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Small-incision versus open cholecystectomy for patients with symptomatic cholecystolithiasis (Review)

Keus F, de Jong J, Gooszen HG, Laarhoven CJHM

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[Intervention Review]

Small-incision versus open cholecystectomy for patients with symptomatic cholecystolithiasis

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ABSTRACT

Background

Cholecystectomy is one of the most frequently performed operations. Open cholecystectomy has been the gold standard for over 100 years. Small-incision cholecystectomy is a less frequently used alternative.

Objectives

To compare the beneficial and harmful effects of small-incision versus open cholecystectomy for patients with symptomatic cholecystolithiasis.

Search methods

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register* (6 April 2004), *The Cochrane Library* (Issue 1, 2004), *MEDLINE* (1966 to January 2004), *EMBASE* (1980 to January 2004), *Web of Science* (1988 to January 2004), and *CINAHL* (1982 to January 2004) for randomised trials.

Selection criteria

All published and unpublished randomised trials in patients with symptomatic cholecystolithiasis comparing any kind of small-incision or other kind of minimal incision cholecystectomy versus any kind of open cholecystectomy. No language limitations were applied.

Data collection and analysis

Two authors independently performed selection of trials and data extraction. The methodological quality of the generation of the allocation sequence, allocation concealment, blinding, and follow-up was evaluated to assess bias risk. Analyses were based on the intention-to-treat principle. Authors were requested additional information in case of missing data. Sensitivity and subgroup analyses were performed if appropriate.

Main results

Seven trials randomised 571 patients. Bias risk was high in the included trials. No mortality was reported. The total complication proportions are respectively 9.9% and 9.3% in the small-incision and open group, which is not significantly different (risk difference all trials, random-effects 0.00, 95% confidence interval (CI) -0.06 to 0.07). There are also no significant differences considering severe complications and bile duct injuries. However, small-incision cholecystectomy has a shorter hospital stay (weighted mean difference, random-effects -2.8 days (95% CI -4.9 to -0.6)) compared to open cholecystectomy.

Authors' conclusions

Small-incision and open cholecystectomy seem to be equivalent regarding risks of complications, but the latter method is associated with a significantly longer hospital stay. The quicker recovery of small-incision cholecystectomy compared with open cholecystectomy confirms the existing preference of this technique over open cholecystectomy.

PLAIN LANGUAGE SUMMARY

Small-incision cholecystectomy and open cholecystectomy seem equivalent considering complications, but small-incision cholecystectomy is associated with a shorter hospital stay

The classical open cholecystectomy and the minimally invasive small-incision cholecystectomy are two alternative operations for removal of the gallbladder. There seem to be no significant differences in mortality and complications between these two techniques. Hospital stay is shorter using the small-incision operation. This review shows that the small-incision and open cholecystectomy should be considered equal, apart from a shorter hospital stay using the small-incision technique.

BACKGROUND

Gallstones are one of the major causes of morbidity in western society. It is estimated that the incidence of symptomatic cholecystolithiasis is up to 2.17 per thousand inhabitants (Legorreta 1993; Steiner 1994) with an annual performance rate of cholecystectomies of more than 500,000 in the USA (Olsen 1991; NIH Consensus 1993; Roslyn 1993). Until the end of the 1980s, open cholecystectomy was the gold standard for treatment of stones in the gallbladder. As incisions for cholecystectomy were shortened resulting in 'small-incision' cholecystectomy, morbidity and complications seemed to decline and patients recovered faster. In the early 1970s small-incision cholecystectomy was introduced as a minimally invasive procedure (Dubois 1982; Goco 1983), and has been compared in trials with open cholecystectomy. Conflicting data on clinical outcome and effectiveness arose from these randomised trials.

Laparoscopic cholecystectomy was introduced in 1985 (Mühe 1986) and rapidly became the method of choice for surgical removal of the gallbladder (NIH Consensus 1993) although the evidence of superiority over small-incision and open cholecystectomy was absent. After this consensus, attention was focused on laparoscopic cholecystectomy and the primary question of the comparison of the small-incision cholecystectomy to the classical open cholecystectomy was never answered.

Differences in primary outcomes like mortality and complication proportions (particularly bile duct injuries) are important reasons to choose one of the operative techniques. When these primary outcomes show no significant difference, then secondary outcomes like non-severe complications, pulmonary outcomes, differences in health status related quality-of-life, hospital stay, and differences in cost-effectiveness analysis should help decide which technique is superior.

Up to now, despite the availability of numerous randomised trials on this topic, no systematic review or meta-analysis of randomised trials has been conducted comparing small-incision and open cholecystectomy. This lack of evidence was the main reason for writing this systematic review. The objective was to evaluate the assumed superiority of the small-incision cholecystectomy.

OBJECTIVES

To evaluate the beneficial and harmful effects of two different types of cholecystectomy for patients with symptomatic cholecystolithiasis. To assess whether small-incision and open cholecystectomy are different in terms of primary (mortality, complications, and relief of symptoms) and secondary outcomes (conversions to open cholecystectomy, operative time, hospital stay, and convalescence). If data were present, differences in other secondary outcomes like analgesic use, postoperative pain, pulmonary function, and costs were compared as well.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised clinical trials comparing small-incision or other kinds of minimal-incision open cholecystectomy to any kind of classical open cholecystectomy. Trials were included irrespectively of blinding, number of patients randomised, and language of the article. Quasi-randomised studies were excluded.

Types of participants

Patients with one or more stones in the gallbladder confirmed by ultrasonography or other imaging technique and symptoms attributable to them, scheduled for cholecystectomy. Acute cholecystitis is a disease with different operative results including the number of complications and conversions. Cholecystectomy in patients suffering from acute cholecystitis should be distinguished from cholecystectomy in patients suffering from symptomatic cholecystolithiasis. Therefore, randomised trials only including patients with acute cholecystitis were excluded from this review. Randomised trials including both symptomatic cholecystolithiasis and acute cholecystitis were included in the review only if the large majority (more than half) of the included patients were operated on because of symptomatic cholecystolithiasis.

Types of interventions

Any kind of small-incision cholecystectomy was assessed versus any kind of open cholecystectomy.

The following classifications of the surgical procedures (based on intention-to-treat) were used:
Only if the words 'small-incision', 'minimal access', 'minilaparotomy', or similar as intended terms were mentioned in the primary classification of the procedure, the surgical intervention was classified as a 'small-incision' cholecystectomy (ie, length of incision of less than 8 cm). The length of incision up to 8 cm was chosen arbitrary as in literature most authors used this as a cut-off point between small-incision and (conversion to) open cholecystectomy.

In all other cases the surgical intervention was classified as 'open cholecystectomy'; this traditional procedure can be carried out through a larger subcostal or transverse incision or a median laparotomy.

Types of outcome measures

The primary outcome measures are mortality, complication proportions (intra-operative, severe, bile duct injuries, and total complications; except minor complications), and relief of symptoms (pain relief). Although relief of symptoms is the aim of cholecystectomy, some patients continue to suffer from their complaints and have persistent pain. Most important in obtaining a high proportion of patients with relief of symptoms is adequate decision making in setting the indication to operate or not. However, it cannot be ruled out that some of this persistent pain should be attributed to the way of incision for cholecystectomy. Therefore it is of interest to include pain relief as a primary outcome.

Secondary outcome measures are all other outcomes assessed in comparing the two operative techniques. We assessed the following secondary outcomes: operative time, hospital stay, convalescence, analgesic use, postoperative pain (visual analogue scale), pulmonary outcome (pulmonary function tests by flow-volume curves), and cost-effectiveness if data were available.

Search methods for identification of studies

We searched the following databases: *The Cochrane Hepato-Biliary Group Controlled Trials Register* (6 April 2004), the *Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects (DARE),* the *Cochrane Central Register of Controlled Trials (CENTRAL), Health Technology Assessment (HTA) Database, NHS Economic Evaluation Database,* all in *The Cochrane Library* (Issue 1, 2004), *The National Library of Medicine (MEDLINE)* (1966 to January 2004), *The Intelligent Gateway to Biomedical & Pharmacological Information (EMBASE)* (1980 to January 2004), *ISI Web of Knowledge (Web of Science)* (1988 to January 2004), and *CINAHL* (1982 to January 2004). The search strategies used are provided in Appendix 1.

Our aim was to perform a maximal sensitive search in order to conduct a more complete review. As describing an operation of the gallbladder in medical terms without the word cholecystectomy is impossible, a maximal sensitive search with the term cholecystectomy was used. For our *MEDLINE* search, a more sophisticated strategy, advised by the Dutch Cochrane Centre and listed in Appendix 1 was used (with help from Geert van der Heijden, Julius Center, Utrecht).

Additional relevant trials were looked for by cross reference checking of identified randomised trials. Finally all authors of included trials were requested by letter for additional information on any published, unpublished, or ongoing trials.

Furthermore, during data extraction it turned out that in a large number of trials essential data and information on methods were missing. To improve the quality of the analysis, individual trialists were contacted and asked for missing data.

Data collection and analysis

The review was conducted according to the present protocol (Keus 2004) and the recommendations by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2005). All identified trials were listed in the 'Characteristics of included studies' table and an evaluation whether the trials fulfilled the inclusion criteria was made. Excluded trials and the reasons for exclusion were listed as well (table with 'Characteristics of excluded studies').

Assessment of methodological quality

Inadequate methodological quality in randomised clinical trials carries the risk of overestimating intervention effects (Schulz 1995; Moher 1998; Kjaergard 2001). Methodological quality, study design, and reporting quality have been recognised as criteria which can restrict bias in the comparisons of interventions (Moher 1998; Kjaergard 2001). Therefore the methodological quality of the randomised clinical trials was assessed using the following components.

Generation of the allocation sequence

- Adequate, if the allocation sequence was generated by a computer or random number table. Drawing of lots, tossing of a coin, shuffling of cards, or throwing dice was considered as adequate if a person who was not otherwise involved in the recruitment of participants performed the procedure.
- Unclear, if the trial was described as randomised, but the method used for the allocation sequence generation was not described.
- Inadequate, if a system involving dates, names, or admittance numbers were used for the allocation of patients. These studies are known as quasi-randomised and were excluded from the present review.

Allocation concealment

- Adequate, if the allocation of patients involved a central independent unit, on-site locked computer, or sealed envelopes.
- Unclear, if the trial was described as randomised, but the method used to conceal the allocation was not described.
- Inadequate, if the allocation sequence was known to the investigators who assigned participants or if the study was quasi-randomised.

Blinding

- Adequate, if the trial was described (at least) as blind to participants or assessors and the method of blinding was described. We are well aware that it is very difficult to properly blind trials comparing surgical treatments.
- Unclear, if the trial was described as (double) blind, but the method of blinding was not described.
- Not performed, if the trial was not blinded.

Follow-up

- Adequate, if the numbers and reasons for dropouts and withdrawals in all intervention groups were described or if it was specified that there were no dropouts or withdrawals.
- Unclear, if the report gave the impression that there had been no dropouts or withdrawals, but this was not specifically stated.
- Inadequate, if the number or reasons for dropouts and withdrawals were not described.

Extraction of data

Inclusion and exclusion criteria used in each trial.

The following data on the randomisation procedure have been extracted:
1. Number of randomised patients.
2. Number of patients not randomised and reasons for non-randomisation.
3. Exclusion after randomisation.
4. Drop-outs.
5. 'Intention-to-treat' analysis.

Also information on sample size, single- or multicentre study design, assessment of primary and secondary outcome measures, use of antibiotic prophylaxis, surgical experience, and intra-operative cholangiography was registered (Table 1).

General descriptive data (like sex, age, body mass index (BMI), and American Society of Anaesthesiology (ASA) classification) are supposed to be equally divided due to randomisation (Assmann 2000). These data are presented in Table 2 as far as available. Outcome data on mortality, complications, health-related quality-of-life, pulmonary function, pain, duration of operation, hospital stay, and convalescence were extracted according to availability.

Statistical analysis

With adequate binary data available, a priori presentation in odds ratios was preferred, based on clinical considerations and statistical

robustness of the odds ratio. From this, results could be presented in relative risk (ratio) (RR(R)) or numbers needed to treat (NNT) by recalculation. However, exploring the data showed that for many binary data the outcome was rare or zero in both arms. Odds ratios (OR) and risk ratios (RR) are not estimable in trials with zero events in both arms (Sweeting 2004). Binary outcomes with zero events in both arms can merely be presented in risk differences (RD). Although risk differences are statistically less robust and result in conservative estimates, they are simple measures, easy to understand, and useful for public communication.

For continuous data, authors generally present their results in medians with ranges due to suspicion of skewed data. However, for the analysis of data in a meta-analysis, means with their corresponding standard deviations (SD) are needed to calculate mean differences (MD) or weighted mean differences (WMD) with 95% confidence intervals (CI). Using means from all trials would ignore a non-Gaussian distribution. Therefore, skewness ratios (mean divided by the standard deviation) were calculated first (Higgins 2005, page 96). With a ratio larger than two, skewness is ruled out, whereas skewness is suggested when the ratio is between one and two and a ratio less than one indicates strong evidence of skewness. In situations where skewness could be ruled out, assumptions on equality of median to mean was made and used in the sensitivity analyses. For trials presenting confidence intervals or standard error of means, we performed a recalculation to a standard deviation (SD) (Higgins 2005, page 90-91). In case no data on standard deviation was available, we calculated an average standard deviation from those observed in other studies and imputed this value for the standard deviation in the sensitivity analysis (Higgins 2005, page 92).

Results were considered according to the four different criteria of quality. The existence of an overall difference in outcome was clear when all four criteria showed significance. However, when the different quality criteria showed contradicting results, then an overall conclusion considering one outcome was not obvious and had to be made individually. In each individual component, results from high-quality trials subgroups were given more weight compared to analyses including all trials or low-quality trials subgroups. Results with confidence intervals that touched, but did not cross, the line of equivalence were considered not significant.

Apart from comparisons in the four individual quality criteria, we also performed a comparison with trials divided into low-bias risk trials (high methodological quality) and high-bias risk trials (low methodological quality). Only trials that were assessed as adequate regarding all the four methodological criteria were considered low-bias risk trials. All trials that were not assessed as adequate with regard to all the four methodological criteria were considered high-bias risk trials.

Bias detection

We have used funnel plots to provide a visual assessment of whether treatment estimates were associated with study size. The presence of publication bias and other biases (Begg 1994; Egger 1997; Macaskill 2001) varies with the magnitude of the treatment effect, the distribution of study size, and whether a one- or two-tailed test is used (Macaskill 2001).

Both the random-effects model (DerSimonian 1986) and the fixed-effect model (DeMets 1987) for pooling effect estimates were explored.

- In case of no discrepancy (and no heterogeneity) the fixed-effect models were presented.
- In case of discrepancy between the two models (ie, one giving a significant intervention effect and the other no significant intervention effect) both results were reported. Discrepancy will only occur when substantial heterogeneity is present.
- Most weight was put on the results of the fixed-effect model if the meta-analysis included one or more large trials, provided that they had adequate methodology. (By large trials we refer to those that outnumber the rest of the included trials in terms of numbers of outcomes and participants (ie, more than half of all included events and participants)).
- Otherwise, most weight was put on the results of the random-effects model as it incorporated heterogeneity. The reason for this was that the random-effects model increases the weight of small trials. Small trials however are more often than large trials conducted with unclear or inadequate methods (Kjaergard 2001).
- In situations of excessive heterogeneity we refrained from reporting a pooled estimate when inappropriate.

The main focus of looking at heterogeneity in meta-analysis is to discriminate true effect modifiers from other sources of heterogeneity. Heterogeneity was calculated by the Cochrane Q test and quantified by measuring I^2 (Higgins 2002). If excessive heterogeneity occurred, data were re-checked first and then adjusted. Extreme outliers were excluded (and tested in sensitivity analyses) when adequate reasons were available. If excessive heterogeneity still remained, depending on the specific research question, alternative methods were considered: subgroup analysis and meta-regression if appropriate.

Subgroup analysis

Subgroup analyses were performed to compare the effects of the interventions according to the methodological quality of the trials (adequate compared to unclear/inadequate). Furthermore, causes of heterogeneity (defined as the presence of statistical heterogeneity by chi-squared test with significance set at P-value < 0.10 and measured by the quantities of heterogeneity by I^2 (Higgins 2002)) were explored by comparing different groups of trials stratified to level of experience of the surgeon and other factors that may explain heterogeneity.

Sensitivity analyses were performed imputing medians and using average standard deviations for missing data. In case of outliers and borderline trials sensitivity analyses were performed as well. Subgroup analyses were performed testing the influence of antibiotic prophylaxis, surgical experience and intra-operative cholangiography on operative time, complications and hospital stay. These subgroup and sensitivity analyses were performed as far as data were available.

The statistical package (RevMan Analyses) was used (RevMan 2003). The statistical analyses were performed by FK and CL.

RESULTS

Description of studies

Searches and trial identification

For the search strategies used and the number of hits we refer to Appendix 1.

The search was conducted in *The Cochrane Hepato-Biliary Group Controlled Trials Register* (840 hits, 65 selected) and *The Cochrane Library*, Issue 1, 2004 with the following results: the *Cochrane Database of Systematic Reviews* (33 hits, none were selected), the *Database of Abstracts of Reviews on Effects* (*DARE*) (17 hits, 5 selected), the *Cochrane Central Register of Controlled Trials (CENTRAL)* (1343 hits, 146 selected), the *Health Technology Assessment (HTA) Database (*11 hits, 4 selected), and the *NHS Economic Evaluation Database (*43 hits, 6 selected).

The search further comprised the following databases: The National Library of Medicine (*MEDLINE*) (8354 hits, 347 selected), The Intelligent Gateway to Biomedical & Pharmacological Information (*EMBASE*) (685 hits, 131 selected), ISI Web of Knowledge *(Web of Science)* (1163 hits, 148 selected), and *CINAHL* (740 hits, 9 selected).

Altogether, the search resulted in 13229 hits. The first selection process was performed based on the title of the publications. In each step of selection, we included the publication in case of any doubt. The total number of selections by title from this group of 13229 publications was 911 hits. After correction for duplicates, 586 remained.

The abstracts of these 586 publications were reviewed independently by two reviewers (FK and JJ) in order to evaluate whether the study should be included in the review. Differences between FK and JJ were discussed with CL. A total of 428 publications could be rejected based on their abstract. Initially, trials which did not clearly mention whether they were randomised clinical trials or not, were given the benefit of the doubt. If appropriate, they were excluded later on. Eventually, 158 publications were selected for further evaluation and these are all listed in this review with reasons for in- or exclusion.

A total of 150 publications were excluded (see table with 'Characteristics of excluded studies'). A total of eight publications describing seven trials including 571 patients were included (see table with 'Characteristics of included studies' and Table 1). Critical appraisal and data extraction of these seven trials were done by FK, JJ, and CL, separately. Any disagreements were solved in several consensus meetings.

As no language restrictions were used, one publication (Coelho 1992a) was translated. Double publications of the trial results by the same research group are listed in the references of included studies, and are considered as one trial (eg, Wani 2002). After contacting individual trialists, no additional data or information were obtained.

Patient characteristics

All included trials used similar inclusion criteria, ie, patients with symptomatic cholecystolithiasis who were scheduled for elective cholecystectomy. The extensiveness in which exclusion criteria were described varied among the trials, but nearly all trials excluded acute cholecystitis. Trials with exclusively acute cholecystitis as inclusion criterion for cholecystectomy were excluded. Trials that included minorities of patients with acute cholecystitis next to patients with symptomatic cholecystolithiasis were included.

Trial designs

Only one trial used a three-arm design (Coelho 1993). All other trials used a two-arm parallel-group design.

Surgical interventions

Some trials using the small-incision technique did not mention the size of the incision. We classified these trials as a small-incision cholecystectomy and not an open cholecystectomy, based on how the author labelled the operation procedure. Two trials performed small-incision cholecystectomy by a 5 cm midline incision, the others by a transverse incision in the right hypochondrium, some with muscle splitting, others by transsection of the rectus or oblique muscles. Open cholecystectomy was normally performed by a subcostal or transverse incision, sometimes by midline laparotomy.

Antibiotic prophylaxis administered at induction of anaesthesia was explicitly mentioned in some trials. In others the explicit omission of antibiotic prophylaxis was mentioned, but most trials did not report on its use. Information on surgical experience (one or a few highly experienced surgeons performing all operations or also involving registrars) and intra-operative cholangiography (attempted in all or only in selected patients) was recorded as well.

Outcome measures

A problem considering relief of symptoms and pain is how this outcome is defined and measured. Apart from differences in measurement, very few trials reported on this outcome. Therefore, we were unable to report results considering relief of symptoms and pain. Nearly all trials reported on complications, operative time, and hospital stay. Trials did not clearly mention mortality. Because of the wide range of the types of complications described, we classified (subcategorised) all complications into four subcategories (intra-operative, minor, severe, or bile duct injury) in addition to a total complication proportion (Table 3). Each complication was classified twice: once in one of the four subcategories (intra-operative, minor, severe, or bile duct injury) and once again in the total complication proportion. Consequently, all bile duct complications were registered separately from all other complications (and not counted in the severe and minor subcategories). Likewise, all intra-operative complications (except from the bile duct injuries) were categorised separately from other minor and severe complications.

Pain scores and analgesic use as well as health-related quality of life were frequently examined outcomes, but due to the great variation in the way these were measured and reported, it appeared impossible to pool results. Considering pulmonary function there is some limited data available from randomised trials. However, considering the inconsistency in the type of effect measure reported, as well as the difference in moments in time the outcome was measured, and the statistical problems that arise in pooling these results, we decided to refrain from reporting these results.

Risk of bias in included studies

We evaluated the internal validity of the trials by considering the four quality components, resulting in the following number of high-quality (ie, adequate) trials. Information that was not mentioned in a trial was scored 'unclear'. When necessary information about randomisation, blinding procedure, or follow-up was unclear or missing, the authors were contacted to obtain specific additional

information on these issues. Trials of which no response was received, remained classified as 'unclear' trials.

Of the seven included trials we assessed the quality as adequate as follows: generation of allocation sequence one trial (14.3%), allocation concealment two trials (28.6%), blinding no trials (0%), and follow-up one trial (14.3%) (Table 4; Figure 1; Figure 2).

Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

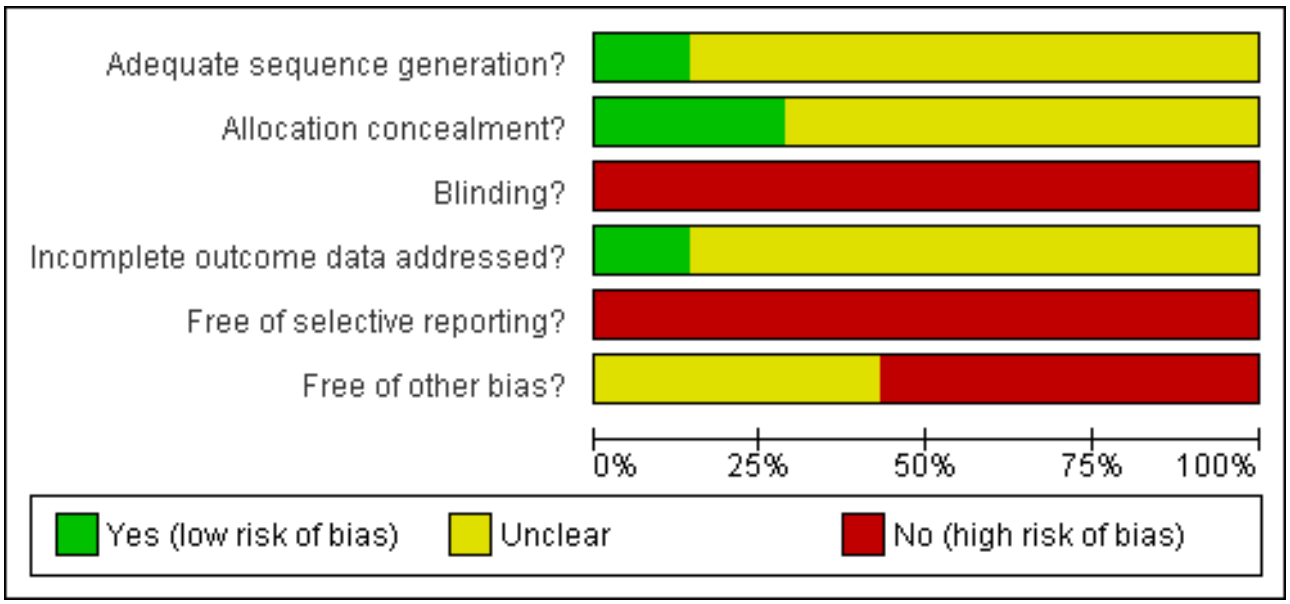
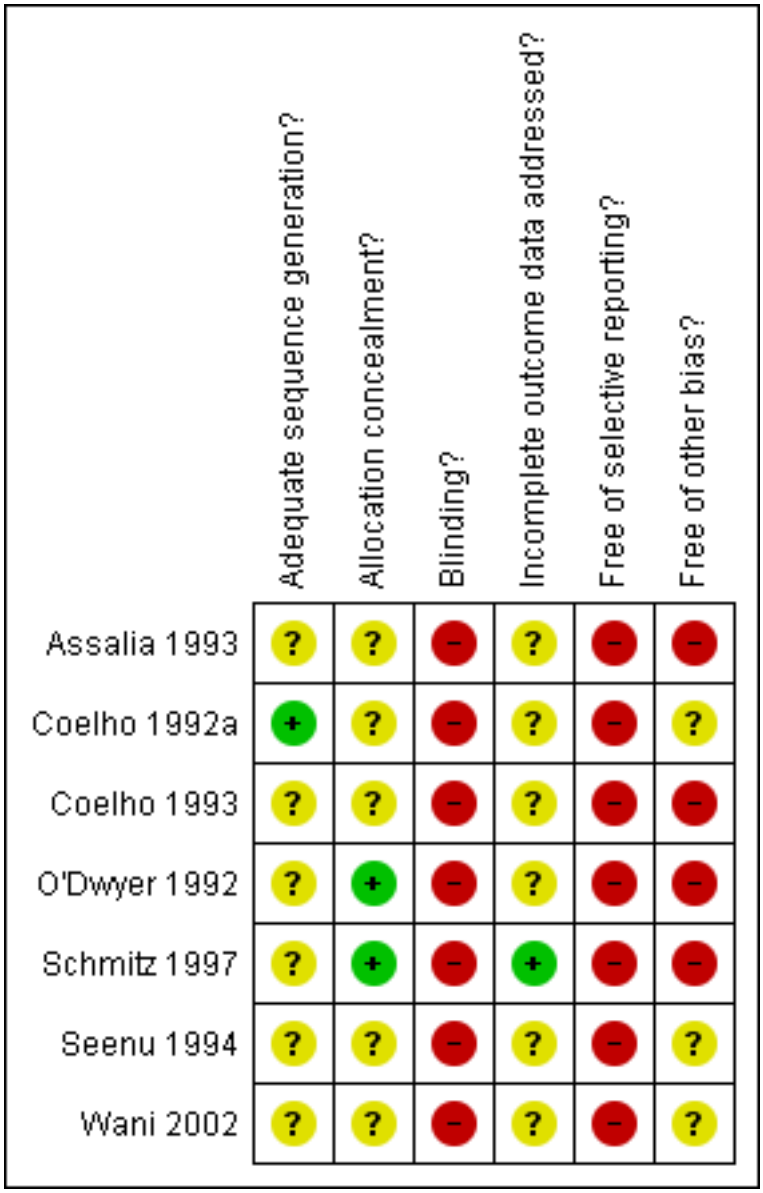


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



A comparison dividing trials into low-bias risk trials (adequate methodological quality in all four criteria) versus high-bias risk trials could not be performed as there was no low-bias risk trial present.

Effects of interventions

We conducted five analyses: four comparisons based on the four methodological quality components including the subgroups high- and low-quality trials, and a fifth comparison containing sensitivity and subgroup analyses. Background data of all trials on age, sex, body mass index (BMI), and American Society of Anaesthesiology (ASA) classification are shown in Table 2 as far as data were available.

We identified a total of seven randomised trials comparing small-incision versus open cholecystectomy. A total of 292 and 279 patients were included in the small-incision and open groups, respectively. Data were presented in Table 1 together with data on antibiotic prophylaxis, performance of cholangiography, and experience of the surgeon.

In the analyses, there were no significant differences in mortality, intra-operative complications, severe complications, bile duct injuries, and operative time considering all trials, neither in the subgroups high-quality and low-quality trials, nor between the fixed-effect model and the random-effects model. As 'concealment of allocation' is regarded as the most important component of methodological quality, all subgroup results considering this aspect (except for the fore-mentioned results that were not significantly different) were presented in additional Table 5.

Sensitivity analyses were performed imputing medians and standard deviations for missing data (operative time and hospital

stay) and omitting one outlier in total complications. Other subgroup and sensitivity analyses were considered inappropriate as data were missing.

Mortality

Mortality was not explicitly mentioned in all seven trials, therefore there were no results for calculating a pooled estimate.

Intra-operative complications

In all seven trials complications were explicitly reported, of which zero intra-operative complications. Consequently, there was no significant difference between the small-incision and open technique.

Minor complications

The minor complication proportions were 8.6% and 6.8% in the small-incision and open groups, respectively. In analysis of all trials there was no significant difference in minor complications (risk difference all trials 0.01, 95% CI -0.03 to 0.05). As heterogeneity was present, the random-effects method has been applied. In the high-quality subgroup in the 'concealment of allocation' comparison only (including two trials) a significant difference is present. In the other subgroups there were no significant differences.

Severe complications

The severe complication proportions were 1.4% and 2.5% in the small-incision and open group, respectively. There were no significant differences between the small-incision and open technique in all four methodological comparisons in all subgroups. As there was no heterogeneity, the fixed-effect method has been used (risk difference all trials -0.01, 95% CI -0.04 to 0.02).

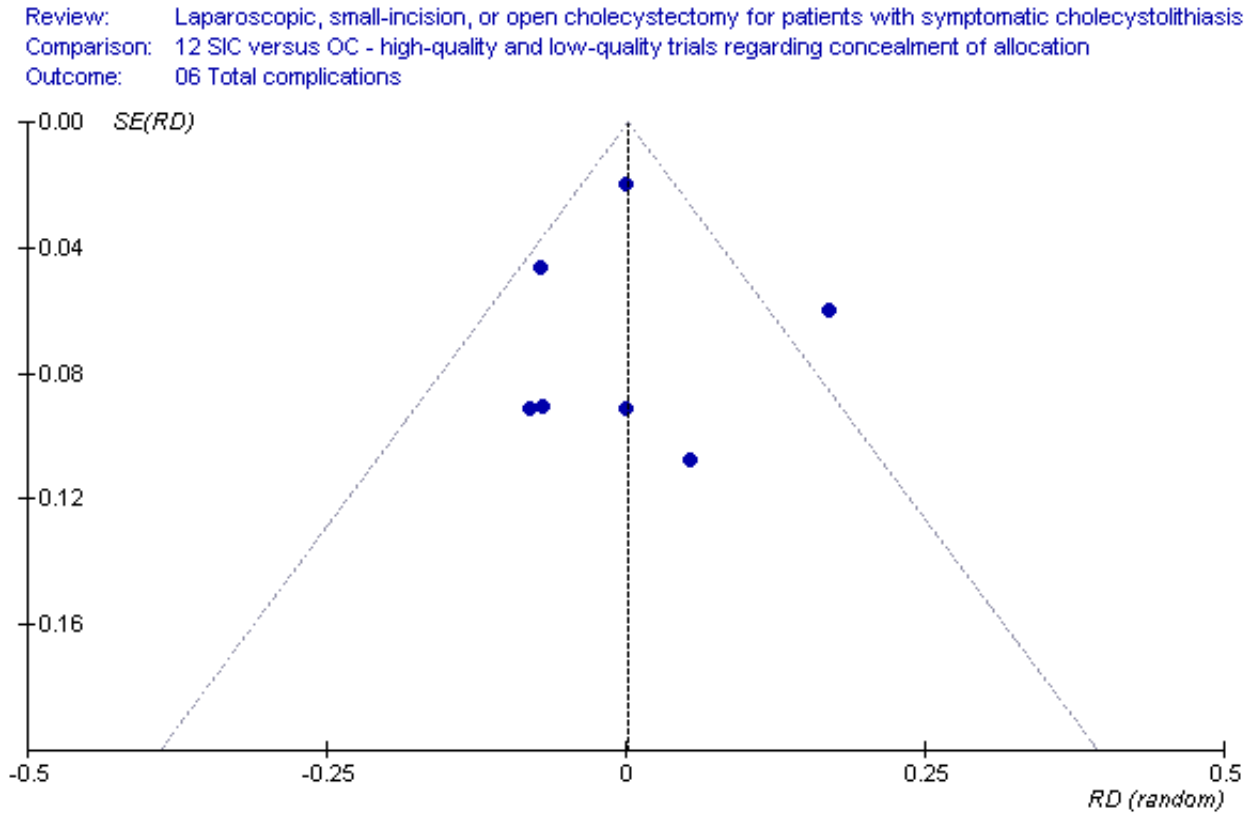
Bile duct injury

In all seven trials no bile duct injuries were reported. Consequently, there was no significant difference between the small-incision and open technique.

Total complications

In a funnel plot using total complication proportions we did not find indication of publication bias (Figure 3). The total complication proportions were 9.9% and 9.3% in the small-incision and open group, respectively (Table 3). Reoperation proportions are 0.7% and 0% respectively. We have found no significant difference in analysis of all trials (risk difference all trials, random-effects 0.00, 95% CI -0.06 to 0.07). Only in the high-quality trials subgroups in the 'allocation concealment' and 'follow-up' comparisons, applying the random-effects model, a significant difference favouring the open group has been found (caused by one trial only). Performing a sensitivity analysis (15-3) by omitting the outlier (Schmitz 1997a) led to a reduction of heterogeneity (22%) and showed no significant difference (risk difference, fixed-effect -0.04, 95% CI -0.09 to 0.01).

Figure 3. Funnel plot on small-incision versus open cholecystectomy regarding concealment of allocation considering total complications, including 95% confidence interval lines. No arguments for bias.



Operative time

There were no significant differences between the small-incision and open technique in all four methodological comparisons considering operative time. As only little heterogeneity was present, the fixed-effect method was presented (WMD all trials, 1.94 minutes, 95% CI -1.37 to 5.25).

All available data were shown in Table 6. In a sensitivity analysis (15-1) including the assumptions on standard deviations and medians considering skewness, there was no significant difference. As heterogeneity was present, the random-effects method was used (WMD -2.98 minutes, 95% CI -7.86 to 1.90).

Hospital stay

There was a significantly shorter hospital stay favouring the small-incision technique. As severe heterogeneity was present, the random-effects method was presented (WMD all trials, random-effects -2.78 days, 95% CI -4.94 to -0.62). However, this concerns the data of only two trials.

All available data were presented in Table 7. In a sensitivity analysis (15-2) including the assumptions on standard deviations and medians considering skewness, there was a significant shorter hospital stay in the small-incision group (WMD, random-effects -1.97 days, 95% CI -2.56 to -1.39).

Convalescence

No data on convalescence were available.

DISCUSSION

The present systematic review contains three major findings. First, the comparison of the clinical outcome of small-incision cholecystectomy with open cholecystectomy has been conducted in seven randomised clinical trials, including only 571 patients, and no trial could be classified as low-bias risk trial (adequate in all four methodological criteria). Secondly, the total numbers of patients with complications were not significantly different for the two procedures. Thirdly, hospital stay was shorter for small-incision cholecystectomy.

Considering the bias risks as well as the limited data on outcomes in the included trials, there are several questions that remain unanswered like pulmonary consequences after surgery, cost aspects, and more detailed questions on convalescence. High-quality trials are more likely to estimate the 'true' effects of the interventions (Schulz 1995; Moher 1998; Kjaergard 2001; Jüni 2001; Egger 2003). Remembering this linkage between unclear / inadequate methodological quality to significant overestimation of beneficial effects and underreporting of adverse effects, the question is whether improvement in methodological quality of randomised trials will alter results.

No trial reported on mortality. There was no significant difference in complication proportions. All trials reported on total complications: 9.9% (small-incision cholecystectomy) and 9.3% (open cholecystectomy). Intra-operative, severe, and bile duct injury complications were not significantly different applying both the fixed-effect and the random-effects models. However, in subgroup analyses on 'allocation concealment' and 'follow-up' as methodological quality aspect, total complications differed in the high-quality group in favour of the open cholecystectomy group, both in the fixed-effect and the random-effects models. Both results are based on the outcome of one trial (Schmitz 1997a). In the other two methodological quality components, however, there were no significant differences in the subgroups. Therefore, total complications cannot be regarded as significantly different for the small-incision group compared to the open group. In a sensitivity analysis the outlying trial (Schmitz 1997a) was omitted from the pooled results, which did not result in a significantly different outcome. The methodological quality of the seven randomised trials comparing small-incision to open cholecystectomy was rather disappointing. Therefore total complication proportions (9.9% and 9.3%) must be interpreted with care. No clear indication of publication bias were found analysing total complication proportions (Figure 3).

There were no significant differences in operative time. In all subgroup comparisons, no significant differences in operating time were found (fixed-effect and random-effects models). However, only three trials could be included in the analysis due to missing data. In the sensitivity analysis on operative time, with assumptions on values for missing standard deviations and means and checking for skewness (additional Table 6) again no significant difference was found. Hospital stay was significantly shorter in the small-incision group in all four subgroup analyses after incorporating the severe heterogeneity in the random-effects model. In sensitivity analysis on hospital stay, using assumptions on values for missing data, and checking for skewness (additional Table 7), small-incision cholecystectomy had a shorter hospital stay. No data on convalescence were available.

AUTHORS' CONCLUSIONS

Implications for practice

We were unable to demonstrate significant differences between small-incision versus open cholecystectomy regarding primary outcomes. We observed a significantly shorter duration of hospital stay in patients being treated by small-incision cholecystectomy. Rationally, if expertise for the small-incision approach is available, the small-incision technique is preferable for these patients. Moreover, an intra-operative conversion to open cholecystectomy remains possible without restrictions.

We recommend that every surgical department is able to offer this kind of elective surgery for patients with symptomatic cholecystolithiasis.

Implications for research

Future trials on implementation issues of minimally invasive open and laparoscopic techniques in general will dominate surgical research. Randomised comparisons should be made of both minimally invasive techniques as well as traditional open techniques, both regarding clinical and oncological outcome measures as well as cost differences.

In accordance with research in general, the overall quality of the randomised trials included in this systematic review varied, with the majority of trials having several methodological deficiencies. In line with conclusions from other systematic reviews, the quality of included trials needs to improve in order to limit bias. Reports can be improved importantly by adopting the CONSORT Statement while conducting and reporting trials (www.consort-statement.org).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Assalia 1993

Methods	Single-centre randomised trial. Generation of allocation: unclear. Allocation concealment: unclear. Blinding: not performed. Follow-up: unclear. Drop-outs: none mentioned. Intention-to-treat: not mentioned. Sample size calculations: no.

Assalia 1993 *(Continued)*

Participants	Elective cholecystectomy for symptomatic cholelithiasis. In- and exclusion criteria: not mentioned. Comparability groups: well matched.
Interventions	SIC versus OC. Minicholecystectomy: initial 5 cm (no preoperative ultrasound location), extended in stages each 1 cm long. Retrograde (fundus down) technique was performed. Open cholecystectomy: technique was left to the individual surgeon. Length of incision: offer comfortable exposure, however, not too generous. Antibiotic prophylaxis: yes. Intra-operative cholangiography: selectively carried out according to clinical and laboratory indications.
Outcomes	Primary and secondary outcome: not mentioned. Outcomes: difficulty of the procedure, operative time, degree of pain, total amount of analgesia, hospital stay, patient satisfaction, physical activity limitations. Duration of follow-up: 2 weeks.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear
Blinding? All outcomes	High risk	
Free of selective reporting?	High risk	
Free of other bias?	High risk	short follow-up of 2 weeks

Coelho 1992a

Methods	Single-centre trial. Generation of allocation: adequate, by cards. (aleatoriamente = randomised). Allocation concealment: unclear. Blinding: not performed. Follow-up: unclear. Drop-outs: none mentioned. Intention-to-treat: not mentioned. Sample size calculations: no.
Participants	Patients admitted for cholecystectomy. In- and exclusion criteria: not very well described.

Coelho 1992a *(Continued)*

	Comparability groups: well matched.
Interventions	SIC versus OC. Both procedures not further specified. Antibiotic prophylaxis: not mentioned. Intra-operative cholangiography: routinely performed in both groups.
Outcomes	Primary and secondary outcome: not described. Outcome measures: clinical results. Duration of follow-up: hospital stay.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	
Allocation concealment?	Unclear risk	B - Unclear
Blinding? All outcomes	High risk	
Free of selective reporting?	High risk	

Coelho 1993

Methods	Single-centre trial. Generation of allocation: unclear. Patients randomly and prospectively divided into three groups. Allocation concealment: unclear. Blinding: not performed. Follow-up: unclear. Drop-outs: none mentioned. Intention-to-treat: not mentioned. Sample size calculations: no.
Participants	Chronic calculous cholecystitis admitted for elective cholecystectomy. In- and exclusion criteria: not described. Comparability groups: well matched.
Interventions	LC versus SIC versus OC. LC: four-trocar technique, carbon dioxide insufflated. SIC: right upper quadrant transverse incision of 5 to 8 cm. OC: right upper quadrant subcostal incision of 15 to 20 cm. Antibiotic prophylaxis: not mentioned.

Coelho 1993 *(Continued)*

	Intra-operative cholangiography: not mentioned.
Outcomes	Primary and secondary outcome: not defined. Outcome measures: comparison of reduction in pulmonary function. Duration of follow-up: not mentioned.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear
Blinding? All outcomes	High risk	
Free of selective reporting?	High risk	
Free of other bias?	High risk	unclear duration of follow-up

O'Dwyer 1992

Methods	Two-centre trial. Generation of allocation: unclear. Allocation concealment: adequate (sealed envelope). Blinding: not performed. Follow-up: unclear. Drop-outs: none mentioned. Intention-to-treat: not mentioned. Sample size calculations: no.
Participants	Patients having cholecystectomy for symptomatic gallstones. In- and exclusion criteria: well described. Comparability groups: well matched.
Interventions	SIC versus OC. SIC: through 6 cm incision, rectus muscle divided. OC: not further described. Antibiotic prophylaxis: not mentioned. Routine operative cholangiography in all patients.
Outcomes	Primary and secondary outcome: not specified. Outcome measures: pulmonary, function tests, analgesia requirements, hospital stay. Duration of follow-up: hospital stay.
Notes	

O'Dwyer 1992 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate
Blinding? All outcomes	High risk	
Free of selective reporting?	High risk	
Free of other bias?	High risk	short follow-up (hospital stay)

Schmitz 1997

Methods	Randomised clinical single-centre trial. Generation of allocation: unclear. Allocation concealment: adequate. Blinding: not performed. Follow-up: adequate. Drop-outs: none; postoperative observation was extended to complete the investigation. Intention-to-treat: not mentioned. Sample size calculations: no.
Participants	Patients for elective cholecystectomy. In- and exclusion criteria: not very well described. Comparability groups: well matched.
Interventions	SIC versus OC. SIC: 6 cm subcostal transverse incision with diathermy transsection of the right rectus abdominis muscle. OC: a 13 cm subcostal incision with additional partial extension into the muscle spaces of the right lateral epigastric region. Antibiotic prophylaxis: not mentioned. Intra-operative cholangiography: not mentioned.
Outcomes	Primary and secondary outcome: not mentioned. Outcome measures: operating times, level of subjective pain, analgesic intake, complications. Duration of follow-up: not mentioned.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Schmitz 1997 *(Continued)*

Blinding? All outcomes	High risk	
Incomplete outcome data addressed? All outcomes	Low risk	
Free of selective reporting?	High risk	
Free of other bias?	High risk	unclear duration of follow-up

Seenu 1994

Methods	Single-centre randomised trial, operations performed by consultants and senior residents. Generation of allocation: unclear. Allocation concealment: unclear. Blinding: not performed. Follow-up: unclear. Drop-outs: none mentioned. Intention-to-treat: not mentioned. Sample size calculations: no.
Participants	Patients undergoing elective cholecystectomy. In- and exclusion criteria: not very well described. Comparability groups: not very well described.
Interventions	SIC versus OC. SIC: very well described, a 5 cm transverse incision in the right upper quadrant. OC: vertical midline incision. Antibiotic prophylaxis: not mentioned. Intra-operative cholangiography: no, selective pre-operative cholangiogram was performed when necessary.
Outcomes	Primary and secondary outcome: not mentioned. Outcome measures: complications, operative time, hospital stay. Duration of follow-up: 30 days.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear
Blinding? All outcomes	High risk	

Seenu 1994 *(Continued)*

Free of selective reporting?	High risk

Wani 2002

Methods	Single-centre trial. Randomised trial: prospective study with patients systematically divided. Generation of allocation: unclear. Allocation concealment: unclear. Blinding: not performed. Follow-up: unclear. Drop-outs: none mentioned. Intention-to-treat: not mentioned. Sample size calculations: no.
Participants	Patients with chronic calculus cholecystitis. In- and exclusion criteria: not very well described. Comparability groups: well matched.
Interventions	SIC versus OC. SIC: incision of 5 cm to 7 cm length with two well illuminated retractors, dissected either duct first or fundus first. OC: right subcostal incision of 10 cm to 15 cm. Antibiotic prophylaxis: not mentioned. Intra-operative cholangiography: not mentioned
Outcomes	Primary and secondary outcome: not mentioned. Outcome measures: pulmonary function. Duration of follow-up: not mentioned (hospital stay).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear
Blinding? All outcomes	High risk	
Free of selective reporting?	High risk	
Free of other bias?	Unclear risk	short follow-up

LC - laparoscopic cholecystectomy,
SIC - small-incision cholecystectomy,
OC - open cholecystectomy.

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

Study	Reason for exclusion
Agnifili 1993	Randomised trial evaluating laparoscopic and open cholecystectomy.
Al Tameem 1995	Prospective study on three different types of small-incision cholecystectomy, not randomised.
Alexander 1997	Review on pain after laparoscopy; not a randomised trial.
Allen 2002	Comparison of costs of LC between ten surgeons; no comparison of operative procedures.
Alponat 2002	Randomised clinical trial on conventional LC (two 10 mm and two 5 mm ports) and LC by small instruments (one 10 mm and three 2 mm ports); thus comparison of two types of LC.
Anonymous 1995	Editorial: discussion of other article.
Assalia 1997	Randomised trial only including patients with acute cholecystitis.
Bablekos 2003	Correspondence with GD Bablekos on 11 October 2004: separating patients in triads with allocation according to registration sequence at the emergency ward: quasi-randomised study of LC versus OC.
Barkun 1992	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Barkun 1993	Comparison of three different time periods; not a randomised trial.
Baxter 1992	Debate, consideration.
Bellon 1998	Randomised trial evaluating laparoscopic and open cholecystectomy.
Berggren 1994	Randomised trial evaluating laparoscopic and open cholecystectomy.
Bernard 1994	Economic evaluation.
Bigard 1995	Review on indications and methods of cholecystectomy in treatment of gallstones.
Blanc-Louvry 2000	Randomised trial evaluating laparoscopic and open cholecystectomy.
Blomstedt 1972	Study on the frequency of incisional hernias after different types of conventional cholecystectomy; not a randomised trial.
Bolke 2000	Quasi-randomised trial: "... patients were randomised by alternate number to LC or OC ...".
Bruce 1999	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Bukan 2004	Randomised trial evaluating laparoscopic and open cholecystectomy.
Byrne 1994	Prospective, not randomised study: " ... equipment was only made available on an intermittent basis ...".
Calland 2001	Prospective study on outpatient LC, comparing with historical (inpatient) LC; not a randomised trial.
Caplan 1999	Study on costs and patient satisfaction before and after re-engineering of a surgical service in LC patients and elective herniorrhaphy; no comparison of different types of cholecystectomy.

Study	Reason for exclusion
Champault 2002	One-arm prospective study on costs; not a randomised trial (not two arms).
Charlo 1995	Randomised trial evaluating laparoscopic and open cholecystectomy.
Chaudhary 1999	Randomised trial evaluating laparoscopic and open cholecystectomy.
Chumillas 1998	Randomised trial evaluating laparoscopic and open cholecystectomy.
Clezy 1996	Letter.
Coelho 1992	Not a randomised trial; prospective study of small-incision cholecystectomy.
Coskun 2000	Randomised trial evaluating laparoscopic and open cholecystectomy.
Da Costa 1995	Prospective study, not randomised: "... patients were not randomised as it was felt that it was unethical to do so ...".
Dauleh 1995	Randomised trial evaluating laparoscopic and open cholecystectomy.
Decker 1993	Not randomised; prospective study.
Delogu 1999	Stress response in LC and OC patients, not randomised: "... 22 patients underwent OC and the other 24 had LC according to the availability of laparoscopic equipment ...".
Demirer 2000	Randomised trial evaluating laparoscopic and open cholecystectomy.
Dionigi 1994	Randomised trial evaluating laparoscopic and open cholecystectomy.
Dohrmann 1993	Not randomised; randomisation was not possible as most patients opted for the laparoscopic technique.
Eickhoff 1997	Not a randomised trial: patients who were operated by LC or OC were analysed.
Engin 1998	Randomised trial evaluating laparoscopic and open cholecystectomy
Essen 1995	Randomised trial evaluating laparoscopic and open cholecystectomy.
Frazee 1991	No correct randomisation between two operative techniques: "... patients were randomly assigned to individual staff surgeons, as is our customary practice ...".
Gal 1997	Randomised trial evaluating laparoscopic and open cholecystectomy.
Galizia 2001	Randomised trial evaluating laparoscopic and open cholecystectomy.
GarciaCaballero 1993	Randomised trial evaluating laparoscopic and open cholecystectomy.
Glaser 1995	Prospective study with control group, not randomised: "... because of the ethical problems associated with randomisation of LC and OC, we decided to conduct a prospective trial without randomisation, but with a control group ...".
Go 1995	Retrospective study on cost-effectiveness between extracorporeal shock-wave lithotripsy, conventional cholecystectomy, and laparoscopic cholecystectomy.
Grande 2002	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.

Study	Reason for exclusion
Hagmuller 1997	Not randomised: the authors felt that randomisation was not possible on ethical grounds.
Hasukic 2002	Randomised trial evaluating laparoscopic and open cholecystectomy.
Hauer-Jensen 1986	Randomised trial comparing performing cholecystectomy with or without a routine cholangiography.
Hendolin 2000	Randomised trial evaluating laparoscopic and open cholecystectomy.
Hobbs 1995	Considerations on laparoscopic cholecystectomy, not a randomised trial.
Huang 1996	Randomised trial evaluating laparoscopic and open cholecystectomy.
Huguier 1997	Considerations on laparoscopic digestive surgery, not a randomised trial.
Hunter 2001	Editorial.
Iwase 1992	Not a randomised trial.
Jan 1993	Randomised trial evaluating laparoscopic and open cholecystectomy.
Johnson 1997	Considerations on laparoscopic surgery.
Johnson 1998	Personal view: consideration on efficacy, safety and training; not a randomised trial.
Johnson 1998a	Letter.
Karayiannakis 1997	Randomised trial evaluating laparoscopic and open cholecystectomy.
Karayiannakis 2002	Prospective study in patients having LC and OC, but no randomisation: "... twelve patients who had OC were recruited and served as the control group ...".
Kehlet 1993	Consideration of gallstone treatment modalities.
Keus 2006	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Kiviluoto 1997	Randomised trial between LC and OC on acute cholecystitis.
Kjaersgaard 1994	Randomised trial evaluating laparoscopic and open cholecystectomy.
Koprulu 1996	Randomised trial evaluating laparoscopic and open cholecystectomy.
Krasinski 1998	Prospective study on patients who underwent LC: patients with uncomplicated LC were compared to patients who had conversion from LC to OC.
Krawczyk 1993	Not a randomised trial: "the groups were not randomised".
Kunz 1992	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Kurzawinski 1992	Prospective study, but not randomised: "... patients were randomly allocated to either LC or OC, based on the availability of laparoscopic equipment ...".
Lam 1996	Survey in Scotland on cholecystectomy rate; not a randomised trial.
Lausten 1999 (1)	Randomised trial evaluating laparoscopic and open cholecystectomy.

Study	Reason for exclusion
Lausten 1999 (2)	Randomised trial evaluating laparoscopic and open cholecystectomy.
Lujan 1998	Randomised trial evaluating laparoscopic and open cholecystectomy.
Lukichev 1983	Cohort of patients treated by one technique; not a randomised trial.
Luo 2003	Randomised trial evaluating laparoscopic and open cholecystectomy.
Majeed 1996	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Makinen 1995	Only pilot phase of trial; in pilot phase no randomisation: SIC was performed when LC instruments were not available.
Malaysian HTA 2005	Systematic review on different types of minimal access surgery; not a randomised trial.
Maruszynski 1995	Patients with acute cholecystitis only.
Matsunaga 1996	Comparison of two different types of anaesthesia in cholecystectomy.
McGinn 1995	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
McKellar 1995	Comparison of historical cohorts.
McMahon 1994	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
McMahon 1996	Letter, not a randomised trial.
Mealy 1992	An unselected group of patients undergoing LC in one hospital was compared with a group undergoing OC in another hospital.
Milheiro 1994	Randomised trial evaluating laparoscopic and open cholecystectomy.
Mimica 2000	Randomised trial evaluating laparoscopic and open cholecystectomy.
Mrksic 2001	No randomisation.
Novitsky 2002	Randomised controlled trial on two types of laparoscopic cholecystectomy (mini-port LC (2 mm) versus conventional LC).
Ogawa 2001	Retrospective study on LC versus OC in patients with cardiac valve replacement.
Olsen 1993	Review of literature from 1970 to 1992 on mini-lap cholecystectomy: only articles in English were included and data on conventional and laparoscopic cholecystectomy were obtained from large series reported in literature.
Ortega 1996	Randomised trial evaluating laparoscopic and open cholecystectomy.
Plaisier 1995	Prospective not randomised study: "... allocation to either laparoscopic or conventional cholecystectomy depended on the availability of a laparoscopic set ...".
Prisco 2000	Randomised trial evaluating laparoscopic and open cholecystectomy.
Putensen-Himmer 1992	Randomised trial evaluating laparoscopic and open cholecystectomy.

Study	Reason for exclusion
Rademaker 1992	Patients underwent conventional subcostal cholecystectomy whenever the instrumentation for laparoscopic surgery was not available; the laparoscopic group had on alternating basis general anaesthesia combined with epidural analgesia or general anaesthesia alone; not randomised.
Redmond 1994	Study evaluating laparoscopic and small-incision cholecystectomy.
Rhodes 1996	Not a randomised trial; comment on other article.
Romana 2000	Not randomised: "patients were divided into two groups".
Ros 2001	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Rovina 1996	Randomised trial evaluating laparoscopic and open cholecystectomy.
Schauer 1993	No correct randomisation of surgical techniques: ".. patients were randomly assigned to one of four general surgical services; two of these used only the open cholecystectomy technique, and the other two used the laparoscopic approach ..".
Schauer 1995	Not randomised; ".. procedure was determined by the attending physician ..".
Schaupp 1988	Randomised clinical trial on two types of conventional cholecystectomy (with nasogastric tube, iv infusion and subhepatic drain versus no tube, no infusion and no drain).
Secco 2002	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Srivastava 2001	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Tate 1993	Randomised trial evaluating laparoscopic and small-incision cholecystectomy.
Thaler 1995	Trial on LC and OC patients, but no randomisation as the authors found that laparoscopic cholecystectomy was the method of first choice.
Toouli 1998	Review on gallstones; not a randomised trial.
Trondsen 1993	Randomised trial evaluating laparoscopic and open cholecystectomy.
Ueo 1994	Prospective comparison between IL-6 levels in LC and OC patients, but not randomised: " ... patients who underwent cholecystectomy, 12 each for OC and LC, were chosen as subjects in this study ...".
Volpino 1998	Randomised trial evaluating laparoscopic and open cholecystectomy.
Williams 1993	Prospective study on LC and OC pulmonary function, but not randomised: "... selection for OC or LC depended upon surgeon ...".
Yerdel 1997	Prospective study in cirrhotic patients on laparoscopic versus open cholecystectomy; not randomised ("... all cirrhotic patients were offered LC ...").
Zajac 1998	Randomised trial evaluating laparoscopic and open cholecystectomy.
Zulfikaroglu 2002	Randomised trial evaluating laparoscopic and open cholecystectomy.

LC: laparoscopic cholecystectomy;
OC: open cholecystectomy.

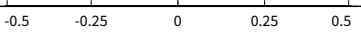
DATA AND ANALYSES

Comparison 1. SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Intra-operative complications	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
1.1 High-quality trials	1	50	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.07, 0.07]
1.2 Low-quality trials	6	521	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
2 Minor complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
2.1 High-quality trials	1	50	Risk Difference (M-H, Random, 95% CI)	-0.04 [-0.21, 0.13]
2.2 Low-quality trials	6	521	Risk Difference (M-H, Random, 95% CI)	0.02 [-0.04, 0.07]
3 Severe complications (without bile duct injuries)	7	571	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
3.1 High-quality trials	1	50	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.14, 0.06]
3.2 Low-quality trials	6	521	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
4 Bile duct injuries	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
4.1 High-quality trials	1	50	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.07, 0.07]
4.2 Low-quality trials	6	521	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
5 Total complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.06, 0.07]
5.1 High-quality trials	1	50	Risk Difference (M-H, Random, 95% CI)	-0.08 [-0.26, 0.10]
5.2 Low-quality trials	6	521	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.06, 0.08]
6 Operative time (minutes)	3	210	Mean Difference (IV, Fixed, 95% CI)	1.94 [-1.37, 5.25]
6.1 High-quality trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Low-quality trials	3	210	Mean Difference (IV, Fixed, 95% CI)	1.94 [-1.37, 5.25]
7 Hospital stay (days)	2	180	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.94, -0.62]
7.1 High-quality trials	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Low-quality trials	2	180	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.94, -0.62]

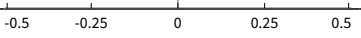
Analysis 1.1. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 1 Intra-operative complications.

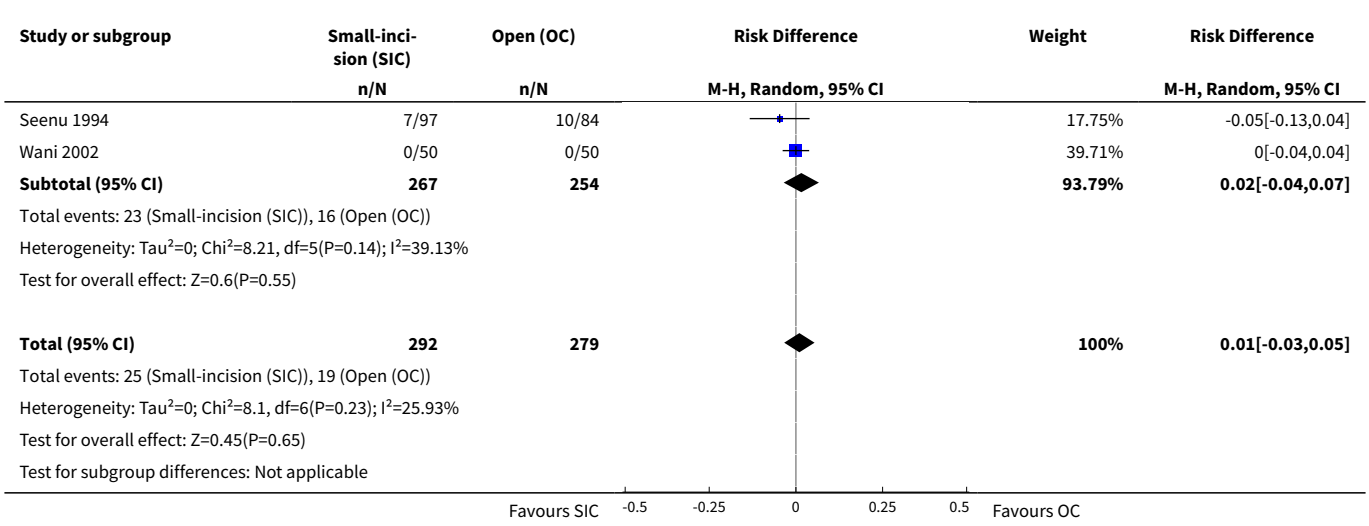
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
1.1.1 High-quality trials					
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Subtotal (95% CI)	**25**	**25**		**8.77%**	**0[-0.07,0.07]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.1.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
O'Dwyer 1992	0/16	0/14		5.24%	0[-0.12,0.12]
Schmitz 1997	0/65	0/65		22.81%	0[-0.03,0.03]
Seenu 1994	0/97	0/84		31.6%	0[-0.02,0.02]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]
Subtotal (95% CI)	**267**	**254**		**91.23%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=5(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=6(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					



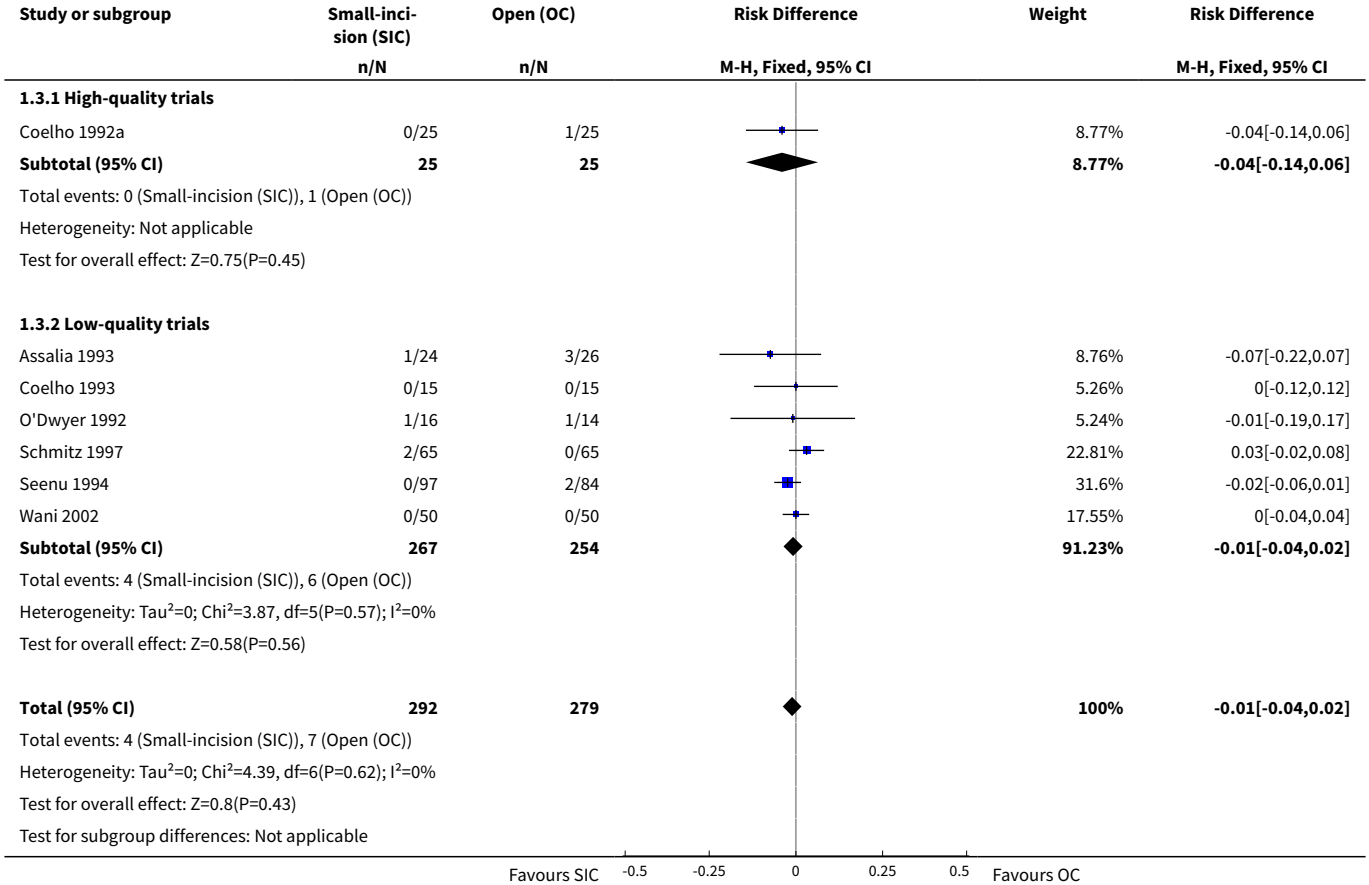
Analysis 1.2. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 2 Minor complications.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
1.2.1 High-quality trials					
Coelho 1992a	2/25	3/25		6.21%	-0.04[-0.21,0.13]
Subtotal (95% CI)	**25**	**25**		**6.21%**	**-0.04[-0.21,0.13]**
Total events: 2 (Small-incision (SIC)), 3 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.47(P=0.64)					
1.2.2 Low-quality trials					
Assalia 1993	1/24	1/26		12.61%	0[-0.11,0.11]
Coelho 1993	1/15	1/15		5.45%	0[-0.18,0.18]
O'Dwyer 1992	1/16	0/14		6.44%	0.06[-0.1,0.23]
Schmitz 1997	13/65	4/65		11.82%	0.14[0.03,0.25]



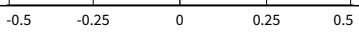


Analysis 1.3. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 3 Severe complications (without bile duct injuries).



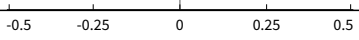
Analysis 1.4. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 4 Bile duct injuries.

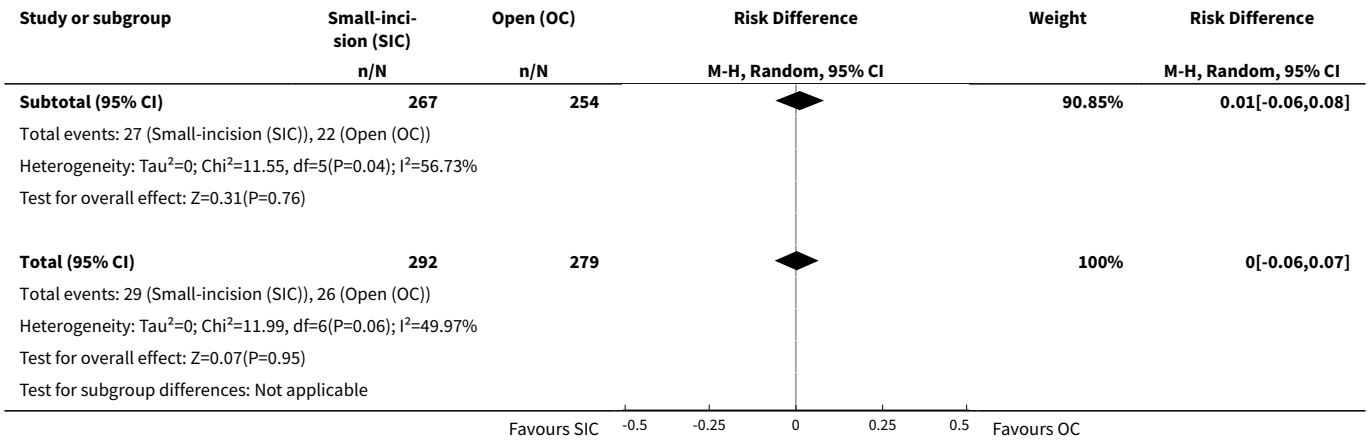
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
1.4.1 High-quality trials					
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Subtotal (95% CI)	**25**	**25**		**8.77%**	**0[-0.07,0.07]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
1.4.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
O'Dwyer 1992	0/16	0/14		5.24%	0[-0.12,0.12]
Schmitz 1997	0/65	0/65		22.81%	0[-0.03,0.03]
Seenu 1994	0/97	0/84		31.6%	0[-0.02,0.02]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]
Subtotal (95% CI)	**267**	**254**		**91.23%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=5(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=6(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					



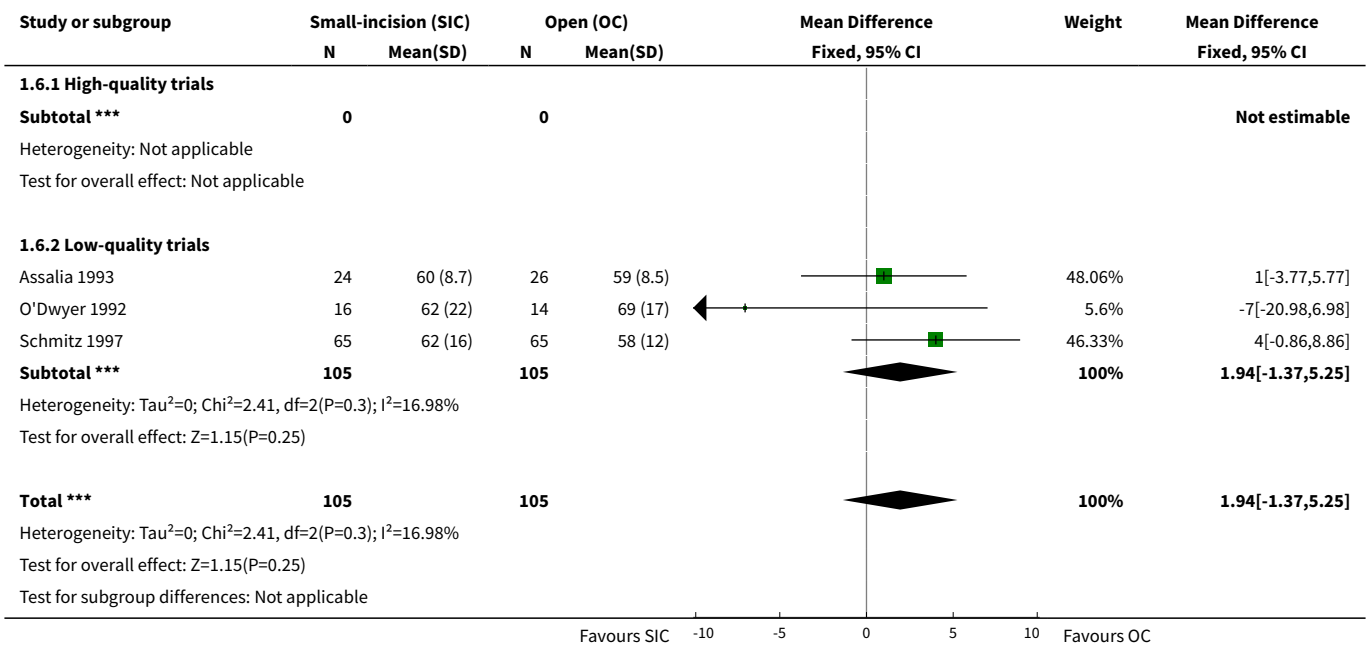
Analysis 1.5. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 5 Total complications.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
1.5.1 High-quality trials					
Coelho 1992a	2/25	4/25		9.15%	-0.08[-0.26,0.1]
Subtotal (95% CI)	**25**	**25**		**9.15%**	**-0.08[-0.26,0.1]**
Total events: 2 (Small-incision (SIC)), 4 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.88(P=0.38)					
1.5.2 Low-quality trials					
Assalia 1993	2/24	4/26		9.26%	-0.07[-0.25,0.11]
Coelho 1993	1/15	1/15		9.17%	0[-0.18,0.18]
O'Dwyer 1992	2/16	1/14		7.12%	0.05[-0.16,0.26]
Schmitz 1997	15/65	4/65		15.53%	0.17[0.05,0.29]
Seenu 1994	7/97	12/84		19.87%	-0.07[-0.16,0.02]
Wani 2002	0/50	0/50		29.9%	0[-0.04,0.04]

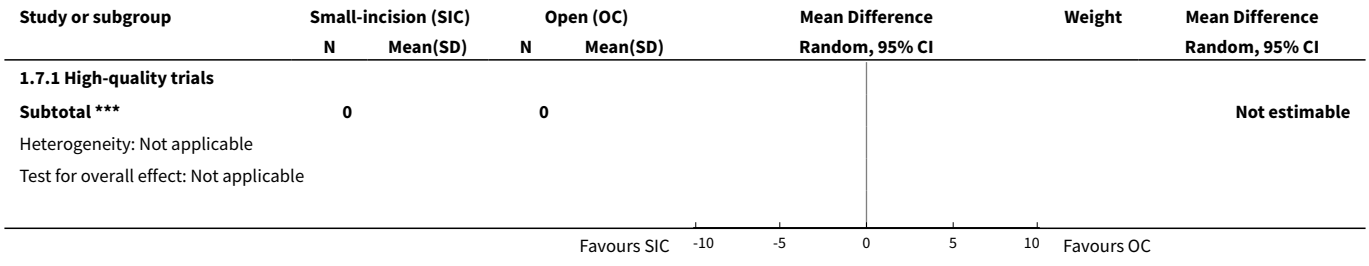


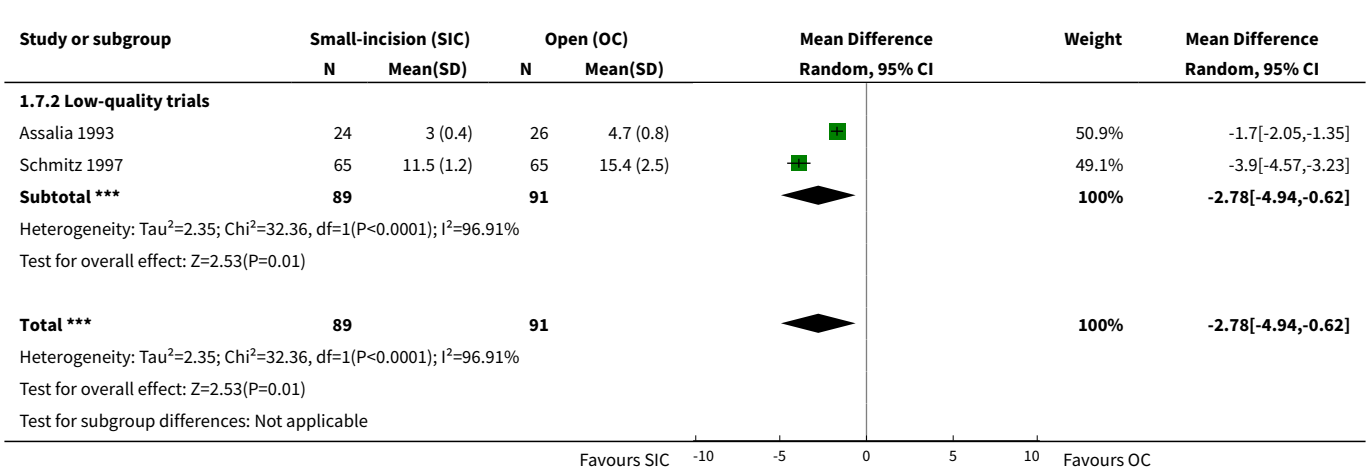


Analysis 1.6. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 6 Operative time (minutes).



Analysis 1.7. Comparison 1 SIC versus OC - high-quality and low-quality trials regarding generation of the allocation sequence, Outcome 7 Hospital stay (days).





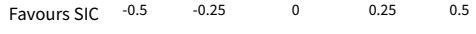
Comparison 2. SIC versus OC - high-quality and low-quality trials regarding concealment of allocation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Intra-operative complications	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
1.1 High-quality trials	2	160	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.03, 0.03]
1.2 Low-quality trials	5	411	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
2 Minor complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
2.1 High-quality trials	2	160	Risk Difference (M-H, Random, 95% CI)	0.11 [0.02, 0.21]
2.2 Low-quality trials	5	411	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.04, 0.02]
3 Severe complications (without bile duct injuries)	7	571	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
3.1 High-quality trials	2	160	Risk Difference (M-H, Fixed, 95% CI)	0.02 [-0.03, 0.08]
3.2 Low-quality trials	5	411	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.06, 0.01]
4 Bile duct injuries	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
4.1 High-quality trials	2	160	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.03, 0.03]
4.2 Low-quality trials	5	411	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
5 Total complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.06, 0.07]
5.1 High-quality trials	2	160	Risk Difference (M-H, Random, 95% CI)	0.14 [0.04, 0.24]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.2 Low-quality trials	5	411	Risk Difference (M-H, Random, 95% CI)	-0.03 [-0.10, 0.03]
6 Operative time (minutes)	3	210	Mean Difference (IV, Fixed, 95% CI)	1.94 [-1.37, 5.25]
6.1 High-quality trials	2	160	Mean Difference (IV, Fixed, 95% CI)	2.81 [-1.78, 7.41]
6.2 Low-quality trials	1	50	Mean Difference (IV, Fixed, 95% CI)	1.0 [-3.77, 5.77]
7 Hospital stay (days)	2	180	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.94, -0.62]
7.1 High-quality trials	1	130	Mean Difference (IV, Random, 95% CI)	-3.9 [-4.57, -3.23]
7.2 Low-quality trials	1	50	Mean Difference (IV, Random, 95% CI)	-1.70 [-2.05, -1.35]

Analysis 2.1. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 1 Intra-operative complications.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
2.1.1 High-quality trials					
O'Dwyer 1992	0/16	0/14		5.24%	0[-0.12,0.12]
Schmitz 1997	0/65	0/65		22.81%	0[-0.03,0.03]
Subtotal (95% CI)	**81**	**79**		**28.05%**	**0[-0.03,0.03]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=1(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
2.1.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
Seenu 1994	0/97	0/84		31.6%	0[-0.02,0.02]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]
Subtotal (95% CI)	**211**	**200**		**71.95%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=4(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=6(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

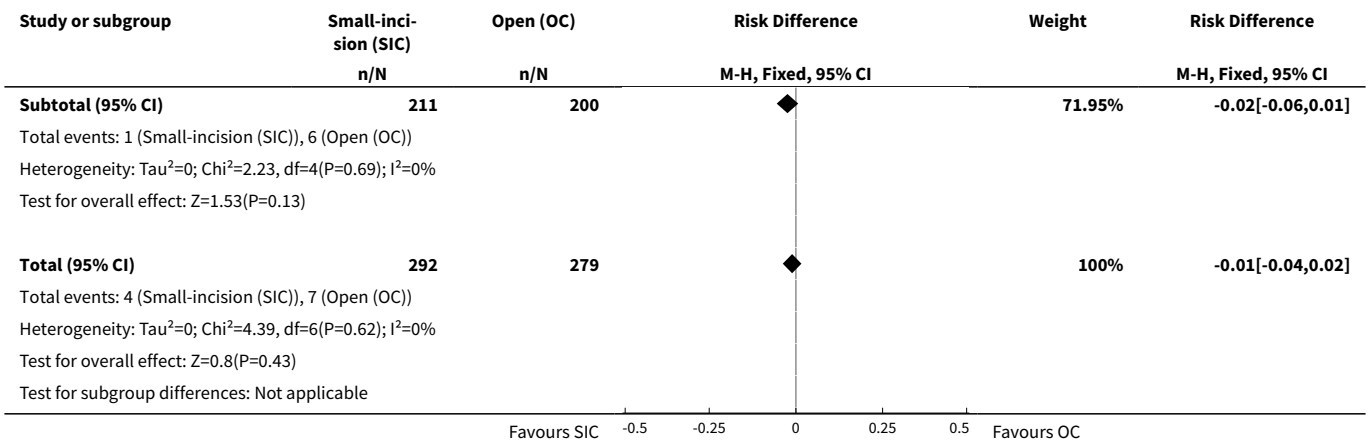


Analysis 2.2. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 2 Minor complications.

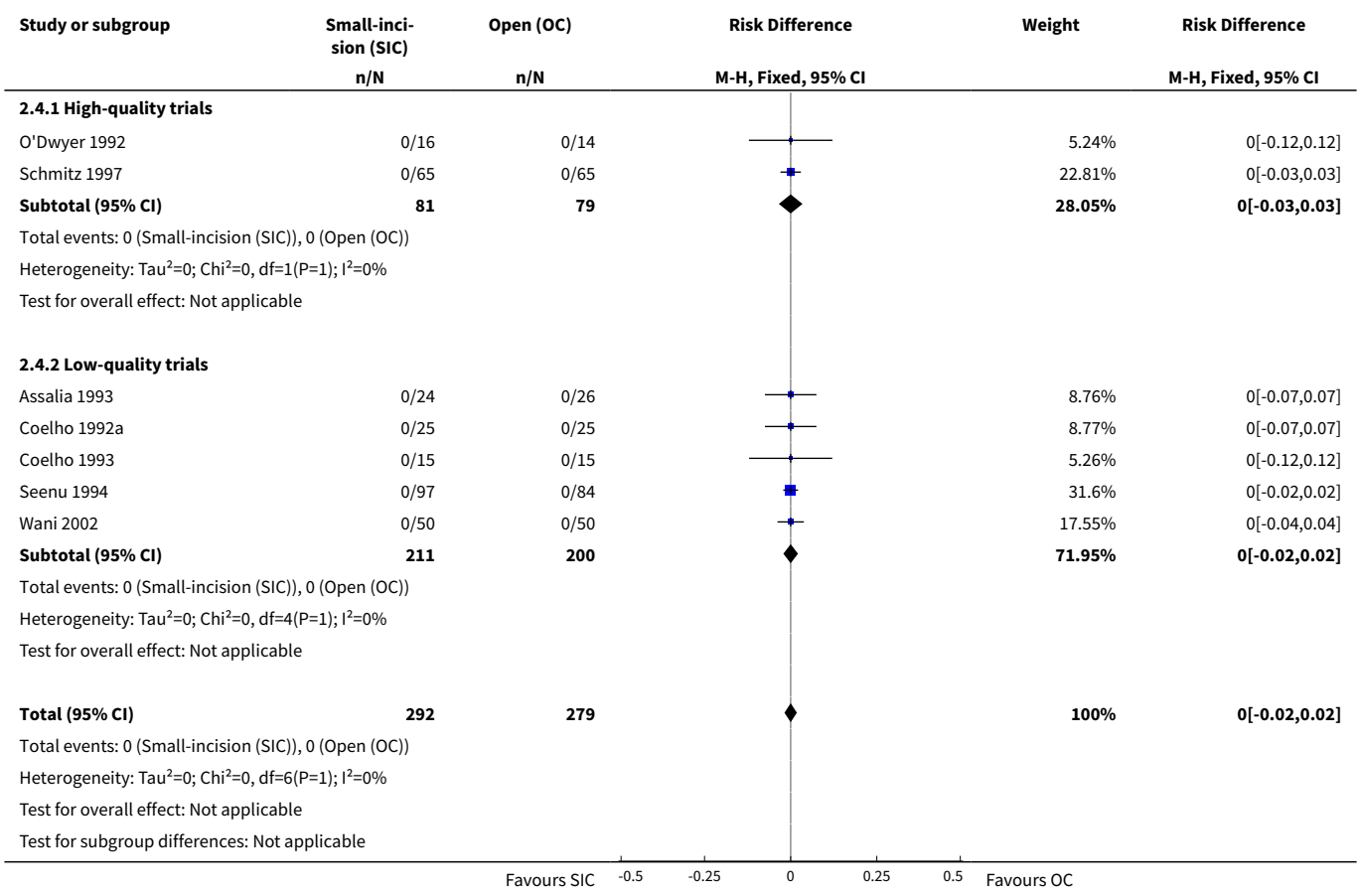
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
2.2.1 High-quality trials					
O'Dwyer 1992	1/16	0/14		6.44%	0.06[-0.1,0.23]
Schmitz 1997	13/65	4/65		11.82%	0.14[0.03,0.25]
Subtotal (95% CI)	**81**	**79**		**18.27%**	**0.11[0.02,0.21]**
Total events: 14 (Small-incision (SIC)), 4 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=0.61, df=1(P=0.43); I^2=0%					
Test for overall effect: Z=2.39(P=0.02)					
2.2.2 Low-quality trials					
Assalia 1993	1/24	1/26		12.61%	0[-0.11,0.11]
Coelho 1992a	2/25	3/25		6.21%	-0.04[-0.21,0.13]
Coelho 1993	1/15	1/15		5.45%	0[-0.18,0.18]
Seenu 1994	7/97	10/84		17.75%	-0.05[-0.13,0.04]
Wani 2002	0/50	0/50		39.71%	0[-0.04,0.04]
Subtotal (95% CI)	**211**	**200**		**81.73%**	**-0.01[-0.04,0.02]**
Total events: 11 (Small-incision (SIC)), 15 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=2.26, df=4(P=0.69); I^2=0%					
Test for overall effect: Z=0.47(P=0.64)					
Total (95% CI)	**292**	**279**		**100%**	**0.01[-0.03,0.05]**
Total events: 25 (Small-incision (SIC)), 19 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=8.1, df=6(P=0.23); I^2=25.93%					
Test for overall effect: Z=0.45(P=0.65)					
Test for subgroup differences: Not applicable					

Analysis 2.3. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 3 Severe complications (without bile duct injuries).

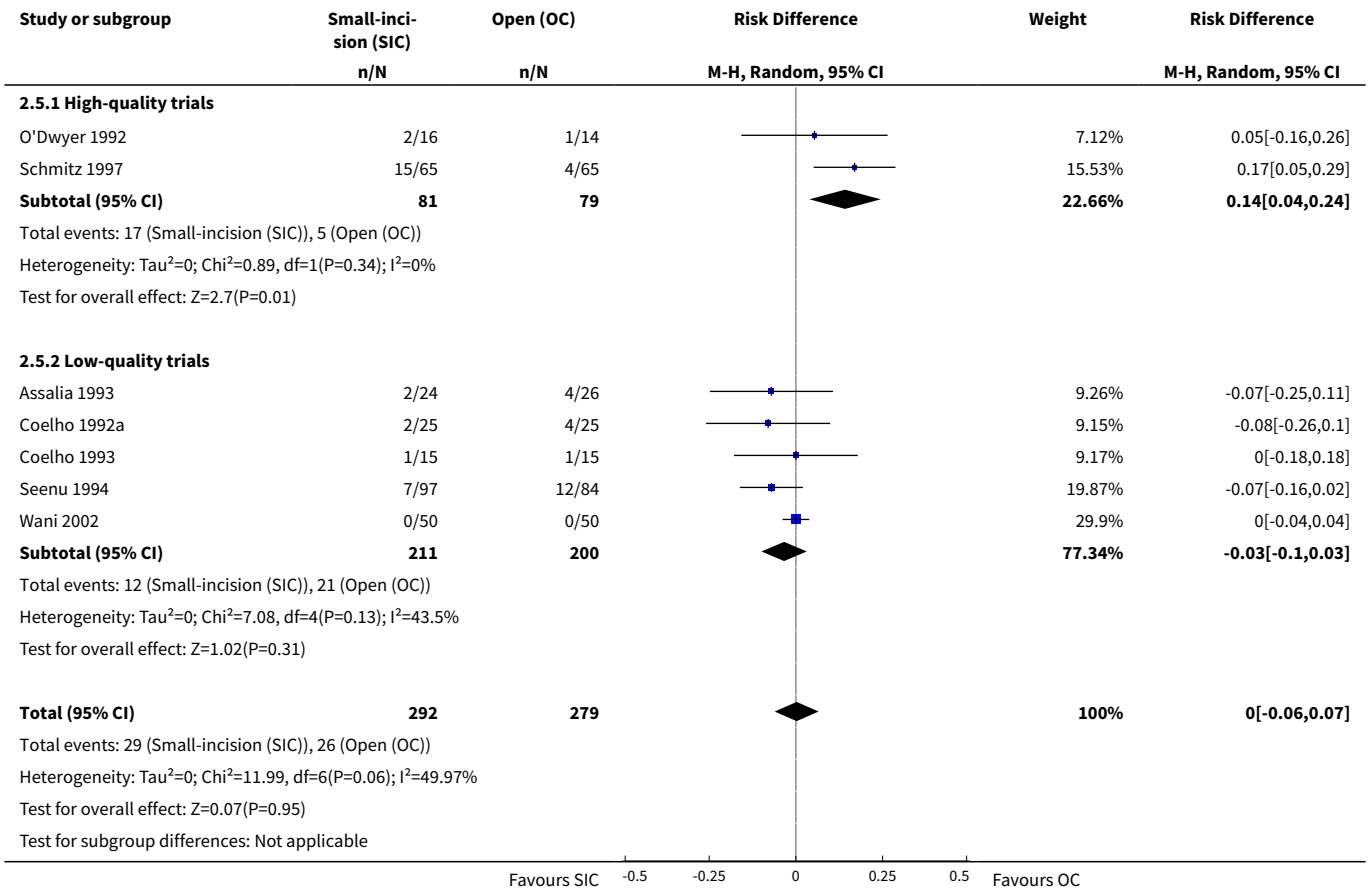
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
2.3.1 High-quality trials					
O'Dwyer 1992	1/16	1/14		5.24%	-0.01[-0.19,0.17]
Schmitz 1997	2/65	0/65		22.81%	0.03[-0.02,0.08]
Subtotal (95% CI)	**81**	**79**		**28.05%**	**0.02[-0.03,0.08]**
Total events: 3 (Small-incision (SIC)), 1 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=0.21, df=1(P=0.65); I^2=0%					
Test for overall effect: Z=0.85(P=0.39)					
2.3.2 Low-quality trials					
Assalia 1993	1/24	3/26		8.76%	-0.07[-0.22,0.07]
Coelho 1992a	0/25	1/25		8.77%	-0.04[-0.14,0.06]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
Seenu 1994	0/97	2/84		31.6%	-0.02[-0.06,0.01]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]



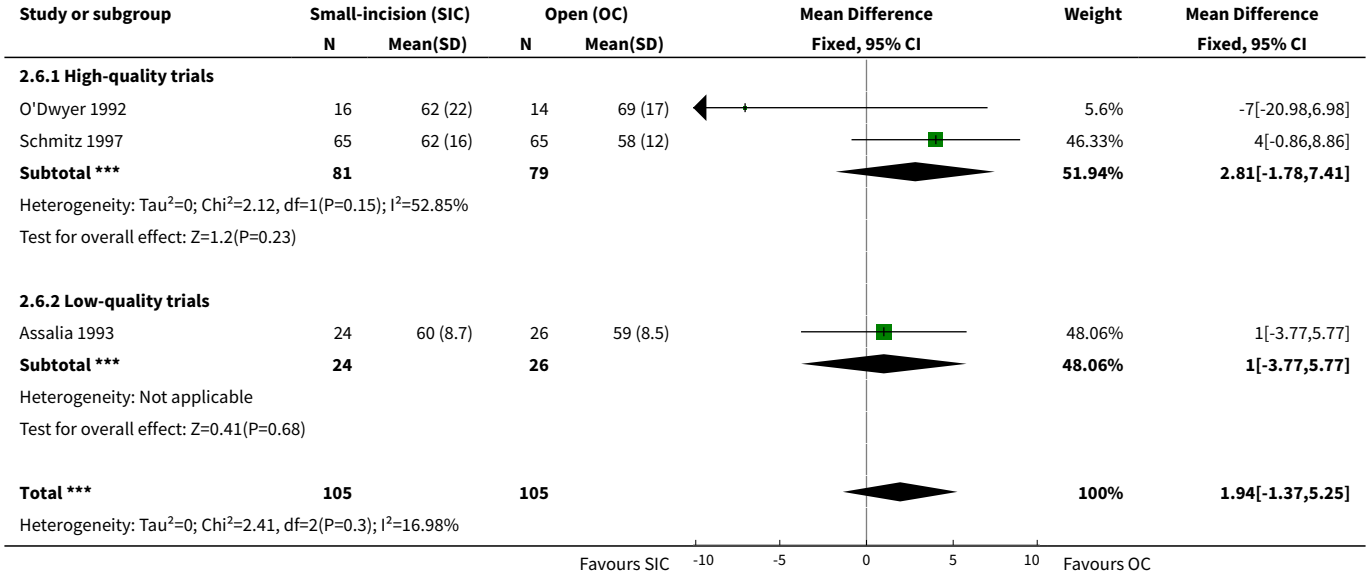
Analysis 2.4. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 4 Bile duct injuries.

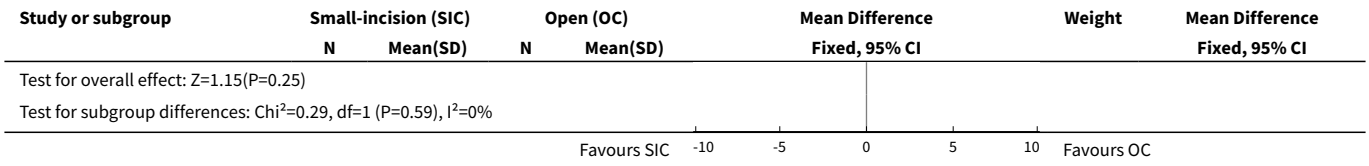


Analysis 2.5. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 5 Total complications.

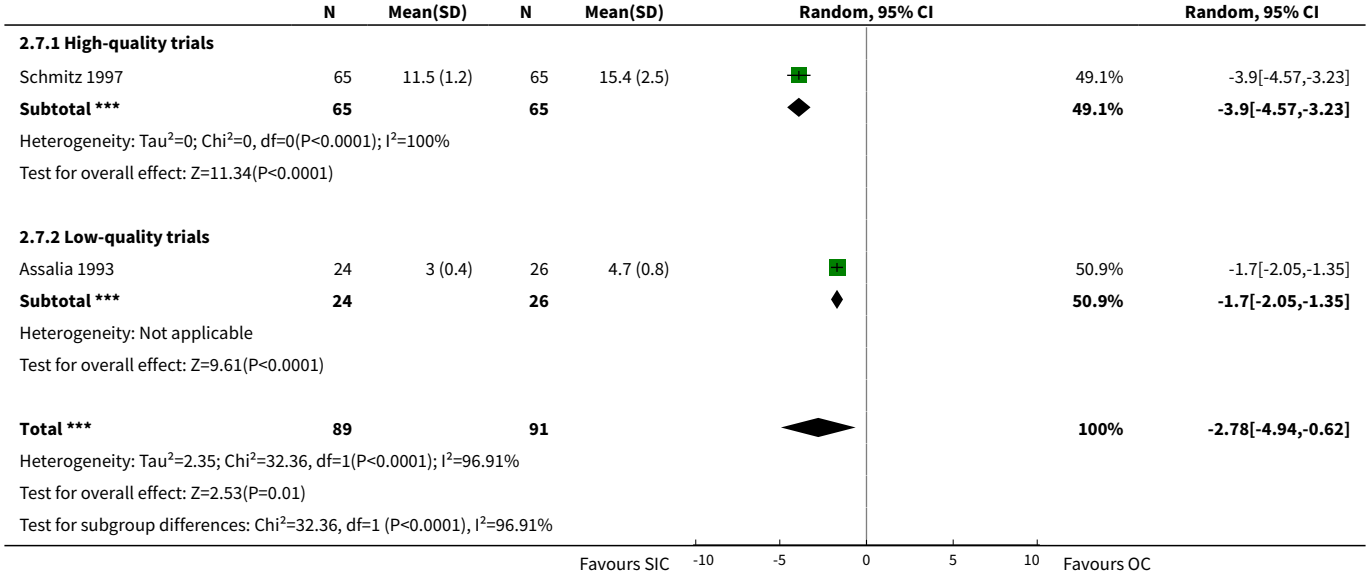


Analysis 2.6. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 6 Operative time (minutes).





Analysis 2.7. Comparison 2 SIC versus OC - high-quality and low-quality trials regarding concealment of allocation, Outcome 7 Hospital stay (days).



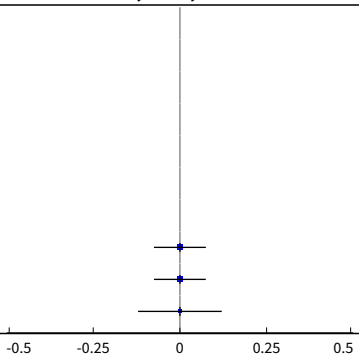
Comparison 3. SIC versus OC - high-quality and low-quality trials regarding blinding

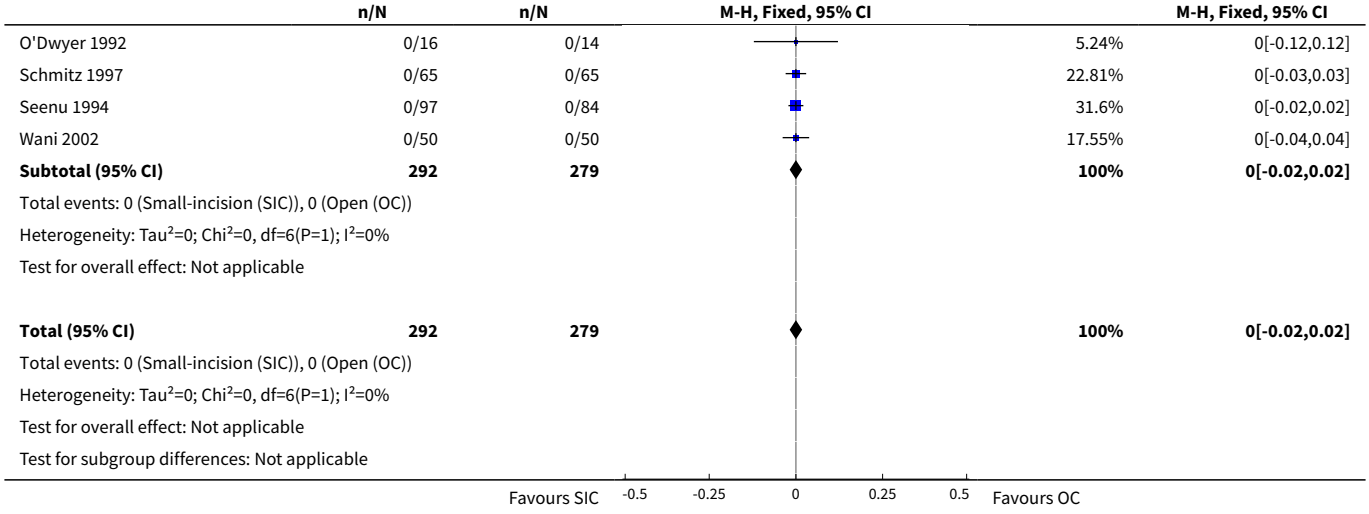
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Intra-operative complications	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
1.1 High-quality trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Low-quality trials	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
2 Minor complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
2.1 High-quality trials	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
2.2 Low-quality trials	7	571	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Severe complications (without bile duct injuries)	7	571	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
3.1 High-quality trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Low-quality trials	7	571	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
4 Bile duct injuries	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
4.1 High-quality trials	0	0	Risk Difference (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Low-quality trials	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
5 Total complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.06, 0.07]
5.1 High-quality trials	0	0	Risk Difference (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.2 Low-quality trials	7	571	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.06, 0.07]
6 Operative time (minutes)	3	210	Mean Difference (IV, Fixed, 95% CI)	1.94 [-1.37, 5.25]
6.1 High-quality trials	0	0	Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Low-quality trials	3	210	Mean Difference (IV, Fixed, 95% CI)	1.94 [-1.37, 5.25]
7 Hospital stay (days)	2	180	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.94, -0.62]
7.1 High-quality trials	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7.2 Low-quality trials	2	180	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.94, -0.62]

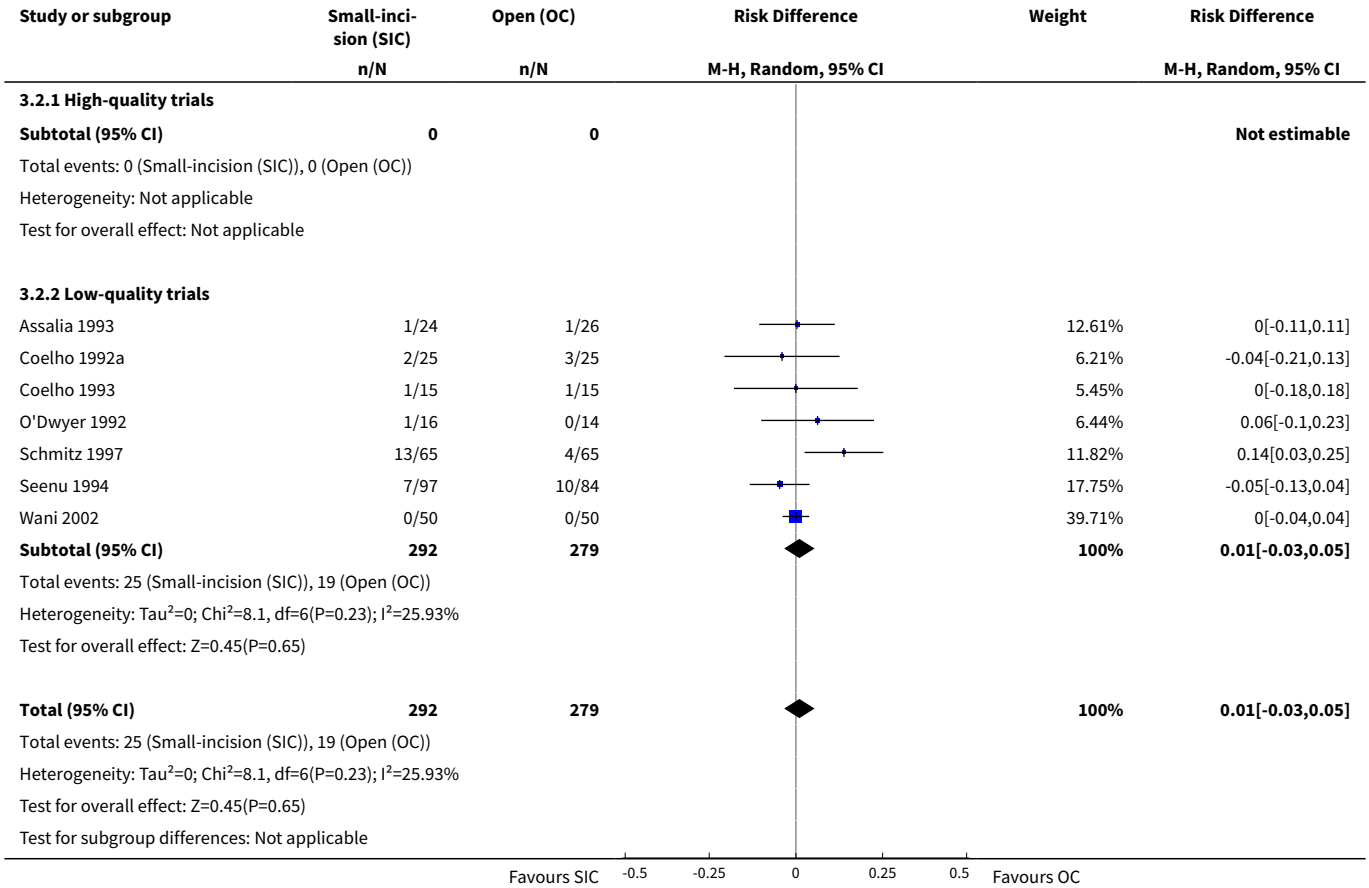
Analysis 3.1. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 1 Intra-operative complications.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
3.1.1 High-quality trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.1.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]



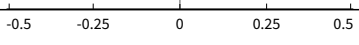


Analysis 3.2. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 2 Minor complications.



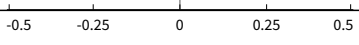
Analysis 3.3. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 3 Severe complications (without bile duct injuries).

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
3.3.1 High-quality trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.3.2 Low-quality trials					
Assalia 1993	1/24	3/26		8.76%	-0.07[-0.22,0.07]
Coelho 1992a	0/25	1/25		8.77%	-0.04[-0.14,0.06]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
O'Dwyer 1992	1/16	1/14		5.24%	-0.01[-0.19,0.17]
Schmitz 1997	2/65	0/65		22.81%	0.03[-0.02,0.08]
Seenu 1994	0/97	2/84		31.6%	-0.02[-0.06,0.01]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]
Subtotal (95% CI)	**292**	**279**		**100%**	**-0.01[-0.04,0.02]**
Total events: 4 (Small-incision (SIC)), 7 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=4.39, df=6(P=0.62); I^2=0%					
Test for overall effect: Z=0.8(P=0.43)					
Total (95% CI)	**292**	**279**		**100%**	**-0.01[-0.04,0.02]**
Total events: 4 (Small-incision (SIC)), 7 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=4.39, df=6(P=0.62); I^2=0%					
Test for overall effect: Z=0.8(P=0.43)					
Test for subgroup differences: Not applicable					

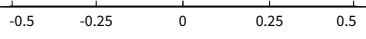


Analysis 3.4. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 4 Bile duct injuries.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
3.4.1 High-quality trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.4.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
O'Dwyer 1992	0/16	0/14		5.24%	0[-0.12,0.12]
Schmitz 1997	0/65	0/65		22.81%	0[-0.03,0.03]
Seenu 1994	0/97	0/84		31.6%	0[-0.02,0.02]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]

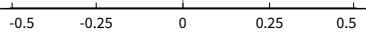


Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Subtotal (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=0, df=6(P=1); I^2=0%					
Test for overall effect: Not applicable					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=0, df=6(P=1); I^2=0%					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

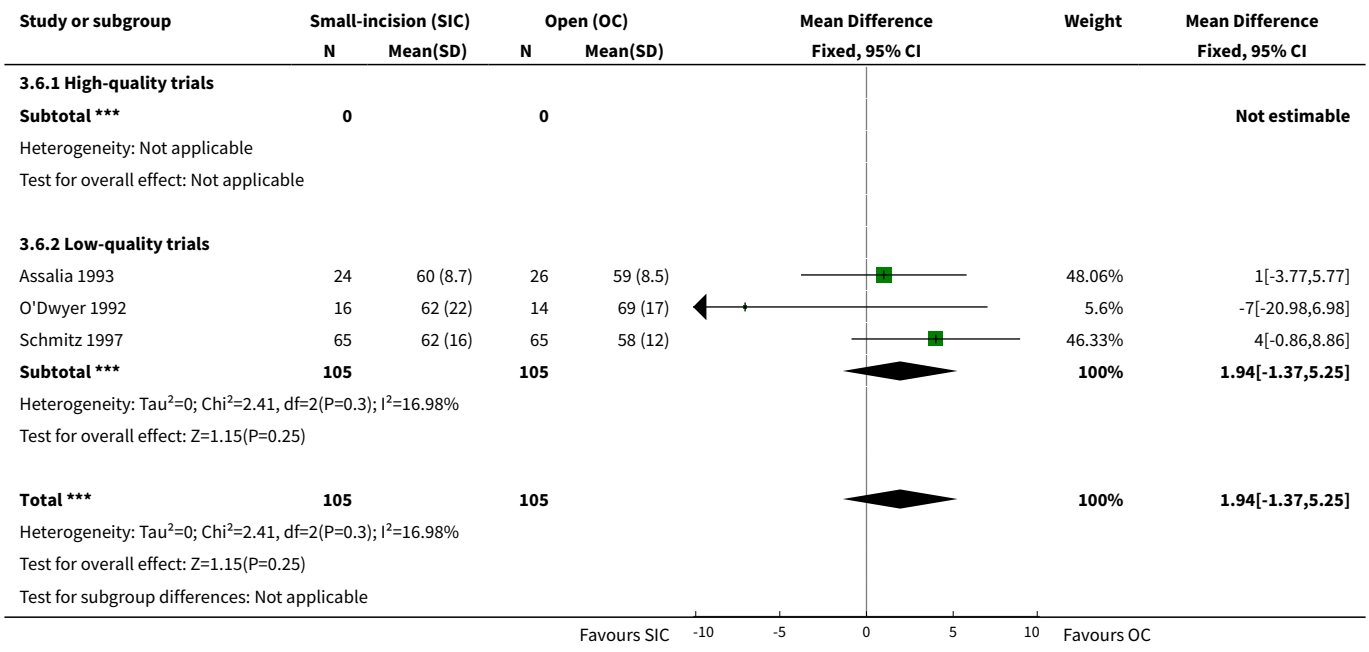


Analysis 3.5. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 5 Total complications.

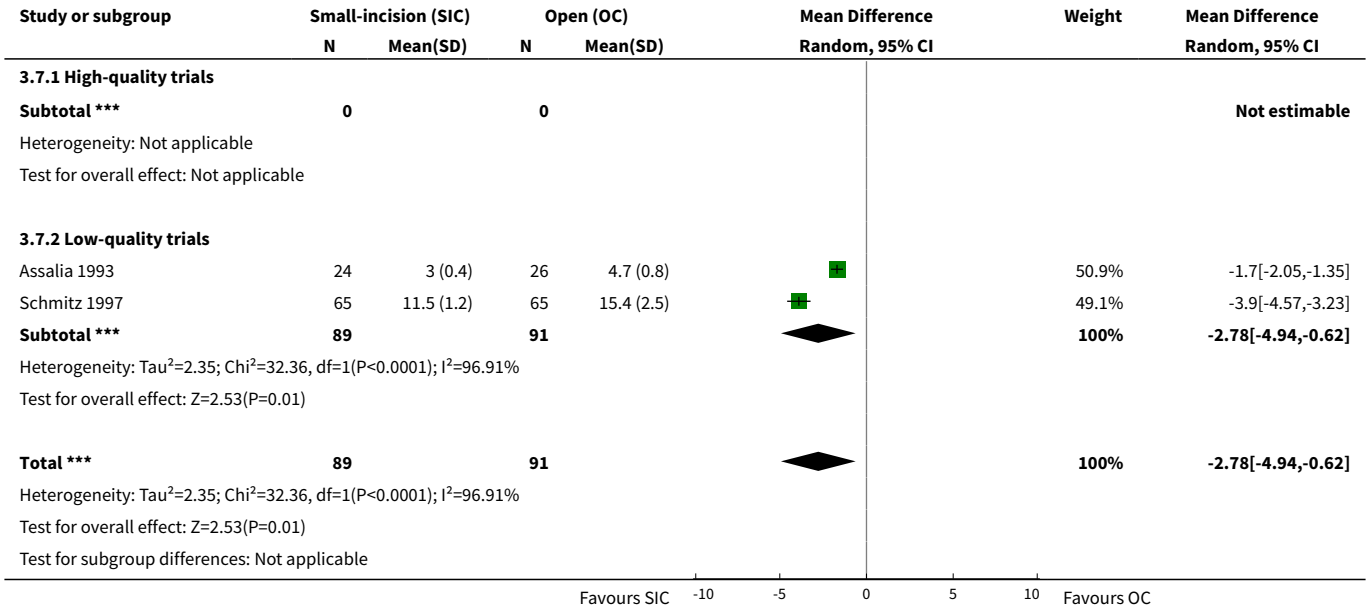
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
3.5.1 High-quality trials					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
3.5.2 Low-quality trials					
Assalia 1993	2/24	4/26		9.26%	-0.07[-0.25,0.11]
Coelho 1992a	2/25	4/25		9.15%	-0.08[-0.26,0.1]
Coelho 1993	1/15	1/15		9.17%	0[-0.18,0.18]
O'Dwyer 1992	2/16	1/14		7.12%	0.05[-0.16,0.26]
Schmitz 1997	15/65	4/65		15.53%	0.17[0.05,0.29]
Seenu 1994	7/97	12/84		19.87%	-0.07[-0.16,0.02]
Wani 2002	0/50	0/50		29.9%	0[-0.04,0.04]
Subtotal (95% CI)	**292**	**279**		**100%**	**0[-0.06,0.07]**
Total events: 29 (Small-incision (SIC)), 26 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=11.99, df=6(P=0.06); I^2=49.97%					
Test for overall effect: Z=0.07(P=0.95)					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.06,0.07]**
Total events: 29 (Small-incision (SIC)), 26 (Open (OC))					
Heterogeneity: Tau^2=0; Chi^2=11.99, df=6(P=0.06); I^2=49.97%					
Test for overall effect: Z=0.07(P=0.95)					
Test for subgroup differences: Not applicable					



Analysis 3.6. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 6 Operative time (minutes).



Analysis 3.7. Comparison 3 SIC versus OC - high-quality and low-quality trials regarding blinding, Outcome 7 Hospital stay (days).

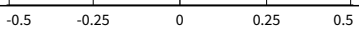


Comparison 4. SIC versus OC - high-quality and low-quality trials regarding follow-up

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Intra-operative complications	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
1.1 High-quality trials	1	130	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.03, 0.03]
1.2 Low-quality trials	6	441	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
2 Minor complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.01 [-0.03, 0.05]
2.1 High-quality trials	1	130	Risk Difference (M-H, Random, 95% CI)	0.14 [0.03, 0.25]
2.2 Low-quality trials	6	441	Risk Difference (M-H, Random, 95% CI)	-0.01 [-0.04, 0.03]
3 Severe complications (without bile duct injuries)	7	571	Risk Difference (M-H, Fixed, 95% CI)	-0.01 [-0.04, 0.02]
3.1 High-quality trials	1	130	Risk Difference (M-H, Fixed, 95% CI)	0.03 [-0.02, 0.08]
3.2 Low-quality trials	6	441	Risk Difference (M-H, Fixed, 95% CI)	-0.02 [-0.05, 0.01]
4 Bile duct injuries	7	571	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
4.1 High-quality trials	1	130	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.03, 0.03]
4.2 Low-quality trials	6	441	Risk Difference (M-H, Fixed, 95% CI)	0.0 [-0.02, 0.02]
5 Total complications	7	571	Risk Difference (M-H, Random, 95% CI)	0.00 [-0.06, 0.07]
5.1 High-quality trials	1	130	Risk Difference (M-H, Random, 95% CI)	0.17 [0.05, 0.29]
5.2 Low-quality trials	6	441	Risk Difference (M-H, Random, 95% CI)	-0.02 [-0.07, 0.03]
6 Operative time (minutes)	3	210	Mean Difference (IV, Fixed, 95% CI)	1.94 [-1.37, 5.25]
6.1 High-quality trials	1	130	Mean Difference (IV, Fixed, 95% CI)	4.0 [-0.86, 8.86]
6.2 Low-quality trials	2	80	Mean Difference (IV, Fixed, 95% CI)	0.16 [-4.35, 4.68]
7 Hospital stay (days)	2	180	Mean Difference (IV, Random, 95% CI)	-2.78 [-4.94, -0.62]
7.1 High-quality trials	1	130	Mean Difference (IV, Random, 95% CI)	-3.9 [-4.57, -3.23]
7.2 Low-quality trials	1	50	Mean Difference (IV, Random, 95% CI)	-1.70 [-2.05, -1.35]

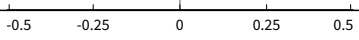
Analysis 4.1. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 1 Intra-operative complications.

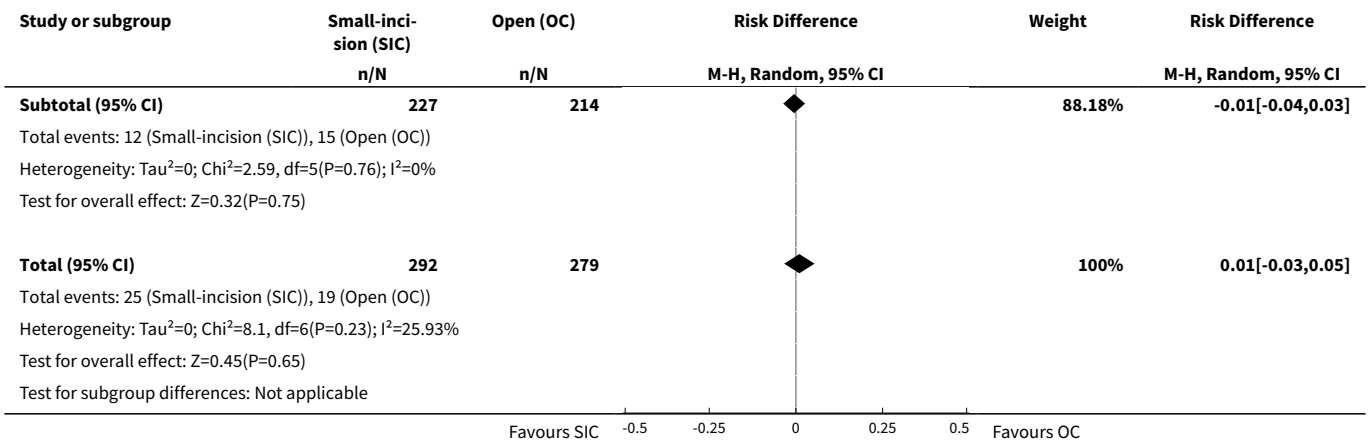
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
4.1.1 High-quality trials					
Schmitz 1997	0/65	0/65		22.81%	0[-0.03,0.03]
Subtotal (95% CI)	**65**	**65**		**22.81%**	**0[-0.03,0.03]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.1.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
O'Dwyer 1992	0/16	0/14		5.24%	0[-0.12,0.12]
Seenu 1994	0/97	0/84		31.6%	0[-0.02,0.02]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]
Subtotal (95% CI)	**227**	**214**		**77.19%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=5(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=6(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					



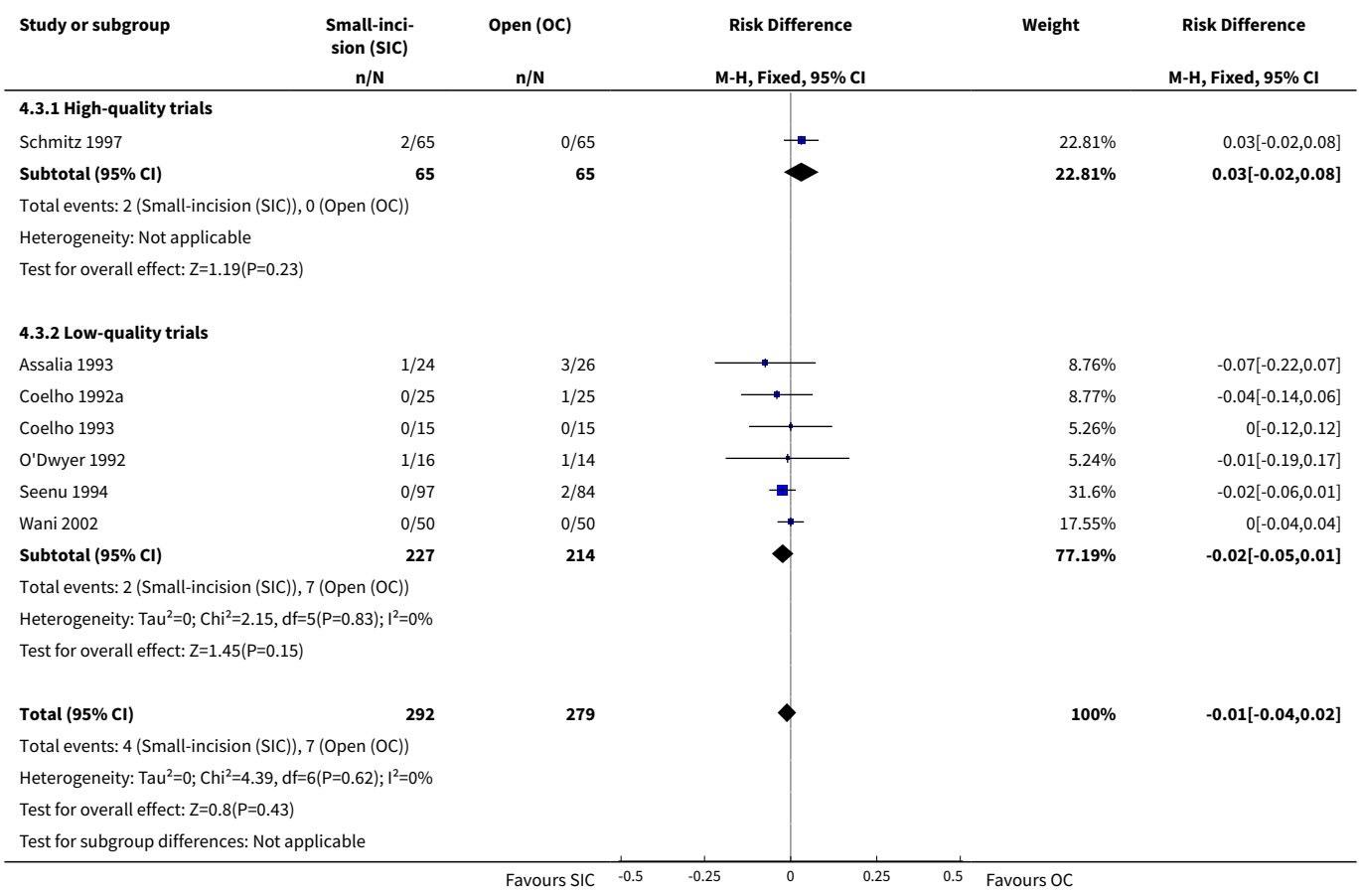
Analysis 4.2. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 2 Minor complications.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
4.2.1 High-quality trials					
Schmitz 1997	13/65	4/65		11.82%	0.14[0.03,0.25]
Subtotal (95% CI)	**65**	**65**		**11.82%**	**0.14[0.03,0.25]**
Total events: 13 (Small-incision (SIC)), 4 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.39(P=0.02)					
4.2.2 Low-quality trials					
Assalia 1993	1/24	1/26		12.61%	0[-0.11,0.11]
Coelho 1992a	2/25	3/25		6.21%	-0.04[-0.21,0.13]
Coelho 1993	1/15	1/15		5.45%	0[-0.18,0.18]
O'Dwyer 1992	1/16	0/14		6.44%	0.06[-0.1,0.23]
Seenu 1994	7/97	10/84		17.75%	-0.05[-0.13,0.04]
Wani 2002	0/50	0/50		39.71%	0[-0.04,0.04]



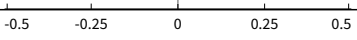


Analysis 4.3. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 3 Severe complications (without bile duct injuries).



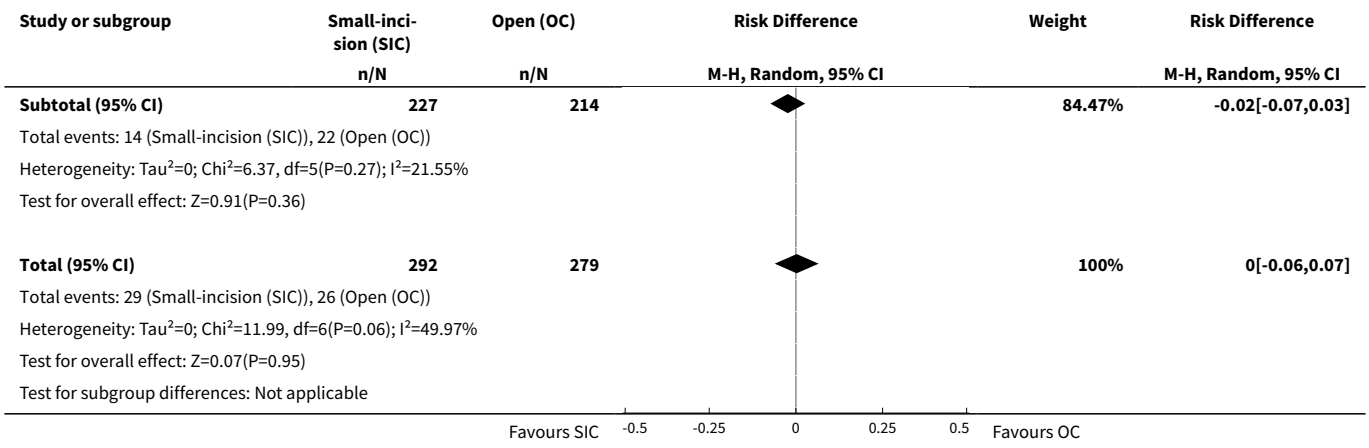
Analysis 4.4. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 4 Bile duct injuries.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
4.4.1 High-quality trials					
Schmitz 1997	0/65	0/65		22.81%	0[-0.03,0.03]
Subtotal (95% CI)	**65**	**65**		**22.81%**	**0[-0.03,0.03]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
4.4.2 Low-quality trials					
Assalia 1993	0/24	0/26		8.76%	0[-0.07,0.07]
Coelho 1992a	0/25	0/25		8.77%	0[-0.07,0.07]
Coelho 1993	0/15	0/15		5.26%	0[-0.12,0.12]
O'Dwyer 1992	0/16	0/14		5.24%	0[-0.12,0.12]
Seenu 1994	0/97	0/84		31.6%	0[-0.02,0.02]
Wani 2002	0/50	0/50		17.55%	0[-0.04,0.04]
Subtotal (95% CI)	**227**	**214**		**77.19%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=5(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Total (95% CI)	**292**	**279**		**100%**	**0[-0.02,0.02]**
Total events: 0 (Small-incision (SIC)), 0 (Open (OC))					
Heterogeneity: $Tau^2=0$; $Chi^2=0$, df=6(P=1); $I^2=0\%$					
Test for overall effect: Not applicable					
Test for subgroup differences: Not applicable					

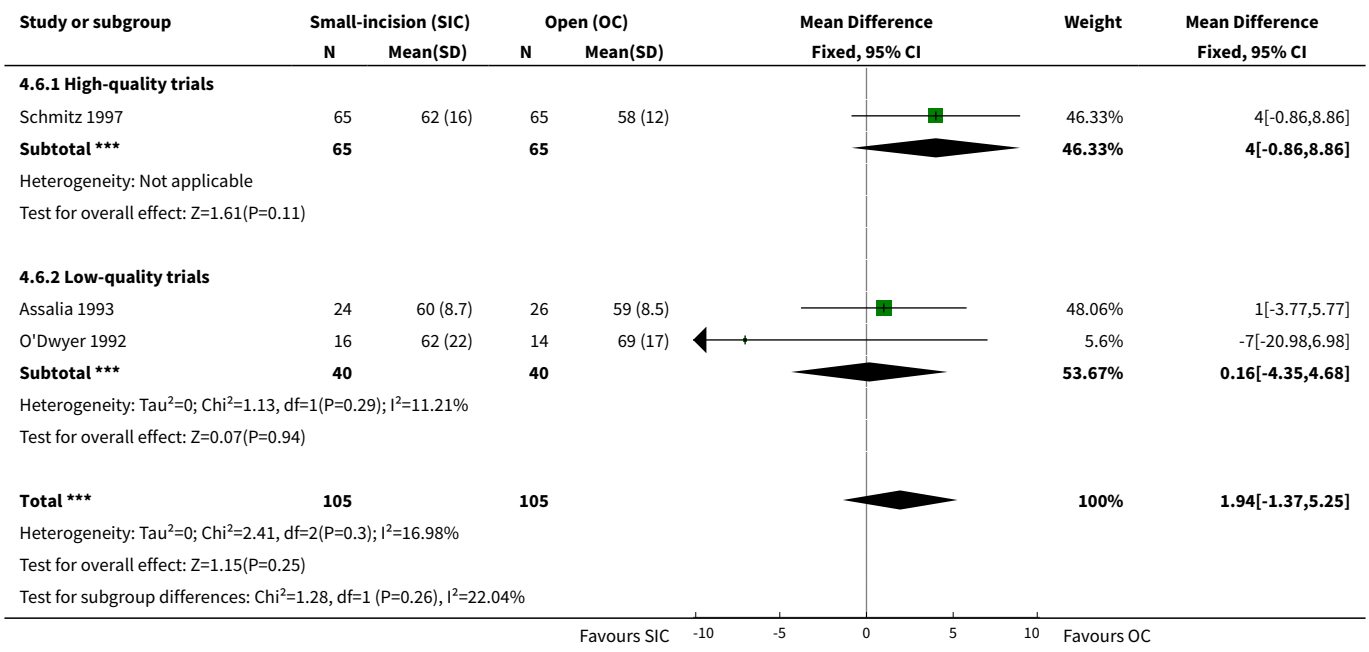


Analysis 4.5. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 5 Total complications.

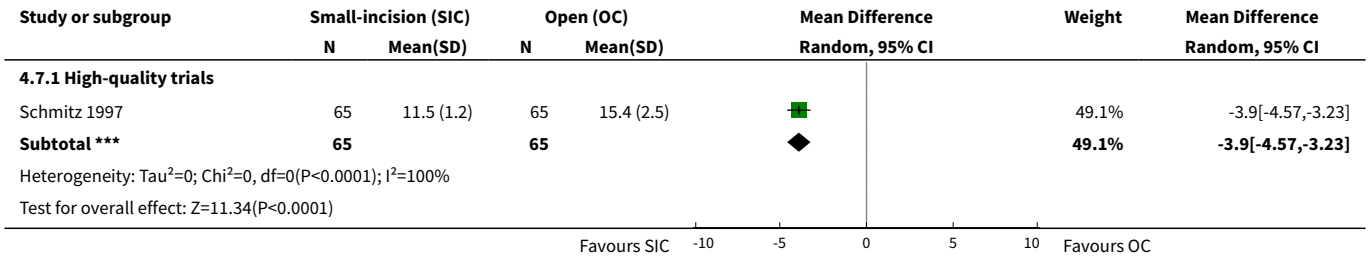
Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Random, 95% CI	Weight	Risk Difference M-H, Random, 95% CI
4.5.1 High-quality trials					
Schmitz 1997	15/65	4/65		15.53%	0.17[0.05,0.29]
Subtotal (95% CI)	**65**	**65**		**15.53%**	**0.17[0.05,0.29]**
Total events: 15 (Small-incision (SIC)), 4 (Open (OC))					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.81(P=0)					
4.5.2 Low-quality trials					
Assalia 1993	2/24	4/26		9.26%	-0.07[-0.25,0.11]
Coelho 1992a	2/25	4/25		9.15%	-0.08[-0.26,0.1]
Coelho 1993	1/15	1/15		9.17%	0[-0.18,0.18]
O'Dwyer 1992	2/16	1/14		7.12%	0.05[-0.16,0.26]
Seenu 1994	7/97	12/84		19.87%	-0.07[-0.16,0.02]
Wani 2002	0/50	0/50		29.9%	0[-0.04,0.04]

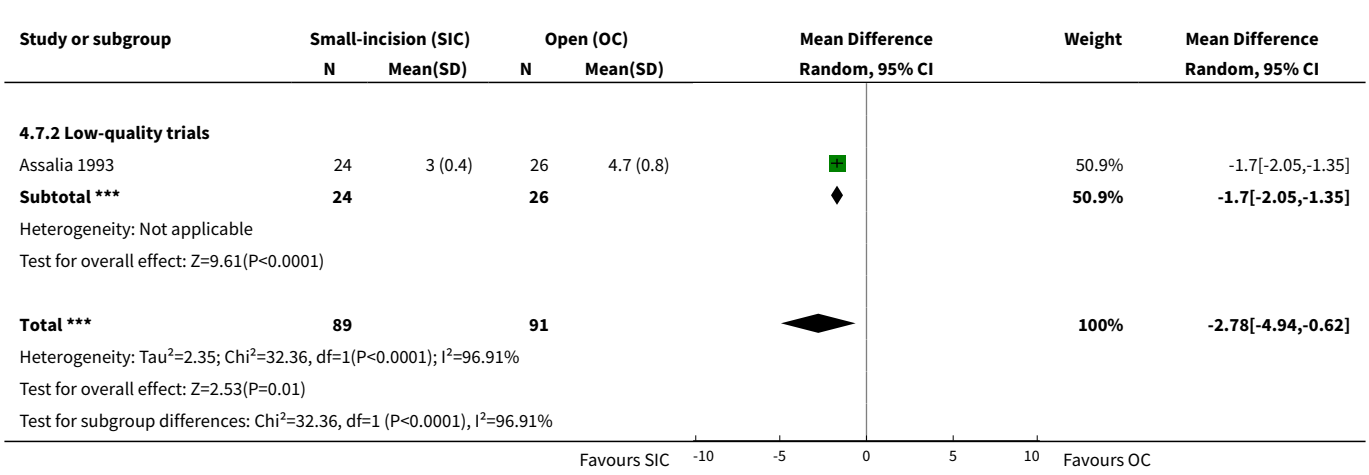


Analysis 4.6. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 6 Operative time (minutes).



Analysis 4.7. Comparison 4 SIC versus OC - high-quality and low-quality trials regarding follow-up, Outcome 7 Hospital stay (days).

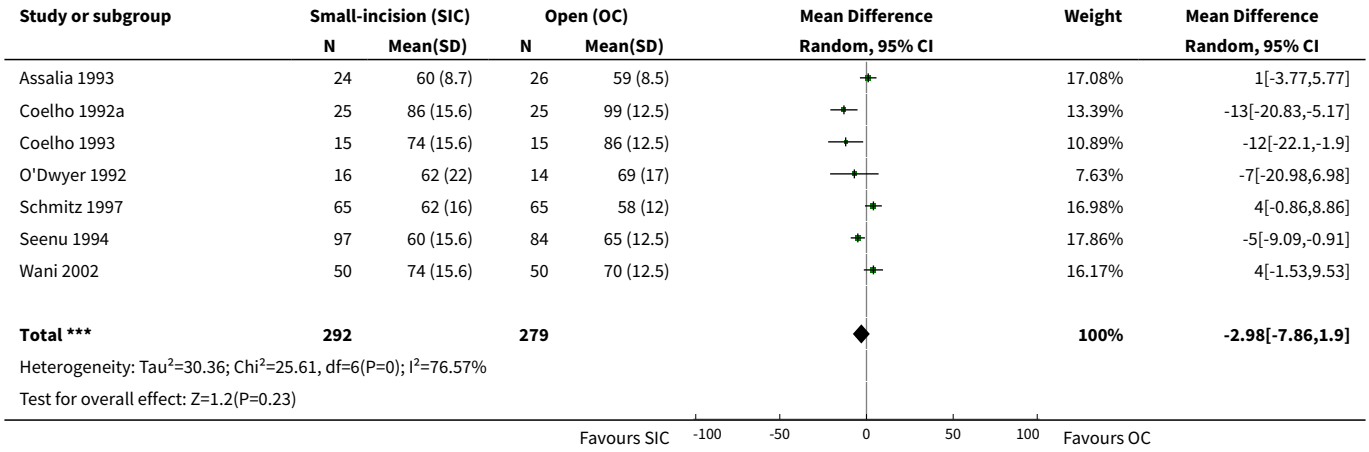




Comparison 5. SIC versus OC - sensitivity analysis imputing medians and standard deviations for missing data

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sensitivity analysis 1: Operative time (minutes)	7	571	Mean Difference (IV, Random, 95% CI)	-2.98 [-7.86, 1.90]
2 Sensitivity analysis 2: Hospital stay (days)	7	571	Mean Difference (IV, Random, 95% CI)	-1.97 [-2.56, -1.39]
3 Sensitivity analysis 3: Omitting outlier Schmitz in total complications	6	441	Risk Difference (M-H, Fixed, 95% CI)	-0.04 [-0.09, 0.01]

Analysis 5.1. Comparison 5 SIC versus OC - sensitivity analysis imputing medians and standard deviations for missing data, Outcome 1 Sensitivity analysis 1: Operative time (minutes).

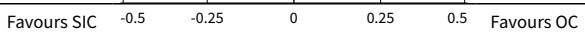


Analysis 5.2. Comparison 5 SIC versus OC - sensitivity analysis imputing medians and standard deviations for missing data, Outcome 2 Sensitivity analysis 2: Hospital stay (days).

Study or subgroup	Small-incision (SIC) N	Small-incision (SIC) Mean(SD)	Open (OC) N	Open (OC) Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Assalia 1993	24	3 (0.4)	26	4.7 (0.8)		16.4%	-1.7[-2.05,-1.35]
Coelho 1992a	25	1.7 (0.8)	25	3.5 (1.7)		13.8%	-1.8[-2.52,-1.08]
Coelho 1993	15	1 (0.8)	15	2 (1.7)		12.13%	-1[-1.93,-0.07]
O'Dwyer 1992	16	3 (0.8)	14	5 (1.7)		11.96%	-2[-2.95,-1.05]
Schmitz 1997	65	11.5 (1.2)	65	15.4 (2.5)		14.15%	-3.9[-4.57,-3.23]
Seenu 1994	97	2.6 (0.8)	84	4 (1.7)		16.17%	-1.4[-1.79,-1.01]
Wani 2002	50	3 (0.8)	50	5 (1.7)		15.39%	-2[-2.51,-1.49]
Total ***	**292**		**279**			**100%**	**-1.97[-2.56,-1.39]**
Heterogeneity: Tau²=0.52; Chi²=45.1, df=6(P<0.0001); I²=86.7%							
Test for overall effect: Z=6.59(P<0.0001)							

Analysis 5.3. Comparison 5 SIC versus OC - sensitivity analysis imputing medians and standard deviations for missing data, Outcome 3 Sensitivity analysis 3: Omitting outlier Schmitz in total complications.

Study or subgroup	Small-incision (SIC) n/N	Open (OC) n/N	Risk Difference M-H, Fixed, 95% CI	Weight	Risk Difference M-H, Fixed, 95% CI
Assalia 1993	2/24	4/26		11.35%	-0.07[-0.25,0.11]
Coelho 1992a	2/25	4/25		11.37%	-0.08[-0.26,0.1]
Coelho 1993	1/15	1/15		6.82%	0[-0.18,0.18]
O'Dwyer 1992	2/16	1/14		6.79%	0.05[-0.16,0.26]
Seenu 1994	7/97	12/84		40.94%	-0.07[-0.16,0.02]
Wani 2002	0/50	0/50		22.73%	0[-0.04,0.04]
Total (95% CI)	**227**	**214**		**100%**	**-0.04[-0.09,0.01]**
Total events: 14 (Small-incision (SIC)), 22 (Open (OC))					
Heterogeneity: Tau²=0; Chi²=6.37, df=5(P=0.27); I²=21.55%					
Test for overall effect: Z=1.62(P=0.11)					



ADDITIONAL TABLES

Table 1. Randomised, excluded, and included in small-incision vs open cholecystectomy

Trial	Randomised	Excluded	Included SIC	Included OC	Cholangiography	Antibiotics	Surgical expertise
Assalia 1993	50	0	24	26	N	Y	S
Coelho 1992a	50	0	25	25	Y	U	U
Coelho 1993	45*	0	15	15	U	U	U
O'Dwyer 1992a	30	0	16	14	Y	U	R
Schmitz 1997a	130	0	65	65	U	U	U
Seenu 1994	181	0	97	84	U	U	R
Wani 2002	100	0	50	50	U	U	U
Total	586	0	292	279			
* three-arm trial, patients in the LC group not listed in this table.	N = no	Y = yes	U = unknown	S = one surgeon	R = also registrars		

Table 2. Description of background data (age, sex, BMI, and ASA)

Trial	N	Age	Age	Sex (m/f)	Sex (m/f)	BMI	BMI	ASA (I-II-III-IV)	ASA (I-II-III-IV)
SIC vs OC	randomised	SIC	OC	SIC	OC	SIC	OC	SIC	OC
Assalia 1993	24 / 26	60.3 (12.1)	59.2 (13.4)	5 / 19	7 / 19	-	-	-	-
Coelho 1992a	25 / 25	46 (-)	45 (-)	2 / 23	4 / 21	-	-	-	-
Coelho 1993	15 / 15	42.5 (25-66)	45.4 (18-73)	2 / 13	3 / 12	-	-	-	-
O'Dwyer 1992a	16 / 14	46 (27-74)	51 (38-73)	3 / 13	4 / 10	-	-	16 - 0 - 0 - 0	14 - 0 - 0 - 0
Schmitz 1997a	65 / 65	52.6 (14.6)	54.1 (12.2)	20 / 45	23 / 42	-	-	-	-

Table 2. Description of background data (age, sex, BMI, and ASA) *(Continued)*

Seenu 1994	97 / 84	-	-	-	-	-	-	-	-
Wani 2002	50 / 50	34.8 (5.6)	37.4 (6.2)	5 / 45	5 / 45	21.5 (1.9)	21.6 (1.8)	-	-
		mean (standard deviation / range)							

Table 3. Complications specified per operative technique: small-incision vs open cholecys

Complications	SIC	OC
INTRA-OPERATIVE	(0)	(0)
POSTOPERATIVE - MINOR	(25 / 8.6%)	(19 / 6.8%)
wound hematoma	12	4
wound infection	12	15
urinary retention	1	0
POSTOPERATIVE - SEVERE	(4 / 1.4%)	(7 / 2.5%)
stone left in cystic duct (re-operation)	1	0
pneumonia	1	5
atelectasis	1	0
cardiovascular	1	0
upper GI bleeding (endoscopy / conservative)	0	2
BILE DUCT INJURY	(0)	(0)
TOTAL COMPLICATIONS	29 (9.9%)	26 (9.3%)
RE-OPERATIONS (all complications)	2 (0.7%)	0
TOTAL NUMBER OF PATIENTS INCLUDED (all trials)	292	279

Table 4. Internal validity assessment of included trials: small-incision vs open cholecys

Trial	Generation of alloc	Concealment of al-loc	Blinding	Follow-up
Assalia 1993	U	U	N	U
Coelho 1992a	A	U	N	U
Coelho 1993	U	U	N	U
O'Dwyer 1992a	U	A	N	U

Table 4. Internal validity assessment of included trials: small-incision vs open cholecys *(Continued)*

Schmitz 1997a	U	A	N	A
Seenu 1994	U	U	N	U
Wani 2002	U	U	N	U
A: Adequate	U: Unclear	I: Inadequate	N: Not performed	

Table 5. Results of small-incision vs open cholecystectomy: alloc. concealment (compar.2)

Outcome	RD/WMD	HQ/LQ/AT	Fixed	Random	Discrepancy	Emphasize	HQ-LQ difference	Significant
Minor complications	RD	HQ	0.12 (0.03, 0.22) *	0.11 (0.02, 0.21) *	no			
		LQ	-0.03 (-0.07, 0.02)	-0.01 (-0.04, 0.02)	no			
		AT	0.02 (-0.03, 0.06)	0.01 (-0.03, 0.05)	no	random	yes	yes/no
Total complications	RD	HQ	0.15 (0.04, 0.25) *	0.14 (0.04, 0.24) *	no			
		LQ	-0.05 (-0.10, 0.00)	-0.03 (-0.10, 0.03)	no			
		AT	0.01 (-0.04, 0.05)	0.00 (-0.06, 0.07)	no	random	yes	yes/no
Hospital stay	WMD	HQ	-3.90 (-4.57, -3.23) *	-3.90 (-4.57, -3.23) *	no			
		LQ	-1.70 (-2.05, -1.35) *	-1.70 (-2.05, -1.35) *	no			
		AT	-2.16 (-2.47, -1.85) *	-2.78 (-4.94, -0.62) *	no	random	no	yes
* significant result	HQ: high-quality trials	LQ: low-quality trials	AT: all trials	RD: risk difference	WMD: weighted mean difference	random: random-effects model		

Table 6. Operative time small-incision vs open cholecystectomy: all available data

Trial	Type of data	SIC - mean/median	SIC - SD/range	OC - mean/median	OC - SD/range	Skewness SIC	Skewness OC
Assalia 1993	A - SD	60	8.7	59	8.5	6.90	6.94
Coelho 1992a	A -	86	-	99	-	-	-
Coelho 1993	A - range	74	40 - 125	86	40 - 140	-	-
O'Dwyer 1992a	A - SD	62	22	69	17	2.82	4.06

Table 6. Operative time small-incision vs open cholecystectomy: all available data *(Continued)*

Schmitz 1997a	A - SD	62	16	58	12	3.88	4.83
Seenu 1994	A - range	60	30 - 100	65	20 - 90	-	-
Wani 2002	A - range	74	40 - 125	70	50 - 125	-	-
	A: Average / mean	SD: standard deviation					

Table 7. Hospital stay small-incision vs open cholecystectomy: all available data

Trial	Type of data	SIC - mean/median	SIC - SD/range	OC - mean/median	OC - SD/range	Skewness SIC	Skewness OC
Assalia 1993	A - SD	3	0.4	4.7	0.8	7.5	5.88
Coelho 1992a	A -	1,7	-	3,5	-	-	-
Coelho 1993	A - range	1	1 - 1	2	2 - 3	-	-
O'Dwyer 1992a	M - range	3	1 - 10	5	3 - 8	-	-
Schmitz 1997a	A - SD	11.5	1.2	15.4	2.5	9.58	6.16
Seenu 1994	A - range	2.6	1 - 4	4	3 - 8	-	-
Wani 2002	A -	3	-	5	-	-	-
	A: Average / mean	SD: standard deviation	M: median				

APPENDICES

Appendix 1. Search strategies

Database	Timespan of search	Search strategy	Hits	Titles selected
The Cochrane Hepato-Biliary Group Controlled Trials Register	6 April 2004	"cholelithiasis OR gallstones OR cholecystectomy"	843	65
Cochrane Database of Systematic Reviews in The Cochrane Library	Issue 1, 2004	"cholecystectomy"	33	0
Database of Abstracts of Reviews of Effects in The Cochrane Library	Issue 1, 2004	"cholecystectomy"	17	5
Cochrane Central Register of Controlled Trials in The Cochrane Library	Issue 1, 2004	"cholecystectomy"	1343	146
Health Technology Assessment Database in The Cochrane Library	Issue 1, 2004	"cholecystectomy"	11	4
NHS Economic Evaluation Database in The Cochrane Library	Issue 1, 2004	"cholecystectomy"	43	6
MEDLINE	1950 to January 2004	(((Gallbladder[Tiab] AND (Surgery[Tiab] OR Endoscopy[Tiab] OR Surgical[Tiab] OR Laparoscopy[Tiab])) OR Cholecystectomy[Tiab]) OR ((("Gallbladder"[MeSH] OR "Gallbladder Diseases"[MeSH]) AND ("Surgery"[MeSH] OR "surgery"[Subheading] OR "Endoscopy, Gastrointestinal"[MeSH] OR "Surgical Procedures, Operative"[MeSH] OR "Surgical Procedures, Minor"[MeSH] OR "Laparoscopy"[MeSH])) OR "Cholecystectomy"[MeSH])) AND (randomized controlled trial[PTYP] OR randomized controlled trials OR controlled clinical trial[PTYP] OR clinical trial[PTYP] OR clinical trials OR (clinical AND trial) OR random allocation OR random* OR double blind method OR single blind method OR (singl* OR doubl* OR trebl* OR tripl*) OR blind* OR mask* OR placebo* OR placebos OR research design OR comparative study OR evaluation studies OR follow up studies OR prospective studies OR control OR controlled OR prospectiv* OR volunteer*)	8354	347
EMBASE	1966 to January 2004	"cholecystectomy"	685	131

(Continued)

Web of Science	1988 to January 2004	TS=(cholecystectomy AND random*)	1163	148
CINAHL	1982 to January 2004	"cholecystectomy"	740	9
Total			13232	586

WHAT'S NEW

Date	Event	Description
23 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

F Keus: literature searches and selection, data extraction, statistical analysis, and text writing.
JAF de Jong: literature selection and data extraction.
HG Gooszen: text editing and supervision.
CJHM van Laarhoven: data extraction, statistical analysis, text writing, and final supervision.

DECLARATIONS OF INTEREST

We (FK, HG, CL) are the coordinating authors of an unpublished trial (Keus 2006), which will be published in the near future.

SOURCES OF SUPPORT

Internal sources

- Department of Surgery, University Medical Center, Utrecht, Netherlands.
- Department of Surgery, St. Elisabeth Hospital, Tilburg, Netherlands.

External sources

- No sources of support supplied

NOTES

The protocol for this systematic review was first published in Issue 3, 1997 of The Cochrane Library. The reviewers, Dr T Jørgensen and H Laugesen have abandoned the preparation of the systematic review. This necessitated that an update of the protocol and preparation of the review be performed by a new team of reviewers. They are F Keus, JAF de Jong, HG Gooszen, and CJHM van Laarhoven. Due to the large number of identified trials it was considered wiser in terms of clarity and usability to produce three separate reviews. Thus this review is one of the three.

Correction of name
Eric Keus, the lead author of the protocol, and Frederik Keus, the lead author of the review, is one and the same person.

INDEX TERMS

Medical Subject Headings (MeSH)

Cholecystectomy [*methods]; Cholecystolithiasis [*surgery]; Minimally Invasive Surgical Procedures; Randomized Controlled Trials as Topic

MeSH check words

Humans