| Comparison | Outcome | Number of studies (Participants) | Domains pertaining to strength of evidence | Magnitude of effectStrength of evidence |
| --- | --- | --- | --- | --- |
|  |  |  | Risk of bias | Consistency | Directness | Precision |  |
| TNF-alpha inhibitor vs no TNF-alpha inhibitor | Mortality | 12 RCTs3,896 CD1 prospective2 retrospective6,464 CD1,409 IBD | Moderate | Consistent | Direct | Very imprecise | Neither favoredObservational RR range 0.8 – 4.3Low |
| Infliximab + IMM vs infliximab | Mortality | 3 RCTs535 CD3 retrospective1 unclear690 CD221 IBD | High | Inconsistent | Direct | Very imprecise | Neither favoredLow |
| Infliximab + IMM vs IMM | Mortality | 1 RCT340 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Infliximab + corticosteroids vs infliximab | Mortality | 2 retrospective71 CD100 IBD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Infliximab vs IMM | Mortality | 1 RCT324 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Natalizumab vs placebo | Mortality | 3 RCTs1,414 CD | Moderate | Consistent | Direct | Very imprecise | Neither favoredLow |
| IMM vs no IMM | Mortality | 3 RCTs425 CD2 prospective2 retrospective11,829 CD19,486 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredObservational RR range 0.7 – 1.3 Low |
| Azathioprine vs corticosteroids | Mortality | 2 RCTs336 CD | Moderate | Consistent | Direct | Very imprecise | Neither favoredLow |
| Azathioprine vs sulfasalazine | Mortality | 1 RCT245 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Azathioprine + prednisone vs prednisone | Mortality | 1 RCT81 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Corticosteroids vs no corticosteroids | Mortality | 2 RCTs547 CD1 prospective3 retrospective15,070 CD554 IBD | High | Inconsistent | Direct | Imprecise | No corticosteroids favoredObservational RR range 1.0 – 2.5Low |
| Corticosteroids vs ASA | Mortality | 2 RCTs508 CD | Moderate | Consistent | Direct | Very imprecise | Neither favoredLow |
| Corticosteroids + ASA vs placebo, corticosteroids or ASA | Mortality | 1 RCT452 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| ASA vs no ASA | Mortality | 4 RCTs674 CD1 retrospective3,241 CD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredObservational RR 0.7Low |
| TNF-alpha inhibitor vs no TNF-alpha inhibitor | Lymphoma | 8 RCTs2,704 CD 3 retrospective9,389 CD1,409 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredObservational RR range 0.6 – 1.7Low |
| TNF-alpha inhibitor + IMM + steroids vs no therapy | Lymphoma | 1 retrospectiveNR CD | High | NA | Direct | Very imprecise | Neither favored Low |
| Infliximab + IMM vs infliximab | Lymphoma | 1 retrospective100 IBD | High | NA | Direct | Very imprecise | Neither favoredLow |
| TNF-alpha inhibitor + IMM vs no therapy | Lymphoma | 1 retrospectiveNR CD | High | NA | Direct | Imprecise | Neither favoredObservational RR = 1.5Low |
| Infliximab + corticosteroids vs infliximab | Lymphoma | 1 retrospective100 IBD | High | NA | Direct | Very imprecise | Neither favoredLow |
| TNF-alpha inhibitor + corticosteroids vs no therapy | Lymphoma | 1 retrospectiveNR CD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Natalizumab vs placebo | Lymphoma | 3 RCTs1,414 CD | Moderate | Consistent | Direct | Very imprecise | Neither favoredLow |
| Natalizumab + infliximab vs infliximab | Lymphoma | 1 RCT79 CD | Low | NA | Direct | Very imprecise | Neither favoredLow |
| IMM vs no IMM | Lymphoma | 1 prospective4 retrospective1 case-control8,581 CD54,939 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredObservational RR range 0.3 – 5.3 Low |
| IMM + corticosteroids vs no therapy | Lymphoma | 1 retrospectiveNR CD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Azathioprine + ASA vs azathioprine | Lymphoma | 1 retrospective104 CD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Corticosteroids vs no therapy | Lymphoma | 1 retrospectiveNR CD | High | NA | Direct | Very imprecise | Neither favoredObservation HR 1.0Low |
| Corticosteroids vs no corticosteroids | Lymphoma | 1 retrospective15,164 IBD | High | NA | Direct | Imprecise | Neither favoredObservational OR 1.0Low |
| ASA vs no ASAMs; aminosalicylates; rval; se Questionnaire; ership skillsield of computer science/engineerig. | Lymphoma | 1 retrospective15,164 IBD | High | NA | Direct | Imprecise | Neither favoredObservational OR 1.0Low |
| TNF-alpha inhibitor vs no TNF-alpha inhibitor | Cervical cancer | 1 RCT371 CD women3 retrospective1,567 IBD women | High | Inconsistent | Direct | Imprecise | Neither favored; Low |
| IMM vs no IMM | Cervical cancer | 4 retrospective1,942 IBD women | High | Inconsistent | Direct | Imprecise | Neither favored; Low |
| Corticosteroids vs no corticosteroids | Cervical cancer | 2 retrospective1,205 IBD women | High | Inconsistent | Direct | Imprecise | Neither favored; Low |
| ASA vs no ASA | Cervical cancer | 1 retrospective1,165 IBD women | High | NA | Direct | Imprecise | Neither favored; Low |
| TNF-alpha inhibitor vs no TNF-alpha inhibitor | Cancers | 8 RCTs3,393 CD3 retrospective1,966 CD1,409 IBD1 case-control1,935 CD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredObservational RR range 0.2 – 3.6Low |
| TNF-alpha inhibitor + IMM + steroids vs no therapy | Cancers | 1 retrospective8,581 CD | High | NA | Direct | Imprecise | Neither favoredObservational RR 0.7 – 0.9Low |
| TNF-alpha inhibitor + IMM versus no TNF-alpha inhibitor + no IMM | Cancers | 1 case-control1,935 CD | High | NA | Direct | Precise | No TNF + No IMM favoredObservational RR range 5.9 – 6.8Low |
| Infliximab + IMM vs infliximab | Cancers | 3 RCTs441 CD2 retrospective573 CD100 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredObservational RR 2.9Low |
| Infliximab + IMM vs IMM | Cancers | 2 RCTs435 CD | Moderate | Consistent | Direct | Very imprecise | Neither favoredLow |
| TNF-alpha inhibitor + IMM vs no therapy | Cancers | 1 retrospective8,581 CD | High | NA | Direct | Imprecise | Neither favoredObservational RR range 0.9 – 1.1Low |
| Infliximab + corticosteroids vs infliximab | Cancers | 2 retrospective221 IBD | High | NA | Direct | Very imprecise | Neither favoredLow |
| TNF-alpha inhibitor + corticosteroids vs no therapy | Cancers | 1 retrospective8,581 CD | High | NA | Direct | Imprecise | Neither favoredObservational RR range 0.3 – 0.6 Low |
| Infliximab vs IMM | Cancers | 1 RCT324 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Natalizumab vs placebo | Cancers | 3 RCTs1,414 CD | Moderate | Consistent | Direct | Very imprecise | Neither favoredLow |
| Natalizumab + infliximab vs infliximab | Cancers | 1 RCT79 CD | Low | NA | Direct | Very imprecise | Neither favoredLow |
| IMM vs no IMM | Cancers | 1 RCT291 CD1 prospective 3 retrospective 5 case-control10,551 CD39,527 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredObservational RR range 0 – 10.8Low |
| IMM + corticosteroids vs no therapy | Cancers | 1 retrospective8,581 CD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Azathioprine vs prednisone | Cancers | 1 RCT259 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Azathioprine vs sulfasalazine | Cancers | 1 RCT245 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| Azathioprine + ASA vs azathioprine | Cancers | 1 retrospective104 CD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Corticosteroids vs no corticosteroids | Cancers | 1 RCT324 CD1 retrospective3 case-control8,616 CD1,584 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredObservation RR range 1.0 – 1.6Low |
| Prednisone vs sulfasalazine | Cancers | 1 RCT278 CD | Moderate | NA | Direct | Very imprecise | Neither favoredLow |
| ASA vs no ASA | Cancers | 1 RCT310 CD1 retrospective3 case-control35 CD10.328 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredObservational RR 0.2 – 1.2 Low |
| TNF-alpha inhibitor versus no TNF-alpha inhibitor | Infections | 13 RCTs4,059 CD1 prospective1 retrospective1 case-control6,290 CD1,709 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRCT RR range 0.3 – 5.5Observational RR range 0.7 – 11.1Low |
| Infliximab + IMM vs infliximab | Infections | 3 RCTs607 CD1 retrospective1 uclear57 CD121 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRR range 0.8 – 3.2Low |
| Infliximab + IMM vs IMM | Infections | 2 RCTs340 CD1 retrospective10,141 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRR 1.1Low |
| Infliximab + IMM vs corticosteroids | Infections | 1 RCT129 CD | Moderate | NA | Direct | Imprecise | Neither favoredLow |
| Infliximab vs IMM | Infections | 1 RCT324 CD1 retrospective3.404 IBD | Moderate | NA | Direct | Imprecise | Neither favoredRCT RR range 0.9 – 1.0Observational RR range 0.7 – 1.1Low |
| TNF-alpha inhibitor + IMM vs no therapy | Infections | 1 retrospective1 case-control8,581 CD300 IBD | High | NA | Direct | Imprecise | Neither favoredRR range 0.7 – 4.8Low |
| TNF-alpha inhibitor + IMM + corticosteroids vs no therapy | Infections | 1 retrospective1 case control8,581 CD300 IBD | High | NA | Direct | Imprecise | Neither favoredRR range 2.4 – 4.1Low |
| TNF-alpha inhibitor + corticosteroids vs no therapy | Infections | 1 retrospective8,581 CD | High | NA | Direct | Imprecise | Neither favoredRR range 0.7 – 5.6Low |
| Natalizumab versus placebo | Infections | 3 RCTs1,414 CD | Moderate |  Inconsistent | Direct | Imprecise | Neither favoredRR range 0.3 – 1.3Low |
| Natalizumab + infliximab vs infliximab | Infections | 1 RCT79 CD | Moderate | NA | Direct | Imprecise | Neither favoredRR 0.9Low |
| IMM vs no IMM | Infections | 3 RCTs463 CD1 retrospective, 1 prospective6253 CD302 IBD | Moderate | NA | Direct | Imprecise | Neither favoredRR range 0.6 – 2.0Low |
| IMM vs no therapy | Infections | 1 retrospective2 case-control10,141 CD2,538 IBD | High | NA | Direct | Imprecise | Neither favoredRR range 0.6 – 4.1Low |
| IMM vs corticosteroids | Infections | 2 RCTs336 CD1 retrospective10,141 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRR range 0.3 – 2.9Low |
| Azathioprine vs sulfasalazine | Infections | 1 RCT245 CD | Moderate | NA | Direct | Imprecise | Neither favoredRR 0.6Low |
| IMM + steroids vs steroids | Infections | 3 RCTs263 CD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRR range 0.9 – 1.3Low |
| Azathioprine + ASA vs azathioprine | Infections | 1 retrospective199 IBD | High | NA | Direct | Very imprecise | Neither favoredLow |
| IMM + corticosteroids vs no therapy | Infections | 1 retrospective2 case-control8,581 CD2,538 IBD | High | NA | Direct  | Imprecise | Neither favoredRR range 1.2 – 17.5Low |
| Corticosteroids vs no corticosteroids | Infections | 2 RCTs362 CD1 prospective 1 retrospective6,253 CD554 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRR range 0.4 – 2.9Low |
| Corticosteroids vs no therapy | Infections | 1 retrospecitvie2 case-control 8,581 CD2,538 IBD | High | NA | Direct | Imprecise | Neither favoredRR range 0.9 – 3.4Low |
| Corticosteroids vsASA | Infections | 2 RCTs216 CD | Moderate | NA | Direct | Imprecise | Neither favoredRR range 0.4 – 2.8Low |
| Prednisone + sulfasalazine vs prednisone | Infections | 1 RCT89 CD | Moderate | NA | Direct | Precise | PRED + SUL favoredRR = 0.3Moderate |
| Sulfasalazine vs placebo | Infections | 1 RCT159 CD | Moderate | NA | Direct | Imprecise | Neither favoredRR range 1.1 – 1.8Low |
| Mesalamine vs no therapy | Infections | 1 case-control2,238 IBD | High | NA | Direct | Imprecise | Neither favoredRR 0.9Low |
| TNF-alpha inhibitor vs placebo | Tuberculosis | 5 RCTs2,374 CD | Moderate | Consistent | Direct | Imprecise | 4 cases observed in TNF treated, 0 in untreatedLow |
| Infliximab + azathioprine vs infliximab | Tuberculosis | 1 RCT340 CD | Moderate | NA | Direct | Imprecise | 1 case in infliximab + azathioprine, 0 in infliximabLow |
| Infliximab + IMM vs IMM | Tuberculosis | 1 RCT342 CD | Moderate | NA | Direct | Imprecise | 1 case in infliximab + azathioprine, 0 in infliximab Low |
| TNF-alpha inhibitor vs placebo | Infusion and injection-site reactions | 13 RCTs4,389 CD | Moderate | Inconsistent | Direct | Precise | Placebo favored for infliximab and adalimumabRCT RR range 1.1 – 3.2LowNeither favored for CP RCT RR range 0.2 – 6.4 Low |
| Infliximab + IMM vs infliximab | Infusion and injection-site reactions | 3 RCTs468 CD1 prospective 8 retrospective 1,025 CD1,184 IBD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRCT RR range 0.3 – 1.5Observational RR range 0.3 – 1.4Low |
| Infliximab + IMM vs IMM | Infusion and injection-site reactions | 2 RCTs453 CD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRCT RR 0.9Low |
| Infliximab vs azathioprine | Infusion and injection-site reactions | 1 RCT324 CD | Low | NA | Direct | Precise | Azathioprine favoredRCT RR 3.0High |
| Infliximab + thiopurines vs infliximab + methotrexate | Infusion and injection-site reactions | 1 prospective 2 retrospective 291 CD 144 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredObservational RR range 0.8 – 1.4Low |
| Infliximab + steroids vs infliximab + no steroids | Infusion and injection-site reactions | 3 retrospective 964 IBD | High | Inconsistent | Direct | Imprecise | Neither favoredLow |
| Natalizumab vs placebo | Infusion and injection-site reactions | 3 RCTs1,414 CD | Moderate | Inconsistent | Direct | Imprecise | Neither favoredRCT RR range 0.8 – 1.5Low |
| Natalizumab + infliximab vs infliximab | Infusion and injection-site reactions | 1 RCT79 CD | High | NA | Direct | Very imprecise | Neither favoredLow |
| Azathioprine vs placebo | Infusion and injection-site reactions | 1 RCT96 CD | Low | NA | Direct | Precise | Placebo favoredRCT RR 5.8High |
| Budesonide vs. Prednisolone | Fractures | 1 RCT271 CD | Low | NA | Direct | Imprecise | Neither favoredModerate |
| Corticosteroids vs. no corticosteroids | Fractures | 3207 CD554 IBD | High | Consistent | Direct | Imprecise | Neither favoredLow |

ASA = aminosalicylate; CD = Crohn’s disease; CP = certolizumab pegol; HR = hazard ratio; IBD = inflammatory bowel disease; IMM = immunomodulator; NA = not applicable because only one study reported; NR = not reported; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk, Steroids = corticosteroids; TNF = tumor necrosis factor; vs = versus

The strength of the evidence was defined as follows: High = High confidence that the evidence reflects the true effect. Further research is unlikely to change our confidence in the estimate of the effect. Moderate = Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate. Low = Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate. Insufficient = Evidence is unavailable.