Risk of bias judgements and strength of conclusions in meta-evidence from the Cochrane Colorectal Cancer Group

John Delaney¹,²*, Rebecca Cui² and Alexander Engel¹,³

Abstract

Background: The Cochrane Collaboration records risk of bias (ROB) judgements on the original studies it analyses. The aim of this review is to perform an audit of all literature produced by the Cochrane Colorectal Cancer Group (CCCG), focusing on whether intervention type has any relationship with ROB and the ability of a review to inform clinical practice.

Methods: The most recent version of every CCCG review from January 2000 to the end of July 2018 was included. Conclusions were categorized as informing clinical practice (I) or not (N). Both I and N categories were divided into firm (F) or tempered (T) based on the definitiveness of their language. ROB judgements were aggregated. Reviews were classed as Medical (M), Surgical (S), Medical & Surgical (MS) or Other (O) based on their intervention, with O reviews then excluded. Data were analyzed in SPSS.

Results: Ninety-five reviews were included, covering 1892 studies. Sixty-two percent (n = 59/95) informed clinical practice (I). Thirty-eight percent (n = 36/95) did not inform clinical practice (N). Of the N group, 53% (n = 19/36) were completely equivocal (firm) while 47% (n = 17/36) were moderately so (tempered). In the I group, 46% (n = 27/59) gave a conclusion that was firm and 54% (n = 32/59) were tempered. Seven thousand five hundred sixty-four cases of bias were assessed. Risk of bias was low in 43%, high in 20% and unclear in 37%. A review that regarded a medical intervention alone was significantly more likely to be comprised of studies with a low risk of bias than a review that included a surgical intervention (p < 0.001).

Conclusion: The Cochrane Colorectal Cancer Group finds the risk of bias to be low in less than half of its judgements. A review that included a surgical intervention was less likely to display low risk of bias. Risk of bias was associated with whether a review informed clinical practice, but intervention type was not. Readers of colorectal literature should be cautious when considering original and meta-evidence in this field, particularly where a surgical intervention is assessed.

Keywords: Meta-analysis, Systematic review, Cochrane, Risk of bias, Epidemiologic methods

Background

The Cochrane Collaboration is an independent [1] global medical research organization [2], well regarded as having a high standard of methodology and rigor [3]. As part of their assessment of original evidence for inclusion in reviews, the Cochrane Collaboration typically assess each study’s risk of bias (ROB), recording a judgement of “low risk”, “high risk” or “unclear risk” across seven standard criteria [4]. The criteria, familiar to many readers, were based on consensus expert review [5] and are intended to focus on the internal validity of studies. Assessment of ROB using the Cochrane tool has been previously noted to have high inter-rater variability [6], and the impact on effect size that a judgement of high or unclear bias in a particular domain has may vary according to the intervention and design of an original study [5]. A judgement of “unclear” may reflect a deficiency in the quality of reporting, rather than poor internal validity of the study. However, Cochrane’s approach is regarded as the gold standard for risk of bias assessment in meta-evidence [7].

* Correspondence: jdel2642@uni.sydney.edu.au
1 Northern Clinical School, Sydney Medical School, University of Sydney, Sydney, Australia
2 Royal Prince Alfred Hospital, Sydney, Australia
Full list of author information is available at the end of the article

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Judgements of high or unclear risk have been associated with an over-appreciation of effect size [6]. The domains are listed in Table 1. Risk of bias judgements are collated and published in the finished reviews. Cochrane reviews are usually based on randomized control trials and do not consider “real-world data”.

Cochrane’s colorectal cancer group is the CCCG, the Cochrane Colorectal Cancer Group [8]. Each review published by the CCCG typically includes a recording of the ROB judgements of the relevant group of original studies. The overall picture of bias within the literature assessed by the CCCG has yet to be aggregated. This paper will collect and analyze all ROB judgements published by the CCCG, giving an overview of the risk of bias found in colorectal original research. The combined data will provide a view of the quality of a sample of colorectal literature over time, and a snapshot of its current status. It will also offer insight into the level of clinical utility of scientific publications within the colorectal domain; that is, when Cochrane reviews the colorectal literature, how often is it able to inform clinical practice?

As a subset of surgical intervention, laparoscopic surgery presents an example of the surgical research dilemma; technology precedes evidence, and the barriers to surgeons using new devices are low [9]. The learning curve of a new surgical implement and the pre-existing challenges of surgical research make robust conclusions about best practice difficult, particularly in the early phase of implementation [10]. This is in a commercial setting of high public demand and great marketing potential for new surgical technologies, as may also be seen currently with the popularity of robotic surgery [11, 12]. Laparoscopic surgery (“key-hole” surgery) became widespread prior to significant evidence demonstrating its superiority over open approaches [13] and even now there remain some areas of controversy [14]. Subgroup analysis on laparoscopic papers from within the CCCG output was planned for this review as a means of assessing the meta-evidence support for this surgical technique.

### Methods

#### Literature search

In collaboration with the CCCG, a list of all of that group’s reviews from January 2000 to the end of July 2018 was acquired. The recorded ROB judgements for each study were also provided. The provided database was compared by two independent reviewers (JD and RC) with reviews retrieved from the Cochrane Library to check accuracy.

#### Definitions

Risk of bias judgements are defined in the Cochrane Collaboration handbook [4]. Conclusion type was classified as “informs clinical practice—firm” (I-F), “informs clinical practice—tempered” (I-T), “does not inform clinical practice—tempered” (N-T) and “does not inform clinical practice—firm” (N-F). The definitions for these categories are outlined in Table 2 and have been described and used previously [15].

Reviews were classed as Medical (M), Surgical (S), Medical & Surgical (MS) or Other (O) based on the intervention. An M paper considered an intervention that was exclusively medical, whereas an S paper examined an intervention that was exclusively surgical in nature. An MS paper was one where a surgical intervention was assessed in the setting of medical intervention or vice versa, for example, Epidural local anesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery [16]. A review that did not assess an intervention or incorporated a therapy that was neither surgical nor medical (for instance, radiotherapy) was classified as “Other” (O).

#### Inclusion and exclusion criteria

Included papers were systematic reviews and meta-analyses produced by the Cochrane Colorectal Cancer Group from January 2000 to the end of July 2018 that were classified as M, MS or S. Where more than one version of a review had been produced, the most up-to-date version was preferred. Reviews that were classified as O (that is, reviews that considered no intervention, or an intervention that was neither

| Table 1 The Cochrane risk of bias tool |
|---------------------------------------|
| Risk of bias domain                      | Judgement                                                      |
| Random sequence generation                | Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence. |
| Allocation concealment                   | Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment. |
| Blinding of participants and personnel   | Performance bias due to knowledge of the allocated interventions by participants and personnel during the study. |
| Blinding of outcome assessment           | Detection bias due to knowledge of the allocated interventions by outcome assessors. |
| Incomplete outcome data                  | Attrition bias due to amount, nature or handling of incomplete outcome data. |
| Selective reporting                      | Reporting bias due to selective outcome reporting. |
| Other bias                               | Bias due to problems not covered elsewhere in the table. |
considered the impact of a perioperative blood transfusion in one review, 3 regarded dietary modifications and 1 regarding its role in the prevention of complications. Five reviews concerned radiotherapy, 4 examined diagnostic techniques, and 2 focused on the role of nutritional support in surgical patients. Of those reviews (a "word cloud"), 48% (M = 50%, S = 42%, \( p < 0.001 \)) found to be more likely than S reviews in the category of blinding of participants and personnel (M = 50%, S = 42%, \( p < 0.001 \)), and 37% (MS = 21%, \( p = 0.012 \)) of the time (n = 2783). Bias judgements for each intervention type may be found in Table 3. A chi-square test was performed, and a significant relationship found between the intervention type and the likelihood of a study to show differing bias (chi-square, df 4, \( p = 0.001 \)). Comparison of individual groups using chi-square with a Bonferroni correction (\( \alpha = 0.0024 \)) revealed M to be more likely than S and MS to have studies with a low risk of bias (M = 50% > S = 42%, \( p < 0.001 \)), (MS = 50% > MS = 42%, \( p = 0.002 \)). No difference was found in the likelihood of a low-risk bias when comparing S with MS (\( p = 0.831 \)). Figure 2 displays low-risk judgements by intervention as a percentage of judgements made across Cochrane's seven categories. Assessments of the likelihood of high-risk judgements showed S reviews to be more likely than M reviews to show a high risk of bias (S = 21% \( p = 0.001 \)). MS reviews were also more likely than M to display high risk (MS = 20% > M = 16%, \( p < 0.001 \)). There was no difference in the likelihood of a high risk of bias between S and MS (\( p = 0.2294 \)). M had the greatest percentage of low-risk judgements across all risk-of-bias categories with the exception of selective reporting, where MS had the greatest percentage. When comparing M with S using chi-square with a Bonferroni correction (\( \alpha = 0.0024 \), M group reviews were found to be significantly more likely to be comprised of studies with a low risk of bias than S reviews in the category of blinding of participants and personnel (M = 35% > S = 21%, \( p < 0.001 \)). No difference was found in the likelihood to display low risk in random sequence generation (M = 50%, S = 42%, \( p = 0.049 \)), allocation concealment (M = 44%, S = 37%, \( p = 0.035 \)), blinding of outcome assessment (M = 32%, S = 22%, \( p = 0.007 \)), incomplete outcome data (M = 71%, S = 67%, \( p = 0.439 \)), selective reporting (M = 64%, S = 54%, \( p = 0.0145 \)) and other bias (M = 35%, S = 37%, \( p = 0.007 \)).

The CCCG made a combined total of 7564 judgements across the seven ROB categories. In 5680 instances, a ROB judgement was not recorded by the Cochrane Group (for example, when a review provided a judgement for some but not all of the ROB criteria). Overall, bias was judged as low 43% of the time (n = 3291), high 20% of the time (n = 1490) and unclear 37% of the time (n = 2783). Bias judgements for each intervention type may be found in Table 3. A chi-square test was performed, and a significant relationship found between the intervention type and the likelihood of a study to show differing bias (chi-square, df 4, \( p = 0.001 \)). Comparison of individual groups using chi-square with a Bonferroni correction (\( \alpha = 0.0024 \)) revealed M to be more likely than S and MS to have studies with a low risk of bias (M = 50% > S = 42%, \( p < 0.001 \)), (MS = 50% > MS = 42%, \( p = 0.002 \)). No difference was found in the likelihood of a low-risk bias when comparing S with MS (\( p = 0.831 \)). Figure 2 displays low-risk judgements by intervention as a percentage of judgements made across Cochrane's seven categories. Assessments of the likelihood of high-risk judgements showed S reviews to be more likely than M reviews to show a high risk of bias (S = 21% \( p = 0.001 \)). MS reviews were also more likely than M to display high risk (MS = 20% > M = 16%, \( p < 0.001 \)). There was no difference in the likelihood of a high risk of bias between S and MS (\( p = 0.2294 \)). M had the greatest percentage of low-risk judgements across all risk-of-bias categories with the exception of selective reporting, where MS had the greatest percentage. When comparing M with S using chi-square with a Bonferroni correction (\( \alpha = 0.0024 \), M group reviews were found to be significantly more likely to be comprised of studies with a low risk of bias than S reviews in the category of blinding of participants and personnel (M = 35% > S = 21%, \( p < 0.001 \)). No difference was found in the likelihood to display low risk in random sequence generation (M = 50%, S = 42%, \( p = 0.049 \)), allocation concealment (M = 44%, S = 37%, \( p = 0.035 \)), blinding of outcome assessment (M = 32%, S = 22%, \( p = 0.007 \)), incomplete outcome data (M = 71%, S = 67%, \( p = 0.439 \)), selective reporting (M = 64%, S = 54%, \( p = 0.0145 \)) and other bias (M =

### Table 2 Categories of conclusion type

| Conclusion type                  | Criteria                                                                 |
|----------------------------------|--------------------------------------------------------------------------|
| Informs clinical practice—firm   | A conclusion that makes a recommendation for practice (positive or negative), with minimal or no caveats. |
| Informs clinical practice—tempered | A conclusion that makes a recommendation for practice, but places significant caveats on that recommendation. |
| Does not inform clinical practice—tempered | A conclusion that is unable to make a recommendation but suggests that a recommendation might be possible soon based on an emerging trend or underlying theory. |
| Does not inform clinical practice—firm | A conclusion that is unable to make a recommendation and is completely uncertain. There may be no evidence at all, or of too poor a quality, or the evidence may be contradictory. |

surgical nor medical) were a priori excluded from this analysis to facilitate comparison of surgical and medical interventions.

### Data extraction

ROB judgements were extracted from each included Cochrane review. Conclusions and intervention type (M, S, MS or O) were scored independently by JD and RC. Each CCCG review was categorized based on its ability to inform clinical practice, using a standardized matrix (Table 2). Any disagreements were resolved by discussion to arrive at a consensus. Collation of data was performed in Microsoft Excel [17].

A subgroup of reviews concerning laparoscopic interventions was isolated and assessed (17 reviews). For visual comparison, a graphical representation of the commentary made on evidence within the conclusions of those reviews (a ‘word cloud’) was generated using Microsoft Word.

### Statistical analysis

Analysis of data was performed using SPSS v24 [18]. Inter-observer agreement was assessed using weighted kappa (\( \kappa \)) [19]. Data that were categorical were analyzed was via cross tabulation with chi-square. A two-tailed test was performed, and a significant relationship found between the intervention type and the likelihood of a study to show differing bias (chi-square, df 4, \( p = 0.001 \)). Comparison of individual groups using chi-square with a Bonferroni correction (\( \alpha = 0.0024 \)) revealed M to be more likely than S and MS to have studies with a low risk of bias (M = 50% > S = 42%, \( p < 0.001 \)), (MS = 50% > MS = 42%, \( p = 0.002 \)). No difference was found in the likelihood of a low-risk bias when comparing S with MS (\( p = 0.831 \)). Figure 2 displays low-risk judgements by intervention as a percentage of judgements made across Cochrane's seven categories. Assessments of the likelihood of high-risk judgements showed S reviews to be more likely than M reviews to show a high risk of bias (S = 21% \( p = 0.001 \)). MS reviews were also more likely than M to display high risk (MS = 20% > M = 16%, \( p < 0.001 \)). There was no difference in the likelihood of a high risk of bias between S and MS reviews (\( p = 0.2294 \)).

M had the greatest percentage of low-risk judgements across all risk-of-bias categories with the exception of selective reporting, where MS had the greatest percentage. When comparing M with S using chi-square with a Bonferroni correction (\( \alpha = 0.0024 \), M group reviews were found to be significantly more likely to be comprised of studies with a low risk of bias than S reviews in the category of blinding of participants and personnel (M = 35% > S = 21%, \( p < 0.001 \)). No difference was found in the likelihood to display low risk in random sequence generation (M = 50%, S = 42%, \( p = 0.049 \)), allocation concealment (M = 44%, S = 37%, \( p = 0.035 \)), blinding of outcome assessment (M = 32%, S = 22%, \( p = 0.007 \)), incomplete outcome data (M = 71%, S = 67%, \( p = 0.439 \)), selective reporting (M = 64%, S = 54%, \( p = 0.0145 \)) and other bias (M =
59%, M = 51%, p = 0.035). S reviews were more likely to display a high risk of bias than M reviews in the domains of random sequence generation (S = 12% > M = 2%, p < 0.001) and AC. (S = 11% > M = 2%, p < 0.001). No difference was found in the chance of a high-risk judgement in the areas of blinding of participants and personnel (S = 41%, M = 44%, p = 0.559), blinding of outcome assessment (S = 48%, M = 45%, p = 0.616), incomplete outcome data (S = 17%, M = 8%, p = 0.005), selective reporting (S = 13%, M = 7%, p = 0.013) and other bias (S = 16%, M = 15%, p = 0.659).

Comparing M with MS, M reviews were significantly more likely to be comprised of studies displaying low bias in random sequence generation (M = 50% > MS = 36%, p < 0.001), allocation concealment (M = 44% > MS = 29%, p < 0.001) and blinding of participants and personnel (M = 32% > MS = 19%, p < 0.001). MS was more likely than M to display low bias in the domain of selective reporting (MS = 88% > M = 64%, p < 0.001). Differences were not found between MS and M groups in the chance of a low-risk judgement in blinding of outcome assessment (M = 32%, MS = 29%, p = 0.534), incomplete outcome data (M = 71%, MS = 68%, p = 0.562) and other (M = 59%, MS = 52%, p = 0.173). MS reviews were more likely to have a judgement of high risk in the areas of allocation concealment (MS = 20% > M = 2%, p < 0.001) and incomplete outcome data (MS = 27% > M = 8%, p < 0.001). M was more likely to show high risk in blinding of participants and personnel (M = 44% > MS = 24%, p < 0.001). No difference in high-risk judgements were found in the areas of random sequence generation (M = 2%, MS = 1%, p = 0.764), blinding of outcome assessment (M = 45%, MS = 45%, p = 0.87), selective reporting (M = 7%, MS = 1%, p = 0.006) or other bias (M = 15%, MS = 5%, p = 0.001).

Contrasting MS with S, MS reviews were significantly more likely to come from original studies with low risk of bias judgements in the categories of selective reporting (MS = 88% > S = 54%, p < 0.001). S reviews were more likely to have a greater proportion of low-risk judgements in the domain of allocation concealment (S = 37% > MS = 29%, p < 0.001). Differences between the two interventions were non-significant in random sequence generation (MS = 36%, S = 42%, p = 0.055), blinding of participants and personnel (MS = 19%, S = 21%, p = 0.038), blinding of outcome assessment (MS = 29%, S = 22%, p = 0.524), incomplete outcome data (MS = 68%, S = 67%, p = 0.826) and other bias (MS = 52%, S = 51%, p = 0.721). S reviews were more likely to have studies with a high risk of bias in the areas of random sequence generation (S = 12% > S = 1%, p < 0.001), selective
## Table 3 Bias judgements by intervention type

| Reviews | Studies | Patients | Total bias judgements made | Low risk of bias (% of judgements made) | High risk of bias (% of judgements made) | Unclear risk of bias (% of judgements made) | Informs clinical practice—firm (% of reviews) | Informs clinical practice—tempered (% of reviews) | Does not inform clinical practice—tempered (% of reviews) | Does not inform clinical practice—firm (% of reviews) |
|---------|---------|----------|----------------------------|----------------------------------------|------------------------------------------|-----------------------------------------------|-----------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| All     | 95      | 1892     | 525,927                    | 7564                                   | 3291 (43)                                | 1490 (20)                                     | 2783 (37)                                   | 32 (34)                                          | 27 (28)                                          | 17 (18)                                          | 19 (20)                                          |
| M       | 21      | 368      | 105,200                    | 1732                                   | 863 (50)                                 | 278 (16)                                      | 591 (34)                                    | 15 (71)                                          | 2 (10)                                           | 1 (5)                                            | 3 (14)                                           |
| S       | 54      | 834      | 198,514                    | 3248                                   | 1348 (42)                                | 694 (21)                                      | 1206 (37)                                   | 11 (20)                                          | 20 (37)                                          | 10 (19)                                          | 13 (24)                                          |
| MS      | 20      | 690      | 221,190                    | 2584                                   | 1080 (42)                                | 518 (20)                                      | 986 (38)                                    | 6 (30)                                           | 5 (25)                                           | 6 (30)                                           | 3 (15)                                           |

* M medical, S surgical, MS medical and surgical
reporting (S = 13% > MS = 1%, p = 0.001), and other bias (S = 16% > MS = 5%, p < 0.001). MS was more likely to have a high risk of bias judgement in allocation concealment (MS = 20% > S = 11%, p < 0.001) and incomplete outcome data (MS = 27% > S = 17%, p < 0.001). No difference was found in blinding of outcome assessment (MS = 45%, S = 48%, p = 0.411).

Overall, the reviews firmly informed clinical practice (I-F) 34% of the time (n = 32/95) and informed practice in a tempered fashion (I-T) 28% of the time (n = 27/95). A conclusion that did not inform clinical practice but was tempered (N-T) was made 18% of the time (n = 17/95) and a conclusion that did not inform clinical fashion and was firm (N-F) was made 20% of the time (n = 19/95). There was substantial [20] inter-observer agreement on the conclusiveness of the reviews (weighted kappa = 0.622). Initial disagreements were primarily found in the differentiation between firm and tempered conclusions; comparison of "informs clinical practice" vs "does not inform clinical practice" decisions revealed a kappa of 0.753. A consensus was achieved for each review.

A chart of the conclusiveness of reviews by intervention is shown in Fig. 3. There was a significant difference between the groups when assessed using chi-square (df 6, 20.274, p = 0.002). Comparison of individual groups using chi-square with a Bonferroni correction (α = 0.004) was performed. M reviews were significantly more likely to provide conclusion that firmly informed clinical practice than S (M = 71% > S = 20%, p < 0.001) but not MS (M = 71%, MS = 30%, p = 0.0294). Reviews informed clinical practice (regardless of whether firm or tempered) in 81% of M reviews, 55% of MS reviews and 57% of S reviews, but there was no significant difference between these groups (M vs S p = 0.066, M vs MS p = 0.1, S vs MS p = 1).

The risk of bias groups and their relationship to conclusion type were examined via chi-square, with a significant difference found between the groups (chi-square, df 6, 311.465, p < 0.001). Comparison of I and N groups using chi-square with a Bonferroni correction (α = 0.0018) revealed a significant difference in the likelihood of input studies being judged as having a low risk of bias between them (I = 46% > N = 35%, p < 0.001).

Chi-square with a Bonferroni correction (α = 0.0018) was used to examine whether there was any association between the seven risk of bias categories and a review’s likelihood to inform clinical practice. Risk of bias domains that had a significant association between low-risk judgements and conclusion type were blinding of outcome assessment (I = 42% low risk > N = 17% low risk, p < 0.001), selective reporting (I = 72% > N = 42%, p < 0.001) and other bias (I = 59% > N = 36%, p > 0.001). There was not a significant association found between random sequence generation (I = 42%, N = 41%, p = 0.939), allocation concealment (I = 37%, N = 30%, p = 0.411), and other bias (I = 16% > N = 5%, p < 0.001).
0.017), blinding of participants and personnel (I = 27%, N = 17%, p = 0.004) and incomplete outcome data (I = 68%, N = 68%, p = 0.871). A chart of risk of bias by ability to inform clinical practice is shown in Fig. 4.

For interest, the conclusions of a subgroup of reviews that considered laparoscopic interventions were assessed, shown in Table 4. Seventeen reviews were found. The modal recommendation was I-T in 8 (47%), followed by N-F in 5 (29%), N-T in 2 (12%) and I-F in 2 (12%). A “word cloud” made using descriptions of evidence quality from the conclusions of each of these reviews may be seen in Fig. 5.
| Review title                                                                 | Studies | Patients | Rec. | BPP (%) low risk | BOA (%) low risk | IOD (%) low risk | SR (%) low risk | OB (%) low risk | Evidence commentary |
|------------------------------------------------------------------------------|---------|----------|------|------------------|------------------|------------------|-----------------|-----------------|---------------------|
| Closure methods for laparotomy incisions for preventing incisional hernias and other wound complications | 55      | 19,174   |     | 27               | 22               | N/A              | 69              | 93              | 84                  | Based on this moderate-quality body of evidence… |
| Closure methods of the appendix stump for complications during laparoscopic appendectomy | 8       | 850      | N-F  | 50               | 25               | 0                | 13              | 63              | 0                   | Evidence is insufficient at present… |
| Energy source instruments for laparoscopic colectomy                         | 6       | 515      | N-F  | 50               | 83               | N/A              | N/A             | 100             | 100                 | With the current evidence it is not possible… |
| Gases for establishing pneumoperitoneum during laparoscopic abdominal surgery | 7       | 340      | N-T  | 29               | 29               | 57               | 71              | 57              | 71                   | No comment |
| Hand assisted laparoscopic surgery versus conventional laparoscopy for colorectal surgery | 3       | 189      | I-T  | 67               | 0                | 0                | 67              | 67              | N/A                  | No comment |
| Heated insufflation with or without humidification for laparoscopic abdominal surgery | 22      | 1428     | I-F  | 55               | 59               | 74               | 74              | 82              | 86                   | No comment |
| Laparoscopic techniques versus open techniques for inguinal hernia repair      | 40      | 6205     | I-T  | 48               | N/A              | N/A              | N/A             | N/A             | N/A                  | No comment |
| Laparoscopic versus open resection for sigmoid diverticulitis                 | 3       | 392      | N-F  | 67               | 67               | 0                | 0               | 33              | 67                   | evidence to support or refute… is insufficient. |
| Laparoscopic versus Open surgery for small bowel Crohn’s disease             | 4       | 249      | I-T  | 0                | 50               | 0                | 0               | N/A             | 100                  | No comment |
| Laparoscopic versus open surgery for suspected appendicitis                   | 66      | 7148     | I-T  | 37               | 63               | 13               | 13              | 49              | 15                   | In spite of the mediocre quality of the available research data, we would generally recommend… data from retrospective clinical controlled trials… |
| Laparoscopic versus open surgery in small bowel obstruction                    | 0       | 0        | N-F  | N/A              | N/A              | N/A              | N/A             | N/A             | N/A                  | No comment |
| Laparoscopic versus open surgical techniques for ventral or incisional hernia repair | 10      | 880      | N-T  | 60               | 70               | 0                | 0               | 50              | 20                   | No comment |
| Laparoscopic versus open total mesorectal excision for rectal cancer         | 48      | 4067     | I-T  | 0                | N/A              | N/A              | N/A             | N/A             | N/A                  | Based on evidence mainly from non-randomized studies… |
| Long-term results of laparoscopic colorectal cancer resection                 | 12      | 3346     | I-T  | 58               | N/A              | N/A              | N/A             | N/A             | N/A                  | No comment |
| Open versus laparoscopic (assisted) ileo pouch anal anastomosis for ulcerative colitis and familial adenomatous | 11      | 673      | I-T  | 9                | N/A              | N/A              | N/A             | N/A             | N/A                  | No comment |
## Table 4
Reviews assessing laparoscopic interventions (Continued)

| Review title                                                                 | Studies | Patients | Rec. | RSG (% low risk) | AC (% low risk) | BPP (% low risk) | BOA (% low risk) | IOD (% low risk) | SR (% low risk) | OB (% low risk) | Evidence commentary |
|-----------------------------------------------------------------------------|---------|----------|------|------------------|----------------|------------------|------------------|------------------|----------------|----------------|-------------------|
| Short term benefits for laparoscopic colorectal resection                   | 24      | 3474     | I-F  | N/A              | 28             | N/A              | N/A              | N/A              | N/A            | N/A            | No comment         |
| Transabdominal pre-peritoneal (TAPP) vs totally extraperitoneal (TEP) laparoscopic techniques for inguinal hernia repair | 10      | 19,738   | N-F  | N/A              | N/A            | N/A              | N/A              | N/A              | N/A            | N/A            | There is insufficient data. |

*IF informs clinical practice—firm, I-T informs clinical practice—tempered, N-T does not inform clinical practice—tempered, N-F does not inform clinical practice—firm, RSG random sequence generation, AC allocation concealment, BPP blinding of participants and personnel, BOA blinding of outcome assessors, IOD incomplete outcome data, SR selective reporting, OB other bias, N/A no judgements made*
Discussion

This review has gathered previously made judgements on the risk of bias from a large sample of original research within the colorectal field and combined them, forming a portrait of the risk of bias within the discipline generally. We have then added to this data new judgements regarding the type of intervention studied and the clinical relevance of the meta-evidence produced. Using this approach, a view of the quality of data input and data output within colorectal science may be formed. The importance of these results relates to the defining characteristic of intervention-based medical research: the drive to improve patient outcomes. Studies that exhibit a high risk of bias lead to meta-evidence that is less able to guide clinical outcomes, together forming clinical “noise”, from which clinicians are tasked with separating the “signal”. The results of this review illustrate the benchmarks within colorectal science of “signal” and “noise”, and whether there are any associated factors that will help guide the production of useful original and combined evidence.

When the Cochrane Colorectal Cancer Group examines the risk of bias in original studies within colorectal science, it found the risk of bias to be low in the minority of cases. Notably, many of the studies assessed by the CCCG do not specifically address questions surrounding colorectal cancer per se (for instance, “Cisapride for Intestinal Constipation” [21], or “Antibiotics for uncomplicated diverticulitis” [22]), but rather provide an overview of colorectal science in general, with an inclination towards cancer research. The opinion of the Cochrane group was that the risk of bias within this sample was high or unclear in greater than half of cases. If we consider risk of bias judgements that could possibly have been made but were not to be “unclear” the proportion of low-risk judgements to high or unclear drops further. This review suggests that the minority rate of low-risk judgements across all of the CCCG should be noted by researchers and readers in the colorectal discipline. Efforts to minimize the risk of bias within this field should be considered, led by feedback from meta-evidence.

There was an association found between the intervention type and the level of low risk of bias judgements made. Studies concerning a medical intervention (M) were significantly more likely to display low risk of bias than studies concerning a surgical intervention only, or studies with a surgical and medical intervention. Studies that assessed only a surgical intervention were judged to have a low risk of bias at a rate that was not significantly different to studies that assessed a medical and surgical intervention. S reviews and MS reviews were significantly more likely than M reviews to have high-risk judgements. This may suggest that the addition of a surgical intervention may decrease the amount of bias protection inherent in the assessment of a medical intervention.

Across all interventions, the rate of low-risk judgements was 50% or less in random sequence allocation, allocation concealment and blinding of outcome assessment and participants and personnel. That the randomization, concealment and blinding for all studies within the CCCG reviews were judged as having high or unclear risk of bias in more than half of cases is cause for reflection. Previous research has demonstrated that high-risk judgements from the Cochrane risk of bias tool are associated with increased effect sizes [6, 23]. It should be noted that within this sample over 5000 risk of bias judgements that could have been made were not, which potentially dilutes the generalizability and impact of this finding.

Despite a significant difference in low risk of bias findings between M and S overall, analysis of each domain did not reveal a deeper pattern, though a significant difference was found in the blinding of participants and personnel, and a near-significant difference seen in the blinding of outcome assessors. Perhaps surprisingly, the rate of high-risk judgements made regarding blinding was not significantly different between M and S reviews. Both M and S reviews were judged to be high risk for binding in nearly half of all cases. Difficulty in adequately blinding is the nature of the surgical intervention and remains a systemic challenge to rigorous science in surgery. However, the result for the M group suggests that where practical, medical colorectal studies may benefit from paying particular attention to the risk of bias due to inadequate blinding.

M and MS groups were significantly different across a range of bias categories, with M being more likely than MS to have a low risk of bias in random sequence allocation, allocation concealment and blinding of participants and personnel, and MS being more likely to display low risk in selective reporting. As discussed, the inclusion of a surgical intervention in a study makes participant and personnel blinding...
difficult, which may explain why MS reviews were less likely than M to have a low risk of bias in this domain. Errors in reporting may explain the difference in random sequence generation, as MS was no more likely to be judged as high risk in this area, suggesting the discrepancy to be related to a large proportion of “unclear” judgements. Within allocation concealment, however, MS reviews were more likely to have less low-risk judgements and they were significantly more likely to have a high-risk judgement. The increased exposure to bias from poor allocation concealment within MS reviews is also present when contrasting MS with S reviews. This result is attributable to the impact of a single MS review, “Antimicrobial prophylaxis for colorectal surgery” [24], which had a high-risk judgement rate for allocation concealment of 45% and provided 115 of the 133 allocation concealment judgements made.

Intervention type was not associated with whether or not a review would be able to inform clinical practice. The likelihood that a review will make a conclusion that informs clinical practice is similar between surgical, medical and combined medical and surgical meta-evidence, despite the fact that studies that incorporate a surgical intervention are more likely to display high or unclear bias. In contrast, there was an association between whether a review informed clinical practice and the risk of bias. M reviews were better protected against bias than S and MS reviews but were no less likely to inform clinical practice. Where a conclusion did inform practice, the likelihood that it would be firm, rather than tempered, was significantly different M and S reviews, but not M and MS. Reviews that examined a surgical intervention exclusively were less confident about their conclusions but were willing to inform practice. It is speculative, but this may suggest that the threshold for a clinical recommendation within surgical evidence is lower than that in medical evidence. Readers of these reviews should be conscious of the GRADE quality assessments that accompany modern Cochrane reviews [25] and consider all low-quality clinical recommendations cautiously. It may be possible that a new weighting metric for meta-evidence, which combines a weighted risk of bias quality score with the cohort size of each study, may deliver meta-analysis that better accounts for varying input quality.

The subgroup analysis of laparoscopic surgery, including the “word cloud”, shows a negative view of the quality of the input studies and a lack of confidence regarding the evidence. In spite of this, a conclusion that informs clinical practice is made in nearly half of all cases, albeit tempered. The following quoted conclusion, regarding the use of laparoscopic or open techniques in the management of suspected appendicitis, one of surgery’s most common ailments, illustrates the challenge surgeons face; “In spite of the mediocre quality of the available research data, we would generally recommend to use laparoscopy...in patients with suspected appendicitis unless laparoscopy itself is contraindicated or not feasible” [26].

These findings suggest that the original input studies informing meta-evidence within surgery may be inherently biased in a way that makes evidence synthesis in this field less applicable. In the face of this, evidence-based surgery remains elusive. Novel ways of thinking about surgical research may need to be employed. This is not a new revelation [27], but perhaps there are technological advances now that afford surgical research an opportunity not present before. In particular, cloud-based “big data” collection and machine learning analysis may be useful; an approach where high-fidelity patient and practitioner data are automatically recorded for analysis across multiple centres may provide a better avenue to approximate the real-world impact of surgical interventions.

Strengths and limitations
The strengths of this “review of reviews” are the large number of Cochrane reviews included in our assessment and the dual independent extraction of data. Cochrane is viewed as the gold standard of systematic reviews. Assessment of risk of bias is standardized across Cochrane trials, which enables comparison. Our methods and definitions have been clearly outlined.

The limitations of this study include the restriction of data to Cochrane reviews only, introducing the possibility of selection bias. The CCCG did not record a judgement in over 5000 of the instances where it could have, creating potential bias. The risk of bias judgements recorded by Cochrane are subjective and open to bias. Likewise, the judgements made by the authors of this review regarding the conclusiveness of each of the Cochrane reviews are subjective.

Conclusion
The findings of this study highlight a need for more detailed reporting and a greater degree of methodological rigor within original colorectal research. Although the type of intervention was associated with a higher risk of bias, it was not associated with the likelihood of a review to inform clinical practice. Surgical studies, in particular, are prone to a higher degree of bias risk and must be interpreted with caution; a review that included a surgical intervention was likely to have a higher risk of bias but was just as likely to inform clinical practice. This may be reflective of the systemic challenges of surgical research.
## Appendix

### Table 5 Excluded reviews

| Review                                                                 | Year | Reason for exclusion  |
|------------------------------------------------------------------------|------|-----------------------|
| Blood CEA levels for detecting recurrent colorectal cancer             | 2015 | Non-interventional     |
| Chinese medical herbs for chemotherapy side effects in colorectal cancer patients | 2005 | Herbal                 |
| Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum | 2016 | Non-interventional     |
| Concomitant hyperthermia and radiation therapy for treating locally advanced rectal cancer | 2009 | Radiotherapy           |
| Dietary calcium supplementation for preventing colorectal cancer and adenomatous polyps | 2008 | Dietary               |
| Dietary fiber for the prevention of recurrent colorectal adenomas and carcinomas | 2017 | Dietary               |
| Dietary flavonoid for preventing colorectal neoplasms                  | 2012 | Dietary               |
| Flexible sigmoidoscopy versus fecal occult blood testing for colorectal cancer screening in asymptomatic individuals | 2013 | Non-interventional     |
| Follow-up strategies for patients treated for non-metastatic colorectal cancer | 2007 | Non-interventional     |
| Herbal medicines for advanced colorectal cancer                        | 2012 | Herbal                |
| Narrow band imaging versus conventional white light colonoscopy for the detection of colorectal polyps | 2012 | Non-interventional     |
| Oral traditional Chinese medication for adhesive small bowel obstruction | 2012 | Herbal                |
| Perioperative blood transfusions and recurrence of colorectal cancer    | 2012 | Blood transfusion      |
| Pre-operative radiotherapy and curative surgery for the management of localized rectal carcinoma | 2007 | Radiotherapy           |
| Preoperative chemoradiation versus radiation alone for stage II and III resectable rectal cancer | 2013 | Radiotherapy           |
| Radiofrequency ablation in the treatment of liver metastases from colorectal cancer | 2012 | Radiotherapy           |
| Screening for colorectal cancer using the fecal occult blood test, Hemoccult | 2007 | Non-interventional     |
| Selective internal radiation therapy for liver metastases from colorectal cancer | 2009 | Radiotherapy           |
| Virtual reality simulation training for health professions trainees in gastrointestinal endoscopy | 2012 | Non-interventional     |
| Workload and surgeon’s specialty for outcome after colorectal cancer surgery | 2012 | Non-interventional     |
| Traditional Chinese Medicine herbs for stopping bleeding from hemorrhoids | 2010 | Herbal                |
| Transparent cap colonoscopy versus standard colonoscopy to improve caecal intubation | 2012 | Non-interventional     |

### Table 6 Included reviews

| Review                                                                 | Year | Author                  | Intervention | Conclusion |
|------------------------------------------------------------------------|------|-------------------------|--------------|------------|
| Abdominal drainage to prevent intra-peritoneal abscess after open appendectomy for complicated appendicitis | 2015 | Nelson RL, et al.       | Surgical     | N-F        |
| Adjuvant chemotherapy for small intestine adenocarcinoma               | 2007 | Singhal N, Singhal D    | Medical      | N-F        |
| Adjuvant Therapy for completely resected Stage II Colon Cancer         | 2008 | Figueredo A, et al.     | Medical & Surgical | I-T      |
| Analgesia in patients with acute abdominal pain                        | 2011 | Manterola C, et al.     | Medical      | I-F        |
| Anti-angiogenic therapies for metastatic colorectal cancer             | 2009 | Wagner ADADW, et al.    | Medical      | I-F        |
| Antibiotic prophylaxis for hernia repair                              | 2012 | Sanchez-Manuel FJ, et al. | Medical & Surgical | N-T      |
| Antibiotic regimens for secondary peritonitis of gastrointestinal origin in adults | 2005 | Wong PF, et al.         | Medical      | I-F        |
| Antibiotics for uncomplicated diverticulitis                          | 2012 | Shabanzadeh DM, Willie-Jørgensen P | Medical | N-T       |
| Antibiotics versus placebo for prevention of postoperative infection after appendicectomy. | 2005 | BR Andersen, et al.    | Medical & Surgical | I-F       |
| Antimicrobial prophylaxis for colorectal surgery                       | 2014 | Nelson RL, et al.       | Medical & Surgical | I-F       |
| Appendectomy versus antibiotic treatment for acute appendicitis       | 2011 | Wilms IMHA, et al.      | Medical & Surgical | I-T       |
| Cesarean delivery for the prevention of anal incontinence              | 2010 | Nelson RL, et al.       | Surgical     | I-F        |
| Review                                                                 | Year | Author                                | Intervention       | Conclusion |
|-----------------------------------------------------------------------|------|---------------------------------------|--------------------|------------|
| Chewing gum for postoperative recovery of gastrointestinal function  | 2015 | Short V, et al.                        | Surgical           | N-T        |
| Cisapride for Intestinal Constipation                                 | 2009 | Aboumarzouk OM, et al.                 | Medical            | I-F        |
| Closure methods for laparotomy incisions for preventing incisional hernias and other wound complications | 2017 | Patel SV, et al.                      | Surgical           | I-T        |
| Closure methods of the appendix stump for complications during laparoscopic appendectomy | 2017 | Mannu GS, et al.                      | Surgical           | N-F        |
| Colorectal stents for the management of malignant colonic obstructions | 2011 | Sagar J                               | Surgical           | I-T        |
| Combination chemotherapy versus single-agent chemotherapy during preoperative chemoradiation for resectable rectal cancer | 2015 | Resende HM, et al.                    | Medical & Surgical | N-F        |
| Conventional versus LigaSure hemorrhoidectomy for patients with symptomatic Hemorrhoids | 2009 | Nienhuijs SW, et al.                 | Surgical           | I-T        |
| Covering ileo- or colostomy in anterior resection for rectal carcinoma | 2010 | Montedori A, et al.                  | Surgical           | I-T        |
| Curative surgery for obstruction from primary left colorectal carcinoma- Primary or staged resection? | 2004 | De Salvo GL, et al.                 | Surgical           | N-F        |
| Daikenchuto for reducing postoperative ileus in patients undergoing elective abdominal surgery | 2018 | Hoshino N, et al.                    | Medical & Surgical | N-F        |
| Duration of adjuvant chemotherapy for patients with non-metastatic colorectal cancer | 2010 | Des Guet G, et al.                   | Medical            | I-F        |
| Early enteral nutrition within 24 h of colorectal surgery versus later commencement of feeding for postoperative complications | 2006 | Andersen HK, et al.                 | Surgical           | N-T        |
| Early versus delayed appendicectomy for appendiceal phlegmon or abscess | 2017 | Cheng Y, et al.                      | Surgical           | N-F        |
| Energy source instruments for laparoscopic colectomy                  | 2011 | Tou S, et al.                         | Surgical           | N-F        |
| Epidermal growth factor receptor (EGFR) inhibitors for metastatic colorectal cancer | 2017 | Chan DLH, et al.                     | Medical            | I-F        |
| Epidural local anesthetics versus opioid-based analgesic regimens for postoperative gastrointestinal paralysis, vomiting and pain after abdominal surgery | 2016 | Guay J, et al.                      | Medical & Surgical | I-F        |
| Fast track surgery versus conventional recovery strategies for colorectal surgery | 2011 | Spanjersberg WR, et al.              | Surgical           | N-T        |
| Fluoropyrimidine-HAI (hepatic arterial infusion) versus systemic chemotherapy (SCT) for unresectable liver metastases from colorectal cancer | 2009 | Mocellin S, et al.                   | Medical            | I-F        |
| Gases for establishing pneumoperitoneum during laparoscopic abdominal surgery | 2013 | Cheng Y, et al.                      | Surgical           | N-T        |
| Hand assisted laparoscopic surgery versus conventional laparoscopy for colorectal surgery | 2010 | Spanjersberg WR, et al.              | Surgical           | I-T        |
| Heated insufflation with or without humidification for laparoscopic abdominal surgery | 2016 | Birch DW, et al.                    | Surgical           | I-F        |
| Heparins and mechanical methods for thromboprophylaxis in colorectal surgery | 2004 | Wille-Jørgensen P, et al.            | Medical & Surgical | I-F        |
| Hepatic artery adjuvant chemotherapy for patients having resection or ablation of colorectal cancer metastatic to the liver | 2006 | Nelson RL, Freels S                 | Medical & Surgical | N-T        |
| Histamine type 2 receptor antagonists as adjuvant treatment for resected colorectal cancer | 2012 | Deva S, Jameson M                    | Medical            | I-T        |
| Ileostomy or colostomy for temporary decompression of colorectal anastomosis | 2007 | Güenaga KF, et al.                  | Surgical           | N-T        |
| Incision and drainage of perianal abscess with or without treatment of anal fistula | 2010 | Malik AI, et al.                    | Surgical           | I-F        |
| Interventions for anal canal intraepithelial neoplasia                  | 2012 | Macaya A, et al.                     | Surgical           | N-F        |
| Intra-abdominal drains for the prophylaxis of anastomotic leak in elective colorectal surgery | 2004 | Rolph R, et al.                     | Surgical           | N-F        |
| Intra-peritoneal prophylactic agents for preventing adhesions and adhesive intestinal obstruction after non-gynecological abdominal surgery | 2009 | Kumar S, et al.                     | Medical & Surgical | N-T        |
| Irinotecan chemotherapy combined with fluoropyrimidines versus irinotecan alone for overall survival and progression-free survival in patients with advanced and/or metastatic colorectal cancer | 2016 | Wulaningsih W, et al.               | Medical            | N-F        |
| Lactulose versus Polyethylene Glycol for Chronic Constipation          | 2010 | Lee-Robichaud H, et al.              | Medical            | I-F        |
| Laparoscopic techniques versus open techniques for inguinal hernia repair | 2003 | Willaert W, et al.                  | Surgical           | I-T        |
| Review                                                                 | Year  | Author                          | Intervention   | Conclusion |
|------------------------------------------------------------------------|-------|---------------------------------|----------------|------------|
| Laparoscopic versus open resection for sigmoid diverticulitis          | 2017  | Abraha I, et al.                | Surgical       | N-F        |
| Laparoscopic versus open surgery for small bowel Crohn’s disease       | 2011  | Dasari BVM, et al.              | Surgical       | I-T        |
| Laparoscopic versus open surgery in small bowel obstruction            | 2010  | Cirocchi R, et al.              | Surgical       | N-F        |
| Laparoscopic versus open surgery for suspected appendicitis            | 2010  | Sauerland S, et al.             | Surgical       | I-T        |
| Laparoscopic versus open surgical techniques for ventral or incisional hernia repair | 2011 | Sauerland S, et al. | Surgical | N-T        |
| Laparoscopic versus open total mesorectal excision for rectal cancer   | 2014  | S Vennix, et al.                | Surgical       | I-T        |
| Lateral pararectal versus transrectal stoma placement for prevention of parastomal herniation | 2013 | Hardt J, et al.                | Surgical       | N-F        |
| Laxatives for the treatment of hemorrhoids.                            | 2005  | Alonso-Coello P, et al.         | Medical        | I-F        |
| Long-term results of laparoscopic colorectal cancer resection          | 2008  | E Kuhry, et al.                 | Surgical       | I-T        |
| Management for intussusception in children                             | 2017  | Gluckman S, et al.              | Medical & Surgical | N-T    |
| Mechanical bowel preparation for elective colorectal surgery           | 2011  | Güenaga KF, et al.              | Surgical       | N-T        |
| Mesalamine (5-ASA) for the prevention of recurrent diverticulitis      | 2017  | Carter F, et al.                | Medical        | N-F        |
| Mesh fixation with glue versus suture for chronic pain and recurrence in Lichtenstein inguinal hernioplasty | 2017 | Sun P, et al.                  | Surgical       | I-T        |
| Nitrous Oxide for Colonoscopy                                          | 2011  | Aboumarzouk OM, et al.          | Surgical       | I-T        |
| Nonsteroidal anti-inflammatory drugs (NSAID) and aspirin for preventing colorectal adenomas and carcinomas | 2004  | Asano TK, McLeod RS            | Medical        | I-F        |
| Nonsurgical therapy for anal fissure                                   | 2012  | Nelson RL, et al.               | Medical        | I-F        |
| Non-resection versus resection for an asymptomatic primary tumor in patients with unresectable Stage IV colorectal cancer | 2012 | Cirocchi R, et al. | Medical & Surgical | I-T    |
| Open Mesh versus non-Mesh for groin hernia repair                      | 2001  | Scott N, et al.                 | Surgical       | I-T        |
| Open Preperitoneal Techniques versus Lichtenstein Repair for elective Inguinal Hernias | 2012 | Willaert W, et al.             | Surgical       | I-F        |
| Open surgical procedures for incisional hernias                        | 2008  | D den Hartog, et al.            | Surgical       | N-F        |
| Open versus laparoscopic (assisted) ileo pouch anal anastomosis for ulcerative colitis and familial adenomatous polyposis | 2009  | Ahmed Ali U, et al.            | Surgical       | I-T        |
| Operative procedures for fissure in ano                                | 2001  | Nelson RL, et al.               | Surgical       | I-T        |
| Oral versus intravenous fluoropyrimidines for colorectal cancer        | 2017  | Chionh F, et al.                | Medical        | I-F        |
| Oral water soluble contrast for the management of adhesive small bowel obstruction | 2007 | Abbas S, et al.                 | Medical        | I-F        |
| Palliative chemotherapy for advanced or metastatic colorectal cancer   | 2000  | Best L, et al.                  | Medical        | I-F        |
| Phlebotonics for hemorrhoids                                           | 2012  | Perera N, et al.                | Medical        | I-T        |
| Postoperative adjuvant chemotherapy in rectal cancer operated for cure. | 2012  | Petersen SH, et al.             | Medical & Surgical | I-F    |
| Pre and peri-operative erythropoeitin for reducing allogeneic blood transfusions in colorectal cancer surgery. | 2009  | Devon KM, McLeod RS            | Medical & Surgical | N-F    |
| Pre-operative chemoradiation for non-metastatic locally advanced rectal cancer | 2012 | McCarthy K, et al. | Medical & Surgical | I-T    |
| Pre-operative Nutrition Support in Patients Undergoing Gastrointestinal Surgery. | 2012 | Burden S, et al. | Surgical | N-T        |
| Prolonged thromboprophylaxis with Low Molecular Weight heparin for abdominal or pelvic surgery | 2009 | Rasmussen MS, et al. | Medical & Surgical | I-F    |
| Prophylactic nasogastric decompression after abdominal surgery          | 2007  | Verma R, Nelson RL              | Surgical       | I-F        |
| Propofol for sedation during colonoscopy                               | 2008  | Singh H, et al.                 | Medical & Surgical | I-T    |
| Prosthetic mesh placement for the prevention of parastomal herniation  | 2018  | Jones HG, et al.                | Surgical       | I-T        |
| Quality of life after rectal resection for cancer, with or without permanent colostomy. | 2010 | Pachler J, Wille-Jargensen P    | Surgical       | N-T        |
| Reconstructive Techniques After Rectal Resection for Rectal Cancer      | 2008  | Brown CJ, et al.                | Surgical       | I-F        |
| Review                                                                 | Year | Author                        | Intervention | Conclusion |
|----------------------------------------------------------------------|------|-------------------------------|--------------|------------|
| Resection versus no intervention or other surgical interventions for colorectal cancer liver metastases | 2007 | Fedorowicz Z, et al.         | Medical & Surgical | N-T        |
| Rubber band ligation versus excisional haemorroidectomy for hemorrhoids | 2005 | Shammas V, et al.             | Surgical     | I-T        |
| Second-line systemic therapy for metastatic colorectal cancer         | 2017 | Mocellin S, et al.           | Medical       | I-F        |
| Short term benefits for laparoscopic colorectal resection             | 2005 | Schwenk W, et al.            | Surgical     | I-F        |
| Shouldice technique versus other open techniques for inguinal hernia repair | 2012 | Arnato B, et al.              | Surgical     | I-T        |
| Single incision versus conventional multi-incision appendicectomy for suspected appendicitis | 2011 | Rehman H, et al.             | Surgical     | N-F        |
| Single layer versus double layer suture anastomosis of the gastrointestinal tract | 2012 | Sajid MS, et al.             | Surgical     | I-T        |
| Stapled versus conventional surgery for hemorrhoids                    | 2006 | Lumb KJ, et al.              | Surgical     | I-F        |
| Stapled versus handsewn methods for colorectal anastomosis surgery     | 2001 | Matos D, et al.              | Surgical     | I-F        |
| Stapled versus handsewn methods for ileocolic anastomoses              | 2011 | Choy PYG, et al.             | Surgical     | I-F        |
| Surgical intervention for anorectal fistula                             | 2010 | Jacob TJ, et al.             | Surgical     | N-T        |
| Systemic prokinetic pharmacologic treatment for postoperative adynamic ileus following abdominal surgery in adults | 2008 | Traut U, et al.              | Medical & Surgical | N-T        |
| Transabdominal pre-peritoneal (TAPP) vs totally extraperitoneal (TEP) laparoscopic techniques for inguinal hernia repair | 2005 | Wake B, et al.               | Surgical     | N-F        |
| Transverse versus midline incisions for abdominal surgery              | 2005 | Brown SR, et al.             | Surgical     | N-T        |
| Water infusion versus air insufflation for colonoscopy                 | 2015 | Hafner S, et al.             | Surgical     | I-T        |

I-F informs clinical practice—firm, I-T informs clinical practice—tempered, N-T does not inform clinical practice—tempered, N-F does not inform clinical practice—firm

### Additional file

**Additional file 1:** Prisma 2009 checklist. (DOC 64 kb)

### Abbreviations

CCCG: Cochrane Colorectal Cancer Group; I: Informs clinical practice; I-F: Informs clinical practice—firm; I-T: Informs clinical practice—tempered; M: Medical intervention; MS: Medical and surgical intervention; N: Does not inform clinical practice; N-F: Does not inform clinical practice—firm; N-T: Does not inform clinical practice—tempered; O: Other intervention; ROB: Risk of bias; S: Surgical intervention

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### Authors’ contributions

JD and AE are responsible for the study conception and design. JD and RC are responsible for the acquisition of data. JD, RC and AE are responsible for the analysis and interpretation of data. JD, RC and AE are responsible for writing and the critical revision of the manuscript. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

Not required.

### Consent for publication

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### Author details

1 Northern Clinical School, Sydney Medical School, University of Sydney, Sydney, Australia. 2 Royal Prince Alfred Hospital, Sydney, Australia. 3 Kolling Institute of Medical Research, Sydney, Australia.

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