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Risk of postoperative infectious complications from medical therapies in inflammatory bowel disease (Review)

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[Intervention Review]

Risk of postoperative infectious complications from medical therapies in inflammatory bowel disease

Cindy CY Law[1], Conor Bell[1], Deborah Koh[1], Yueyang Bao[2], Vipul Jairath[3], Neeraj Narula[4]

[1]Department of Medicine, McMaster University, Hamilton, Canada. [2]Department of Biology, McMaster University, Hamilton, Canada. [3]Department of Medicine, University of Western Ontario, London, Canada. [4]Division of Gastroenterology, McMaster University, Hamilton, Canada

Contact: Cindy CY Law, cindy.law@medportal.ca.

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ABSTRACT

Background

Medications used to treat inflammatory bowel disease (IBD) have significantly improved patient outcomes and delayed time to surgery. However, some of these therapies are recognized to increase the general risk of infection and have an unclear impact on postoperative infection risk.

Objectives

To assess the impact of IBD medications on postoperative infection risk within 30 days of surgery.

Search methods

We searched the Cochrane IBD Groups Specialized Register (29 October 2019), MEDLINE (January 1966 to October 2019), EMBASE (January 1985 to October 2019), the Cochrane Library, Clinicaltrials.gov and the WHO International Clinical Trials Registry Platform from inception up to October 2019 and reference lists of articles.

Selection criteria

Randomized controlled trials, quasi-randomized controlled trials, non-randomized controlled trials, prospective cohort studies, retrospective cohort studies, case-control studies and cross-sectional studies comparing patients treated with an IBD medication preoperatively or within 30 days postoperatively to patients who were not taking that medication. Manuscripts and abstracts were included.

Data collection and analysis

Two authors independently screened titles and abstracts and extracted data. The primary outcome was postoperative infection within 30 days of surgery. Secondary outcomes included incisional infections and wound dehiscence, intra-abdominal infectious complications and extra-abdominal infections. Three authors assessed risk of bias using the Newcastle-Ottawa scale. We contacted authors for additional information when data were missing. For the primary and secondary outcomes, we calculated odds ratios (ORs) and corresponding 95% confidence intervals (95% CI) using the generic inverse variance method. When applicable, we analyzed adjusted and unadjusted data separately. The certainty of the evidence was evaluated using GRADE.

Main results

Sixty-eight non-randomized studies were included. Twenty-four studies had low risk of bias while the remaining had very high risk. Based on pooling of adjusted data, overall infectious complications were increased in patients who received anti-TNF agents (OR 1.60; 95% CI 1.20 to 2.13; very low certainty evidence) and corticosteroids (OR 1.70; 95% CI 1.38 to 2.09; low certainty evidence). Use of 5-ASA (OR 0.76; 95% CI 0.51 to 1.14; very low certainty evidence), immunomodulators (OR 1.29; 95% CI 0.95 to 1.76; low certainty evidence) and anti-integrin agents (OR 1.04; 95% CI 0.79 to 1.36; low certainty evidence) had no impact on overall infectious complications. No difference in the odds of wound-related complications was seen in patients using corticosteroids, 5-ASA, immunomodulators, anti-TNF or anti-integrin agents when compared to controls. Both corticosteroids and anti-TNF agents increased odds of intra-abdominal infection (OR 1.53; 95% CI 1.28 to 1.84; very low certainty evidence and OR 1.38; 95% CI 1.04 to 1.82; very low certainty evidence, respectively) whereas no impact was observed with 5-ASA, immunomodulators or anti-integrin agents. The rate of extra-abdominal infections was not affected by corticosteroids, immunomodulators, anti-TNF or anti-integrin agents.

Authors' conclusions

The evidence regarding corticosteroids, 5ASA, immunomodulators, anti-TNF mediations and anti-integrin medications was low or very low in certainty. Thus, the impact of these medications on postoperative infectious complications is uncertain and no firm conclusions can be drawn regarding their safety in the perioperative period. Decisions regarding preoperative IBD medications should be tailored to each patient's unique circumstances. Future studies should focus on controlling for potential confounding factors to generate higher quality evidence.

PLAIN LANGUAGE SUMMARY

Infection risk after surgery in patients using medications for inflammatory bowel disease

Background

More than 1.2 million individuals in North America are affected by inflammatory bowel disease (IBD). It is a condition that involves inflammation in the large and/or small intestine(s), resulting in symptoms such as diarrhea and abdominal pain. Many of the medications used to treat IBD suppress the immune system. As a result, use of these medications increases the risk of infection. This increased risk of infection is particularly concerning in patients undergoing surgery.

Review Question

This systematic review examined the combined data from 68 previously published studies to determine whether patients using IBD medications around the time of surgery had more infections compared to those not using the same medications.

Study Characteristics

This systematic review is current up to 29 October 2019. It included 68 studies in patients with IBD who underwent surgery. Most participants were 18 years or older and both men and women were included. Five IBD medication groups were examined within our study. Infections were tracked up to 30 days after surgery.

Key Results

Analyses of this large set of data revealed that infection risk around the time of surgery varied depending on which type of IBD medication the patients were on. Patients being treated with corticosteroids or anti-TNF agents seemed to have more infections after surgery, while those on 5-ASA, immunomodulators or anti-integrin agents did not seem to have more infections after surgery. These findings should be taken with caution as our review included studies which were of limited quality, and therefore we were not able to draw any firm conclusions.
These findings could help doctors choose which medications to treat IBD patients with before surgery. Decisions should be tailored to each patient's unique health needs. In addition, this study suggests the need to carefully monitor for infections after surgery in patients who are on certain types of IBD medications.

Limitations

One limitation of this systematic review was its dependence on data from a wide range of previously published studies, with various approaches and quality control standards. Most studies examined had very low certainty regarding its conclusions. This review illustrates the need for future high-quality research examining the impact of medications used to treat IBD on infection risk after surgery.

SUMMARY OF FINDINGS

Summary of findings 1. Risk of postoperative infectious complications: corticosteroids compared to control

Risk of postoperative infectious complications: corticosteroids compared to control

Patient or population: inflammatory bowel disease
Setting:
Intervention: Corticosteroids
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with Corticosteroids			
Overall infectious complications within 30 days of surgery	Study population		OR 1.40 (1.23 to 1.60)	41 observational studies	⊕⊖⊖⊖ VERY LOW [1]
	141 per 1,000	187 per 1,000 (168 to 209)			
Overall infectious complications within 30 days of surgery (Adjusted Analysis)	Study population		OR 1.70 (1.38 to 2.09)	17 observational studies	⊕⊕⊖⊖ LOW
	141 per 1,000	219 per 1,000 (185 to 256)			
Overall infectious complications within 30 days of surgery (Unadjusted Analysis)	Study population		OR 1.22 (1.03 to 1.45)	24 observational studies	⊕⊖⊖⊖ VERY LOW [2 3]
	141 per 1,000	167 per 1,000 (145 to 193)			
Incisional infections and wound dehiscence within 30 days of surgery	Study population		OR 1.41 (0.72 to 2.74)	7 observational studies	⊕⊖⊖⊖ VERY LOW [1 3 4]
	20 per 1,000	28 per 1,000 (15 to 53)			
Intra-abdominal infectious complications within 30 days of surgery	Study population		OR 1.53 (1.28 to 1.84)	28 observational studies	⊕⊖⊖⊖ VERY LOW [1]
	60 per 1,000	89 per 1,000 (75 to 105)			
Extra-abdominal infections within 30 days of surgery	Study population		OR 1.23 (0.97 to 1.55)	4 observational studies	⊕⊖⊖⊖ VERY LOW [1 3]
	51 per 1,000	62 per 1,000			

	(50 to 77)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Many studies did not adjust results for important variables such as other medications.
[2] Studies did not adjust results for important variables such as other medications.
[3] Wide confidence interval
[4] High heterogeneity

Summary of findings 2. Risk of postoperative infectious complications: 5-ASA compared to control

Risk of postoperative infectious complications: 5-ASA compared to control

Patient or population: inflammatory bowel disease
Setting:
Intervention: 5-ASA
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with 5-ASA			
Overall infectious complications within 30 days of surgery	Study population		OR 0.76 (0.51 to 1.14)	6 observational studies	⊕⊖⊖⊖ VERY LOW [2 3]
	148 per 1,000 [1]	116 per 1,000 (81 to 165)			
Overall infectious complications within 30 days of surgery (Adjusted Analysis) [1]	Study population		-	0 studies	-
	-	-			
Overall infectious complications within 30 days of surgery (Unadjusted Analysis)	Study population		OR 0.76 (0.51 to 1.14)	6 observational studies	⊕⊖⊖⊖ VERY LOW [2 3]

	148 per 1,000	116 per 1,000 (81 to 165)			
Incisional infections and wound dehiscence within 30 days of surgery	Study population		OR 0.53 (0.30 to 0.95)	1 study	-
	265 per 1,000	160 per 1,000 (98 to 255)			
Intra-abdominal infectious complications within 30 days of surgery	Study population		OR 0.77 (0.45 to 1.33)	3 observational studies	⊕⊖⊖⊖ VERY LOW [2 3]
	108 per 1,000	86 per 1,000 (52 to 139)			
Extra-abdominal infections within 30 days of surgery [1]	Study population		-	0 studies	-
	-	-			

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Analysis was not performed as no appropriate studies were identified
[2] All studies were considered very high risk of bias according to the Newcastle Ottawa Scale
[3] Wide confidence interval
[4] Unable to assess GRADE as only 1 study was identified

Summary of findings 3. Risk of postoperative infectious complications: immunomodulators compared to control

Risk of postoperative infectious complications: immunomodulators compared to control

Patient or population: inflammatory bowel disease
Setting:
Intervention: Immunosuppressive agents
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with Immunosuppressive agents			
Overall infectious complications within 30 days of surgery	Study population		OR 1.11 (0.97 to 1.26)	31 observational studies	⊕⊖⊖⊖ VERY LOW [1]
	151 per 1,000	165 per 1,000 (147 to 183)			
Overall infectious complications within 30 days of surgery (Adjusted Analysis)	Study population		OR 1.29 (0.95 to 1.76)	9 observational studies	⊕⊕⊖⊖ LOW
	151 per 1,000	187 per 1,000 (145 to 239)			
Overall infectious complications within 30 days of surgery (Unadjusted Analysis)	Study population		OR 1.07 (0.93 to 1.24)	22 observational studies	⊕⊖⊖⊖ VERY LOW [1]
	151 per 1,000	160 per 1,000 (142 to 181)			
Incisional infections and wound dehiscence within 30 days of surgery	Study population		OR 1.35 (0.96 to 1.89)	11 observational studies	⊕⊖⊖⊖ VERY LOW [1 2]
	62 per 1,000	82 per 1,000 (60 to 111)			
Intra-abdominal infectious complications within 30 days of surgery	Study population		OR 0.86 (0.66 to 1.12)	20 observational studies	⊕⊖⊖⊖ VERY LOW [1]
	82 per 1,000	71 per 1,000 (55 to 91)			
Extra-abdominal infections within 30 days of surgery	Study population		OR 1.17 (0.80 to 1.71)	4 observational studies	⊕⊖⊖⊖ VERY LOW [1 2]
	0 per 1,000	0 per 1,000 (0 to 0)			

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Many studies did not perform adjusted analyses and were considered to have a high risk of bias according to the Newcastle Ottawa Scale
[2] Wide confidence interval

Summary of findings 4. Risk of postoperative infectious complications: anti-TNF agents compared to control

Anti-TNF-α agents compared to control in inflammatory bowel disease

Patient or population: inflammatory bowel disease
Setting:
Intervention: Anti-TNF-α agents
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with Anti-TNF-α agents			
Overall infectious complications within 30 days of surgery	Study population		OR 1.27 (1.09 to 1.47)	54 observational studies	⊕⊖⊖⊖ VERY LOW [1 2 3]
	112 per 1,000	138 per 1,000 (121 to 156)			
Overall infectious complications within 30 days of surgery (Adjusted Analysis)	Study population		OR 1.60 (1.20 to 2.13)	17 observational studies	⊕⊖⊖⊖ VERY LOW [3]
	112 per 1,000	167 per 1,000 (131 to 211)			
Overall infectious complications within 30 days of surgery (Unadjusted Analysis)	Study population		OR 1.14 (0.96 to 1.36)	37 observational studies	⊕⊖⊖⊖ VERY LOW [2 3 4 5]
	112 per 1,000	125 per 1,000 (108 to 146)			
Incisional infections and wound dehiscence within 30 days of surgery	Study population		OR 1.18 (0.83 to 1.68)	24 observational studies	⊕⊖⊖⊖ VERY LOW [1 2 3]
	45 per 1,000	53 per 1,000 (38 to 74)			
Intra-abdominal infectious complications within 30 days of surgery	Study population		OR 1.38 (1.04 to 1.82)	39 observational studies	⊕⊖⊖⊖ VERY LOW [1 3 6]
	66 per 1,000	89 per 1,000			

		(69 to 115)			
Extra-abdominal infections within 30 days of surgery	Study population		OR 1.34 (0.96 to 1.87)	13 observational studies	⊕⊖⊖⊖ VERY LOW [1 3]
	13 per 1,000	18 per 1,000 (13 to 25)			

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Many studies did not perform adjusted analyses and were considered to have a high risk of bias according to the Newcastle Ottawa Scale
[2] Many confidence intervals do not overlap
[3] Wide confidence interval
[4] Many studies did not performed adjusted analyses and were considered to have a high risk of bias according to the Newcastle Ottawa Scale
[5] Studies did not perform adjusted analyses and were considered to have a high risk of bias according to the Newcastle Ottawa Scale
[6] High degree of heterogeneity

Summary of findings 5. Risk of postoperative infectious complications: anti-integrin agents compared to control

Risk of postoperative infectious complications: anti-integrin agents compared to control

Patient or population: inflammatory bowel disease
Setting:
Intervention: Anti-integrin agents
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with Anti-integrin agents			
Overall infectious complications within 30 days of surgery	Study population		OR 1.11 (0.76 to 1.62)	9 observational studies	⊕⊖⊖⊖ VERY LOW [1 2]
	136 per 1,000	149 per 1,000			

		(107 to 203)			
Overall infectious complications within 30 days of surgery (Adjusted Analysis)	Study population		OR 1.04 (0.79 to 1.36)	2 observational studies	⊕⊕⊖⊖ LOW
	136 per 1,000	141 per 1,000 (111 to 176)			
Overall infectious complications within 30 days of surgery (Unadjusted Analysis)	Study population		OR 1.06 (0.54 to 2.10)	7 observational studies	⊕⊖⊖⊖ VERY LOW [1 2]
	136 per 1,000	143 per 1,000 (78 to 248)			
Incisional infections and wound dehiscence within 30 days of surgery	Study population		OR 1.64 (0.77 to 3.50)	6 observational studies	⊕⊖⊖⊖ VERY LOW [1 2 3]
	20 per 1,000	32 per 1,000 (15 to 67)			
Intra-abdominal infectious complications within 30 days of surgery	Study population		OR 0.40 (0.14 to 1.20)	5 observational studies	⊕⊖⊖⊖ VERY LOW [1 2]
	88 per 1,000	37 per 1,000 (13 to 104)			
Extra-abdominal infections within 30 days of surgery	Study population		OR 1.15 (0.43 to 3.08)	5 observational studies	⊕⊖⊖⊖ VERY LOW [1 2 3]
	28 per 1,000	32 per 1,000 (12 to 81)			

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] Many studies did not performed adjusted analyses and were considered to have a high risk of bias according to the Newcastle Ottawa Scale
[2] Wide confidence interval
[3] High degree of heterogeneity

BACKGROUND

Description of the condition

Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a chronic and incurable disorder characterized by inflammation of the gastrointestinal tract. Inflammation in UC is generally limited to the mucosa of the colon and rectum while Crohn's disease is associated with transmural inflammation in any portion of the gastrointestinal tract. In addition, both conditions can be associated with extraintestinal manifestations in areas such as the skin, joints, and eyes. Over 1.2 million individuals have a diagnosis of IBD in North America and the worldwide prevalence of this disease is projected to increase exponentially over the next decade (Kaplan 2015).

The goal of IBD treatment is to achieve remission of clinical symptoms and resolution of gut inflammation. Several pharmacological and, if necessary, surgical options are available for the treatment of IBD. Traditionally, depending on the severity of inflammation and symptoms, 5-aminosalicylates, corticosteroids, immunomodulators and biologic medications have been used. More recently, biosimilars and small molecules have also been incorporated into the treatment algorithm for IBD.

Description of the intervention

A diverse array of medications are available for the treatment of IBD. These medications can be categorized into several broad categories: aminosalicylates, corticosteroids, immunomodulators, biologics, and small molecules.

Some of the oldest drugs used for the treatment of IBD are aminosalicylates. Aminosalicylates refers to a group of drugs that contain the active ingredient 5-aminosalicylic acid (Sales-Campos 2015). Commonly used aminosalicylates include mesalamine, balsalazide, olsalazine and sulfasalazine and these drugs can be administered orally in pill form or topically as suppositories and enemas. Aminosalicylates are mainly used for the induction and maintenance of remission in mild to moderate UC. Evidence for the use of aminosalicylates in CD is limited.

Another category of medication used to treat IBD is corticosteroids. Commonly prescribed corticosteroids include prednisone, prednisolone, methylprednisolone and budesonide. Corticosteroids can be administered orally, intravenously or rectally. Corticosteroids are effective at inducing remission of CD and UC but are less suitable as long-term therapy due to numerous adverse effects such as increased risk of infection, hyperglycemia, osteoporosis, and hypertension (Sales-Campos 2015).

Immunomodulators include thiopurines, methotrexate, cyclosporine and tacrolimus. Thiopurines include 6-mercaptopurine and its prodrug, azathioprine. Thiopurines are commonly used maintenance therapies for UC and CD but are not suitable for induction of remission given the slow onset of action of these drugs (Zenlea 2014). Patients treated with thiopurines require regular monitoring due to the potential for serious adverse effects such as hepatotoxicity and bone marrow suppression. Patients are also at increased risk of infections and malignancies such as non-melanoma skin cancers with long-term use (Zenlea 2014).

Methotrexate is a folic acid antagonist that can be used for the induction and maintenance of remission of CD. Its role in UC is limited (Herfarth 2018; Sales-Campos 2015). Uncommon but important adverse effects include opportunistic infections, hypersensitivity pneumonitis, leukopenia and hepatotoxicity (Zenlea 2014). Methotrexate should also be used cautiously in women of childbearing age, as it is teratogenic.

There is limited literature on the use of calcineurin inhibitors such as cyclosporine and tacrolimus for the treatment of IBD. Tacrolimus has been used for the treatment of fistulizing CD and refractory UC but data are limited to small studies (Triantafillidis 2011). Cyclosporine is associated with potentially serious adverse effects such as seizure and permanent nephrotoxicity, and has a narrow therapeutic range. Thus, it is reserved as a rescue therapy for steroid resistant, acute severe UC and as a bridge to other immunosuppressive medications (Zenlea 2014).

Biologics are medications derived partly or completely from living cells (Rawla 2018). The introduction of biologic medications in the late 1990s revolutionized the treatment of IBD. While biologics are effective, these drugs can cause undesired adverse effects such as infections, antibody formation and malignancies. Biologics used for the treatment of IBD include anti-tumor necrosis factor-alpha (TNF-α) antibodies, anti-integrin antibodies (natalizumab and vedolizumab), and anti-interleukin antibodies (ustekinumab). Anti-TNF-α medications approved for use in CD include infliximab, adalimumab and certolizumab pegol. Infliximab, adalimumab and golimumab are approved medications for UC.

Natalizumab and vedolizumab are anti-integrins. Natalizumab's use is limited due to its association with progressive multifocal leukoencephalopathy (PML) (Reinglas 2018; Zenlea 2014). Vedolizumab is approved for treatment of moderate to severe CD and UC. Natalizumab inhibits both α4β1 integrin and α4β7 integrin as opposed to vedolizumab, which acts only on the α4β7 integrin. As it is more selective, vedolizumab does not carry the same level of risk for PML (Zenlea 2014). However, theoretical concerns have been raised that vedolizumab could impair postoperative wound healing because it targets leukocyte migration, a necessary component of wound healing (Law 2018).

Biosimilars have also entered treatment algorithms. There are four biosimilars approved by the FDA for infliximab and four for adalimumab as of February 2020. Indications for these biosimilars are the same as the licensed indications for the originator product. Studies evaluating switching from originator drugs to biosimilars have generally not shown inferiority (Reinglas 2018).

Lastly, small molecules are an emerging class of IBD therapy. Tofacitinib is a new oral medication approved for the treatment of UC in the United States in 2018. Studies of tofacitinib in UC patients reported an elevated risk of herpes zoster, particularly in patients treated with higher dosing (i.e. 10mg BID) (Reinglas 2018).

How the intervention might work

The aim of medical therapy in IBD is to decrease inflammation and hence alleviate symptoms and allow mucosal healing (Rawla 2018). Current medications target different stages of the inflammatory cascade that is believed to underpin IBD pathogenesis. Aminosalicylates topically decrease inflammation in the colon through three main ways: inhibition of macrophage chemotaxis, increase in intestinal epithelial cell proliferation, and activation of peroxisome proliferator activated receptor γ (Sales-

Campos 2015). Corticosteroids systemically suppress inflammation by down regulating the transcription of proinflammatory genes involved in cytokine production and inhibiting the recruitment of immune cells (Sales-Campos 2015). Thiopurines inhibit lymphocyte proliferation and induce apoptosis of activated T-lymphocytes (Sales-Campos 2015; Zenlea 2014). Methotrexate is a folic acid antagonist, which increases adenosine, inhibits interleukin-1 and suppresses T cell function (Zenlea 2014). Cyclosporine and tacrolimus are calcineurin inhibitors. These drugs act by suppressing cytokine production and T-cell activation (Triantafillidis 2011; Zenlea 2014).

Biologics work by targeting various pro-inflammatory molecules. Anti-TNF drugs inhibit tumor necrosis factor-α, a key cytokine in the pathogenesis of IBD (Sales-Campos 2015). Infliximab is a chimeric human-mouse monoclonal antibody. It has increased specificity and affinity to the TNF receptor and hence blocks TNF-α from binding (Rawla 2018). Adalimumab is a fully human monoclonal antibody that inhibits TNF-α and its ability to interact with p55 and p75 cell surface receptors (Rawla 2018). Other anti-TNF medications used to treat IBD include certolizumab, a recombinant antigen-binding fragment antibody against TNF-α conjugated to polyethylene glycol, and golimumab, a fully human monoclonal antibody that binds to and inhibits soluble and transmembrane forms of anti-TNF (Rawla 2018). Ustekinumab functions by blocking the activity of interleukin 12 and interleukin 23, which play a role in the activation of natural killer cells and CD4 T lymphocytes (Rawla 2018; Reinglas 2018). Natalizumab is a humanized monoclonal antibody that is an antagonist to both α4β1 integrins and α4β7 integrins. It works by inhibiting the translocation of leukocytes across blood vessel membranes (Rawla 2018). In comparison, vedolizumab is a monoclonal antibody to only the α4β7 integrin. As a result, vedolizumab is gut-selective. It prevents T cell activation and adhesion through blocking the binding of mucosal addressin cell adhesion molecule-1 to the integrin receptor (Rawla 2018).

Biosimilars are biological medications that are highly similar to the reference product and work in the same ways. There are minor differences in clinically inactive components with no clinically meaningful differences in safety and efficacy (Reinglas 2018). Tofacitinib is an inhibitor of janus kinase enzymes, and functions by suppressing cytokine signaling in mucosal cells (Reinglas 2018).

Why it is important to do this review

The growth of medical treatment options has improved physicians' ability to manage IBD medically and in many cases, delay or avoid surgery (Frolkis 2013; Lichtenstein 2005; Rungoe 2014). However, despite these advances, a meta-analysis found that nearly half of CD patients and 16% of UC patients required surgery within 10 years of diagnosis (Frolkis 2013). Many medications commonly used to treat IBD such as corticosteroids, immunomodulators, and biologics are recognized to increase the general risk of infection (Rawla 2018). However, the impact of these medications on surgical outcomes is controversial. Concerns have been raised that preoperative treatment with these medications could theoretically impair wound healing and in turn, increase postoperative infections and other complications (Appau 2008; Lightner 2017b; Magro 2017). Of particular concern are biologic medications, as long-term information on safety, especially with regards to the perioperative setting, is scarce and limited mostly to observational studies. Given the important role TNF-α plays in stimulating dermal fibroblast proliferation and activity, investigators have examined its impact on wound healing in rat models. Lee et al demonstrated that continuous suppression of TNF-α decreased wound breaking strength in rats, raising the possibility of a similar outcome in humans treated with anti-TNF medications (Lee 2000). Additionally, anti-integrins such as vedolizumab function by blocking leukocyte migration to the gut. However, leukocytes are also critical to wound healing, and thus theoretically could impair anastomotic and stoma healing (Argollo 2018; Lightner 2017b). Current studies evaluating this topic have yielded conflicting results (Argollo 2018; Kopylov 2012; Law 2018; Narula 2013; Yang 2012; Yang 2014; Xu 2019). Therefore, a systematic review of the literature would be valuable to study the impact of perioperative IBD medications on the risk of postoperative infectious complications.

OBJECTIVES

The primary objective of this review was to assess the impact of perioperative IBD medications on the risk of postoperative infections within 30 days of surgery.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials, quasi-randomized controlled trials, non-randomized controlled trials, prospective cohort studies, retrospective cohort studies, case-control studies and cross-sectional studies were considered for inclusion. Meta-analyses, systematic reviews, case series, and case reports were excluded. Studies lacking a comparison or control group were also excluded. Studies reporting complications that occurred greater than 30 days after surgery were excluded as infections outside this time period may be less likely to be related to the surgery. Manuscripts as well as abstracts were considered for inclusion.

Types of participants

The majority of patients in each study were required to be adults (at least 18 years in age). Patients needed to have a diagnosis of Crohn's disease, ulcerative colitis, or indeterminate colitis and have undergone surgery, including both abdominal and non-abdominal surgeries.

Types of interventions

We included studies comparing patients treated with an IBD medication (preoperatively or within 30 days postoperatively, as treatment during this time period could potentially influence rates of early infectious complications) to patients who were not taking that medication. What constituted preoperative treatment was not fixed and was based on the definitions used by the authors of the primary studies. Comparison groups could include another active medication, placebo, or a no treatment control. Studies that compared post-operative outcomes between two biologics (e.g. vedolizumab versus infliximab) were excluded as these studies generally all suffered from confounding by indication.
We examined the following classes of medications:
1. Aminosalicylates (5-ASA): balsalazide, mesalamine, olsalazine, sulfasalazine;
2. Corticosteroids: budesonide, methylprednisolone, prednisolone, prednisone;

3. Immunomodulators: azathioprine, 6-mercaptopurine, methotrexate, cyclosporine, tacrolimus;
4. Anti-TNF medications: adalimumab, certolizumab, golimumab, infliximab;
5. Anti-interleukin medications: ustekinumab;
6. Anti-integrin medications: vedolizumab, natalizumab; and
7. Small Molecules: tofacitinib.

Types of outcome measures

We investigated the following postoperative infectious complications.

Primary outcomes

The primary outcome was postoperative infection within 30 days of surgery.

Secondary outcomes

The secondary outcomes were:

1. Incisional infections and wound dehiscence;

2. Intra-abdominal infectious complications including anastomotic leak, intra-abdominal abscess and enterocutaneous fistula; and

3. Extra-abdominal infections including pneumonia, urinary tract infection, bacteremia, catheter associated infections and other infections.

Search methods for identification of studies

Electronic searches

We searched the following databases from inception up to October 29, 2019: MEDLINE, Embase, the Cochrane Library, the Cochrane IBD Group Specialized Register, Clinicaltrials.gov, and the WHO International Clinical Trials Registry Platform. The search strategies for each database are reported in Appendix 1.

Searching other resources

To identify additional studies, we screened the bibliographies of applicable systematic reviews.

Data collection and analysis

Selection of studies

Two investigators (CL and YB) independently screened the titles and abstracts identified by the literature search. Potentially relevant articles were reviewed in full to determine eligibility for inclusion. When necessary, we attempted to contact study authors for clarification. Any disagreements were resolved through consensus and evaluation by a third investigator (NN).

Data extraction and management

Three investigators (CL, CB and NN) performed data extraction independently. In cases where data were missing, we attempted to contact authors for additional information. The following information was extracted from the studies:
1. Study Characteristics: Author, year of publication, time period of study, country of origin, format (paper/abstract), study design, inclusion and exclusion criteria;
2. Patient and IBD Disease Characteristics: Mean age, gender, number of patients by IBD subtype, type of surgery performed, perioperative IBD medication(s), last dose of medication prior to surgery, emergency versus elective surgery; and
3. Outcome Assessment: Length of follow-up period, rate of overall postoperative infectious complications, rate of incisional infections/wound dehiscence, rate of intra-abdominal infectious complications, rate of extra-abdominal infections.

Assessment of risk of bias in included studies

Four investigators (CL, CB, DK and YB) independently assessed the methodological quality of included studies using the Newcastle-Ottawa Scale (Wells 2019). Studies were evaluated based on the selection of the study groups (four questions), the comparability of the groups (two questions), and the ascertainment of either the exposure or outcome of interest (three questions) for case-control or cohort studies respectively. A maximum of 1 point was awarded for each question. Studies with 3 points in the selection domain, and 1 point in the comparability domain, and 2 points in the outcome domain were considered to have a low risk of bias. Studies with 2 points in the selection domain, and 1 point in the comparability domain, and 2 points in the outcome domain were deemed to have a high risk of bias. Finally, studies with 1 point in the selection domain, or 0 points in the comparability domain, or 1 point in the outcome domain were considered to have a very high risk of bias.
We planned to have four authors (CL, CB, DK and YB) independently assess the risk of bias of RCTs using the Cochrane risk of bias tool. Each study was to be assessed based on sequence generation, allocation sequence concealment, incomplete outcome data, selective outcome reporting and other potential sources of bias. However, no RCTs were identified for inclusion.

Measures of treatment effect

Data was analyzed using Review Manager 5.3. Odds ratio (OR) with corresponding 95% confidence intervals (95% CI) were calculated. Since adjusted odds ratios reported by studies were used where available, the generic inverse variance method was used for obtaining overall pooled OR estimates.
For continuous data, we planned to calculate the mean difference (MD) or standardized mean difference (SMD) with corresponding 95% CI as appropriate. If only the MD was reported by a study, the generic inverse variance method was used. However, no continuous data were reported by included studies.

Unit of analysis issues

Whenever possible, we analyzed count data as dichotomous data by extracting the proportion of participants who experienced at least one infection. We attempted to contact authors for clarification whenever necessary.
For studies with multiple treatment groups, depending on the situation, one of three strategies was used. If only one of the treatment arms was relevant to the study, the other treatment arms were ignored and the remaining treatment arm was compared to the control group. If two or more treatment arms were relevant and similar (e.g. two types of immunomodulators), these treatment arms were combined into one group. If it was not appropriate to combine the treatment arms (e.g. immunomodulator and anti-TNF medication), data were analyzed separately. We did not divide the control group between the treatment groups, as the data for each treatment group were used in entirely separate analyses.
We planned to use paired analysis with the generic inverse variance method for cross-over studies, however, these were not

encountered. We also did not encounter any cluster-randomized trials.

Dealing with missing data

For missing dichotomous outcomes, an intention-to-treat analysis was used. Patients who were lost to follow-up or have missing outcome data were considered to have experienced an infection. We attempted to contact authors to provide missing data.
We planned to estimate the value of missing continuous outcomes from other values provided in the applicable study. If this was not possible, we planned to impute the value from the mean of the standard deviations of the other studies in the meta analysis. If possible, we also planned to perform a sensitivity analysis of per protocol data. As no studies reported continuous outcomes, these methods were not required in our analysis.

Assessment of heterogeneity

We assessed heterogeneity by visual inspection of forest plots and by calculating the Chi^2 and I^2 statistics. For the Chi^2 test, we considered a P value less than 0.10 to be statistically significant. I^2 values of greater than 50% were considered to indicate substantial heterogeneity. A priori subgroup analyses were performed to explore potential sources of heterogeneity.

Assessment of reporting biases

Publication bias was assessed using funnel plots, provided at least 10 studies were included.

Data synthesis

Data were pooled by like interventions. We planned to conduct separate analyses for corticosteroids, immunosuppressive agents, anti-TNF agents, biosimilars of anti-TNF agents, anti-integrin agents, anti-interleukin agents, and small molecules, provided at least 2 studies were available for each type of medication. Additionally, data from individual studies were pooled for meta-analysis only if the interventions, patient groups and outcomes were sufficiently similar (determined by consensus). We planned to analyze randomized and observational data separately but this was not necessary as no randomized studies were identified. For evaluation of the primary outcome, we analyzed adjusted and unadjusted data separately.
For dichotomous outcomes, we calculated a pooled OR and 95% CI. For continuous outcomes, we planned to calculate the pooled MD or SMD with corresponding 95% CI. A random-effects model was used as we anticipated significant heterogeneity in the studies.

Subgroup analysis and investigation of heterogeneity

We performed the following subgroup analyses:
1. Crohn's disease patients versus ulcerative colitis patients;
2. Studies conducted prior to 1998 (year of introduction of the first biologic for IBD) versus studies conducted after 1998;
3. Last dose of biologic within eight weeks prior to surgery versus last dose of biologic greater than eight weeks prior to surgery.

Sensitivity analysis

Sensitivity analysis excluding studies with very high risk of bias according to the Newcastle-Ottawa Scale, abstracts, and non-randomized studies was performed. For this analysis, unadjusted and adjusted odds ratios were c ombined.

We performed two ad-hoc sensitivity analyses. The first analysis excluded studies with patients who underwent surgery to alleviate a fistula/abscess or who were found to have an intra-abdominal abscess intraoperatively. The second analysis excluded studies with potential unit of analysis issues (i.e. studies for which we estimated the overall rate of infection by summation of different types of infections).

Summary of findings and assessment of the certainty of the evidence

We used the GRADE approach to assess the certainty of the evidence in the review (Guyatt 2008). Evidence for the primary (overall postoperative infectious complications) and secondary outcomes (incisional infections and wound dehiscence, intra-abdominal infectious complications and extra-abdominal infections) were evaluated and reported in the 'Summary of findings' tables. Data from RCTs begin as high-certainty and observational randomized studies begin as low-certainty evidence. The certainty of the evidence can be downgraded due to risk of bias, inconsistency, indirectness, imprecision or publication bias. The certainty of the evidence can be upgraded due to a large magnitude of effect, dose response gradient, and a result that opposes any plausible residual confounding (Guyatt 2008). Ultimately, the certainty of the evidence for each outcome was determined to be high (further research is unlikely to change our confidence in the estimate of effect), moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low (further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (any estimate of effect is very uncertain). We resolved disagreements by discussion and consensus.

RESULTS

Description of studies

We included 68 studies in total in this review; forty one evaluated perioperative corticosteroid therapy, six evaluated perioperative 5ASA therapy, thirty one evaluated perioperative immunomodulator therapy, fifty four evaluated perioperative anti-TNF therapy, nine evaluated perioperative anti-integrin therapy and one evaluated perioperative anti-interleukin therapy.

Results of the search

We conducted a literature search on August 30, 2018, which identified 12,248 citations. Two additional studies were identified through other sources. Duplicate studies were counted as secondary publications of those studies that were included. 9709 studies remained for screening. 9594 studies were excluded after review of the titles and abstracts. We retrieved the full text of the remaining 115 studies. Of these, 52 studies were excluded and 63 studies were included in the review (Figure 1).

An updated literature search was performed on October 29, 2019. The time period of the updated search was August 1, 2018 to October 29, 2019 and it identified 1726 citations. Duplicate studies were counted as secondary publications of studies that were included. 1690 studies were excluded after review of titles and abstracts. 21 studies remained for full text review and of these, 5 studies were included (Figure 2).

Figure 1. Flow diagram of original search (inception to August 30, 2018).

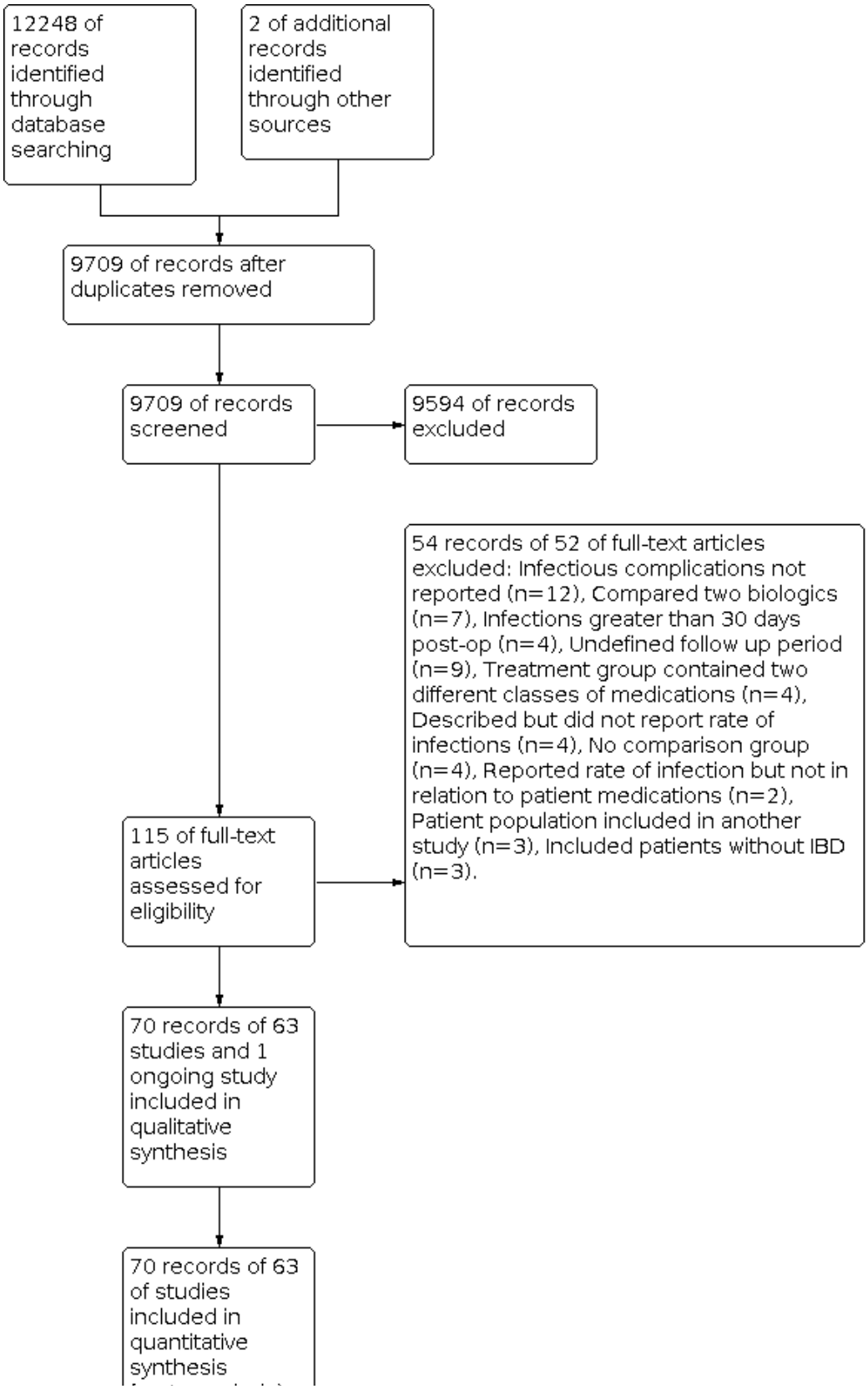


Figure 1. (Continued)

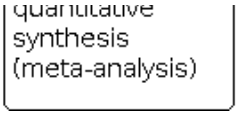
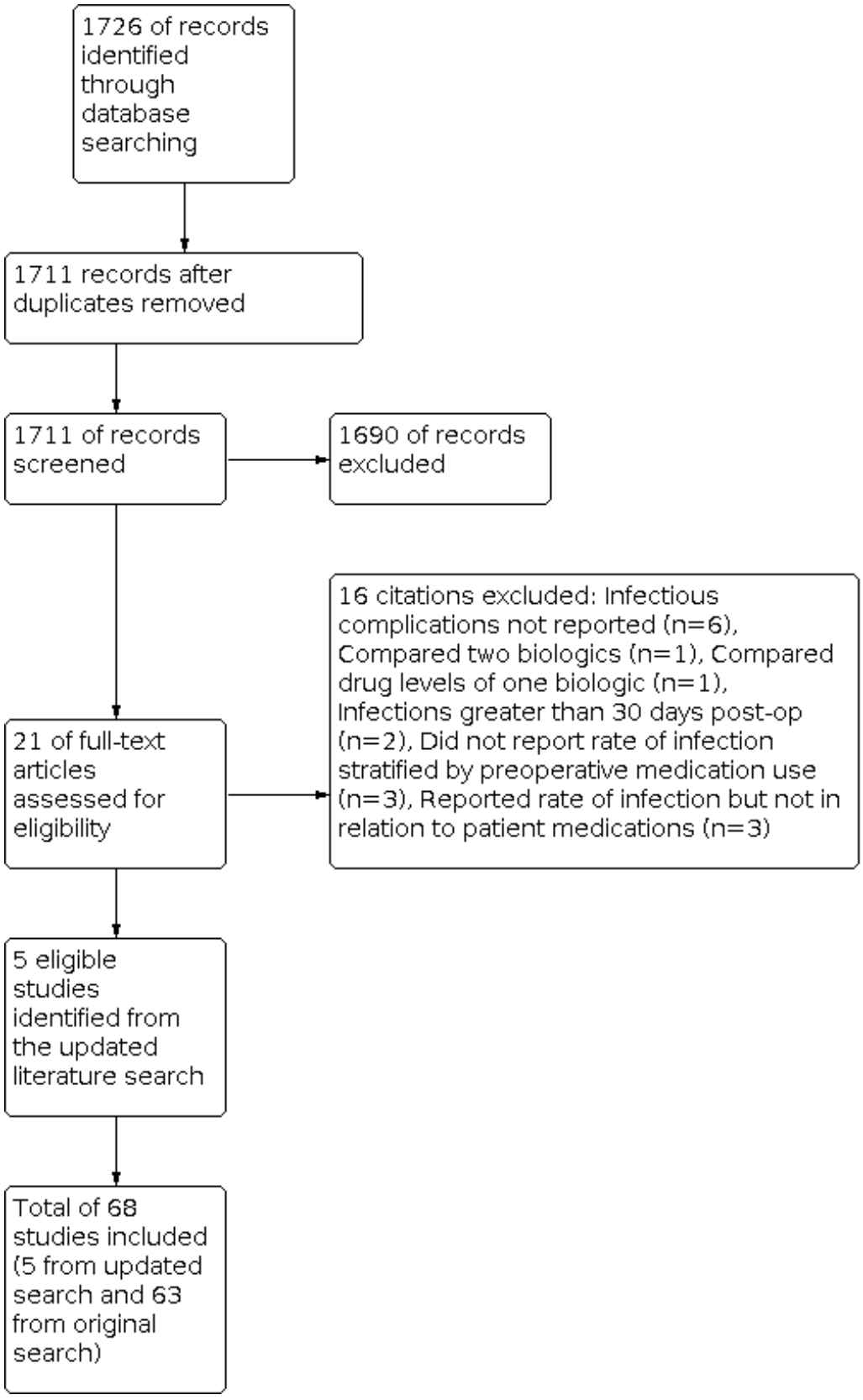


Figure 2. Flow diagram of updated search from August 1, 2018 to October 29, 2019.



Included studies

A total of 68 studies were included in the review. All were observational studies. There were 5 prospective studies (Araki 2014; Brouquet 2018; Fumery 2017; Myrelid 2009; Cohen 2019) and 63 retrospective studies. From these, 60 were manuscripts and 8 were abstracts. All the prospective studies except for one (Cohen 2019) are currently published as manuscripts.

The included studies were heterogenous in their patient selection criteria. The specific criteria for each study are outlined in the Characteristics of included studies section. Some studies focused on only CD or UC patients, while others included a combination of the two. A small percentage of studies also included patients with indeterminate colitis.
Both elective and emergent surgeries were included in our study. All selected studies examined patients who underwent abdominal surgery.

With regards to the type of preoperative medication studied, 41 studies examined corticosteroids (Aberra 2003; Alves 2007; Appau 2008; Bregnbak 2012; Colombel 2004; De Buck Van Overstraeten 2017; El-Hussuna 2012; Ferrante 2009; Ferrante 2017; Fumery 2017; Gainsbury 2011; Guo 2017; Jouvin 2018; Krane 2013; Kunitake 2008; Liang 2017; Lightner 2018 B; McKenna 2018; Mor 2008; Morar 2015; Myrelid 2009; Myrelid 2014; Nasir 2010; Nguyen 2014; Regadas 2011; Rizzo 2011; Schils 2017; Selvasekar 2007; Serradori 2013;Shaib 2017; Tzivanakis 2012; Uchino 2015; Uchino 2019; Wilson 2014; Yamada 2017; Yamamoto 2000; Yamamoto 2016; Yu 2019; Zittan 2016; Ziv 1996; Zuo 2014), 6 examined 5ASAs (Ferrante 2017; Guo 2017; Liang 2017; Morar 2015; Myrelid 2009; Uchino 2013a), 31 examined immunomodulators (Aberra 2003; Afzali 2016; Araki 2014; Appau 2008; Colombel 2004; El-Hussuna 2012; Ferrante 2009; Ferrante 2017; Gainsbury 2011; Guo 2017; Jouvin 2018; Krane 2013; Liang 2017; Lightner 2018b; Mahadevan 2002; McKenna 2018; Mor 2008; Morar 2015; Myrelid 2009; Myrelid 2014; Nasir 2010; Regadas 2011; Rizzo 2011; Selvasekar 2007; Uchino 2010; Uchino 2013a; Uchino 2013b; Uchino 2015; Uchino 2019; Yamamoto 2016, Yu 2019), 54 examined anti-TNF agents (Appau 2008; Ayoub 2018; Bregnbak 2012; Brouquet 2018; Cohen 2019; Canedo 2011; Colombel 2004; Coquet-Reinier 2010; De Buck Van Overstraeten 2017; El-Hussuna 2012; Eshuis 2013; Ferrante 2009; Ferrante 2017; Fumery 2017; Gainsbury 2011; Gu 2013; Guasch 2016; Gudsoorkar 2018; Guo 2017; Jouvin 2018; Kim 2018; Kotze 2017; Krane 2013; Kunitake 2008; Liang 2017; Lightner 2018 A; Lightner 2018 B; Marchal 2004; McKenna 2018; Mor 2008; Morar 2015; Myrelid 2014; Nasir 2010; Norgard 2012; Norgard 2013; Novello 2020; Regadas 2011; Rizzo 2011; Schils 2017; Schluender 2007; Selvasekar 2007; Serradori 2013; Shwaartz 2016; Syed 2013; Uchino 2013a; Uchino 2013b; Uchino 2015; Uchino 2019; Ward 2018; Waterman 2013; Yamada 2017; Yamamoto 2016; Yu 2019; Zittan 2016), 9 examined anti-integrin agents (Ayoub 2018; Ferrante 2017; Gudsoorkar 2018; Kim 2018; Liang 2017; Lightner 2018 A; Novello 2020; Schils 2017; Yamada 2017) and only 1 study examined ustekinumab (Liang 2017). No studies regarding small molecules or biosimilars were found.

Among the studies examining preoperative corticosteroids, a variety of doses were used. Among the studies examining anti-TNF medications, the timing of the last dose prior to surgery also varied from study to study. For instance, 17 studies considered a patient to have been treated preoperatively with an anti-TNF agent only if they received a dose within 8 weeks of surgery. Thirty four studies used a longer cut off time and the remaining 3 did not specify the time of last dose of anti-TNF medication.

All postoperative infectious outcomes occurred within 30 days of surgery. A diverse array of infections was reported by each study. Commonly reported outcomes included overall infectious complications, wound infections, anastomotic leaks, intra-abdominal abscesses, pneumonia and urinary tract infections.

While some studies grouped infections into categories such as intra-abdominal infections and extra-abdominal infections, others studies reported each type of infection individually. To allow for comparability between trials, we categorized infections as incisional, intra-abdominal and extra-abdominal. Some studies also provided an overall rate of infection. When this was not available, we estimated the overall rate of infections by combining the rates of individual infections reported in a study. As some patients could have had more than one postoperative infection, this could potentially create a unit of analysis error. The corresponding author of Schils 2017 kindly provided additional data, which allowed us to identify patients that experienced more than one postoperative infection.

Excluded studies

Following full-text review, 68 studies were excluded for the following reasons:

Overall postoperative complications but not specifically infectious complications were reported in 18 studies (Achkasov 2015; Bafford 2013; Braun 2018, Chaparro 2018; Coscia 2012; Fronda 1999; Gamaleldin 2018; Gonzalez 2013; Grant 2019, Justiniano 2019; Kamel 2019; Li 2016; Melo-Pinto 2018; Monsinjon 2017; Quade 2013; Scarpa 2015; Watson 2018; Weber 2017). We attempted to contact the authors for additional information but were unsuccessful.

Seven studies did not provide numerical data regarding incidence of infections stratified by patients' preoperative medication use (Adegbola 2018; Benichou 2018; Desai 2012; Kimura 2019; Lau 2013; Oh 2014; Yamamoto 2016a). We attempted to contact authors for additional information but were unsuccessful.

Eight studies were excluded because they compared postoperative outcomes between two biologic medications (Aelvoet 2016; Lightner 2017a; Lightner 2018a; Lightner 2018b; Novello 2019; Park 2018; Poylin 2018; Shim 2018). One study was excluded because it compared preoperative drug levels in patient treated with ustekinumab and their subsequent rates of postoperative infection (Parrish 2019). Six studies were excluded for including postoperative infections that occurred more than 30 days after surgery (Andrew 2017; Balachandran 2015; Bewtra 2013; Gregory 2019; Kulaylat 2017; Rizvi 2019). Nine studies did not define their follow up period (Bruewer 2003;De Silva 2011; Eisner 2014; Hyde 2001; Kasparek 2012; Krupa 2012; Nagao 2016; Sahami 2016; Shimada 2016). Four studies were excluded because the treatment group included multiple medications (e.g. anti-TNF medications and tacrolimus) (Abou-Khalil 2016; Stewart 2009; Valizadeh 2017; Yamamoto 2018). Four studies were excluded because they lacked a comparison group (Chiplunker 2015; Domenech 2016; Labidi 2018; Stringfield 2016). Five studies did not explore the relation between infectious complications and preoperative medications (Abelson 2018; Fu 2014; Heimann 1985; Kline 2020; Lim 2018). Three studies were excluded due to overlap of patients with another, larger study

that is included in this review (Kotze 2017a; Kotze 2011; Lightner 2017). Finally, 3 studies were excluded because they included non-IBD patients (George 2017; Kotze 2018; Strassle 2017).

Risk of bias in included studies

Risk of bias was assessed using the Newcastle-Ottawa Scale and the results are summarized in Figure 3.

Figure 3. Risk of bias summary for cohort studies (Newcastle Ottawa Scale): review authors' judgements about each risk of bias item for each included study.

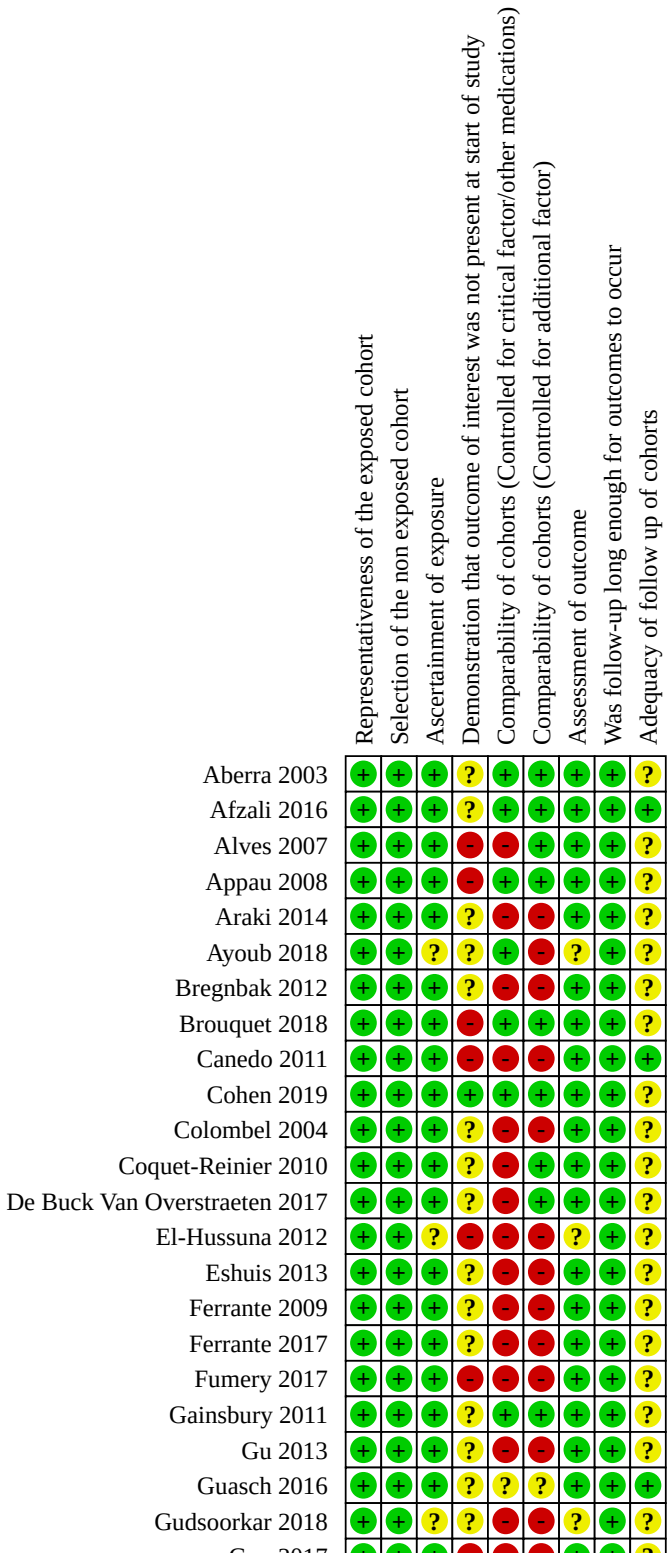
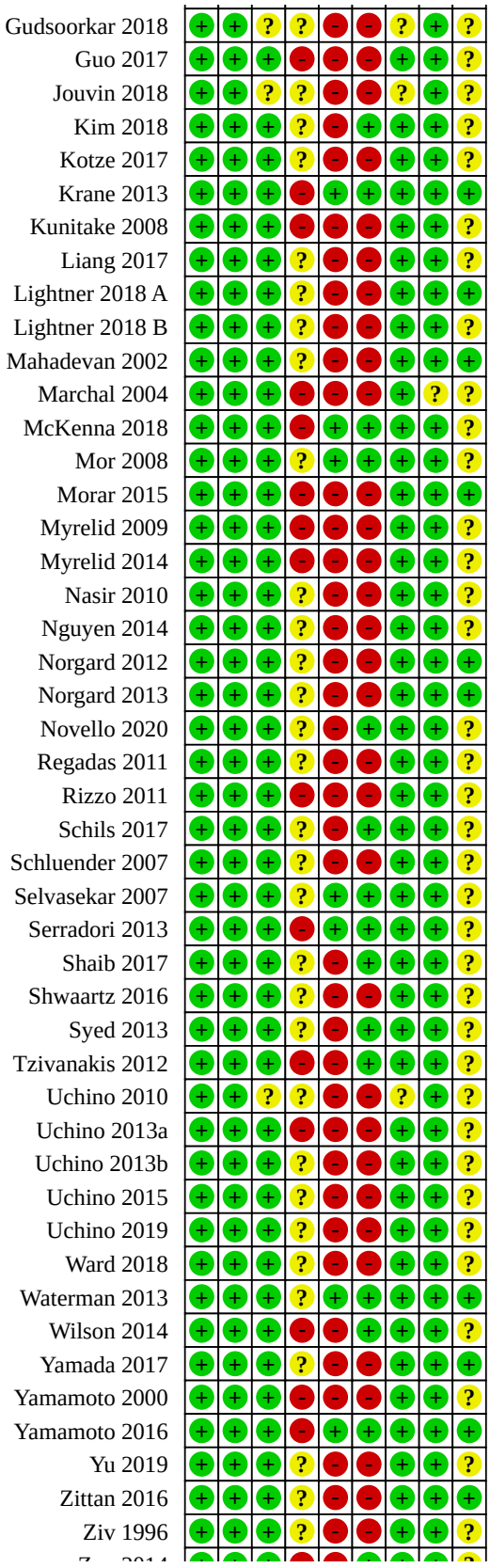


Figure 3. (Continued)



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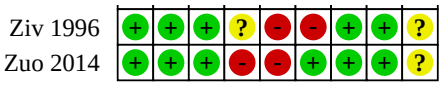


Selection

All 63 studies received 1 point for representativeness of the exposed cohort. All the studies included unselected adult patients with CD or UC who underwent surgery, which is representative of the average IBD patient requiring surgery.

All studies received 1 point for selection of the non-exposed cohort. The non-exposed cohorts were all drawn from either the same hospitals or databases as the exposed cohort.

Five studies (Ayoub 2018; El-Hussuna 2012; Gudsoorkar 2018; Jouvin 2018; Uchino 2010) received 0 points for ascertainment of exposure due to not explicitly stating the source of their data.

Another point criterion was for demonstrating that infection was not present at the start of the study, however, no study qualified. In fact, in 25 studies, surgery was performed to alleviate a fistula/abscess, or an intra-abdominal abscess was discovered intraoperatively (Alves 2007; Appau 2008; Brouquet 2018; Canedo 2011; Cohen 2019; El-Hussuna 2012; Fumery 2017; Guo 2017; Krane 2013; Kunitake 2008; Lightner 2018 B; Marchal 2004; McKenna 2018; Morar 2015; Myrelid 2009; Myrelid 2014; Rizzo 2011; Serradori 2013; Tzivanakis 2012; Uchino 2013a; Wilson 2014; Yamamoto 2000; Yamamoto 2016; Yu 2019; Zuo 2014).

Comparability

One point was awarded if the study controlled for use of a concomitant medication(s) as we considered it to be the most significant potential confounding factor. Another point was awarded if the study controlled for any other potential confounding factor(s) such as age or length of surgery.

The majority of studies reported the event rate of infectious complications and therefore did not control for other variables. Adjusted analyses were performed in 26 studies (Aberra 2003; Afzali 2016; Alves 2007; Appau 2008; Ayoub 2018; Brouquet 2018; Cohen 2019; Coquet-Reinier 2010; De Buck Van Overstraeten 2017; Gainsbury 2011; Kim 2018; Krane 2013; Marchal 2004; McKenna 2018; Mor 2008; Novello 2020; Selvasekar 2007; Serradori 2013; Shaib 2017; Syed 2013; Tzivanakis 2012; Uchino 2019; Waterman 2013; Wilson 2014; Yamamoto 2016; Zuo 2014). Of these, 9 studies controlled for concomitant immunomodulator use (Aberra 2003, Appau 2008, Cohen 2019, Gainsbury 2011, Krane 2013, McKenna 2018, Mor 2008, Yamamoto 2016, Selvasekar 2007), 15 studies controlled for concomitant corticosteroid use (Aberra 2003,Afzali 2016,Appau 2008, Ayoub 2018, Brouquet 2018, Cohen 2019, Gainsbury 2011, Krane 2013, McKenna 2018, Mor 2008, Waterman 2013, Yamamoto 2016, Zuo 2014, Selvasekar 2007, Serradori 2013) and 5 studies controlled for concomitant anti-TNF use (Appau 2008, McKenna 2018, Yamamoto 2016, Selvasekar 2007, Serradori 2013).

In addition, studies controlled for a variety of other potential confounding factors including age (Aberra 2003, Appau 2008, Cohen 2019, Coquet-Reinier 2010, Kim 2018, Marchal 2004, Novello 2020, Selvasekar 2007, Serradori 2013, Tzivanakis 2012, Waterman 2013, Yamamoto 2016, Uchino 2019), gender (Appau 2008, Cohen 2019, Coquet-Reinier 2010, Kim 2018, Marchal 2004, Novello 2020, Shaib 2017, Tzivanakis 2012, Yamamoto 2016), BMI (Afzali 2016, Gainsbury 2011, Syed 2013, Wilson 2014, Zuo 2014), smoking (Afzali 2016, Shaib 2017, Wilson 2014, Yamamoto 2016, Zuo 2014), combordities (Appau 2008, Cohen 2019, Krane 2013, Wilson 2014) and duration of surgery (Aberra 2003, Brouquet 2018, Shaib 2017, Wilson 2014, Uchino 2019). More information about the factors each study controlled for can be found in the Characteristics of included studies tables.

Outcome

Five studies (Ayoub 2018; El-Hussuna 2012; Gudsoorkar 2018; Jouvin 2018; Uchino 2010) received 0 points for assessment of outcomes as they did not specify their data collection methodology.

One point for length of follow up was awarded to all studies except Marchal 2004 as patients in this study were followed for only 10 days post-surgery.

Only thirteen studies were awarded a point for adequacy of follow up as most studies did not comment on this area. Three studies reported a negligible percentage of patients lost to follow up (Afzali 2016; Mahadevan 2002; Morar 2015), while the presence of complete patient data was mandatory in 10 studies (Canedo 2011; Guasch 2016; Krane 2013; Lightner 2018 A; Norgard 2012; Norgard 2013; Waterman 2013; Yamada 2017; Yamamoto 2016; Zittan 2016).

Effects of interventions

See: **Summary of findings 1** Risk of postoperative infectious complications: corticosteroids compared to control; **Summary of findings 2** Risk of postoperative infectious complications: 5-ASA compared to control; **Summary of findings 3** Risk of postoperative infectious complications: immunomodulators compared to control; **Summary of findings 4** Risk of postoperative infectious complications: anti-TNF agents compared to control; **Summary of findings 5** Risk of postoperative infectious complications: anti-integrin agents compared to control

Analysis 1 Corticosteroids vs Control

Pooling of data from 41 studies comparing preoperative corticosteroids to a no treatment control demonstrated an increase in postoperative infectious complications (OR 1.40; 95% CI 1.23 to 1.60, very low certainty evidence; Analysis 1.1). Low heterogeneity was observed in the overall analysis (I^2= 40%). Based on 17 of the studies, the adjusted pooled OR was 1.70 (95% CI 1.38 to 2.09; I2 35%; low certainty evidence; Analysis 1.1.1). Unadjusted OR, based

on 24 studies was 1.22 (95% CI 1.03 to 1.45; I2 34%; very low certainty evidence; Analysis 1.1.2)

Eleven studies included only patients with ulcerative colitis (OR 1.49; 95% CI 1.10 to 2.02, very low certainty evidence) and 23 studies included only patients with Crohn's disease (OR 1.32; 95% CI 1.11 to 1.57, very low certainty evidence) (Analysis 1.2). A statistically significant subgroup difference was not detected (p=0.50).

Increased postoperative infectious complications were seen in studies performed prior to 1998 (OR 1.79; 95% CI 1.20 to 2.66, very low certainty evidence) as well as after 1998 (OR 1.35; 95% CI 1.17 to 1.56, very low certainty evidence) (Analysis 1.3). A statistically significant subgroup difference was not detected (p=0.20).

In terms of secondary outcomes, there was no difference in incidence of incisional infection and wound dehiscence with preoperative corticosteroid use in the seven trials which reported this (OR 1.41; 95% CI 0.72 to 2.74, very low certainty evidence) (Analysis 1.4). The incidence of intra-abdominal infection (28 studies; OR 1.53; 95% CI 1.28 to 1.84, very low certainty evidence) (Analysis 1.5) was significantly higher in the corticosteroid group, while there was no difference observed in extra-abdominal infections (4 studies; OR 1.23 (95% CI 0.97 to 1.55, very low certainty evidence) (Analysis 1.6).

Primary outcome findings were not affected by excluding very high risk of bias studies (1 5 studies; OR 1.4 3 (95% CI 1.1 3 to 1.8 1) (Analysis 1.7) and studies published as a full manuscript (36 studies; OR 1.48 (95% CI 1.28 to 1.72) (Analysis 1.8). A sensitivity analysis was also performed excluding studies that did not adjust for patients who underwent surgery to repair an intrabdominal abscess/fistula or were found to have an abscess intraoperatively and our findings remained significant (21 studies; OR 1.37 (95% CI 1.14 to 1.65) (Analysis 1.9).

Analysis 2 5ASA vs Control

Pooling of data from the 6 studies (all unadjusted outcomes) comparing preoperative 5ASA versus no 5ASA demonstrated no increase in overall postoperative infectious complications (OR 0.76; 95% CI 0.51 to 1.14, very low certainty evidence) (Analysis 2.1). High heterogeneity was observed in the overall analysis (I^2= 60%).

One study included only patients with ulcerative colitis and 4 studies included only patients with Crohn's disease (OR 0.70; 95% CI 0.45 to 1.07, very low certainty evidence) (Analysis 2.2). A statistically significant subgroup difference was not detected (p=0.41).

Studies performed prior to 1998 (OR 1.08; 95% CI 0.47 to 2.51, very low certainty evidence) and studies performed after 1998 (OR 0.71; 95% CI 0.45 to 1.14, very low certainty evidence) both demonstrated no difference in postoperative infectious complications (Analysis 2.3). A statistically significant subgroup difference was not detected (p=0.39).

In terms of secondary outcomes, only 1 study reported rates of incisional infections and wound dehiscence (Analysis 2.4). Data regarding intra-abdominal infections was reported in 3 studies. The OR was 0.77 (95% CI 0.45 to 1.33, very low certainty evidence) (Analysis 2.5). No studies reported rates of extra-abdominal infections.

Primary outcome findings were not significantly changed within a sensitivity analysis excluding studies that did not adjust for patients who underwent surgery to repair an intrabdominal abscess/fistula or were found to have an abscess intraoperatively (2 studies; OR 0.79; 95% CI 0.36 to 1.73) (Analysis 2.7). Other pre-planned sensitivity analyses were not performed as no studies were classified as low risk of bias and all 6 studies were manuscripts.

Analysis 3 Immunomodulators vs Control

Pooling of data from the 31 studies comparing preoperative immunomodulators versus no immunomodulator treatment demonstrated no difference in the incidence postoperative infectious complications (OR 1.11; 95% CI 0.97 to 1.26, very low certainty evidence) (Analysis 3.1). Low heterogeneity was observed in the overall analysis (I^2= 0%). Based on 9 of the studies, the adjusted pooled OR was 1.29 (95% CI 0.95 to 1.76; I2 0%; low certainty evidence; Analysis 3.1.1). Unadjusted OR, based on 22 studies, was 1.07 (95% CI 0.93 to 1.24; I2 0%; very low certainty evidence; Analysis 1.1.2)

Eleven studies included only patients with ulcerative colitis (OR 1.10; 95% CI 0.86 to 1.39, very low certainty evidence) and 14 studies included patients with Crohn's disease only (OR 1.11; 95% CI 0.90 to 1.36, very low certainty evidence) (Analysis 3.2). A statistically significant subgroup difference was not detected (p=0.95)

Studies performed prior to 1998 showed an increased postoperative infectious complications incidence (OR 1.85; 95% CI 1.14 to 3.01, very low certainty evidence) while studies performed after 1998 demonstrated no difference (OR 1.06; 95% CI 0.93 to 1.22, very low certainty evidence) (Analysis 3.3). The test of subgroup differences suggests that there is a statistically significant subgroup effect (p=0.03)

In terms of secondary outcomes, eleven studies reported rates of incisional infection and wound dehiscence and demonstrated no increase with preoperative immunomodulator use (OR 1.35; 95% CI 0.96 to 1.89, very low certainty evidence) (Analysis 3.4). Similar findings were seen in regards to rates of intra-abdominal infections (20 studies; OR 0.86; 95% CI 0.66 to 1.12, very low certainty evidence) (Analysis 3.5) and extra-abdominal infections (4 studies; OR1.17 (95% CI 0.80 to 1.71, very low certainty evidence;) (Analysis 3.6) in the immunomodulator group.

Primary outcome findings were not affected by excluding very high risk of bias studies (9 studies; OR 1.29 (95% CI 0.95 to 1.76) (Analysis 3.7) and studies published as a full manuscript (30 studies; OR 1.11 (95% CI 0.97 to 1.27) (Analysis 3.8). A sensitivity analysis was also performed excluding studies that included patients who underwent surgery to repair an intrabdominal abscess/fistula or were found to have an abscess intraoperatively and our findings remained stable (18 studies; OR 1.09; 95% CI 0.93 to 1.29) (Analysis 3.9). The findings were also not affected by excluding studies with potential unit of analysis error (overall rate of infection estimated by summation of different types of infection) (30 studies; OR 1.11; 95% CI 0.97 to 1.26) (Analysis 3.10).

Analysis 4 Anti-TNF agents vs Control

Pooling of data from the 54 studies comparing preoperative anti-TNF therapy versus no anti-TNF treatment demonstrated a modestly increased incidence of postoperative infectious complications (OR 1.27; 95% CI 1.09 to 1.47, very low certainty evidence) (Analysis 4.1). Substantial heterogeneity was not observed in the overall analysis (I^2= 46%). Based on 17 of the studies, the adjusted pooled OR was 1.60 (95% CI 1.20 to 2.13; I2 48%; low certainty evidence; Analysis 4.1.1). Unadjusted OR, based on 37 studies was 1.14 (95% CI 0.96 to 1.36; I2 42%; very low certainty evidence; Analysis 4.1.2)

Seventeen studies included only patients with ulcerative colitis (OR 1.04; 95% CI 0.79 to 1.36, very low certainty evidence) and 27 studies included patients with Crohn's disease only (OR 1.43; 95% CI 1.09 to 1.87, very low certainty evidence) (Analysis 4.2). A statistically significant subgroup difference was not detected (p=0.10)

In the 17 studies that included patients treated with anti-TNF therapy within 8 weeks of surgery, increased incidence of postoperative infectious complications was found (OR 1.44; 95% CI 1.08 to 1.94, very low certainty evidence) (Analysis 4.3). This was not the case in the 34 studies with patients whose last dose of TNF-therapy was more than 8 weeks before surgery (OR 1.18 95% CI 0.99 to 1.40, very low certainty evidence). A statistically significant subgroup difference was not detected (p=0.25)

In terms of secondary outcomes, twenty four studies reported rates of incisional infection and wound dehiscence and demonstrated no increase with preoperative anti-TNF therapy (OR 1.18; 95% CI 0.83 to 1.68, very low certainty evidence) (Analysis 4.4). While the incidence of intra-abdominal infections was higher in the anti-TNF group (39 studies; OR 1.38; 95% CI 1.04 to 1.82, very low certainty evidence) (Analysis 4.5), there was no difference in extra-abdominal infections (13 studies; OR 1.34 (95% CI 0.96 to 1.87, very low certainty evidence) (Analysis 4.6).

Primary outcome findings were not affected by excluding very high risk of bias studies (16 studies; OR 1.67 (95% CI 1.31 to 2.13) (Analysis 4.7) and studies published as a full manuscript (47 studies; OR 1.26 (95% CI 1.07 to 1.48) (Analysis 4.8). A sensitivity analysis was also performed restricting the analysis to studies that did not include patients who underwent surgery to repair an intrabdominal abscess/fistula or were found to have an abscess intraoperatively and the findings remained significant (37 studies; OR 1.31; 95% CI 1.10 to 1.56) (Analysis 4.9). The findings were also not affected by excluding studies with potential unit of analysis error (overall rate of infection estimated by summation of different types of infection) (46 studies; OR 1.22; 95% CI 1.02 to 1.45) (Analysis 4.10).

Analysis 5 Anti-integrin agents vs Control

Pooling of data from the 9 studies comparing preoperative anti-integrin therapy versus no anti-integrin treatment demonstrated no difference in postoperative infectious complications (OR 1.11; 95% CI 0.76 to 1.62, very low certainty evidence) (Analysis 5.1). Substantial heterogeneity was observed in the overall analysis (I^2= 55%). Based on 2 of the studies, the adjusted pooled OR was 1.04 (95% CI 0.79 to 1.36; I2 22%; low certainty evidence; Analysis 5.1.1). Unadjusted OR, based on 7 studies was 1.06 (95% CI 0.54 to 2.10; I2 62%; very low certainty evidence; Analysis 5.1.2)

Two studies included only patients with ulcerative colitis (OR 0.61; 95% CI 0.28 to 1.36, very low certainty evidence) and 4 studies included only patients with Crohn's disease (OR 1.32; 95% CI 0.51 to 3.42, very low certainty evidence) (Analysis 5.2). A statistically significant subgroup difference was not detected (p=0.22).

In terms of secondary outcomes, six studies reported rates of incisional infection and wound dehiscence and demonstrated no increased incidence with preoperative anti-integrin therapy (OR 1.64; 95% CI 0.77 to 3.50, very low certainty evidence) (Analysis 5.3). Similarly, there was no increase in intra-abdominal infections (5 studies; OR 0.40; 95% CI 0.14 to 1.20, very low certainty evidence) (Analysis 5.4) or extra-abdominal infections (5 studies; OR 1.15 (95% CI 0.43 to 3.08, very low certainty evidence) (Analysis 5.5) in the anti-integrin group.

Primary outcome findings were not affected by excluding very risk of bias studies (3 studies, OR 1.10 (95% CI 0.79 to 1.52) (Analysis 5.6) and studies published as a full manuscript (5 studies, OR 1.06 (95% CI 0.58 to 1.96) (Analysis 5.7). A sensitivity analysis was also performed restricting the analysis to studies that did not include patients who underwent surgery to repair an intrabdominal abscess/fistula or were found to have an abscess intraoperatively and the findings remained non-significant (9 studies; OR 1.11; 95% CI 0.76 to 1.62) (Analysis 5.8).The findings were also not affected by excluding studies with potential unit of analysis error (overall rate of infection estimated by summation of different types of infection) (7 studies; OR 0.97; 95% CI 0.73 to 1.29) (Analysis 5.9).

Analysis 6 Anti-interleukin agents vs Control

As only 1 study regarding anti-interleukin agents met the inclusion criteria, a meta-analysis was not performed. Liang et al. reported no difference in risk of overall postoperative infection (OR 0.80; 95% CI 0.10 to 6.51, very low certainty evidence) (Liang 2017).

Analysis 7 Small molecules vs Control

No studies regarding small molecules meeting our inclusion criteria were identified.

Analysis 8 Biosimilars versus Control

No studies regarding biosimilars meeting our inclusion criteria were identified.

DISCUSSION

Summary of main results

This systematic review included 68 observational studies that evaluated the risk of postoperative infectious complications from IBD medications. Separate analyses were performed for corticosteroids, 5ASAs, immunomodulators, anti-TNF medications, and anti-integrin medications. Meta-analysis was not performed for anti-interleukin medications, small molecules and biosimilars due to lack of appropriate studies.

Patients taking corticosteroids were found to have an increase in postoperative infectious complications within our meta-analysis. These findings were associated with low heterogeneity and low imprecision. Furthermore, the results remained similar in subgroup analyses of UC and CD patients, as well as subgroup analyses of studies performed before and after 1998. With regards to the secondary outcomes, we observed increased intra-

abdominal infections within the group treated with preoperative corticosteroids but no difference in the incidence of wound infections/dehiscence and of extra-abdominal infections. The lack of difference discovered for wound infections/dehiscence and for extra-abdominal infections may have been related to inadequate power to detect a difference, as from 41 studies, only 7 and 4 reported these outcomes, respectively. Of note, we included patients treated with any dose of corticosteroids. The strength of these findings could potentially be enhanced by evaluating whether there is a dose dependent impact on postoperative infectious complications.

We found no difference in postoperative infectious complications in patients treated with 5ASA. This result was associated with high heterogeneity and high imprecision. No difference was found in incidence of postoperative intra-abdominal infections. Analysis of incisional infections/wound dehiscence and extra-abdominal infections was not performed as an insufficient number of studies reported this information.

This meta-analysis did not find increased postoperative infectious complications in patients using immunomodulators. This result was associated with low heterogeneity and low imprecision. The findings remained stable in subgroup analyses of UC and CD patients. Interestingly, subgroup analysis of studies performed prior to 1998 revealed an increase in postoperative infectious complications that was not seen after 1998. Prior to the biologic era, immunomodulators were used more often for those with severe disease, so it is possible this finding is due to confounding by disease severity rather than a true biological effect. There was no difference observed in wound infection/dehiscence, intra-abdominal infections, or extra-abdominal infections within the group treated with immunomodulators.

For patients prescribed anti-TNF therapy, the incidence of postoperative infectious complications was higher within studies that reported adjusted data, but no different in the studies that reported unadjusted data. The risk of confounding within the unadjusted data must be considered, therefore it is more likely that anti-TNF therapy is associated with increased postoperative infectious complications based on our results. In subgroup analyses, the increased incidence of postoperative infectious complications remained significant only in CD patients and in patients who were treated with anti-TNF medications within 8 weeks of surgery. The increase in infectious complications seen only in patients receiving anti-TNF therapy within eight weeks before surgery could be explained by the pharmacokinetics of the drug class. Patients receiving their last dose of anti-TNF therapy greater than eight weeks before surgery may not have had significant drug levels at the time of surgery. Further studies could look at testing serum drug levels in postoperative IBD patients to compare infection rates in patients with and without therapeutic anti-TNF levels. It is not entirely clear why postoperative infectious complications on anti-TNF therapy was only increased in patients with CD, especially as no differences in results were found for CD compared to UC patients for other outcomes within this review. Secondary outcomes revealed mixed results, which may be explained by lower sample sizes, inclusion of both UC and CD patients, as well as variation in the timing of the last dose of medication.

We found no difference in postoperative infectious complications in patients treated with anti-integrin medications compared to those not using these therapies. This finding was associated with low heterogeneity but was also imprecise, likely due to a small sample size. Results were consistent in all subgroup analyses and analyses of secondary outcomes. Given the assumed gut selective mechanism of vedolizumab, intra-abdominal infections were of particular interest. We did not find an increase in intra-abdominal infections in patients prescribed anti-integrin agents.

Preplanned analyses for anti-interleukin medications, small molecule and biosimilars were not performed due to insufficient number of studies.

Overall completeness and applicability of evidence

The literature search was designed with the assistance of an experienced research librarian and was designed to include studies from around the world regardless of publication form, language, or date of publication. Hence, we believe this review is comprehensive and reflects the available evidence.

There were 41 studies on corticosteroids, 31 on immunomodulators and 54 reporting on anti-TNF medications. Data regarding 5ASA (6 studies), anti-integrin medications (9 studies), and anti-interleukin medications (1 study) was sparse and completely lacking in the case of biosimilars and small molecules. As anti-integrins, anti-interleukins, biosimilars and small molecules were relatively recently approved for the treatment of IBD, there will likely be more data regarding these medications in coming years.

We believe the results of this study to be generalizable to UC and CD patients but with some caveats. As most of the studies were performed at tertiary centers, the results may be less applicable to hospitals with less expertise in IBD-related surgeries. Also, the results of this study may not be applicable to patients undergoing non-abdominal surgery. We originally planned to perform subgroup analyses of studies containing abdominal and non-abdominal surgeries. However, this analysis could not be performed as patients only underwent abdominal procedures within the included studies. It is also important to be mindful that some studies excluded emergency surgeries and surgeries performed for the management of dysplasia/malignancy, and thus applicability of the results of this study to these specific patient populations may be limited. Furthermore, as many studies did not control for concomitant medication use, it may be difficult to apply these findings to clinical contexts where patients may be on multiple IBD medications. This is especially true regarding decisions around anti-TNF agents and corticosteroids since they were associated with increased postoperative infectious complications.

Quality of the evidence

Risk of bias according to the Newcastle-Ottawa Scale was deemed low in 24 studies and very high in 44 studies. Studies commonly lost points in the comparability section because many studies did not control for important factors such as disease severity and concomitant medications. Fourteen studies (Aberra 2003; Afzali 2016; Brouquet 2018; Cohen 2019; Gainsbury 2011; Krane 2013; McKenna 2018; Selvasekar 2007; Serradori 2013; Yamamoto 2016; Ayoub 2018; Appau 2008; Mor 2008; Waterman 2013) controlled for concomitant steroid us and 5 studies controlled for anti-TNF agents (McKenna 2018; Selvasekar 2007; Serradori 2013; Yamamoto 2016; Appau 2008). Also, many studies did not account for pre-existing infections. We acknowledge it may be impossible to guarantee that infections were not present prior to surgery as infections require some time to incubate before symptoms manifest. However, in cases where there are known preoperative infections such as when surgery is performed for management of an abdominal abscess, it may be prudent to adjust for this factor.

Overall, our assessment based on GRADE suggests that the certainty of evidence supporting the outcomes of this review is very low due to the observational nature of the data and very serious risk of bias. As well, many outcomes also demonstrated substantial levels of imprecision.

Potential biases in the review process

We explored publication bias by creating funnel plots for the primary outcome of each class of medication. Funnel plots were not created for the 5ASA and anti-integrin analyses due to insufficient (<10) number of studies. Publication bias was not detected based on visual inspection of these funnel plots (Figure 4; Figure 5; Figure 6). Limitations of this review include the paucity of prospective studies, small number of studies regarding 5ASA and anti-integrin medications, as well as sparse reporting of secondary outcomes.

Several studies did not provide an overall rate of infection, but rather reported different types of infections separately. In these situations, we contacted the authors for additional information, but if they did not provide the requested details, we estimated the overall rate of infection by summation of the different types of infection reported. This created the possibility of unit of analysis error. Reassuringly, sensitivity analyses excluding studies with potential unit of analysis issues did not result in significant changes to our findings.

In addition, 18 studies reported overall postoperative complications but not specifically infectious complications and 7 studies did not provide numerical data regarding incidence of infections stratified by patients' preoperative medication use. Efforts to contact authors for additional information were made. We did not hear back from the authors and thus, the above studies were excluded from our analysis. The data may be unavailable because the above studies had different areas of focus and did not specifically examine postoperative infections. It is also possible that data on postoperative infections was recorded but not reported, which would result in a publication bias.

Lastly, there were variations between studies as to what constituted an infectious complication. For example, some studies focused on only intra-abdominal infections, while others reported both intra-abdominal and extra-abdominal outcomes. Standardization in the method of reporting postoperative infections would allow for more accurate comparisons between studies.

Figure 4. Funnel plot of comparison: 1 Corticosteroids versus control, outcome: 1.1 Postoperative infection within 30 days of surgery.

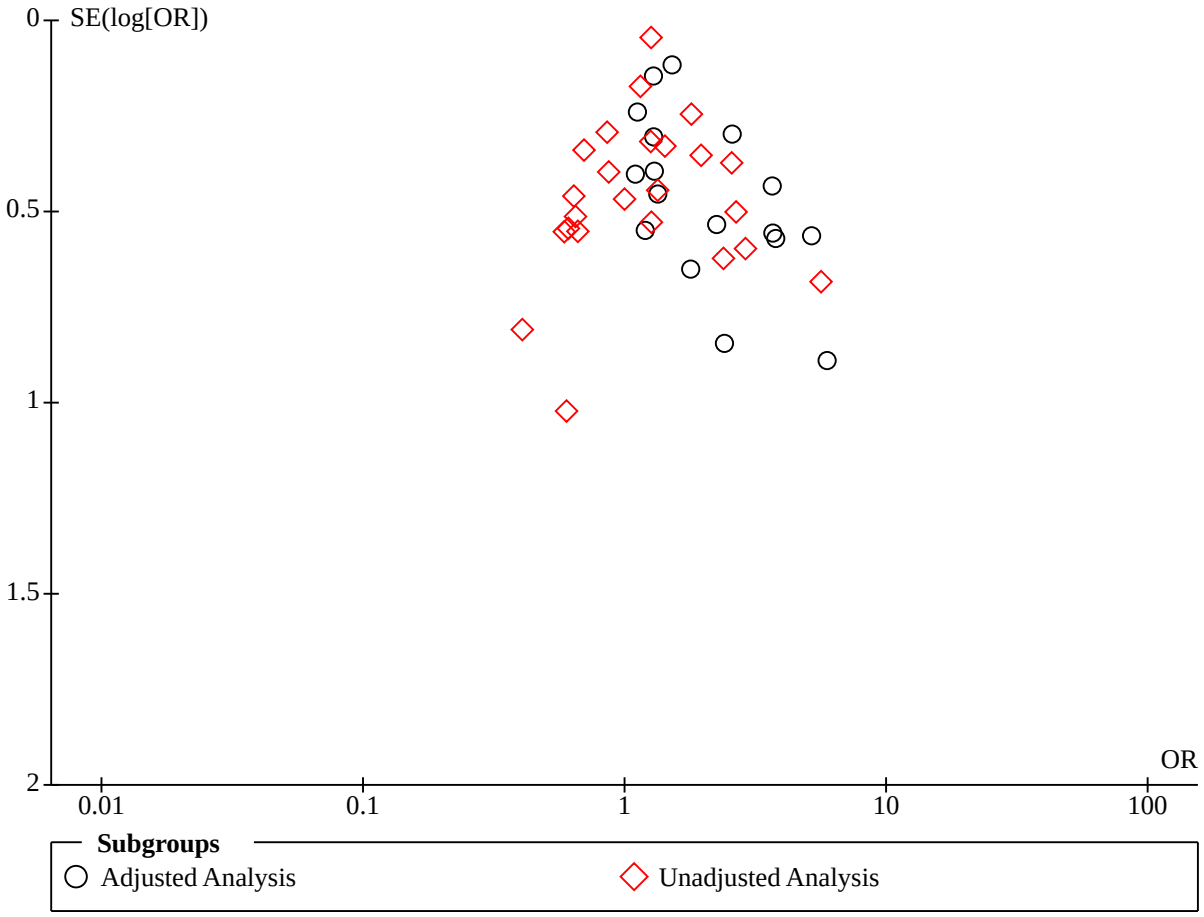


Figure 5. Funnel plot of comparison: 3 Immunosuppressive agents versus control, outcome: 3.1 Postoperative infection within 30 days of surgery.

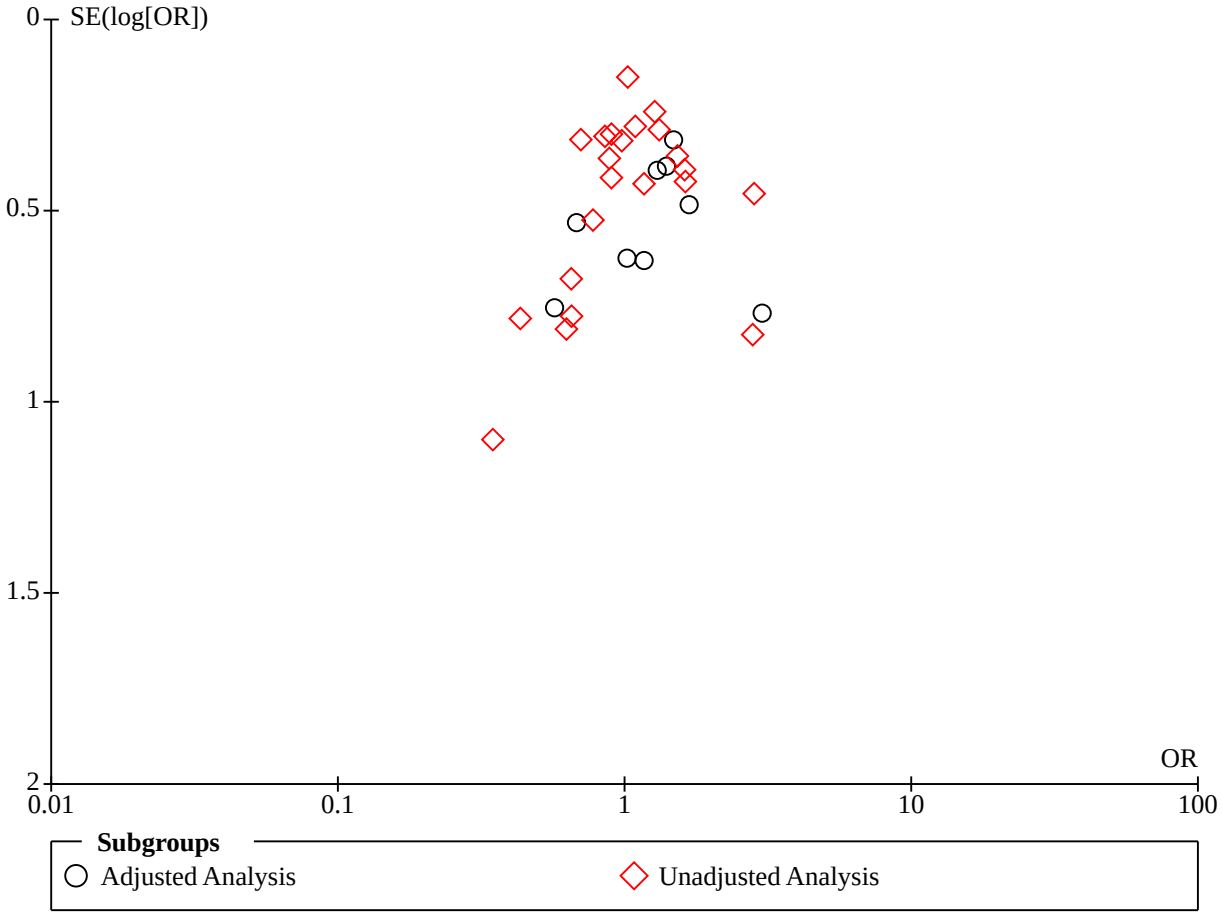
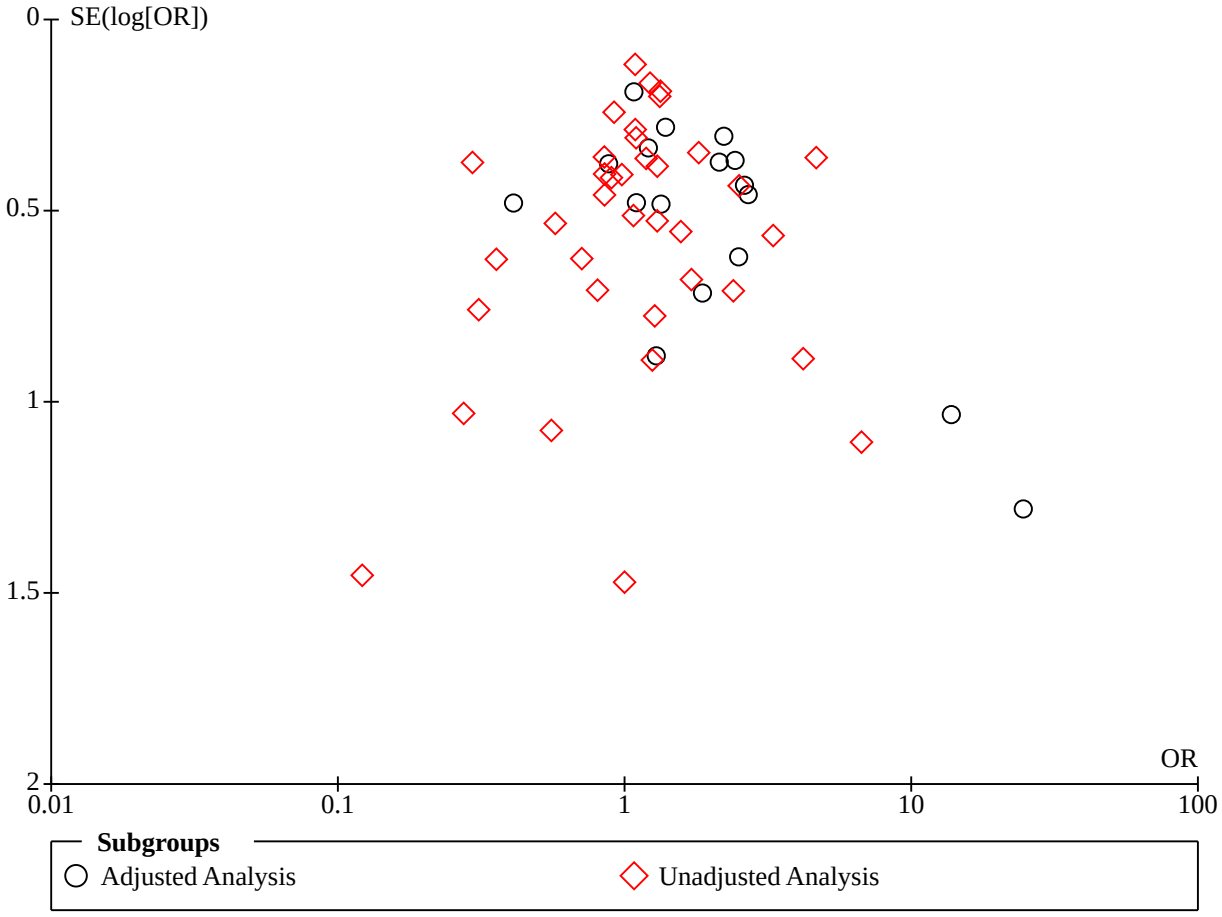


Figure 6. Funnel plot of comparison: 4 Anti-TNF-α agents versus control, outcome: 4.1 Postoperative infection within 30 days of surgery.



Agreements and disagreements with other studies or reviews

Our findings were similar to those reported in previous meta-analyses on this topic.

Subramanian et al. performed a meta-analysis on the risk of postoperative complications in IBD patients treated with corticosteroids. It examined infectious outcomes in addition to total postoperative outcomes (Subramanian 2008). In their analysis of postoperative infections, 5 studies were included and an increase in odds of infections within 30 days of surgery was reported (OR 1.68; 95% CI 1.24 to 2.28). Ali et al also studied the association between corticosteroid and postoperative infections (Ali 2014). They included 10 studies and reported a RR of 1.55 (95% CI 1.23 to 1.95). Our findings were in agreement with both studies and also had a narrower confidence interval, likely due to the larger sample size of our analysis.

To our knowledge, there are no previous meta-analyses examining the association between 5ASA therapy and postoperative infections in IBD patients.

We found two previous systematic reviews studying preoperative immunomodulator use and postoperative infections (Ali 2014; Subramanian 2006). Ali et al pooled data from 7 studies and found no difference in infectious complications (RR 1.23; 95% CI 0.66 to 2.29). Subramanian et al did not perform a meta-analysis but identified two studies (Aberra 2003; Colombel 2004) that both reported no significant increase in the risk of postoperative infection.

Numerous meta-analyses have been performed examining the association between anti-TNF therapy and postoperative infections (Billioud 2013; Ehteshami-Afshar 2011; El-Hussuna 2013; Kopylov 2012; Narula 2013; Waterland 2016; Xu 2019; Yang 2014; Yang 2012). For unclear reasons, conclusions of these studies have been inconsistent. Three studies examined odds of infection in IBD patients (UC and CD combined): Billoud et al (OR 1.27; 95% CI 0.87 to 1.85) and Ehtshami et al (OR 1.56; 95% CI 0.71 to 3.44) reported no difference in infection, while Narula et al (OR 1.56; 95% CI 1.09 to 2.24) reported a modest increase. However, both Billoud et al (OR 1.45; 95% CI 1.03 to 2.05) and Narula et al (OR 1.94; 95% CI 1.28 to 2.89) found a significant increase in CD patients with no difference in UC patients. One potential reason for the difference in findings amongst these reviews could be related to the variation in the accepted definition of preoperative anti-TNF administration. For

example, Billioud et al included studies that reported the last dose of anti-TNF infusion anywhere from 2-24 weeks preoperatively. In contrast, Ehtshami et al did not provide information on the time of last infusion but did provide the total length of time a patient had been on anti-TNF therapy.

Among studies that examined CD patients exclusively, El-Hussana et al (RR 0.91; 95% CI 0.56 to 1.47) did not find an increase in risk, but Kopylov et al (OR 1.50; 95% CI 1.14 to 2.03), Waterland et al (OR 1.52; 95% CI 1.14 to 2.03), Xu et al (OR 1.23; 95% CI 0.87 to 1.74) and Yang et al (OR 1.47; 95% CI 1.08 to 1.99) all reported an increased odds. In a separate publication, Yang et al also studied UC patients and reported no difference (OR 1.10; 95% CI 0.51 to 2.38) (Yang 2012). Our study found that there appears to be a mildly increased risk of postoperative infection in IBD patients overall and particularly in CD patients, which is consistent with the majority of these previous meta-analyses.

Two systematic reviews studying anti-integrin medications and postoperative infection were identified (Law 2018; Yung 2018). Neither identified any increase in risk of infectious complications (Law: RR 0.92; 95% CI 0.44 to 1.92; Yung: OR 0.72; 95% CI 0.19 to 2.74), which is consistent with the results of our study.

AUTHORS' CONCLUSIONS

Implications for practice

This is the largest and most comprehensive meta-analysis to date on this topic. The evidence regarding corticosteroids, 5ASA, immunomodulators, anti-TNF mediations and anti-integrin medications was very low in certainty. Thus, the impact of these medications on postoperative infectious complications is uncertain and no firm conclusions can be drawn regarding their safety in the perioperative period. The decision to stop IBD medications prior to surgery involves potential risks and benefits. Holding therapies prior to surgery could result in a disease flare and in the case of biologic medications, could lead to sensitization and the formation of antibodies. Thus, the decision should involve careful consideration of each patient's circumstances, treatment history, preferences and values.

Implications for research

This review has highlighted areas for further research. Prospective studies and studies controlling for potential confounding factors such as disease severity and concomitant medications are required to generate higher quality evidence. Furthermore, data regarding anti-interleukin and anti-integrin medications was sparse and no studies are currently available on small molecules and biosimilars. Undoubtedly, more studies are required before firm conclusions can be drawn regarding these medications. Incorporation of preoperative drug levels in future studies would also be helpful as it could delineate a potential dose-dependent risk and help stratify patients' risks for potential infection. Lastly, standardization of which and how postoperative infections are reported would greatly aid in comparison of studies.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Aberra 2003

Study characteristics	
Methods	Retrospective cohort. Study period: 1992 to 2000
Participants	Country: USA. Patients with UC or CD who underwent elective bowel surgery. Patients treated with infliximab, mycophenolate, or tacrolimus were excluded
Interventions	1. Azathioprine/6-mercaptopurine within 2 weeks of surgery (n=52) 2. Preoperative corticosteroids (n=90) 3. No preoperative immunosuppressants or corticosteroids (n=51)

Aberra 2003 *(Continued)*

Outcomes	Wound infection, sepsis, p n e umonia, peritonitis, abdominal abscess and wound dehiscence within 30 days of surgery
Notes	NOS low risk of bias overall. Adjusted O Rs for corticosteroids and azathioprine/6-mercaptopurine were obtained from multivariate regression model.

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	All UC and CD patients undergoing elective bowel surgery at University of Pennsylvania Health system from 1992 to 2000
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	All charts were manually searched to determine medication exposure
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information was provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Azathioprine/6-mercaptopurine analysis controlled for corticosteroids and vice versa
Comparability of cohorts (Controlled for additional factor)	Low risk	Also controlled for CD, disease refractory to medication, age >38 years, and surgery duration >241 minutes
Assessment of outcome	Low risk	Inpatient medical records were examined
Was follow-up long enough for outcomes to occur	Low risk	Patients were followed until discharge from hospital (median 8 days, range 1-37 days)
Adequacy of follow up of cohorts	Unclear risk	No information was provided

Afzali 2016

Study characteristics	
Methods	Retrospective cohort. Study period: 1992 to 2012
Participants	Country: USA. UC and CD patients who underwent either urgent or elective abdominal surgery.
Interventions	1.Preoperative methotrexate (n=15) 2. Preoperative azathioprine or 6-mercaptopurine (n= 52) 3. No preoperative methotrexate (n=165) 4. No preoperative azathioprine or 6-mercaptopurine (n=128)

Afzali 2016 *(Continued)*

Outcomes	Wound infection, anastomotic leak, abscess, fistula and extraabdominal infection within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted ORs for methotrexate and azathioprine were obtained from multivariate logistic regression model.

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	All CD and UC who underwent abdominal surgery at the Univerity of Washington Medical Center from 1993 to 2012
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records were examined
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information was provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Adjusted for steroid use
Comparability of cohorts (Controlled for additional factor)	Low risk	Also adjusted for albumin, hematocrit, smoking status, and BMI
Assessment of outcome	Low risk	Medical records were examined
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	61 patients excluded from analysis due to missing BMI measurement

Alves 2007

Study characteristics

Methods	Retrospective cohort. Study period: 1984 to 2004.
Participants	Country: France. CD patients who underwent their first ileocecal resection with primary anastomosis. Patients with temporary stomas were excluded.
Interventions	1. Preoperative steroids (n= 59) 2. No preoperative steroids (n=102)
Outcomes	Anastomotic leak and intra-abdominal abscess within 30 days of surgery

Alves 2007 *(Continued)*

Notes	NOS low risk of bias overall Adjusted OR for st eroids was obtained from stepwise multivariate analysis model.

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD database of patients who underwent surgery from 1984 to 2004
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	CD database
Demonstration that outcome of interest was not present at start of study	High risk	Some patients were found to have Intra-abdominal abscesses during surgery
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not report controlling for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for poor nutritional status
Assessment of outcome	Low risk	CD database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	NOS low risk of bias overall

Appau 2008

Study characteristics

Methods	Retrospective cohort. Study period: 1998 to 2007.
Participants	Country: USA. CD patients who underwent ileocolonic resection with anastomosis.
Interventions	1. Preoperative infliximab (n= 60) within 3 months of surgery 2. No preoperative infliximab (n=329)
Outcomes	Wound infection, wound complications, anastomotic leak, sepsis and intraabdominal abscess within 30 days of surgery
Notes	NOS low risk of bias overall A djusted OR s for infliximab, 6MP/azathioprine/ methotrexate, and steroids were obtained from multivariate logistic regression model.

Appau 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD database of all patients who underwent ileocolonic resection at the Cleveland Clinic
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medication use verified with pharmacy department and patients were called to confirm last dose of infliximab infusion
Demonstration that outcome of interest was not present at start of study	High risk	Some patient were noted to have intraabdominal abscesses preoperatively
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Adjusted for methotrexate, 6-mercaptopurine, azathioprine, infliximab and steroid use
Comparability of cohorts (Controlled for additional factor)	Low risk	Also adjusted for age, gender, comorbidities, penetrating abscess before surgery, diverting stoma, and disease phenotype
Assessment of outcome	Low risk	Medical charts were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information was provided

Araki 2014

Study characteristics	
Methods	Prospective, multicenter (13 institutions), observational cohort study. Study period: 2009 to 2010
Participants	Country: Japan. UC patients who underwent colorectal surgery
Interventions	1. Preoperative immunomodulator therapy (n= 92) 2. No preoperative immunomodulator (n= 103)
Outcomes	Superficial, deep and organ space surgical site infections within 30 days
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement

Araki 2014 *(Continued)*

Representativeness of the exposed cohort	Low risk	All UC patients who underwent colorectal surgery from 2009 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Data collection prospectively on a standardized form by physicians
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information was provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data collection prospectively on a standardized form by physicians
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information was provided

Ayoub 2018

Study characteristics	
Methods	Retrospective cohort. Study period: 2014 to 2016.
Participants	Country: USA. CD and UC patients who underwent major abdominal surgery. Patients actively treated with steroids were excluded
Interventions	1. Vedolizumab (n= 16) within 8 weeks of surgery 2. Biologics other than vedolizumab (n= 37) within 8 weeks of surgery 3. No preoperative biologic therapy (n=18)
Outcomes	Surgical site infection within 30 days of surgery
Notes	This study is an abstract. NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	All patients who underwent major abdominal procedures due to IBD were screened

Ayoub 2018 *(Continued)*

Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Unclear risk	No information provided
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Excluded patients actively treated with steroids
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for any other variables
Assessment of outcome	Unclear risk	No information provided
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Bregnbak 2012

Study characteristics	
Methods	Retrospective cohort. Study period: 2005 to 2010
Participants	Country: Denmark. UC patients who underwent colectomy. Patients with colonic malignancy or dysplasia were excluded.
Interventions	1. Preoperative infliximab (n=20) within 90 days of surgery. 2. Preoperative corticosteroids (n=48) 3. No preoperative infliximab (n=51) 4. No preoperative corticosteroids (n=23)
Outcomes	Infectious complications within 30 days postoperative
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	All patients with UC based on clinical, endoscopic and histological criteria who underwent colectomy from 2005 to 2010.
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period

Bregnbak 2012 *(Continued)*

Ascertainment of exposure	Low risk	Danish National Health Reigster and examination of patient records
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other factors
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for other factors
Assessment of outcome	Low risk	Medical records were examined
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Brouquet 2018

Study characteristics	
Methods	Prospective, multicenter (19 institutions), cohort study. Study period: 2013 to 2015
Participants	Country: France. Patients with ileocolonic CD who underwent abdominal surgery. Patients with perianal CD or colonic CD were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 143) within 3 months of surgery 2. No preoperative anti-TNF therapy (n= 449)
Outcomes	Peritonitis, anastomotic leak, and intraabdominal abscess within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted OR for anti-TNF medications was obtained from multivariate m odel with propensity s core analysis .

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	All patients who underwent surgery for ileocolonic CD from 2013 to 2015
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Data prospectively collected on an electronic dedicated clinical research form

Brouquet 2018 *(Continued)*

Demonstration that outcome of interest was not present at start of study	High risk	18% patients had intraoperative finding of abscess
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Controlled for systemic steroids and budesonide
Comparability of cohorts (Controlled for additional factor)	Low risk	Also controlled for recurrent CD, hemoglobin, TPN, laparoscopic approach, and operative time
Assessment of outcome	Low risk	Prospectively collected on an electronic dedicated clinical research form
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Canedo 2011

Study characteristics	
Methods	Retrospective cohort study. Study period: 2000 to 2008
Participants	Country: USA. CD patients who underwent intestinal or colorectal resection. Patients who had stoma creation without resection, stoma reversal and lysis of adhesions were excluded
Interventions	1. Preoperative infliximab (n= 65) within 3 months of surgery 2. No preoperative biologics (n= 75)
Outcomes	Wound infection, pulmonary infection, abscess and anastomotic leak within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Consecutive patients with CD who underwent surgical intestinal and colorectal resection from 2000 to 2008
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Retrospective analysis of a prospective surgical database
Demonstration that outcome of interest was not present at start of study	High risk	Firstula/abscess was indication for surgery for 72 patients

Canedo 2011 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other factors
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for other factors
Assessment of outcome	Low risk	Retrospective analysis of a prospective surgical database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Patients with incomplete data were excluded

Cohen 2019

Study characteristics	
Methods	Multicentre prospective cohort study. Study period 2014 to 2017.
Participants	Country: USA. Crohn's and ulcerative colitis patients undergoing intra-abdominal surgery.
Interventions	1. Preoperative anti-TNF therapy (n= 382) within 12 weeks of surgery. 2. No preoperative anti-TNF exposure (n= 573)
Outcomes	30 post operative infectious complications (any infection and surgical site infection)
Notes	NOS low risk of bias overall Adjusted OR for preoperative anti-TNF therapy was obtained from m ultivariable logistic regression model.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Prospective cohort of IBD patients who underwent intra-abdominal surgery from 2014 to 2017
Selection of the non exposed cohort	Low risk	Both groups obtained from same centres and time period
Ascertainment of exposure	Low risk	Prospective database. Data obtained by patient interview and chart abstraction
Demonstration that outcome of interest was not present at start of study	Low risk	Controlled for pre-operative non-abdominal infection

Cohen 2019 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Performed multivariable analysis controlling for preoperative methotrexate and steroids
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for multiple other factors including age, BMI, gender and comorbid disease
Assessment of outcome	Low risk	Prospective database. Data obtained by patient interview and chart abstraction
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Authors did not comment whether any patients were lost to follow up

Colombel 2004

Study characteristics	
Methods	Retrospective cohort. Study period: 1998 to 2001
Participants	Country: USA. CD patients who underwent surgical resection, stricturoplasty, or intestinal bypass. Patients who received cyclosporine, tacrolimus, or investigational therapy within 8 weeks of surgery were excluded. Patients who underwent perianal surgery were also excluded.
Interventions	1. Preoperative infliximab (n= 52) 8 weeks prior to surgery and within 30 days after surgery 2. Preoperative azathioprine/6-mercatopurine/methotrexate (n= 105) 3. Preoperative moderate/high dose steroids (n= 77) 4. No preoperative infliximab (n= 218) 5. No preoperative azathioprine/6-mercatopurine/methotrexate (n= 165) 6. Low dose/no preoperative steroids (n=193)
Outcomes	Wound sepsis, intraabdominal infections and extraabdominal infections within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent surgical resection, stricturoplastly or intestinal bypass from 1998 to 2001
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records were examined

Colombel 2004 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis only
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis only
Assessment of outcome	Low risk	Medical records were examined
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Coquet-Reinier 2010

Study characteristics		
Methods	Matched retrospective cohort study. Study period: 1998 to 2008	
Participants	Country: France. UC patients who underwent laproscopic restorative proctocolectomy with ileal pouch anal anastomosis	
Interventions	1. Preoperative infliximab (n=13) 2. No preoperative infliximab (n=13)	
Outcomes	Pelvic abscess and anastomotic leak within 30 days of surgery	
Notes	NOS low risk of bias overall	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent laparoscopic IPAA since 1999
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records were examined
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided

Coquet-Reinier 2010 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Matched for gender, age and procedure type (2 or 3 stage)
Assessment of outcome	Low risk	Medical records were examined
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

De Buck Van Overstraeten 2017

Study characteristics	
Methods	Retrospective cohort. Study period: 1998 to 2013
Participants	Country: Belgium. CD patients who underwent primary ileocecal resection
Interventions	1. Preoperative anti-TNF therapy (n= 111) within 12 weeks of surgery 2. Preoperative steroids (n=278) 3. No preoperative anti-TNF therapy (n=427) 4. No preopera tive steroids (n= 260)
Outcomes	Anastomotic leak within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted ORs for preoperative steroids and anti-TNF therapy were obtained from multivariate logistic regression model .

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Patients with CD operated on for terminal ileocecal disease
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical charts reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided

De Buck Van Overstraeten 2017 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Corrected for institution and time since first surgical procedure
Assessment of outcome	Low risk	Medical charts reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

El-Hussuna 2012

Study characteristics	
Methods	Retrospective, multicenter (4 institutions) cohort. Study period: 2000 to 2007.
Participants	Country: Denmark. CD patients who underwent resection and anastomosis or with stricturoplasty
Interventions	1. Preoperative infliximab/certolizumab (n= 32) within 3 months of surgery 2. Azathioprine/6-mercaptopurine/methotrexate (n= 166) within 1 month o surgery 3. Preoperative steroids (n= 66) 4. No preoperative anti-TNF medication (n= 385) 5. No preoperative immunosuppressants (n= 251) 6. No preoperative steroids (n= 351)
Outcomes	Intraabdominal septic complications (anastomotic dehiscence, fistula, abscess), septic complications, other infective complications within 30 days of surgery
Notes	NOS very high risk of bias overall
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent resection form 2000 to 2007
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Unclear risk	No information provided

El-Hussuna 2012 *(Continued)*

Demonstration that outcome of interest was not present at start of study	High risk	20% patients had preoperative intraabdominal infection
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Unclear risk	No information provided
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Eshuis 2013

Study characteristics		
Methods	Retrospective cohort. Study period: 2006 to 2010	
Participants	Country: Netherlands. UC patients who underwent restorative proctocolectomy. Patients who had surgery for dysplasia or malignancy were excluded.	
Interventions	1. Preoperative infliximab (n= 38) 2. No preoperative infliximab (n =34)	
Outcomes	Pelvic sepsis, intraabdominal asbcess, surgical site infection, extraabdominal infection within 30 days of surgery	
Notes	NOS very high risk of bias overall	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	All patients requiring restorative proctocolectomy for refactory UC from 2006 to 2010.
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical charts reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided

Eshuis 2013 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for other factors
Assessment of outcome	Low risk	Medical charts reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Ferrante 2009

Study characteristics	
Methods	Retrospective cohort. Study period: 1998 to 2008
Participants	Country: Belgium. UC and unclassified IBD patients who underwent restorative proctocolectomy
Interventions	1. Preoperative infliximab (n= 22) within 12 weeks of surgery 2. Preoperative immunomodulators (n= 78) 3. Preoperative steroids(n= 64) 4. No preoperative infliximab (n= 119) 5. No preoperative immunomodulators (n= 63) 6. no preoperative steroids (n= 77)
Outcomes	Pouch sepcific complications, surgical site infections, and non-surgical site infections within 30 days of surgery
Notes	NOS very high risk of bias overall Adjusted OR for preoperative steroids was obtained from multiv ariate model. Unadjusted ORs for preoperative infliximab and immunomodulators were obtained from univariate analysis.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Consecutive UC/IBDU patients who underwent restorative proctocolectomy from 1998 to 2008
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Clinical charts reviewed

Ferrante 2009 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Clinical charts reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Ferrante 2017

Study characteristics	
Methods	Retrospective cohort. Enrolment period: 2006 to 2016
Participants	Country: Belgium. UC patients who underwent colectomy. Patients who were treated with investigational products and who were anticipated to have a permant ileostomy were excluded
Interventions	1. Preoperative mesalamine (n= 97) 2. Preoperative thiopurine/methotrexate (n= 38) 3. Preoperative steroids (n= 32) 4. Preoperative anti-TNF medications within 8 weeks of surgery (n= 60) 5. Preoperative vedolizumab within 16 weeks of surgery (n= 34) 6. No preoperative mesalamine (n= 73) 7. No preoperative thiopurine/methotrexate (n= 132) 8. No preoperative steroids (n= 138) 9. No preoperative anti-TNF medications (n= 110) 10. No preoperative vedolizumab (n= 136)
Outcomes	Pouch specific infectious complications, surgical site infections, non-surgical site infections within 30 days of surgery
Notes	NOS very high risk of bias overall Unadjusted ORs for preoperative mesalamine, thiopurine/methotrexate, steroids, anti-TNF therapy, and vedolizumab were obtained from univariate regre ssion models.

Ferrante 2017 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	All UC patients who underwent colectomy from 2006 to 2016
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Patient charts reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not adjust for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not adjust for additional factors
Assessment of outcome	Low risk	Patient charts reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Fumery 2017

Study characteristics	
Methods	Prospective, multicenter (9 institutions) cohort. Study period: 2010 to 2014
Participants	Country: France. CD patients who underwent ileocecal resection. Pregnant patients and those who had surgery for dysplasia were excluded
Interventions	1. Preoperative steroids (n= 45) 2. Preoperative anti-TNF therapy (n= 93) within 4 weeks of surgery 3. No preoperative steroid (n= 164) 4. No preoperative anti-TNF therapy (n= 165)
Outcomes	Abdominal infections and extaabdominal infections within 30 days of surgery
Notes	NOS very high risk of bias overall
Risk of bias	

Fumery 2017 *(Continued)*

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	All adult CD patients who underwent ileocecal resection from 2010 to 2014
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Data collected prospectively in a standardized format by gastroenterologist
Demonstration that outcome of interest was not present at start of study	High risk	42% surgeries performed due to fistula/abscess
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control of other factors
Assessment of outcome	Low risk	Data collected prospectively in a standardized format and reviewed in detail
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Gainsbury 2011

Study characteristics	
Methods	Retrospective cohort. Study period: 2005 to 2009
Participants	Country: USA. UC patients who underwent ileal pounch-anal anastomosis
Interventions	1. Preoperative infliximab (n= 29) within 12 weeks of surgery 2. No preoperative infliximab (n= 52)
Outcomes	Pelvic/intraabdominal abscess or wound infection
Notes	NOS low risk of bias overall Adjusted ORs f or preoperative infliximab, 6MP and corticosteroids were obtained from multivariate logistic regression models.

Risk of bias

Bias	Authors' judgement	Support for judgement

Gainsbury 2011 *(Continued)*

Representativeness of the exposed cohort	Low risk	UC patients who underwent ileal pounch-anal anastomosis from 2005 to 2009
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Medical records were reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Adjusted for steroids, 6-mercaptopurine, and methotrexate
Comparability of cohorts (Controlled for additional factor)	Low risk	Also adjusted for BMI, laproscopic colectomy, and failed medical therapy
Assessment of outcome	Low risk	Medical records were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Gu 2013

Study characteristics	
Methods	Retrospective cohort. Study period 2006 to 2010
Participants	Country: USA. UC or indeterminate colitis ptints who underwent total proctocolectomy or subtotal colectomy with end ileostomy. Patients who underwent surgery for toxic megacolon, massive hemorrhage, colonic perforation, dyplasia or malignancy were exlcuded
Interventions	1. Anti-TNF medication (n= 167) within 12 weeks of surgery for infliximab and within 4 weeks of surgery for adalimumab/certolizumab 2. No preoperative anti-TNF medication (n= 421)
Outcomes	Pelvic sepsis, wound infection, anastomotic leak within 30 days
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC or indeterminate colitis ptints who underwent total proctocolectomy or subtotal colectomy with end ileostomy

Gu 2013 *(Continued)*

Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Information obtained from prospective database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Did not provide information
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control of other factors
Assessment of outcome	Low risk	Information obtained from prospective database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Guasch 2016

Study characteristics	
Methods	Retrospective cohort. Study period: 2009 to 2014
Participants	Country: Spain. CD patients who underwent intestinal resection
Interventions	1. Preoperative anti-TNF treatment (n= 44) within 3 months of surgery 2. No preoperative anti-TNF treatment (n= 56)
Outcomes	Septic complications within 30 days of surgery
Notes	This study is an abstract. NOS risk of bias very high overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	All CD patients who underwent intestinal resection from 2009 to 2014
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Electronic medical record reviewed

Guasch 2016 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	Unclear risk	No information provided
Comparability of cohorts (Controlled for additional factor)	Unclear risk	No information provided
Assessment of outcome	Low risk	Electronic medical record reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	All patients had at least 1 year of follow up

Gudsoorkar 2018

Study characteristics	
Methods	Retrospective cohort. Study period: 2015 to 2017
Participants	CD and UC patients who underwent IBD-related surgery
Interventions	1. Preoperative anti-TNF medication (n= 20) 2. Preoperative vedolizumab (n= 16) 3. No preoperative biologic therapy (n= 12)
Outcomes	Infectious complications within 30 days
Notes	This study is an abstract. NOS risk of bias very high overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD and UC patients who underwent IBD-related surgery
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Unclear risk	Information not provided
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided

Gudsoorkar 2018 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not adjust for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not adjust for additional factors
Assessment of outcome	Unclear risk	Information not provided
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Guo 2017

Study characteristics	
Methods	Retrospective cohort. Study period: 2013 to 2015
Participants	Country: China. Patients with fistulizing CD who underwent abodminal surgery. Excluded stricturoplasty, resection of perianal disease, ileostomy/colostomy closure, reoperations for postoperative complications
Interventions	1. Preoperative 5ASA (n= 45) 2. Preoperative immunomodulator (n= 7) 3. Preoperative steroids (n= 22) 4. Preoperative anti-TNF medication (n= 11) 5. No preoperative 5ASA (N= 73) 6. No preoperative immunomodulator (n= 111) 7. No preoperative steroids (n= 96) 8. No preoperative anti-TNF medication (n= 107)
Outcomes	Surgical site infection within 30 days
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Patients with fistulizing CD who underwent abodminal surgery.
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period

Guo 2017 *(Continued)*

Ascertainment of exposure	Low risk	Medical records reviewed
Demonstration that outcome of interest was not present at start of study	High risk	13 patients had preoperative intraabdominal abscess
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factors
Assessment of outcome	Low risk	Medical records reviewed
Was follow-up long enough for outcomes to occur	Low risk	Surgical site infection within 30 days of surgery
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Jouvin 2018

Study characteristics	
Methods	Retrospective cohort. Study period: 2002 to 2013
Participants	Country: France. CD patients who underwent ileocolic resection. Patients requiring ileorectal or ileoanal anastomosis were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 55) within 8 weeks of surgery 2. Preoperative immunomodulator (n= 147) 3. Preoperative steroids (n= 154) 4. No preoperative anti-TNF therapy (n= 305) 5. No preoperative immunomodulator (n= 213) 6. No preoperative steroids (n= 206)
Outcomes	Intraabdominal septic complications, septic complications within 30 days of surgery
Notes	NOS very high risk of bias overall Adjusted OR for preoperative anti-TNF therapy was obtained from multivaria ble regression model.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent ileocolic resection from 2002 to 2013

Jouvin 2018 *(Continued)*

Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Unclear risk	Information not provided
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for other factors
Assessment of outcome	Unclear risk	Information not provided
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Kim 2018

Study characteristics	
Methods	Matched cohort study. Enrolment period: unknown
Participants	CD patients who underwent colorectal surgery. Patients matched for age and gender
Interventions	1. Preoperative vedolizumab (n= 13) 2. Preoperative anti-TNF (n= 39) 3. No preoperative biologic (n= 29)
Outcomes	Surgical site infection within 30 days of surgery
Notes	This study is an abstract. NOS low risk of bias Adjusted OR for preoperative vedolizumab was obtained from a multivariate regression model.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent colorectal surgery
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period. Patients matched for age and gender

Kim 2018 *(Continued)*

Ascertainment of exposure	Low risk	Information obtained from prospective database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for age and gender
Assessment of outcome	Low risk	Information obtained from prospective database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Kotze 2017

Study characteristics	
Methods	Retrospective, multicenter (2 institutions) cohort. Study period: 2007 to 2014
Participants	Country: Brazil. CD patients who underwent elective intestinal resection. Stricuroplasty, diverting stomas and emergency surgeries were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 81) within 8 weeks of surgery 2. No preoperative anti-TNF therapy (n= 52)
Outcomes	Intraabdominal abscess, anastomotic dehiscence, surgical site infection, other infections within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent elective intestinal resection from 2007 to 2014
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Medical records examined

Kotze 2017 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factors
Assessment of outcome	Low risk	Medical records examined
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Krane 2013

Study characteristics	
Methods	Retrospective cohort. Study period: 2004 to 2011
Participants	Country: USA. CD, UC and indeterminate colitis patients who underwent laparascopic resection. Stricturoplasty, multiorgan resection, stoma formation without colorectal resection, emergency surgery, and robot-assisted surgery were excluded.
Interventions	1. Preoperative infliximab (n= 142) within 12 weeks of surgery 2. No preoperative infliximab (n= 376)
Outcomes	Surgical site infections and non-surgical site infections within 30 days of surgery
Notes	Only patients with minimum of 6 months of follow were included. NOS low risk of bias overall Adjusted ORs for preoperative infliximab, steroi ds and immunomodulators were obtained from a multivariate regression model.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD, UC and indeterminate colitis patients who underwent laparascopic resection
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospitals and time period
Ascertainment of exposure	Low risk	Prospectively collected database

Krane 2013 *(Continued)*

Demonstration that outcome of interest was not present at start of study	High risk	24 patients had preoperative C. difficile infection
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Adjusted for steroids and immunosuppressants
Comparability of cohorts (Controlled for additional factor)	Low risk	Adjusted for type of IBD, disease activity, comorbidities
Assessment of outcome	Low risk	Prospectively collected database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Only patients with minimum of 6 months of follow were included

Kunitake 2008

Study characteristics	
Methods	Retrospective cohort. Study period: 1993 to 2007
Participants	Country: USA. CD, UC and indeterminate colitis patients who underwent abdominal surgery
Interventions	1. Preoperative infliximab (n= 101) within 12 weeks of surgery 2. No preoperative infliximab (n= 312)
Outcomes	Anastomotic leak, sepsis, intraabdominal abscess, wound infection, wound dehiscence, pneumonia
Notes	NOS very high risk of bias overall Adjusted ORs for preoperative infliximab and c orticosteroids were obtained fr om multivariate regression model.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD, UC and indeterminate colitis patients who underwent abdominal surgery
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Electronic medical records were reviewed
Demonstration that outcome of interest was not present at start of study	High risk	Indication for surgery was intraabdominal abscess in 38 patients

Kunitake 2008 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Reported event rates
Comparability of cohorts (Controlled for additional factor)	High risk	Reported event rates
Assessment of outcome	Low risk	Electronic medical records were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Liang 2017

Study characteristics	
Methods	Retrospective cohort. Study period: 2014 to 2016
Participants	Country: USA. UC and CD patients who underwent lower GI surgery
Interventions	1. Preoperative anti-TNF therapy (n= 686) within 12 weeks of surgery 2. Preoperative vedolizumab (n= 114) 3. Preoperative ustekinumab (n= 8) 4. Preoperative 5ASA (n= 733) 5. Preoperative corticosteroids (n= 674) 6. Preoperative immunosuppressants (n= 382) 7. No preoperative anti-TNF therapy (n= 2674) 8. No preoperativ vedolizumab (n= 3246) 9. No preoperative ustekinumab (n= 3352) 10. No preoperative 5ASA (n= 2627) 11. No preoperative corticosteroids (n= 2686) 12. No preoperative immunosuppressants (n= 2978)
Outcomes	Wound infection, peritonitis, retroperitoneal infection, sepsis within 30 days of surgery
Notes	NOS very high risk of bias overall Adjusted OR for preoperative corticosteroids was obtained from multivariate regression model.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Liang 2017 *(Continued)*

Representativeness of the exposed cohort	Low risk	UC and CD patients who underwent lower GI surgery
Selection of the non exposed cohort	Low risk	Both groups obtained from Clinformatics DataMart database and time period
Ascertainment of exposure	Low risk	Identified exposures using medical and pharmacy claims
Demonstration that outcome of interest was not present at start of study	Unclear risk	Did not provide information
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Identified outcomes using ICD codes, facility claims and provider claims
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Did not provide information

Lightner 2018 A

Study characteristics	
Methods	Retrospective cohort. Study period: 2014 to 2016
Participants	Country: USA. CD patients who underwent elective major abdominal surgery.
Interventions	1. Preoperative vedolizumab (n= 100) within 12 weeks of surgery 2. Preoperative anti-TNF therapy (n= 107) within 12 weeks of surgery 3. No preoperative biologic therapy (n= 105)
Outcomes	Surgical site infection, mucocutaneous separation, anastomotic leak, extraabdominal infections within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent elective major abdominal surgery from 2014 to 2016

Lightner 2018 A *(Continued)*

Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Electronic medical records reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factors
Assessment of outcome	Low risk	Electronic medical records reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Excluded patients with less than 30 days of follow up

Lightner 2018 B

Study characteristics	
Methods	Retrospective cohort. Study period 2010 to 2017.
Participants	Country: USA. Adult patients undergoing ileocolic resection with primary anastomosis for Crohn's disease
Interventions	1. Preoperative steroid use 2. Preoperative immunomodulator use 3. Preoperative biologics 4. Dual therapy 5. Triple therapy 6. No preoperative medication
Outcomes	Intra-abdominal sepsis, defined as an intraperitoneal abscess or anastomotic leak
Notes	NOS very high risk of bias overall Unadjusted ORs for preoperative steroids, immunomodulators and biologics were obtained from univari ate analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement

Lightner 2018 B *(Continued)*

Representativeness of the exposed cohort	Low risk	Retrospective cohort of patients undergoing ileocolic resection for Crohn's disease
Selection of the non exposed cohort	Low risk	Both groups obtained from same centres and time period
Ascertainment of exposure	Low risk	Chart review was performed
Demonstration that outcome of interest was not present at start of study	Unclear risk	No information provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Unadjusted odds ratios were reported
Comparability of cohorts (Controlled for additional factor)	High risk	Unadjusted odd ratios were reported
Assessment of outcome	Low risk	Chart review was performed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Mahadevan 2002

Study characteristics	
Methods	Retrospective cohort. Study period: 1997 to 1999
Participants	Country: USA. UC patients who underwent proctocolectomy with IPAA
Interventions	1. Preoperative immunosuppressants (n= 58) 2. No preoperative immunosuppressants (n= 151)
Outcomes	Anastomotic leak, wound dehiscence, pelvic sepsis, perianal fistula/abscess, other infectious complications within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent proctocolectomy with IPAA from 1997 to 1999
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period

Mahadevan 2002 *(Continued)*

Ascertainment of exposure	Low risk	Medical records reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factors
Assessment of outcome	Low risk	Medical records reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	All 209 patients were included in the analysis of early complications

Marchal 2004

Study characteristics	
Methods	Matched retrospective cohort study. Study period: 1998 to 2002
Participants	Country: Belgium. CD patients who underwent intestinal resection
Interventions	1. Preoperative infliximab (n= 40) 2. No preoperative infliximab (n= 39)
Outcomes	Sepsis, anastomotic leak, peritonitis, fistula, abscess, wound infection within 10 days of surgery
Notes	NOS low risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent intestinal resection
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records reviewed
Demonstration that outcome of interest was not present at start of study	High risk	Indication for surgery was fistula/abscess in 31 patients

Marchal 2004 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Control group adjusted for age, gender and surgical procedure
Assessment of outcome	Low risk	Medical records reviewed
Was follow-up long enough for outcomes to occur	Unclear risk	10 days only
Adequacy of follow up of cohorts	Unclear risk	Information was not provided

McKenna 2018

Study characteristics	
Methods	Retrospective cohort. Study period: 2007 to 2017
Participants	Country: USA. CD patients who underwent ileocolic resection with primary anastomosis. Patients who underwent ileocolic resection with primary anastomosis and diverting loop ileostomy were excluded
Interventions	1. Preoperative steroids (n= 37) 2. Preoperative immunomodulators (n =57) 3. Preoperative anti-TNF therapy (n= 322) within 12 weeks of surgery 4. No preoperative steroids (n= 584) 5. No preoperative immunomodulators (n= 564) 6. No preoperative anti-TNF therapy (n= 299)
Outcomes	Intraabdominal sepsis within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted ORs for preoperative steroids, immunomodulators, and anti-TNF therapy were obtained from multivariate regression model.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent ileocolic resection with primary anastomosis from 2007 to 2017
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical charts were reviewed

McKenna 2018 *(Continued)*

Demonstration that outcome of interest was not present at start of study	High risk	61 patients had an abscess at the time of surgery
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Controlled for other medications (corticosteroids, immunomodulators, anti-TNF)
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for previous intestinal resection, tobacco use
Assessment of outcome	Low risk	Medical charts were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Mor 2008

Study characteristics	
Methods	Matched retrospective cohort study. Study period: 2000 to 2006
Participants	Country: USA. UC and indeterminate colitis patients who underwent two stage restorative proctocolectomy
Interventions	1. Preoperative infliximab (n= 46) 2. No preoperative infliximab (n= 46)
Outcomes	Pelvis sepsis within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted ORs for preoperative steroids, immunomodulators, and anti-TNF were obtained from multivariate regression analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC and indeterminate colitis patients who underwent two stage restorative proctocolectomy from 2000 to 2006
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records were reviewed

Mor 2008 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Adjusted for dose of steroids and other immunomodulators
Comparability of cohorts (Controlled for additional factor)	Low risk	Patients matched for age, gender, date of operation and indication for surgery
Assessment of outcome	Low risk	Medical records were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Morar 2015

Study characteristics	
Methods	Retrospective cohort. Study period: 2005 to 2010
Participants	Country: United Kingdom. CD patients who underwent ileocolonic resection. Patients with previous segmental or subtotal colectomy were excluded
Interventions	1. Preoperative steroids (n= 34) 2. Preoperative immunomodulators (n= 64) 3. Preoperative 5ASA (n= 43) 4. Preoperative anti-TNF therapy (n= 4) within 4 weeks of surgery 5. No preoperative steroids (n= 104) 6. No preoperative immunomodulators (n= 193) 7. No preoperative 5ASA (n= 82) 8. No preoper a tive anti-TNF therapy (n= 126)
Outcomes	Intrabdominal septic complication including anastomotic leak, intraabdominal collection, enter o cutaneous fistula formation within 30 days of surgery
Notes	NOS very high risk of bias ov erall Adjusted OR for preoperative anti-TNF therapy was obtained from multivariate regression model.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Morar 2015 *(Continued)*

Representativeness of the exposed cohort	Low risk	CD patients who underwent ileocolonic resection from 2005 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same databases and time period
Ascertainment of exposure	Low risk	Clinical case records were examined
Demonstration that outcome of interest was not present at start of study	High risk	Fistula/abscess was indication for surgery for some patients
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Clinical case records were examined
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Low percentage of patients had missing data (<15%)

Myrelid 2009

Study characteristics	
Methods	Prospective cohort. Enrolment period: 1989 to 2002
Participants	Country: Sweden. CD patients who underwent a surgery for CD involving an anastomosis/strictureplasty. Proceudres including diverting or permantent stomas and reconstructions after stomas were excluded
Interventions	1. Preoperative steroids (n=87) 2. Preoperative 5ASA (n= 113) 3. Preoperative azathioprine (n= 51) 4. No preoperative steroids (n= 256) 5. No preoperative 5ASA (n= 230) 6. No preoeprative azathioprine (n= 292)
Outcomes	Intraabdominal septic complications (including fistula, abscess, and dehiscence) and extraabdominal infection within 30 days of surgery
Notes	NOS very high risk of bias overall

Myrelid 2009 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD patients who underwent a surgery for CD involving an anastomosis/stricture plasty
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database
Ascertainment of exposure	Low risk	Data obtained from a prospectively maintained database
Demonstration that outcome of interest was not present at start of study	High risk	12% of patients had preoperative intraabdominal infection
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data obtained from a prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Myrelid 2014

Study characteristics	
Methods	Retrospective cohort. Study period not provided
Participants	Country: Sweden. CD patients who underwent resection with primary anastomoses and/or stircture-plasties. Patients with stomas were excluded
Interventions	1. Preoperative infliximab (n= 111) within 2 months of surgery 2. No preoperative infliximab (n= 187)
Outcomes	Infectious complications within 30 days of surgery
Notes	NOS very high risk of bias overall Unadjusted ORs for preoperative steroids, immunomodulators and anti-TNF were o btained from regression analysis.

Risk of bias

Myrelid 2014 *(Continued)*

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD patients who underwent resection with primary anastomoses and/or stricturetureplasties.
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital database and time period
Ascertainment of exposure	Low risk	Data obtained from database
Demonstration that outcome of interest was not present at start of study	High risk	Indication for surgery was abscess/fistula in 61 patients
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data obtained from database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	No information provided

Nasir 2010

Study characteristics	
Methods	Retrospective cohort. Study period: 2005 to 2009
Participants	Country: USA. CD patients who underwent operations resulting in an anastomosis. Emergency surgeries and proximal diversions were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 119) within 8 weeks of surgery 2. No preoperative anti-TNF therapy (n= 251)
Outcomes	Intraabdominal abscess and anastomotic leak within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD patients who underwent operations resulting in an anastomosis from 2005 to 2009

Nasir 2010 *(Continued)*

Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital database and time period
Ascertainment of exposure	Low risk	Data obtained from prospectively maintained database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factors
Assessment of outcome	Low risk	Data obtained from prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Nguyen 2014

Study characteristics	
Methods	Retrospective cohort. Study period: 2005 to 2012.
Participants	Country: Canada. CD and UC patients who underwent abdominal surgery in the ACS-NSQIP database.
Interventions	1. Preoperative steroids (n= 6281) 2. No preoperative steroids (n= 9214)
Outcomes	Superficial and deep wound infection, intraabdominal infection, extraabdominal infection within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD and UC patients who underwent abdominal surgery in the ACS-NSQIP database from 2005 to 2012
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Patients identified by ICD-9 codes

Nguyen 2014 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factor
Assessment of outcome	Low risk	Obtained fron ACS-NSQIP database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Norgard 2012

Study characteristics	
Methods	Retrospective cohort. Study period: 2003 to 2010
Participants	Country: Denmark. UC patients who underwent colectomy in the Danish National Patient Registry
Interventions	1. Preoperative anti-TNF therapy (n= 199) within 12 weeks of surgery 2. No preoperative anti-TNF therapy (n= 1027)
Outcomes	Anastomotic leak, intraabdominal asbcess within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent colectomy from 2003 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Exposure identified by codes from the National Patient Registry and prescription database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided

Norgard 2012 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	OR adjusted for age, gender, comorbidity, steroids, duration of UC, year and length of inpatient stay was available for anastomotic leak and intraabodminal abscess outcomes separately. Combined event rate of anastomotic leak and intraabdominal abscess was used for our analysis.
Comparability of cohorts (Controlled for additional factor)	High risk	See above
Assessment of outcome	Low risk	Outcome identified by codes from the National Patient Registry
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	All patients had 30 and 60 day follow up data after surgery

Norgard 2013

Study characteristics	
Methods	Retrospective cohort. Study period: 2003 to 2010
Participants	Country: Denmark. CD patients who underwent abdominal surgery in the Danish National Patient Registry
Interventions	1. Preoperative anti-TNF therapy (n= 214) within 12 weeks 2. No preoperative anti-TNF therapy (n= 2079)
Outcomes	Anastomotic leak, intraabdominal abscess, bacteremia within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD patients who underwent abdominal surgery from 2003 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Exposure identified by codes from the National Patient Registry and prescription database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	OR adjusted for age, gender, comorbidity, steroids, duration of CD, year and length of inpatient stay was available for anastomotic leak and intraabodminal

Norgard 2013 *(Continued)*

		abscess outcomes separately. Combined event rate of anastomotic leak and intraabdominal abscess was used for our analysis.
Comparability of cohorts (Controlled for additional factor)	High risk	See above
Assessment of outcome	Low risk	Outcome identified by codes from the National Patient Registry
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	All patients had 30 and 60 day follow up data after surgery

Novello 2020

Study characteristics	
Methods	Retrospective cohort study. Study period 2012 to 2017
Participants	IBD patiests who underwent elective abdominal surgery. Excluded patients undergoing anorectal surgery alone.
Interventions	1. Preoperative vedolizumab use within 12 weeks of surgery 2. Preoperative infliximab use within 12 weeks of surgery 3. No preoperative biologic use
Outcomes	Infectious complications within 30 days of surgery, including organ space SSI, superficial SSI, perineal wound infection, pneumonia, UTI, anastomotic leak, rectal stump leak, other enteric leak, stoma separation and Clostridium difficile infection
Notes	Case-matched analysis was performed but we used the data from the analysis conducted on the full, unmatched sample. NOS low risk of bias overall Adjusted ORs were obtained for preoperative vedolizumab and infliximab treatment from multivariable logistic regression models.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Consecutive patients with IBD who underwent abdominal surgery
Selection of the non exposed cohort	Low risk	Both groups obtained from same centres and time period
Ascertainment of exposure	Low risk	Chart review performed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided

Novello 2020 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Multivariate analysis did not control for other preoperative medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for other factors including hemoglobin, BMI, surgery time and diagnosis (CD vs UC)
Assessment of outcome	Low risk	Chart review performed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Regadas 2011

Study characteristics	
Methods	Retrospective cohort. Study period: 2001 to 2008
Participants	Country: USA. CD, UC and indeterminate colitis patients who underwent ileostomy reversal
Interventions	1. Preoperative infliximab (n= 28) within 2 months of surgery 2. Preoperative steroids (n= 72) 3. Preoperative immunosuppressive therapy (n= 35) 4. No preoperative immunosuppressive therapy (n= 114)
Outcomes	Wound infection, anastomotic leak, intraabdominal abscess and enterocutaneous fistula within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD, UC and indeterminate colitis patients who underwent ileostomy reversal from 2001 to 2008
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Data obtained from a prospectively maintained database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided

Regadas 2011 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control for additional factors
Assessment of outcome	Low risk	Data obtained from a prospectively maintained databas
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Rizzo 2011

Study characteristics		
Methods	Retrospective cohort. Study period: 2004 to 2010	
Participants	Country: Italy. CD or UC patients who underwent abdominal surgery	
Interventions	1. Preoperative anti-TNF therapy (n= 54) within 12 weeks of surgery 2. No preoperative anti-TNF therapy (n= 60)	
Outcomes	Wound infection, intraabdominal abscess, anastomotic leak, pelvic abscess, extraabdominal infection within 30 days of surgery	
Notes	NOS very high risk of bias overall	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD or UC patients who underwent abdominal surgery from 2004 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Medical records were reviewed
Demonstration that outcome of interest was not present at start of study	High risk	Indication for surgery was perforation in 6 patients
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis

Rizzo 2011 *(Continued)*

Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Medical records were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Schils 2017

Study characteristics	
Methods	Matched retrospective cohort study. Study period 2006 to 2016
Participants	Country: Belgium. CD patients who underwent right hemicolectomy with ileocolonic anastomosis
Interventions	1. Preoperative vedolizumab (n= 12) within 14 weeks of surgery 2. Preoperative anti-TNF therapy (n= 12) within 8 weeks of surgery 3. Preoperative steroids (n= 12) 4. No preoperative therapy (n= 12)
Outcomes	Infectious complications and anastomotic leak within 30 days of surgery
Notes	This study is an abstract. Additional information was provided by the authors of Schils et al. NOS low risk of bias overall.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent right hemicolectomy with ileocolonic anastomosis from 2006 to 2016
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period. Matched for age and gender
Ascertainment of exposure	Low risk	Medical charts were reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications

Schils 2017 *(Continued)*

Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for age and gender
Assessment of outcome	Low risk	Medical charts were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Schluender 2007

Study characteristics	
Methods	Retrospective cohort. Study period: 2000 to 2005
Participants	Country: USA. UC patients who underwent colectomy. Patients with indeterminate colitis, surgery for dysplasia or carcinoma were excluded
Interventions	1. Preoperative infliximab (n= 17) 2. No preoperative infliximab (n= 134)
Outcomes	Infectious complications within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent colectomy from 2000 to 2005
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Information obtained from a prospectively maintained database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	High risk	Did not control of additional factors
Assessment of outcome	Low risk	Information obtained from a prospectively maintained database

Schluender 2007 *(Continued)*

Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Selvasekar 2007

Study characteristics		
Methods	Retrospective cohort. Study period: 2002 to 2005	
Participants	Country: USA. UC patients who underwent ileal pouch anal anastomosis	
Interventions	1. Preoperative infliximab (n= 47) 2. No preoperative infliximab (n= 254)	
Outcomes	Anastomotic leak, intraabdominal abscess, superficial and deep wound infections within 30 days of surgery	
Notes	NOS low risk of bias overall Adjusted ORs for steroids, azathioprine and anti-TNF were obtained from multivariate regression analysis.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent ileal pouch anal anastomosis from 2002 to 2005
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Medical charts reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Adjusted for steroids, infliximab and azathioprine use
Comparability of cohorts (Controlled for additional factor)	Low risk	Also adjusted for age and severity of colitis
Assessment of outcome	Low risk	Medical charts reviewed

Selvasekar 2007 *(Continued)*

Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Serradori 2013

Study characteristics		
Methods	Retrospective, multicenter (3 institutions) cohort. Study period: 2000 to 2010	
Participants	Country: France. CD patients who underwent ileocecal or ileocolonic resection. Patients with temporary stomas were excluded.	
Interventions	1. Preoperative anti-TNF within 8 weeks of surgery 2. Preoperative steroids	
Outcomes	Intraabdominal abscess, anastomotic leak, fistula within 30 days of surgery	
Notes	NOS low risk of bias overall Adjusted ORs for preoperative anti-TNF and corticosteroids were obtained from multivariate regression analysis.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent ileocecal or ileocolonic resection from 2000 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Medical charts reviewed
Demonstration that outcome of interest was not present at start of study	High risk	30 patients had an abscess at the time of surgery
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Controlled for steroids and anti-TNF use
Comparability of cohorts (Controlled for additional factor)	Low risk	Also controlled for age, Montreal classification
Assessment of outcome	Low risk	Medical charts reviewed

Serradori 2013 *(Continued)*

Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Shaib 2017

Study characteristics		
Methods	Retrospective cohort (NSQIP database). Study period: not provided	
Participants	Country: USA. UC and CD patients who underwent colectomy	
Interventions	1. Preoperative steroid 2. No preoperative steroid	
Outcomes	Anastomotic leak within 30 days of surgery	
Notes	This study is an abstract. NOS very high risk of bias overall Adjusted OR for preoperative corticosteroids was obtained from multivariate regression analysis.	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC and CD patients who underwent colectomy
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database
Ascertainment of exposure	Low risk	Information obtained from NSQIP database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for gender, operation time, smoking, emergency surgeries, subtype of IBD
Assessment of outcome	Low risk	Information obtained from NSQIP database
Was follow-up long enough for outcomes to occur	Low risk	30 days

Shaib 2017 *(Continued)*

Adequacy of follow up of cohorts	Unclear risk	Information not provided

Shwaartz 2016

Study characteristics	
Methods	Retrospective cohort. Study period: 2013 to 2015
Participants	Country: USA. UC and CD patients who underwent intestinal surgery with primary anastomosis. Emergency surgeries were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 73). Last dose of infliximab within 8 weeks and last dose of adalimumab and certolizumab within 4 weeks of surgery 2. No preoperative anti-TNF therapy (n= 209)
Outcomes	Anastomotic leak, intraabdominal abscess, extraabdominal infection within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC and CD patients who underwent intestinal surgery with primary anastomosis from 2013 to 2015
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Analysis for overall infectious complications did not control for other factors.
Comparability of cohorts (Controlled for additional factor)	High risk	See above
Assessment of outcome	Low risk	Medical records reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Syed 2013

Study characteristics	
Methods	Retrospective cohort. Study period 2004 to 2011
Participants	Country: USA. CD patients who underwent abdominal surgery. Isolated perianal surgieres were excluded.
Interventions	1. Preoperative anti-TNF therapy (n= 150) within 8 weeks of surgery 2. No preoperative anti-TNF therapy (n= 175)
Outcomes	Intraabdominal infectious complication, surgical site complication, any infectious complication within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted OR for preoperative anti-TNF was obtained from multivariate regression analysis.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent abdominal surgery from 2004 to 2011
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Electronic medical record and clinic charts were reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for BMI, stricture, open surgery, perforation, ASA >2
Assessment of outcome	Low risk	Electronic medical record and clinic charts were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Tzivanakis 2012

Study characteristics

Tzivanakis 2012 *(Continued)*

Methods	Retrospective cohort. Study period: 2000 to 2010
Participants	Country: UK. CD patients who underwent ileocecal and ileocolic resection. Strictureplasties, mulitple resections, subtotal or isolated colonic resections were excluded
Interventions	1. Preoperative steroids (n= 56) 2. No preoperative steroids (n= 117)
Outcomes	Anastomotic leak, intraabdominal abscess, fistula within 30 days of surgery
Notes	NOS low risk of bias overall Unadjusted OR for preoperative corticosteroids was ob tained from regression analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD patients who underwent ileocecal and ileocolic resection from 2000 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Data from propsective database that was audited weekly to ensure accurate entry of data
Demonstration that outcome of interest was not present at start of study	High risk	Preoperative abscess was found to an independent predictor of anastomotic-associated complication
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for age, sex, malnutrition, preoperative serum albumin, smoking, urgency of surgery, mode of surgery, presence of abscess or fistula at the time of surgery and previous resection for CD
Assessment of outcome	Low risk	Data from propsective database that was audited weekly to ensure accurate entry of data
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Uchino 2010

Study characteristics

Methods	Retrospective cohort. Study period: 2006 to 2008

Uchino 2010 *(Continued)*

Participants	Country: Japan. UC patients who underwent laparotomy. Patients who had subtotal colectomy with mucous fistula before IPAA or ileostomy closure were excluded.
Interventions	1. Preoperative immunosuppressants (n= 20) 2. No preoperative immunosuppressants (n= 172)
Outcomes	Superficial incisional, deep incisional, and organ space surgical site infection within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	UC patients who underwent laparotomy from 2006 to 2008
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Unclear risk	Information not provided
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univerariate analysis
Assessment of outcome	Unclear risk	Information not provided
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Uchino 2013a

Study characteristics

Methods	Retrospective cohort. Study period: 2008 to 2011
Participants	Country: Japan. CD patients who underwent laparotomy. Perianal procedures were excluded
Interventions	1. Preoperative infliximab (n= 79) within 12 weeks of surgery 2. Preoperative immunosuppressants (n= 6)

Uchino 2013a *(Continued)*

	3. Preoperative 5ASA (n= 322) 4. No preoperative infliximab (n= 326) 5. No preoperative immunosuppressants (n= 399) 6. No preoperative 5ASA (n= 83)
Outcomes	Incisional surgical site infection, organ space surgical site infeciton within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	CD patients who underwent laparotomy from 2008 to 2011
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Data was obtained from a prospectively maintained database
Demonstration that outcome of interest was not present at start of study	High risk	27 patients classified as wound class IV (dirty/infected)
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data was obtained from a prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Uchino 2013b

Study characteristics

Methods	Retrospective cohort. 2010 to 2012
Participants	Country: Japan. UC patients who underwent laparotomy. Patients who had subtotal colectomy with mucous fistula before IPAA or ileostomy closure were excluded.
Interventions	1. Preoperative infliximab (n= 22) within 12 weeks of surgery 2. Properative immunomodulators (n= 94)

Uchino 2013b *(Continued)*

	3. No preoperative infliximab (n= 174) 4. No preoperative immunomodulators (n= 102)
Outcomes	Superficial incisional, deep incisional, organ space surgical site infection, and extraabdominal infections within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	UC patients who underwent laparotomy from 2010 to 2012
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Data was obtained from a prospectively maintained database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Included patients with contaminated wounds
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univiariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data was obtained from a prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Uchino 2015

Study characteristics

Methods	Retrospective cohort. Study period: 2012 to 2014
Participants	Country: Japan. UC patients who underwent IPAA. Patients who underwent with total colectomy without IPAA were ex c luded
Interventions	1. Preoperative biologic (n=44) within 12 weeks of surgery 2. Preoperative immunomodulator (n= 105) 3. Preoperative steroids (n= 113)

Uchino 2015 *(Continued)*

Outcomes	Surgical site infection within 30 days of surgery
Notes	NOS very high risk of bias overall Adjusted OR preoperative steroids, immunomodulators, and biologics were obtained from multivariate regression analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	UC patients who underwent IPAA from 2012 to 2014
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Data was obtained from a prospectively maintained database
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data was obtained from a prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Uchino 2019

Study characteristics

Methods	Retrospective cohort study. Study period 2015 to 2018
Participants	Country: Japan. Patients with ulcerative colitis who underwent total colectomy with ileostomy, total proctocolectomy with end ileostomy or ileal pouch anal anastomosis
Interventions	1. Preoperative steroids (n=117) 2. Preoperative azathioprine/6MP (n=121) 3. Preoperative anti-TNF agents within 12 weeks of surgery (n=146)
Outcomes	Surgical site infection (incisional infection and organ/space infection) within 30 days of surgery

Uchino 2019 *(Continued)*

Notes	NOS very high risk of bias overall Adjusted OR for preoperative anti-TNF therapy was obtained from multivariable regression model. Unadjusted OR for preoperative steroid therapy was obtained from univariate regression model.

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	301 consecutive patients with UC who underwent abdominal surgery
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Retrospective evaluation of a prospective database at Hyogo College of Medicine
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not perform
Comparability of cohorts (Controlled for additional factor)	High risk	Multivariate analysis only for anti-TNF administration (age, pre-op albumin, transfusion, ASA score, wound class, urgent/emergent surgery, intra-operative blood loss and duration of surgery). Univariate analysis for steroids and azathioprine/6M
Assessment of outcome	Low risk	Retrospective evaluation of a prospective database at Hyogo College of Medicine
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Ward 2018

Study characteristics

Methods	Retrospective cohort. Study period: 2006 to 2015
Participants	Country: UK. UC patients who underwent subtotal colectomy
Interventions	1. Preoperative anti-TNF therapy (n= 418) within 4 weeks of surgery 2. No preoperative anti-TNF therapy (n= 5807)
Outcomes	Infectious complications within 30 days of surgery

Ward 2018 *(Continued)*

Notes	NOS very high risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement
Representativeness of the exposed cohort	Low risk	UC patients who underwent subtotal colectomy from 2006 to 2015
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period
Ascertainment of exposure	Low risk	Information obtained using Office of Population Censuses and Surveys codes
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Information obtained using ICD codes
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Waterman 2013

Study characteristics

Methods	Matched retrospective cohort study. Study period: 2000 to 2010
Participants	Country: Canada. CD and UC patients who underwent abdominal surgery.
Interventions	1. Preoperative infliximab (n= 195) within 180 days of surgery 2. No preoperative infliximab (n= 278)
Outcomes	Wound infection, anastomotic leak, intraabdominal abscess, extraabdominal infections within 30 days of surgery
Notes	NOS low risk of bias overall

Risk of bias

Bias	Authors' judgement	Support for judgement

Waterman 2013 *(Continued)*

Representativeness of the exposed cohort	Low risk	CD and UC patients who underwent abdominal surgery from 2000 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period.
Ascertainment of exposure	Low risk	Patient charts reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Groups matched for steroids
Comparability of cohorts (Controlled for additional factor)	Low risk	Groups also matched for surgical procedure, IBD subtype and patient age
Assessment of outcome	Low risk	Patient charts reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Patients without adequate clinical records documenting 30 day outcomes were excluded

Wilson 2014

Study characteristics	
Methods	Retrospective cohort. Study period: 2005 to 2010
Participants	Country: USA. CD patients in National Surgical Quality Improvement Project database who underwent ileocolectomy
Interventions	1. Preoperative steroid therapy (n= 954) 2. No preoperative steroid therapy (n= 1515)
Outcomes	Organ space surgical site infection within 30 days of surgery
Notes	NOS low risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients in National Surgical Quality Improvement Project database who underwent ileocolectomy from 2005 to 2010
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period.

Wilson 2014 *(Continued)*

Ascertainment of exposure	Low risk	NSQIP database
Demonstration that outcome of interest was not present at start of study	High risk	Wound class classification IV in 12% of patients
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications
Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for BMI, diabetes, smoking, ASA classification, extended operative time, open procedure, preoperative SIRS, emergent procedure, and wound classification
Assessment of outcome	Low risk	NSQIP database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Yamada 2017

Study characteristics	
Methods	Retrospective cohort. Study period: 2014 to 2016
Participants	Country: USA. UC and CD patients who underwent major and minor abdominal surgeries. Patients with less than 30 days of follow up data or missing data were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 129) within 4 weeks of surgery 2. Preoperative vedolizumab (n= 64) within 4 weeks 3. No preoperative biologic therapy (n= 250)
Outcomes	Infectious complications (wound infection or dehiscence, anastomotic leak, abscess, sepsis, fistula, pulmonary infection, UTI) within 30 days of surgery
Notes	NOS very high risk of bias overall Adjusted OR for preoperative steroids was obtained from multivariate model.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC and CD patients who underwent major and minor abdominal surgeries from 2014 to 2016
Selection of the non exposed cohort	Low risk	Both groups obtained from the same database and time period.
Ascertainment of exposure	Low risk	Data was obtained from a prospectively maintained database

Yamada 2017 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Data was obtained from a prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Patients with less than 30 days of follow up data or missing data were excluded

Yamamoto 2000

Study characteristics	
Methods	Retrospective cohort. Study period: 1980 to 1997
Participants	Country: UK. CD patients who underwent at least one intestinal anastomosis. Closure of loop ileostomy/colostomy and reoperations for early postoperative complications were excluded
Interventions	1. Preoperative steroids (n= 220) 2. No preoperative steroids (n= 346)
Outcomes	Anastomotic leak, intraabdominal abscess, fistula within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent at least one intestinal anastomosis from 1980 to 1997
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period.
Ascertainment of exposure	Low risk	Medical records were reviewed
Demonstration that outcome of interest was not present at start of study	High risk	121 patients were found to have an abscess at the time of laparotomy

Yamamoto 2000 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Medical records were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Yamamoto 2016

Study characteristics	
Methods	Retrospective multicenter (7 institutions) cohort. Study period: 2008 to 2013
Participants	Countries: Japan, Brazil and Italy. CD patients who underwent ileocolonic resection with primary anastomosis. Patients who had covering ileostomy or with insufficient data for analysis were excluded
Interventions	1. Preoperative steroids (n= 68) 2. Preoperative immunomodulators (n= 65) 3. Preoperative biologics (n= 79) within 8 weeks of surgery 4. No preoperative steroids (n= 163) 5. No preoperative immunomodulators (n= 166) 6. No preoperative biologics (n= 152)
Outcomes	Anastomotic leak, intraabdominal abscess, fistula within 30 days of surgery
Notes	NOS low risk of bias overall Adjusted ORs for preoperative steroids, immunomodulators and biologics were obtained from multivariate analysis.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD patients who underwent ileocolonic resection with primary anastomosis from 2008 to 2013
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Data was obtained from a prospectively maintained database

Yamamoto 2016 *(Continued)*

Demonstration that outcome of interest was not present at start of study	High risk	43% of patients had perforating disease at baseline
Comparability of cohorts (Controlled for critical factor/other medications)	Low risk	Controlled for steroids, immunosuppressants, biologics
Comparability of cohorts (Controlled for additional factor)	Low risk	Also controlled for age, gender, behavior of CD, smoking, previous resections, blood transfusions, surgical approach and type of anastomosis
Assessment of outcome	Low risk	Data was obtained from a prospectively maintained database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Patients with insuffi ci ent data for analysis were excluded

Yu 2019

Study characteristics	
Methods	Retrospective cohort. Study period 2006 to 2015
Participants	Country: Korea. Patients with Crohn's disease who underwent bowel resection with or without anastomosis or strictureplasty. Patients excluded if they had open biopsy or stoma formation/reversal only
Interventions	1. Preoperative steroids (n= 39) 2. Preoperative immunomodulators (azathioprine, 6MP, methotrexate) (n= 211) 3. Preoperative anti-TNF medications within 8 weeks of surgery (n= 32)
Outcomes	30 day infectious and non-infectious postoperative complications. Infectious complications include intra-abdominal sepsis, enterocutaneous fistula, wound infection and extra-abdominal infection
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	Patients with Crohn's disease who underwent bowel resection with or without anastomosis or strictureplasty.
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records reviewed

Yu 2019 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Medical records reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Zittan 2016

Study characteristics	
Methods	Retrospective cohort. Study period: 2002 to 2013
Participants	Country: Canada. UC patients who underwent IPAA. Patients with less than 30 days of follow up data were excluded. Patients without adequate clinical documentation of the 30 day postoperative period were excluded
Interventions	1. Preoperative anti-TNF therapy (n= 196) within 180 days of surgery 2. No preoperative anti-TNF therapy (n= 562)
Outcomes	Pelvic abcess, anastomotic leak, and wound infection within 30 days of surgery
Notes	NOS very high risk of bias overall Adjusted OR for preoperative corticosteroid s was obtained from multivariable analysis.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent IPAA from 2002 to 2013
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical charts were reviewed

Zittan 2016 *(Continued)*

Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Medical charts were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Low risk	Patients without adequate clinical documentation of the 30 day postoperative period were excluded

Ziv 1996

Study characteristics	
Methods	Retrospective cohort. Study period: 1983 to 1992
Participants	Country: USA. UC patients who underwent IPAA
Interventions	1. Preoperative steroids (n= 361) 2. No preoperative steroids (n= 310)
Outcomes	Sepsis, anastomotic leak, fistula, parapouch abscess within 30 days of surgery
Notes	NOS very high risk of bias overall

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	UC patients who underwent IPAA from 1983 to 1992
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Medical records were reviewed
Demonstration that outcome of interest was not present at start of study	Unclear risk	Information not provided

Ziv 1996 *(Continued)*

Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Univariate analysis
Comparability of cohorts (Controlled for additional factor)	High risk	Univariate analysis
Assessment of outcome	Low risk	Medical records were reviewed
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

Zuo 2014

Study characteristics	
Methods	Retrospective cohort. Study period: 1999 to 2004
Participants	Country: China. CD who underwent abdominal surgery. Patients with intestinal TB, gastrointestinal malignancy, Behcet's or who underwent perianal surgery were excluded
Interventions	1. Preoperative steroids (n= 32) 2. No preoperative steroids (n= 684)
Outcomes	Intraabdominal abscess, fistula, anastomotic leak within 30 days
Notes	NOS low risk of bias overall Adjusted OR for preoperative corticosteroids was obtained from multivariate analysis.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Representativeness of the exposed cohort	Low risk	CD who underwent abdominal surgery from 1999 to 2004
Selection of the non exposed cohort	Low risk	Both groups obtained from the same hospital and time period
Ascertainment of exposure	Low risk	Data extracted from hospital database
Demonstration that outcome of interest was not present at start of study	High risk	Proportion of patients were found to have abscesses at the time of surgery
Comparability of cohorts (Controlled for critical factor/other medications)	High risk	Did not control for other medications

Zuo 2014 *(Continued)*

Comparability of cohorts (Controlled for additional factor)	Low risk	Controlled for preoperative albumin, CRP, enteral nutrition, preoperative infection, ostomy, resection and anastomosis
Assessment of outcome	Low risk	Data extracted from hospital database
Was follow-up long enough for outcomes to occur	Low risk	30 days
Adequacy of follow up of cohorts	Unclear risk	Information not provided

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

Study	Reason for exclusion
Abelson 2018	Compared rates of surgical complications in IBD patients who underwent surgery between 1995 and 2005 vs 2005 and 2013. Did not compare preoperative medications.
Abou-Khalil 2016	Studied patients with CD who were treated with immunosuppressants compared with those who were not. Authors clarified that the immunosuppressant group included patients treated with any of the following: mycophenolate mofetil, adalimumab, etanercept, azathioprine, cyclosporine, tacrolimus, sirolimus, infliximab, natalizumab, methotrexate and certolizumab pegol.
Achkasov 2015	Reported combined outcome of surgical site infection and parastomal complications. Unable to contact authors to obtain rate of only the infectious complications.
Adegbola 2018	Reported rates of intra-abdominal septic complications in IBD patients who underwent ileocolonic resection. Did not report pre-operative medications in patients who developed septic complications and those who did not develop septic complications. Unable to contact author for more information.
Aelvoet 2016	Compared patients treated with vedolizumab to those treated with infliximab.
Andrew 2017	Infectious outcomes were collected within the first 60 postoperative days.
Bafford 2013	Reported overall postoperative complications and not specifically infectious complications. Unable to contact authors for additional information.
Balachandran 2015	Recorded complications occurring within 3 months of surgery.
Benichou 2018	Did not specify number of patients with postoperative infections who were treated with and without anti-TNF agents.
Bewtra 2013	Recorded complications occurring within 90 days of surgery.
Braun 2018	Did not report postoperative infectious complications.
Bruewer 2003	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Chaparro 2018	Described characteristics and indications for surgical interventions. Did not report postoperative complications.

Study	Reason for exclusion
Chiplunker 2015	No comparison group
Coscia 2012	Reported overall postoperative complications. Unable to contact authors to obtain rate of infectious complications.
Desai 2012	Postoperative infection was a secondary outcome but results were not reported in the abstract. Unable to obtain information from authors.
De Silva 2011	Complications were recorded from time of surgery to time of discharge from hospital. Range or mean length of stay in hospital was not reported. While infectious complications were reported, patients' medications were not specified. Unable to contact authors.
Domenech 2016	No comparison group.
Eisner 2014	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Fronda 1999	Did not specifically report infectious complications.
Fu 2014	Study did not compare rates of postoperative infection in IBD patients treated with different medications
Gamaleldin 2018	Did not report postoperative infections
George 2017	Included patients who did not have a diagnosis of IBD
Gonzalez 2013	Did not report postoperative infections
Grant 2019	Reported rates of wound healing following proctectomy but not postoperative infectious complications.
Gregory 2019	Reported 90 day postoperative infectious complications.
Heimann 1985	Reported postoperative infections but did not report how many of these patients were treated with steroids and how many were not treated with steroids. Unable to contact authors for confirmation.
Hyde 2001	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Justiniano 2019	Only reported postoperative mortality.
Kamel 2019	Reported effect of biologic agents on operative outcomes (length of small bowel resection, intraoperative blood loss and total operative time) but not postoperative infectious complications.
Kasparek 2012	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Kimura 2019	Did not provide rates of postoperative infectious complications for each category of preoperative medication.
Kline 2020	Did not examine relationship between preoperative medications and postoperative infectious complications.
Kotze 2011	Patient population included in Kotze 2017.
Kotze 2017a	Patient population included in Kotze 2017.

Study	Reason for exclusion
Kotze 2018	Comparison group included patients without IBD
Krupa 2012	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Kulaylat 2017	Recorded complications occurring within 90 days of surgery.
Labidi 2018	There was no comparison group.
Lau 2013	Reported rates of postoperative infection in a graph, which was illegible. Unable to contact authors for additional information.
Li 2016	Reported overall postoperative complications but not specifically infectious complications.
Lightner 2017	Significant overlap with patients in Lightner 2018.
Lightner 2017a	Compared vedolizumab treated patients to anti-TNF treated patients.
Lightner 2018a	Compared patients treated with ustekinumab to patients treated with anti-TNF medications.
Lightner 2018b	Compared patients treated with vedolizumab to patients treated with anti-TNF medications.
Lim 2018	Reported surgical trends over time. Did not examine relationship between preoperative medications and postoperative infectious complications.
Melo-Pinto 2018	Reported overall postoperative complications but not specifically infectious complications.
Monsinjon 2017	Reported overall postoperative complications but not specifically infectious complications.
Nagao 2016	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Novello 2019	Compared patients treated with ustekinumab to patients treated with vedolizumab.
Oh 2014	Mentioned that the rate of infectious complications was similar between treatment and comparison groups but did not actually report the rate. Unable to contact authors for additional information.
Park 2018	Compared patients treated with ustekinumab to patients treated with vedolizumab.
Parrish 2019	Did not compare different preoperative medications. Compared patients treated with ustekinumab with detectable levels before surgery to patients treated with ustekinumab with undetectable levels.
Poylin 2018	Compared patients treated with vedolizumab to those treated with an anti-TNF agent.
Quade 2013	Reported overall postoperative complications but not specifically infectious complications.
Rizvi 2019	Reported postoperative infectious complications up to 6 months after surgery.
Sahami 2016	Did not specify time frame for postoperative complications. Unable to contact authors for confirmation.
Scarpa 2015	Reported overall postoperative complications but not specifically infectious complications.

Study	Reason for exclusion
Shim 2018	Compared patients treated with ustekinumab to patients treated with anti-TNF medications.
Shimada 2016	Did not specify time frame for postoperative complications or rate of complications in the comparison group. Unable to contact authors for confirmation.
Stewart 2009	Reported infectious complications in a group of patients on some form of immunosuppression such as infliximab, cyclosporine, prednisone, or azathioprine. Contacted authors for separate rates of infectious complications in patients treated with each of these medications. However, the authors were unable to obtain this data.
Strassle 2017	Included patients with ulcerative colitis, Crohn's disease, or familial adenomatous polyposis.
Stringfield 2016	Lacked a comparison group.
Valizadeh 2017	Reported infectious complications in patients treated with either immunosuppressant medications or steroids. Did not analyse each type of medications separately.
Watson 2018	Reports rates of any postoperative complication but not specifically infectious complications.
Weber 2017	Did not report postoperative infectious complications.
Yamamoto 2016a	Stated that neither immunosuppressive nor biologic therapy prior to surgery was significantly associated with the incidence of septic complications. Also stated that high dose steroid therapy significantly increased the risk of septic complications. Did not report any rates, odd ratio or risk ratio. Unable to contact author for additional information.
Yamamoto 2018	Included patients treated with either anti-TNF medication or tacrolimus into one group in their analysis.

DATA AND ANALYSES

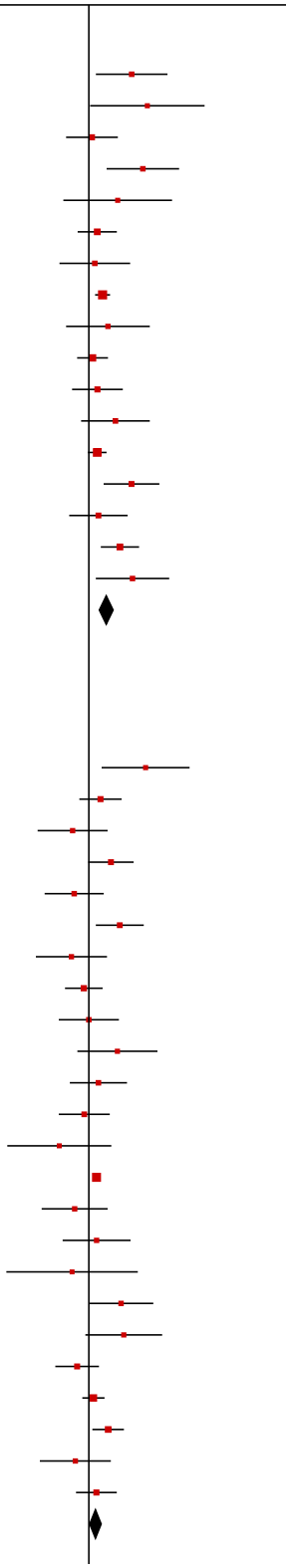
Comparison 1. Corticosteroids versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Postoperative infection within 30 days of surgery	41		Odds Ratio (IV, Random, 95% CI)	Subtotals only
1.1.1 Adjusted Analysis	17		Odds Ratio (IV, Random, 95% CI)	1.70 [1.38, 2.09]
1.1.2 Unadjusted Analysis	24		Odds Ratio (IV, Random, 95% CI)	1.22 [1.03, 1.45]
1.2 Postoperative infection within 30 days of surgery: subgroup UC vs CD	33		Odds Ratio (IV, Random, 95% CI)	1.36 [1.18, 1.57]
1.2.1 Ulcerative colitis	11		Odds Ratio (IV, Random, 95% CI)	1.49 [1.10, 2.02]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2.2 Crohn's disease	23		Odds Ratio (IV, Random, 95% CI)	1.32 [1.11, 1.57]
1.3 Postoperative infection within 30 days of surgery: subgroup pre 1998 versus 1998 or after	15		Odds Ratio (IV, Random, 95% CI)	1.72 [1.37, 2.16]
1.3.1 Pre 1998	2		Odds Ratio (IV, Random, 95% CI)	4.22 [1.67, 10.64]
1.3.2 1998 or after	13		Odds Ratio (IV, Random, 95% CI)	1.62 [1.30, 2.01]
1.4 Incisional infections and wound dehiscence	7		Odds Ratio (IV, Random, 95% CI)	1.41 [0.72, 2.74]
1.5 Intra-abdominal infectious complications	28		Odds Ratio (IV, Random, 95% CI)	1.53 [1.28, 1.84]
1.6 Extra-abdominal infections	4		Odds Ratio (IV, Random, 95% CI)	1.23 [0.97, 1.55]
1.7 Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias	15		Odds Ratio (IV, Random, 95% CI)	1.43 [1.13, 1.81]
1.8 Postoperative infection within 30 days of surgery: sensitivity exclude abstract	36		Odds Ratio (IV, Random, 95% CI)	1.48 [1.28, 1.72]
1.9 Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess	21		Odds Ratio (IV, Random, 95% CI)	1.37 [1.14, 1.65]
1.9.1 Adjusted Analysis	9		Odds Ratio (IV, Random, 95% CI)	1.79 [1.35, 2.38]
1.9.2 Unadjusted Analysis	12		Odds Ratio (IV, Random, 95% CI)	1.07 [0.81, 1.40]

Analysis 1.1. Comparison 1: Corticosteroids versus control, Outcome 1: Postoperative infection within 30 days of surgery

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.1.1 Adjusted Analysis				
Aberra 2003	1.3056	0.5564	3.1%	3.69 [1.24 , 10.98]
Alves 2007	1.7834	0.8899	1.3%	5.95 [1.04 , 34.04]
Appau 2008	0.0953	0.4023	5.3%	1.10 [0.50 , 2.42]
Ferrante 2009	1.6467	0.5635	3.1%	5.19 [1.72 , 15.66]
Gainsbury 2011 (1)	0.8796	0.845	1.5%	2.41 [0.46 , 12.63]
Krane 2013	0.2562	0.3047	7.8%	1.29 [0.71 , 2.35]
Kunitake 2008	0.1823	0.5494	3.2%	1.20 [0.41 , 3.52]
Liang 2017	0.4187	0.1164	17.3%	1.52 [1.21 , 1.91]
McKenna 2018	0.5822	0.6507	2.4%	1.79 [0.50 , 6.41]
Mor 2008	0.1133	0.2398	10.4%	1.12 [0.70 , 1.79]
Selvasekar 2007	0.2624	0.3945	5.5%	1.30 [0.60 , 2.82]
Serradori 2013	0.8109	0.534	3.4%	2.25 [0.79 , 6.41]
Shaib 2017	0.2546	0.1455	15.5%	1.29 [0.97 , 1.72]
Yamada 2017	1.3002	0.4332	4.7%	3.67 [1.57 , 8.58]
Yamamoto 2016	0.2927	0.4543	4.4%	1.34 [0.55 , 3.26]
Zittan 2016	0.9478	0.2975	8.1%	2.58 [1.44 , 4.62]
Zuo 2014	1.331	0.5706	3.0%	3.78 [1.24 , 11.58]
Subtotal (95% CI)			**100.0%**	**1.70 [1.38 , 2.09]**
Heterogeneity: Tau² = 0.05; Chi² = 24.52, df = 16 (P = 0.08); I² = 35%				
Test for overall effect: Z = 4.97 (P < 0.00001)				
1.1.2 Unadjusted Analysis				
Bregnbak 2012	1.7301	0.6836	1.5%	5.64 [1.48 , 21.54]
Colombel 2004	0.3554	0.3289	5.1%	1.43 [0.75 , 2.72]
De Buck Van Overstraeten 2017	-0.4943	0.5441	2.3%	0.61 [0.21 , 1.77]
El-Hussuna 2012	0.6741	0.353	4.6%	1.96 [0.98 , 3.92]
Ferrante 2017	-0.4463	0.4596	3.1%	0.64 [0.26 , 1.58]
Fumery 2017	0.9433	0.3727	4.3%	2.57 [1.24 , 5.33]
Guo 2017	-0.5306	0.5529	2.2%	0.59 [0.20 , 1.74]
Jouvin 2018	-0.1534	0.2925	6.0%	0.86 [0.48 , 1.52]
Lightner 2018 B	0	0.4675	3.0%	1.00 [0.40 , 2.50]
Morar 2015	0.8709	0.6226	1.8%	2.39 [0.71 , 8.09]
Myrelid 2009	0.2919	0.4443	3.2%	1.34 [0.56 , 3.20]
Myrelid 2014	-0.1393	0.3965	3.9%	0.87 [0.40 , 1.89]
Nasir 2010	-0.9001	0.8089	1.1%	0.41 [0.08 , 1.98]
Nguyen 2014	0.2339	0.0448	16.9%	1.26 [1.16 , 1.38]
Regadas 2011	-0.4318	0.5131	2.5%	0.65 [0.24 , 1.78]
Rizzo 2011	0.2364	0.5279	2.4%	1.27 [0.45 , 3.56]
Schils 2017	-0.5108	1.022	0.7%	0.60 [0.08 , 4.45]
Tzivanakis 2012	0.9821	0.5011	2.6%	2.67 [1.00 , 7.13]
Uchino 2015	1.0647	0.597	1.9%	2.90 [0.90 , 9.34]
Uchino 2019	-0.3567	0.3393	4.9%	0.70 [0.36 , 1.36]
Wilson 2014	0.1398	0.1726	10.6%	1.15 [0.82 , 1.61]
Yamamoto 2000	0.5884	0.2452	7.5%	1.80 [1.11 , 2.91]
Yu 2019	-0.4112	0.5519	2.2%	0.66 [0.22 , 1.96]
Ziv 1996	0.2303	0.3169	5.4%	1.26 [0.68 , 2.34]
Subtotal (95% CI)			**100.0%**	**1.22 [1.03 , 1.45]**
Heterogeneity: Tau² = 0.04; Chi² = 35.04, df = 23 (P = 0.05); I² = 34%				

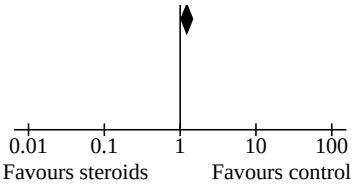


Analysis 1.1. (Continued)

Subtotal (95% CI)	**100.0%**	**1.22 [1.03 , 1.45]**

Heterogeneity: Tau² = 0.04; Chi² = 35.04, df = 23 (P = 0.05); I² = 34%

Test for overall effect: Z = 2.28 (P = 0.02)

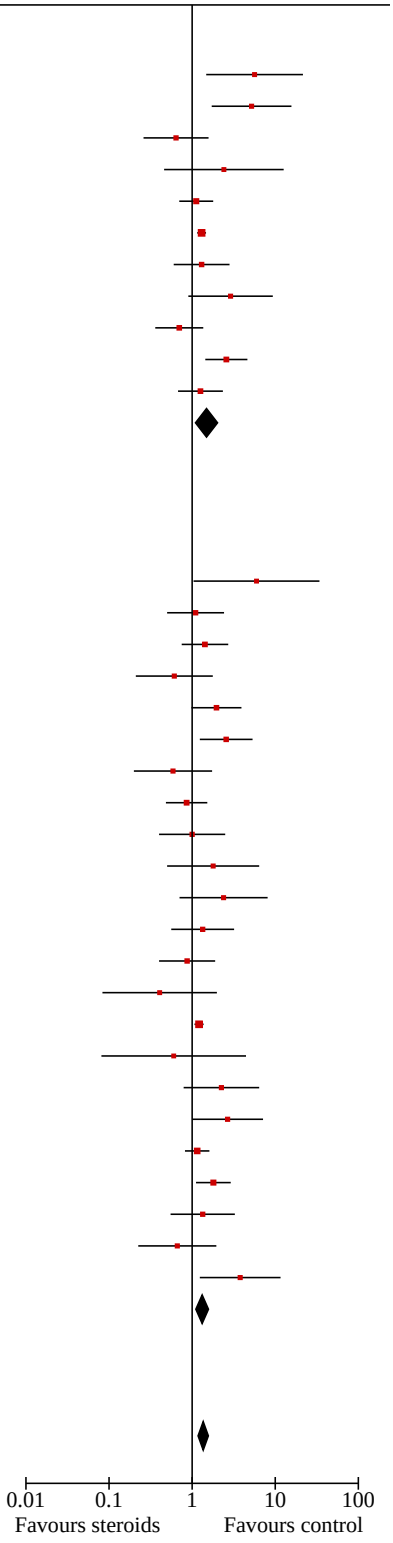


Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

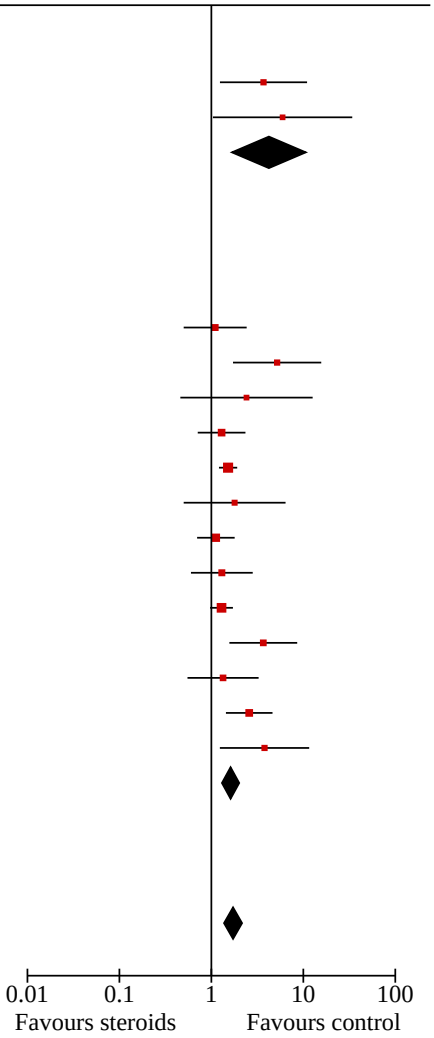
Analysis 1.2. Comparison 1: Corticosteroids versus control, Outcome 2: Postoperative infection within 30 days of surgery: subgroup UC vs CD

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.2.1 Ulcerative colitis				
Bregnbak 2012	1.7301	0.6836	1.0%	5.64 [1.48 , 21.54]
Ferrante 2009	1.6467	0.5635	1.5%	5.19 [1.72 , 15.66]
Ferrante 2017	-0.4463	0.4596	2.1%	0.64 [0.26 , 1.58]
Gainsbury 2011	0.8796	0.845	0.7%	2.41 [0.46 , 12.63]
Mor 2008	0.1133	0.2398	5.3%	1.12 [0.70 , 1.79]
Nguyen 2014	0.2623	0.0626	11.5%	1.30 [1.15 , 1.47]
Selvasekar 2007	0.2624	0.3945	2.7%	1.30 [0.60 , 2.82]
Uchino 2015	1.0647	0.597	1.3%	2.90 [0.90 , 9.34]
Uchino 2019	-0.3567	0.3393	3.3%	0.70 [0.36 , 1.36]
Zittan 2016	0.9478	0.2975	4.0%	2.58 [1.44 , 4.62]
Ziv 1996	0.2303	0.3169	3.7%	1.26 [0.68 , 2.34]
Subtotal (95% CI)			**37.1%**	**1.49 [1.10 , 2.02]**
Heterogeneity: Tau² = 0.12; Chi² = 24.26, df = 10 (P = 0.007); I² = 59%				
Test for overall effect: Z = 2.56 (P = 0.01)				
1.2.2 Crohn's disease				
Alves 2007	1.7834	0.8899	0.6%	5.95 [1.04 , 34.04]
Appau 2008	0.0953	0.4023	2.6%	1.10 [0.50 , 2.42]
Colombel 2004	0.3554	0.3289	3.5%	1.43 [0.75 , 2.72]
De Buck Van Overstraeten 2017	-0.4943	0.5441	1.6%	0.61 [0.21 , 1.77]
El-Hussuna 2012	0.6741	0.353	3.2%	1.96 [0.98 , 3.92]
Fumery 2017	0.9433	0.3727	2.9%	2.57 [1.24 , 5.33]
Guo 2017	-0.5306	0.5529	1.5%	0.59 [0.20 , 1.74]
Jouvin 2018	-0.1534	0.2925	4.1%	0.86 [0.48 , 1.52]
Lightner 2018 B	0	0.4675	2.0%	1.00 [0.40 , 2.50]
McKenna 2018	0.5822	0.6507	1.1%	1.79 [0.50 , 6.41]
Morar 2015	0.8709	0.6226	1.2%	2.39 [0.71 , 8.09]
Myrelid 2009	0.2919	0.4443	2.2%	1.34 [0.56 , 3.20]
Myrelid 2014	-0.1393	0.3965	2.6%	0.87 [0.40 , 1.89]
Nasir 2010	-0.9001	0.8089	0.8%	0.41 [0.08 , 1.98]
Nguyen 2014	0.1908	0.0645	11.5%	1.21 [1.07 , 1.37]
Schils 2017	-0.5108	1.022	0.5%	0.60 [0.08 , 4.45]
Serradori 2013	0.8109	0.534	1.6%	2.25 [0.79 , 6.41]
Tzivanakis 2012	0.9821	0.5011	1.8%	2.67 [1.00 , 7.13]
Wilson 2014	0.1398	0.1726	7.3%	1.15 [0.82 , 1.61]
Yamamoto 2000	0.5884	0.2452	5.2%	1.80 [1.11 , 2.91]
Yamamoto 2016	0.2927	0.4543	2.1%	1.34 [0.55 , 3.26]
Yu 2019	-0.4112	0.5519	1.5%	0.66 [0.22 , 1.96]
Zuo 2014	1.331	0.5706	1.4%	3.78 [1.24 , 11.58]
Subtotal (95% CI)			**62.9%**	**1.32 [1.11 , 1.57]**
Heterogeneity: Tau² = 0.04; Chi² = 30.19, df = 22 (P = 0.11); I² = 27%				
Test for overall effect: Z = 3.12 (P = 0.002)				
Total (95% CI)			**100.0%**	**1.36 [1.18 , 1.57]**
Heterogeneity: Tau² = 0.04; Chi² = 55.01, df = 33 (P = 0.009); I² = 40%				
Test for overall effect: Z = 4.23 (P < 0.0001)				
Test for subgroup differences: Chi² = 0.46, df = 1 (P = 0.50), I² = 0%				



Analysis 1.3. Comparison 1: Corticosteroids versus control, Outcome 3: Postoperative infection within 30 days of surgery: subgroup pre 1998 versus 1998 or after

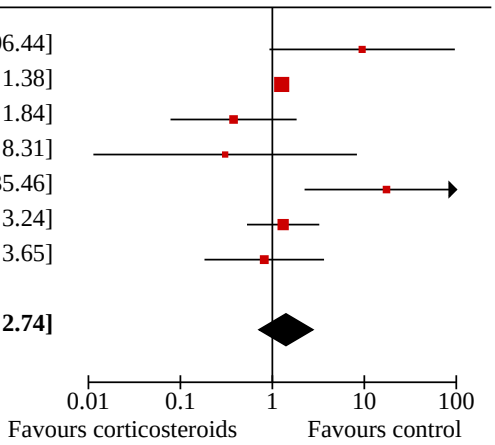
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.3.1 Pre 1998				
Aberra 2003	1.3056	0.5564	3.6%	3.69 [1.24 , 10.98]
Alves 2007	1.7834	0.8899	1.6%	5.95 [1.04 , 34.04]
Subtotal (95% CI)			**5.1%**	**4.22 [1.67 , 10.64]**
Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.65); I² = 0%				
Test for overall effect: Z = 3.05 (P = 0.002)				
1.3.2 1998 or after				
Appau 2008	0.0953	0.4023	5.9%	1.10 [0.50 , 2.42]
Ferrante 2009	1.6467	0.5635	3.5%	5.19 [1.72 , 15.66]
Gainsbury 2011	0.8796	0.845	1.7%	2.41 [0.46 , 12.63]
Krane 2013	0.2562	0.3047	8.5%	1.29 [0.71 , 2.35]
Liang 2017	0.4187	0.1164	17.3%	1.52 [1.21 , 1.91]
McKenna 2018	0.5822	0.6507	2.7%	1.79 [0.50 , 6.41]
Mor 2008	0.1133	0.2398	11.0%	1.12 [0.70 , 1.79]
Selvasekar 2007	0.2624	0.3945	6.1%	1.30 [0.60 , 2.82]
Shaib 2017	0.2546	0.1455	15.7%	1.29 [0.97 , 1.72]
Yamada 2017	1.3002	0.4332	5.3%	3.67 [1.57 , 8.58]
Yamamoto 2016	0.2927	0.4543	4.9%	1.34 [0.55 , 3.26]
Zittan 2016	0.9478	0.2975	8.8%	2.58 [1.44 , 4.62]
Zuo 2014	1.331	0.5706	3.4%	3.78 [1.24 , 11.58]
Subtotal (95% CI)			**94.9%**	**1.62 [1.30 , 2.01]**
Heterogeneity: Tau² = 0.05; Chi² = 19.03, df = 12 (P = 0.09); I² = 37%				
Test for overall effect: Z = 4.36 (P < 0.0001)				
Total (95% CI)			**100.0%**	**1.72 [1.37 , 2.16]**
Heterogeneity: Tau² = 0.06; Chi² = 23.82, df = 14 (P = 0.05); I² = 41%				
Test for overall effect: Z = 4.71 (P < 0.00001)				
Test for subgroup differences: Chi² = 3.92, df = 1 (P = 0.05), I² = 74.5%				



Analysis 1.4. Comparison 1: Corticosteroids versus control, Outcome 4: Incisional infections and wound dehiscence

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Gainsbury 2011	2.2481	1.1841	6.7%	9.47 [0.93 , 96.44]
Nguyen 2014	0.2339	0.0448	35.2%	1.26 [1.16 , 1.38]
Regadas 2011	-0.9714	0.8054	11.9%	0.38 [0.08 , 1.84]
Schils 2017	-1.182	1.6833	3.7%	0.31 [0.01 , 8.31]
Uchino 2015	2.8576	1.0465	8.2%	17.42 [2.24 , 135.46]
Uchino 2019	0.27	0.4617	21.5%	1.31 [0.53 , 3.24]
Yu 2019	-0.2027	0.7636	12.8%	0.82 [0.18 , 3.65]
Total (95% CI)			**100.0%**	**1.41 [0.72 , 2.74]**

Heterogeneity: Tau² = 0.33; Chi² = 12.46, df = 6 (P = 0.05); I² = 52%
Test for overall effect: Z = 1.00 (P = 0.32)
Test for subgroup differences: Not applicable



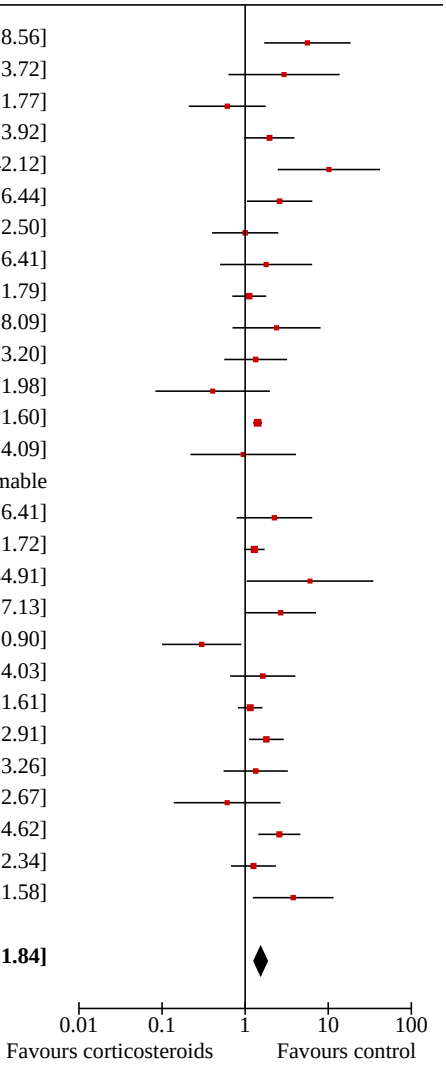
Analysis 1.5. Comparison 1: Corticosteroids versus control, Outcome 5: Intra-abdominal infectious complications

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Alves 2007	1.7254	0.6099	2.0%	5.61 [1.70 , 18.56]
Appau 2008	1.0784	0.786	1.3%	2.94 [0.63 , 13.72]
De Buck Van Overstraeten 2017	-0.4943	0.5441	2.4%	0.61 [0.21 , 1.77]
El-Hussuna 2012	0.6741	0.353	4.5%	1.96 [0.98 , 3.92]
Ferrante 2009	2.3224	0.7236	1.5%	10.20 [2.47 , 42.12]
Fumery 2017	0.9555	0.4626	3.1%	2.60 [1.05 , 6.44]
Lightner 2018 B	0	0.4675	3.0%	1.00 [0.40 , 2.50]
McKenna 2018	0.5822	0.6507	1.8%	1.79 [0.50 , 6.41]
Mor 2008	0.1133	0.2398	6.9%	1.12 [0.70 , 1.79]
Morar 2015	0.8709	0.6226	1.9%	2.39 [0.71 , 8.09]
Myrelid 2009	0.2919	0.4443	3.3%	1.34 [0.56 , 3.20]
Nasir 2010	-0.9001	0.8089	1.2%	0.41 [0.08 , 1.98]
Nguyen 2014	0.3457	0.0636	11.8%	1.41 [1.25 , 1.60]
Regadas 2011	-0.0536	0.7463	1.4%	0.95 [0.22 , 4.09]
Schils 2017	0	0		Not estimable
Serradori 2013	0.8109	0.534	2.5%	2.25 [0.79 , 6.41]
Shaib 2017	0.2546	0.1455	9.6%	1.29 [0.97 , 1.72]
Shwaartz 2016	1.7984	0.8951	1.0%	6.04 [1.05 , 34.91]
Tzivanakis 2012	0.9821	0.5011	2.7%	2.67 [1.00 , 7.13]
Uchino 2015	-1.204	0.5605	2.3%	0.30 [0.10 , 0.90]
Uchino 2019	0.4886	0.4613	3.1%	1.63 [0.66 , 4.03]
Wilson 2014	0.1398	0.1726	8.8%	1.15 [0.82 , 1.61]
Yamamoto 2000	0.5884	0.2452	6.7%	1.80 [1.11 , 2.91]
Yamamoto 2016	0.2927	0.4543	3.2%	1.34 [0.55 , 3.26]
Yu 2019	-0.4983	0.7554	1.4%	0.61 [0.14 , 2.67]
Zittan 2016	0.9478	0.2975	5.5%	2.58 [1.44 , 4.62]
Ziv 1996	0.2303	0.3169	5.1%	1.26 [0.68 , 2.34]
Zuo 2014	1.331	0.5706	2.2%	3.78 [1.24 , 11.58]
Total (95% CI)			**100.0%**	**1.53 [1.28 , 1.84]**

Heterogeneity: Tau² = 0.07; Chi² = 47.37, df = 26 (P = 0.006); I² = 45%

Test for overall effect: Z = 4.58 (P < 0.00001)

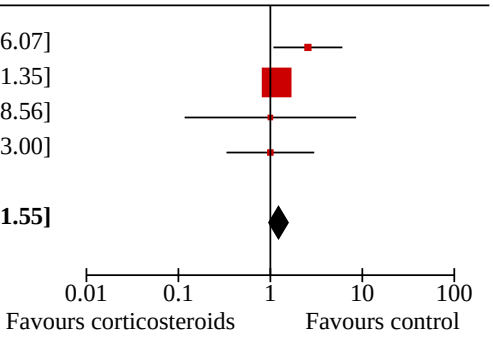
Test for subgroup differences: Not applicable



Analysis 1.6. Comparison 1: Corticosteroids versus control, Outcome 6: Extra-abdominal infections

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Fumery 2017	0.94	0.4403	7.1%	2.56 [1.08 , 6.07]
Nguyen 2014	0.157	0.0712	87.3%	1.17 [1.02 , 1.35]
Schils 2017	0	1.0954	1.2%	1.00 [0.12 , 8.56]
Yu 2019	0	0.5605	4.5%	1.00 [0.33 , 3.00]
Total (95% CI)			**100.0%**	**1.23 [0.97 , 1.55]**

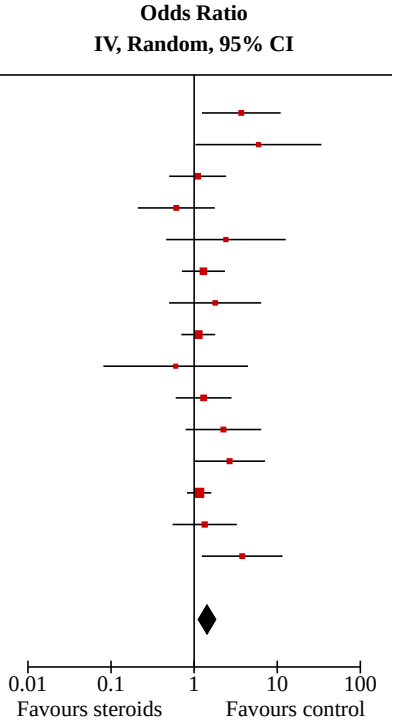
Heterogeneity: Tau² = 0.01; Chi² = 3.21, df = 3 (P = 0.36); I² = 6%
Test for overall effect: Z = 1.69 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1: Corticosteroids versus control, Outcome 7: Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aberra 2003	1.3056	0.5564	4.2%	3.69 [1.24 , 10.98]
Alves 2007	1.7834	0.8899	1.8%	5.95 [1.04 , 34.04]
Appau 2008	0.0953	0.4023	7.4%	1.10 [0.50 , 2.42]
De Buck Van Overstraeten 2017	-0.4943	0.5441	4.4%	0.61 [0.21 , 1.77]
Gainsbury 2011	0.8796	0.845	2.0%	2.41 [0.46 , 12.63]
Krane 2013	0.2562	0.3047	11.3%	1.29 [0.71 , 2.35]
McKenna 2018	0.5822	0.6507	3.2%	1.79 [0.50 , 6.41]
Mor 2008	0.1133	0.2398	15.4%	1.12 [0.70 , 1.79]
Schils 2017	-0.5108	1.022	1.4%	0.60 [0.08 , 4.45]
Selvasekar 2007	0.2624	0.3945	7.6%	1.30 [0.60 , 2.82]
Serradori 2013	0.8109	0.534	4.6%	2.25 [0.79 , 6.41]
Tzivanakis 2012	0.9821	0.5011	5.1%	2.67 [1.00 , 7.13]
Wilson 2014	0.1398	0.1726	21.7%	1.15 [0.82 , 1.61]
Yamamoto 2016	0.2927	0.4543	6.0%	1.34 [0.55 , 3.26]
Zuo 2014	1.331	0.5706	4.0%	3.78 [1.24 , 11.58]
Total (95% CI)			**100.0%**	**1.43 [1.13 , 1.81]**

Heterogeneity: Tau² = 0.04; Chi² = 17.25, df = 14 (P = 0.24); I² = 19%
Test for overall effect: Z = 2.93 (P = 0.003)
Test for subgroup differences: Not applicable



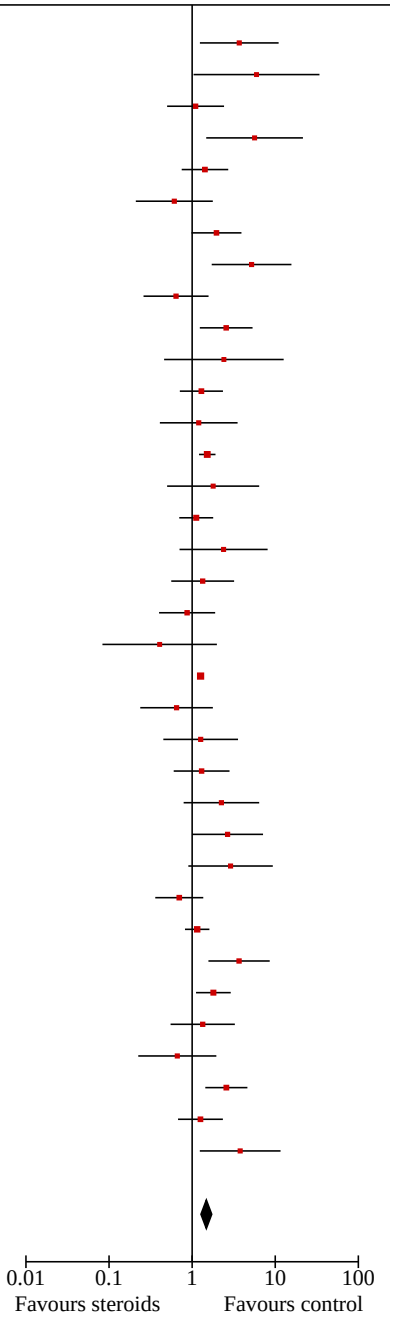
Analysis 1.8. Comparison 1: Corticosteroids versus control, Outcome 8: Postoperative infection within 30 days of surgery: sensitivity exclude abstract

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aberra 2003	1.3056	0.5564	1.6%	3.69 [1.24 , 10.98]
Alves 2007	1.7834	0.8899	0.7%	5.95 [1.04 , 34.04]
Appau 2008	0.0953	0.4023	2.6%	1.10 [0.50 , 2.42]
Bregnbak 2012	1.7301	0.6836	1.1%	5.64 [1.48 , 21.54]
Colombel 2004	0.3554	0.3289	3.5%	1.43 [0.75 , 2.72]
De Buck Van Overstraeten 2017	-0.4943	0.5441	1.6%	0.61 [0.21 , 1.77]
El-Hussuna 2012	0.6741	0.353	3.2%	1.96 [0.98 , 3.92]
Ferrante 2009	1.6467	0.5635	1.5%	5.19 [1.72 , 15.66]
Ferrante 2017	-0.4463	0.4596	2.2%	0.64 [0.26 , 1.58]
Fumery 2017	0.9433	0.3727	2.9%	2.57 [1.24 , 5.33]
Gainsbury 2011	0.8796	0.845	0.7%	2.41 [0.46 , 12.63]
Krane 2013	0.2562	0.3047	3.9%	1.29 [0.71 , 2.35]
Kunitake 2008	0.1823	0.5494	1.6%	1.20 [0.41 , 3.52]
Liang 2017	0.4187	0.1164	8.2%	1.52 [1.21 , 1.91]
McKenna 2018	0.5822	0.6507	1.2%	1.79 [0.50 , 6.41]
Mor 2008	0.1133	0.2398	5.1%	1.12 [0.70 , 1.79]
Morar 2015	0.8709	0.6226	1.3%	2.39 [0.71 , 8.09]
Myrelid 2009	0.2919	0.4443	2.3%	1.34 [0.56 , 3.20]
Myrelid 2014	-0.1393	0.3965	2.7%	0.87 [0.40 , 1.89]
Nasir 2010	-0.9001	0.8089	0.8%	0.41 [0.08 , 1.98]
Nguyen 2014	0.2339	0.0448	9.8%	1.26 [1.16 , 1.38]
Regadas 2011	-0.4318	0.5131	1.8%	0.65 [0.24 , 1.78]
Rizzo 2011	0.2364	0.5279	1.7%	1.27 [0.45 , 3.56]
Selvasekar 2007	0.2624	0.3945	2.7%	1.30 [0.60 , 2.82]
Serradori 2013	0.8109	0.534	1.7%	2.25 [0.79 , 6.41]
Tzivanakis 2012	0.9821	0.5011	1.9%	2.67 [1.00 , 7.13]
Uchino 2015	1.0647	0.597	1.4%	2.90 [0.90 , 9.34]
Uchino 2019	-0.3567	0.3393	3.4%	0.70 [0.36 , 1.36]
Wilson 2014	0.1398	0.1726	6.7%	1.15 [0.82 , 1.61]
Yamada 2017	1.3002	0.4332	2.4%	3.67 [1.57 , 8.58]
Yamamoto 2000	0.5884	0.2452	4.9%	1.80 [1.11 , 2.91]
Yamamoto 2016	0.2927	0.4543	2.2%	1.34 [0.55 , 3.26]
Yu 2019	-0.4112	0.5519	1.6%	0.66 [0.22 , 1.96]
Zittan 2016	0.9478	0.2975	4.0%	2.58 [1.44 , 4.62]
Ziv 1996	0.2303	0.3169	3.7%	1.26 [0.68 , 2.34]
Zuo 2014	1.331	0.5706	1.5%	3.78 [1.24 , 11.58]
Total (95% CI)			**100.0%**	**1.48 [1.28 , 1.72]**

Heterogeneity: Tau² = 0.06; Chi² = 61.55, df = 35 (P = 0.004); I² = 43%

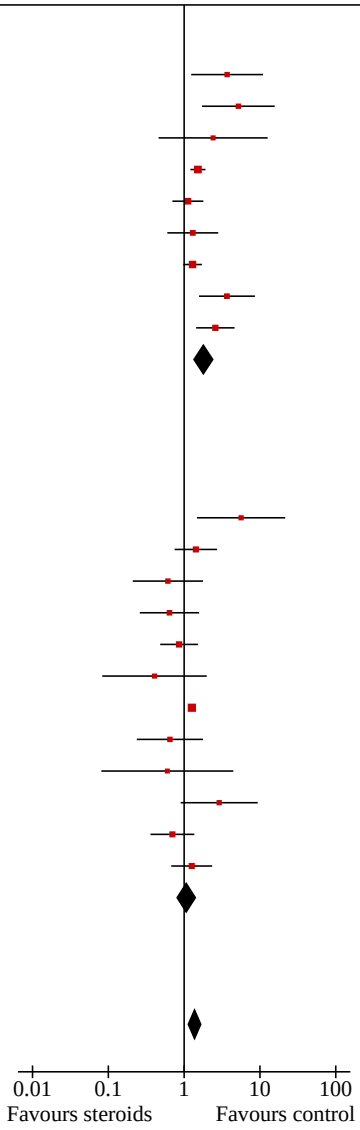
Test for overall effect: Z = 5.18 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 1.9. Comparison 1: Corticosteroids versus control, Outcome 9: Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.9.1 Adjusted Analysis				
Aberra 2003	1.3056	0.5564	2.5%	3.69 [1.24 , 10.98]
Ferrante 2009	1.6467	0.5635	2.4%	5.19 [1.72 , 15.66]
Gainsbury 2011 (1)	0.8796	0.845	1.2%	2.41 [0.46 , 12.63]
Liang 2017	0.4187	0.1164	11.7%	1.52 [1.21 , 1.91]
Mor 2008	0.1133	0.2398	7.5%	1.12 [0.70 , 1.79]
Selvasekar 2007	0.2624	0.3945	4.2%	1.30 [0.60 , 2.82]
Shaib 2017	0.2546	0.1455	10.6%	1.29 [0.97 , 1.72]
Yamada 2017	1.3002	0.4332	3.6%	3.67 [1.57 , 8.58]
Zittan 2016	0.9478	0.2975	6.0%	2.58 [1.44 , 4.62]
Subtotal (95% CI)			**49.6%**	**1.79 [1.35 , 2.38]**
Heterogeneity: Tau² = 0.08; Chi² = 17.85, df = 8 (P = 0.02); I² = 55%				
Test for overall effect: Z = 4.03 (P < 0.0001)				
1.9.2 Unadjusted Analysis				
Bregnbak 2012	1.7301	0.6836	1.7%	5.64 [1.48 , 21.54]
Colombel 2004	0.3554	0.3289	5.3%	1.43 [0.75 , 2.72]
De Buck Van Overstraeten 2017	-0.4943	0.5441	2.5%	0.61 [0.21 , 1.77]
Ferrante 2017	-0.4463	0.4596	3.3%	0.64 [0.26 , 1.58]
Jouvin 2018	-0.1534	0.2925	6.1%	0.86 [0.48 , 1.52]
Nasir 2010	-0.9001	0.8089	1.3%	0.41 [0.08 , 1.98]
Nguyen 2014	0.2339	0.0448	13.7%	1.26 [1.16 , 1.38]
Regadas 2011	-0.4318	0.5131	2.8%	0.65 [0.24 , 1.78]
Schils 2017	-0.5108	1.022	0.8%	0.60 [0.08 , 4.45]
Uchino 2015	1.0647	0.597	2.2%	2.90 [0.90 , 9.34]
Uchino 2019	-0.3567	0.3393	5.1%	0.70 [0.36 , 1.36]
Ziv 1996	0.2303	0.3169	5.6%	1.26 [0.68 , 2.34]
Subtotal (95% CI)			**50.4%**	**1.07 [0.81 , 1.40]**
Heterogeneity: Tau² = 0.08; Chi² = 19.47, df = 11 (P = 0.05); I² = 44%				
Test for overall effect: Z = 0.45 (P = 0.65)				
Total (95% CI)			**100.0%**	**1.37 [1.14 , 1.65]**
Heterogeneity: Tau² = 0.07; Chi² = 44.36, df = 20 (P = 0.001); I² = 55%				
Test for overall effect: Z = 3.29 (P = 0.001)				
Test for subgroup differences: Chi² = 6.66, df = 1 (P = 0.010), I² = 85.0%				



Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

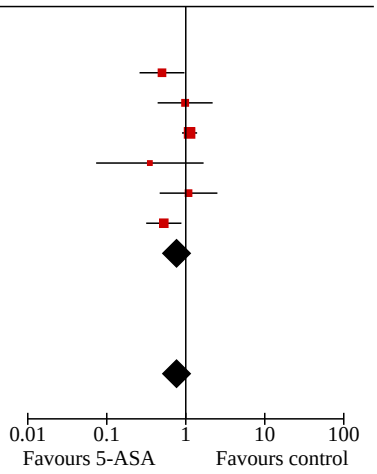
Comparison 2. 5-ASA versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Postoperative infection within 30 days of surgery	6	5030	Odds Ratio (IV, Random, 95% CI)	0.76 [0.51, 1.14]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1.1 Unadjusted Analysis	6	5030	Odds Ratio (IV, Random, 95% CI)	0.76 [0.51, 1.14]
2.2 Postoperative infection within 30 days of surgery: subgroup UC vs CD	5		Odds Ratio (IV, Random, 95% CI)	0.63 [0.45, 0.89]
2.2.1 Ulcerative colitis	1		Odds Ratio (IV, Random, 95% CI)	0.50 [0.26, 0.96]
2.2.2 Crohn's disease	4		Odds Ratio (IV, Random, 95% CI)	0.70 [0.45, 1.07]
2.3 Postoperative infection within 30 days of surgery: subgroup pre 1998 versus 1998 or after	6		Odds Ratio (IV, Random, 95% CI)	0.76 [0.51, 1.14]
2.3.1 Pre 1998	1		Odds Ratio (IV, Random, 95% CI)	1.08 [0.47, 2.51]
2.3.2 1998 or after	5		Odds Ratio (IV, Random, 95% CI)	0.71 [0.45, 1.14]
2.4 Incisional infections and wound dehiscence	1		Odds Ratio (IV, Random, 95% CI)	0.53 [0.30, 0.95]
2.5 Intra-abdominal infectious complications	3		Odds Ratio (IV, Random, 95% CI)	0.77 [0.45, 1.33]
2.6 Postoperative infection within 30 days of surgery: sensitivity exclude abstract	6		Odds Ratio (IV, Random, 95% CI)	0.76 [0.51, 1.14]
2.7 Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess	2		Odds Ratio (IV, Random, 95% CI)	0.79 [0.36, 1.73]
2.7.1 Unadjusted Analysis	2		Odds Ratio (IV, Random, 95% CI)	0.79 [0.36, 1.73]

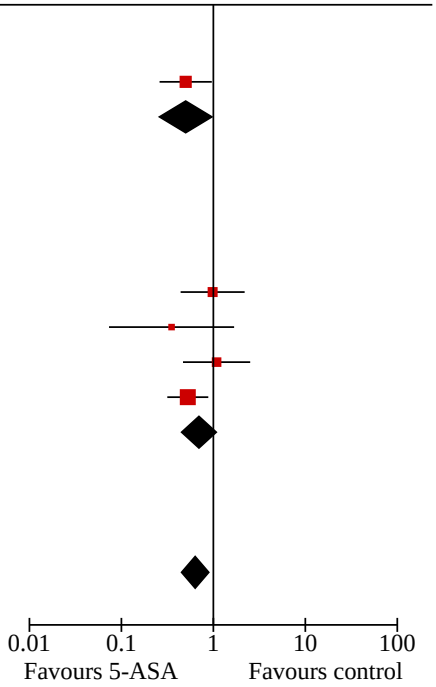
Analysis 2.1. Comparison 2: 5-ASA versus control, Outcome 1: Postoperative infection within 30 days of surgery

Study or Subgroup	log[OR]	SE	5-ASA Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI
2.1.1 Unadjusted Analysis						
Ferrante 2017	-0.6931	0.3336	97	73	17.2%	0.50 [0.26 , 0.96]
Guo 2017	-0.0184	0.4089	45	73	14.0%	0.98 [0.44 , 2.19]
Liang 2017	0.1112	0.1122	854	3015	29.3%	1.12 [0.90 , 1.39]
Morar 2015	-1.0463	0.7989	43	82	5.4%	0.35 [0.07 , 1.68]
Myrelid 2009	0.0809	0.4292	113	230	13.2%	1.08 [0.47 , 2.51]
Uchino 2013a	-0.6402	0.2618	322	83	21.0%	0.53 [0.32 , 0.88]
Subtotal (95% CI)			**1474**	**3556**	**100.0%**	**0.76 [0.51 , 1.14]**
Heterogeneity: Tau² = 0.13; Chi² = 12.47, df = 5 (P = 0.03); I² = 60%						
Test for overall effect: Z = 1.33 (P = 0.18)						
Total (95% CI)			**1474**	**3556**	**100.0%**	**0.76 [0.51 , 1.14]**
Heterogeneity: Tau² = 0.13; Chi² = 12.47, df = 5 (P = 0.03); I² = 60%						
Test for overall effect: Z = 1.33 (P = 0.18)						
Test for subgroup differences: Not applicable						



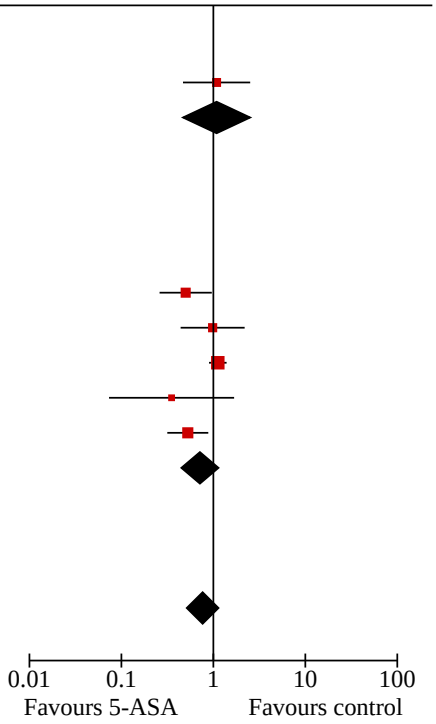
Analysis 2.2. Comparison 2: 5-ASA versus control, Outcome 2: Postoperative infection within 30 days of surgery: subgroup UC vs CD

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
2.2.1 Ulcerative colitis				
Ferrante 2017	-0.6931	0.3336	24.7%	0.50 [0.26 , 0.96]
Subtotal (95% CI)			**24.7%**	**0.50 [0.26 , 0.96]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.08 (P = 0.04)				
2.2.2 Crohn's disease				
Guo 2017	-0.0184	0.4089	16.9%	0.98 [0.44 , 2.19]
Morar 2015	-1.0463	0.7989	4.6%	0.35 [0.07 , 1.68]
Myrelid 2009	0.0809	0.4292	15.4%	1.08 [0.47 , 2.51]
Uchino 2013a	-0.6402	0.2618	38.3%	0.53 [0.32 , 0.88]
Subtotal (95% CI)			**75.3%**	**0.70 [0.45 , 1.07]**
Heterogeneity: Tau² = 0.04; Chi² = 3.62, df = 3 (P = 0.31); I² = 17%				
Test for overall effect: Z = 1.64 (P = 0.10)				
Total (95% CI)			**100.0%**	**0.63 [0.45 , 0.89]**
Heterogeneity: Tau² = 0.01; Chi² = 4.26, df = 4 (P = 0.37); I² = 6%				
Test for overall effect: Z = 2.63 (P = 0.008)				
Test for subgroup differences: Chi² = 0.69, df = 1 (P = 0.41), I² = 0%				



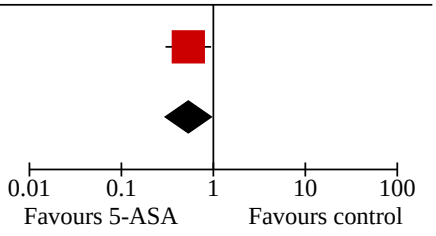
Analysis 2.3. Comparison 2: 5-ASA versus control, Outcome 3: Postoperative infection within 30 days of surgery: subgroup pre 1998 versus 1998 or after

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
2.3.1 Pre 1998				
Myrelid 2009	0.0809	0.4292	13.2%	1.08 [0.47 , 2.51]
Subtotal (95% CI)			**13.2%**	**1.08 [0.47 , 2.51]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.19 (P = 0.85)				
2.3.2 1998 or after				
Ferrante 2017	-0.6931	0.3336	17.2%	0.50 [0.26 , 0.96]
Guo 2017	-0.0184	0.4089	14.0%	0.98 [0.44 , 2.19]
Liang 2017	0.1112	0.1122	29.3%	1.12 [0.90 , 1.39]
Morar 2015	-1.0463	0.7989	5.4%	0.35 [0.07 , 1.68]
Uchino 2013a	-0.6402	0.2618	21.0%	0.53 [0.32 , 0.88]
Subtotal (95% CI)			**86.8%**	**0.71 [0.45 , 1.14]**
Heterogeneity: Tau² = 0.17; Chi² = 12.34, df = 4 (P = 0.01); I² = 68%				
Test for overall effect: Z = 1.42 (P = 0.16)				
Total (95% CI)			**100.0%**	**0.76 [0.51 , 1.14]**
Heterogeneity: Tau² = 0.13; Chi² = 12.47, df = 5 (P = 0.03); I² = 60%				
Test for overall effect: Z = 1.33 (P = 0.18)				
Test for subgroup differences: Chi² = 0.72, df = 1 (P = 0.39), I² = 0%				



Analysis 2.4. Comparison 2: 5-ASA versus control, Outcome 4: Incisional infections and wound dehiscence

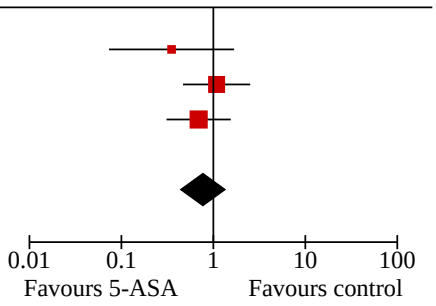
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Uchino 2013a	-0.6273	0.2912	100.0%	0.53 [0.30 , 0.95]
Total (95% CI)			**100.0%**	**0.53 [0.30 , 0.95]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.15 (P = 0.03)				
Test for subgroup differences: Not applicable				



Analysis 2.5. Comparison 2: 5-ASA versus control, Outcome 5: Intra-abdominal infectious complications

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Morar 2015	-1.0463	0.7989	12.1%	0.35 [0.07 , 1.68]
Myrelid 2009	0.0809	0.4292	41.9%	1.08 [0.47 , 2.51]
Uchino 2013a	-0.368	0.4099	46.0%	0.69 [0.31 , 1.55]
Total (95% CI)			**100.0%**	**0.77 [0.45 , 1.33]**

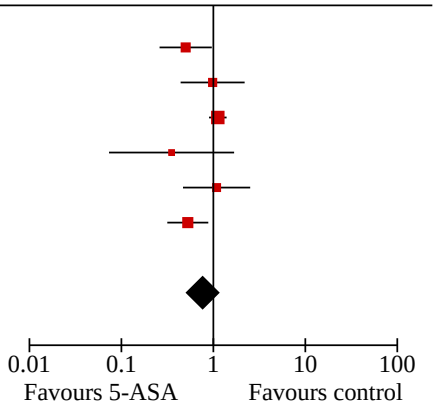
Heterogeneity: Tau² = 0.00; Chi² = 1.67, df = 2 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.94 (P = 0.35)
Test for subgroup differences: Not applicable



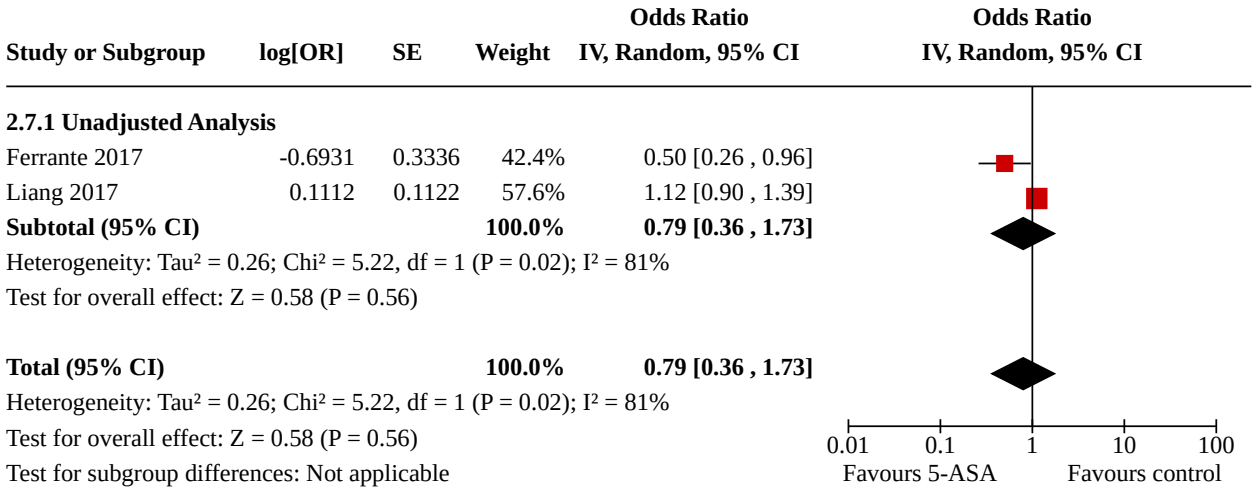
Analysis 2.6. Comparison 2: 5-ASA versus control, Outcome 6: Postoperative infection within 30 days of surgery: sensitivity exclude abstract

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Ferrante 2017	-0.6931	0.3336	17.2%	0.50 [0.26 , 0.96]
Guo 2017	-0.0184	0.4089	14.0%	0.98 [0.44 , 2.19]
Liang 2017	0.1112	0.1122	29.3%	1.12 [0.90 , 1.39]
Morar 2015	-1.0463	0.7989	5.4%	0.35 [0.07 , 1.68]
Myrelid 2009	0.0809	0.4292	13.2%	1.08 [0.47 , 2.51]
Uchino 2013a	-0.6402	0.2618	21.0%	0.53 [0.32 , 0.88]
Total (95% CI)			**100.0%**	**0.76 [0.51 , 1.14]**

Heterogeneity: Tau² = 0.13; Chi² = 12.47, df = 5 (P = 0.03); I² = 60%
Test for overall effect: Z = 1.33 (P = 0.18)
Test for subgroup differences: Not applicable



Analysis 2.7. Comparison 2: 5-ASA versus control, Outcome 7: Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess



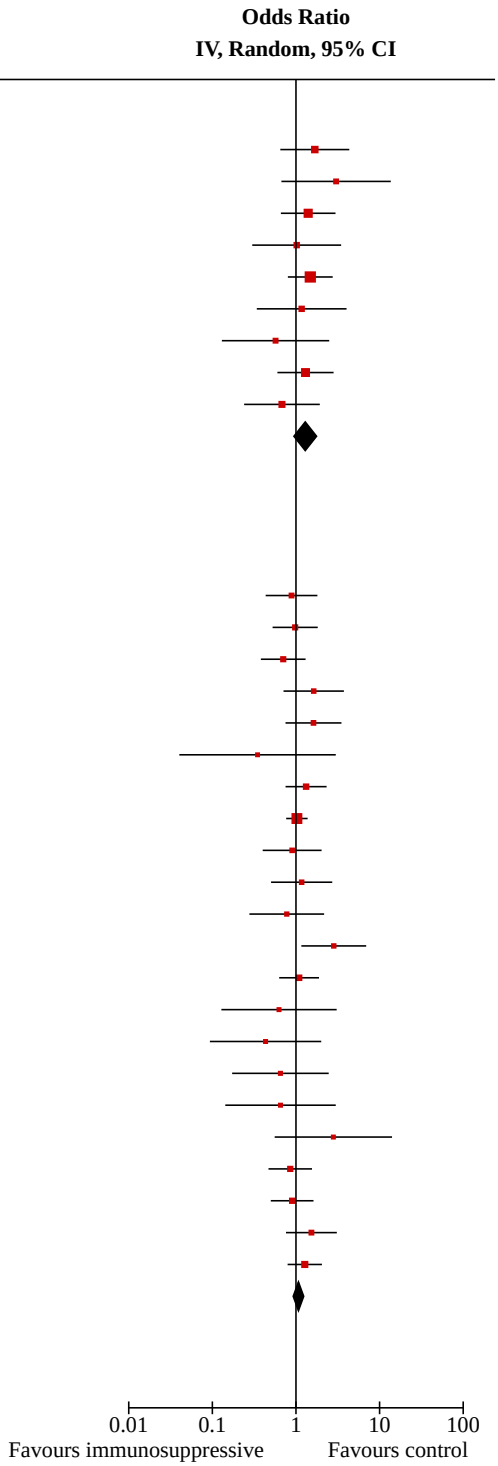
Comparison 3. Immunosuppressive agents versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Postoperative infection within 30 days of surgery	31		Odds Ratio (IV, Random, 95% CI)	Subtotals only
3.1.1 Adjusted Analysis	9		Odds Ratio (IV, Random, 95% CI)	1.29 [0.95, 1.76]
3.1.2 Unadjusted Analysis	22		Odds Ratio (IV, Random, 95% CI)	1.07 [0.93, 1.24]
3.2 Postoperative infection within 30 days of surgery: subgroup UC vs CD	25		Odds Ratio (IV, Random, 95% CI)	1.10 [0.95, 1.29]
3.2.1 Ulcerative colitis	11		Odds Ratio (IV, Random, 95% CI)	1.10 [0.86, 1.39]
3.2.2 Crohn's disease	14		Odds Ratio (IV, Random, 95% CI)	1.11 [0.90, 1.36]
3.3 Postoperative infection within 30 days of surgery: subgroup pre 1998 vs 1998 or after	31		Odds Ratio (IV, Random, 95% CI)	1.11 [0.97, 1.26]
3.3.1 Pre 1998	4		Odds Ratio (IV, Random, 95% CI)	1.85 [1.14, 3.01]
3.3.2 1998 or after	27		Odds Ratio (IV, Random, 95% CI)	1.06 [0.93, 1.22]
3.4 Incisional infections and wound dehiscence	11		Odds Ratio (IV, Random, 95% CI)	1.35 [0.96, 1.89]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.5 Intra-abdominal infectious complications	20		Odds Ratio (IV, Random, 95% CI)	0.86 [0.66, 1.12]
3.6 Extra-abdominal infections	4		Odds Ratio (IV, Random, 95% CI)	1.17 [0.80, 1.71]
3.7 Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias	9		Odds Ratio (IV, Random, 95% CI)	1.29 [0.95, 1.76]
3.8 Postoperative infection within 30 days of surgery: sensitivity exclude abstract	30		Odds Ratio (IV, Random, 95% CI)	1.11 [0.97, 1.27]
3.9 Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess	18		Odds Ratio (IV, Random, 95% CI)	1.09 [0.93, 1.29]
3.9.1 Adjusted Analysis	5		Odds Ratio (IV, Random, 95% CI)	1.34 [0.83, 2.16]
3.9.2 Unadjusted Analysis	13		Odds Ratio (IV, Random, 95% CI)	1.06 [0.89, 1.27]
3.10 Postoperative infection within 30 days of surgery: sensitivity excluding sum of infection studies	30		Odds Ratio (IV, Random, 95% CI)	1.11 [0.97, 1.26]
3.10.1 Adjusted Analysis	9		Odds Ratio (IV, Random, 95% CI)	1.29 [0.95, 1.76]
3.10.2 Unadjusted Analysis	21		Odds Ratio (IV, Random, 95% CI)	1.07 [0.92, 1.24]

Analysis 3.1. Comparison 3: Immunosuppressive agents versus control, Outcome 1: Postoperative infection within 30 days of surgery

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
3.1.1 Adjusted Analysis				
Aberra 2003	0.5188	0.4845	10.7%	1.68 [0.65 , 4.34]
Afzali 2016	1.1053	0.7682	4.3%	3.02 [0.67 , 13.61]
Appau 2008	0.3365	0.3837	17.1%	1.40 [0.66 , 2.97]
Gainsbury 2011 (1)	0.0198	0.6244	6.5%	1.02 [0.30 , 3.47]
Krane 2013	0.3941	0.3149	25.4%	1.48 [0.80 , 2.75]
McKenna 2018	0.157	0.6305	6.3%	1.17 [0.34 , 4.03]
Mor 2008	-0.5621	0.7541	4.4%	0.57 [0.13 , 2.50]
Selvasekar 2007	0.2624	0.3945	16.2%	1.30 [0.60 , 2.82]
Yamamoto 2016	-0.3857	0.5314	8.9%	0.68 [0.24 , 1.93]
Subtotal (95% CI)			**100.0%**	**1.29 [0.95 , 1.76]**
Heterogeneity: Tau² = 0.00; Chi² = 4.56, df = 8 (P = 0.80); I² = 0%				
Test for overall effect: Z = 1.61 (P = 0.11)				
3.1.2 Unadjusted Analysis				
Araki 2014	-0.1221	0.3633	4.1%	0.89 [0.43 , 1.80]
Colombel 2004	-0.0223	0.3171	5.4%	0.98 [0.53 , 1.82]
El-Hussuna 2012	-0.3508	0.3142	5.5%	0.70 [0.38 , 1.30]
Ferrante 2009	0.4886	0.424	3.0%	1.63 [0.71 , 3.74]
Ferrante 2017	0.4824	0.3929	3.5%	1.62 [0.75 , 3.50]
Guo 2017	-1.0578	1.099	0.4%	0.35 [0.04 , 2.99]
Jouvin 2018	0.2784	0.2883	6.5%	1.32 [0.75 , 2.32]
Liang 2017	0.0258	0.1505	23.9%	1.03 [0.76 , 1.38]
Lightner 2018 B	-0.1054	0.4137	3.2%	0.90 [0.40 , 2.02]
Mahadevan 2002	0.1565	0.4297	2.9%	1.17 [0.50 , 2.71]
Morar 2015	-0.2535	0.5247	2.0%	0.78 [0.28 , 2.17]
Myrelid 2009	1.041	0.4555	2.6%	2.83 [1.16 , 6.92]
Myrelid 2014	0.0862	0.2797	6.9%	1.09 [0.63 , 1.89]
Nasir 2010	-0.4667	0.8098	0.8%	0.63 [0.13 , 3.07]
Regadas 2011	-0.8372	0.7821	0.9%	0.43 [0.09 , 2.01]
Rizzo 2011	-0.428	0.6783	1.2%	0.65 [0.17 , 2.46]
Uchino 2010	-0.4257	0.7761	0.9%	0.65 [0.14 , 2.99]
Uchino 2013a	1.0296	0.8244	0.8%	2.80 [0.56 , 14.09]
Uchino 2013b	-0.1577	0.3056	5.8%	0.85 [0.47 , 1.55]
Uchino 2015	-0.1054	0.2999	6.0%	0.90 [0.50 , 1.62]
Uchino 2019	0.4253	0.357	4.3%	1.53 [0.76 , 3.08]
Yu 2019	0.2422	0.2411	9.3%	1.27 [0.79 , 2.04]
Subtotal (95% CI)			**100.0%**	**1.07 [0.93 , 1.24]**
Heterogeneity: Tau² = 0.00; Chi² = 17.53, df = 21 (P = 0.68); I² = 0%				
Test for overall effect: Z = 0.93 (P = 0.35)				
Test for subgroup differences: Chi² = 1.14, df = 1 (P = 0.29), I² = 12.3%				

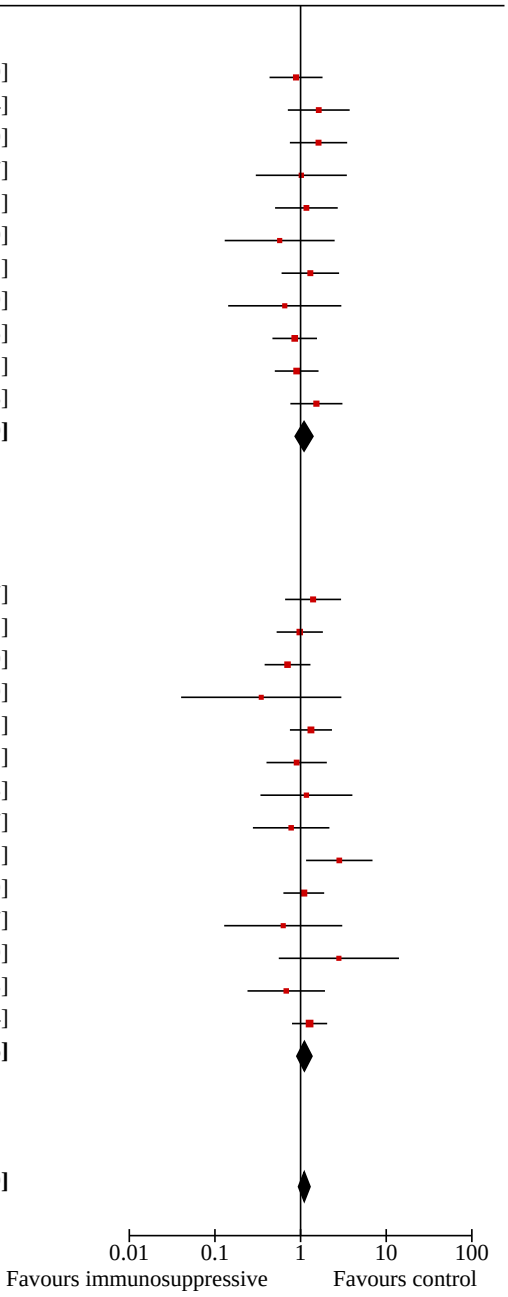


Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

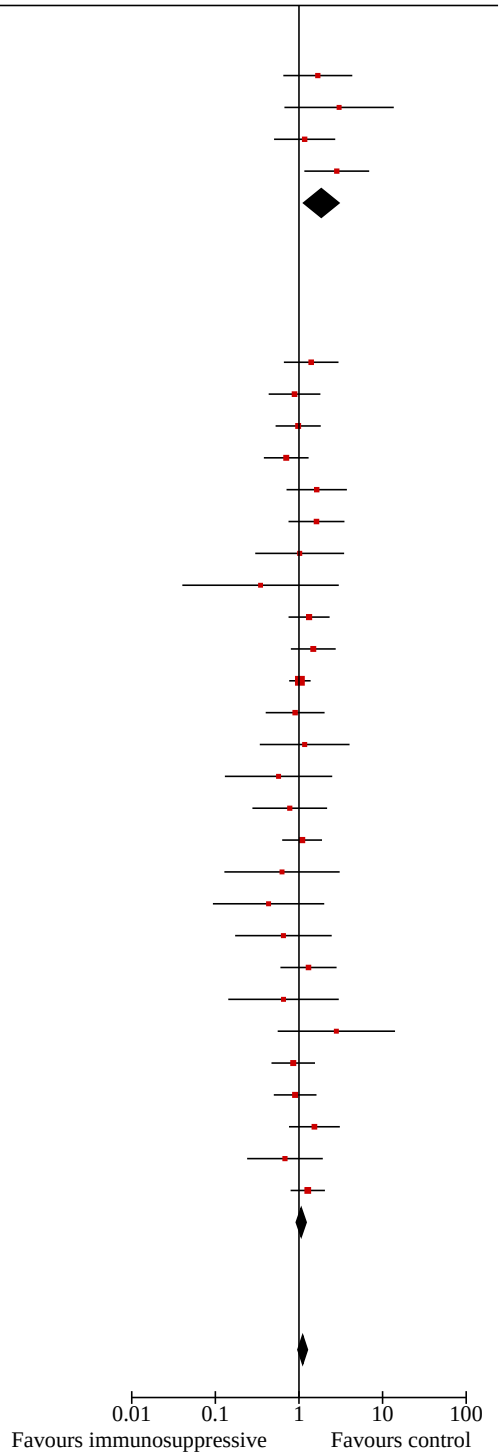
Analysis 3.2. Comparison 3: Immunosuppressive agents versus control, Outcome 2: Postoperative infection within 30 days of surgery: subgroup UC vs CD

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
3.2.1 Ulcerative colitis				
Araki 2014	-0.1221	0.3633	4.7%	0.89 [0.43 , 1.80]
Ferrante 2009	0.4886	0.424	3.5%	1.63 [0.71 , 3.74]
Ferrante 2017	0.4824	0.3929	4.0%	1.62 [0.75 , 3.50]
Gainsbury 2011	0.0198	0.6244	1.6%	1.02 [0.30 , 3.47]
Mahadevan 2002	0.1565	0.4297	3.4%	1.17 [0.50 , 2.71]
Mor 2008	-0.5621	0.7541	1.1%	0.57 [0.13 , 2.50]
Selvasekar 2007	0.2624	0.3945	4.0%	1.30 [0.60 , 2.82]
Uchino 2010	-0.4257	0.7761	1.0%	0.65 [0.14 , 2.99]
Uchino 2013b	-0.1577	0.3056	6.7%	0.85 [0.47 , 1.55]
Uchino 2015	-0.1054	0.2999	6.9%	0.90 [0.50 , 1.62]
Uchino 2019	0.4253	0.357	4.9%	1.53 [0.76 , 3.08]
Subtotal (95% CI)			**41.9%**	**1.10 [0.86 , 1.39]**
Heterogeneity: Tau² = 0.00; Chi² = 5.60, df = 10 (P = 0.85); I² = 0%				
Test for overall effect: Z = 0.77 (P = 0.44)				
3.2.2 Crohn's disease				
Appau 2008	0.3365	0.3837	4.2%	1.40 [0.66 , 2.97]
Colombel 2004	-0.0223	0.3171	6.2%	0.98 [0.53 , 1.82]
El-Hussuna 2012	-0.3508	0.3142	6.3%	0.70 [0.38 , 1.30]
Guo 2017	-1.0578	1.099	0.5%	0.35 [0.04 , 2.99]
Jouvin 2018	0.2784	0.2883	7.5%	1.32 [0.75 , 2.32]
Lightner 2018 B	-0.1054	0.4137	3.6%	0.90 [0.40 , 2.02]
McKenna 2018	0.157	0.6305	1.6%	1.17 [0.34 , 4.03]
Morar 2015	-0.2535	0.5247	2.3%	0.78 [0.28 , 2.17]
Myrelid 2009	1.041	0.4555	3.0%	2.83 [1.16 , 6.92]
Myrelid 2014	0.0862	0.2797	8.0%	1.09 [0.63 , 1.89]
Nasir 2010	-0.4667	0.8098	1.0%	0.63 [0.13 , 3.07]
Uchino 2013a	1.0296	0.8244	0.9%	2.80 [0.56 , 14.09]
Yamamoto 2016	-0.3857	0.5314	2.2%	0.68 [0.24 , 1.93]
Yu 2019	0.2422	0.2411	10.7%	1.27 [0.79 , 2.04]
Subtotal (95% CI)			**58.1%**	**1.11 [0.90 , 1.36]**
Heterogeneity: Tau² = 0.00; Chi² = 12.00, df = 13 (P = 0.53); I² = 0%				
Test for overall effect: Z = 0.99 (P = 0.32)				
Total (95% CI)			**100.0%**	**1.10 [0.95 , 1.29]**
Heterogeneity: Tau² = 0.00; Chi² = 17.61, df = 24 (P = 0.82); I² = 0%				
Test for overall effect: Z = 1.25 (P = 0.21)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.95), I² = 0%				



Analysis 3.3. Comparison 3: Immunosuppressive agents versus control, Outcome 3: Postoperative infection within 30 days of surgery: subgroup pre 1998 vs 1998 or after

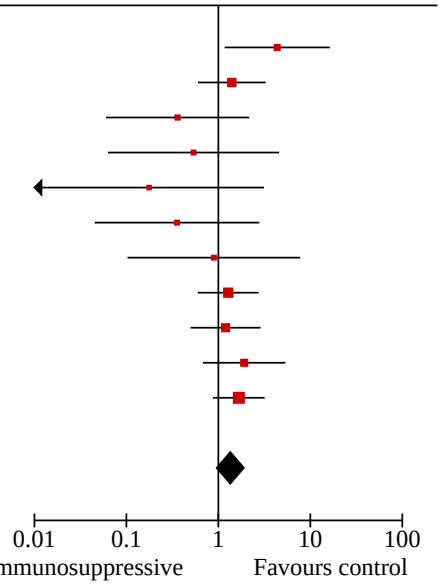
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
3.3.1 Pre 1998				
Aberra 2003	0.5188	0.4845	1.9%	1.68 [0.65 , 4.34]
Afzali 2016	1.1053	0.7682	0.8%	3.02 [0.67 , 13.61]
Mahadevan 2002	0.1565	0.4297	2.4%	1.17 [0.50 , 2.71]
Myrelid 2009	1.041	0.4555	2.2%	2.83 [1.16 , 6.92]
Subtotal (95% CI)			**7.2%**	**1.85 [1.14 , 3.01]**
Heterogeneity: Tau² = 0.00; Chi² = 2.46, df = 3 (P = 0.48); I² = 0%				
Test for overall effect: Z = 2.47 (P = 0.01)				
3.3.2 1998 or after				
Appau 2008	0.3365	0.3837	3.0%	1.40 [0.66 , 2.97]
Araki 2014	-0.1221	0.3633	3.4%	0.89 [0.43 , 1.80]
Colombel 2004	-0.0223	0.3171	4.4%	0.98 [0.53 , 1.82]
El-Hussuna 2012	-0.3508	0.3142	4.5%	0.70 [0.38 , 1.30]
Ferrante 2009	0.4886	0.424	2.5%	1.63 [0.71 , 3.74]
Ferrante 2017	0.4824	0.3929	2.9%	1.62 [0.75 , 3.50]
Gainsbury 2011	0.0198	0.6244	1.1%	1.02 [0.30 , 3.47]
Guo 2017	-1.0578	1.099	0.4%	0.35 [0.04 , 2.99]
Jouvin 2018	0.2784	0.2883	5.4%	1.32 [0.75 , 2.32]
Krane 2013	0.3941	0.3149	4.5%	1.48 [0.80 , 2.75]
Liang 2017	0.0258	0.1505	19.7%	1.03 [0.76 , 1.38]
Lightner 2018 B	-0.1054	0.4137	2.6%	0.90 [0.40 , 2.02]
McKenna 2018	0.157	0.6305	1.1%	1.17 [0.34 , 4.03]
Mor 2008	-0.5621	0.7541	0.8%	0.57 [0.13 , 2.50]
Morar 2015	-0.2535	0.5247	1.6%	0.78 [0.28 , 2.17]
Myrelid 2014	0.0862	0.2797	5.7%	1.09 [0.63 , 1.89]
Nasir 2010	-0.4667	0.8098	0.7%	0.63 [0.13 , 3.07]
Regadas 2011	-0.8372	0.7821	0.7%	0.43 [0.09 , 2.01]
Rizzo 2011	-0.428	0.6783	1.0%	0.65 [0.17 , 2.46]
Selvasekar 2007	0.2624	0.3945	2.9%	1.30 [0.60 , 2.82]
Uchino 2010	-0.4257	0.7761	0.7%	0.65 [0.14 , 2.99]
Uchino 2013a	1.0296	0.8244	0.7%	2.80 [0.56 , 14.09]
Uchino 2013b	-0.1577	0.3056	4.8%	0.85 [0.47 , 1.55]
Uchino 2015	-0.1054	0.2999	5.0%	0.90 [0.50 , 1.62]
Uchino 2019	0.4253	0.357	3.5%	1.53 [0.76 , 3.08]
Yamamoto 2016	-0.3857	0.5314	1.6%	0.68 [0.24 , 1.93]
Yu 2019	0.2422	0.2411	7.7%	1.27 [0.79 , 2.04]
Subtotal (95% CI)			**92.8%**	**1.06 [0.93 , 1.22]**
Heterogeneity: Tau² = 0.00; Chi² = 16.17, df = 26 (P = 0.93); I² = 0%				
Test for overall effect: Z = 0.89 (P = 0.37)				
Total (95% CI)			**100.0%**	**1.11 [0.97 , 1.26]**
Heterogeneity: Tau² = 0.00; Chi² = 23.22, df = 30 (P = 0.81); I² = 0%				
Test for overall effect: Z = 1.52 (P = 0.13)				
Test for subgroup differences: Chi² = 4.59, df = 1 (P = 0.03), I² = 78.2%				



Analysis 3.4. Comparison 3: Immunosuppressive agents versus control, Outcome 4: Incisional infections and wound dehiscence

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Afzali 2016	1.4733	0.6719	6.4%	4.36 [1.17 , 16.28]
Araki 2014	0.3365	0.4323	14.8%	1.40 [0.60 , 3.27]
Gainsbury 2011	-1.0217	0.9142	3.5%	0.36 [0.06 , 2.16]
Mahadevan 2002	-0.6217	1.0935	2.5%	0.54 [0.06 , 4.58]
Regadas 2011	-1.7346	1.4681	1.4%	0.18 [0.01 , 3.14]
Uchino 2010	-1.0354	1.0516	2.7%	0.36 [0.05 , 2.79]
Uchino 2013a	-0.113	1.1031	2.4%	0.89 [0.10 , 7.76]
Uchino 2013b	0.2473	0.3873	18.1%	1.28 [0.60 , 2.74]
Uchino 2015	0.1823	0.4467	13.9%	1.20 [0.50 , 2.88]
Uchino 2019	0.6471	0.5269	10.2%	1.91 [0.68 , 5.36]
Yu 2019	0.5125	0.3301	24.1%	1.67 [0.87 , 3.19]
Total (95% CI)			**100.0%**	**1.35 [0.96 , 1.89]**

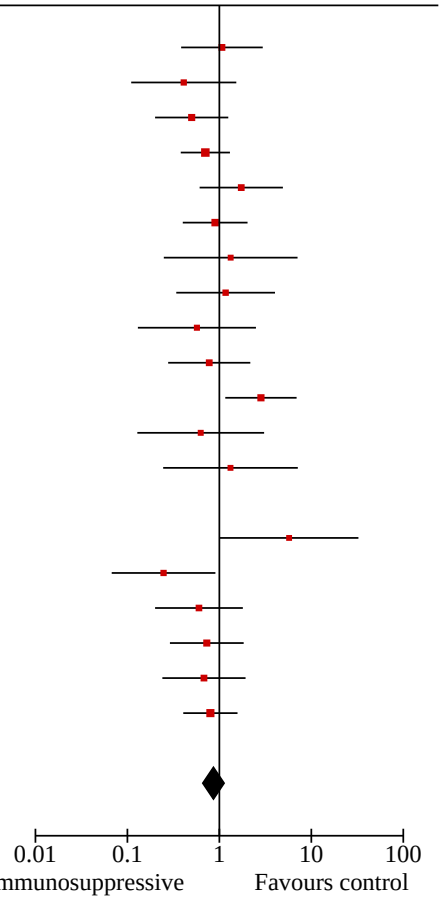
Heterogeneity: Tau² = 0.02; Chi² = 10.47, df = 10 (P = 0.40); I² = 4%
Test for overall effect: Z = 1.73 (P = 0.08)
Test for subgroup differences: Not applicable



Analysis 3.5. Comparison 3: Immunosuppressive agents versus control, Outcome 5: Intra-abdominal infectious complications

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Afzali 2016	0.0647	0.5211	5.5%	1.07 [0.38 , 2.96]
Appau 2008	-0.8916	0.6713	3.6%	0.41 [0.11 , 1.53]
Araki 2014	-0.6931	0.4675	6.6%	0.50 [0.20 , 1.25]
El-Hussuna 2012	-0.3508	0.3142	11.6%	0.70 [0.38 , 1.30]
Ferrante 2009	0.5481	0.5319	5.4%	1.73 [0.61 , 4.91]
Lightner 2018 B	-0.1054	0.4137	8.0%	0.90 [0.40 , 2.02]
Mahadevan 2002	0.2831	0.8542	2.3%	1.33 [0.25 , 7.08]
McKenna 2018	0.157	0.6305	4.0%	1.17 [0.34 , 4.03]
Mor 2008	-0.5621	0.7541	2.9%	0.57 [0.13 , 2.50]
Morar 2015	-0.2535	0.5247	5.5%	0.78 [0.28 , 2.17]
Myrelid 2009	1.041	0.4555	6.9%	2.83 [1.16 , 6.92]
Nasir 2010	-0.4667	0.8098	2.6%	0.63 [0.13 , 3.07]
Regadas 2011	0.2785	0.8599	2.3%	1.32 [0.24 , 7.13]
Shwaartz 2016	0	0		Not estimable
Uchino 2013a	1.7465	0.8854	2.2%	5.73 [1.01 , 32.52]
Uchino 2013b	-1.3973	0.6624	3.7%	0.25 [0.07 , 0.91]
Uchino 2015	-0.5108	0.5605	4.9%	0.60 [0.20 , 1.80]
Uchino 2019	-0.3147	0.471	6.5%	0.73 [0.29 , 1.84]
Yamamoto 2016	-0.3857	0.5314	5.4%	0.68 [0.24 , 1.93]
Yu 2019	-0.2247	0.3465	10.2%	0.80 [0.41 , 1.58]
Total (95% CI)			**100.0%**	**0.86 [0.66 , 1.12]**

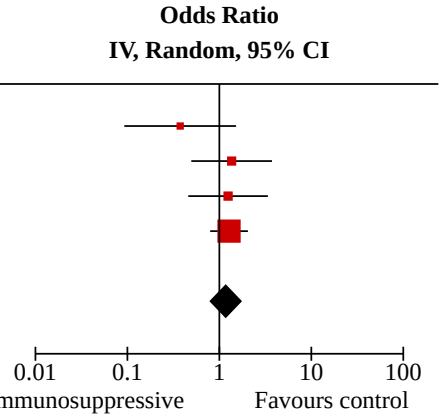
Heterogeneity: Tau² = 0.06; Chi² = 21.86, df = 18 (P = 0.24); I² = 18%
Test for overall effect: Z = 1.09 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 3.6. Comparison 3: Immunosuppressive agents versus control, Outcome 6: Extra-abdominal infections

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Afzali 2016	-0.9808	0.7139	7.3%	0.38 [0.09 , 1.52]
Mahadevan 2002	0.3075	0.5154	14.0%	1.36 [0.50 , 3.73]
Uchino 2013b	0.2184	0.5084	14.4%	1.24 [0.46 , 3.37]
Yu 2019	0.2422	0.2411	64.2%	1.27 [0.79 , 2.04]
Total (95% CI)			**100.0%**	**1.17 [0.80 , 1.71]**

Heterogeneity: Tau² = 0.00; Chi² = 2.76, df = 3 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.82 (P = 0.41)
Test for subgroup differences: Not applicable



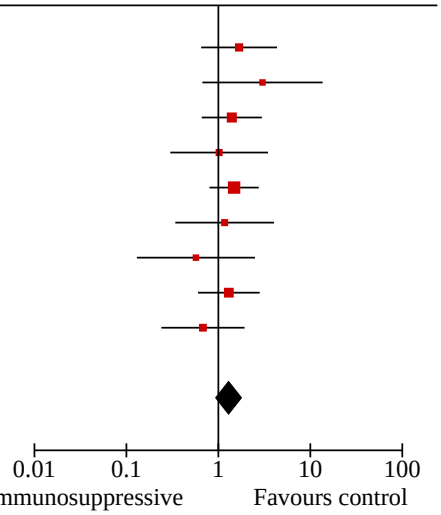
Analysis 3.7. Comparison 3: Immunosuppressive agents versus control, Outcome 7: Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aberra 2003	0.5188	0.4845	10.7%	1.68 [0.65 , 4.34]
Afzali 2016	1.1053	0.7682	4.3%	3.02 [0.67 , 13.61]
Appau 2008	0.3365	0.3837	17.1%	1.40 [0.66 , 2.97]
Gainsbury 2011	0.0198	0.6244	6.5%	1.02 [0.30 , 3.47]
Krane 2013	0.3941	0.3149	25.4%	1.48 [0.80 , 2.75]
McKenna 2018	0.157	0.6305	6.3%	1.17 [0.34 , 4.03]
Mor 2008	-0.5621	0.7541	4.4%	0.57 [0.13 , 2.50]
Selvasekar 2007	0.2624	0.3945	16.2%	1.30 [0.60 , 2.82]
Yamamoto 2016	-0.3857	0.5314	8.9%	0.68 [0.24 , 1.93]
Total (95% CI)			**100.0%**	**1.29 [0.95 , 1.76]**

Heterogeneity: Tau² = 0.00; Chi² = 4.56, df = 8 (P = 0.80); I² = 0%

Test for overall effect: Z = 1.61 (P = 0.11)

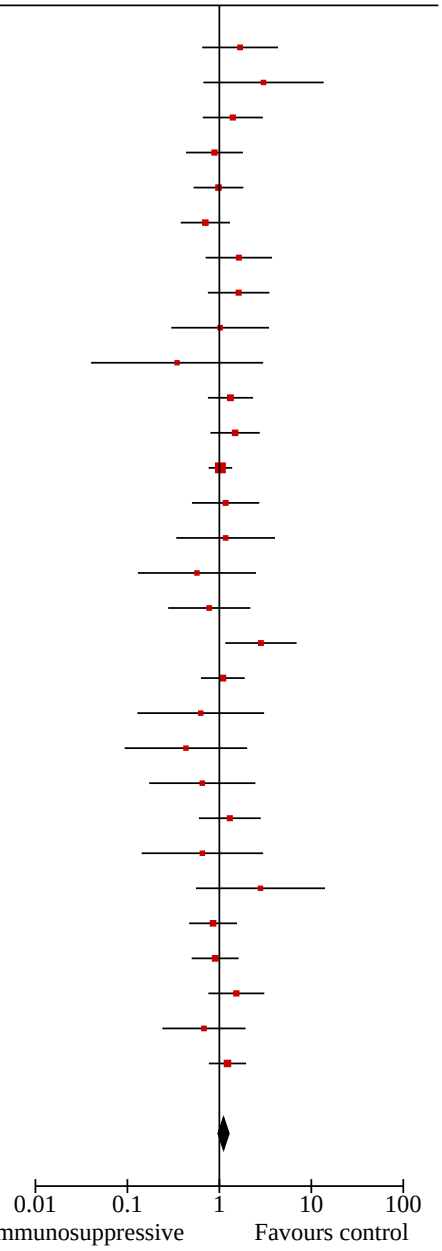
Test for subgroup differences: Not applicable



Analysis 3.8. Comparison 3: Immunosuppressive agents versus control, Outcome 8: Postoperative infection within 30 days of surgery: sensitivity exclude abstract

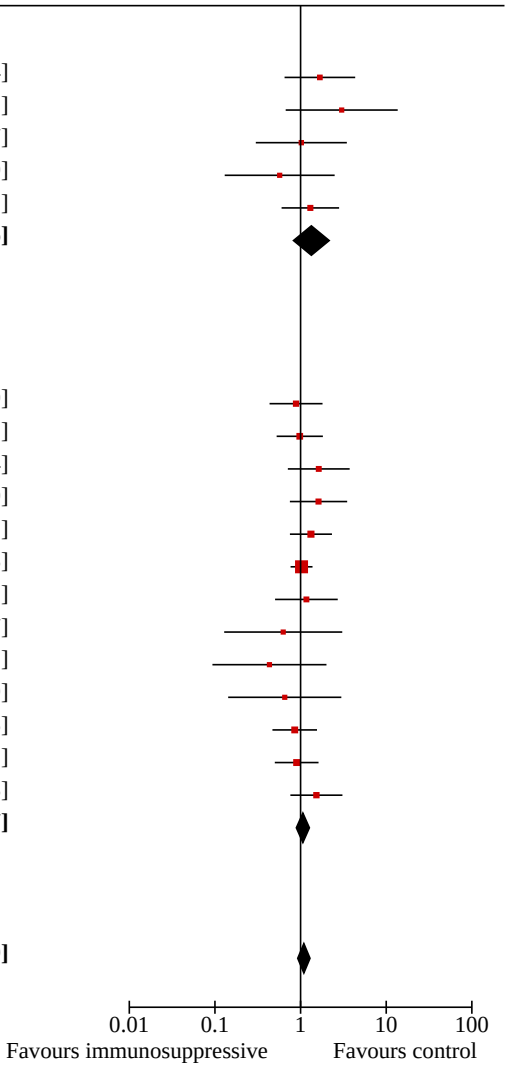
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Aberra 2003	0.5188	0.4845	1.9%	1.68 [0.65 , 4.34]
Afzali 2016	1.1053	0.7682	0.8%	3.02 [0.67 , 13.61]
Appau 2008	0.3365	0.3837	3.1%	1.40 [0.66 , 2.97]
Araki 2014	-0.1221	0.3633	3.5%	0.89 [0.43 , 1.80]
Colombel 2004	-0.0223	0.3171	4.5%	0.98 [0.53 , 1.82]
El-Hussuna 2012	-0.3508	0.3142	4.6%	0.70 [0.38 , 1.30]
Ferrante 2009	0.4886	0.424	2.5%	1.63 [0.71 , 3.74]
Ferrante 2017	0.4824	0.3929	3.0%	1.62 [0.75 , 3.50]
Gainsbury 2011	0.0198	0.6244	1.2%	1.02 [0.30 , 3.47]
Guo 2017	-1.0578	1.099	0.4%	0.35 [0.04 , 2.99]
Jouvin 2018	0.2784	0.2883	5.5%	1.32 [0.75 , 2.32]
Krane 2013	0.3941	0.3149	4.6%	1.48 [0.80 , 2.75]
Liang 2017	0.0258	0.1505	20.2%	1.03 [0.76 , 1.38]
Mahadevan 2002	0.1565	0.4297	2.5%	1.17 [0.50 , 2.71]
McKenna 2018	0.157	0.6305	1.1%	1.17 [0.34 , 4.03]
Mor 2008	-0.5621	0.7541	0.8%	0.57 [0.13 , 2.50]
Morar 2015	-0.2535	0.5247	1.7%	0.78 [0.28 , 2.17]
Myrelid 2009	1.041	0.4555	2.2%	2.83 [1.16 , 6.92]
Myrelid 2014	0.0862	0.2797	5.8%	1.09 [0.63 , 1.89]
Nasir 2010	-0.4667	0.8098	0.7%	0.63 [0.13 , 3.07]
Regadas 2011	-0.8372	0.7821	0.7%	0.43 [0.09 , 2.01]
Rizzo 2011	-0.428	0.6783	1.0%	0.65 [0.17 , 2.46]
Selvasekar 2007	0.2624	0.3945	2.9%	1.30 [0.60 , 2.82]
Uchino 2010	-0.4257	0.7761	0.8%	0.65 [0.14 , 2.99]
Uchino 2013a	1.0296	0.8244	0.7%	2.80 [0.56 , 14.09]
Uchino 2013b	-0.1577	0.3056	4.9%	0.85 [0.47 , 1.55]
Uchino 2015	-0.1054	0.2999	5.1%	0.90 [0.50 , 1.62]
Uchino 2019	0.4253	0.357	3.6%	1.53 [0.76 , 3.08]
Yamamoto 2016	-0.3857	0.5314	1.6%	0.68 [0.24 , 1.93]
Yu 2019	0.2027	0.2378	8.1%	1.22 [0.77 , 1.95]
Total (95% CI)			**100.0%**	**1.11 [0.97 , 1.27]**

Heterogeneity: Tau² = 0.00; Chi² = 22.81, df = 29 (P = 0.79); I² = 0%
Test for overall effect: Z = 1.54 (P = 0.12)
Test for subgroup differences: Not applicable



Analysis 3.9. Comparison 3: Immunosuppressive agents versus control, Outcome 9: Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
3.9.1 Adjusted Analysis				
Aberra 2003	0.5188	0.4845	3.0%	1.68 [0.65 , 4.34]
Afzali 2016	1.1053	0.7682	1.2%	3.02 [0.67 , 13.61]
Gainsbury 2011 (1)	0.0198	0.6244	1.8%	1.02 [0.30 , 3.47]
Mor 2008	-0.5621	0.7541	1.2%	0.57 [0.13 , 2.50]
Selvasekar 2007	0.2624	0.3945	4.5%	1.30 [0.60 , 2.82]
Subtotal (95% CI)			**11.7%**	**1.34 [0.83 , 2.16]**
Heterogeneity: Tau² = 0.00; Chi² = 2.82, df = 4 (P = 0.59); I² = 0%				
Test for overall effect: Z = 1.18 (P = 0.24)				
3.9.2 Unadjusted Analysis				
Araki 2014	-0.1221	0.3633	5.3%	0.89 [0.43 , 1.80]
Colombel 2004	-0.0223	0.3171	7.0%	0.98 [0.53 , 1.82]
Ferrante 2009	0.4886	0.424	3.9%	1.63 [0.71 , 3.74]
Ferrante 2017	0.4824	0.3929	4.6%	1.62 [0.75 , 3.50]
Jouvin 2018	0.2784	0.2883	8.5%	1.32 [0.75 , 2.32]
Liang 2017	0.0258	0.1505	31.0%	1.03 [0.76 , 1.38]
Mahadevan 2002	0.1565	0.4297	3.8%	1.17 [0.50 , 2.71]
Nasir 2010	-0.4667	0.8098	1.1%	0.63 [0.13 , 3.07]
Regadas 2011	-0.8372	0.7821	1.1%	0.43 [0.09 , 2.01]
Uchino 2010	-0.4257	0.7761	1.2%	0.65 [0.14 , 2.99]
Uchino 2013b	-0.1577	0.3056	7.5%	0.85 [0.47 , 1.55]
Uchino 2015	-0.1054	0.2999	7.8%	0.90 [0.50 , 1.62]
Uchino 2019	0.4253	0.357	5.5%	1.53 [0.76 , 3.08]
Subtotal (95% CI)			**88.3%**	**1.06 [0.89 , 1.27]**
Heterogeneity: Tau² = 0.00; Chi² = 7.16, df = 12 (P = 0.85); I² = 0%				
Test for overall effect: Z = 0.69 (P = 0.49)				
Total (95% CI)			**100.0%**	**1.09 [0.93 , 1.29]**
Heterogeneity: Tau² = 0.00; Chi² = 10.74, df = 17 (P = 0.87); I² = 0%				
Test for overall effect: Z = 1.05 (P = 0.29)				
Test for subgroup differences: Chi² = 0.77, df = 1 (P = 0.38), I² = 0%				

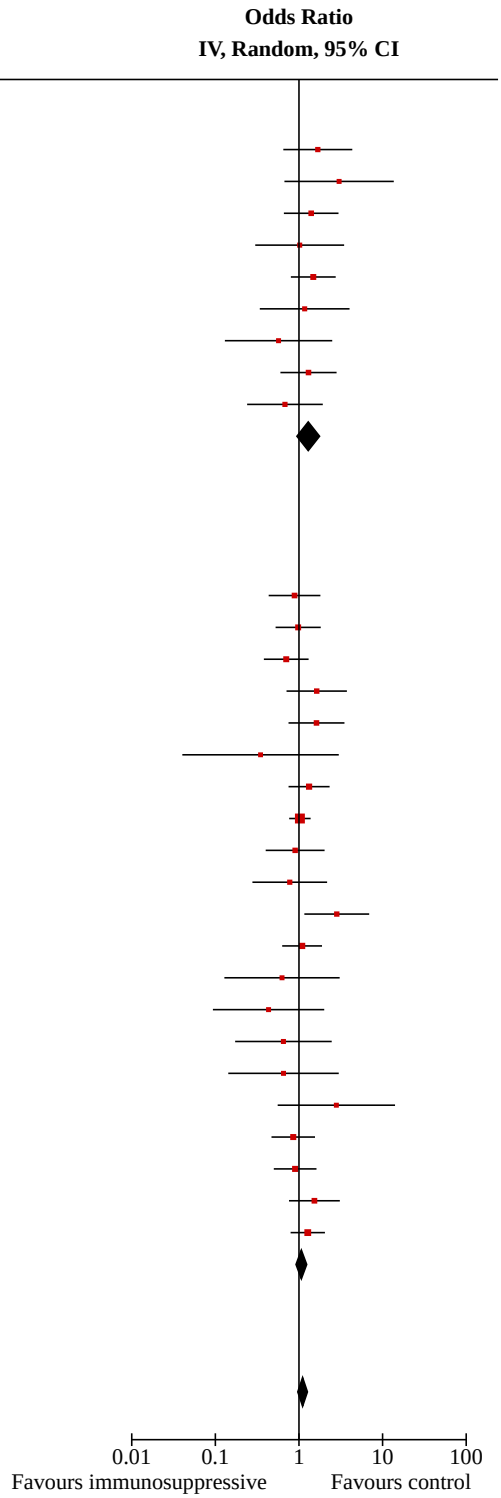


Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

Analysis 3.10. Comparison 3: Immunosuppressive agents versus control, Outcome 10: Postoperative infection within 30 days of surgery: sensitivity excluding sum of infection studies

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
3.10.1 Adjusted Analysis				
Aberra 2003	0.5188	0.4845	1.9%	1.68 [0.65 , 4.34]
Afzali 2016	1.1053	0.7682	0.8%	3.02 [0.67 , 13.61]
Appau 2008	0.3365	0.3837	3.1%	1.40 [0.66 , 2.97]
Gainsbury 2011 (1)	0.0198	0.6244	1.2%	1.02 [0.30 , 3.47]
Krane 2013	0.3941	0.3149	4.6%	1.48 [0.80 , 2.75]
McKenna 2018	0.157	0.6305	1.1%	1.17 [0.34 , 4.03]
Mor 2008	-0.5621	0.7541	0.8%	0.57 [0.13 , 2.50]
Selvasekar 2007	0.2624	0.3945	2.9%	1.30 [0.60 , 2.82]
Yamamoto 2016	-0.3857	0.5314	1.6%	0.68 [0.24 , 1.93]
Subtotal (95% CI)			**18.1%**	**1.29 [0.95 , 1.76]**
Heterogeneity: Tau² = 0.00; Chi² = 4.56, df = 8 (P = 0.80); I² = 0%				
Test for overall effect: Z = 1.61 (P = 0.11)				
3.10.2 Unadjusted Analysis				
Araki 2014	-0.1221	0.3633	3.5%	0.89 [0.43 , 1.80]
Colombel 2004	-0.0223	0.3171	4.5%	0.98 [0.53 , 1.82]
El-Hussuna 2012	-0.3508	0.3142	4.6%	0.70 [0.38 , 1.30]
Ferrante 2009	0.4886	0.424	2.5%	1.63 [0.71 , 3.74]
Ferrante 2017	0.4824	0.3929	3.0%	1.62 [0.75 , 3.50]
Guo 2017	-1.0578	1.099	0.4%	0.35 [0.04 , 2.99]
Jouvin 2018	0.2784	0.2883	5.5%	1.32 [0.75 , 2.32]
Liang 2017	0.0258	0.1505	20.2%	1.03 [0.76 , 1.38]
Lightner 2018 B	-0.1054	0.4137	2.7%	0.90 [0.40 , 2.02]
Morar 2015	-0.2535	0.5247	1.7%	0.78 [0.28 , 2.17]
Myrelid 2009	1.041	0.4555	2.2%	2.83 [1.16 , 6.92]
Myrelid 2014	0.0862	0.2797	5.8%	1.09 [0.63 , 1.89]
Nasir 2010	-0.4667	0.8098	0.7%	0.63 [0.13 , 3.07]
Regadas 2011	-0.8372	0.7821	0.7%	0.43 [0.09 , 2.01]
Rizzo 2011	-0.428	0.6783	1.0%	0.65 [0.17 , 2.46]
Uchino 2010	-0.4257	0.7761	0.8%	0.65 [0.14 , 2.99]
Uchino 2013a	1.0296	0.8244	0.7%	2.80 [0.56 , 14.09]
Uchino 2013b	-0.1577	0.3056	4.9%	0.85 [0.47 , 1.55]
Uchino 2015	-0.1054	0.2999	5.1%	0.90 [0.50 , 1.62]
Uchino 2019	0.4253	0.357	3.6%	1.53 [0.76 , 3.08]
Yu 2019	0.2422	0.2411	7.9%	1.27 [0.79 , 2.04]
Subtotal (95% CI)			**81.9%**	**1.07 [0.92 , 1.24]**
Heterogeneity: Tau² = 0.00; Chi² = 17.48, df = 20 (P = 0.62); I² = 0%				
Test for overall effect: Z = 0.88 (P = 0.38)				
Total (95% CI)			**100.0%**	**1.11 [0.97 , 1.26]**
Heterogeneity: Tau² = 0.00; Chi² = 23.21, df = 29 (P = 0.77); I² = 0%				
Test for overall effect: Z = 1.48 (P = 0.14)				
Test for subgroup differences: Chi² = 1.17, df = 1 (P = 0.28), I² = 14.3%				



Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

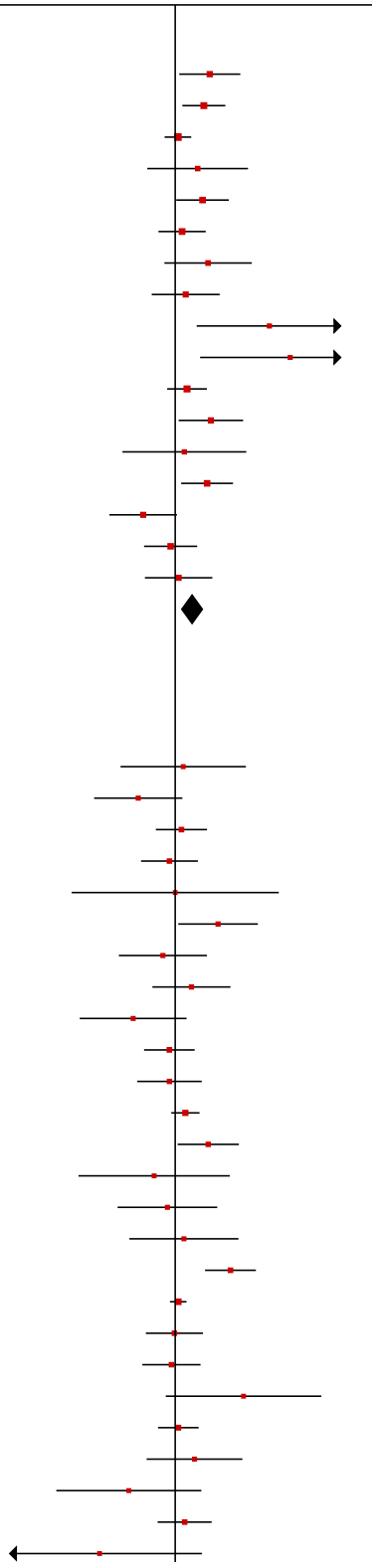
Comparison 4. Anti-TNF-α agents versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Postoperative infection within 30 days of surgery	54		Odds Ratio (IV, Random, 95% CI)	Subtotals only
4.1.1 Adjusted Analysis	17		Odds Ratio (IV, Random, 95% CI)	1.60 [1.20, 2.13]
4.1.2 Unadjusted Analysis	37		Odds Ratio (IV, Random, 95% CI)	1.14 [0.96, 1.36]
4.2 Postoperative infection within 30 days of surgery: subgroup UC vs CD	43		Odds Ratio (IV, Random, 95% CI)	1.26 [1.03, 1.53]
4.2.1 Ulcerative colitis	17		Odds Ratio (IV, Random, 95% CI)	1.04 [0.79, 1.36]
4.2.2 Crohn's disease	27		Odds Ratio (IV, Random, 95% CI)	1.43 [1.09, 1.87]
4.3 Postoperative infection within 30 days of surgery: subgroup biologics < 8 weeks before surgery vs > 8 weeks before surgery	51		Odds Ratio (IV, Random, 95% CI)	1.25 [1.08, 1.46]
4.3.1 < 8 weeks before surgery	17		Odds Ratio (IV, Random, 95% CI)	1.44 [1.08, 1.94]
4.3.2 > 8 weeks before surgery	34		Odds Ratio (IV, Random, 95% CI)	1.18 [0.99, 1.40]
4.4 Incisional infections and wound dehiscence	24		Odds Ratio (IV, Random, 95% CI)	1.18 [0.83, 1.68]
4.5 Intra-abdominal infectious complications	39		Odds Ratio (IV, Random, 95% CI)	1.38 [1.04, 1.82]
4.6 Extra-abdominal infections	13		Odds Ratio (IV, Random, 95% CI)	1.34 [0.96, 1.87]
4.7 Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias	16		Odds Ratio (IV, Random, 95% CI)	1.67 [1.31, 2.13]
4.8 Postoperative infection within 30 days of surgery: sensitivity exclude abstract	47		Odds Ratio (IV, Random, 95% CI)	1.26 [1.07, 1.48]
4.9 Postoperative infection within 30 days of surgery: sensitivity exclude surgery for abscess	37		Odds Ratio (IV, Random, 95% CI)	1.31 [1.10, 1.56]
4.9.1 Adjusted Analysis	8		Odds Ratio (IV, Random, 95% CI)	1.61 [0.98, 2.65]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.9.2 Unadjusted Analysis	29		Odds Ratio (IV, Random, 95% CI)	1.24 [1.03, 1.50]
4.10 Postoperative infection within 30 days of surgery: sensitivity excluding sum of infection studies	46		Odds Ratio (IV, Random, 95% CI)	1.22 [1.02, 1.45]
4.10.1 Adjusted Analysis	17		Odds Ratio (IV, Random, 95% CI)	1.60 [1.20, 2.13]
4.10.2 Unadjusted Analysis	29		Odds Ratio (IV, Random, 95% CI)	1.01 [0.82, 1.24]

Analysis 4.1. Comparison 4: Anti-TNF-α agents versus control, Outcome 1: Postoperative infection within 30 days of surgery

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.1.1 Adjusted Analysis				
Appau 2008	0.9632	0.4336	6.2%	2.62 [1.12 , 6.13]
Brouquet 2018	0.7975	0.3054	8.7%	2.22 [1.22 , 4.04]
Cohen 2019	0.0751	0.1892	11.3%	1.08 [0.74 , 1.56]
Gainsbury 2011 (1)	0.6259	0.7156	3.2%	1.87 [0.46 , 7.60]
Jouvin 2018	0.7608	0.3731	7.3%	2.14 [1.03 , 4.45]
Krane 2013	0.1914	0.3359	8.0%	1.21 [0.63 , 2.34]
Kunitake 2008	0.9163	0.6209	3.9%	2.50 [0.74 , 8.44]
McKenna 2018	0.2927	0.483	5.5%	1.34 [0.52 , 3.45]
Mor 2008	2.6247	1.0336	1.7%	13.80 [1.82 , 104.64]
Morar 2015	3.2027	1.2804	1.2%	24.60 [2.00 , 302.55]
Novello 2020	0.3293	0.2819	9.2%	1.39 [0.80 , 2.42]
Selvasekar 2007	0.9933	0.4581	5.9%	2.70 [1.10 , 6.63]
Serradori 2013	0.2546	0.8798	2.3%	1.29 [0.23 , 7.24]
Syed 2013	0.8879	0.3686	7.4%	2.43 [1.18 , 5.00]
Uchino 2015	-0.8916	0.4801	5.5%	0.41 [0.16 , 1.05]
Uchino 2019	-0.1278	0.3774	7.2%	0.88 [0.42 , 1.84]
Yamamoto 2016	0.0953	0.4792	5.6%	1.10 [0.43 , 2.81]
Subtotal (95% CI)			**100.0%**	**1.60 [1.20 , 2.13]**
Heterogeneity: Tau² = 0.15; Chi² = 31.02, df = 16 (P = 0.01); I² = 48%				
Test for overall effect: Z = 3.23 (P = 0.001)				
4.1.2 Unadjusted Analysis				
Ayoub 2018	0.2231	0.8909	0.9%	1.25 [0.22 , 7.17]
Bregnbak 2012	-1.0296	0.6273	1.6%	0.36 [0.10 , 1.22]
Canedo 2011	0.1736	0.3634	3.5%	1.19 [0.58 , 2.43]
Colombel 2004	-0.1604	0.4041	3.1%	0.85 [0.39 , 1.88]
Coquet-Reinier 2010	0	1.472	0.3%	1.00 [0.06 , 17.90]
De Buck Van Overstraeten 2017	1.1939	0.5652	1.9%	3.30 [1.09 , 9.99]
El-Hussuna 2012	-0.3434	0.6255	1.6%	0.71 [0.21 , 2.42]
Eshuis 2013	0.452	0.5548	2.0%	1.57 [0.53 , 4.66]
Ferrante 2009	-1.1712	0.7592	1.2%	0.31 [0.07 , 1.37]
Ferrante 2017	-0.1625	0.3597	3.6%	0.85 [0.42 , 1.72]
Fumery 2017	-0.1609	0.4589	2.6%	0.85 [0.35 , 2.09]
Gu 2013	0.2829	0.2011	6.0%	1.33 [0.89 , 1.97]
Guasch 2016	0.9203	0.435	2.8%	2.51 [1.07 , 5.89]
Gudsoorkar 2018	-0.5878	1.075	0.6%	0.56 [0.07 , 4.57]
Guo 2017	-0.2167	0.7081	1.3%	0.81 [0.20 , 3.23]
Kim 2018	0.2426	0.7754	1.1%	1.27 [0.28 , 5.83]
Kotze 2017	1.5396	0.3613	3.5%	4.66 [2.30 , 9.47]
Liang 2017	0.0851	0.1174	7.5%	1.09 [0.87 , 1.37]
Lightner 2018 A	-0.0217	0.4057	3.1%	0.98 [0.44 , 2.17]
Lightner 2018 B	-0.1054	0.4137	3.0%	0.90 [0.40 , 2.02]
Marchal 2004	1.903	1.1056	0.6%	6.71 [0.77 , 58.55]
Myrelid 2014	0.0862	0.2879	4.5%	1.09 [0.62 , 1.92]
Nasir 2010	0.5373	0.6803	1.4%	1.71 [0.45 , 6.49]
Norgard 2012	-1.2921	1.0304	0.7%	0.27 [0.04 , 2.07]
Norgard 2013	0.2627	0.3838	3.3%	1.30 [0.61 , 2.76]
Regadas 2011	-2.107	1.454	0.4%	0.12 [0.01 , 2.10]



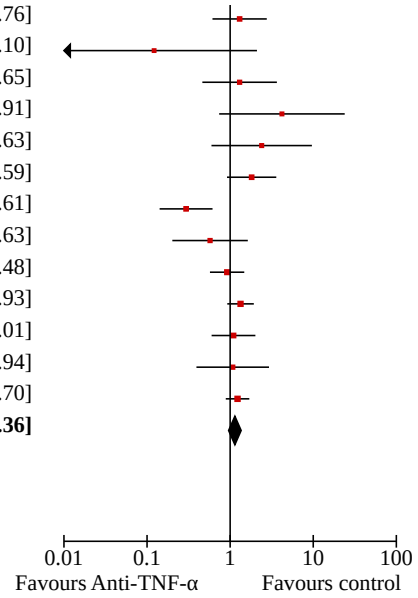
Analysis 4.1. (Continued)

Norgard 2013	0.2627	0.3838	3.3%	1.30 [0.61 , 2.76]
Regadas 2011	-2.107	1.454	0.4%	0.12 [0.01 , 2.10]
Rizzo 2011	0.2624	0.5268	2.1%	1.30 [0.46 , 3.65]
Schils 2017	1.4351	0.8873	0.9%	4.20 [0.74 , 23.91]
Schluender 2007	0.8738	0.7098	1.3%	2.40 [0.60 , 9.63]
Shwaartz 2016	0.5958	0.3483	3.7%	1.81 [0.92 , 3.59]
Uchino 2013a	-1.2214	0.374	3.4%	0.29 [0.14 , 0.61]
Uchino 2013b	-0.5564	0.5334	2.1%	0.57 [0.20 , 1.63]
Ward 2018	-0.0842	0.2425	5.2%	0.92 [0.57 , 1.48]
Waterman 2013	0.2882	0.1875	6.2%	1.33 [0.92 , 1.93]
Yamada 2017	0.0929	0.3095	4.2%	1.10 [0.60 , 2.01]
Yu 2019	0.0715	0.5129	2.2%	1.07 [0.39 , 2.94]
Zittan 2016	0.205	0.1665	6.6%	1.23 [0.89 , 1.70]
Subtotal (95% CI)			**100.0%**	**1.14 [0.96 , 1.36]**

Heterogeneity: Tau² = 0.09; Chi² = 61.69, df = 36 (P = 0.005); I² = 42%

Test for overall effect: Z = 1.48 (P = 0.14)

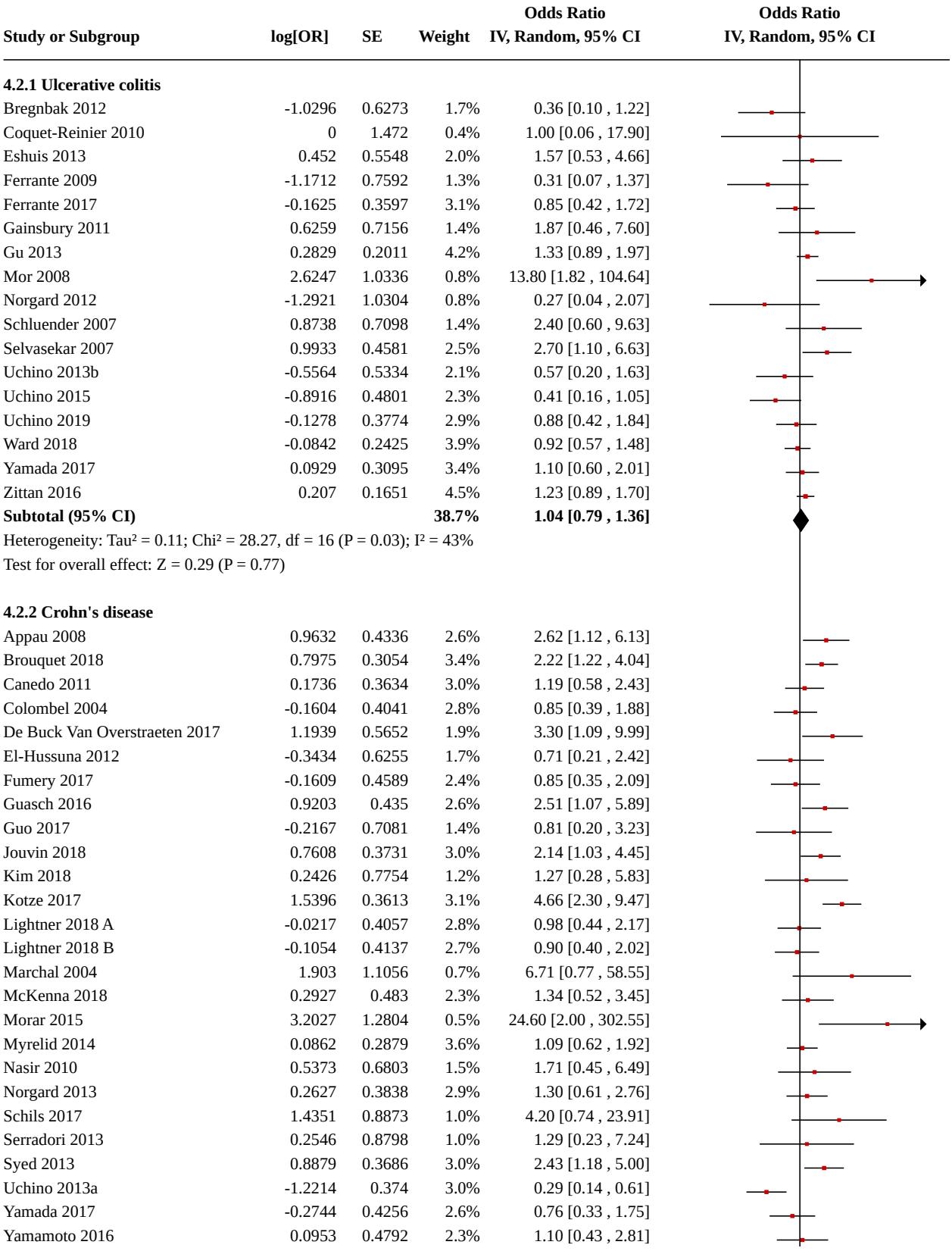
Test for subgroup differences: Chi² = 3.96, df = 1 (P = 0.05), I² = 74.8%



Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

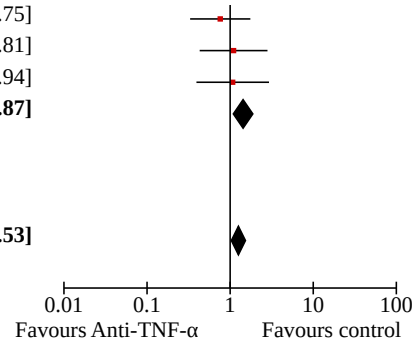
Analysis 4.2. Comparison 4: Anti-TNF-α agents versus control, Outcome 2: Postoperative infection within 30 days of surgery: subgroup UC vs CD



Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.2.1 Ulcerative colitis				
Bregnbak 2012	-1.0296	0.6273	1.7%	0.36 [0.10 , 1.22]
Coquet-Reinier 2010	0	1.472	0.4%	1.00 [0.06 , 17.90]
Eshuis 2013	0.452	0.5548	2.0%	1.57 [0.53 , 4.66]
Ferrante 2009	-1.1712	0.7592	1.3%	0.31 [0.07 , 1.37]
Ferrante 2017	-0.1625	0.3597	3.1%	0.85 [0.42 , 1.72]
Gainsbury 2011	0.6259	0.7156	1.4%	1.87 [0.46 , 7.60]
Gu 2013	0.2829	0.2011	4.2%	1.33 [0.89 , 1.97]
Mor 2008	2.6247	1.0336	0.8%	13.80 [1.82 , 104.64]
Norgard 2012	-1.2921	1.0304	0.8%	0.27 [0.04 , 2.07]
Schluender 2007	0.8738	0.7098	1.4%	2.40 [0.60 , 9.63]
Selvasekar 2007	0.9933	0.4581	2.5%	2.70 [1.10 , 6.63]
Uchino 2013b	-0.5564	0.5334	2.1%	0.57 [0.20 , 1.63]
Uchino 2015	-0.8916	0.4801	2.3%	0.41 [0.16 , 1.05]
Uchino 2019	-0.1278	0.3774	2.9%	0.88 [0.42 , 1.84]
Ward 2018	-0.0842	0.2425	3.9%	0.92 [0.57 , 1.48]
Yamada 2017	0.0929	0.3095	3.4%	1.10 [0.60 , 2.01]
Zittan 2016	0.207	0.1651	4.5%	1.23 [0.89 , 1.70]
Subtotal (95% CI)			**38.7%**	**1.04 [0.79 , 1.36]**
Heterogeneity: Tau² = 0.11; Chi² = 28.27, df = 16 (P = 0.03); I² = 43%				
Test for overall effect: Z = 0.29 (P = 0.77)				
4.2.2 Crohn's disease				
Appau 2008	0.9632	0.4336	2.6%	2.62 [1.12 , 6.13]
Brouquet 2018	0.7975	0.3054	3.4%	2.22 [1.22 , 4.04]
Canedo 2011	0.1736	0.3634	3.0%	1.19 [0.58 , 2.43]
Colombel 2004	-0.1604	0.4041	2.8%	0.85 [0.39 , 1.88]
De Buck Van Overstraeten 2017	1.1939	0.5652	1.9%	3.30 [1.09 , 9.99]
El-Hussuna 2012	-0.3434	0.6255	1.7%	0.71 [0.21 , 2.42]
Fumery 2017	-0.1609	0.4589	2.4%	0.85 [0.35 , 2.09]
Guasch 2016	0.9203	0.435	2.6%	2.51 [1.07 , 5.89]
Guo 2017	-0.2167	0.7081	1.4%	0.81 [0.20 , 3.23]
Jouvin 2018	0.7608	0.3731	3.0%	2.14 [1.03 , 4.45]
Kim 2018	0.2426	0.7754	1.2%	1.27 [0.28 , 5.83]
Kotze 2017	1.5396	0.3613	3.1%	4.66 [2.30 , 9.47]
Lightner 2018 A	-0.0217	0.4057	2.8%	0.98 [0.44 , 2.17]
Lightner 2018 B	-0.1054	0.4137	2.7%	0.90 [0.40 , 2.02]
Marchal 2004	1.903	1.1056	0.7%	6.71 [0.77 , 58.55]
McKenna 2018	0.2927	0.483	2.3%	1.34 [0.52 , 3.45]
Morar 2015	3.2027	1.2804	0.5%	24.60 [2.00 , 302.55]
Myrelid 2014	0.0862	0.2879	3.6%	1.09 [0.62 , 1.92]
Nasir 2010	0.5373	0.6803	1.5%	1.71 [0.45 , 6.49]
Norgard 2013	0.2627	0.3838	2.9%	1.30 [0.61 , 2.76]
Schils 2017	1.4351	0.8873	1.0%	4.20 [0.74 , 23.91]
Serradori 2013	0.2546	0.8798	1.0%	1.29 [0.23 , 7.24]
Syed 2013	0.8879	0.3686	3.0%	2.43 [1.18 , 5.00]
Uchino 2013a	-1.2214	0.374	3.0%	0.29 [0.14 , 0.61]
Yamada 2017	-0.2744	0.4256	2.6%	0.76 [0.33 , 1.75]
Yamamoto 2016	0.0953	0.4792	2.3%	1.10 [0.43 , 2.81]

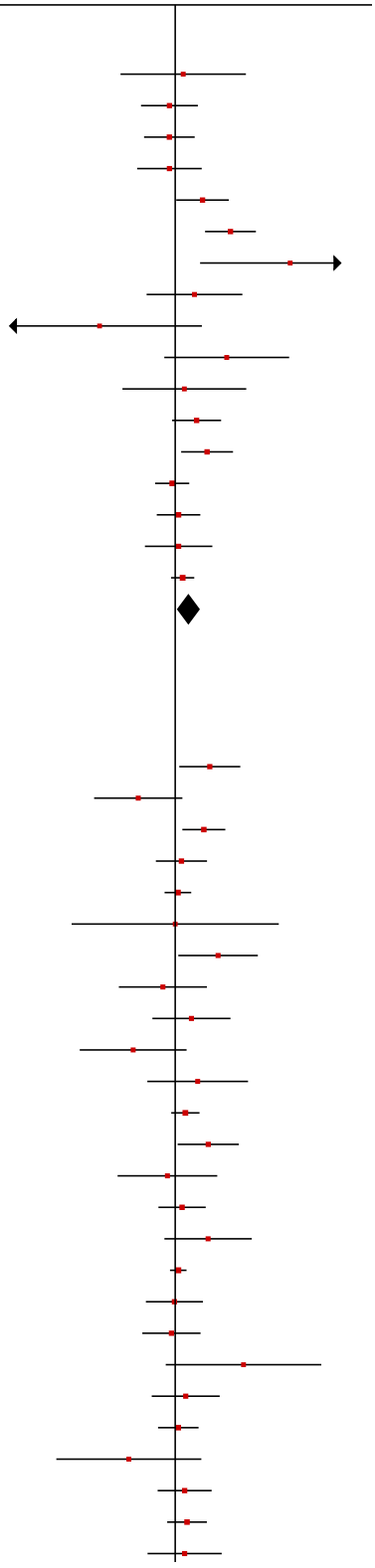
Analysis 4.2. (Continued)

Yamada 2017	-0.2744	0.4256	2.6%	0.76 [0.33 , 1.75]
Yamamoto 2016	0.0953	0.4792	2.3%	1.10 [0.43 , 2.81]
Yu 2019	0.0715	0.5129	2.2%	1.07 [0.39 , 2.94]
Subtotal (95% CI)			**61.3%**	**1.43 [1.09 , 1.87]**
Heterogeneity: Tau² = 0.26; Chi² = 59.08, df = 26 (P = 0.0002); I² = 56%				
Test for overall effect: Z = 2.61 (P = 0.009)				
Total (95% CI)			**100.0%**	**1.26 [1.03 , 1.53]**
Heterogeneity: Tau² = 0.19; Chi² = 91.41, df = 43 (P < 0.0001); I² = 53%				
Test for overall effect: Z = 2.30 (P = 0.02)				
Test for subgroup differences: Chi² = 2.67, df = 1 (P = 0.10), I² = 62.5%				



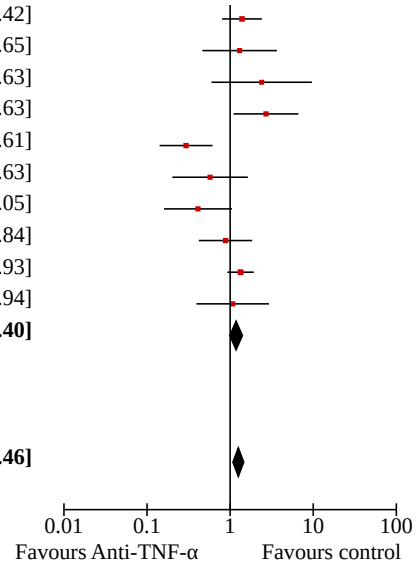
Analysis 4.3. Comparison 4: Anti-TNF-α agents versus control, Outcome 3: Postoperative infection within 30 days of surgery: subgroup biologics < 8 weeks before surgery vs > 8 weeks before surgery

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.3.1 < 8 weeks before surgery				
Ayoub 2018	0.2231	0.8909	0.6%	1.25 [0.22 , 7.17]
Colombel 2004	-0.1604	0.4041	2.2%	0.85 [0.39 , 1.88]
Ferrante 2017	-0.1625	0.3597	2.5%	0.85 [0.42 , 1.72]
Fumery 2017	-0.1609	0.4589	1.8%	0.85 [0.35 , 2.09]
Jouvin 2018	0.7608	0.3731	2.4%	2.14 [1.03 , 4.45]
Kotze 2017	1.5396	0.3613	2.5%	4.66 [2.30 , 9.47]
Morar 2015	3.2027	1.2804	0.3%	24.60 [2.00 , 302.55]
Nasir 2010	0.5373	0.6803	1.0%	1.71 [0.45 , 6.49]
Regadas 2011	-2.107	1.454	0.3%	0.12 [0.01 , 2.10]
Schils 2017	1.4351	0.8873	0.7%	4.20 [0.74 , 23.91]
Serradori 2013	0.2546	0.8798	0.7%	1.29 [0.23 , 7.24]
Shwaartz 2016	0.5958	0.3483	2.6%	1.81 [0.92 , 3.59]
Syed 2013	0.8879	0.3686	2.4%	2.43 [1.18 , 5.00]
Ward 2018	-0.0842	0.2425	3.5%	0.92 [0.57 , 1.48]
Yamada 2017	0.0929	0.3095	2.9%	1.10 [0.60 , 2.01]
Yamamoto 2016	0.0953	0.4792	1.7%	1.10 [0.43 , 2.81]
Zittan 2016	0.207	0.1651	4.4%	1.23 [0.89 , 1.70]
Subtotal (95% CI)			**32.4%**	**1.44 [1.08 , 1.94]**
Heterogeneity: Tau² = 0.16; Chi² = 33.63, df = 16 (P = 0.006); I² = 52%				
Test for overall effect: Z = 2.45 (P = 0.01)				
4.3.2 > 8 weeks before surgery				
Appau 2008	0.9632	0.4336	2.0%	2.62 [1.12 , 6.13]
Bregnbak 2012	-1.0296	0.6273	1.2%	0.36 [0.10 , 1.22]
Brouquet 2018	0.7975	0.3054	2.9%	2.22 [1.22 , 4.04]
Canedo 2011	0.1736	0.3634	2.4%	1.19 [0.58 , 2.43]
Cohen 2019	0.0751	0.1892	4.1%	1.08 [0.74 , 1.56]
Coquet-Reinier 2010	0	1.472	0.3%	1.00 [0.06 , 17.90]
De Buck Van Overstraeten 2017	1.1939	0.5652	1.4%	3.30 [1.09 , 9.99]
El-Hussuna 2012	-0.3434	0.6255	1.2%	0.71 [0.21 , 2.42]
Eshuis 2013	0.452	0.5548	1.4%	1.57 [0.53 , 4.66]
Ferrante 2009	-1.1712	0.7592	0.9%	0.31 [0.07 , 1.37]
Gainsbury 2011	0.6259	0.7156	0.9%	1.87 [0.46 , 7.60]
Gu 2013	0.2829	0.2011	4.0%	1.33 [0.89 , 1.97]
Guasch 2016	0.9203	0.435	2.0%	2.51 [1.07 , 5.89]
Guo 2017	-0.2167	0.7081	1.0%	0.81 [0.20 , 3.23]
Krane 2013	0.1914	0.3359	2.7%	1.21 [0.63 , 2.34]
Kunitake 2008	0.9163	0.6209	1.2%	2.50 [0.74 , 8.44]
Liang 2017	0.0851	0.1174	4.9%	1.09 [0.87 , 1.37]
Lightner 2018 A	-0.0217	0.4057	2.2%	0.98 [0.44 , 2.17]
Lightner 2018 B	-0.1054	0.4137	2.1%	0.90 [0.40 , 2.02]
Marchal 2004	1.903	1.1056	0.4%	6.71 [0.77 , 58.55]
McKenna 2018	0.2927	0.483	1.7%	1.34 [0.52 , 3.45]
Myrelid 2014	0.0862	0.2879	3.1%	1.09 [0.62 , 1.92]
Norgard 2012	-1.2921	1.0304	0.5%	0.27 [0.04 , 2.07]
Norgard 2013	0.2627	0.3838	2.3%	1.30 [0.61 , 2.76]
Novello 2020	0.3293	0.2819	3.1%	1.39 [0.80 , 2.42]
Rizzo 2011	0.2624	0.5268	1.5%	1.30 [0.46 , 3.65]



Analysis 4.3. (Continued)

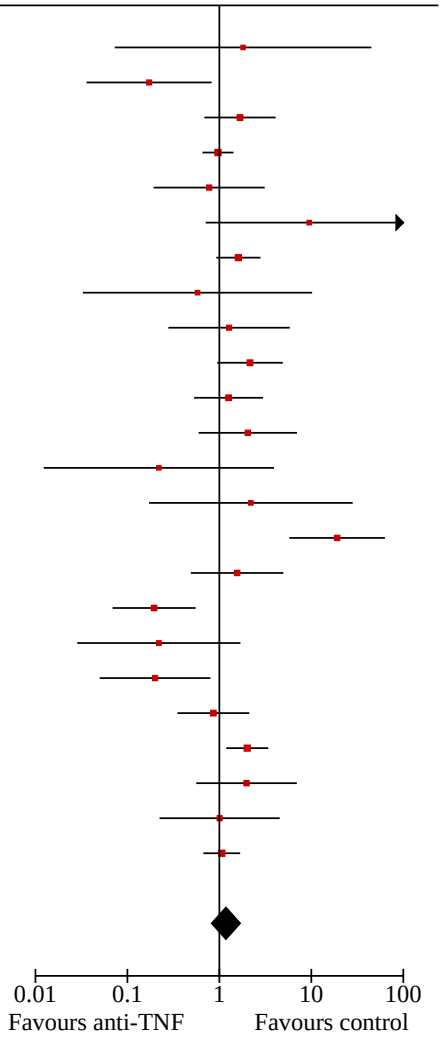
Novello 2020	0.3293	0.2819	3.1%	1.39 [0.80 , 2.42]
Rizzo 2011	0.2624	0.5268	1.5%	1.30 [0.46 , 3.65]
Schluender 2007	0.8738	0.7098	1.0%	2.40 [0.60 , 9.63]
Selvasekar 2007	0.9933	0.4581	1.8%	2.70 [1.10 , 6.63]
Uchino 2013a	-1.2214	0.374	2.4%	0.29 [0.14 , 0.61]
Uchino 2013b	-0.5564	0.5334	1.5%	0.57 [0.20 , 1.63]
Uchino 2015	-0.8916	0.4801	1.7%	0.41 [0.16 , 1.05]
Uchino 2019	-0.1278	0.3774	2.3%	0.88 [0.42 , 1.84]
Waterman 2013	0.2882	0.1875	4.1%	1.33 [0.92 , 1.93]
Yu 2019	0.0715	0.5129	1.6%	1.07 [0.39 , 2.94]
Subtotal (95% CI)			**67.6%**	**1.18 [0.99 , 1.40]**
Heterogeneity: Tau² = 0.09; Chi² = 56.32, df = 33 (P = 0.007); I² = 41%				
Test for overall effect: Z = 1.86 (P = 0.06)				
Total (95% CI)			**100.0%**	**1.25 [1.08 , 1.46]**
Heterogeneity: Tau² = 0.11; Chi² = 91.72, df = 50 (P = 0.0003); I² = 45%				
Test for overall effect: Z = 2.98 (P = 0.003)				
Test for subgroup differences: Chi² = 1.35, df = 1 (P = 0.25), I² = 25.7%				



Analysis 4.4. Comparison 4: Anti-TNF-α agents versus control, Outcome 4: Incisional infections and wound dehiscence

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Appau 2008	0.5933	1.639	1.1%	1.81 [0.07 , 44.96]
Bregnbak 2012	-1.759	0.7986	3.2%	0.17 [0.04 , 0.82]
Canedo 2011	0.5164	0.4552	5.5%	1.68 [0.69 , 4.09]
Cohen 2019	-0.0348	0.1983	7.7%	0.97 [0.65 , 1.42]
Ferrante 2017	-0.2556	0.7095	3.7%	0.77 [0.19 , 3.11]
Gainsbury 2011	2.2502	1.3228	1.5%	9.49 [0.71 , 126.83]
Gu 2013	0.4761	0.2817	7.1%	1.61 [0.93 , 2.80]
Gudsoorkar 2018	-0.5465	1.4641	1.3%	0.58 [0.03 , 10.21]
Kim 2018	0.2426	0.7754	3.3%	1.27 [0.28 , 5.83]
Kotze 2017	0.7671	0.4195	5.8%	2.15 [0.95 , 4.90]
Krane 2013	0.2317	0.4405	5.6%	1.26 [0.53 , 2.99]
Lightner 2018 A	0.7131	0.6285	4.2%	2.04 [0.60 , 6.99]
Regadas 2011	-1.515	1.4704	1.3%	0.22 [0.01 , 3.92]
Schils 2017	0.7885	1.3003	1.6%	2.20 [0.17 , 28.14]
Selvasekar 2007	2.9495	0.6105	4.3%	19.10 [5.77 , 63.18]
Shwaartz 2016	0.4447	0.5908	4.5%	1.56 [0.49 , 4.97]
Uchino 2013a	-1.6345	0.5306	4.9%	0.20 [0.07 , 0.55]
Uchino 2013b	-1.5157	1.0425	2.2%	0.22 [0.03 , 1.69]
Uchino 2015	-1.6094	0.7073	3.7%	0.20 [0.05 , 0.80]
Uchino 2019	-0.1508	0.4587	5.5%	0.86 [0.35 , 2.11]
Waterman 2013	0.6985	0.2681	7.2%	2.01 [1.19 , 3.40]
Yamada 2017	0.681	0.642	4.1%	1.98 [0.56 , 6.95]
Yu 2019	0.007	0.7678	3.3%	1.01 [0.22 , 4.54]
Zittan 2016	0.0599	0.2349	7.4%	1.06 [0.67 , 1.68]
Total (95% CI)			**100.0%**	**1.18 [0.83 , 1.68]**

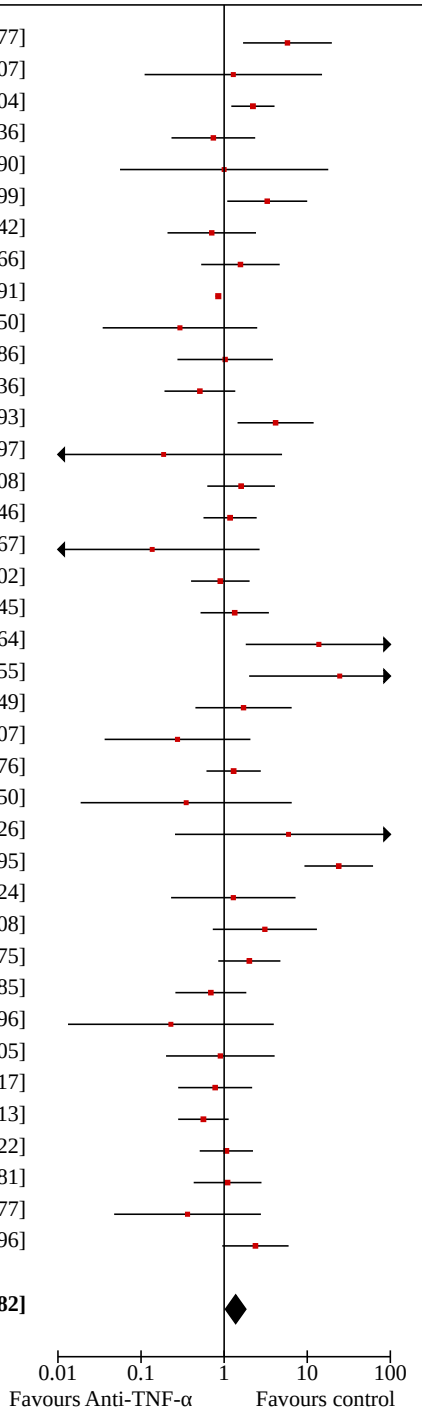
Heterogeneity: Tau² = 0.38; Chi² = 62.75, df = 23 (P < 0.0001); I² = 63%
Test for overall effect: Z = 0.91 (P = 0.36)
Test for subgroup differences: Not applicable



Analysis 4.5. Comparison 4: Anti-TNF-α agents versus control, Outcome 5: Intra-abdominal infectious complications

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Appau 2008	1.7544	0.6274	2.7%	5.78 [1.69 , 19.77]
Bregnbak 2012	0.2542	1.2542	1.1%	1.29 [0.11 , 15.07]
Brouquet 2018	0.7975	0.3054	4.4%	2.22 [1.22 , 4.04]
Canedo 2011	-0.2991	0.5917	2.8%	0.74 [0.23 , 2.36]
Coquet-Reinier 2010	0	1.472	0.8%	1.00 [0.06 , 17.90]
De Buck Van Overstraeten 2017	1.1939	0.5652	2.9%	3.30 [1.09 , 9.99]
El-Hussuna 2012	-0.3434	0.6255	2.7%	0.71 [0.21 , 2.42]
Eshuis 2013	0.452	0.5548	3.0%	1.57 [0.53 , 4.66]
Ferrante 2009	-0.1625	0.0373	5.4%	0.85 [0.79 , 0.91]
Ferrante 2017	-1.2249	1.0924	1.3%	0.29 [0.03 , 2.50]
Gainsbury 2011	0.0282	0.6746	2.5%	1.03 [0.27 , 3.86]
Gu 2013	-0.6723	0.5004	3.3%	0.51 [0.19 , 1.36]
Guasch 2016	1.4255	0.5377	3.1%	4.16 [1.45 , 11.93]
Gudsoorkar 2018	-1.6767	1.674	0.6%	0.19 [0.01 , 4.97]
Kotze 2017	0.47	0.4779	3.4%	1.60 [0.63 , 4.08]
Krane 2013	0.1646	0.376	4.0%	1.18 [0.56 , 2.46]
Lightner 2018 A	-1.9935	1.5181	0.8%	0.14 [0.01 , 2.67]
Lightner 2018 B	-0.1054	0.4137	3.7%	0.90 [0.40 , 2.02]
McKenna 2018	0.2927	0.483	3.4%	1.34 [0.52 , 3.45]
Mor 2008	2.6247	1.0336	1.4%	13.80 [1.82 , 104.64]
Morar 2015	3.2027	1.2804	1.0%	24.60 [2.00 , 302.55]
Nasir 2010	0.5373	0.6803	2.4%	1.71 [0.45 , 6.49]
Norgard 2012	-1.2921	1.0304	1.4%	0.27 [0.04 , 2.07]
Norgard 2013	0.2627	0.3838	3.9%	1.30 [0.61 , 2.76]
Regadas 2011	-1.0519	1.492	0.8%	0.35 [0.02 , 6.50]
Schils 2017	1.7838	1.6048	0.7%	5.95 [0.26 , 138.26]
Selvasekar 2007	3.1757	0.485	3.4%	23.94 [9.25 , 61.95]
Serradori 2013	0.2546	0.8798	1.8%	1.29 [0.23 , 7.24]
Shwaartz 2016	1.1282	0.7362	2.2%	3.09 [0.73 , 13.08]
Syed 2013	0.6981	0.4391	3.6%	2.01 [0.85 , 4.75]
Uchino 2013a	-0.3682	0.5014	3.3%	0.69 [0.26 , 1.85]
Uchino 2013b	-1.4755	1.4544	0.8%	0.23 [0.01 , 3.96]
Uchino 2015	-0.1054	0.7674	2.1%	0.90 [0.20 , 4.05]
Uchino 2019	-0.2485	0.5227	3.2%	0.78 [0.28 , 2.17]
Waterman 2013	-0.5744	0.3568	4.1%	0.56 [0.28 , 1.13]
Yamada 2017	0.061	0.3765	4.0%	1.06 [0.51 , 2.22]
Yamamoto 2016	0.0953	0.4792	3.4%	1.10 [0.43 , 2.81]
Yu 2019	-1.0145	1.0372	1.4%	0.36 [0.05 , 2.77]
Zittan 2016	0.8671	0.4686	3.4%	2.38 [0.95 , 5.96]
Total (95% CI)			**100.0%**	**1.38 [1.04 , 1.82]**

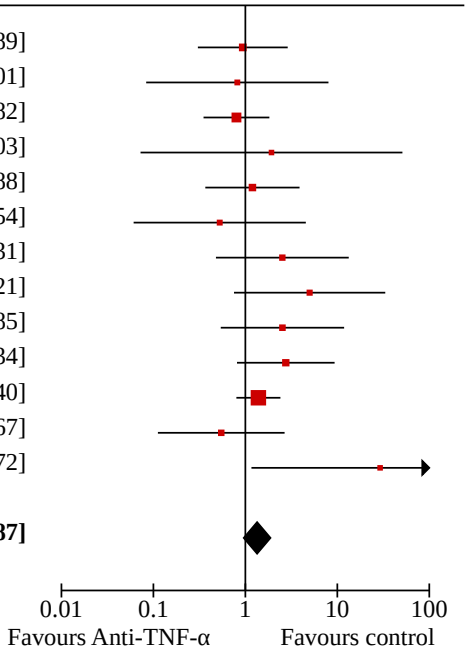
Heterogeneity: Tau² = 0.38; Chi² = 120.91, df = 38 (P < 0.00001); I² = 69%
Test for overall effect: Z = 2.23 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 4.6. Comparison 4: Anti-TNF-α agents versus control, Outcome 6: Extra-abdominal infections

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bregnbak 2012	-0.0645	0.5737	8.8%	0.94 [0.30 , 2.89]
Canedo 2011	-0.2012	1.1642	2.1%	0.82 [0.08 , 8.01]
Ferrante 2017	-0.2231	0.4205	16.4%	0.80 [0.35 , 1.82]
Gudsoorkar 2018	0.6539	1.6727	1.0%	1.92 [0.07 , 51.03]
Kotze 2017	0.177	0.6018	8.0%	1.19 [0.37 , 3.88]
Krane 2013	-0.642	1.0999	2.4%	0.53 [0.06 , 4.54]
Lightner 2018 A	0.926	0.8482	4.0%	2.52 [0.48 , 13.31]
Schils 2017	1.6094	0.9661	3.1%	5.00 [0.75 , 33.21]
Shwaartz 2016	0.9282	0.788	4.7%	2.53 [0.54 , 11.85]
Uchino 2013b	1.0124	0.6234	7.5%	2.75 [0.81 , 9.34]
Waterman 2013	0.3264	0.2812	36.3%	1.39 [0.80 , 2.40]
Yamada 2017	-0.6039	0.8092	4.4%	0.55 [0.11 , 2.67]
Yu 2019	3.3738	1.6437	1.1%	29.19 [1.16 , 731.72]
Total (95% CI)			**100.0%**	**1.34 [0.96 , 1.87]**

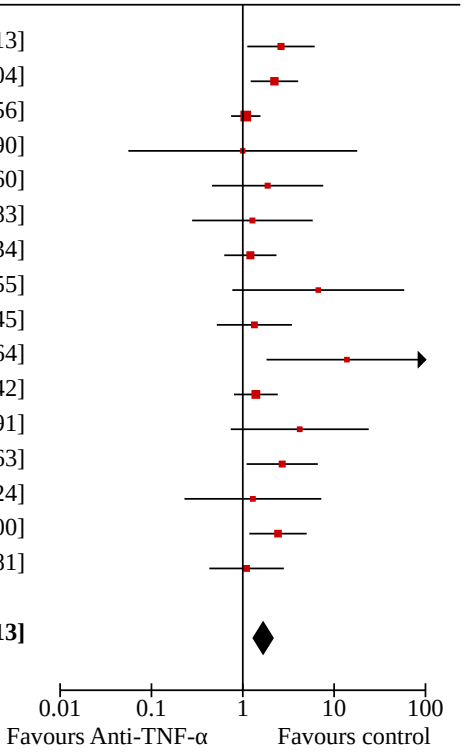
Heterogeneity: Tau² = 0.00; Chi² = 12.03, df = 12 (P = 0.44); I² = 0%
Test for overall effect: Z = 1.72 (P = 0.09)
Test for subgroup differences: Not applicable



Analysis 4.7. Comparison 4: Anti-TNF-α agents versus control, Outcome 7: Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias

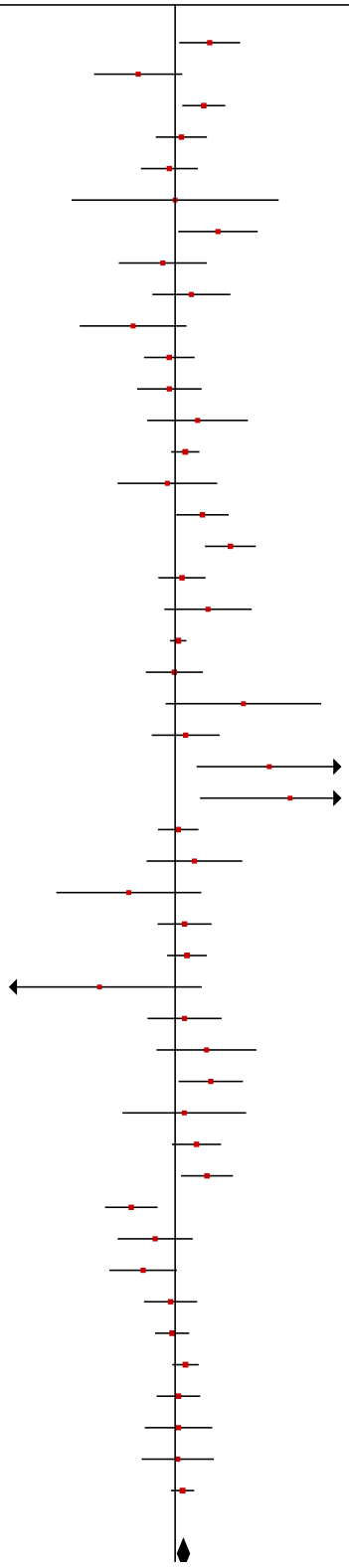
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Appau 2008	0.9632	0.4336	6.8%	2.62 [1.12 , 6.13]
Brouquet 2018	0.7975	0.3054	11.5%	2.22 [1.22 , 4.04]
Cohen 2019	0.0751	0.1892	19.9%	1.08 [0.74 , 1.56]
Coquet-Reinier 2010	0	1.472	0.7%	1.00 [0.06 , 17.90]
Gainsbury 2011	0.6259	0.7156	2.8%	1.87 [0.46 , 7.60]
Kim 2018	0.2426	0.7754	2.4%	1.27 [0.28 , 5.83]
Krane 2013	0.1914	0.3359	10.1%	1.21 [0.63 , 2.34]
Marchal 2004	1.903	1.1056	1.2%	6.71 [0.77 , 58.55]
McKenna 2018	0.2927	0.483	5.7%	1.34 [0.52 , 3.45]
Mor 2008	2.6247	1.0336	1.4%	13.80 [1.82 , 104.64]
Novello 2020	0.3293	0.2819	12.8%	1.39 [0.80 , 2.42]
Schils 2017	1.4351	0.8873	1.9%	4.20 [0.74 , 23.91]
Selvasekar 2007	0.9933	0.4581	6.2%	2.70 [1.10 , 6.63]
Serradori 2013	0.2546	0.8798	1.9%	1.29 [0.23 , 7.24]
Syed 2013	0.8879	0.3686	8.8%	2.43 [1.18 , 5.00]
Yamamoto 2016	0.0953	0.4792	5.8%	1.10 [0.43 , 2.81]
Total (95% CI)			**100.0%**	**1.67 [1.31 , 2.13]**

Heterogeneity: Tau² = 0.04; Chi² = 18.53, df = 15 (P = 0.24); I² = 19%
Test for overall effect: Z = 4.08 (P < 0.0001)
Test for subgroup differences: Not applicable



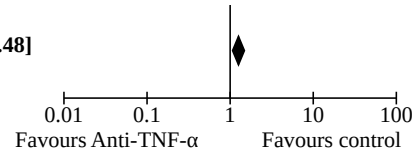
Analysis 4.8. Comparison 4: Anti-TNF-α agents versus control, Outcome 8: Postoperative infection within 30 days of surgery: sensitivity exclude abstract

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Appau 2008	0.9632	0.4336	2.2%	2.62 [1.12 , 6.13]
Bregnbak 2012	-1.0296	0.6273	1.3%	0.36 [0.10 , 1.22]
Brouquet 2018	0.7975	0.3054	3.2%	2.22 [1.22 , 4.04]
Canedo 2011	0.1736	0.3634	2.7%	1.19 [0.58 , 2.43]
Colombel 2004	-0.1604	0.4041	2.4%	0.85 [0.39 , 1.88]
Coquet-Reinier 2010	0	1.472	0.3%	1.00 [0.06 , 17.90]
De Buck Van Overstraeten 2017	1.1939	0.5652	1.6%	3.30 [1.09 , 9.99]
El-Hussuna 2012	-0.3434	0.6255	1.3%	0.71 [0.21 , 2.42]
Eshuis 2013	0.452	0.5548	1.6%	1.57 [0.53 , 4.66]
Ferrante 2009	-1.1712	0.7592	1.0%	0.31 [0.07 , 1.37]
Ferrante 2017	-0.1625	0.3597	2.7%	0.85 [0.42 , 1.72]
Fumery 2017	-0.1609	0.4589	2.1%	0.85 [0.35 , 2.09]
Gainsbury 2011	0.6259	0.7156	1.1%	1.87 [0.46 , 7.60]
Gu 2013	0.2829	0.2011	4.2%	1.33 [0.89 , 1.97]
Guo 2017	-0.2167	0.7081	1.1%	0.81 [0.20 , 3.23]
Jouvin 2018	0.7608	0.3731	2.6%	2.14 [1.03 , 4.45]
Kotze 2017	1.5396	0.3613	2.7%	4.66 [2.30 , 9.47]
Krane 2013	0.1914	0.3359	2.9%	1.21 [0.63 , 2.34]
Kunitake 2008	0.9163	0.6209	1.4%	2.50 [0.74 , 8.44]
Liang 2017	0.0851	0.1174	4.9%	1.09 [0.87 , 1.37]
Lightner 2018 A	-0.0217	0.4057	2.4%	0.98 [0.44 , 2.17]
Marchal 2004	1.903	1.1056	0.5%	6.71 [0.77 , 58.55]
McKenna 2018	0.2927	0.483	1.9%	1.34 [0.52 , 3.45]
Mor 2008	2.6247	1.0336	0.6%	13.80 [1.82 , 104.64]
Morar 2015	3.2027	1.2804	0.4%	24.60 [2.00 , 302.55]
Myrelid 2014	0.0862	0.2879	3.3%	1.09 [0.62 , 1.92]
Nasir 2010	0.5373	0.6803	1.2%	1.71 [0.45 , 6.49]
Norgard 2012	-1.2921	1.0304	0.6%	0.27 [0.04 , 2.07]
Norgard 2013	0.2627	0.3838	2.5%	1.30 [0.61 , 2.76]
Novello 2020	0.3293	0.2819	3.4%	1.39 [0.80 , 2.42]
Regadas 2011	-2.107	1.454	0.3%	0.12 [0.01 , 2.10]
Rizzo 2011	0.2624	0.5268	1.7%	1.30 [0.46 , 3.65]
Schluender 2007	0.8738	0.7098	1.1%	2.40 [0.60 , 9.63]
Selvasekar 2007	0.9933	0.4581	2.1%	2.70 [1.10 , 6.63]
Serradori 2013	0.2546	0.8798	0.8%	1.29 [0.23 , 7.24]
Shwaartz 2016	0.5958	0.3483	2.8%	1.81 [0.92 , 3.59]
Syed 2013	0.8879	0.3686	2.7%	2.43 [1.18 , 5.00]
Uchino 2013a	-1.2214	0.374	2.6%	0.29 [0.14 , 0.61]
Uchino 2013b	-0.5564	0.5334	1.7%	0.57 [0.20 , 1.63]
Uchino 2015	-0.8916	0.4801	2.0%	0.41 [0.16 , 1.05]
Uchino 2019	-0.1278	0.3774	2.6%	0.88 [0.42 , 1.84]
Ward 2018	-0.0842	0.2425	3.8%	0.92 [0.57 , 1.48]
Waterman 2013	0.2882	0.1875	4.3%	1.33 [0.92 , 1.93]
Yamada 2017	0.0929	0.3095	3.1%	1.10 [0.60 , 2.01]
Yamamoto 2016	0.0953	0.4792	2.0%	1.10 [0.43 , 2.81]
Yu 2019	0.0715	0.5129	1.8%	1.07 [0.39 , 2.94]
Zittan 2016	0.207	0.1651	4.5%	1.23 [0.89 , 1.70]
Total (95% CI)			**100.0%**	**1.26 [1.07 , 1.48]**



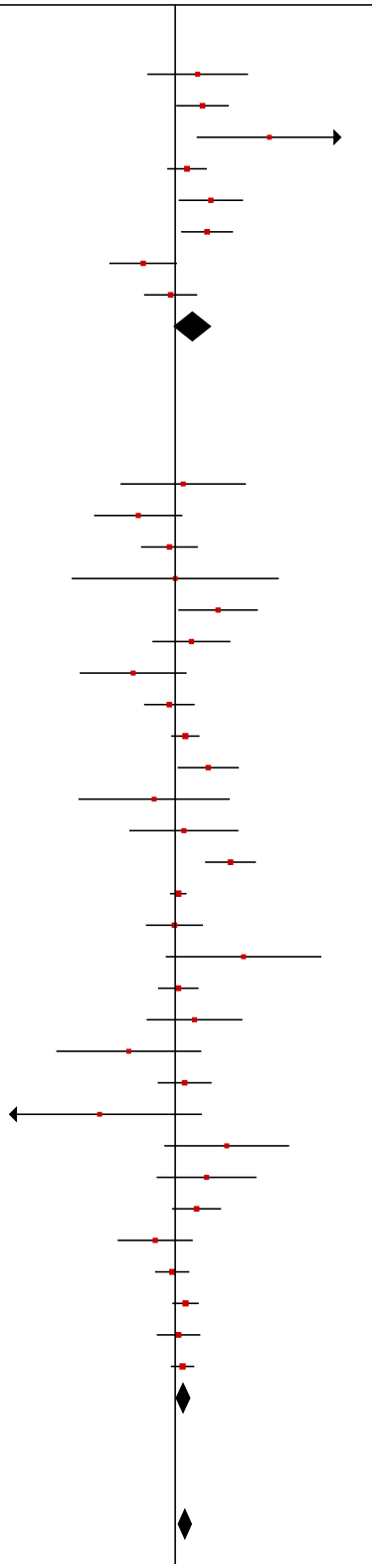
Analysis 4.8. (Continued)

Total (95% CI)	**100.0%**	**1.26 [1.07 , 1.48]**
Heterogeneity: Tau² = 0.13; Chi² = 91.53, df = 46 (P < 0.0001); I² = 50%		
Test for overall effect: Z = 2.76 (P = 0.006)		
Test for subgroup differences: Not applicable		



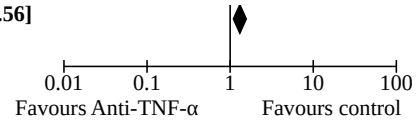
Analysis 4.9. Comparison 4: Anti-TNF-α agents versus control, Outcome 9: Postoperative infection within 30 days of surgery: sensitivity exclude surgery for abscess

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.9.1 Adjusted Analysis				
Gainsbury 2011 (1)	0.6259	0.7156	1.3%	1.87 [0.46 , 7.60]
Jouvin 2018	0.7608	0.3731	3.4%	2.14 [1.03 , 4.45]
Mor 2008	2.6247	1.0336	0.7%	13.80 [1.82 , 104.64]
Novello 2020	0.3293	0.2819	4.5%	1.39 [0.80 , 2.42]
Selvasekar 2007	0.9933	0.4581	2.6%	2.70 [1.10 , 6.63]
Syed 2013	0.8879	0.3686	3.4%	2.43 [1.18 , 5.00]
Uchino 2015	-0.8916	0.4801	2.4%	0.41 [0.16 , 1.05]
Uchino 2019	-0.1278	0.3774	3.3%	0.88 [0.42 , 1.84]
Subtotal (95% CI)			**21.6%**	**1.61 [0.98 , 2.65]**
Heterogeneity: Tau² = 0.30; Chi² = 18.31, df = 7 (P = 0.01); I² = 62%				
Test for overall effect: Z = 1.88 (P = 0.06)				
4.9.2 Unadjusted Analysis				
Ayoub 2018	0.2231	0.8909	0.9%	1.25 [0.22 , 7.17]
Bregnbak 2012	-1.0296	0.6273	1.6%	0.36 [0.10 , 1.22]
Colombel 2004	-0.1604	0.4041	3.1%	0.85 [0.39 , 1.88]
Coquet-Reinier 2010	0	1.472	0.4%	1.00 [0.06 , 17.90]
De Buck Van Overstraeten 2017	1.1939	0.5652	1.9%	3.30 [1.09 , 9.99]
Eshuis 2013	0.452	0.5548	2.0%	1.57 [0.53 , 4.66]
Ferrante 2009	-1.1712	0.7592	1.2%	0.31 [0.07 , 1.37]
Ferrante 2017	-0.1625	0.3597	3.5%	0.85 [0.42 , 1.72]
Gu 2013	0.2829	0.2011	5.7%	1.33 [0.89 , 1.97]
Guasch 2016	0.9203	0.435	2.8%	2.51 [1.07 , 5.89]
Gudsoorkar 2018	-0.5878	1.075	0.7%	0.56 [0.07 , 4.57]
Kim 2018	0.2426	0.7754	1.2%	1.27 [0.28 , 5.83]
Kotze 2017	1.5396	0.3613	3.5%	4.66 [2.30 , 9.47]
Liang 2017	0.0851	0.1174	6.9%	1.09 [0.87 , 1.37]
Lightner 2018 A	-0.0217	0.4057	3.0%	0.98 [0.44 , 2.17]
Marchal 2004	1.903	1.1056	0.6%	6.71 [0.77 , 58.55]
Myrelid 2014	0.0862	0.2879	4.4%	1.09 [0.62 , 1.92]
Nasir 2010	0.5373	0.6803	1.4%	1.71 [0.45 , 6.49]
Norgard 2012	-1.2921	1.0304	0.7%	0.27 [0.04 , 2.07]
Norgard 2013	0.2627	0.3838	3.3%	1.30 [0.61 , 2.76]
Regadas 2011	-2.107	1.454	0.4%	0.12 [0.01 , 2.10]
Schils 2017	1.4351	0.8873	0.9%	4.20 [0.74 , 23.91]
Schluender 2007	0.8738	0.7098	1.3%	2.40 [0.60 , 9.63]
Shwaartz 2016	0.5958	0.3483	3.6%	1.81 [0.92 , 3.59]
Uchino 2013b	-0.5564	0.5334	2.1%	0.57 [0.20 , 1.63]
Ward 2018	-0.0842	0.2425	5.0%	0.92 [0.57 , 1.48]
Waterman 2013	0.2882	0.1875	5.9%	1.33 [0.92 , 1.93]
Yamada 2017	0.0929	0.3095	4.1%	1.10 [0.60 , 2.01]
Zittan 2016	0.205	0.1665	6.2%	1.23 [0.89 , 1.70]
Subtotal (95% CI)			**78.4%**	**1.24 [1.03 , 1.50]**
Heterogeneity: Tau² = 0.07; Chi² = 45.95, df = 28 (P = 0.02); I² = 39%				
Test for overall effect: Z = 2.32 (P = 0.02)				
Total (95% CI)			**100.0%**	**1.31 [1.10 , 1.56]**
Heterogeneity: Tau² = 0.10; Chi² = 66.46, df = 36 (P = 0.001); I² = 46%				



Analysis 4.9. (Continued)

Total (95% CI)	**100.0%**	**1.31 [1.10 , 1.56]**
Heterogeneity: Tau² = 0.10; Chi² = 66.46, df = 36 (P = 0.001); I² = 46%		
Test for overall effect: Z = 2.97 (P = 0.003)		
Test for subgroup differences: Chi² = 0.92, df = 1 (P = 0.34), I² = 0%		

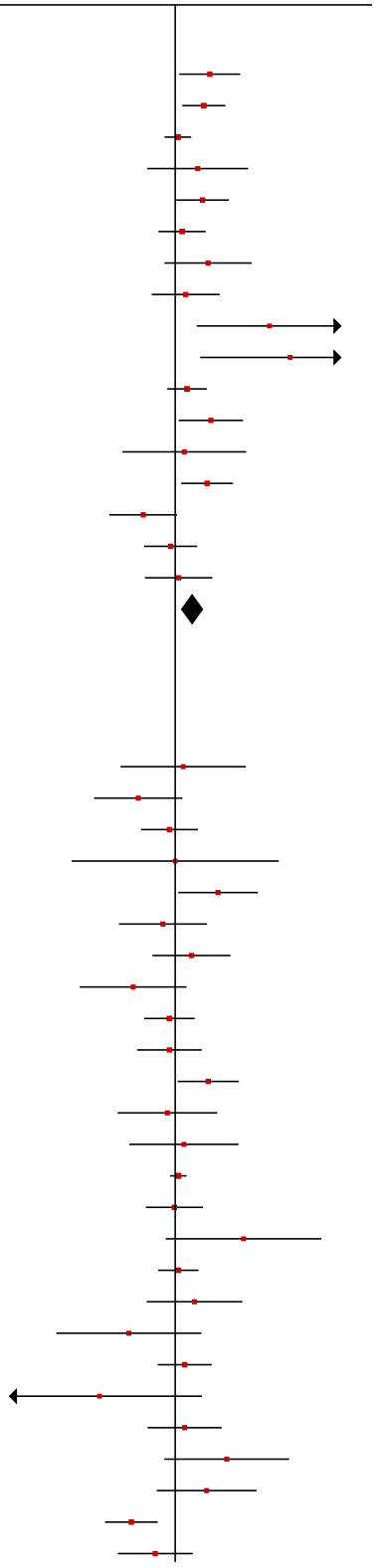


Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

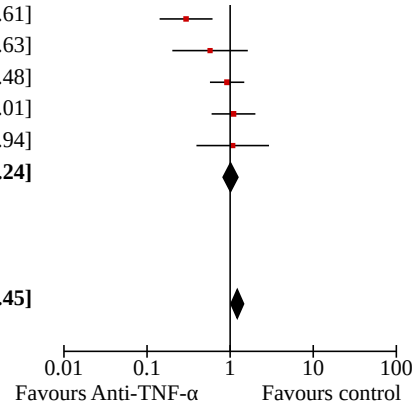
Analysis 4.10. Comparison 4: Anti-TNF-α agents versus control, Outcome 10: Postoperative infection within 30 days of surgery: sensitivity excluding sum of infection studies

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.10.1 Adjusted Analysis				
Appau 2008	0.9632	0.4336	2.5%	2.62 [1.12 , 6.13]
Brouquet 2018	0.7975	0.3054	3.6%	2.22 [1.22 , 4.04]
Cohen 2019	0.0751	0.1892	4.9%	1.08 [0.74 , 1.56]
Gainsbury 2011 (1)	0.6259	0.7156	1.2%	1.87 [0.46 , 7.60]
Jouvin 2018	0.7608	0.3731	3.0%	2.14 [1.03 , 4.45]
Krane 2013	0.1914	0.3359	3.3%	1.21 [0.63 , 2.34]
Kunitake 2008	0.9163	0.6209	1.6%	2.50 [0.74 , 8.44]
McKenna 2018	0.2927	0.483	2.2%	1.34 [0.52 , 3.45]
Mor 2008	2.6247	1.0336	0.7%	13.80 [1.82 , 104.64]
Morar 2015	3.2027	1.2804	0.5%	24.60 [2.00 , 302.55]
Novello 2020	0.3293	0.2819	3.9%	1.39 [0.80 , 2.42]
Selvasekar 2007	0.9933	0.4581	2.4%	2.70 [1.10 , 6.63]
Serradori 2013	0.2546	0.8798	0.9%	1.29 [0.23 , 7.24]
Syed 2013	0.8879	0.3686	3.0%	2.43 [1.18 , 5.00]
Uchino 2015	-0.8916	0.4801	2.2%	0.41 [0.16 , 1.05]
Uchino 2019	-0.1278	0.3774	3.0%	0.88 [0.42 , 1.84]
Yamamoto 2016	0.0953	0.4792	2.2%	1.10 [0.43 , 2.81]
Subtotal (95% CI)			**41.0%**	**1.60 [1.20 , 2.13]**
Heterogeneity: Tau² = 0.15; Chi² = 31.02, df = 16 (P = 0.01); I² = 48%				
Test for overall effect: Z = 3.23 (P = 0.001)				
4.10.2 Unadjusted Analysis				
Ayoub 2018	0.2231	0.8909	0.9%	1.25 [0.22 , 7.17]
Bregnbak 2012	-1.0296	0.6273	1.5%	0.36 [0.10 , 1.22]
Colombel 2004	-0.1604	0.4041	2.7%	0.85 [0.39 , 1.88]
Coquet-Reinier 2010	0	1.472	0.3%	1.00 [0.06 , 17.90]
De Buck Van Overstraeten 2017	1.1939	0.5652	1.8%	3.30 [1.09 , 9.99]
El-Hussuna 2012	-0.3434	0.6255	1.5%	0.71 [0.21 , 2.42]
Eshuis 2013	0.452	0.5548	1.8%	1.57 [0.53 , 4.66]
Ferrante 2009	-1.1712	0.7592	1.1%	0.31 [0.07 , 1.37]
Ferrante 2017	-0.1625	0.3597	3.1%	0.85 [0.42 , 1.72]
Fumery 2017	-0.1609	0.4589	2.4%	0.85 [0.35 , 2.09]
Guasch 2016	0.9203	0.435	2.5%	2.51 [1.07 , 5.89]
Guo 2017	-0.2167	0.7081	1.3%	0.81 [0.20 , 3.23]
Kim 2018	0.2426	0.7754	1.1%	1.27 [0.28 , 5.83]
Liang 2017	0.0851	0.1174	5.6%	1.09 [0.87 , 1.37]
Lightner 2018 A	-0.0217	0.4057	2.7%	0.98 [0.44 , 2.17]
Marchal 2004	1.903	1.1056	0.6%	6.71 [0.77 , 58.55]
Myrelid 2014	0.0862	0.2879	3.8%	1.09 [0.62 , 1.92]
Nasir 2010	0.5373	0.6803	1.3%	1.71 [0.45 , 6.49]
Norgard 2012	-1.2921	1.0304	0.7%	0.27 [0.04 , 2.07]
Norgard 2013	0.2627	0.3838	2.9%	1.30 [0.61 , 2.76]
Regadas 2011	-2.107	1.454	0.4%	0.12 [0.01 , 2.10]
Rizzo 2011	0.2624	0.5268	2.0%	1.30 [0.46 , 3.65]
Schils 2017	1.4351	0.8873	0.9%	4.20 [0.74 , 23.91]
Schluender 2007	0.8738	0.7098	1.3%	2.40 [0.60 , 9.63]
Uchino 2013a	-1.2214	0.374	3.0%	0.29 [0.14 , 0.61]
Uchino 2013b	-0.5564	0.5334	1.9%	0.57 [0.20 , 1.63]



Analysis 4.10. (Continued)

Uchino 2013a	-1.2214	0.374	3.0%	0.29 [0.14 , 0.61]
Uchino 2013b	-0.5564	0.5334	1.9%	0.57 [0.20 , 1.63]
Ward 2018	-0.0842	0.2425	4.3%	0.92 [0.57 , 1.48]
Yamada 2017	0.0929	0.3095	3.6%	1.10 [0.60 , 2.01]
Yu 2019	0.0715	0.5129	2.0%	1.07 [0.39 , 2.94]
Subtotal (95% CI)			**59.0%**	**1.01 [0.82 , 1.24]**
Heterogeneity: Tau² = 0.08; Chi² = 40.31, df = 28 (P = 0.06); I² = 31%				
Test for overall effect: Z = 0.10 (P = 0.92)				
Total (95% CI)			**100.0%**	**1.22 [1.02 , 1.45]**
Heterogeneity: Tau² = 0.13; Chi² = 80.72, df = 45 (P = 0.0009); I² = 44%				
Test for overall effect: Z = 2.21 (P = 0.03)				
Test for subgroup differences: Chi² = 6.59, df = 1 (P = 0.01), I² = 84.8%				



Footnotes

(1) Zeros indicate the study reported the OR rather than the number of participants

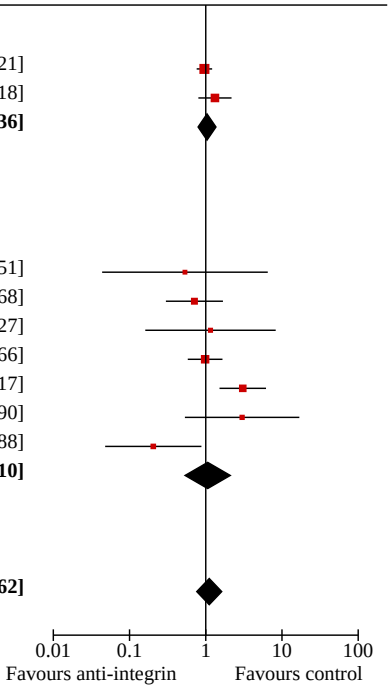
Comparison 5. Anti-integrin agents versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Postoperative infection within 30 days of surgery	9	5157	Odds Ratio (IV, Random, 95% CI)	1.11 [0.76, 1.62]
5.1.1 Adjusted Analysis	2	1022	Odds Ratio (IV, Random, 95% CI)	1.04 [0.79, 1.36]
5.1.2 Unadjusted Analysis	7	4135	Odds Ratio (IV, Random, 95% CI)	1.06 [0.54, 2.10]
5.2 Postoperative infection within 30 days of surgery: subgroup UC vs CD	5		Odds Ratio (IV, Random, 95% CI)	1.04 [0.52, 2.07]
5.2.1 Ulcerative colitis	2		Odds Ratio (IV, Random, 95% CI)	0.61 [0.28, 1.36]
5.2.2 Crohn's disease	4		Odds Ratio (IV, Random, 95% CI)	1.32 [0.51, 3.42]
5.3 Incisional infections and wound dehiscence	6		Odds Ratio (IV, Random, 95% CI)	1.64 [0.77, 3.50]
5.4 Intra-abdominal infectious complications	5		Odds Ratio (IV, Random, 95% CI)	0.40 [0.14, 1.20]
5.5 Extra-abdominal infections	5		Odds Ratio (IV, Random, 95% CI)	1.15 [0.43, 3.08]
5.6 Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias	3		Odds Ratio (IV, Random, 95% CI)	1.10 [0.79, 1.52]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.7 Postoperative infection within 30 days of surgery: sensitivity exclude abstract	5		Odds Ratio (IV, Random, 95% CI)	1.06 [0.58, 1.96]
5.8 Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess	9		Odds Ratio (IV, Random, 95% CI)	1.11 [0.76, 1.62]
5.8.1 Adjusted Analysis	2		Odds Ratio (IV, Random, 95% CI)	1.04 [0.79, 1.36]
5.8.2 Unadjusted Analysis	7		Odds Ratio (IV, Random, 95% CI)	1.06 [0.54, 2.10]
5.9 Postoperative infection within 30 days of surgery: sensitivity excluding sum of infection studies	7		Odds Ratio (IV, Random, 95% CI)	0.97 [0.73, 1.29]
5.9.1 Adjusted Analysis	2		Odds Ratio (IV, Random, 95% CI)	1.04 [0.79, 1.36]
5.9.2 Unadjusted Analysis	5		Odds Ratio (IV, Random, 95% CI)	0.78 [0.42, 1.47]

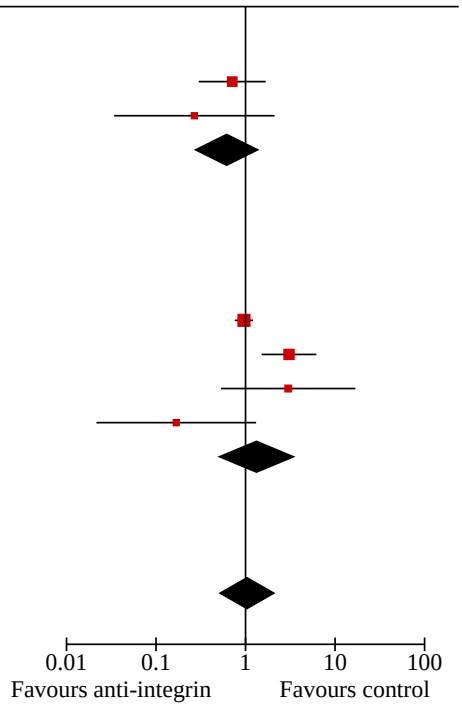
Analysis 5.1. Comparison 5: Anti-integrin agents versus control, Outcome 1: Postoperative infection within 30 days of surgery

Study or Subgroup	log[OR]	SE	Anti-integrin Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI
5.1.1 Adjusted Analysis						
Kim 2018	-0.0408	0.1192	13	29	24.4%	0.96 [0.76 , 1.21]
Novello 2020	0.2776	0.2555	141	839	18.2%	1.32 [0.80 , 2.18]
Subtotal (95% CI)			**154**	**868**	**42.6%**	**1.04 [0.79 , 1.36]**
Heterogeneity: Tau² = 0.01; Chi² = 1.28, df = 1 (P = 0.26); I² = 22%						
Test for overall effect: Z = 0.28 (P = 0.78)						
5.1.2 Unadjusted Analysis						
Ayoub 2018	-0.6286	1.2764	16	18	2.1%	0.53 [0.04 , 6.51]
Ferrante 2017	-0.3425	0.4395	34	136	11.2%	0.71 [0.30 , 1.68]
Gudsoorkar 2018	0.1431	1.0051	16	12	3.2%	1.15 [0.16 , 8.27]
Liang 2017	-0.0192	0.2674	114	3246	17.7%	0.98 [0.58 , 1.66]
Lightner 2018 A	1.118	0.3583	100	105	13.9%	3.06 [1.52 , 6.17]
Schils 2017	1.0986	0.8819	12	12	4.0%	3.00 [0.53 , 16.90]
Yamada 2017	-1.5851	0.7417	64	250	5.4%	0.20 [0.05 , 0.88]
Subtotal (95% CI)			**356**	**3779**	**57.4%**	**1.06 [0.54 , 2.10]**
Heterogeneity: Tau² = 0.44; Chi² = 15.96, df = 6 (P = 0.01); I² = 62%						
Test for overall effect: Z = 0.17 (P = 0.87)						
Total (95% CI)			**510**	**4647**	**100.0%**	**1.11 [0.76 , 1.62]**
Heterogeneity: Tau² = 0.14; Chi² = 17.69, df = 8 (P = 0.02); I² = 55%						
Test for overall effect: Z = 0.55 (P = 0.58)						
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%						



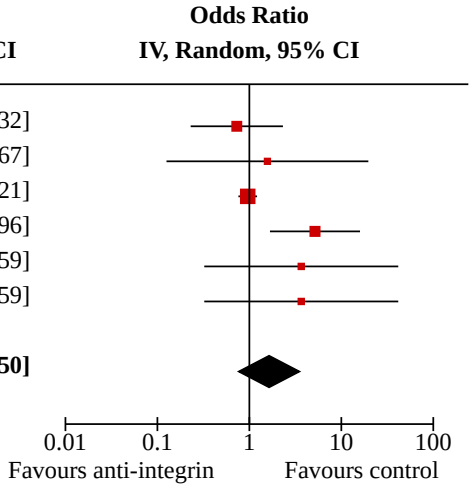
Analysis 5.2. Comparison 5: Anti-integrin agents versus control, Outcome 2: Postoperative infection within 30 days of surgery: subgroup UC vs CD

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
5.2.1 Ulcerative colitis				
Ferrante 2017	-0.3425	0.4395	20.6%	0.71 [0.30 , 1.68]
Yamada 2017	-1.3163	1.0526	8.2%	0.27 [0.03 , 2.11]
Subtotal (95% CI)			**28.8%**	**0.61 [0.28 , 1.36]**
Heterogeneity: Tau² = 0.00; Chi² = 0.73, df = 1 (P = 0.39); I² = 0%				
Test for overall effect: Z = 1.20 (P = 0.23)				
5.2.2 Crohn's disease				
Kim 2018	-0.0408	0.1192	29.4%	0.96 [0.76 , 1.21]
Lightner 2018 A	1.118	0.3583	23.1%	3.06 [1.52 , 6.17]
Schils 2017	1.0986	0.8819	10.4%	3.00 [0.53 , 16.90]
Yamada 2017	-1.7822	1.0477	8.2%	0.17 [0.02 , 1.31]
Subtotal (95% CI)			**71.2%**	**1.32 [0.51 , 3.42]**
Heterogeneity: Tau² = 0.61; Chi² = 13.90, df = 3 (P = 0.003); I² = 78%				
Test for overall effect: Z = 0.58 (P = 0.56)				
Total (95% CI)			**100.0%**	**1.04 [0.52 , 2.07]**
Heterogeneity: Tau² = 0.41; Chi² = 16.39, df = 5 (P = 0.006); I² = 69%				
Test for overall effect: Z = 0.10 (P = 0.92)				
Test for subgroup differences: Chi² = 1.48, df = 1 (P = 0.22), I² = 32.5%				



Analysis 5.3. Comparison 5: Anti-integrin agents versus control, Outcome 3: Incisional infections and wound dehiscence

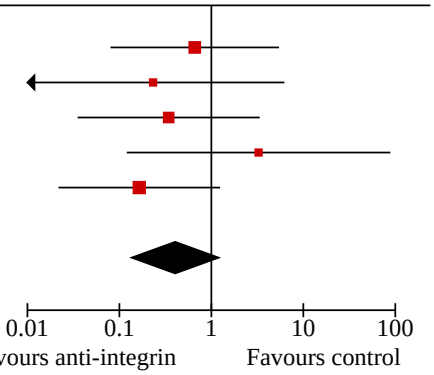
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Ferrante 2017	-0.3147	0.5893	20.1%	0.73 [0.23 , 2.32]
Gudsoorkar 2018	0.452	1.2893	7.3%	1.57 [0.13 , 19.67]
Kim 2018	-0.0408	0.1192	36.5%	0.96 [0.76 , 1.21]
Lightner 2018 A	1.6432	0.5751	20.6%	5.17 [1.68 , 15.96]
Schils 2017	1.2993	1.2391	7.7%	3.67 [0.32 , 41.59]
Yamada 2017	1.2993	1.2391	7.7%	3.67 [0.32 , 41.59]
Total (95% CI)			**100.0%**	**1.64 [0.77 , 3.50]**
Heterogeneity: Tau² = 0.39; Chi² = 10.76, df = 5 (P = 0.06); I² = 54%				
Test for overall effect: Z = 1.28 (P = 0.20)				
Test for subgroup differences: Not applicable				



Analysis 5.4. Comparison 5: Anti-integrin agents versus control, Outcome 4: Intra-abdominal infectious complications

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Ferrante 2017	-0.4155	1.0767	26.6%	0.66 [0.08 , 5.45]
Gudsoorkar 2018	-1.4596	1.6776	10.9%	0.23 [0.01 , 6.22]
Lightner 2018 A	-1.0688	1.1633	22.7%	0.34 [0.04 , 3.36]
Schils 2017	1.182	1.6833	10.9%	3.26 [0.12 , 88.34]
Yamada 2017	-1.8048	1.0323	28.9%	0.16 [0.02 , 1.24]
Total (95% CI)			**100.0%**	**0.40 [0.14 , 1.20]**

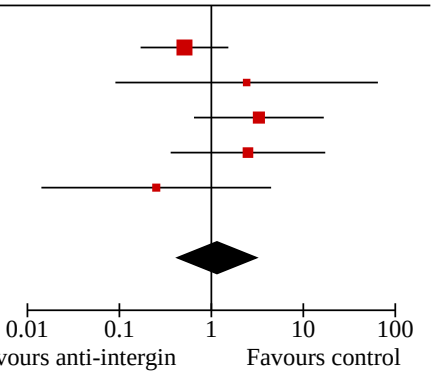
Heterogeneity: Tau² = 0.00; Chi² = 2.63, df = 4 (P = 0.62); I² = 0%
Test for overall effect: Z = 1.63 (P = 0.10)
Test for subgroup differences: Not applicable



Analysis 5.5. Comparison 5: Anti-integrin agents versus control, Outcome 5: Extra-abdominal infections

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Ferrante 2017	-0.6733	0.5605	38.3%	0.51 [0.17 , 1.53]
Gudsoorkar 2018	0.8835	1.6767	8.0%	2.42 [0.09 , 64.70]
Lightner 2018 A	1.19	0.8289	24.5%	3.29 [0.65 , 16.69]
Schils 2017	0.9163	0.9874	19.1%	2.50 [0.36 , 17.31]
Yamada 2017	-1.3796	1.4673	10.1%	0.25 [0.01 , 4.46]
Total (95% CI)			**100.0%**	**1.15 [0.43 , 3.08]**

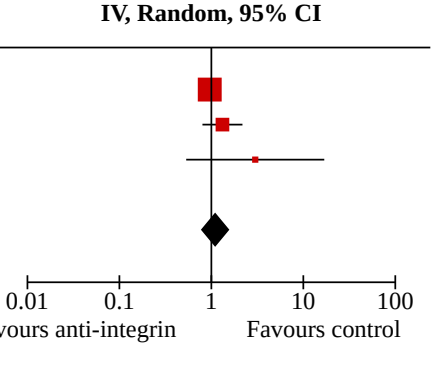
Heterogeneity: Tau² = 0.35; Chi² = 5.52, df = 4 (P = 0.24); I² = 28%
Test for overall effect: Z = 0.28 (P = 0.78)
Test for subgroup differences: Not applicable



Analysis 5.6. Comparison 5: Anti-integrin agents versus control, Outcome 6: Postoperative infection within 30 days of surgery: sensitivity excluding very high risk of bias

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Kim 2018	-0.0408	0.1192	66.5%	0.96 [0.76 , 1.21]
Novello 2020	0.2776	0.2555	30.0%	1.32 [0.80 , 2.18]
Schils 2017	1.0986	0.8819	3.5%	3.00 [0.53 , 16.90]
Total (95% CI)			**100.0%**	**1.10 [0.79 , 1.52]**

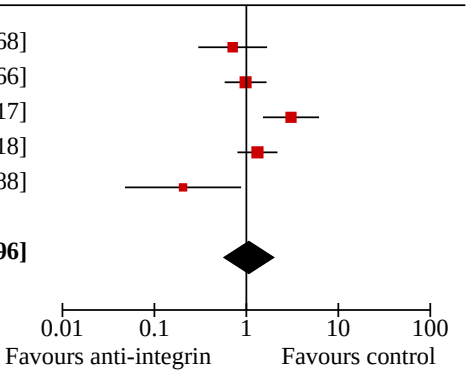
Heterogeneity: Tau² = 0.03; Chi² = 2.76, df = 2 (P = 0.25); I² = 28%
Test for overall effect: Z = 0.56 (P = 0.57)
Test for subgroup differences: Not applicable



Analysis 5.7. Comparison 5: Anti-integrin agents versus control, Outcome 7: Postoperative infection within 30 days of surgery: sensitivity exclude abstract

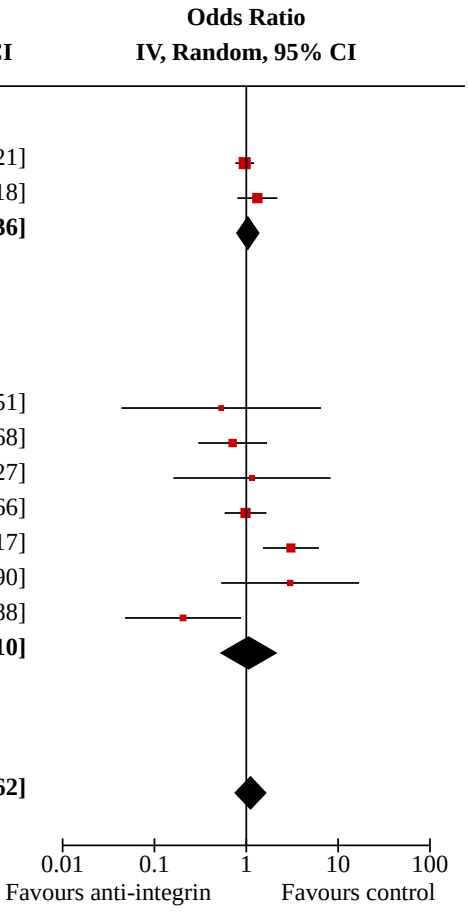
Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
Ferrante 2017	-0.3425	0.4395	18.6%	0.71 [0.30 , 1.68]
Liang 2017	-0.0192	0.2674	24.3%	0.98 [0.58 , 1.66]
Lightner 2018 A	1.118	0.3583	21.3%	3.06 [1.52 , 6.17]
Novello 2020	0.2776	0.2555	24.7%	1.32 [0.80 , 2.18]
Yamada 2017	-1.5851	0.7417	11.1%	0.20 [0.05 , 0.88]
Total (95% CI)			**100.0%**	**1.06 [0.58 , 1.96]**

Heterogeneity: Tau² = 0.33; Chi² = 14.63, df = 4 (P = 0.006); I² = 73%
Test for overall effect: Z = 0.20 (P = 0.84)
Test for subgroup differences: Not applicable



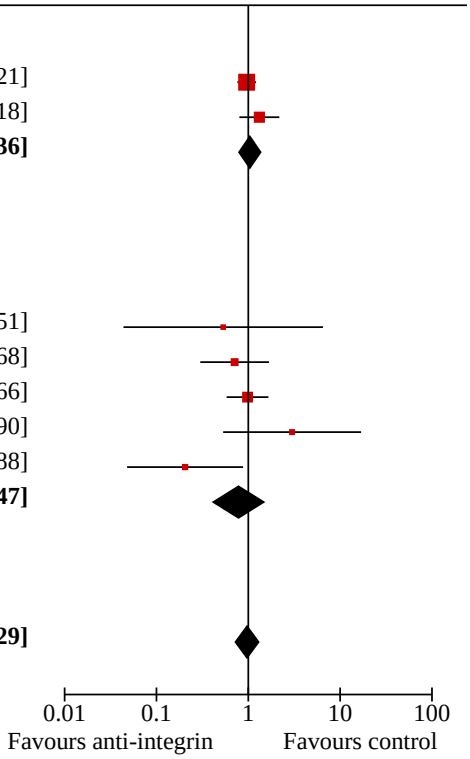
Analysis 5.8. Comparison 5: Anti-integrin agents versus control, Outcome 8: Postoperative infection within 30 days of surgery: sensitivity excluding surgery for abscess

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
5.8.1 Adjusted Analysis				
Kim 2018	-0.0408	0.1192	24.4%	0.96 [0.76 , 1.21]
Novello 2020	0.2776	0.2555	18.2%	1.32 [0.80 , 2.18]
Subtotal (95% CI)			**42.6%**	**1.04 [0.79 , 1.36]**
Heterogeneity: Tau² = 0.01; Chi² = 1.28, df = 1 (P = 0.26); I² = 22%				
Test for overall effect: Z = 0.28 (P = 0.78)				
5.8.2 Unadjusted Analysis				
Ayoub 2018	-0.6286	1.2764	2.1%	0.53 [0.04 , 6.51]
Ferrante 2017	-0.3425	0.4395	11.2%	0.71 [0.30 , 1.68]
Gudsoorkar 2018	0.1431	1.0051	3.2%	1.15 [0.16 , 8.27]
Liang 2017	-0.0192	0.2674	17.7%	0.98 [0.58 , 1.66]
Lightner 2018 A	1.118	0.3583	13.9%	3.06 [1.52 , 6.17]
Schils 2017	1.0986	0.8819	4.0%	3.00 [0.53 , 16.90]
Yamada 2017	-1.5851	0.7417	5.4%	0.20 [0.05 , 0.88]
Subtotal (95% CI)			**57.4%**	**1.06 [0.54 , 2.10]**
Heterogeneity: Tau² = 0.44; Chi² = 15.96, df = 6 (P = 0.01); I² = 62%				
Test for overall effect: Z = 0.17 (P = 0.87)				
Total (95% CI)			**100.0%**	**1.11 [0.76 , 1.62]**
Heterogeneity: Tau² = 0.14; Chi² = 17.69, df = 8 (P = 0.02); I² = 55%				
Test for overall effect: Z = 0.55 (P = 0.58)				
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%				



Analysis 5.9. Comparison 5: Anti-integrin agents versus control, Outcome 9: Postoperative infection within 30 days of surgery: sensitivity excluding sum of infection studies

Study or Subgroup	log[OR]	SE	Weight	Odds Ratio IV, Random, 95% CI
5.9.1 Adjusted Analysis				
Kim 2018	-0.0408	0.1192	41.9%	0.96 [0.76 , 1.21]
Novello 2020	0.2776	0.2555	21.1%	1.32 [0.80 , 2.18]
Subtotal (95% CI)			**63.0%**	**1.04 [0.79 , 1.36]**
Heterogeneity: Tau² = 0.01; Chi² = 1.28, df = 1 (P = 0.26); I² = 22%				
Test for overall effect: Z = 0.28 (P = 0.78)				
5.9.2 Unadjusted Analysis				
Ayoub 2018	-0.6286	1.2764	1.3%	0.53 [0.04 , 6.51]
Ferrante 2017	-0.3425	0.4395	9.4%	0.71 [0.30 , 1.68]
Liang 2017	-0.0192	0.2674	19.9%	0.98 [0.58 , 1.66]
Schils 2017	1.0986	0.8819	2.7%	3.00 [0.53 , 16.90]
Yamada 2017	-1.5851	0.7417	3.7%	0.20 [0.05 , 0.88]
Subtotal (95% CI)			**37.0%**	**0.78 [0.42 , 1.47]**
Heterogeneity: Tau² = 0.18; Chi² = 6.31, df = 4 (P = 0.18); I² = 37%				
Test for overall effect: Z = 0.76 (P = 0.45)				
Total (95% CI)			**100.0%**	**0.97 [0.73 , 1.29]**
Heterogeneity: Tau² = 0.04; Chi² = 8.21, df = 6 (P = 0.22); I² = 27%				
Test for overall effect: Z = 0.22 (P = 0.83)				
Test for subgroup differences: Chi² = 0.66, df = 1 (P = 0.42), I² = 0%				

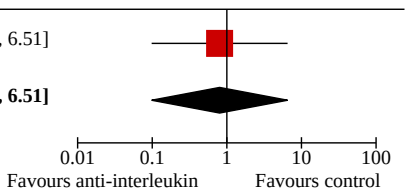


Comparison 6. Anti-interleukin agents versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Postoperative infection within 30 days of surgery	1	3360	Odds Ratio (IV, Random, 95% CI)	0.80 [0.10, 6.51]

Analysis 6.1. Comparison 6: Anti-interleukin agents versus control, Outcome 1: Postoperative infection within 30 days of surgery

Study or Subgroup	log[OR]	SE	Anti-interleukin Total	Control Total	Weight	Odds Ratio IV, Random, 95% CI
Liang 2017	-0.2234	1.0701	8	3352	100.0%	0.80 [0.10 , 6.51]
Total (95% CI)			**8**	**3352**	**100.0%**	**0.80 [0.10 , 6.51]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.21 (P = 0.83)						
Test for subgroup differences: Not applicable						



APPENDICES

Appendix 1. Search strategies

MEDLINE

1. random$.tw.

2. factorial$.tw.

3. (crossover$ or cross over$ or cross-over$).tw.

4. placebo$.tw.

5. single blind.mp.

6. double blind.mp.

7. triple blind.mp.

8. (singl$ adj blind$).tw.

9. (double$ adj blind$).tw.

10. (tripl$ adj blind$).tw.

11 assign$.tw.

12. allocat$.tw.

13. randomized controlled trial/

14. or/1-13

15. exp cohort studies/

16. exp case-control studies/

17. exp retrospective studies/

18. exp Epidemiologic Studies/

19. case-control studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or cross-sectional studies/

20.(cohort$ or prospective$ or retrospective$).mp.

21. or/15-20

22. 14 or 21

23. Exp Inflammatory bowel disease/

24. (inflammatory bowel disease* or IBD).mp.

25. Exp Crohn disease/ or crohn*.mp.

26. Exp ulcerative colitis/ or (colitis and ulcerat*).mp.

27. or/23-26

28. (Anti-TNF* OR anti TNF* or Biologic*).mp.

29. Integrin receptor antagonist.mp.

30. (Corticosteroid* or steroid*).mp.

31. (immunosuppress* or immunomodulator*).mp.

32. Antibiotic*.mp.

33. Aminosalicylate*.mp.

34. (Adalimumab or Certolizumab* or Golimumab or Infliximab or Natalizumab or Ustekinumab or Vedolizumab).mp.

35. (Tofacitinib or Ozanimod).mp.

36. (Budesonide or Methylprednisolone or Prednisolone or Prednisone).mp.

37. (Azathioprine or 6-MP or 6-mercaptopurine or Cyclosporine or Mercaptopurine or Methotrexate or Tacrolimus).mp.

38. (Ciprofloxain or Metronidazole).mp.

39. (5-ASA or Balsalazide or Mesalamine or Olsalazine or Sulfasalazine).mp.

40. or/28-39

41. (Post-operation or Post-operative or Post-op* or postoperative* or postsurgical* or post-surg*).mp.

42. (operation* or surg* or strictureplasty or resection or colectomy or proctocolectomy).mp.

43. 41 or 42

44. (Infect* or complication* or heal* or re-operation or reoperation or outcome* or adverse* or adverse event* or side effect*).mp.

45. 22 and 27 and 40 and 43 and 44

Embase

1. random$.mp.

2. factorial$.mp.

3. (crossover$ or cross over$ or cross-over$).mp.

4. placebo$.mp.

5. single blind.mp.

6. double blind.mp.

7. triple blind.mp.

8. (singl$ adj blind$).mp.

9. (double$ adj blind$).mp.

10. (tripl$ adj blind$).mp.

11. assign$.mp.

12. allocat$.mp.

13. crossover procedure/

14. double blind procedure/

15. single blind procedure/

16. triple blind procedure/

17. randomized controlled trial/

18. or/1-17

19. exp cohort studies/

20. exp case-control studies/

21. exp retrospective studies/

22. exp Epidemiologic Studies/

23. case-control studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or cross-sectional studies/

24. (cohort$ or prospective$ or retrospective$).mp.

25. or/19-24

26. 18 or 25

27. Exp Inflammatory bowel disease/

28. (inflammatory bowel disease* or IBD).mp.

29. Exp Crohn disease/ or crohn*.mp.

30. Exp ulcerative colitis/ or (colitis and ulcerat*).mp.

31. or/27-30

32. (Anti-TNF* OR anti TNF* or Biologic*).mp.

33. Integrin receptor antagonist.mp.

34. (Corticosteroid* or steroid*).mp.

35. (immunosuppress* or immunomodulator*).mp.

36. Antibiotic*.mp.

37. (Aminosalicylate* or Aminosalicylic*).mp.

38. (Adalimumab or Certolizumab* or Golimumab or Infliximab or Natalizumab or Ustekinumab or Vedolizumab).mp.

39. (Tofacitinib or Ozanimod).mp.

40. (Budesonide or Methylprednisolone or Prednisolone or Prednisone).mp.

41. (Azathioprine or 6-MP or 6-mercaptopurine or Cyclosporine or Mercaptopurine or Methotrexate or Tacrolimus).mp.

42. (Ciprofloxain or Metronidazole).mp.

43. (5-ASA or Balsalazide or Mesalamine or Olsalazine or Sulfasalazine).mp.

44. or/32-43

45. (Post-operation or Post-operative or Post-op* or postoperative* or postsurgical* or post-surg*).mp.

46. (operation* or surg* or strictureplasty or resection or colectomy or proctocolectomy).mp.

47. 45 or 46

48. (Infect* or complication* or heal* or re-operation or reoperation or outcome* or adverse* or adverse event* or side effect*).mp.

49. 26 and 31 and 44 and 47 and 48

CENTRAL

#1 MeSH: [Inflammatory bowel disease] explode all trees

#2 IBD

#3 Crohn

#4 ulcerative colitis

#5 #1 or #2 or #3 or #4

#6 MeSH: [Biological factors] explode all trees

#7 MeSH: [Receptors, Steroid] explode all trees

#8 MeSH: [Immunosuppressive Agents] explode all trees

#9 MeSH: [Anti-bacterial agents] explode all trees

#10 MeSH: [Aminosalicylic Acids] explode all trees

#11 Adalimumab or Certolizumab* or Golimumab or Infliximab or Natalizumab or Ustekinumab or Vedolizumab

#12 Tofacitinib or Ozanimod

#13 Budesonide or Methylprednisolone or Prednisolone or Prednisone

#14 Azathioprine or 6MP or mercaptopurine or Cyclosporine or Mercaptopurine or Methotrexate or Tacrolimus

#15 Ciprofloxain or Metronidazole

#16 5ASA or Balsalazide or Mesalamine or Olsalazine or Sulfasalazine

#17 #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16

#18 Post-operation or Post-operative or Post-op* or postoperative* or postsurgical* or post-surg*

#19 operation* or surg* or strictureplasty or resection or colectomy or proctocolectomy

#20 #18 or #19

#21 Infect* or complication* or heal* or re-operation or reoperation or outcome* or adverse* or adverse event* or side effect*

#22 #5 and #17 and #20 and #21

Cochrane IBD Group Specialized Register

1. Operation and infection

2. Post-opera and outcome

3. Operation and complication

4. Surgery and Crohn's disease

5. Surgery and ulcerative colitis

Clinicaltrials.gov

1. Inflammatory bowel disease and operation/surgery

2. Inflammatory bowel disease and surgical complication

WHO trials registry (ICTRP)

1. Inflammatory bowel disease and operation/surgery

2. Inflammatory bowel disease and surgical complication

WHAT'S NEW

Date	Event	Description
4 November 2021	Amended	This amendment addresses post-publication feedback. Changes include updates to the analyses and risk of bias assessments. These changes did not impact the conclusions or certainty of the evidence.

HISTORY

Protocol first published: Issue 2, 2019
Review first published: Issue 10, 2020

CONTRIBUTIONS OF AUTHORS

Cindy CY Law: Data acquisition, data analysis and drafting of the manuscript.

Conor Bell: Data acquisition and drafting of the manuscript.

Deborah Koh: Data acquisition and drafting of the manuscript.

Yueyang Bao: Data acquisition and critical revision of the manuscript.

Vipul Jairath: Study concept and critical revision of the manuscript.

Neeraj Narula: Study concept, data analysis and critical revision of the manuscript.

DECLARATIONS OF INTEREST

Cindy CY Law: None known

Conor Bell: None known

Deborah Koh: None known

Yueyang Bao: None known

Vipul Jairath has received has received consulting fees from AbbVie, Eli Lilly, GlaxoSmithKline, Arena pharmaceuticals, Genetech, Pendopharm, Sandoz, Merck, Takeda, Janssen, Robarts Clinical Trials, Topivert, Celltrion; speakers fees from Takeda, Janssen, Shire, Ferring, Abbvie, and Pfizer.

Neeraj Narula has received fees for consultancy from Abbvie, Takeda. Janssen, and Lupin; payment for lectures from Abbvie, Takeda, Janssen, and Pfizier; and payment for educational presentations from Abbvie and Janssen.

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- No sources of support provided

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Several modifications were made to the protocol.

Firstly, we clarified that patients with a diagnosis of indeterminate colitis could be included. With regards to the classes of medications included in the study, we separated the biologics category into three separate categories entitled anti-TNF medications, anti-interleukin medications, and anti-integrin medications. Also, we decided that studies comparing two biologics (i.e. vedolizumab versus infliximab) would be excluded due to issues with confounding by indication. Furthermore, we clarified that we would exclude studies that reported complications outside the 30-day postoperative period.

In the Data extraction and management section, we updated that the investigators CL, CB and NN performed data extraction instead of CL, DK, and YB. We clarified that we attempted to contact authors in cases where data was missing.

In the Assessment of risk of bias in included studies section, we updated that four investigators assessed the methodological quality of the studies instead of three. Definitions of low, high, and very high risk of bias for the Newcastle-Ottawa Scale were added to provide clarification to readers.

In instances where a study included two treatment arms (e.g. immunomodulator and anti-TNF medication), we had originally stated in the protocol that we would divide the control group between the treatment groups. For our analysis, we elected not to divide the control

group between the treatment groups because the data for each treatment group was used in separate analyses and thus, would not create a unit of analysis error.

Information on the GRADE analysis was moved from this section to the 'Summary of findings and assessment of the certainty of the evidence' section.
Two sensitivity analyses were added. We excluded studies that included patients who underwent surgery to alleviate a fistula/abscess or who were found to have an intra-abdominal abscess intraoperatively. We performed this sensitivity analysis as the presence of a pre-operative abscess is likely a confounding factor. Another ad-hoc sensitivity analysis was performed excluding studies with potential unit of analysis issues (studies for which we estimated the overall rate of infection by summation of different types of infections).
In the protocol, we stated that data from randomized and non-randomized studies would be pooled. We amended the Methods section to reflect that, if applicable, we would analyze randomized and non-randomized studies separately. In addition, we had planned to select a random effects or fixed effects model based on the amount of heterogeneity in the results. However, we later decided that a random effects model would be used for all analyses given that significant heterogeneity was anticipated in the studies and this would be best accounted for using a random effects model.
Lastly, some studies reported adjusted data while others reported unadjusted results. We modified our Methods so that adjusted and unadjusted data would be analyzed separately for the primary outcome of interest.

INDEX TERMS

Medical Subject Headings (MeSH)

Adrenal Cortex Hormones [adverse effects]; Aminosalicylic Acids [adverse effects]; Bias; Colitis, Ulcerative [drug therapy]; Confidence Intervals; Crohn Disease [drug therapy]; Immunologic Factors [adverse effects]; Infections [*chemically induced] [epidemiology]; Inflammatory Bowel Diseases [*drug therapy]; Integrins [antagonists & inhibitors]; Observational Studies as Topic [statistics & numerical data]; Odds Ratio; Postoperative Complications [*chemically induced] [epidemiology]; Surgical Wound Dehiscence [chemically induced] [epidemiology]; Surgical Wound Infection [chemically induced] [epidemiology]; Time Factors; Tumor Necrosis Factor-alpha [antagonists & inhibitors]

MeSH check words

Adult; Female; Humans; Male