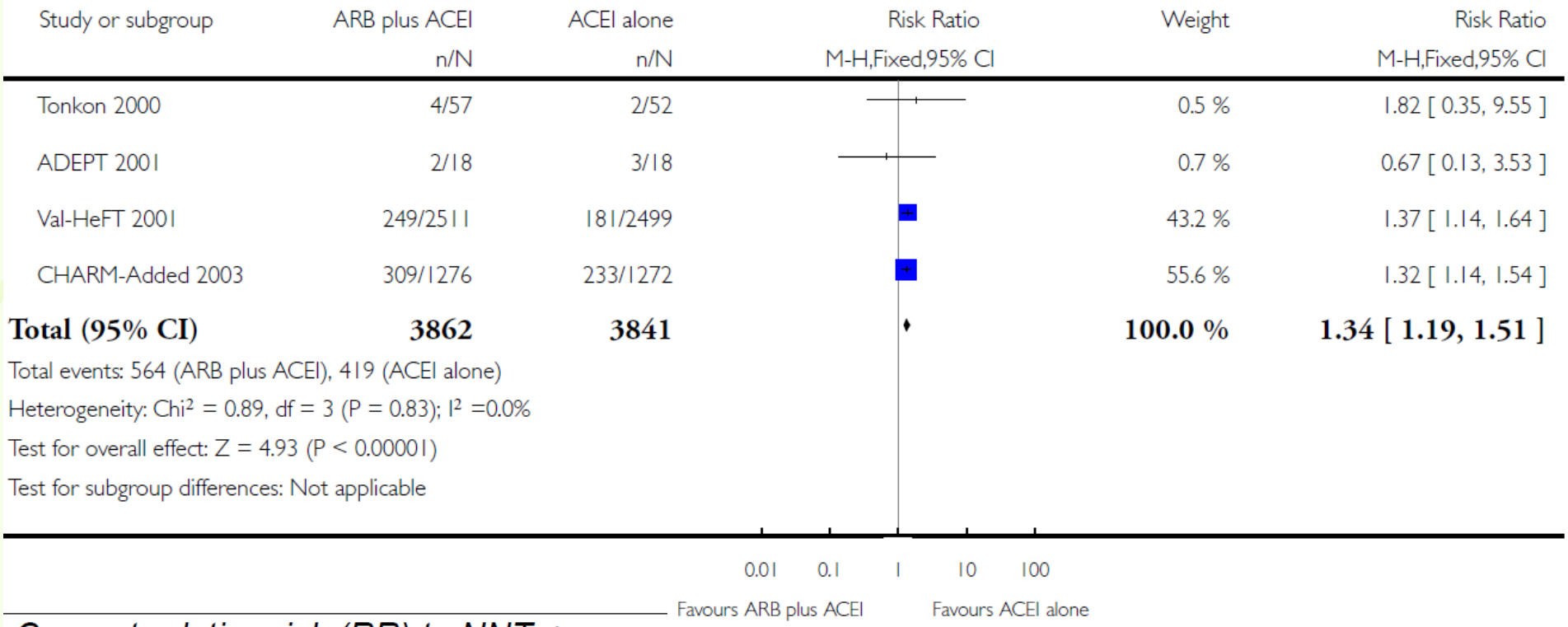
For OR > 1:

$$NNH = \frac{1 + \{PEER \times (OR - 1)\}}{(1 - PEER) \times PEER \times (OR - 1)}$$

- OR = 0.42
- 1-OR = 1-0.42 = 0.58
- PEER = CER = 159/457 = 0.348
- **NNT** = $\frac{1 - (0.348 \times 0.58)}{(1-0.348) \times 0.348 \times 0.58}$

  = 0.798/0.132 = 6.05 = **7**

Outcome: 9 WDAE (Withdrawal Due to Adverse Effects)



Convert relative risk (RR) to NNT :

For RR < 1 : $\rightarrow NNT = \frac{1}{[(1-RR)\times PEER]}$

For RR > 1 : $\rightarrow NNT = \frac{1}{[(RR-1)\times PEER]}$

RR = 1.34

PEER = CER = (2+3+181+233)/3841 = 419/3841 = 0.109

NNH = 1/[(1.34-1) x 0.109] = 1/0.037 = 27.027 = 27

重點提示

- 必須有 risk ratio 或 odds ratio 才有辦法算 NNT(number needed to treat) 或 NNH(number needed to harm)。

- 統計上無意義的話就不必算 NNT或 NNH了。

- NNT —— 小數點無條件進位
- NNH —— 小數點無條件捨棄

7. How precise are the results?

- 結果有多精確？

- What is the confidence interval ?
- Narrow confidence interval is more precise.

Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

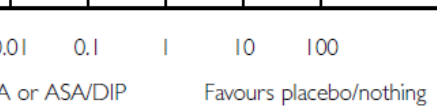
Study or subgroup	Favours ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	11/78	22/70		18.3 %	0.36 [0.16, 0.81]
Donaldson 1985	4/33	15/32		13.4 %	0.16 [0.04, 0.55]
Goldman 1984	7/22	19/31		14.4 %	0.29 [0.09, 0.93]
Green 1982	8/32	12/17		12.8 %	0.14 [0.04, 0.52]
Kohler 1984	22/44	17/44		17.9 %	1.59 [0.68, 3.70]
McCollum 1991	63/286	74/263		23.1 %	0.72 [0.49, 1.06]
Total (95% CI)	**495**	**457**		**100.0 %**	**0.42 [0.22, 0.83]**

Total events: 115 (Favours ASA or ASA/DIP), 159 (Placebo or nothing)

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 18.07$, df = 5 (P = 0.003); $I^2 = 72\%$

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



Confidences interval = 0.83-0.22 = 0.61

Analysis 3.3. Comparison 3 ASA or ASA/DIP versus pentoxifylline (PTX), all grafts, Outcome 3 Primary graft patency, 6 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 3 ASA or ASA/DIP versus pentoxifylline (PTX), all grafts

Outcome: 3 Primary graft patency, 6 months

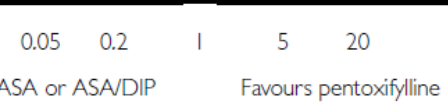
Study or subgroup	ASA or ASA/DIP n/N	PTX n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Lucas 1984	5/19	2/14		18.5 %	2.14 [0.35, 13.12]
Raithel 1987	10/59	9/59		81.5 %	1.13 [0.42, 3.03]
Total (95% CI)	**78**	**73**		**100.0 %**	**1.32 [0.56, 3.11]**

Total events: 15 (ASA or ASA/DIP), 11 (PTX)

Heterogeneity: $Chi^2 = 0.37$, df = 1 (P = 0.54); $I^2 = 0.0\%$

Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable



Confidences interval = 3.11-0.56 = 2.55

Wide confidences interval

Analysis 1.5. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 5 Mortality.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 5 Mortality

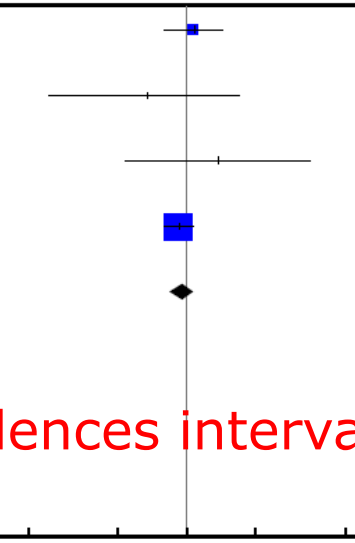
Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Clyne 1987	11/78	8/70		14.2 %	1.27 [0.48, 3.37]
Goldman 1984	0/22	2/31		4.0 %	0.26 [0.01, 5.74]
Green 1982	2/32	0/17		1.2 %	2.87 [0.13, 63.22]
McCollum 1991	40/286	46/263		80.7 %	0.77 [0.48, 1.22]
Total (95% CI)	**418**	**381**		**100.0 %**	**0.84 [0.56, 1.26]**

Total events: 53 (ASA or ASA/DIP), 56 (Placebo or nothing)

Heterogeneity: $Chi^2 = 2.00$, $df = 3$ ($P = 0.57$); $I^2 = 0.0\%$

Test for overall effect: $Z = 0.83$ ($P = 0.41$)

Test for subgroup differences: Not applicable



0.005 0.1 1 10 200

Favours ASA or ASA/DIP Favours placebo/nothing

Confidences interval = 1.26-0.56 = 0.7

Narrow confidences interval

實證醫學的五個步驟

1) Ask an answerable question〔問可以回答的問題〕
2) Search for the best evidences〔搜尋最佳證據〕
3) Critically appraise those evidences〔嚴格的文獻評讀〕
4) Apply to the patient〔臨床應用〕
5) Evaluate our performance〔評估與稽核以上步驟〕

8. Can the results be applied to the local population?

Yes

Can't Tell

No

- **此研究是否可應用到你的病患？**

  我們的病患與研究中的病患是否不同？

  我們是否有這種藥或設備？

  治療的方法是否與我們的病患相似？

Characteristics of included studies *[ordered by study ID]*

Becquemin 1997

Methods	***Study type:*** Multicentre, double-blind, randomised controlled trial ***Study aim:*** To determine whether ticlopidine (TIC) could reduce the rate of late occlusion of saphenous-vein grafts below the knee ***Country:*** France
Participants	***Number randomised:*** Total n = 243 (TIC n = 122; placebo n = 121) ***Age- mean years:*** TIC 67.1; placebo 67.7 ***Gender n (M/F):*** TIC 96/26; placebo 92/29 ***Inclusion criteria:*** All patients 18 to 80 years old who required femoropopliteal or femorotibial bypass graft for atheromatous occlusive disease; had a saphenous vein suitable for grafting ***Exclusion criteria:*** Acute ischaemia or aneurysm; marked stenosis in the ipsilateral iliac artery; previous arterial surgery on the same limb; reduced life expectancy; pregnancy; inability to comply with the protocol; associated conditions requiring treatment with platelet-inhibiting drugs or anticoagulants; abnormalities of haemostasis ***Co-morbidity:*** current angina or previous MI (TIC 20.5%; placebo 24.8%), impaired left ventricular function (TIC 10.7%; placebo 7.4%), arrhythmia (TIC 9.0%; placebo 15.7%), carotid stenosis (TIC 22.1%; placebo 21.5%), hypertension (TIC 48.4%; placebo 53.7%), current smoker (TIC 25.4%; placebo 19.0%), diabetes (TIC 27.0%; placebo 21.5%), hyperlipidaemia (TIC 23.8%; placebo 25.6%), previous vascular surgery (TIC 32.8%; placebo 30.6%) ***Severity of occlusive disease:*** Leriche-Fontaine stage of disease- stage IIb (TIC 27.0; placebo 22.3), stage III (TIC 30.3; placebo 41.3), stage IV (TIC 42.6; placebo 36.4) ***Site of distal anastomosis:*** popliteal (TIC n = 66; placebo n = 82), tibial (TIC n = 56; placebo n = 39) ***Type of graft:*** autologous saphenous-vein grafts More than 70% of the participants in both groups suffered from critical limb ischaemia

CASPAR 2010

Methods	***Study type:*** Multicentre, prospective, randomised, placebo-controlled trial ***Study aim:*** To determine whether clopidogrel plus ASA had better limb outcomes compared to ASA alone, in patients undergoing below-knee bypass grafting ***Country:*** UK
Participants	***Number randomised:*** Total n = 851 (Clopidogrel + ASA n = 425; ASA + placebo n = 426) ***Age- mean years (SD):*** Clopidogrel + ASA 66.5 (8.7); ASA + placebo 65.6 (8.5) ***Gender- M%:*** Clopidogrel + ASA 75.5%; ASA + placebo 75.8% ***Inclusion criteria:*** ≥ 40 and ≤ 80 years; informed consent obtained before conducting any study-related procedure; chronic background treatment with daily ASA of any done, started at least 4 weeks before surgery; a post-randomisation dose of ASA between 75 and 100 mg/day; unilateral below-knee bypass graft for atherosclerotic PAD; patent index graft demonstrated during bypass surgery or between surgery and time of randomisation; no clinical evidence of graft occlusion at randomisation ***Exclusion criteria:*** Onset of PAD symptoms before age of 40; nonatherosclerotic vascular disease; patients receiving aortobifemoral, iliac-femoral or cross-over (femoral-femoral) grafts or undergoing peripheral transcutaneous angioplasty during the same surgery; significant bleeding risk such as current active bleeding at the surgical site; withdrawal of an epidural catheter less than 12 hours before randomisation; peptic ulceration within 12 months of randomisation; previous or current intracranial haemorrhage or haemorrhagic stroke; any history of severe spontaneous bleeding; current warfarin therapy or anticipated need for warfarin; concomitant additional antiplatelet agents or thrombolytic agents ***Co-morbidity:*** Hypertension (Clopidogrel + ASA 70.1%, ASA + placebo 70.0%); Hyperlipidemia (Clopidogrel + ASA 50.4%, ASA + placebo 48.8%); CAD and/or CRVD (Clopidogrel + ASA 38.4%, ASA + placebo 31.0%); Diabetes (Clopidogrel + ASA 37.4%, ASA + placebo 38.0%), claudication only (Clopidogrel + ASA 34.1%, ASA + placebo 32.6%), rest pain (Clopidogrel + ASA 26.1%, ASA + placebo 26.5%), ulcers/gangrene (Clopidogrel + ASA 39.3%, ASA + placebo 39.9%) ***Severity of occlusive disease (determined by ABPI):*** ABPI (SD) - Clopidogrel + ASA 0.44 (0.25), ASA + placebo 0.46 (0.26) ***Site of distal anastomosis:*** Below-knee popliteal (Clopidogrel + ASA 75.5%, ASA + placebo 74.8%); below-knee popliteal crural (Clopidogrel + ASA 20.7%, ASA + placebo 22.1%); beyond popliteal pedal (Clopidogrel + ASA 3.8%, ASA + placebo 3.1%) ***Type of graft:*** venous and prosthetic grafts (Clopidogrel + ASA venous = 297 prosthetic = 128; ASA + placebo venous = 301 prosthetic = 125)

1. Aspirin (ASA) or aspirin and dipyridamole (ASA/DIP) versus placebo or nothing (Clyne 1987; Donaldson 1985; Goldman 1984; Green 1982; Kohler 1984; McCollum 1991)
2. ASA or ASA/DIP versus pentoxifylline (PTX) (Lucas 1984; Raithel 1987)
3. ASA/DIP versus indobufen (IND), a reversible cyclo-oxygenase inhibitor (D'Addato 1992)
4. ASA or ASA/DIP versus vitamin K antagonists (VKA) (BOA 2000; Schneider 1979)
5. ASA/DIP versus low molecular weight heparin (LMWH) (Edmondson 1994)
6. Ticlopidine (TIC) versus placebo (Becquemin 1997)
7. ASA versus prostaglandin E1 (Gruss 1991)
8. ASA versus naftidrofuryl (Noppeney 1988)
9. Clopidogrel and ASA versus ASA alone (CASPAR 2010)

Details of the study designs are shown in the table 'Characteristics of included studies' and in Table 1.

9. Were all important outcomes considered?

Yes	
Can't Tell	
No	

- **是否所有重要的結果都被考量到？**
- 是否有呈現我們想要看的臨床重要結果 ？

Analysis 1.1. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 1 Primary graft patency at 12 months.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 1 Primary graft patency at 12 months

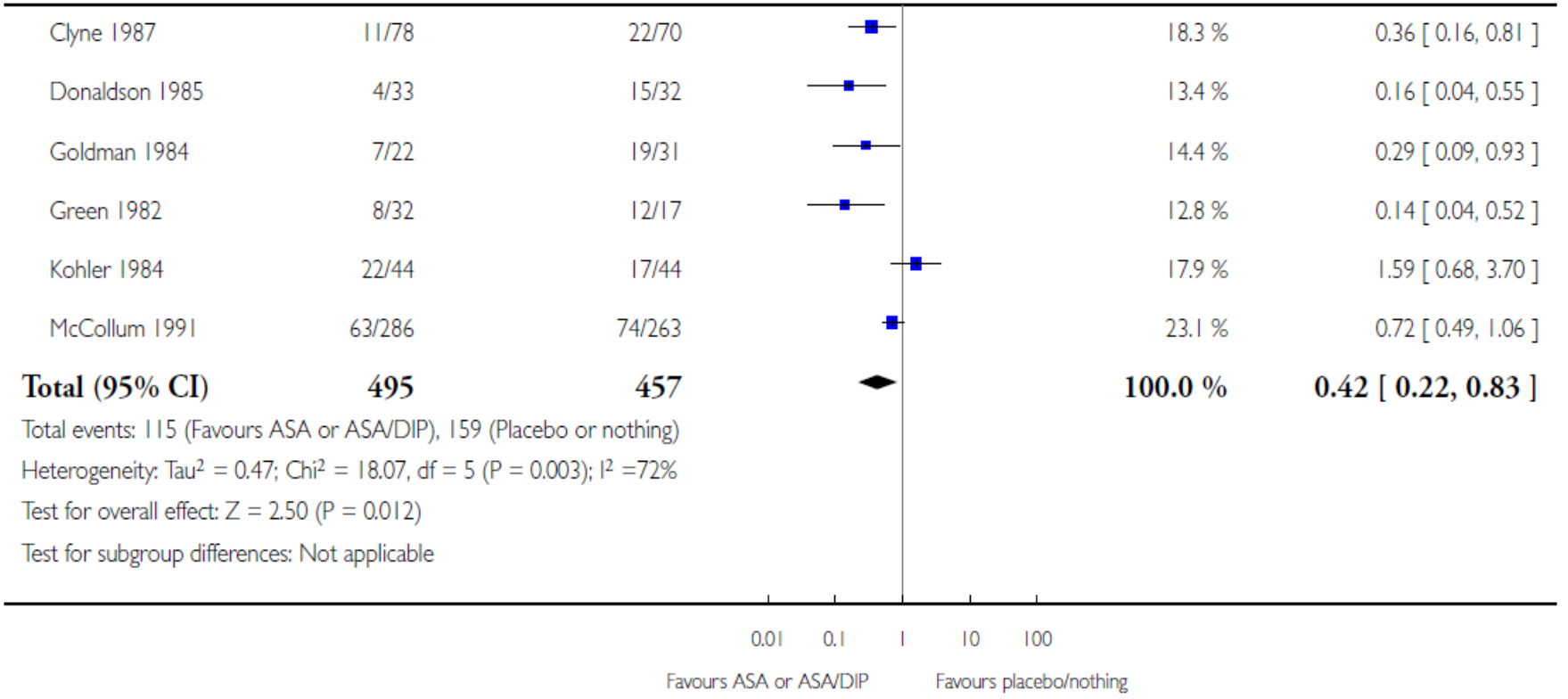
Study or subgroup	Favours ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	11/78	22/70		18.3 %	0.36 [0.16, 0.81]
Donaldson 1985	4/33	15/32		13.4 %	0.16 [0.04, 0.55]
Goldman 1984	7/22	19/31		14.4 %	0.29 [0.09, 0.93]
Green 1982	8/32	12/17		12.8 %	0.14 [0.04, 0.52]
Kohler 1984	22/44	17/44		17.9 %	1.59 [0.68, 3.70]
McCollum 1991	63/286	74/263		23.1 %	0.72 [0.49, 1.06]
Total (95% CI)	**495**	**457**		**100.0 %**	**0.42 [0.22, 0.83]**

Total events: 115 (Favours ASA or ASA/DIP), 159 (Placebo or nothing)

Heterogeneity: $Tau^2 = 0.47$; $Chi^2 = 18.07$, df = 5 (P = 0.003); $I^2 = 72\%$

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 4 Cardiovascular events.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 4 Cardiovascular events

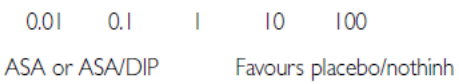
Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Clyne 1987	5/78	2/70		23.0 %	2.33 [0.44, 12.41]
Donaldson 1985	4/32	1/33		16.0 %	4.57 [0.48, 43.34]
Green 1982	3/32	1/17		15.1 %	1.66 [0.16, 17.25]
McCollum 1991	35/286	53/263		45.8 %	0.55 [0.35, 0.88]
Total (95% CI)	**428**	**383**		**100.0 %**	**1.27 [0.43, 3.80]**

Total events: 47 (ASA or ASA/DIP), 57 (Placebo or nothing)

Heterogeneity: $Tau^2 = 0.62$; $Chi^2 = 6.19$, df = 3 (P = 0.10); $I^2 = 52\%$

Test for overall effect: Z = 0.44 (P = 0.66)

Test for subgroup differences: Not applicable



Analysis 1.5. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 5 Mortality.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

Outcome: 5 Mortality

Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Clyne 1987	11/78	8/70		14.2 %	1.27 [0.48, 3.37]
Goldman 1984	0/22	2/31		4.0 %	0.26 [0.01, 5.74]
Green 1982	2/32	0/17		1.2 %	2.87 [0.13, 63.22]
McCollum 1991	40/286	46/263		80.7 %	0.77 [0.48, 1.22]
Total (95% CI)	**418**	**381**		**100.0 %**	**0.84 [0.56, 1.26]**

Total events: 53 (ASA or ASA/DIP), 56 (Placebo or nothing)

Heterogeneity: $Chi^2 = 2.00$, df = 3 (P = 0.57); $I^2 = 0.0\%$

Test for overall effect: Z = 0.83 (P = 0.41)

Test for subgroup differences: Not applicable

10. Are the benefits worth the harms and costs?

- 這些好處隨之而來的傷害和花費是否值得？

What is the adverse effect ?

What is the cost ?

Analysis 1.2. Comparison 1 ASA or ASA/DIP vs placebo or nothing, all grafts, Outcome 2 Side effects and complications.

Review: Antiplatelet agents for preventing thrombosis after peripheral arterial bypass surgery

Comparison: 1 ASA or ASA/DIP vs placebo or nothing, all grafts

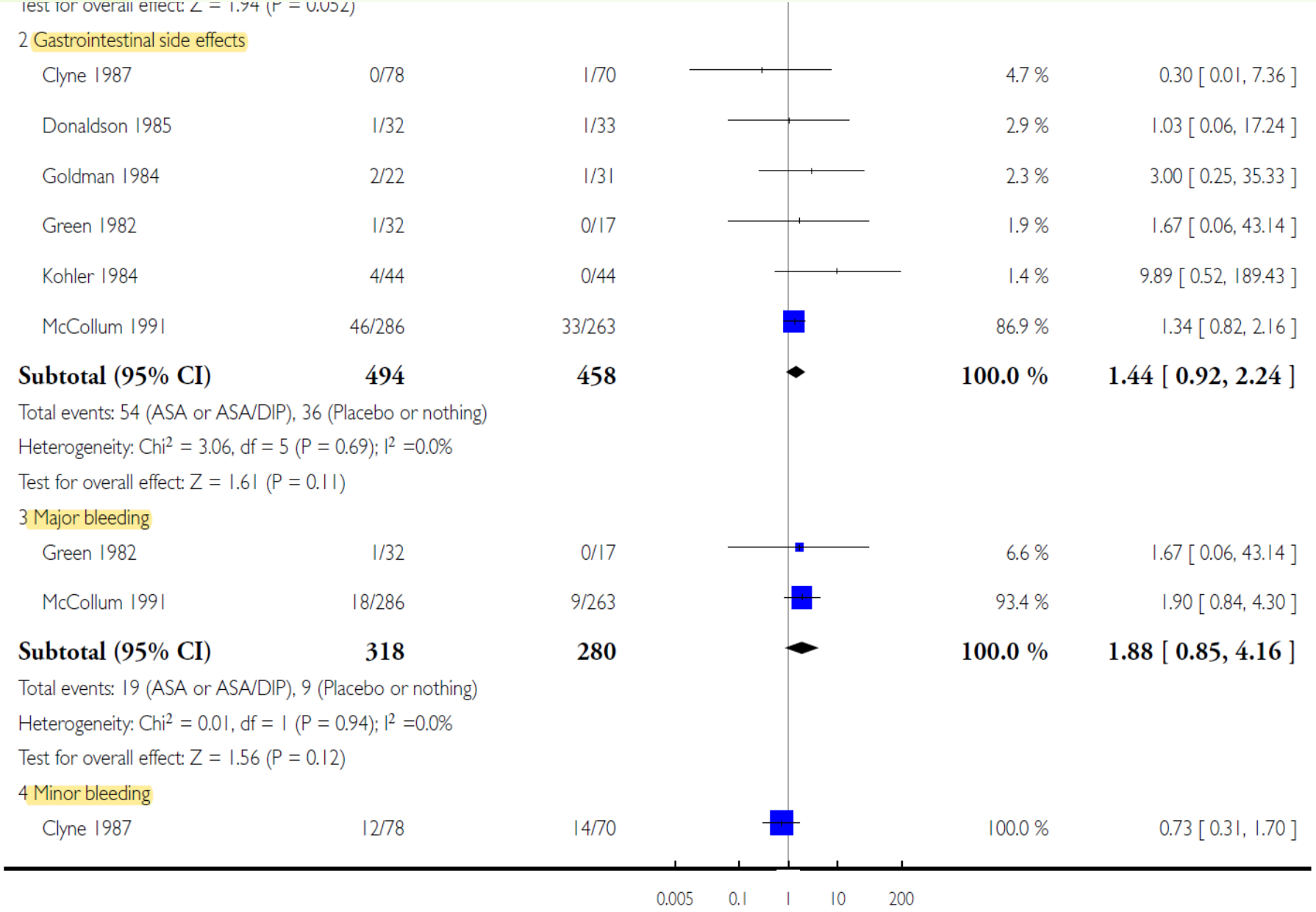
Outcome: 2 Side effects and complications

Study or subgroup	ASA or ASA/DIP n/N	Placebo or nothing n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Side effects- general					
Clyne 1987	6/78	1/70		3.0 %	5.75 [0.67, 49.00]
Donaldson 1985	1/32	1/33		3.0 %	1.03 [0.06, 17.24]
Green 1982	1/32	0/17		1.9 %	1.67 [0.06, 43.14]
Kohler 1984	4/51	1/51		2.9 %	4.26 [0.46, 39.46]
McCollum 1991	46/286	33/263		89.3 %	1.34 [0.82, 2.16]
Subtotal (95% CI)	**479**	**434**		**100.0 %**	**1.55 [1.00, 2.41]**

Total events: 58 (ASA or ASA/DIP), 36 (Placebo or nothing)

Heterogeneity: $Chi^2 = 2.67$, df = 4 (P = 0.61); $I^2 = 0.0\%$

Test for overall effect: Z = 1.94 (P = 0.052)


Test for overall effect: Z = 1.94 (P = 0.052)
2 Gastrointestinal side effects
Clyne 1987 0/78 1/70 4.7 % 0.30 [0.01, 7.36]
Donaldson 1985 1/32 1/33 2.9 % 1.03 [0.06, 17.24]
Goldman 1984 2/22 1/31 2.3 % 3.00 [0.25, 35.33]
Green 1982 1/32 0/17 1.9 % 1.67 [0.06, 43.14]
Kohler 1984 4/44 0/44 1.4 % 9.89 [0.52, 189.43]
McCollum 1991 46/286 33/263 86.9 % 1.34 [0.82, 2.16]
Subtotal (95% CI) 494 458 100.0 % 1.44 [0.92, 2.24]
Total events: 54 (ASA or ASA/DIP), 36 (Placebo or nothing)
Heterogeneity: Chi² = 3.06, df = 5 (P = 0.69); I² =0.0%
Test for overall effect: Z = 1.61 (P = 0.11)
3 Major bleeding
Green 1982 1/32 0/17 6.6 % 1.67 [0.06, 43.14]
McCollum 1991 18/286 9/263 93.4 % 1.90 [0.84, 4.30]
Subtotal (95% CI) 318 280 100.0 % 1.88 [0.85, 4.16]
Total events: 19 (ASA or ASA/DIP), 9 (Placebo or nothing)
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² =0.0%
Test for overall effect: Z = 1.56 (P = 0.12)
4 Minor bleeding
Clyne 1987 12/78 14/70 100.0 % 0.73 [0.31, 1.70]
0.005
0.1
1
10
200

Thank You