

Crohn's disease

Appendix E

Clinical Guideline <...>

Excluded studies

10 October 2012

NICE's original guidance on Crohn's disease: management in adults, children and young people was published in October 2012; it was partially updated in May 2016 when a new recommendation on inducing remission was added. It has now undergone a further partial update published in May 2019. The full, current recommendations can be found on the NICE website.

This document preserves evidence for areas of the guideline that have not been updated in 2019. Black shading indicates text from 2012 replaced by the 2019 update.

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1.1 Induction

1.1.1 Glucocorticosteroid

Excluded studies: glucocorticosteroid versus placebo, 5-ASA, immunosuppressives		
Study	Reason for exclusion	Topic of study
1. Brooke BN, Javett SL, Davison OW. Further experience with azathioprine for Crohn's disease. <i>Lancet</i> . 1970; 2(7682):1050-1053.	Case report	AZA
2. Charpignon C, Beau P. Methotrexate as single therapy in Crohn's disease: is its long-term efficacy limited? <i>Gastroenterologie Clinique Et Biologique</i> . 2008; 32(2):153-157.	Not RCT	MTX
3. Chong RY, Hanauer SB, Cohen RD. Efficacy of parenteral methotrexate in refractory Crohn's disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(1):35-44.	Not RCT	MTX
4. Christensen LA, Fallingborg J, Jacobsen BA, Abildgaard K, Rasmussen HH, Rasmussen SN, Hansen SH. Bioavailability of 5-aminosalicylic acid from slow release 5-aminosalicylic acid drug and sulfasalazine in normal children. <i>Digestive Diseases and Sciences</i> . 1993; 38(10):1831-1836.	Case series; not question	5-ASA
5. Clarke DF, George D, Milsap RL. Sulfasalazine metabolite pharmacokinetics in pediatric patients with inflammatory bowel disease: Effects of disease activity, acetylator phenotype, and age. <i>Pediatric Pharmacology</i> . 1982; 2(4):323-333.	Narrative review	5-ASA (sulfasalazine)
6. Cuffari C, Theoret Y, Latour S, Seidman G. 6-Mercaptopurine metabolism in Crohn's disease: correlation with efficacy and toxicity. <i>Gut</i> . 1996; 39(3):401-406.	Not question	MP
7. Din S, Dahele A, Fennel J, Aitken S, Shand AG, Arnott ID, Satsangi J. Use of methotrexate in refractory Crohn's disease: the Edinburgh experience. <i>Inflammatory Bowel Diseases</i> . 2008; 14(6):756-762.	Not RCT	MTX
8. Egan LJ, Sandborn WJ, Tremaine WJ, Leighton JA, Mays DC, Pike MG, Zinsmeister AR, Lipsky JJ. A randomized dose-response and	Mixed IBD population	MTX

Excluded studies: glucocorticosteroid versus placebo, 5-ASA, immunosuppressives		
pharmacokinetic study of methotrexate for refractory inflammatory Crohn's disease and ulcerative colitis. <i>Alimentary Pharmacology and Therapeutics</i> . 1999; 13(12):1597-1604.		
9. Feagan BG. Aminosalicylates for active disease and in the maintenance of remission in Crohn's disease. <i>European Journal of Surgery</i> . 1998; 164(12):903-909.	Narrative	5-ASA
10. Feagan BG. Methotrexate treatment for Crohn's disease. <i>Inflammatory Bowel Diseases</i> . 1998; 4(2):120-121.	Review	MTX
11. Goldstein F, Menduke H, Thornton JJ, III, Abramson J. Anti-inflammatory drug treatment of Crohn's disease: a prospective evaluation of 100 consecutively treated patients. <i>Journal of Clinical Gastroenterology</i> . 1980; 2(1):77-85.	Not RCT	5-ASA (sulfasalazine)
12. Irving PM, Geary RB, Sparrow MP, Gibson PR. Review article: Appropriate use of corticosteroids in Crohn's disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2007; 26(3):313-329.	Narrative review	Use of glucocorticosteroids
13. Jakobovits J, Schuster MM. Metronidazole therapy for Crohn's disease and associated fistulae. <i>American Journal of Gastroenterology</i> . 1984; 79(7):533-540.	Case series	MTX
14. Kim SC, Ferry GD. Inflammatory bowel diseases in pediatric and adolescent patients: clinical, therapeutic, and psychosocial considerations. <i>Gastroenterology</i> . 2004; 126(6):1550-1560.	Narrative	Paediatric CD
15. Korelitz BI, Present DH. Methotrexate for Crohn's disease. <i>New England Journal of Medicine</i> . 1995; 333(9):600-601.	Not RCT	MTX
16. Mack DR, Young R, Kaufman SS, Ramey L, Vanderhoof JA. Methotrexate in patients with Crohn's disease after 6-mercaptopurine. <i>Journal of Pediatrics</i> . 1998; 132(5):830-835.	Not RCT	MTX
17 Markowitz J, Hyams J, Mack D, LeLeiko N, Evans J, Kugathasan S, Pfefferkorn M, Mezoff A, Rosh J, Tolia V, Otley A, Griffiths A, Moyer	Not RCT	Paediatric glucocorticosteroid

Excluded studies: glucocorticosteroid versus placebo, 5-ASA, immunosuppressives		
MS, Oliva-Hemker M, Wyllie R, Rothbaum R, Bousvaros A, Del Rosario JF, Hale S, Lerer T, Pediatric IBD Collaborative Research Group. Corticosteroid therapy in the age of infliximab: acute and 1-year outcomes in newly diagnosed children with Crohn's disease. <i>Clinical Gastroenterology and Hepatology</i> . 2006; 4(9):1124-1129.		
18. Papp JP, Watson DW, Bull FE. Azathioprine treatment in Crohn's disease. <i>American Journal of Gastroenterology</i> . 1974; 61(2):136-142.	Case series	AZA
19. Punati J, Markowitz J, Lerer T, Hyams J, Kugathasan S, Griffiths A, Otley A, Rosh J, Pfefferkorn M, Mack D, Evans J, Bousvaros A, Moyer MS, Wyllie R, Oliva-Hemker M, Mezoff A, LeLeiko N, Keljo D, Crandall W, Pediatric IBD Collaborative Research Group. Effect of early immunomodulator use in moderate to severe pediatric Crohn disease ⁴²⁰ . <i>Inflammatory Bowel Diseases</i> . 2008; 14(7):949-954.	Not RCT	Paediatric AZA, MP
20. Rijk MC, van Hogezaand RA, van Lier HJ, van Tongeren JH. Sulphasalazine and prednisone compared with sulphasalazine for treating active Crohn disease. A double-blind, randomized, multicenter trial. <i>Annals of Internal Medicine</i> . 1991; 114(6):445-450.	Not question	Comparison of two indices – Van Hees and CDAI
21. Rutgeerts PJ. Review article: the limitations of corticosteroid therapy in Crohn's disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(10):1515-1525.	Narrative	Glucocorticosteroid
22. Sandborn WJ. Steroid-dependent Crohn's disease. <i>Canadian Journal of Gastroenterology</i> . 2000; 14 Suppl C:17C-22C.	Not question	AZA IV
23. Sandborn WJ, Tremaine WJ, Wolf DC, Targan SR, Sninsky CA, Sutherland LR, Hanauer SB, McDonald JWD, Feagan BG, Fedorak RN, Isaacs KL, Pike MG, Mays DC, Lipsky JJ, Gordon S, Kleoudis CS, Murdock RH, Jr. Lack of effect of intravenous administration on time to respond	Narrative	Glucocorticosteroid

Excluded studies

Excluded studies: glucocorticosteroid versus placebo, 5-ASA, immunosuppressives		
to azathioprine for steroid-treated Crohn's disease. Gastroenterology. 1999; 117(3):527-535.		
24. Turner D, Grossman AB, Rosh J, Kugathasan S, Gilman AR, Baldassano R, Griffiths AM. Methotrexate following unsuccessful thiopurine therapy in pediatric Crohn's disease. American Journal of Gastroenterology. 2007; 102(12):2804-2812.	Not RCT	Paediatric MTX
25. van Bodegraven AA, Mulder CJ. Indications for 5-aminosalicylate in inflammatory bowel disease: is the body of evidence complete? World Journal of Gastroenterology. 2006; 12(38):6115-6123.	Narrative	5-ASA

1.1.2 5-aminosalicylates

Study reference	Reason for exclusion
1. Aithal GP, Mansfield JC. Review article: The risk of lymphoma associated with inflammatory bowel disease and immunosuppressive treatment. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(8):1101-1108.	Narrative review
2. American Journal of Nursing. Drug watch. Methotrexate-induced lung injury. <i>American Journal of Nursing</i> . 1998; 98(5):56.	Wrong diagnosis
3. Andrews JM, Travis SP, Gibson PR, Gasche C. Systematic review: does concurrent therapy with 5-ASA and immunomodulators in inflammatory bowel disease improve outcomes? <i>Alimentary Pharmacology and Therapeutics</i> . 2009; 29(5):459-469.	Systematic review: used for quality assurance
4. Bebb JR, Scott BB. Systematic review: How effective are the usual treatments for Crohn's disease? <i>Alimentary Pharmacology and Therapeutics</i> . 2004; 20(2):151-159.	Systematic review: used for quality assurance
5. Beck IT, Hudacin J, Paterson WG, Depew WT, Simon JB, Groll A. Mesalazine in the treatment of active Crohn's disease. <i>Canadian Journal of Gastroenterology</i> . 1988; 2(SUPPL. A):63A-70A.	Not RCT
6. Bergman R, Parkes M. Systematic review: The use of mesalazine in inflammatory bowel disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2006; 23(7):841-855.	Systematic review: used for quality assurance
7. Bjarnason I, Macpherson AJ. Delivery, safety and efficacy of 5-aminosalicylate preparations. <i>Inflammopharmacology</i> . 1993; 2(3):277-287.	Narrative review
8. Brimblecombe R. Mesalazine: A global safety evaluation. <i>Scandinavian Journal of Gastroenterology - Supplement</i> . 1990; 25(172):66-68.	Narrative review
9. Cash JM. Does methotrexate cause pulmonary fibrosis? <i>Journal of Musculoskeletal Medicine</i> . 1994; 11(10):11-12.	Narrative
10. Christensen LA, Fallingborg J, Jacobsen BA, Abildgaard K, Rasmussen HH, Rasmussen SN, Hansen SH. Bioavailability of 5-aminosalicylic acid from slow release 5-aminosalicylic acid drug and sulfasalazine in normal children. <i>Digestive Diseases and Sciences</i> . 1993; 38(10):1831-1836.	Not question
11. Clarke DF, George D, Milsap RL. Sulfasalazine metabolite pharmacokinetics in pediatric patients with inflammatory bowel disease: Effects of disease activity, acetylator phenotype, and age. <i>Pediatric Pharmacology</i> . 1982; 2(4):323-333.	Not question
12. Feagan BG. Aminosaliclates for active disease and in the maintenance of remission in Crohn's disease. <i>European Journal of Surgery</i> . 1998; 164(12):903-909.	Narrative
13. Floren CH, Ahren B, Bengtsson M, Bartosik J, Obrant K. Bone mineral density in patients with	Not outcome of interest

Excluded studies

Study reference	Reason for exclusion
Crohn's disease during long-term treatment with azathioprine. <i>Journal of Internal Medicine</i> . 1998; 243(2):123-126.	
14. Ford AC, Kane SV, Khan KJ, Achkar JP, Talley NJ, Marshall JK, Moayyedi P. Efficacy of 5-Aminosalicylates in Crohn's Disease: Systematic Review and Meta-Analysis. <i>American Journal of Gastroenterology</i> . 2011; 106(4):617-629.	Systematic review – used for quality assessment
15. Gisbert JP, Nino P, Cara C, Rodrigo L. Comparative effectiveness of azathioprine in Crohn's disease and ulcerative colitis: prospective, long-term, follow-up study of 394 patients. <i>Alimentary Pharmacology and Therapeutics</i> . 2008; 28(2):228-238.	Not RCT
16. Juillerat P, Pittet V, Felley C, Mottet C, Froehlich F, Vader JP, Gonvers JJ, Michetti P. Drug safety in Crohn's disease therapy. <i>Digestion</i> . 2007; 76(2):161-168.	Narrative
17. Muller AF, Stevens PE, Mcintyre AS, Ellison H, Logan RF. Experience of 5-aminosalicylate nephrotoxicity in the United Kingdom. <i>Alimentary Pharmacology and Therapeutics</i> . 2005; 21(10):1217-1224.	Narrative
18. Rasmussen SN, Binder V, Maier K, Bondesen S, Fischer C, Klotz U, Hansen SH, Hvidberg EF. Treatment of Crohn's disease with peroral 5-aminosalicylic acid. <i>Gastroenterology</i> . 1983; 85(6):1350-1353.	Not RCT
19. Rijk MC, van Hogezaand RA, van Lier HJ, van Tongeren JH. Sulphasalazine and prednisone compared with sulphasalazine for treating active Crohn disease. A double-blind, randomized, multicenter trial. <i>Annals of Internal Medicine</i> . 1991; 114(6):445-450.	Comparison of two indices
20. Smith MA, Irving PM, Marinaki AM, Sanderson JD. Review article: malignancy on thiopurine treatment with special reference to inflammatory bowel disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2010; 32(2):119-130.	Narrative review
21. Su C, Lichtenstein GR, Krok K, Brensinger C, Lewis JD. A Meta-Analysis of the Placebo Rates of Remission and Response in Clinical Trials of Active Crohn's Disease. <i>Gastroenterology</i> . 2004; 126(5):1257-1269.	Not question
22. Subramanian V, Pollok RC, Kang JY, Kumar D. Systematic review of postoperative complications in patients with inflammatory bowel disease treated with immunomodulators. <i>British Journal of Surgery</i> . 2006; 93(7):793-799.	Post operative
23. van Hees PA, van Lier HJ, Van Elteren PH, Driessen M, van Hogezaand RA, Ten Velde GP, Bakker JH, van Tongeren JH. Effect of sulphasalazine in patients with active Crohn's disease: a controlled double-blind study	CDAI not used to measure remission

Excluded studies

Study reference	Reason for exclusion
2696. Gut. 1981; 22(5):404-409.	
24. Van Staa TP, Travis S, Leufkens HG, Logan RF. 5-aminosalicylic acids and the risk of renal disease: a large British epidemiologic study. Gastroenterology. 2004; 126(7):1733-1739.	Not drug of interest
25. Vestergaard P, Rejnmark L, Mosekilde L. Methotrexate, azathioprine, cyclosporine, and risk of fracture. Calcified Tissue International. 2006; 79(2):69-75.	Outcome not of interest

1.1.3 Budesonide

Budesonide Cochrane update search study reference	Reason for exclusion
1. Budesonide Capsules Cause Fewer Glucocorticoid-Related Adverse Effects Than Prednisolone During Short-Term Therapy for Active Crohn's Disease in Adults. <i>Drugs & Therapy Perspectives</i> . 2003; 19(6):1-4.	Narrative review
2. Kane SV, Schoenfeld P, Sandborn WJ, Tremaine W, Hofer T, Feagan BG. Systematic Review: The Effectiveness of Budesonide Therapy for Crohn's Disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2002; 16(8):1509-1517.	Systematic review: used for quality assurance
3. Mantzaris GJ, Christidou A, Sfakianakis M, Roussos A, Koilakou S, Petraki K, Polyzou P. Azathioprine Is Superior to Budesonide in Achieving and Maintaining Mucosal Healing and Histologic Remission in Steroid-Dependent Crohn's Disease. <i>Inflammatory Bowel Diseases</i> . 2009; 15(3):375-382	Maintenance of remission
4. Novacek G, Kleinberger M, Vogelsang H, Moser G, Lochs H. Budesonide in Glucocorticoid Dependent Chronic Active Crohn's Disease; a Pilot Study. <i>Zeitschrift Fur Gastroenterologie</i> . 1995; 33(5):251-254.	Not RCT
5. Papi C, Luchetti R, Gili L, Montanti S, Koch M, Capurso L. Budesonide in the Treatment of Crohn's Disease: A Meta-Analysis. <i>Alimentary Pharmacology and Therapeutics</i> . 2000; 14(11):1419-1428.	Meta-analysis: used for quality assurance

1.1.4 Azathioprine/mercaptopurine

Study reference	Reason for exclusion
1. Aithal GP, Mansfield JC. Review article: The risk of lymphoma associated with inflammatory bowel disease and immunosuppressive treatment. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(8):1101-1108.	Narrative review
2. American Journal of Nursing. Drug watch. Methotrexate-induced lung injury. <i>American Journal of Nursing</i> . 1998; 98(5):56.	Wrong diagnosis
3. Andrews JM, Travis SP, Gibson PR, Gasche C. Systematic review: does concurrent therapy with 5-ASA and immunomodulators in inflammatory bowel disease improve outcomes? <i>Alimentary Pharmacology and Therapeutics</i> . 2009; 29(5):459-469.	Systematic review: used for quality assurance
4. Bebb JR, Scott BB. Systematic review: How effective are the usual treatments for Crohn's disease? <i>Alimentary Pharmacology and Therapeutics</i> . 2004; 20(2):151-159.	Systematic review: used for quality assurance
5. Brooke BN, Javett SL, Davison OW. Further experience with azathioprine for Crohn's disease. <i>Lancet</i> . 1970; 2(7682):1050-1053.	Case report
6. Cash JM. Does methotrexate cause pulmonary fibrosis? <i>Journal of Musculoskeletal Medicine</i> . 1994; 11(10):11-12.	Narrative
7. D'Haens G, Baert F, Van Assche G, Caenepeel P, Vergauwe P, Tuynman H, De Vos M, van Deventer S, Stitt L, Donner A, Vermeire S, Van De Mierop FJ, Coche JC, van der Woude J, Ochsenuhn T, van Bodegraven AA, Van Hooitegem PP, Lambrecht GL, Mana F, Rutgeerts P, Feagan BG, Hommes D. Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn's disease: an open randomised trial. <i>Lancet</i> . 2008; 371(9613):660-667.	Infliximab
8. Floren CH, Ahren B, Bengtsson M, Bartosik J, Obrant K. Bone mineral density in patients with Crohn's disease during long-term treatment with azathioprine. <i>Journal of Internal Medicine</i> . 1998; 243(2):123-126.	Not outcome of interest
9. Gisbert JP, Nino P, Cara C, Rodrigo L. Comparative effectiveness of azathioprine in Crohn's disease and ulcerative colitis: prospective, long-term, follow-up study of 394 patients. <i>Alimentary Pharmacology and Therapeutics</i> . 2008; 28(2):228-238.	Not RCT
10. Juillerat P, Pittet V, Felley C, Mottet C, Froehlich F, Vader JP, Gonvers JJ, Michetti P. Drug safety in Crohn's disease therapy. <i>Digestion</i> . 2007; 76(2):161-168.	Narrative
11. Leung Y, Sparrow MP, Schwartz M, Hanauer SB. Long term efficacy and safety of allopurinol and azathioprine or 6-mercaptopurine in patients with inflammatory bowel disease. <i>Journal of Crohn's and</i>	Small retrospective review

Excluded studies

Study reference	Reason for exclusion
Colitis. 2009; 3(3):162-167.	
12. McGovern DPB, Jewell DP. Risks and benefits of azathioprine therapy. <i>Gut</i> . 2005; 54(8):1055-1059.	Commentary
13. Rhodes J, Bainton D, Beck P. Azathioprine in Crohn's disease. <i>Lancet</i> . 1970; 2(7683):1142.	Commentary
14. Rhodes J. Azathioprine in the treatment of Crohn's disease. <i>British Journal of Surgery</i> . 1972; 59(10):819-821.	Commentary
15. Sandborn WJ, Tremaine WJ, Wolf DC, Targan SR, Sninsky CA, Sutherland LR, Hanauer SB, McDonald JWD, Feagan BG, Fedorak RN, Isaacs KL, Pike MG, Mays DC, Lipsky JJ, Gordon S, Kleoudis CS, Murdock RH, Jr. Lack of effect of intravenous administration on time to respond to azathioprine for steroid-treated Crohn's disease. <i>Gastroenterology</i> . 1999; 117(3):527-535.	Not question
16. Smith MA, Irving PM, Marinaki AM, Sanderson JD. Review article: malignancy on thiopurine treatment with special reference to inflammatory bowel disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2010; 32(2):119-130.	Narrative review
17. Su C, Lichtenstein GR, Krok K, Brensinger C, Lewis JD. A Meta-Analysis of the Placebo Rates of Remission and Response in Clinical Trials of Active Crohn's Disease. <i>Gastroenterology</i> . 2004; 126(5):1257-1269.	Not question
18. Subramanian V, Pollok RC, Kang JY, Kumar D. Systematic review of postoperative complications in patients with inflammatory bowel disease treated with immunomodulators. <i>British Journal of Surgery</i> . 2006; 93(7):793-799.	Post op
19. Van Staa TP, Travis S, Leufkens HG, Logan RF. 5-aminosalicylic acids and the risk of renal disease: a large British epidemiologic study. <i>Gastroenterology</i> . 2004; 126(7):1733-1739.	Not drug of interest
20. Vestergaard P, Rejnmark L, Mosekilde L. Methotrexate, azathioprine, cyclosporine, and risk of fracture. <i>Calcified Tissue International</i> . 2006; 79(2):69-75.	Outcome not of interest

1.2 Maintenance

1.2.1 Conventional glucocorticosteroid

Study reference	Reason for exclusion
1. Brignola C, Campieri M, Farruggia P, Tragnone A, Pasquali S, Iannone P, Lanfranchi GA, Barbara L. The Possible Utility of Steroids in the Prevention of Relapses of Crohn's Disease in Remission. A Preliminary Study. <i>Journal of Clinical Gastroenterology</i> . 1988; 10(6):631-634. (Guideline Ref ID 660)	Follow-up less than 12 months
2. Faubion J, Loftus J, Harmsen WS, Zinsmeister AR, Sandborn WJ. The Natural History of Glucocorticosteroid Therapy for Inflammatory Bowel Disease: A Population-Based Study. <i>Gastroenterology</i> . 2001; 121(2):255-260. (Guideline Ref ID 20315)	Not RCT
3. Feagan BG. Review: Glucocorticosteroid Therapy Does Not Reduce the Rate of Relapse in Crohn Disease... Commentary on Steinhart AH, Ewe K, Griffiths AM Et Al. Glucocorticosteroid Therapy for Maintenance of Remission in Crohn's Disease. <i>Cochrane Review</i> , Latest Version 23 Jun 1998. In: <i>The Cochrane Library</i> . Oxford: Update Software. <i>ACP Journal Club</i> . 1999; 130(2):36. (Guideline Ref ID 2216)	Commentary
4. Hoes JN, Jacobs JW, Verstappen SM, Bijlsma JW, Van der Heijden GJ. Adverse Events of Low- to Medium-Dose Oral Glucocorticoids in Inflammatory Diseases: a Meta-Analysis. <i>Annals of the Rheumatic Diseases</i> . 2009; 68(12):1833-1838. (Guideline Ref ID 41)	Not RCT
5. Papi C, Luchetti R, Gili L, Montanti S, Koch M, Capurso L. Budesonide in the Treatment of Crohn's Disease: A Meta-Analysis. <i>Alimentary Pharmacology and Therapeutics</i> . 2000; 14(11):1419-1428. (Guideline Ref ID 1966)	Not ongoing glucocorticosteroid
6. Plevy SE. Glucocorticosteroid-Sparing Treatments in Patients With Crohn's Disease. <i>American Journal of Gastroenterology</i> . 2002; 97(7):1607-1617. (Guideline Ref ID 210)	Narrative review
7. Rutgeerts PJ. Review Article: the Limitations of Glucocorticosteroid Therapy in Crohn's Disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(10):1515-1525. (Guideline Ref ID 225)	Narrative review
8. Weldon D. The Effects of Glucocorticosteroids on Bone Growth and Bone Density. <i>Annals of Allergy, Asthma and Immunology</i> . 2009; 103(1):3-11. (Guideline Ref ID 913)	Not CD specific
9. Johnson T, Macdonald S, Hill SM, Thomas A, Murphy MS. Treatment of Active Crohn's Disease in Children Using Partial Enteral Nutrition With Liquid Formula: a Randomised Controlled Trial. <i>Gut</i> . 2006; 55(3):356-361. (Guideline Ref ID 845)	No maintenance treatment

Excluded studies

Study reference	Reason for exclusion
10. Winship DH, Summers RW, Singleton JW, Best WR, Beckett JM, Lenk LF, Kern F, Jr. National Cooperative Crohn's Disease Study: Study Design and Conduct of the Study. <i>Gastroenterology</i> . 1979; 77(4 Pt 2):829-842. (Guideline Ref ID 2	Description of methods on for NCCD study; no results included in the study

1.2.2 5-aminosalicylates

Study reference	Reason for exclusion
1. Actis GC, Paziienza P, Rosina F. Mesalamine for Inflammatory Bowel Disease: Recent Reappraisals. <i>Inflammation and Allergy Drug Targets</i> . 2008; 7(1):1-5. (Guideline Ref ID 98)	Not RCT
2. Akobeng AK, Gardener E. Oral 5-Aminosalicylic Acid for Maintenance of Medically-Induced Remission in Crohn's Disease. <i>Cochrane Database of Systematic Reviews</i> . 2005;(1) (Guideline Ref ID 246)	Cochrane Review used for reference and quality assurance
3. Bonapace CR, Mays DA. The Effect of Mesalamine and Nicotine in the Treatment of Inflammatory Bowel Disease. <i>Annals of Pharmacotherapy</i> . 1997; 31(7-8):907-913. (Guideline Ref ID 567)	Not RCT
4. Camma C, Giunta M, Rosselli M, Cottone M. Mesalamine in the Maintenance Treatment of Crohn's Disease: a Meta-Analysis Adjusted for Confounding Variables. <i>Gastroenterology</i> . 1997; 113:1465-1473. (Guideline Ref ID 1112)	Meta-analysis used for quality assurance
5. Campbell S, Ghosh S. Effective Maintenance of Inflammatory Bowel Disease Remission by Azathioprine Does Not Require Concurrent 5-Aminosalicylate Therapy. <i>European Journal of Gastroenterology and Hepatology</i> . 2001; 13(11):1297-1301. (Guideline Ref ID 20336)	Not RCT
6. Cezard JP, Munck A, Mouterde O, Morali A, Lenaerts C, Lachaux A, Turck D, Schmitz J, Maurage C, Girardet J-P, Belli D, Lamireau T, Sarles J, 7.Chouraqui JP, Descos B, Dabadi A, Meyer M, Olives J-P, Mary J-Y. Prevention of Relapse by Mesalazine (Pentasa) in Pediatric Crohn's Disease: A Multicenter, Double-Blind, Randomized, Placebo-Controlled Trial. <i>Gastroenterologie Clinique Et Biologique</i> . 2009; 33(1 PART 1):31-40. (Guideline Ref ID 992)	Patients with active disease
8. Dewit O, Vanheuverzwyn R, Desager JP, Horsmans Y. Interaction Between Azathioprine and Aminosalicylates: an in Vivo Study in Patients With Crohn's Disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2002; 16(1):79-85. (Guideline Ref ID 401)	Not RCT
9. Duricova D, Pedersen N, Elkjaer M, Jensen JKS, Munkholm P. 5-Aminosalicylic Acid Dependency in Crohn's Disease: A Danish Crohn Colitis Database Study. <i>Journal of Crohn's and Colitis</i> . 2010; 4(5):575-581. (Guideline Ref ID 894)	Not RCT
10. Feagan BG. Aminosalicylates for Active Disease and in the Maintenance of Remission in Crohn's Disease. <i>European Journal of Surgery</i> . 1998; 164(12):903-909. (Guideline Ref ID 1374)	Narrative review
11. Feagan BG. Maintenance Therapy for Inflammatory Bowel Disease. <i>American Journal of Gastroenterology</i> . 2003; 98(12 SUPPL.):S6-S17. (Guideline Ref ID 1795)	Narrative review
12. Ford AC, Kane SV, Khan KJ, Achkar JP, Talley NJ,	Meta-analysis used for quality assurance

Excluded studies

Study reference	Reason for exclusion
Marshall JK, Moayyedi P. Efficacy of 5-Aminosalicylates in Crohn's Disease: Systematic Review and Meta-Analysis. <i>American Journal of Gastroenterology</i> . 2011; 106(4):617-629. (Guideline Ref ID 20322)	
13. Ford AC, Kane SV, Khan KJ, Achkar JP, Talley NJ, Marshall JK, Moayyedi P. Efficacy of 5-Aminosalicylates in Crohn's Disease: Systematic Review and Meta-Analysis. <i>American Journal of Gastroenterology</i> . 2011; 106(4):617-629.	Systematic review – used for quality assessment
14. Hanauer SB. The Case for Using 5-Aminosalicylates in Crohn's Disease: Pro. <i>Inflammatory Bowel Diseases</i> . 2005; 11(6):609-612. (Guideline Ref ID 1450)	Not RCT
15. Hanauer SB, Krawitt EL, Robinson M, Rick GG, Safdi MA, Alpert E, Martin MC, DiMarino J, Atin MD, Ionna SL, Letzdowitz S, Ruffini RA, Zfass AM, Elson Iii CO, Lee A, Goshgarian-Patrick P, Gitnick GL, Korentz R, Abbey H. Long-Term Management of Crohn's Disease With Mesalamine Capsules (Pentasa). <i>American Journal of Gastroenterology</i> . 1993; 88(9):1343-1351. (Guideline Ref ID 1892)	Not RCT
16. Howaldt S, Raedler A, Reinecker HC, Berghaus D, Hoyer S, Kaiser B, Schreiber S. Comparative Trial of Remission Prophylaxis in Quiescent Crohn's Disease With Oral 4-Aminosalicylic Acid Versus 5-Aminosalicylic Acid Slow Release Tablets. <i>Canadian Journal of Gastroenterology</i> . 1993; 7:241-244. (Guideline Ref ID 2477)	Not question of interest
17. Lennard-Jones JE. Sulphasalazine in Asymptomatic Crohn's Disease. A Multicentre Trial 2766. <i>Gut</i> . 1977; 18(1):69-72. (Guideline Ref ID 2766)	No validated index
18. Lim W-C, Hanauer SB. Controversies With Aminosalicylates in Inflammatory Bowel Disease. <i>Reviews in Gastroenterological Disorders</i> . 2004; 4(3):104-117. (Guideline Ref ID 1728)	Not RCT
19. Malchow H, Ewe K, Brandes JW, Goebell H, Ehms H, Sommer H, Jesdinsky H. European Cooperative Crohn's Disease Study (ECCDS): Results of Drug Treatment. <i>Gastroenterology</i> . 1984; 86(2):249-266. (Guideline Ref ID 21)	Randomised in active phase
20. Modigliani R, Colombel JF, Dupas JL, Dapoigny M, Costil V, Veyrac M, Duclos B, Soule JC, Gendre JP, Galmiche JP, Danne O, Cadiot G, Lamouliatte H, Belaiche J, Mary JY. Mesalamine in Crohn's Disease With Steroid-Induced Remission: Effect on Steroid Withdrawal and Remission Maintenance, Groupe D'Etudes Therapeutiques Des Affections Inflammatoires Digestives. <i>Gastroenterology</i> . 1996; 110(3):688-693. (Guideline Ref ID 2040)	Randomised in active phase
21. Present DH, Korelitz BI, Wisch N. Treatment of Crohn's Disease With 6-Mercaptopurine. A Long-Term, Randomized, Double-Blind Study. <i>New</i>	Randomised in active phase

Excluded studies

Study reference	Reason for exclusion
England Journal of Medicine. 1980; 302(18):981-987. (Guideline Ref ID 1485)	
22. Singleton JW, Summers RW, Kern F, Jr., Becketl JM, Best WR, Hansen RN, Winship DH. A Trial of Sulfasalazine As Adjunctive Therapy in Crohn's Disease. Gastroenterology. 1979; 77(4 Pt 2):887-897. (Guideline Ref ID 929)	Less than one year follow-up
23. Steinhart AH, Forbes A, Mills EC, Rodgers-Gray BS, Travis SP. Systematic Review: the Potential Influence of Mesalazine Formulation on Maintenance of Remission in Crohn's Disease. [44 Refs]. Alimentary Pharmacology and Therapeutics. 2007; 25(12):1389-1399. (Guideline Ref ID 20340)	Systematic review used for quality assessment
24. Sutherland LR, Martin F, Bailey RJ, Fedorak RN, Poleski M, Dallaire C, Rossman R, Saibil F, Lariviere L. A Randomized, Placebo-Controlled, Double-Blind Trial of Mesalamine in the Maintenance of Remission of Crohn's Disease. The Canadian Mesalamine for Remission of Crohn's Disease Study Group. Gastroenterology. 1997; 112(4):1069-1077. (Guideline Ref ID 988)	Study period less than one year
25. Thomson AB. Review Article: New Developments in the Use of 5-Aminosalicylic Acid in Patients With Inflammatory Bowel Disease. [130 Refs]. Alimentary Pharmacology and Therapeutics. 1991; 5(5):449-470. (Guideline Ref ID 728)	Narrative review
26. Wong JM, Wei SC. Efficacy of Pentasa Tablets for the Treatment of Inflammatory Bowel Disease. Journal of the Formosan Medical Association. 2003; 102(9):613-619. (Guideline Ref ID 20341)	Not RCT

1.2.3 Budesonide

Study reference	Reason for exclusion
1. Andus T, Gross V, Caesar I, Schulz HJ, Lochs H, Strohm WD, Gierend M, Weber A, Ewe K, Scholmerich J, German/Austrian Budesonide Study Group. Replacement of Conventional Glucocorticoids by Oral PH-Modified Release Budesonide in Active and Inactive Crohn's Disease: Results of an Open, Prospective, Multicenter Trial. <i>Digestive Diseases and Sciences</i> . 2003; 48(2):373-378. (Guideline Ref ID 299)	Not RCT
2. Benchimol EI, Seow CH, Otley AR, Steinhart AH. Budesonide for Maintenance of Remission in Crohn's Disease. <i>Cochrane Database of Systematic Reviews</i> . 2009;(1) (Guideline Ref ID 196)	Cochrane Review used for reference and quality assurance
3. Caesar I, Gross V, Roth M, Andus T, Schmidt C, Raedsch R, Weber A, Gierend M, Ewe K, Scholmerich J. Treatment of Active and Postactive Ileal and Colonic Crohn's Disease With Oral PH-Modified-Release Budesonide. German Budesonide Study Group. <i>Hepato-Gastroenterology</i> . 1997; 44(14):445-451. (Guideline Ref ID 504)	Not RCT
4. Cortot A, Colombel J-F, Rutgeerts P, Lauritsen K, Malchow H, Hamling J, Winter T, Van GA, Persson T, Pettersson E. Switch From Systemic Steroids to Budesonide in Steroid-Dependent Patients With Inactive Crohn's Disease. <i>Drugs of Today</i> . 2000; 36(Suppl G):33-37. (Guideline Ref ID 2053)	Follow-up less than one year
5. Ford AC, Bernstein CN, Khan KJ, Abreu MT, Marshall JK, Talley NJ, Moayyedi P. Glucocorticosteroid Therapy in Inflammatory Bowel Disease: Systematic Review and Meta-Analysis. <i>American Journal of Gastroenterology</i> . 2011; 106(4):590-599. (Guideline Ref ID 20323)	Meta-analysis used for reference and quality assurance
6. Green JR, Lobo AJ, Giaffer M, Travis S, Watkins HC, Freedom Investigator Group. Maintenance of Crohn's Disease Over 12 Months: Fixed Versus Flexible Dosing Regimen Using Budesonide Controlled Ileal Release Capsules. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(9):1331-1341. (Guideline Ref ID 20316)	Dose comparison– not question of interest
7. Lichtenstein GR, Bengtsson B, Hapten-White L, Rutgeerts P. Oral Budesonide for Maintenance of Remission of Crohn's Disease: a Pooled Safety Analysis. <i>Alimentary Pharmacology and Therapeutics</i> . 2009; 29(6):643-653. (Guideline Ref ID 20317)	Review of adverse events
8. Lichtenstein GR, Feagan BG, Cohen RD, Salzberg BA, Diamond RH, Chen DM, Pritchard ML, Sandborn WJ. Serious Infections and Mortality in Association With Therapies for Crohn's Disease: TREAT Registry. [Erratum Appears in <i>Clin Gastroenterol Hepatol</i> . 2006 Jul;4(7):931]. <i>Clinical Gastroenterology and Hepatology</i> . 2006; 4(5):621-630. (Guideline Ref ID 185)	Review of adverse events

Excluded studies

Study reference	Reason for exclusion
9. McNatty D. Crohn's Disease - Strategies to Improve Quality of Life. Pharmacy Times. 2008; 74(9):42+44. (Guideline Ref ID 20386)	Not RCT
10. Sandborn WJ, Lofberg R, Feagan BG, Hanauer SB, Campieri M, Greenberg GR. Budesonide for Maintenance of Remission in Patients With Crohn's Disease in Medically Induced Remission: a Predetermined Pooled Analysis of Four Randomized, Double-Blind, Placebo-Controlled Trials. American Journal of Gastroenterology. 2005; 100(8):1780-1787. (Guideline Ref ID 217)	Pooled analysis used for reference and quality assurance
11. Simonoska CM, Glavas DM, Goracinova K. Chitosan Coated Ca-Alginate Microparticles Loaded With Budesonide for Delivery to the Inflamed Colonic Mucosa. European Journal of Pharmaceutics and Biopharmaceutics. 2008; 68(3):565-578. (Guideline Ref ID 20388)	Not question of interest

1.2.4 Azathioprine/mercaptopurine

Study reference	Reason for exclusion
1. No authors listed. Crohn's disease and immunosuppressive therapy. <i>Med J Aust.</i> 1972;2(11):579-80. (Guideline Ref ID 433)	Not RCT
2. Belaiche J, Desager JP, Horsmans Y, Louis E. Therapeutic drug monitoring of azathioprine and 6-mercaptopurine metabolites in Crohn disease. <i>Scand J Gastroenterol.</i> 2001;36(1):71-6. (Guideline Ref ID 1322)	Not RCT
3. Bokemeyer B, Teml A, Roggel C, Hartmann P, Fischer C, Schaeffeler E, Schwab M. Adherence to thiopurine treatment in out-patients with Crohn's disease. <i>Aliment Pharmacol Ther.</i> 2007;26(2):217-25. (Guideline Ref ID 20335)	Not question of interest
4. Bouhnik Y, Lémann M, Mary JY, Scemama G, Taï R, Matuchansky C, Modigliani R, Rambaud JC. Long-term follow-up of patients with Crohn's disease treated with azathioprine or 6-mercaptopurine. <i>Lancet.</i> 1996;347(8996):215-9. (Guideline Ref ID 811)	Not RCT
5. Chebli JM, Gaburri PD, De Souza AF, Pinto AL, Chebli LA, Felga GE, Forn CG, Pimentel CF. Long-term results with azathioprine therapy in patients with glucocorticosteroid-dependent Crohn's disease: open-label prospective study. <i>J Gastroenterol Hepatol.</i> 2007;22(2):268-74. (Guideline Ref ID 90)	Not RCT
6. Christodoulou D, Katsanos K, Baltayannis G, Tzabouras N, Tsianos EV. A report on efficacy and safety of azathioprine in a group of inflammatory bowel disease patients in northwest Greece. <i>Hepatogastroenterology.</i> 2003;50(52):1021-4. (Guideline Ref ID 334)	Not RCT
7. Cosnes J, Nion-Larmurier I, Beaugerie L, Afchain P, Tiret E, Gendre JP. Impact of the increasing use of immunosuppressants in Crohn's disease on the need for intestinal surgery. <i>Gut.</i> 2005;54(2):237-41. (Guideline Ref ID 1080)	Not RCT
8. Cuffari C, Théorêt Y, Latour S, Seidman G. 6-Mercaptopurine metabolism in Crohn's disease: correlation with efficacy and toxicity. <i>Gut.</i> 1996;39(3):401-6. (Guideline Ref ID 306)	Not question of interest
9. Goldstein F. Maintenance treatment for Crohn's disease: has the time arrived? <i>Am J Gastroenterol.</i> 1992;87(5):551-6. (Guideline Ref ID 343)	Not RCT
10. Gupta P, Gokhale R, Kirschner BS. 6-mercaptopurine metabolite levels in children with inflammatory bowel disease. <i>J Pediatr Gastroenterol Nutr.</i> 2001;33(4):450-4. (Guideline Ref ID 763)	Not question of interest
11. Jacobstein DA, Baldassano RN. Use of 6-mercaptopurine/azathioprine as the immunomodulator of choice for moderately active Crohn's disease: balance. <i>Inflamm Bowel Dis.</i> 2005;11(2):203-5. (Guideline Ref ID 1061)	Not RCT
12. Jaspers GJ, Verkade HJ, Escher JC, de Ridder L,	Not RCT

Study reference	Reason for exclusion
Taminiau JA, Rings EH. Azathioprine maintains first remission in newly diagnosed pediatric Crohn's disease. <i>Inflamm Bowel Dis</i> . 2006;12(9):831-6. (Guideline Ref ID 678)	
13. Juillerat P, Vader JP, Felley C, Pittet V, Gonvers JJ, Mottet C, Bemelman WA, Lémann M, Oresland T, Michetti P, Froehlich F; EPACT II Study Group. Appropriate maintenance treatment for Crohn's disease: Results of a multidisciplinary international expert panel - EPACT II. <i>J Crohns Colitis</i> . 2009;3(4):241-9. (Guideline Ref ID 238)	Not RCT
14. Kader HA, Raynor SC, Young R, Kaufman SS, Vanderhoof J, Ruby EI, Mack DR. Introduction of 6-mercaptopurine in Crohn's disease patients during the perioperative period: a preliminary evaluation of recurrence of disease. <i>J Pediatr Gastroenterol Nutr</i> . 1997;25(1):93-7. (Guideline Ref ID 304)	Not RCT
15. Kim PS, Zlatanic J, Korelitz BI, Gleim GW. Optimum duration of treatment with 6-mercaptopurine for Crohn's disease. <i>Am J Gastroenterol</i> . 1999;94(11):3254-7. (Guideline Ref ID 20337)	Not RCT
16. Klein M, Binder HJ, Mitchell M, Aaronson R, Spiro H. Treatment of Crohn's disease with azathioprine: a controlled evaluation. <i>Gastroenterology</i> . 1974;66(5):916-22. (Guideline Ref ID 2791)	Not maintenance therapy
17. Hanauer SB. Remission of Crohn disease with current drugs: A meta-analysis. <i>Annals of Internal Medicine</i> 1992;117(SUPPL. 3), 69. (Guideline Ref ID 828)	Not RCT
18. Kornbluth A, George J, Sachar DB. Immunosuppressive drugs in Crohn's disease. <i>Gastroenterologist</i> . 1994;2(3):239-46. (Guideline Ref ID 326)	Not RCT
19. Lavy A, Chowers Y, Odes HS, Eliakim R; Israel gastroenterology association. Position statement: immunomodulator therapy for inflammatory Bowel disease. <i>Isr Med Assoc J</i> . 2003;5(3):164-9. (Guideline Ref ID 121)	Not RCT
20. Ludwig D, Stange EF. Efficacy of azathioprine in the treatment of chronic active Crohn's disease: prospective one-year follow-up study. German Imurek Study Group. <i>Z Gastroenterol</i> . 1999;37(11):1085-91. (Guideline Ref ID 1759)	Not RCT
21. Mantzaris GJ, Roussos A, Christidou A, Koilakou S, Kalantzis CN, Petraki K, Sfakianakis M, Karagiannidis A, Polyzou P. The long-term efficacy of azathioprine does not wane after four years of continuous treatment in patients with steroid-dependent luminal Crohn's disease. <i>J Crohns Colitis</i> . 2007;1(1):28-34. (Guideline Ref ID 785)	Not RCT
22. Markowitz J, Rosa J, Grancher K, Aiges H, Daum F. Long-term 6-mercaptopurine treatment in adolescents with Crohn's disease. <i>Gastroenterology</i> .	Not RCT

Study reference	Reason for exclusion
1990;99(5):1347-51. (Guideline Ref ID 347)	
23. Nielsen OH, Vainer B, Rask-Madsen J. Review article: the treatment of inflammatory bowel disease with 6-mercaptopurine or azathioprine. <i>Aliment Pharmacol Ther.</i> 2001;15(11):1699-708. (Guideline Ref ID 20338)	Not RCT
24. Nyman M, Hansson I, Eriksson S. Long-term immunosuppressive treatment in Crohn's disease. <i>Scand J Gastroenterol.</i> 1985;20(10):1197-203. (Guideline Ref ID 6321)	Not RCT
25. O'Brien JJ, Bayless TM, Bayless JA. Use of azathioprine or 6-mercaptopurine in the treatment of Crohn's disease. <i>Gastroenterology.</i> 1991;101(1):39-46. (Guideline Ref ID 20339)	Not RCT
26. Picco MF, Zubiaurre I, Adluni M, Cangemi JR, Shelton D. Immunomodulators are associated with a lower risk of first surgery among patients with non-penetrating non-stricturing Crohn's disease. <i>Am J Gastroenterol.</i> 2009;104(11):2754-9. (Guideline Ref ID 598)	Not RCT
27. Pinto AL, Chebli LA, Ribeiro MS, Pace FH, Moraes JP, do Amaral FJ Jr, Gaburri PD, Meirelles de Souza AF, Chebli JM. Azathioprine therapy in steroid-dependent patients with Crohn disease: results of a 10-year longitudinal follow-up study. <i>Med Sci Monit.</i> 2009;15(5):PI19-26. (Guideline Ref ID 447)	Not RCT
28. Plevy SE. Glucocorticosteroid-sparing treatments in patients with Crohn's disease. <i>Am J Gastroenterol.</i> 2002;97(7):1607-17. (Guideline Ref ID 210)	Not RCT
29. Present DH, Meltzer SJ, Krumholz MP, Wolke A, Korelitz BI. 6-Mercaptopurine in the management of inflammatory bowel disease: short- and long-term toxicity. <i>Ann Intern Med.</i> 1989;111(8):641-9 (Guideline Ref ID 501)	Not RCT
30. Present DH, Korelitz BI, Wisch N, Glass JL, Sachar DB, Pasternack BS. Behandlung des Morbus Crohn mit 6-Mercaptopurine. <i>Inn. Med.</i> 1980;7: 147-8 (Guideline Ref ID 1533)	Non-English language
31. Carter MJ, Lobo AJ. Lack of effect of intravenous azathioprine on time to respond for steroid treated Crohn's disease. <i>Gut.</i> 2001;48(3):295-6. (Guideline Ref ID 6315)	Not question of interest
32. Steinhart H. Maintenance therapy in Crohn's disease. <i>Can J Gastroenterol.</i> 2000;14 Suppl C:23C-28C. (Guideline Ref ID 249)	Not RCT
33. Szamosi T, Banai J, Lakatos L, Czegledi Z, David G, Zsigmond F, Pandur T, Erdelyi Z, Gemela O, Papp M, Papp J, Lakatos PL. Early azathioprine/biological therapy is associated with decreased risk for first surgery and delays time to surgery but not reoperation in both smokers and nonsmokers with Crohn's disease, while smoking decreases the risk of colectomy in ulcerative colitis. <i>Eur J Gastroenterol</i>	Not question of interest

Excluded studies

Study reference	Reason for exclusion
Hepatology. 2010;22(7):872-9 (Guideline Ref ID 387)	
34. Treton X, Bouhnik Y, Mary JY, Colombel JF, Duclos B, Soule JC, Lerebours E, Cosnes J, Lemann M; Groupe D'Etude Thérapeutique Des Affections Inflammatoires Du Tube Digestif (GETAID). Azathioprine withdrawal in patients with Crohn's disease maintained on prolonged remission: a high risk of relapse. Clin Gastroenterol Hepatol. 2009;7(1):80-5. (Guideline Ref ID 63)	Not question of interest
35. Zheng JJ, Chu XQ, Shi XH, Zhou CL, Seng BW. Efficacy and safety of azathioprine maintenance therapy in a group of Crohn's disease patients in China. J Dig Dis. 2008;9(2):84-8. (Guideline Ref ID 6323)	Not RCT
36. Viazis N, Vlachogiannakos J., Georgiadis D., Keyoglou A., Vasianopoulou P., Markoutsaki Th., Komninou E., Markoglou K., Gouma P., Karamanolis D.G. Azathioprine use in patients with Inflammatory Bowel Disease. Adherence to treatment and adverse events. A single center experience. Annals of Gastroenterology 2009;22(3):173-7 (Guideline Ref ID 20248)	Not RCT
37. Treton X, Bouhnik Y, Mary JY, Colombel JF, Duclos B, Soule JC, Lerebours E, Cosnes J, Lemann M; Groupe D'Etude Thérapeutique Des Affections Inflammatoires Du Tube Digestif (GETAID). Azathioprine withdrawal in patients with Crohn's disease maintained on prolonged remission: a high risk of relapse. Clin Gastroenterol Hepatol. 2009;7(1):80-5. (Guideline Ref ID 63)	Not RCT – study already included (Ref ID: 6334 Lémann et al. 2005)
38. Fuentes D, Torrente F, Keady S, Thirrupathy K, Thomson MA, Walker-Smith JA, Murch SH, Heuschkel RB. High-dose azathioprine in children with inflammatory bowel disease. Aliment Pharmacol Ther. 2003;17(7):913-21. (Guideline Ref ID 1033)	Not RCT
39. Present DH, Wisch N, Glass JL, Korelitz BI. The efficacy of immunosuppressive therapy in Crohn's Disease. A randomized long term double blind study. Gastroenterology 1977;72(5II), A-91. (Guideline Ref ID 948)	Crossover study
40. Boyle B, Mackner L, Ross C, Moses J, Kumar S, Crandall W. A single-center experience with methotrexate after thiopurine therapy in pediatric Crohn disease. J Pediatr Gastroenterol Nutr. 2010;51(6):714-7. (Guideline Ref ID 602)	Not RCT
41. Pearson DC, May GR, Fick GH, Sutherland LR. Azathioprine and 6-mercaptopurine in Crohn disease. A meta-analysis. Ann Intern Med. 1995;123(2):132-42. (Guideline Ref ID 6380)	Not RCT (used for quality assessment)
42. Candy S, Wright J, Gerber M, Adams G, Gerig M, Goodman R. A controlled double blind study of azathioprine in the management of Crohn's disease. Gut. 1995;37(5):674-8. (Guideline Ref ID 319)	Active disease at randomisation

Excluded studies

Study reference	Reason for exclusion
43. Maté-Jiménez J, Hermida C, Cantero-Perona J, Moreno-Otero R. 6-mercaptopurine or methotrexate added to prednisone induces and maintains remission in steroid-dependent inflammatory bowel disease. <i>Eur J Gastroenterol Hepatol.</i> 2000;12(11):1227-33. (Guideline Ref ID 6332)	Active disease at randomisation
44. Rosenberg JL, Levin B, Wall AJ, Kirsner JB. A controlled trial of azathioprine in Crohn's disease. <i>Am J Dig Dis.</i> 1975;20(8):721-6. (Guideline Ref ID 418)	Trial lasted less than 12 months
45. Willoughby JM, Beckett J, Kumar PJ, Dawson AM. Controlled trial of azathioprine in Crohn's disease. <i>Lancet.</i> 1971;2(7731):944-7. (Guideline Ref ID 437)	Trial lasted less than 12 months
46. D'Haens GR, Norman M, Van Assche GA, Van Olman G, Aerden I, Wermeire S, Rutgeerts PJ. Combination therapy with metronidazole and azathioprine reduces severe postoperative recurrence of Crohn's disease: a double-blind controlled randomised trial. <i>Gastroenterology.</i> 2007;132:A52. (Guideline Ref ID 6532)	Post-surgical study
47. Hanauer SB, Korelitz BI, Rutgeerts P, Peppercorn MA, Thisted RA, Cohen RD, Present DH. Postoperative maintenance of Crohn's disease remission with 6-mercaptopurine, mesalamine, or placebo: a 2-year trial. <i>Gastroenterology.</i> 2004;127(3):723-9. (Guideline Ref ID 6333)	Post-surgical study
48. Prefontaine E, Sutherland LR, Macdonald JK, Cepoiu M. Azathioprine or 6-mercaptopurine for maintenance of remission in Crohn's disease. <i>Cochrane Database Syst Rev.</i> 2009;(1):CD000067 (Guideline Ref ID 2533)	Not RCT (used for quality assessment)

1.2.5 Methotrexate

Study reference	Reason for exclusion
1. Boyle B, MacKner L, Ross C, Moses J, Kumar S, Crandall W. A Single-center experience with methotrexate after thiopurine therapy in pediatric crohn disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2010; 51(6):714-717.	Not an RCT
2. Charpignon C, Beau P. Methotrexate as single therapy in Crohn's disease: is its long-term efficacy limited? <i>Gastroenterologie Clinique Et Biologique</i> . 2008; 32(2):153-157.	Not an RCT
3. Chong RY, Hanauer SB, Cohen RD. Efficacy of parenteral methotrexate in refractory Crohn's disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2001; 15(1):35-44.	Not and RCT
4. Din S, Dahele A, Fennel J, Aitken S, Shand AG, Arnott ID, Satsangi J. Use of methotrexate in refractory Crohn's disease: the Edinburgh experience. <i>Inflammatory Bowel Diseases</i> . 2008; 14(6):756-762.	Not an RCT
5. Feagan BG, Rochon J, Fedorak RN, Irvine EJ, Wild G, Sutherland L, Steinhart AH, Greenberg GR, Gillies R, Hopkins M. Methotrexate for the treatment of Crohn's disease. The North American Crohn's Study Group Investigators. <i>New England Journal of Medicine</i> . 1995; 332(5):292-297.	Active disease
6. Fraser AG, Morton D, MCGovern D, Travis S, Jewell DP. The efficacy of methotrexate for maintaining remission in inflammatory bowel disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2002; 16(4):693-697.	Not an RCT
7. Egan LJ, Sandborn WJ, Tremaine WJ, Leighton JA, Mays DC, Pike MG, Zinsmeister AR, Lipsky JJ. A randomized dose-response and pharmacokinetic study of methotrexate for refractory inflammatory Crohn's disease and unclerative colitis. <i>Alimentary Pharmacology and Therapeutics</i> . 1999; 13(12):1597-1604.	Mixed IBD population
8. Hausmann J, Zabel K, Herrmann E, Schroder O. Methotrexate for maintenance of remission in chronic active Crohn's disease: long-term single-center experience and meta-analysis of observational studies. <i>Inflammatory Bowel Diseases</i> . 2010; 16(7):1195-1202.	Not an RCT
9. Hayee BH, Harris AW. Methotrexate for Crohn's disease: Experience in a district general hospital. <i>European Journal of Gastroenterology and Hepatology</i> . 2005; 17(9):893-898.	Not an RCT
10. Laharie D, Reffet A, Belleannee G, Chabrun E, Subtil C, Razaire S, Capdepont M, de L, V. Mucosal healing with methotrexate in Crohn's disease: a prospective comparative study with azathioprine and infliximab. <i>Alimentary Pharmacology and Therapeutics</i> . 2011; 33(6):714-721.	Not an RCT

Excluded studies

Study reference	Reason for exclusion
11. Mate-Jimenez J, Hermida C, Cantero-Perona J, Moreno-Otero R. 6-mercaptopurine or methotrexate added to prednisone induces and maintains remission in steroid-dependent inflammatory bowel disease. <i>European Journal of Gastroenterology and Hepatology</i> . 2000; 12(11):1227-1233.	No placebo comparison
12. Oren R, Moshkowitz M, Odes S, Becker S, Keter D, Pomeranz I, Shirin C, Reinfeld I, Broide E, Lavy A, Fich A, Eliakim R, Patz J, Villa Y, Arber N, Gilat T. Methotrexate in chronic active Crohn's disease: a double-blind, randomized, Israeli multicenter trial. <i>American Journal of Gastroenterology</i> . 1997; 92(12):2203-2209.	Active disease
13. Ruemmele FM. Immunomodulation with methotrexate: underused and undervalued? <i>Digestive Diseases</i> . 2009; 27(3):312-314.	Narrative review
14. Turner D, Grossman AB, Rosh J, Kugathasan S, Gilman AR, Baldassano R, Griffiths AM. Methotrexate following unsuccessful thiopurine therapy in pediatric Crohn's disease. <i>American Journal of Gastroenterology</i> . 2007; 102(12):2804-2812.	Not an RCT
15. Uhlen S, Belbouab R, Narebski K, Goulet O, Schmitz J, Cezard JP, Turck D, Ruemmele FM. Efficacy of methotrexate in pediatric Crohn's disease: A French multicenter study. <i>Inflammatory Bowel Diseases</i> . 2006; 12(11):1053-1057.	Not an RCT

1.3 Maintaining remission after surgery

Study reference	Reason for exclusion
Please note that evidence on treatments for post-surgical maintenance of remission in Crohn's disease was reviewed in 2019. The updated evidence review and full current recommendations can be found on the NICE website.	
Drugs reduce recurrence rate after second resection for Crohn disease? <i>Inflammatory Bowel Diseases.</i> 2004; 10(5):491-495.	
3. Anstee QM, Forbes A. The safe use of percutaneous gastrostomy for enteral nutrition in patients with Crohn's disease. <i>European Journal of Gastroenterology and Hepatology.</i> 2000; 12(10):1089-1093.	Not RCT
4. Bernstein CN, Shanahan F. Critical appraisal of enteral nutrition as primary therapy in adults with Crohn's disease. <i>American Journal of Gastroenterology.</i> 1996; 91(10):2075-2079.	Clinical review
5. Besnard M, Jaby O, Mougenot JF, Ferkdadji L, Debrun A, Faure C, Delagausie P, Peuchmaur M, Aigrain Y, Navarro J, Cezard JP. Postoperative outcome of Crohn's disease in 30 children. <i>Gut.</i> 1998; 43(5):634-638.	Not question of interest
6. Blum E, Katz JA. Postoperative therapy for Crohn's disease. <i>Inflammatory Bowel Diseases.</i> 2009; 15(3):463-472.	Review article
7. Braegger CP, Nicholls S, Murch SH, Stephens S, Macdonald TT. Tumour necrosis factor alpha in stool as a marker of intestinal inflammation. <i>Lancet.</i> 1992; 339(8785):89-91.	Narrative review
8. Breslin NP, Sutherland LR. The case against routine post-operative therapy for prevention of recurrence in Crohn's disease. <i>Italian Journal of Gastroenterology and Hepatology.</i> 1998; 30(2):226-230.	Narrative review
9. Cao Y, Gao F, Liao C, Tan A, Mo Z. Meta-analysis of medical treatment and placebo treatment for preventing postoperative recurrence in Crohn's disease (CD). <i>International Journal of Colorectal Disease.</i> 2009; 24(5):509-520.	Meta-analysis used for QA
10. Caprilli R, Cottone M, Tonelli F, Sturniolo G, Castiglione F, Annese V, Papi C, Viscido A, Camma C, Corrao G, Latella G. Two mesalazine regimens in the prevention of the post-operative recurrence of Crohn's disease: a pragmatic, double-blind, randomized controlled trial. <i>Alimentary Pharmacology and Therapeutics.</i> 2003; 17(4):517-523.	Dose comparison – not question of interest
11. Chermesh I, Tamir A, Reshef R, Chowers Y, Suissa A, Katz D, Gelber M, Halpern Z, Bengmark S, Eliakim R. Failure of Synbiotic 2000 to prevent postoperative recurrence of Crohn's disease. <i>Digestive Diseases and Sciences.</i> 2007; 52(2):385-389.	Probiotics – not treatment of interest
12. Cho SM, Cho SW, Regueiro M. Postoperative Management of Crohn Disease. <i>Medical Clinics of North America.</i> 2010; 94(1):179-188.	Narrative review
13. Clarke K, Regueiro M. Prevention and treatment	Narrative review

Study reference	Reason for exclusion
options for postoperative Crohn's disease: A clinical dilemma. <i>Gastroenterology and Hepatology</i> . 2009; 5(8):581-588.	
14. Colombel JF, Rutgeerts P, Malchow H, Jacyna M, Nielsen OH, Rask-Madsen J, van Deventer S, Ferguson A, Desreumaux P, Forbes A, Geboes K, Melani L, Cohard M. Interleukin 10 (Tenovil) in the prevention of postoperative recurrence of Crohn's disease. <i>Gut</i> . 2001; 49(1):42-46.	Not treatment of interest
15. Cottone M, Orlando A, Viscido A, Calabrese E, Camma C, Casa A. Review article: Prevention of postsurgical relapse and recurrence in Crohn's disease. <i>Alimentary Pharmacology and Therapeutics, Supplement</i> . 2003; 17(2):38-42.	Review article
16. Cuillerier E, Lemann M, Bouhnik Y, Allez M, Rambaud JC, Modigliani R. Azathioprine for prevention of postoperative recurrence in Crohn's disease: a retrospective study. <i>European Journal of Gastroenterology and Hepatology</i> . 2001; 13(11):1291-1296.	Not RCT
17. Cunningham MF, Docherty NG, Coffey JC, Burke JP, O'Connell PR. Postsurgical recurrence of ileal Crohn's disease: an update on risk factors and intervention points to a central role for impaired host-microflora homeostasis. <i>World Journal of Surgery</i> . 2010; 34(7):1615-1626.	Review article; not question of interest
18. D'Haens GR, Noman M, Van Assche G, Van Olman G, Aerden I, Wermeire S, Rutgeerts PJ. Combination therapy with metronidazole and azathioprine reduces severe postoperative recurrence of Crohn's disease. <i>Gastroenterology</i> . 2007; 132(4 suppl 2):A52.	Abstract only
19. Doherty G, Bennett G, Patil S, Cheifetz A, Moss AC. Interventions for prevention of post-operative recurrence of Crohn's disease. <i>Cochrane Database of Systematic Reviews</i> . 2009;(1)	Cochrane review – used for QA
20. Doherty GA, Bennett GC, Cheifetz AS, Moss AC. Meta-analysis: targeting the intestinal microbiota in prophylaxis for post-operative Crohn's disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2010; 31(8):802-809.	Not outcome of interest
21. Domenech E, Manosa M, Bernal I, Garcia-Planella E, Cabre E, Pinol M, Lorenzo-Zuniga V, Boix J, Gassull MA. Impact of azathioprine on the prevention of postoperative Crohn's disease recurrence: results of a prospective, observational, long-term follow-up study. <i>Inflammatory Bowel Diseases</i> . 2008; 14(4):508-513.	Not RCT
22. El-Hachem S, Regueiro M. Postoperative Crohn's disease: Prevention and treatment. <i>Expert Review of Gastroenterology and Hepatology</i> . 2009; 3(3):249-256.	Narrative review
23. Esaki M, Matsumoto T, Hizawa K, Nakamura S, Jo Y, Mibu R, Iida M. Preventive effect of nutritional therapy against postoperative recurrence of Crohn disease, with reference to findings determined by intra-operative enteroscopy. <i>Scandinavian Journal of Gastroenterology</i> . 2005; 40(12):1431-1437.	Comparison of types of EN – not question of interest

Study reference	Reason for exclusion
24. Esaki M, Matsumoto T, Nakamura S, Yada S, Fujisawa K, Jo Y, Iida M. Factors affecting recurrence in patients with Crohn's disease under nutritional therapy. <i>Diseases of the Colon and Rectum</i> . 2006; 49(10 Suppl):S68-S74.	Not post-surgical
25. Flasse R, Fontaine F, Vanheuverzwyn R. Prevention of Crohn's disease recurrences after intestinal resection with Eudragis-L-coated 5-aminosalicylic acid. Preliminary results of a one year double-blind placebo controlled study. <i>Gastroenterology</i> . 1991; 100(5 Part 2):A208	Abstract only
26. Florent C, Cortot A, Quandale P, Sahmound T, Modigliani R, Sarfaty E, Valleur P, Dupas JL, Daurat M, Faucheron JL, Lerebours E, Michot F, Belaiche J, Jacquet N, Soule JC, Rothman N, Gendre JP, Malafosse M. Placebo-controlled clinical trial of mesalazine in the prevention of early endoscopic recurrences after resection for Crohn's disease. (Groupe d'Etudes Therapeutiques des Affections Inflammatoires Digestives (GETAID). <i>European Journal of Gastroenterology and Hepatology</i> . 1996; 8(3):229-233.	Treatment time less than one year
27. Ford AC, Khan KJ, Talley NJ, Moayyedi P. 5-aminosalicylates prevent relapse of Crohn's disease after surgically induced remission: Systematic review and meta-analysis. <i>American Journal of Gastroenterology</i> . 2011; 106(3):413-420.	Meta-analysis – used for quality assurance
28. Gordon M, Naidoo K, Thomas AG, Akobeng AK. Oral 5-aminosalicylic acid for maintenance of surgically-induced remission in Crohn's disease. <i>Cochrane Database of Systematic Reviews</i> . 2011;(1)	Cochrane review – used for quality assurance
29. Grivceva SK, Misevska P, Zdravkovska M, Trajkov D, Serafimovski V. Total parenteral nutrition in treatment of patients with inflammatory bowel disease. <i>Makedonska Akademija Na Naukite i Umetnostite Oddelenie Za Bioloski i Meditsinski Nauki Prilozi</i> . 2008; 29(1):21-43.	Not treatment of interest
30. Hawthorne AB, Logan RF, Hawkey CJ, Foster PN, Axon AT, Swarbrick ET, Scott BB, Lennard-Jones JE. Randomised controlled trial of azathioprine withdrawal in ulcerative colitis. <i>BMJ</i> . 1992; 305(6844):20-22.	Ulcerative colitis paper
31. Herfarth H, Tjaden C, Lukas M, Obermeier F, Dilger K, Muller R, Scholmerich J, Study Group. Adverse events in clinical trials with azathioprine and mesalamine for prevention of postoperative recurrence of Crohn's disease. <i>Gut</i> . 2006; 55(10):1525-1526.	Letter to editor; per protocol analysis; underpowered
32. Ikeuchi H, Kusunoki M, Yanagi H, Yamamura T, Fukuda Y, Shimoyama T. Effects of elemental diet (ED) on surgical treatment in Crohn's disease. <i>Hepato-Gastroenterology</i> . 2000; 47(32):390-392.	Pre-surgical treatment
33. Ikeuchi H, Yamamura T, Nakano H, Kosaka T, Shimoyama T, Fukuda Y. Efficacy of nutritional therapy for perforating and non-perforating Crohn's disease. <i>Hepato-Gastroenterology</i> . 2004; 51(58):1050-1052.	Length of treatment time not specified

Excluded studies

Study reference	Reason for exclusion
34. Lake AM, Kim S, Mathis RK, Walker WA. Influence of preoperative parenteral alimentation on postoperative growth in adolescent Crohn's disease. <i>Journal of Pediatric Gastroenterology and Nutrition.</i> 1985; 4(2):182-186.	Pre-surgical study
35. Madsen K, Backer JL, Leddin D, Dieleman LA, Bitton A, Feagan B, Petrunia DM, Chiba N, Enns R, Fedorak R. A Randomized Controlled Trial of VSL#3 for the Prevention of Endoscopic Recurrence Following Surgery for Crohn's Disease. <i>Gastroenterology.</i> 2008; 134(4):A-361.	Not treatment of interest
36. Malireddy K, Larson DW, Sandborn WJ, Loftus EV, Faubion WA, Pardi DS, Qin R, Gullerud RE, Cima RR, Wolff B, Dozois EJ. Recurrence and impact of postoperative prophylaxis in laparoscopically treated primary ileocolic Crohn disease. <i>Archives of Surgery.</i> 2010; 145(1):42-47.	Not RCT
37. Marteau P, Lemann M, Seksik P, Laharie D, Colombel JF, Bouhnik Y, Cadiot G, Soule JC, Bourreille A, Metman E, Lerebours E, Carbonnel F, Dupas JL, Veyrac M, Coffin B, Moreau J, Abitbol V, Blum-Sperisen S, Mary JY. Ineffectiveness of Lactobacillus (Johnsonii LA1 for prophylaxis of postoperative recurrence in Crohn's disease: a randomised, double blind, placebo controlled GETAID trial. <i>Gut.</i> 2006; 55(6):842-847.	Not question of interest
38. McLeod RS, Wolff BG, Ross S, Parkes R, McKenzie M, Investigators of the CAST Trial. Recurrence of Crohn's disease after ileocolic resection is not affected by anastomotic type: results of a multicenter, randomized, controlled trial. <i>Diseases of the Colon and Rectum.</i> 2009; 52(5):919-927.	Not question of interest
39. Myrelid P, Svarm S, Andersson P, Almer S, Bodemar G, Olaison G. Azathioprine as a postoperative prophylaxis reduces symptoms in aggressive Crohn's disease. <i>Scandinavian Journal of Gastroenterology.</i> 2006; 41(10):1190-1195.	Not RCT
40. Ng SC, Lied GA, Arebi N, Phillips RK, Kamm MA. Clinical and surgical recurrence of Crohn's disease after ileocolonic resection in a specialist unit. <i>European Journal of Gastroenterology and Hepatology.</i> 2009; 21(5):551-557.	Not RCT
41. Papay P, Reinisch W, Ho E, Gratzer C, Lissner D, Herkner H, Riss S, Dejaco C, Miehsler W, Vogelsang H, Novacek G. The impact of thiopurines on the risk of surgical recurrence in patients with Crohn's disease after first intestinal surgery. <i>American Journal of Gastroenterology.</i> 2010; 105(5):1158-1164.	Not RCT
42. Papi C, Aratari A, Tornatore V, Koch M, Capurso L, Caprilli R. Long-term prevention of post-operative recurrence in Crohn's disease cannot be affected by mesalazine. <i>Journal of Crohn's and Colitis.</i> 2009; 3(2):109-114.	Not RCT
43. Pascua M, Su C, Lewis JD, Brensinger C, Lichtenstein GR. Meta-analysis: Factors predicting post-operative recurrence with placebo therapy in patients with Crohn's disease. <i>Alimentary</i>	Not question of interest

Study reference	Reason for exclusion
<i>Pharmacology and Therapeutics</i> . 2008; 28(5):545-556.	
44. Peyrin-Biroulet L, Deltenre P, Ardizzone S, D'Haens G, Hanauer SB, Herfarth H, Lemann M, Colombel JF. Azathioprine and 6-mercaptopurine for the prevention of postoperative recurrence in Crohn's disease: a meta-analysis. <i>American Journal of Gastroenterology</i> . 2009; 104(8):2089-2096.	(Meta-analysis – used for quality assurance)
45. Prantera C, Scribano ML, Falasco G, Andreoli A, Luzi C. Ineffectiveness of probiotics in preventing recurrence after curative resection for Crohn's disease: a randomised controlled trial with <i>Lactobacillus GG</i> . <i>Gut</i> . 2002; 51(3):405-409.	Not treatment of interest
46. Regueiro M. Management and prevention of postoperative Crohn's disease. <i>Inflammatory Bowel Diseases</i> . 2009; 15(10):1583-1590.	Clinical review
47. Regueiro M, Schraut W, Baidoo L, Kip KE, Sepulveda AR, Pesci M, Harrison J, Plevy SE. Infliximab prevents Crohn's disease recurrence after ileal resection. <i>Gastroenterology</i> . 2009; 136(2):441-450.	Not question of interest
48. Reinisch W, Angelberger S, Petritsch W, Shonova O, Lukas M, Bar-Meir S, Teml A, Schaeffeler E, Schwab M, Dilger K, Greinwald R, Mueller R, Stange EF, Herrlinger KR, International AZT. Azathioprine versus mesalazine for prevention of postoperative clinical recurrence in patients with Crohn's disease with endoscopic recurrence: efficacy and safety results of a randomised, double-blind, double-dummy, multicentre trial. <i>Gut</i> . 2010; 59(6):752-759.	Study started 6-24 months after surgery
49. Renna S, Orlando A, Mocciaro F, Cottone M. Placebo therapy in Crohn's disease. <i>European Journal of Internal Medicine</i> . 2009; 20(6):572-578.	Not question of interest
50. Rutgeerts P, Van Assche G, Vermeire S, D'Haens G, Baert F, Noman M, Aerden I, de Hertogh G, Geboes K, Hiele M, D'Hoore A, Penninckx F. Ornidazole for prophylaxis of postoperative Crohn's disease recurrence: a randomized, double-blind, placebo-controlled trial. <i>Gastroenterology</i> . 2005; 128(4):856-861.	Ornidazole not available in UK
51. Sampietro GM, Corsi F, Maconi G, Ardizzone S, Frontali A, Corona A, Porro GB, Foschi D. Prospective study of long-term results and prognostic factors after conservative surgery for small bowel Crohn's disease. <i>Clinical Gastroenterology and Hepatology</i> . 2009; 7(2):183-191.	Not RCT
52. Sutherland LR, Martin F, Bailey RJ, Fedorak RN, Poleski M, Dallaire C, Rossman R, Saibil F, Lariviere L. A randomized, placebo-controlled, double-blind trial of mesalamine in the maintenance of remission of Crohn's disease. The Canadian Mesalamine for Remission of Crohn's Disease Study Group. <i>Gastroenterology</i> . 1997; 112(4):1069-1077.	Less than one year treatment
53. Swoger JM, Regueiro M. Preventive therapy in postoperative Crohn's disease. <i>Current Opinion in Gastroenterology</i> . 2010; 26(4):337-343.	Narrative review
54. Takahashi H, Ando T, Watanabe O, Maeda O, Ishiguro K, Ishikawa D, Hasegawa M, Minami M, Goto	Not RCT

Excluded studies

Study reference	Reason for exclusion
<p>Y, Kusugami K, Ina K, Ohmiya N, Niwa Y, Goto H. Relationship between nutritional therapy and surgery in Crohn's disease. <i>Hepato-Gastroenterology</i>. 2009; 56(93):1044-1048.</p>	
<p>55. Van Gossum A, Dewit O, Louis E, de Hertogh G, Baert F, Fontaine F, DeVos M, Enslen M, Paintin M, Franchimont D. Multicenter randomized-controlled clinical trial of probiotics (<i>Lactobacillus johnsonii</i>, LA1) on early endoscopic recurrence of Crohn's disease after ileo-caecal resection. <i>Inflammatory Bowel Diseases</i>. 2007; 13(2):135-142.</p>	<p>Not question of interest</p>
<p>56. Velayos FS, Sandborn WJ. Use of azathioprine and 6MP in postoperative Crohn's: Changing natural history or just along for the ride. <i>American Journal of Gastroenterology</i>. 2009; 104(8):2097-2099.</p>	<p>Narrative review</p>
<p>57. Yamamoto T, Nakahigashi M, Umegae S, Kitagawa T, Matsumoto K. Impact of long-term enteral nutrition on clinical and endoscopic recurrence after resection for Crohn's disease: A prospective, non-randomized, parallel, controlled study. <i>Alimentary Pharmacology and Therapeutics</i>. 2007; 25(1):67-72.</p>	<p>Not RCT</p>
<p>58. Yao GX, Wang XR, Jiang ZM, Zhang SY, Ni AP. Role of perioperative parenteral nutrition in severely malnourished patients with Crohn's disease. <i>World Journal of Gastroenterology</i>. 2005; 11(36):5732-5734.</p>	<p>Not treatment of interest</p>

1.4 Enteral nutrition

1.4.1 Induction

Study reference	Reason for exclusion
1. Afzal, N. A., et al. "Colonic Crohn's disease in children does not respond well to treatment with enteral nutrition if the ileum is not involved." <i>Digestive Diseases and Sciences</i> 50.8 (2005): 1471-75.	Prospective cohort study; no control group
2. Afzal NA, Van Der Zaag-Loonen HJ, Arnaud-Battandier F, Davies S, Murch S, Derkx B, Heuschkel R, Fell JM. Improvement in quality of life of children with acute Crohn's disease does not parallel mucosal healing after treatment with exclusive enteral nutrition. <i>Alimentary Pharmacology and Therapeutics</i> . 2004; 20(2):167-172.	Prospective cohort study; no control group
3. Bascietto C, Borrelli O, Di Nardo G, Ambrosini A, Cirulli M, Bosco S, Cucchiara S. Nutritional Therapy Alone With A Polymeric Diet (Modulen) Is More Effective Than Corticosteroids in Inducing Healing of Intestinal Mucosal Lesions in Active Crohn's Disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2004; 39:S106-S107.	Abstract from poster session
4. Beattie RM, Schiffrin EJ, Donnet-Hughes A, Huggett AC, Domizio P, Macdonald TT, Walker-Smith JA. Polymeric nutrition as the primary therapy in children with small bowel Crohn's disease <i>Alimentary Pharmacology and Therapeutics</i> . 1994; 8(6):609-615.	
5. Berni Canani R., Terrin G, Borrelli O, Romano MT, Manguso F, Coruzzo A, D'Armiento F, Romeo EF, Cucchiara S. Short- and Long-Term Therapeutic Efficacy of Nutritional Therapy and Glucocorticosteroids in Paediatric Crohn's Disease. <i>Digestive and Liver Disease</i> . 2006; 38(6):381-387. (Guideline Ref ID 1208)	Not RCT; uncontrolled descriptive study
6. Buchanan E, Gaunt WW, Cardigan T, Garrick V, McGrogan P, Russell RK. The use of exclusive enteral nutrition for induction of remission in children with Crohn's disease demonstrates that disease phenotype does not influence clinical remission <i>Alimentary Pharmacology and Therapeutics</i> . 2009; 30(5):501-507.	Not RCT
7. Day, A. S., et al. "Systematic review: Nutritional therapy in paediatric Crohn's disease." <i>Alimentary Pharmacology and Therapeutics</i> 27.4 (2008): 293-307.	Narrative review
8. Demetriou, A. A. "Comparison of enteral nutrition and drug treatment in active Crohn's disease: results of the European Cooperative Crohn's Disease Study IV." <i>Journal of Parenteral and Enteral Nutrition</i> 16.1 (1992): 84-85.	Letter
9. Dziechciarz, P., et al. "Meta-analysis: enteral nutrition in active Crohn's disease in children. [47 refs]." <i>Alimentary Pharmacology and Therapeutics</i> 26.6 (2007): 795-806.	Meta-analysis/systematic review used for quality assurance
10. Fell JME, Paintin M, Arnaud-Battandieri F, Beattie	Not RCT

Excluded studies

Study reference	Reason for exclusion
RM, Hollis A, Kitching P, Donnet-Hughes A, Macdonald TT, Walker-Smith JA. Mucosal healing and a fall in mucosal pro-inflammatory cytokine mRNA induced by a specific oral polymeric diet in paediatric Crohn's disease. <i>Alimentary Pharmacology and Therapeutics</i> . 2000; 14(3):281-289.	
11. Fernández-Bañares, F., et al. "How effective is enteral nutrition in inducing clinical remission in active Crohn's disease? A meta-analysis of the randomized clinical trials." <i>Journal of Parenteral and Enteral Nutrition</i> 19.5 (1995): 356-64.	Meta-analysis/systematic review used for quality assurance
12. Griffiths, A. M., et al. "Meta-analysis of enteral nutrition as a primary treatment of active Crohn's disease." <i>Gastroenterology</i> 108.4 (1995): 1056-67.	Meta-analysis/systematic review used for quality assurance
13. Heuschkel, R. B., et al. "Enteral nutrition and glucocorticosteroids in the treatment of acute Crohn's disease in children." <i>Journal of Pediatric Gastroenterology and Nutrition</i> 31.1 (2000): 8-15.	Meta-analysis/systematic review used for quality assurance
14. Koretz, R. L., et al. "Does enteral nutrition affect clinical outcome? A systematic review of the randomized trials. [207 refs]." <i>American Journal of Gastroenterology</i> 102.2 (2007): 412-29.	Meta-analysis/systematic review used for quality assurance
15. Messori, A., et al. "Defined-formula diets versus steroids in the treatment of active Crohn's disease: a meta-analysis." <i>Scandinavian Journal of Gastroenterology</i> 31.3 (1996): 267-72.	Meta-analysis/systematic review used for quality assurance
16. Guidelines for use of home total parenteral nutrition. A.S.P.E.N. Board of Directors. American Society for Parenteral and Enteral Nutrition. <i>Jpen: Journal of Parenteral & Enteral Nutrition</i> 11.4 (1987): 342-44.	Not question of interest
17. Gassull, M. A., et al. "Enteral nutrition in inflammatory bowel disease." <i>Gut</i> 27 Suppl 1 (1986): 76-80.	Not RCT
18. Gonzalez-Huix, F., et al. "Total enteral nutrition with polymeric diets (TENP) as primary treatment in Crohn's disease (CD). Preliminary results of a controlled trial [abstract]." <i>Clinical Nutrition</i> 10 Spec Suppl 2 (1991): 47.	Abstract
19. Griffiths, A. M., et al. "Meta-analysis of enteral nutrition as a primary treatment of active Crohn's disease." <i>Gastroenterology</i> 108.4 (1995): 1056-67.	Abstract
20. Heuschkel, R. "Enteral nutrition should be used to induce remission in childhood Crohn's disease. [81 refs]." <i>Digestive Diseases</i> 27.3 (2009): 297-305.	Narrative review
21. Hunt, J. B., et al. "A randomised controlled trial of elemental diet versus prednisolone in the treatment of new & recurrent Crohns disease [abstract]." <i>Clinical Nutrition</i> 8 Spec Suppl (1989): 80.	Abstract
22. Imes, S., et al. "Effect of Ensure, a defined formula diet, in patients with Crohn's disease." <i>Digestion</i> 35.3 (1986): 158-69.	Not comparison of interest
23. Johnson, T., et al. "Treatment of active Crohn's	Not question of interest

Excluded studies

Study reference	Reason for exclusion
disease in children using partial enteral nutrition with liquid formula: a randomised controlled trial 845." Gut 55.3 (2006): 356-61.	
24 .Lochs, H., et al. "ESPEN Guidelines on Enteral Nutrition: Gastroenterology. [148 refs]." Clinical Nutrition 25.2 (2006): 260-74.	Guideline
25. Mantzaris, G. J., et al. "A Prospective Randomized Trial in Active Crohn's Disease Comparing prednisolone, a Polymeric Diet and a Polymeric Diet Plus Prednisolon [abstract]." Gut 39 Suppl 3 (1996): A166.	Abstract only
26. Matsueda, K. "Therapeutic efficacy of elemental enteral alimentation in Crohn's disease." Journal of Gastroenterology 35.SUPPL. 12 (2000): 19.	Abstract
27. Matsui, T., T. Sakurai, and T. Yao. "Nutritional therapy for Crohn's disease in Japan. [Review] [29 refs]." Journal of Gastroenterology 40 Suppl 16:25-31, 2005 Mar. (2005): 25-31.	Narrative only
28. Moorthy, D., K. L. Cappellano, and I. H. Rosenberg. "Nutrition and Crohn's disease: an update of print and Web-based guidance. [Review] [116 refs]." Nutrition Reviews 66.7 (2008): 387-97.	Narrative
29. Morin, C. L., et al. "Continuous elemental enteral alimentation in the treatment of children and adolescents with Crohn's disease." Journal of Parenteral and Enteral Nutrition 6.3 (1982): 194-99.	Not RCT
30. Munkholm, Larsen P., et al. "Elemental diet: a therapeutic approach in chronic inflammatory bowel disease." Journal of Internal Medicine 225.5 (1989): 325-31.	Not question of interest
31. Murphy, M. S., et al. "Can intensive nutritional supplementation with an elemental diet induce a true remission in Crohn's disease? A randomised controlled trial." Journal of Pediatric Gastroenterology and Nutrition 34.4 (2002): 457.	Abstract
32. Nielsen, A. A., et al. "Impact of enteral supplements enriched with omega-3 fatty acids and/or omega-6 fatty acids, arginine and ribonucleic acid compounds on leptin levels and nutritional status in active Crohn's disease treated with prednisolone." Digestion 75.1 (2007): 10-16.	Not question of interest
33. Nielsen, N. K., et al. "Response pattern recognition in paediatric Crohn's disease patients treated with enteral nutrition." Journal of Crohn's and Colitis 2.3 (2008): 233-36.	Not RCT
34. O'Keefe, S. J., et al. "Glucocorticosteroids versus elemental diet in the treatment of acute Crohn's disease: the effects on in vivo amino acid kinetics, protein catabolism, immunoglobulin, transferrin and albumin synthesis rates." South African Medical Journal 68 (1985): 523.	Abstract
35. O'Keefe, S. J., et al. "Steroids and bowel rest versus elemental diet in the treatment of patients with	Outcome measures of interest not included

Excluded studies

Study reference	Reason for exclusion
Crohn's disease: the effects on protein metabolism and immune function." <i>Journal of Parenteral and Enteral Nutrition</i> 13.5 (1989): 455	
36. O'Morain, C. "Elemental diets and Crohn's disease. [16 refs]." <i>Acta Gastroenterologica Belgica</i> 50.5 (1987): 574	Narrative review
37. O'Morain, C. and M. O'Sullivan. "Nutritional support in Crohn's disease: current status and future directions. [32 refs]." <i>Journal of Gastroenterology</i> 30.Suppl 8 (1995): 102	Narrative review
38. O'Sullivan, M. A. and C. A. O'Morain. "Nutritional therapy in Crohn's disease. [80 refs]." <i>Inflammatory Bowel Diseases</i> 4.1 (1998): 45	Narrative review
39. Okada M, Yao T, Yamamoto T, Takenaka K, Imamura K, Maeda K, Fujita K. Controlled trial comparing an elemental diet with prednisolone in the treatment of active Crohn's disease. <i>Hepato-Gastroenterology</i> . 1990; 37(1):72-80.	Outcome measures of interest not included
40. Papadopoulou, A., et al. "Remission following an elemental diet or prednisolone in Crohn's disease." <i>Acta Paediatrica</i> 84.1 (1995): 79	Not RCT
41. Park, R. H. R., et al. "Double-blind controlled trial of elemental and polymeric diets as primary therapy in active Crohn's disease." <i>European Journal of Gastroenterology and Hepatology</i> 3.6 (1991): 483-90.	Not question of interest
42. Raouf, A. H., et al. "Enteral feeding as sole treatment for Crohn's disease: Controlled trial of whole protein v amino acid based feed and a case study of dietary challenge." <i>Gut</i> 32.6 (1991): 702	Not question of interest
43. Ritchie, J. K., et al. "Controlled multicentre therapeutic trial of an unrefined carbohydrate, fibre rich diet in Crohn's disease." <i>British Medical Journal Clinical Research Ed.</i> 295.6597 (1987): 517	Not question of interest
44. Roggero, P., et al. "A prospective pediatric multicenter trial of enteral nutrition and azathioprine in preventing relapses of Crohn disease: preliminary results." <i>Journal of Pediatric Gastroenterology and Nutrition</i> 36.4 (2003): 543.	Abstract
45. Saverymuttu, S., H. J. Hodgson, and V. S. Chadwick. "Controlled trial comparing prednisolone with an elemental diet plus non	Not comparison of interest
46. Seidman, E., et al. "Nutritional issues in pediatric inflammatory bowel disease." <i>Journal of Pediatric Gastroenterology and Nutrition</i> 12.4 (1991): 424	Abstract
47. Slonim, A. E., M. Grovit, and L. Bulone. "Effect of exclusion diet with nutraceutical therapy in juvenile Crohn's disease." <i>Journal of the American College of Nutrition</i> 28.3 (2009): 277	Not RCT
48. Sylvester, F. A., et al. "A two-year longitudinal study of persistent lean tissue deficits in children with Crohn's disease." <i>Clinical Gastroenterology and Hepatology</i> 7.4 (2009): 452-55.	Not question of interest

Excluded studies

Study reference	Reason for exclusion
49. Yamamoto, T., et al. "Impact of elemental diet on mucosal inflammation in patients with active Crohn's disease: cytokine production and endoscopic and histological findings." <i>Inflammatory Bowel Diseases</i> 11.6 (2005): 580	Not RCT
50. "Impact of long-term enteral nutrition on clinical and endoscopic recurrence after resection for Crohn's disease: A prospective, non-randomized, parallel, controlled study." <i>Alimentary Pharmacology and Therapeutics</i> 25.1 (2007): 67-72.	Not RCT

1.4.2 Maintenance

Study reference	Reason for exclusion
1. Berni Canani R., Terrin G, Borrelli O, Romano MT, Manguso F, Coruzzo A, D'Armiento F, Romeo EF, Cucchiara S. Short- and Long-Term Therapeutic Efficacy of Nutritional Therapy and Glucocorticosteroids in Paediatric Crohn's Disease. <i>Digestive and Liver Disease</i> . 2006; 38(6):381-387. (Guideline Ref ID 1208)	Not RCT
2. Brotherton AM, Judd PA. Quality of Life in Adult Enteral Tube Feeding Patients. <i>Journal of Human Nutrition and Dietetics</i> . 2007; 20(6):513-522. (Guideline Ref ID 1166)	Not question of interest
3. Dray X, Marteau P. The Use of Enteral Nutrition in the Management of Crohn's Disease in Adults. <i>Journal of Parenteral and Enteral Nutrition</i> . 2005; 29(4 Suppl):S166-S169. (Guideline Ref ID 20311)	Review article
4. Esaki M, Matsumoto T, Hizawa K, Nakamura S, Jo Y, Mibu R, Iida M. Preventive Effect of Nutritional Therapy Against Postoperative Recurrence of Crohn Disease, With Reference to Findings Determined by Intra-Operative Enteroscopy. <i>Scandinavian Journal of Gastroenterology</i> . 2005; 40(12):1431-1437. (Guideline Ref ID 2222)	Not question of interest – post operative
5. Giaffer MH, Cann P, Holdsworth CD. Long-Term Effects of Elemental and Exclusion Diets for Crohn's Disease. <i>Alimentary Pharmacology and Therapeutics</i> . 1991; 5(2):115-125. (Guideline Ref ID 816)	Not question of interest
6. Gonzalez-Huix F, De Leon R, Fernandez-Banares F, Esteve M, Cabre E, Acero D, Abad-Lacruz A, Figa M, Guilera M, Planas R, Gassull MA. Polymeric Enteral Diets As Primary Treatment of Active Crohn's Disease: A Prospective Steroid Controlled Trial. <i>Gut</i> . 1993; 34(6):778-782. (Guideline Ref ID 1486)	Mean follow -up less than one year
7. Gorard DA, Hunt JB, Payne-James JJ, Palmer KR, Rees RG, Clark ML, Farthing MJ, Misiewicz JJ, Silk DB. Initial Response and Subsequent Course of Crohn's Disease Treated With Elemental Diet or Prednisolone. <i>Gut</i> . 1993; 34(9):1198-1202. (Guideline Ref ID 6427)	Maintenance diet not described
8. Harries AD, Jones LA, Danis V. Controlled Trial of Supplemented Oral Nutrition in Crohn's Disease. <i>Lancet</i> . 1983; 1(8330):887-890. (Guideline Ref ID 20288)	No long-term follow up
9. Johnson T, Macdonald S, Hill SM, Thomas A, Murphy MS. Treatment of Active Crohn's Disease in Children Using Partial Enteral Nutrition With Liquid Formula: a Randomised Controlled Trial. <i>Gut</i> . 2006; 55(3):356-361. (Guideline Ref ID 845)	No maintenance treatment
10. Knight C, El-Matary W, Spray C, Sandhu BK. Long-Term Outcome of Nutritional Therapy in Paediatric Crohn's Disease. <i>Clinical Nutrition</i> . 2005; 24(5):775-779. (Guideline Ref ID 2223)	No maintenance treatment
11. Koga H, Iida M, Aoyagi K, Matsui T, Fujishima M.	Article in Japanese

Excluded studies

Study reference	Reason for exclusion
[Long-Term Efficacy of Low Residue Diet for the Maintenance of Remission in Patients With Crohn's Disease]. Nippon Shokakibyō Gakkai Zasshi. 1993; 90(11):2882-2888. (Guideline Ref ID 2224)	
12. Matsueda K, Shoda R, Takazoe M, Hiwatashi N, Bamba T, Kobayashi K, Saito T, Terano A, Yao T. Therapeutic Efficacy of Cyclic Home Elemental Enteral Alimentation in Crohn's Disease: Japanese Cooperative Crohn's Disease Study. Journal of Gastroenterology. 1995; 30 Suppl 8:91-94. (Guideline Ref ID 2225)	Questionnaire study
13. Papadopoulou A, Rawashdeh MO, Brown GA, McNeish AS, Booth IW. Remission Following an Elemental Diet or Prednisolone in Crohn's Disease. Acta Paediatrica. 1995; 84(1):79-83. (Guideline Ref ID 726)	No maintenance treatment
14. Yamamoto T, Nakahigashi M, Saniabadi AR, Iwata T, Maruyama Y, Umegae S, Matsumoto K. Impacts of Long-Term Enteral Nutrition on Clinical and Endoscopic Disease Activities and Mucosal Cytokines During Remission in Patients With Crohn's Disease: a Prospective Study. Inflammatory Bowel Diseases. 2007; 13(12):1493-1501. (Guideline Ref ID 20261)	Not outcome of interest
15. Yamamoto T, Nakahigashi M, Umegae S, Kitagawa T, Matsumoto K. Impact of Elemental Diet on Mucosal Inflammation in Patients With Active Crohn's Disease: Cytokine Production and Endoscopic and Histological Findings. Inflammatory Bowel Diseases. 2005; 11(6):580-588. (Guideline Ref ID 6432)	Not outcome of interest

1.5 Surgery

1.5.1 Surgery limited to the distal ileum versus medical management

Study reference	Reason for exclusion
1. Adson MA, Benjamin I, Dockerty MB (1971) Postcolectomy ileitis and related disorders. <i>Archives of Surgery</i> 102 (4): 326-31.	Not question of interest
2. Agrez MV, Valente RM, Pierce W et al. (1982) Surgical history of Crohn's disease in a well-defined population. <i>Mayo Clinic Proceedings</i> 57 (12): 747-52.	Not question of interest
3. Alves A, Panis Y, Joly F et al. (2004) Could immunosuppressive drugs reduce recurrence rate after second resection for Crohn disease? <i>Inflammatory Bowel Diseases</i> 10 (5): 491-5.	Epidemiology of Swedish patients
4. Andersson P, Olaison G, Bodemar G et al. (2002) Surgery for Crohn colitis over a twenty-eight-year period: fewer stomas and the replacement of total colectomy by segmental resection. <i>Scandinavian Journal of Gastroenterology</i> 37 (1): 68-73.	Not question of interest
5. Andrews HA, Lewis P, Allan RN (1989) Prognosis after surgery for colonic Crohn's disease. <i>British Journal of Surgery</i> 76 (11): 1184-90.	Not question of interest
6. Aronson DC, Van CF, Heijmans HS et al. (1993) Surgical treatment of Crohn disease in children and adolescents; how conservative can the paediatrician be? <i>European Journal of Pediatrics</i> 152 (9): 727-9.	Adults vs. children – not question of interest
7. Baldassano RN, Han PD, Jeshion WC et al. (2001) Pediatric Crohn's disease: risk factors for postoperative recurrence. <i>American Journal of Gastroenterology</i> 96 (7): 2169-76.	Not question of interest
8. Bednarz W, Czopnik P, Wojtczak B et al. (2008) Analysis of results of surgical treatment in Crohn's disease. <i>Hepato-Gastroenterology</i> 55 (84): 998-1001.	Not question of interest
9. Bemelman WA, Ivenski M, van Hogezaand RA et al. (2001) How effective is extensive nonsurgical treatment of patients with clinically active Crohn's disease of the terminal ileum in preventing surgery? <i>Digestive Surgery</i> 18 (1): 56-60.	Risk assessment – not question of interest
10. Boeckman CR, Stone R, Schueller K (1981) Crohn's disease in children. <i>American Journal of Surgery</i> 142 (5): 567-8.	Not question of interest
11. Broe PJ, Cameron JL (1982) Surgical management of ileosigmoid fistulas in Crohn's disease. <i>American Journal of Surgery</i> 143 (5): 611-3.	Type of surgery – not question of interest
12. Chardavoyne R, Flint GW, Pollack S et al. (1986) Factors affecting recurrence following resection for Crohn's disease. <i>Diseases of the Colon and Rectum</i> 29 (8): 495-502.	Not question of interest
13. Condie J, Leslie KO, Smiley DF (1987) Surgical treatment for inflammatory bowel disease in the older patient. <i>Surgery Gynecology and Obstetrics</i> 165 (2): 135-42.	Case series

Excluded studies

Study reference	Reason for exclusion
14. Cook L, Al-Hendawi E, Bates AW et al. (2007) Limited ileo-caecal resection for localised Crohn's disease in childhood: Clinical outcome and predictors of further surgery. <i>Journal of Crohn's and Colitis</i> 1 (2): 82-6.	Not question of interest
15. Cristaldi M, Sampietro GM, Danelli PG et al. (2000) Long-term results and multivariate analysis of prognostic factors in 138 consecutive patients operated on for Crohn's disease using "bowel-sparing" techniques. <i>American Journal of Surgery</i> 179 (4): 266-70.	Risk factors – not question of interest
16. Davies G, Evans CM, Shand WS et al. (1990) Surgery for Crohn's disease in childhood: influence of site of disease and operative procedure on outcome. <i>British Journal of Surgery</i> 77 (8): 891-4.	Not question of interest
17. Di Abriola GF, De AP, Dall'oglio L et al. (2003) Strictureplasty: An alternative approach in long segment bowel stenosis Crohn's disease. <i>Journal of Pediatric Surgery</i> 38 (5): 814-8.	Technique - not question of interest
18. Dietz DW, Fazio VW, Laureti S et al. (2002) Strictureplasty in diffuse Crohn's jejunoileitis: safe and durable. <i>Diseases of the Colon and Rectum</i> 45 (6): 764-70.	Technique – not question of interest
19. Dietz DW, Laureti S, Strong SA et al. (2001) Safety and longterm efficacy of strictureplasty in 314 patients with obstructing small bowel Crohn's disease. <i>Journal of the American College of Surgeons</i> 192 (3): 330-7.	Technique – not question of interest
20. Eshuis EJ, Stokkers PC, Bemelman WA (2010) Decision-making in ileocecal Crohn's disease management: surgery versus pharmacotherapy. [64 refs]. <i>Expert review of gastroenterology and hepatology</i> 4 (2): 181-9.	Narrative review - excellent
21. Fazio VW, Tjandra JJ, Lavery IC et al. (1993) Long-term follow-up of strictureplasty in Crohn's disease. <i>Diseases of the Colon and Rectum</i> 36 (4): 355-61.	Technique – not question of interest
22. Hellers G (1979) Crohn's disease in Stockholm County 1955-1974. <i>Acta Chirurgica Scandinavica</i> 145 (Suppl. 490)	Did not report on medicine vs. surgery
23. Kennedy ED, Urbach DR, Krahn MD et al. (2004) Azathioprine or ileocolic resection for steroid-dependent terminal ileal Crohn's disease? A Markov analysis. <i>Diseases of the Colon and Rectum</i> 47 (12): 2120-30.	Economic study
24. Kim NK, Senagore AJ, Luchtefeld MA et al. (1997) Long-term outcome after ileocecal resection for Crohn's disease. <i>American Surgeon</i> 63 (7): 627-33.	Not question of interest
25. Kirkegaard P, Weile F, Henriksen FW et al. (1978) Long-term results after excisional surgery for Crohn's disease of the terminal ileum. <i>Acta Chirurgica Scandinavica</i> 144 (1): 51-4.	Not question of interest
26. Krause U (1978) Post-operative complication and early course of the surgical treatment of Crohn's	Follow up after surgery

Excluded studies

Study reference	Reason for exclusion
disease. <i>Acta Chirurgica Scandinavica</i> 144 (3): 163-74.	
27. Krause U, Ejerblad S, Bergman L (1985) Crohn's disease. A long-term study of the clinical course in 186 patients. <i>Scandinavian Journal of Gastroenterology</i> 20 (4): 516-24.	Not question of interest
28. Michelassi F, Balestracci T, Chappell R et al. (1991) Primary and recurrent Crohn's disease. Experience with 1379 patients. <i>Annals of Surgery</i> 214 (3): 230-8.	Recurrence rate after surgery – not question of interest
29. Ng SC, Lied GA, Arebi N et al. (2009) Clinical and surgical recurrence of Crohn's disease after ileocolonic resection in a specialist unit. <i>European Journal of Gastroenterology and Hepatology</i> 21 (5): 551-7.	Post operative recurrence – not question of interest
30. Norris B, Solomon MJ, Eysers AA et al. (1999) Abdominal surgery in the older Crohn's population. <i>Australian and New Zealand Journal of Surgery</i> 69 (3): 199	Not question of interest
31. Samimi R, Flasar MH, Kavic S et al. (2010) Outcome of medical treatment of stricturing and penetrating Crohn's disease: a retrospective study. <i>Inflammatory Bowel Diseases</i> 16 (7): 1187-94.	Risk for surgery – not question of interest
32. Scarpa M, Ruffolo C, D'Inca R et al. (2007) Health-related quality of life after ileocolonic resection for Crohn's disease: long-term results. <i>Inflammatory Bowel Diseases</i> 13 (4): 462-9.	No comparison with medical treatment
33. Scott NA, Hughes LE (1994) Timing of ileocolonic resection for symptomatic Crohn's disease--the patient's view. <i>Gut</i> 35 (5): 656-7.	Not question of interest
34. Simi M, Leardi S, Minervini S et al. (1990) Early complications after surgery for Crohn's disease. <i>Netherlands Journal of Surgery</i> 42 (4): 105-9.	Post op – not question of interest
35. Speranza V, Simi M, Leardi S et al. (1983) Indications, strategy and results of surgical management in 141 cases of Crohn's disease. <i>Italian Journal of Surgical Sciences</i> 13 (1): 5-12.	No comparison with medical treatment – before and after surgery comparison
36. Thirlby RC, Sobrino MA, Randall JB et al. (2001) The long-term benefit of surgery on health-related quality of life in patients with inflammatory bowel disease. <i>Archives of Surgery</i> 136 (5): 521-7.	No comparison with medical treatment
37. Trnka YM, Glotzer DJ, Kasdon EJ et al. (1982) The long-term outcome of restorative operation in Crohn's disease: influence of location, prognostic factors and surgical guidelines. <i>Annals of Surgery</i> 196 (3): 345-55.	Not question of interest
38. Yazdanpanah Y, Klein O, Gambiez L et al. (1997) Impact of surgery on quality of life in Crohn's disease. <i>American Journal of Gastroenterology</i> 92 (10): 1897-900.	No information about pre-operative treatment

1.5.2 Stricture management

Study reference	Reason for exclusion	Review
1. Alexander-Williams J. Conservative Surgery in Crohn's Disease. <i>Canadian Journal of Gastroenterology</i> . 1988; 2(SUPPL. A):83A-85A.	Data reported elsewhere	Strictureplasty
2. Alos R, Hinojosa J. Timing of Surgery in Crohn's Disease: A Key Issue in the Management. <i>World Journal of Gastroenterology</i> . 2008; 14(36):5532-5539.	Narrative review re. timing of surgery in general in Crohn's	Strictureplasty
3. Baratsis S, Manganas D, Moustafelos P, Alepas P, Bolanis I, Dimogerontas G, Niakas I. Results of Surgical Treatment of Crohn's Disease. <i>Annals of Gastroenterology</i> . 2003; 16(4):334-338.	Insufficient detail: outcomes not presented by type of procedure	Strictureplasty
4. Borley NR, Mortensen NJ, Chaudry MA, Mohammed S, Warren BF, George BD, Clark T, Jewell DP, Kettlewell MG. Recurrence After Abdominal Surgery for Crohn's Disease: Relationship to Disease Site and Surgical Procedure. <i>Diseases of the Colon and Rectum</i> . 2002; 45(3):377-383.	Not specifically intervention of interest	Strictureplasty
5. Breysem Y, Janssens JF, Coremans G, Vantrappen G, Hendrickx G, Rutgeerts P. Endoscopic Balloon Dilation of Colonic and Ileo-Colonic Crohn's Strictures: Long-Term Results. <i>Gastrointestinal Endoscopy</i> . 1992; 38(2):142-147.	Less than 20 patients	Balloon dilation
6. Brooker JC, Beckett CG, Saunders BP, Benson MJ. Long-Acting Steroid Injection After Endoscopic Dilation of Anastomotic Crohn's Strictures May Improve the Outcome: a Retrospective Case Series. <i>Endoscopy</i> . 2003; 35(4):333-337.	Less than 20 patients	Balloon dilation
7. Canin-Endres J, Salky B, Gattorno F, Edey M. Laparoscopically Assisted Intestinal Resection in 88 Patients With Crohn's Disease. <i>Surgical Endoscopy</i> . 1999; 13(6):595-599.	Not specifically intervention of interest	Strictureplasty
8. Dehn TC, Kettlewell MG, Mortensen NJ, Lee EC, Jewell DP. Ten-Year Experience of Strictureplasty for Obstructive	Data reported elsewhere	Strictureplasty

Excluded studies

Study reference	Reason for exclusion	Review
Crohn's Disease. British Journal of Surgery. 1989; 76(4):339-341.		
9. Despott EJ, Gupta A, Burling D, Tripoli E, Konieczko K, Hart A, Fraser C. Effective Dilation of Small-Bowel Strictures by Double-Balloon Enteroscopy in Patients With Symptomatic Crohn's Disease (With Video). Gastrointestinal Endoscopy. 2009; 70(5):1030-1036.	Less than 20 patients	Balloon dilation
10. Detry R, Fiasse R. Role of Surgery in the Management of Crohn's Disease. Acta Endoscopica. 2003; 33(2): 241-248	Less than 20 patients	Strictureplasty
11. East JE, Brooker JC, Rutter MD, Saunders BP. A Pilot Study of Intrastricture Steroid Versus Placebo Injection After Balloon Dilatation of Crohn's Strictures. Clinical Gastroenterology and Hepatology. 2007; 5(9):1065-1069.	Less than 20 patients; not question of interest	Balloon dilation
12. Erkelens GW, van Deventer SJ. Endoscopic Treatment of Strictures in Crohn's Disease. [28 Refs]. Best Practice and Research in Clinical Gastroenterology. 2004; 18(1):201-207.	Narrative review	Balloon dilation
13. Fazio VW. Conservative Surgery for Crohn's Disease of the Small Bowel: the Role of Strictureplasty. Medical Clinics of North America. 1990; 74(1):169-181.	Narrative review	Strictureplasty
14. Fichera A, Lovadina S, Rubin M, Cimino F, Hurst RD, Michelassi F. Patterns and Operative Treatment of Recurrent Crohn's Disease: a Prospective Longitudinal Study. Surgery. 2006; 140(4):649-654.	Not specifically intervention of interest	Strictureplasty
15. Gardiner KR, Kettlewell MGW, Mortensen NJM. Intestinal Haemorrhage After Strictureplasty for Crohn's Disease. International Journal of Colorectal Disease. 1996; 11(4):180-182.	Data reported elsewhere	Strictureplasty
16. Hamel CT, Singh JJ, Weiss EG, Nogueras JJ, Wexner SD. Laparoscopic-Assisted Right Hemicolectomy in Inflammatory Versus Noninflammatory	Not CD	Strictureplasty

Excluded studies

Study reference	Reason for exclusion	Review
Conditions of the Large Bowel. Techniques in Coloproctology. 2000; 4(3):163-167.		
17. Hassan C, Zullo A, De F, V, Ierardi E, Giustini M, Pitidis A, Taggi F, Winn S, Morini S. Systematic Review: Endoscopic Dilatation in Crohn's Disease. [30 Refs]. Alimentary Pharmacology and Therapeutics. 2007; 26(11-12):1457-1464.	Systematic review	Balloon dilation
18. Kendall GP, Hawley PR, Nicholls RJ, Lennard-Jones JE. Strictureplasty. A Good Operation for Small Bowel Crohn's Disease? Diseases of the Colon and Rectum. 1986; 29(5):312-316.	Less than 20 patients	Strictureplasty
19. Kim JH, Shin JH, Di ZH, Ko GY, Yoon HK, Sung KB, Song HY. Benign Duodenal Strictures: Treatment by Means of Fluoroscopically Guided Balloon Dilation. Journal of Vascular and Interventional Radiology. 2005; 16(4):543-548.	Technique – not question of interest	Balloon dilation
20. Laurent S, Detry O, Detroz B, DeRoover A, Joris J, Honore P, Louis E, Belaiche J, Jacquet N. Strictureplasty in Crohn's Disease: Short- and Long-Term Follow-Up. Acta Chirurgica Belgica. 2002; 102(4):253-255.	Less than 20 patients	Strictureplasty
21. Lee ECG, Papaioannou N. Minimal Surgery for Chronic Obstruction in Patients With Extensive or Universal Crohn's Disease. Annals of the Royal College of Surgeons of England. 1982; 64(4):229-233.	Less than 20 patients; data presented elsewhere	Strictureplasty
22 .Loftus EV. The Role of Endoscopy in the Evaluation and Management of Intestinal Strictures in Inflammatory Bowel Disease. Techniques in Gastrointestinal Endoscopy. 2004; 6(4):154-158.	Narrative review	Balloon dilation
23. Maconi G, Sampietro GM, Cristaldi M, Danelli PG, Russo A, Bianchi PG, Taschieri AM. Preoperative Characteristics and Postoperative Behavior of Bowel Wall on Risk of Recurrence After Conservative Surgery in Crohn's Disease: a Prospective Study.	Data reported elsewhere	Strictureplasty

Excluded studies

Study reference	Reason for exclusion	Review
Annals of Surgery. 2001; 233(3):345-352.		
24. Matsui T, Hatakeyama S, Ikeda K, Yao T, Takenaka K, Sakurai T. Long-Term Outcome of Endoscopic Balloon Dilatation in Obstructive Gastroduodenal Crohn's Disease. Endoscopy. 1997; 29(7):640-645.	Less than 20 patients	Balloon dilation
25. Michelassi F, Taschieri A, Tonelli F, Sasaki I, Poggioli G, Fazio V, Upadhyay G, Hurst R, Sampietro GM, Fazi M, Funayama Y, Pierangeli F. An International, Multicenter, Prospective, 26.Observational Study of the Side-to-Side Isoperistaltic Strictureplasty in Crohn's Disease. Diseases of the Colon and Rectum. 2007; 50(3):277-284.	Data reported elsewhere	Strictureplasty
27. Motson RW, Kadirkamanathan SS, Gallegos N. Minimally Invasive Surgery for Ileo-Colic Crohn's Disease. Colorectal Disease. 2002; 4(2):127-131.	Not specifically intervention of interest	Strictureplasty
28. Nomura E, Takagi S, Kikuchi T, Negoro K, Takahashi S, Kinouchi Y, Hiwatashi N, Shimosegawa T. Efficacy and Safety of Endoscopic Balloon Dilatation for Crohn's Strictures. Diseases of the Colon and Rectum. 2006; 49(10 Suppl):S59-S67.	Less than 20 patients	Balloon dilation
29. Nwokolo CU, Tan WC, Andrews HA, Allan RN. Surgical Resections in Parous Patients With Distal Ileal and Colonic Crohn's Disease. Gut. 1994; 35(2):220-223.	Not intervention of interest	Strictureplasty
30. Olaison G, Smedh K, Sjodahl R. Natural Course of Crohn's Disease After Ileocolic Resection: Endoscopically Visualised Ileal Ulcers Preceding Symptoms. Gut. 1992; 33(3):331-335.	Not intervention of interest	Strictureplasty
31. Ozuner G, Fazio VW, Lavery IC, Church JM, Hull TL. How Safe Is Strictureplasty in the Management of Crohn's Disease? American Journal of Surgery. 1996; 171(1):57-60.	Data reported elsewhere	Strictureplasty
32. Ozuner G, Fazio VW, Lavery IC, Milsom JW, Strong SA. Reoperative Rates for Crohn's	Data reported elsewhere	Strictureplasty

Excluded studies

Study reference	Reason for exclusion	Review
Disease Following Strictureplasty. Long-Term Analysis. Diseases of the Colon and Rectum. 1996; 39(11):1199-1203.		
33. Pohl J, May A, Nachbar L, Ell C. Diagnostic and Therapeutic Yield of Push-and-Pull Enteroscopy for Symptomatic Small Bowel Crohn's Disease Strictures. European Journal of Gastroenterology and Hepatology. 2007; 19(7):529-534.	Surgical technique. Less than 20 patients	Balloon dilation
34. Pritchard TJ, Schoetz DJ, Jr., Caushaj FP, Roberts PL, Murray JJ, Collier JA, Veidenheimer MC. Strictureplasty of the Small Bowel in Patients With Crohn's Disease. An Effective Surgical Option. Archives of Surgery. 1990; 125(6):715-717.	Less than 20 patients	Strictureplasty
35. Reese GE, Purkayastha S, Tilney HS, von RA, Yamamoto T, Tekkis PP. Strictureplasty Vs Resection in Small Bowel Crohn's Disease: an Evaluation of Short-Term Outcomes and Recurrence. Colorectal Disease. 2007; 9(8):686-694.	Systematic review comparing surgical techniques	Strictureplasty
36. Resegotti A, Astegiano M, Sostegni R, Garino M, Fusi D, Longhin R. Strictureplasty in Crohn's Disease. Indications and Results. Minerva Chirurgica. 2000; 55(5):313-317.	Not in English	Strictureplasty
37. Roy P, Kumar D. Strictureplasty for Active Crohn's Disease. International Journal of Colorectal Disease. 2006; 21(5):427-432.	Less than 20 patients	Strictureplasty
38. Sampietro GM, Cristaldi M, Maconi G, Parente F, Sartani A, Ardizzone S, Danelli P, Bianchi PG, Taschieri AM. A Prospective, Longitudinal Study of Nonconventional Strictureplasty in Crohn's Disease. Journal of the American College of Surgeons. 2004; 199(1):8-20.	Data reported elsewhere	Strictureplasty
39. Sampietro GM, Cristaldi M, Porretta T, Montecamozzo G, Danelli P, Taschieri AM. Early Perioperative Results and Surgical Recurrence After Strictureplasty and Miniresection for Complicated Crohn's Disease.	Data reported elsewhere	Strictureplasty

Excluded studies

Study reference	Reason for exclusion	Review
Digestive Surgery. 2000; 17(3):261-267.		
40. Sasaki I, Funayama Y, Naito H, Fukushima K, Shibata C, Matsuno S. Extended Strictureplasty for Multiple Short Skipped Strictures of Crohn's Disease. Diseases of the Colon and Rectum. 1996; 39(3):342-344.	Less than 20 patients	Strictureplasty
41. Saunders BP, Brown GJE, Lemann M, Rutgeerts P. Balloon Dilation of Ileocolonic Strictures in Crohn's Disease. Endoscopy. 2004; 36(11):1001-1007.	Narrative review	Balloon dilation
42. Sayfan J, Wilson DA, Allan A, Andrews H, Alexander-Williams J. Recurrence After Strictureplasty or Resection for Crohn's Disease. British Journal of Surgery. 1989; 76(4):335-338.	Data reported elsewhere	Strictureplasty
43. Sharif H, Alexander-Williams J. Strictureplasty for Ileo-Colic Anastomotic Strictures in Crohn's Disease. International Journal of Colorectal Disease. 1991; 6(4):214-216.	Insufficient detail	Strictureplasty
44. Shatari T, Clark MA, Yamamoto T, Menon A, Keh C, Alexander-Williams J, Keighley M. Long Strictureplasty Is As Safe and Effective As Short Strictureplasty in Small-Bowel Crohn's Disease. Colorectal Disease. 2004; 6(6):438-441.	Data reported elsewhere	Strictureplasty
45. Shen B, Fazio VW, Remzi FH, Delaney CP, Achkar J-P, Bennett A, Khandwala F, Brzezinski A, Doumit J, Liu W, Lashner BA. Endoscopic Balloon Dilation of Ileal Pouch Strictures. American Journal of Gastroenterology. 2004; 99(12):2340-2347.	Not question of interest	Balloon dilation
46. Siassi M, Weiger A, Hohenberger W, Kessler H. Changes in Surgical Therapy for Crohn's Disease Over 33 Years: a Prospective Longitudinal Study. International Journal of Colorectal Disease. 2007; 22(3):319-324.	Epidemiology of CD and surgery	Surgery
47. Silverman RE, McLeod RS, Cohen Z. Strictureplasty in Crohn's Disease. Canadian Journal of Surgery. 1989; 32(1):19-22.	Less than 20 patients	Strictureplasty
48. Singh VV, Draganov P,	Less than 20 patients	Balloon dilation

Excluded studies

Study reference	Reason for exclusion	Review
Valentine J. Efficacy and Safety of Endoscopic Balloon Dilatation of Symptomatic Upper and Lower Gastrointestinal Crohn's Disease Strictures. <i>Journal of Clinical Gastroenterology</i> . 2005; 39(4):284-290.		
49. Solt J, Hertelendy A, Szilagyi K. Long-Term Results of Balloon Catheter Dilatation of Lower Gastrointestinal Tract Stenoses. <i>Diseases of the Colon and Rectum</i> . 2004; 47(9):1499-1505.	Crohn's patients not analysed separately	Balloon dilatation
50. Stebbing JF, Jewell DP, Kettlewell MGW, Mortensen M. Long-Term Results of Recurrence and Reoperation After Strictureplasty for Obstructive Crohn's Disease. <i>British Journal of Surgery</i> . 1995; 82(11):1471-1474.	Data presented elsewhere	Strictureplasty
51. Sun B, Shen R, Cheng S, Zhang C, Zhong J. The Role of Double-Balloon Enteroscopy in Diagnosis and Management of Incomplete Small-Bowel Obstruction. <i>Endoscopy</i> . 2007; 39(6):511-515.	Not question of interest	Balloon dilatation
52. Tichansky D, Cagir B, Yoo E, Marcus SM, Fry RD. Strictureplasty for Crohn's Disease: Meta-Analysis. <i>Diseases of the Colon and Rectum</i> . 2000; 43(7):911-919.	SR and MA	Strictureplasty
53. Tjandra JJ, Fazio VW. Strictureplasty for Ileocolic Anastomotic Strictures in Crohn's Disease. <i>Diseases of the Colon and Rectum</i> . 1993; 36(12):1099-1103.	Data reported elsewhere	Strictureplasty
54. Tjandra JJ, Fazio VW. Strictureplasty Without Concomitant Resection for Small Bowel Obstruction in Crohn's Disease. <i>British Journal of Surgery</i> . 1994; 81(4):561-563.	Data reported elsewhere	Strictureplasty
55. Tjandra JJ, Fazio VW, Lavery IC. Results of Multiple Strictureplasties in Diffuse Crohn's Disease of the Small Bowel. <i>Australian and New Zealand Journal of Surgery</i> . 1993; 63(2):95-99.	Data reported elsewhere	Strictureplasty
56. Van Assche G, Vermeire S, Rutgeerts P, Koltun WA. Endoscopic Therapy of Strictures in Crohn's Disease. <i>Inflammatory</i>	Narrative review	Balloon dilatation

Excluded studies

Study reference	Reason for exclusion	Review
Bowel Diseases. 2007; 13(3):356-361.		
57. Wibmer AG, Kroesen AJ, Grone J, Buhr HJ, Ritz JP. Comparison of Strictureplasty and Endoscopic Balloon Dilatation for Stricturing Crohn's Disease-- Review of the Literature. International Journal of Colorectal Disease. 2010; 25(10):1149-1157.	Narrative review	Balloon dilation vs. surgery
58. Worsey MJ, Hull T, Ryland L, Fazio V. Strictureplasty Is an Effective Option in the Operative Management of Duodenal Crohn's Disease. Diseases of the Colon and Rectum. 1999; 42(5):596-600.	Data reported elsewhere	Strictureplasty
59. Yaffe BH, Korelitz BI. Prognosis for Nonoperative Management of Small-Bowel Obstruction in Crohn's Disease. Journal of Clinical Gastroenterology. 1983; 5(3):211-215.	Not procedure of interest	Balloon dilation
60. Yamamoto T, Allan RN, Keighley MRB. Long-Term Outcome of Surgical Management for Diffuse Jejunoileal Crohn's Disease. Surgery. 2001; 129(1):96-102.	Not specific intervention of interest	Strictureplasty
61. Yamamoto T, Fazio VW, Tekkis PP. Safety and Efficacy of Strictureplasty for Crohn's Disease: a Systematic Review and Meta-Analysis. Diseases of the Colon and Rectum. 2007; 50(11):1968-1986.	Meta analysis and review	Strictureplasty
62. Yamamoto T, Keighley MR. Factors Affecting the Incidence of Postoperative Septic Complications and Recurrence After Strictureplasty for Jejunoileal Crohn's Disease. American Journal of Surgery. 1999; 178(3):240-245.	Data reported elsewhere	Strictureplasty
63. Yamamoto T, Keighley MR. Long-Term Results of Strictureplasty for Ileocolonic Anastomotic Recurrence in Crohn's Disease. Journal of Gastrointestinal Surgery. 1999; 3(5):555-560.	Data reported elsewhere	Strictureplasty
64. Yamamoto T, Umegae S, Kitagawa T, Matsumoto K. Postoperative Change of Mucosal Inflammation at Strictureplasty	Less than 20 patients	Strictureplasty

Excluded studies

Study reference	Reason for exclusion	Review
Segment in Crohn's Disease: Cytokine Production and Endoscopic and Histologic Findings. Diseases of the Colon and Rectum. 2005; 48(4):749-757.		

1.6 Monitoring

1.6.1 Osteopenia

Study reference	Reason for exclusion
1. Hill RJ, Brookes DSK, Davies PSW. Bones in pediatric Crohn's disease: a review of fracture risk in children and adults. <i>Inflammatory Bowel Diseases</i> . 2011; 17(5):1223-1228.	Narrative review
2. Leonard MB. Glucocorticoid-induced osteoporosis in children: impact of the underlying disease. <i>Pediatrics</i> . 2007; 119 Suppl 2:S166-S174.	Not question of interest
3. Pappa H, Thayu M, Sylvester F, Leonard M, Zemel B, Gordon C. Skeletal health of children and adolescents with inflammatory bowel disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2011; 53(1):11-25.	Narrative review
4. Mascarenhas MR, Thayu M. Pediatric inflammatory bowel disease and bone health. <i>Nutrition in Clinical Practice</i> . 2010; 25(4):347-352.	Narrative review
5. Persad R, Jaffer I, Issenman RM. The prevalence of long bone fractures in pediatric inflammatory bowel disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2006; 43(5):597-602.	Limited area of investigation
6. Rovner AJ, Zemel BS. Re: Prevalence of long bone fractures in pediatric inflammatory bowel disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2007; 45(2):269-271.	Limited area of investigation
7. Specker BL, Schoenau E. Quantitative bone analysis in children: Current methods and recommendations. <i>Journal of Pediatrics</i> . 2005; 146(6):726-731.	Not question of interest
8. Sylvester FA. IBD and skeletal health: children are not small adults! <i>Inflammatory Bowel Diseases</i> . 2005; 11(11):1020-1023.	Not question of interest
9. Sylvester FA. Do bones crack under the effects of inflammatory bowel disease in children? <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2006; 43(5):563-565.	Narrative review
10. Viswanathan A, Sylvester FA. Chronic pediatric inflammatory diseases: Effects on bone. <i>Reviews in Endocrine and Metabolic Disorders</i> . 2008; 9(2):107-122.	Narrative review

1.6.2 Monitoring for early relapse

Exclusion List	Reason for exclusion
1. Aadland E, Fagerhol MK. Faecal calprotectin: A marker of inflammation throughout the intestinal tract. <i>European Journal of Gastroenterology and Hepatology</i> . 2002; 14(8):823-825.	Narrative review
2. Achkar J-P. Endoscopic evaluation of postoperative recurrence in the patient with Crohn's disease. <i>Techniques in Gastrointestinal Endoscopy</i> . 2004; 6(4):165-168.	Narrative review
3. Allez M, Lemann M. Role of endoscopy in predicting the disease course in inflammatory bowel disease. <i>World Journal of Gastroenterology</i> . 2010; 16(21):2626-2632.	Narrative review
4. Amati L, Passeri ME, Selicato F, Mastronardi ML, Penna A, Jirillo E, Covelli V. New insights into the biological and clinical significance of fecal calprotectin in inflammatory bowel disease. <i>Immunopharmacology and Immunotoxicology</i> . 2006; 28(4):665-681.	Narrative review
5. Angriman I, Scarpa M, D'Inca R, Basso D, Ruffolo C, Polese L, Sturniolo GC, D'Amico DF, Plebani M. Enzymes in feces: useful markers of chronic inflammatory bowel disease. <i>Clinica Chimica Acta</i> . 2007; 381(1):63-68.	Narrative review
6. Aomatsu T, Yoden A, Matsumoto K, Kimura E, Inoue K, Andoh A, Tamai H. Fecal calprotectin is a useful marker for disease activity in pediatric patients with inflammatory bowel disease. <i>Digestive Diseases and Sciences</i> . 2011; 56(8):2372-2377.	Correlation study
7. Arber N, Berliner S, Hallak A, Bujanover Y, Dotan I, Liberman E, Santo M, Moshkowitz M, Ratan J, Dotan G. Increased leucocyte adhesiveness/aggregation is a most useful indicator of disease activity in patients with inflammatory bowel disease. <i>Gut</i> . 1995; 37(1):77-80.	Not question of interest
8. Arber N, Berliner S, Reif S, Dotan I, Liberman E, Aschkenasy M, Vila Y, Gilat T, Bujanover Y. Increased leukocyte adhesiveness/aggregation is the single best biochemical indicator of disease activity in adolescent patients with inflammatory bowel disease. <i>Journal of Medicine</i> . 1996; 27(5-6):319-331.	Not question of interest
9. Arnott ID, Kingstone K, Ghosh S. Abnormal intestinal permeability predicts relapse in inactive Crohn disease. <i>Scandinavian Journal of Gastroenterology</i> . 2000; 35(11):1163-1169	Not question of interest
10. Barnes BH, Borowitz SM, Saulsbury FT, Hellems M, Sutphen JL. Discordant erythrocyte sedimentation rate and C-reactive protein in children with inflammatory bowel disease taking azathioprine or 6-mercaptopurine.	Not question of interest
11. Bernstein CN, Greenberg H, Boulton I, Chubey S, Leblanc C, Ryner L. A prospective comparison study of MRI versus small bowel follow-through in	Correlation study

Exclusion List	Reason for exclusion
recurrent Crohn's disease. American Journal of Gastroente	
12. Biancone L, De NF, Del Vecchio BG, Monteleone I, Vavassori P, Geremia A, Pallone F. Review article: monitoring the activity of Crohn's disease. Alimentary Pharmacology and Therapeutics. 2002; 16 Suppl 4:29-33.	Narrative review
13. Biancone L, Fantini M, Tosti C, Bozzi R, Vavassori P, Pallone F. Fecal alpha 1-antitrypsin clearance as a marker of clinical relapse in patients with Crohn's disease of the distal ileum. European Journal of Gastroenterology and Hepatology. 2003; 15(3):261-266.	Not question of interest
14. Braegger CP, Nicholls S, Murch SH, Stephens S, Macdonald TT. Tumour necrosis factor alpha in stool as a marker of intestinal inflammation. Lancet. 1992; 339(8785):89-91.	Not question of interest
15. Braegger CP, Nicholls S, Murch SH, Stephens S, Macdonald TT. Tumour necrosis factor alpha in stool as a marker of intestinal inflammation. Lancet. 1992; 339(8785):89-91.	'New Index' evaluation without information using individual components
16. Broedl UC, Schachinger V, Lingenhel A, Lehrke M, Stark R, Seibold F, Goke B, Kronenberg F, Parhofer KG, Konrad-Zerna A. Apolipoprotein A-IV is an independent predictor of disease activity in patients with inflammatory bowel disease. Inflammatory Bowel Diseases. 2007; 13(4):391-397.	Not question of interest
17. Bunn SK, Bisset WM, Main MJ, Gray ES, Olson S, Golden BE. Fecal calprotectin: validation as a noninvasive measure of bowel inflammation in childhood inflammatory bowel disease. Journal of Pediatric Gastroenterology and Nutrition. 2001; 33(1):14-22.	Correlation study
18. Caccaro R, D'Inca R, Sturniolo GC. Clinical utility of calprotectin and lactoferrin as markers of inflammation in patients with inflammatory bowel disease. Expert Review of Clinical Immunology. 2010; 6(4):551-558.	Narrative review
19. Canani RB, Rapacciuolo L, Romano MT, Tanturri de HL, Terrin G, Manguso F, Cirillo P, Paparo F, Troncione R. Diagnostic value of faecal calprotectin in paediatric gastroenterology clinical practice. Digestive and Liver Disease. 2004; 36(7):467-470.	Diagnostic study
20. Canani RB, Terrin G, Rapacciuolo L, Miele E, Siani MC, Puzone C, Cosenza L, Staiano A, Troncione R. Faecal calprotectin as reliable non-invasive marker to assess the severity of mucosal inflammation in children with inflammatory bowel disease. Digestive and Liver Disease. 2008; 40(7):547-553.	Correlation study
21. Caprilli R, Castro M, Cirillo LC, Lanfranchi GA, Tragone A, Pallone F, Rossini FP, Tonelli F, Brignola C. Postoperative recurrence in Crohn's disease: Definition, prediction and monitoring.	Not question of interest

Excluded studies

Exclusion List	Reason for exclusion
Gastroenterology International. 1993; 6(3):145-148.	
22. Caprilli R, Taddei G, Viscido A. In favour of prophylactic treatment for post-operative recurrence in Crohn's disease. Italian Journal of Gastroenterology and Hepatology. 1998; 30(2):219-225.	Narrative review
23. Chamouard P, Richert Z, Meyer N, Rahmi G, Baumann R. Diagnostic value of C-reactive protein for predicting activity level of Crohn's disease. Clinical Gastroenterology and Hepatology. 2006; 4(7):882-887.	Diagnostic review
24. Charron M. Inflammatory bowel disease activity assessment with biologic markers and ^{99m} Tc-WBC scintigraphy: Are there different trends in ileitis versus colitis? Journal of Nuclear Medicine. 2003; 44(10):1586-1591.	Not question of interest
24. Clara I, Lix LM, Walker JR, Graff LA, Miller N, Rogala L, Rawsthorne P, Bernstein CN. The manitoba IBD index: Evidence for a new and simple indicator of IBD activity. American Journal of Gastroenterology. 2009; 104(7):1754-1763.	Not question of interest
25. Colombel JF, Solem CA, Sandborn WJ, Booya F, Loftus EV, Jr., Harmsen WS, Zinsmeister AR, Bodily KD, Fletcher JG. Quantitative measurement and visual assessment of ileal Crohn's disease activity by computed tomography enterography: correlation with endoscopic severity and C reactive protein. Gut. 2006; 55(11):1561-1567.	Correlation study
26. Connell W. PRO: Endoscopic surveillance minimizes the risk of cancer. American Journal of Gastroenterology. 2004; 99(9):1631-1633.	Not question of interest
27. Costa F, Mumolo MG, Bellini M, Romano MR, Ceccarelli L, Arpe P, Sterpi C, Marchi S, Maltinti G. Role of faecal calprotectin as non-invasive marker of intestinal inflammation. Digestive and Liver Disease. 2003; 35(9):642-647.	Correlation study
28. Denis MA, Reenaers C, Fontaine F, Belaiche J, Louis E. Assessment of endoscopic activity index and biological inflammatory markers in clinically active Crohn's disease with normal C-reactive protein serum level. Inflammatory Bowel Diseases. 2007; 13(9):1100-1105.	Correlation study
29. Deodhar SD. C-reactive protein: the best laboratory indicator available for monitoring disease activity. Cleveland Clinic Journal of Medicine. 1989; 56(2):126-130.	Narrative review
30. Diamanti A, Colistro F, Basso MS, Papadatou B, Francalanci P, Bracci F, Muraca M, Knafelz D, De AP, Castro M. Clinical role of calprotectin assay in determining histological relapses in children affected by inflammatory bowel diseases. Inflammatory Bowel Diseases. 2008; 14(9):1229-1235.	CD patients not reported separately
31. Efthymiou A, Viazis N, Mantzaris G,	Correlation study

Excluded studies

Exclusion List	Reason for exclusion
Papadimitriou N, Tzourmakliotis D, Raptis S, Karamanolis DG. Does clinical response correlate with mucosal healing in patients with Crohn's disease of the small bowel? A prospective, case-series study using wireless capsule endoscopy. <i>Inflammatory Bowel Diseases</i> . 2008; 14(11):1542-1547.	
32. Erbayrak M, Turkey C, Eraslan E, Cetinkaya H, Kasapoglu B, Bektas M. The role of fecal calprotectin in investigating inflammatory bowel diseases. <i>Clinics</i> . 2009; 64(5):421-425.	Evaluation of FC levels as a reflection of disease activity and correlation of FC with ESR and CRP in 14 CD patients
33. Ergen FB, Akata D, Hayran M, Harmanci O, Arslan S, Basaran C, Hussain HK. Magnetic resonance colonography for the evaluation of colonic inflammatory bowel disease: Correlation with conventional colonoscopy. <i>Journal of Computer Assisted Tomography</i> . 2008; 32(6):848-854.	Correlation study
34. Fagerberg UL, Loof L, Lindholm J, Hansson LO, Finkel Y. Fecal calprotectin: a quantitative marker of colonic inflammation in children with inflammatory bowel disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2007; 45(4):414-420.	Not question of interest
35. Fagerberg UL, Loof L, Myrdal U, Hansson LO, Finkel Y. Colorectal inflammation is well predicted by fecal calprotectin in children with gastrointestinal symptoms. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2005; 40(4):450-455.	Diagnostic study
36. Filik L, Dagli U, Ulker A. C-reactive protein and monitoring the activity of Crohn's disease. <i>Advances in Therapy</i> . 2006; 23(4):655-662.	Correlation study
37. Gaya DR, Lyon TD, Duncan A, Neilly JB, Han S, Howell J, Liddell C, Stanley AJ, Morris AJ, Mackenzie JF. Faecal calprotectin in the assessment of Crohn's disease activity. <i>Qjm</i> . 2005; 98(6):435-441.	Correlation study
38. Gerasimidis K, Nikolaou CK, Edwards CA, McGrogan P. Serial fecal calprotectin changes in children with Crohn's disease on treatment with exclusive enteral nutrition: associations with disease activity, treatment response, and prediction of a clinical relapse. <i>Journal of Clinical Gastroenterology</i> . 2011; 45(3):234-239.	Not question of interest
39. Ghosh S, Drummond HE, Ferguson A. Neglect of growth and development in the clinical monitoring of children and teenagers with inflammatory bowel disease: review of case records. <i>BMJ</i> . 1998; 317(7151):120-121.	Not related to early relapse
40. Gisbert JP, McNicholl AG. Questions and answers on the role of faecal calprotectin as a biological marker in inflammatory bowel disease. <i>Digestive and Liver Disease</i> . 2009; 41(1):56-66.	Narrative
41. Gisbert JP, McNicholl AG, Gomollon F. Questions and answers on the role of fecal lactoferrin as a biological marker in inflammatory bowel disease.	Narrative

Excluded studies

Exclusion List	Reason for exclusion
Inflammatory Bowel Diseases. 2009; 15(11):1746-1754.	
42. Koilakou S, Sailer J, Peloschek P, Ferlitsch A, Vogelsang H, Miehsler W, Fletcher J, Turetschek K, Schima W, Reinisch W. Endoscopy and MR enteroclysis: equivalent tools in predicting clinical recurrence in patients with Crohn's disease after ileocolic resection. <i>Inflammatory Bowel Diseases</i> . 2010; 16(2):198-203.	Correlation study
42. Lamb CA, Mohiuddin MK, Gicquel J, Neely D, Bergin FG, Hanson JM, Mansfield JC. Faecal calprotectin or lactoferrin can identify postoperative recurrence in Crohn's disease. <i>British Journal of Surgery</i> . 2009; 96(6):663-674.	Correlation study
43. Louis E, Belaiche J, van KC, Franchimont D, de GD, Gueenen V, Mary JY. A high serum concentration of interleukin-6 is predictive of relapse in quiescent Crohn's disease. <i>European Journal of Gastroenterology and Hepatology</i> . 1997; 9(10):939-944.	Not question of interest
44. Maconi G, Radice E, Greco S, Bianchi PG. Bowel ultrasound in Crohn's disease. <i>Best Practice and Research in Clinical Gastroenterology</i> . 2006; 20(1):93-112.	Narrative review
45. Maharshak N, Zilberman L, Arbel Y, Shapira I, Berliner S, Arber N, Dotan I. Microinflammation in patients with Crohn's disease in clinical remission. <i>Journal of Crohn's and Colitis</i> . 2008; 2(4):310-314	Correlation study
46. Meijer MJ, Mieremet-Ooms MA, Sier CF, van Hogezaand RA, Lamers CB, Hommes DW, Verspaget HW. Matrix metalloproteinases and their tissue inhibitors as prognostic indicators for diagnostic and surgical recurrence in Crohn's disease. <i>Inflammatory Bowel Diseases</i> . 2009; 15(1):84-92.	Not question of interest
47. Mendoza JL, Abreu MT. Biological markers in inflammatory bowel disease: practical consideration for clinicians. <i>Gastroenterologie Clinique Et Biologique</i> . 2009; 33 Suppl 3:S158-S173.	Narrative review
48. Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, Mitton S, Orchard T, Rutter M, Younge L, Lees C, Ho G-T, Satsangi J, Bloom S. Guidelines for the management of inflammatory bowel disease in adults. <i>Gut</i> . 2011; 60(5):571-607.	No guidance on monitoring
49. Nielsen OH, Vainer B, Madsen SM, Seidelin JB, Heegaard NH. Established and emerging biological activity markers of inflammatory bowel disease. <i>American Journal of Gastroenterology</i> . 2000; 95(2):359-367.	Narrative review
50. Onali S, Calabrese E, Petruzzello C, Zorzi F, Sica GS, Lolli E, Ascolani M, Condino G, Pallone F, Biancone L. Endoscopic vs ultrasonographic findings related to Crohn's disease recurrence: a prospective longitudinal study at 3 years. <i>Journal of Crohn's and</i>	Correlation study

Excluded studies

Exclusion List	Reason for exclusion
Colitis. 2010; 4(3):319-328.	
51. Orlando A, Modesto I, Castiglione F, Scala L, Scimeca D, Rispo A, Teresi S, Mocciaro F, Criscuoli V, Marrone C, Platania P, De FT, Maisano S, Nicoli N, Cottone M. The role of calprotectin in predicting endoscopic post-surgical recurrence in asymptomatic Crohn's disease: a comparison with ultrasound. <i>European Review for Medical and Pharmacological Sciences</i> . 2006; 10(1):17-22.	Correlation study
52. Paduchova Z, Durackova Z. Fecal calprotectin as a promising marker of inflammatory diseases. <i>Bratislavske Lekarske Listy</i> . 2009; 110(10):598-602.	Narrative review
53. Radwan-Kwiatek K, Radwan P, Skrzydło-Radomanska B. C-reactive protein as a valuable marker of the clinical activity of Crohn's disease. <i>Przegląd Gastroenterologiczny</i> . 2007; 2(6):324-327.	Correlation study
54. Sahnoud T, Hochtin-Boes G, Modigliani R, Bitoun A, Colombel JF, Soule JC, Florent C, Gendre JP, Lerebours E, Sylvester R. Identifying patients with a high risk of relapse in quiescent Crohn's disease. The GETAID Group. The Groupe d'Etudes Therapeutiques des Affections Inflammatoires Digestives. <i>Gut</i> . 1995; 37(6):811-818.	Narrative review
55. Schoepfer AM, Beglinger C, Straumann A, Trummler M, Vavricka SR, Bruegger LE, Seibold F. Fecal calprotectin correlates more closely with the Simple Endoscopic Score for Crohn's disease (SES-CD) than CRP, blood leukocytes, and the CDAI. <i>American Journal of Gastroenterology</i> . 2010; 105(1):162-169.	Correlation study
56. Sempere GAJ, Sanjuan VM, Chulia EM, Benages A, Toyosato AT, Canelles P, Bulto A, Quiles F, Puchades I, Cuquerella J, Celma J, Orti E. MRI evaluation of inflammatory activity in Crohn's disease. <i>American Journal of Roentgenology</i> . 2005; 184(6):1829-1835.	Not question of interest
57. Sipponen T, Bjorkesten CG, Farkkila M, Nuutinen H, Savilahti E, Kolho KL. Faecal calprotectin and lactoferrin are reliable surrogate markers of endoscopic response during Crohn's disease treatment. <i>Scandinavian Journal of Gastroenterology</i> . 2010; 45(3):325-331.	Correlation study
58. Sipponen T, Karkkainen P, Savilahti E, Kolho KL, Nuutinen H, Turunen U, Farkkila M. Correlation of faecal calprotectin and lactoferrin with an endoscopic score for Crohn's disease and histological findings. <i>Alimentary Pharmacology and Therapeutics</i> . 2008; 28(10):1221-1229	Correlation study
59. Sipponen T, Kolho KL. Faecal calprotectin in children with clinically quiescent inflammatory bowel disease. <i>Scandinavian Journal of Gastroenterology</i> . 2010; 45(7-8):872-877.	Results for CD not reported
60. Sipponen T, Savilahti E, Kolho KL, Nuutinen H, Turunen U, Farkkila M. Crohn's disease activity	Correlation study

Excluded studies

Exclusion List	Reason for exclusion
assessed by fecal calprotectin and lactoferrin: correlation with Crohn's disease activity index and endoscopic findings. <i>Inflammatory Bowel Diseases</i> . 2008; 14(1):40-46.	
61. Solem CA, Loftus EV, Jr., Tremaine WJ, Harmsen WS, Zinsmeister AR, Sandborn WJ. Correlation of C-reactive protein with clinical, endoscopic, histologic, and radiographic activity in inflammatory bowel disease. <i>Inflammatory Bowel Diseases</i> . 2005; 11(8):707-712.	Correlation study
62. Sostegni R, Daperno M, Scaglione N, Lavagna A, Rocca R, Pera A. Crohn's disease: monitoring disease activity. <i>Alimentary Pharmacology & Therapeutics</i> . 2003; 17(Supplement S2):11-17.	Narrative review
63. Tibble J, Teahon K, Thjodleifsson B, Roseth A, Sigthorsson G, Bridger S, Foster R, Sherwood R, Fagerhol M, Bjarnason I. A simple method for assessing intestinal inflammation in Crohn's disease. <i>Gut</i> . 2000; 47(4):506-513.	Diagnostic study
64. Tilakaratne S, Lemberg DA, Leach ST, Day AS. C-reactive protein and disease activity in children with Crohn's disease. <i>Digestive Diseases and Sciences</i> . 2010; 55(1):131-136.	Narrative review
65. Tomei E, Diacinti D, Marini M, Boirivant M, Paoluzi P. Computed tomography of bowel wall in patients with Crohn's disease: relationship of inflammatory activity to biological indices. <i>Italian Journal of Gastroenterology</i> . 1996; 28(9):487-492.	Correlation study
66. Tsampalieros A, Griffiths AM, Barrowman N, Mack DR. Use of C-reactive protein in children with newly diagnosed inflammatory bowel disease. <i>Journal of Pediatrics</i> . 2011; 159(2):340-342.	Correlation study
67. Vieira A, Fang CB, Rolim EG, Klug WA, Steinwurz F, Rossini LG, Candelaria PA. Inflammatory bowel disease activity assessed by fecal calprotectin and lactoferrin: correlation with laboratory parameters, clinical, endoscopic and histological indexes. <i>BMC Research Notes</i> . 2009; 2:221.	Correlation study
68. Viscido A, Corrao G, Taddei G, Caprilli R. "Crohn's disease activity index" is inaccurate to detect the post-operative recurrence in Crohn's disease. A GISC study. Gruppo Italiano per lo Studio del Colon e del Retto. <i>Italian Journal of Gastroenterology and Hepatology</i> . 1999; 31(4):274-279	Not question of interest
69. Wright JP, Alp NM, Young GO, Tigler-Wybrandi N. Predictors of Acute Relapse of Crohn's disease. <i>Digestive Diseases and Sciences</i> . 1987; 37(2).	Prognostic data not provided
70. Zubcevic N, Mesihovic R, Zubcevic S. Usefulness of laboratory data in estimation of Crohn's disease activity. <i>Medicinski Arhiv</i> . 2010; 64(1):33-36.	Not question of interest

1.7 Patient information and support

Excluded Papers	Reason for exclusion
1. Patient perspective: the woes and wounds of Crohn's. <i>Gastrointestinal Nursing</i> . 2005; 3(7):14-16.	Case study
2. A patient's perspective: my battle with Crohn's disease. <i>American Journal of Gastroenterology</i> . 2007; 102(3):482.	Case study
3. Online help centre for Crohn's patients. <i>Nursing in the Community</i> . 2007; 8(6):5.	Not specific to information needs – not question of interest
4. Agulnik MH. A personal experience: coping with Crohn's disease. <i>CAET Journal</i> . 1994; 13(2):7-9.	Case review
5. Baars JE, Markus T, Kuipers EJ, van der Woude CJ. Patients' preferences regarding shared decision-making in the treatment of inflammatory bowel disease: results from a patient-empowerment study. <i>Digestion</i> . 2010; 81(2):113-119.	Not question of interest
6. Barlow C, Cooke D, Mulligan K, Beck E, Newman S. A critical review of self-management and educational interventions in inflammatory bowel disease. <i>Gastroenterology Nursing</i> . 2010; 33(1):11-18.	Outcomes of education interventions – not question of interest
7. Belling R, McLaren S, Woods L. Specialist nursing interventions for inflammatory bowel disease. <i>Cochrane Database of Systematic Reviews</i> . 2009;(4):CD006597.	Not specific to information needs – not question of interest
8. Bernard A, Langille M, Hughes S, Rose C, Leddin D, Veldhuyzen van ZS. A systematic review of patient inflammatory bowel disease information resources on the World Wide Web. <i>American Journal of Gastroenterology</i> . 2007; 102(9):2070-2077.	Not specific to information needs – not question of interest
9. Borgaonkar MR, Townson G, Donnelly M, Irvine EJ. Providing disease-related information worsens health-related quality of life in inflammatory bowel disease. <i>Inflammatory Bowel Diseases</i> . 2002; 8(4):264-269.	Not question of interest
10. Botoman VA, Bonner GF, Botoman DA. Information from your family doctor. Learning to live with inflammatory bowel disease. <i>American Family Physician</i> . 1998; 57(1):71-72.	Not perspective of interest
11. Daniel JM. Young adults' perceptions of living with chronic inflammatory bowel disease. <i>Gastroenterology Nursing</i> . 2002; 25(3):83-94.	Not question of interest
12. Drossman DA, Patrick DL, Mitchell CM, Zagami EA, Appelbaum MI. Health-related quality of life in inflammatory bowel disease. Functional status and patient worries and concerns. <i>Digestive Diseases and Sciences</i> . 1989; 34(9):1379-1386..	Not question of interest
13. Bregenzer N, Lange A, Furst A, Gross V, Scholmerich J, Andus T. Patient education in inflammatory bowel disease does not influence patients knowledge and long-term psychosocial well-being. <i>Zeitschrift Fur Gastroenterologie</i> . 2005; 43(4):367-371.	Not specific to information needs – not question of interest
14 .Cooper JM, Collier J, James V, Hawkey CJ. Beliefs about personal control and self-management in	Not specific to information needs – not question of interest

Excluded studies

Excluded Papers	Reason for exclusion
30□□□ year olds living with Inflammatory Bowel Disease: A qualitative study. International Journal of Nursing Studies. 2010; 47(12):1500-1509.	
15. Corbett S, Whayman K. Delivering patient education programmes as part of an inflammatory bowel disease service -- what is the way forward? Gastrointestinal Nursing. 2006; 4(5):10-11.	Not specific to information needs – not question of interest
16. Duffy LC, Zielezny MA, Marshall JR, Byers TE, Weiser MM, Phillips JF, Calkins BM, Ogra PL, Graham S. Relevance of major stress events as an indicator of disease activity prevalence in inflammatory bowel disease. Behavioral Medicine. 1991; 17(3):101-110.	Not question of interest
17. Garrett JW, Drossman DA. Health status in inflammatory bowel disease. Biological and behavioral considerations. Gastroenterology. 1990; 99(1):90-96.	Measures of disease - not question of interest
18. Gethins S, Duckett T, Shatford C, Robinson R. Self-management programme for patients with long-term inflammatory bowel disease. Gastrointestinal Nursing. 2011; 9(3):33-37.	Not question of interest
19. Hall A, Porrett T, Cox C. Factors affecting medication compliance in inflammatory bowel disease. Gastrointestinal Nursing. 2006; 4(5):31-40.	Not question of interest
20. Irvine EJ. Quality of Life in inflammatory bowel disease: biases and other factors affecting scores. Scandinavian Journal of Gastroenterology - Supplement. 1995; 208:136-140.	Not question of interest
21. Irvine EJ. Health-related quality-of-life in Crohn's disease. Research and Clinical Forums. 1998; 20(3):49-58.	Not question of interest
22. Irvine EJ. Review article: Patients' fears and unmet needs in inflammatory bowel disease. Alimentary Pharmacology and Therapeutics, Supplement. 2004; 20(4):54-59.	Not specific to information need
23. Janke KH, Klump B, Gregor M, Meisner C, Haeuser W. Determinants of life satisfaction in inflammatory bowel disease. Inflammatory Bowel Diseases. 2005; 11(3):272-286.	Not question of interest
24. Jordan C. Stress and inflammatory bowel disease: encouraging adaptive coping in patients. Gastrointestinal Nursing. 2010; 8(10):28-33.	Not question of interest
25. Kane S. Just a spoonful of sugar helps the medicine go down... If only it was that simple! nonadherence in inflammatory bowel disease. American Journal of Gastroenterology. 2007; 102(7):1427-1428.	Not question of interest
26. Kane SV, Loftus EV, Jr., Dubinsky MC, Sederman R. Disease perceptions among people with Crohn's disease. Inflammatory Bowel Diseases. 2008; 14(8):1097-1101.	Does not include information needs
27. Kennedy A, Gask L, Rogers A. Training professionals to engage with and promote self-management. Health Education Research. 2005; 20(5):567-578.	Not question of interest

Excluded Papers	Reason for exclusion
28. Kennedy AP, Nelson E, Reeves D, Richardson G, Roberts C, Robinson A, Rogers AE, Sculpher M, Thompson DG. A randomised controlled trial to assess the effectiveness and cost of a patient orientated self management approach to chronic inflammatory bowel disease. <i>Gut</i> . 2004; 53(11):1639-1645.	Not question of interest
29. Knopf JM, Hornung RW, Slap GB, DeVellis RF, Britto MT. Views of treatment decision making from adolescents with chronic illnesses and their parents: a pilot study. <i>Health Expectations</i> . 2008; 11(4):343-354.	Not question of interest
30. Mahadev S, Young JM, Selby W, Solomon MJ. Quality of life in perianal Crohn's disease: what do patients consider important? <i>Diseases of the Colon and Rectum</i> . 2011; 54(5):579-585.	Not specific to information needs
31. Mansfield JC, Tanner AR, Bramble MG. Information for patients about inflammatory bowel disease. <i>Journal of the Royal College of Physicians of London</i> . 1997; 31(2):184-187.	Not specific to information needs – not question of interest
32. Mayberry JF. Assessment of an information booklet on pregnancy for patients with inflammatory bowel disease. <i>Journal of Obstetrics and Gynaecology</i> . 1988; 9(1):14-17.	Not specific to information needs. Assessment of booklet – not question of interest
33 .Mayberry JF. Information booklets for patients with inflammatory bowel disease. <i>International Disability Studies</i> . 1988; 10(4):179-180.	Evaluation of booklet - not question of interest
34. Moody GA, Mayberry JF. Quality of life: Its assessment in gastroenterology. <i>European Journal of Gastroenterology and Hepatology</i> . 1992; 4(12):1025-1030.	Quality of life tools - not question of interest
35. Moser G, Tillinger W, Sachs G, Genser D, Maier-Dobersberger T, Spiess K, Wyatt J, Vogelsang H, Lochs H, Gangl A. Disease-related worries and concerns: a study on out-patients with inflammatory bowel disease. <i>European Journal of Gastroenterology and Hepatology</i> . 1995; 7(9):853-858.	Not specific to information needs
36. Nicholas DB, Otley A, Smith C, Avolio J, Munk M, Griffiths AM. Challenges and strategies of children and adolescents with inflammatory bowel disease: a qualitative examination. <i>Health and Quality of Life Outcomes</i> . 2007; 5:28.	Not question of interest
37. Oxelmark L, Magnusson A, Lofberg R, Hilleras P. Group-based intervention program in inflammatory bowel disease patients: effects on quality of life. <i>Inflammatory Bowel Diseases</i> . 2007; 13(2):182-190.	Not question of interest
38. Pallis AG, Mouzas IA. Quality of health care in inflammatory bowel disease and its assessment. <i>Annals of Gastroenterology</i> . 2002; 15(2):143-147.	Not question of interest
39. Pallis AG, Vlachonikolis IG, Mouzas IA. Assessing health-related quality of life in patients with inflammatory bowel disease, in Crete, Greece. <i>BMC Gastroenterology</i> . 2002; 2:1.	No specific information needs
40. Peyrin-Biroulet L. What is the patient's perspective: How important are patient-reported	Measures of disability - not question of interest

Excluded studies

Excluded Papers	Reason for exclusion
outcomes, quality of life and disability? Digestive Diseases. 2010; 28(3):463-471.	
41. Phillips S, Warren J. Supporting the patient with inflammatory bowel disease. Nursing Times. 1995; 91(27):38-39.	Narrative
42. Porrett T, Hall A. Medication concordance in patients with IBD. Gastrointestinal Nursing. 2004; 2(7):12-14.	Narrative
43. Probert CS, Mayberry JF. Inflammatory bowel disease: patients' expectations in the 1990s. Journal of the Royal Society of Medicine. 1991; 84(3):131-132.	Not question of interest
44. Protheroe J, Rogers A, Kennedy AP, Macdonald W, Lee V. Promoting patient engagement with self-management support information: a qualitative meta-synthesis of processes influencing uptake. Implementation Science. 2008; 3:44.	Not question of interest
45. Redmond C, Crino A, Faircloth J. Inflammatory Bowel Disease/Lower Gastrointestinal Bleeding CarePlan Map. -6. 1993. Tucson Medical Center, 5301 East Grant Road, PO Box 42195, Tucson AZ 85733; Phone: (602) 327-5461. http://search.ebscohost.com/login.aspx?direct=true&db=cin20&AN=1997029949&site=ehost-live	Nursing Care plan - exclude
46. Rejler M, Spangeus A, Tholstrup J, Andersson-Gare B. Improved population-based care: Implementing patient-and demand-directed care for inflammatory bowel disease and evaluating the redesign with a population-based registry. Quality Management in Health Care. 2007; 16(1):38-50.	Not question of interest
47. Ringel Y, Drossman DA. Psychosocial Aspects of Crohn's Disease. Surgical Clinics of North America. 81(1); 231-252. 2001.	Not question of interest
48. Robinson A. Review article: improving adherence to medication in patients with inflammatory bowel disease. Alimentary Pharmacology and Therapeutics. 2008; 27 Suppl 1:9-14.	Not question of interest
49. Rogers A, Kennedy A, Nelson E, Robinson A. Patients' experiences of an open access follow up arrangement in managing inflammatory bowel disease. Quality and Safety in Health Care. 2004; 13(5):374-378.	Not question of interest
50. Rubin GP, Hungin AP, Chinn DJ, Dwarakanath D. Quality of life in patients with established inflammatory bowel disease: a UK general practice survey. Alimentary Pharmacology and Therapeutics. 2004; 19(5):529-535.	Not question of interest
51. Sarlo RS, Barreto CR, Domingues TAM. Understanding the experience of patients who have Crohn's disease. Acta Paulista De Enfermagem. 2008; 21(4):629-635.	No specific information needs
52. Scholmerich J, Sedlak P, Hoppe-Seyler P, Gerok W. The information needs and fears of patients with inflammatory bowel disease. Hepato-	Not divided by diagnosis – no CD information

Excluded studies

Excluded Papers	Reason for exclusion
Gastroenterology. 1987; 34(4):182-185.	
53. Searle A, Bennett P. Psychological factors and inflammatory bowel disease: a review of a decade of literature. <i>Psychology, Health & Medicine</i> . 2001; 6(2):121-135.	Not question of interest
54. Sewitch MJ, Abrahamowicz M, Bitton A, Daly D, Wild GE, Cohen A, Katz S, Szego PL, Dobkin PL. Psychological distress, social support, and disease activity in patients with inflammatory bowel disease. <i>American Journal of Gastroenterology</i> . 2001; 96(5):1470-1479.	Not question of interest
55. Sewitch MJ, Abrahamowicz M, Dobkin PL, Tamblyn R. Measuring differences between patients' and physicians' health perceptions: the patient-physician discordance scale. <i>Journal of Behavioral Medicine</i> . 2003; 26(3):245-264.	Good concurrent validity but not question of interest
56. Sewitch MJ, Leffondre K, Dobkin PL. Clustering patients according to health perceptions: relationships to psychosocial characteristics and medication nonadherence. <i>Journal of Psychosomatic Research</i> . 2004; 56(3):323-332.	Not question of interest
57. Skinner N. Crohn's disease: a patients perspective. <i>Care Management</i> . 2001; 7(4):4.	Case study
58. Smart H, Mayberry J, Calcraft B, Morris JS, Rhodes J. Effect of information booklet on patients' anxiety levels and consultation rates in Crohn's disease. <i>Public Health</i> . 1986; 100(3):184-186.	Not question of interest
59. Smolen DM, Topp R. Coping methods of patients with inflammatory bowel disease and prediction of perceived health, functional status, and well-being. <i>Gastroenterology Nursing</i> . 1998; 21(3):112-118.	Not question of interest
60. van Dullemen HM, Kleibeuker JH. Novel approaches in the outpatient care of patients with chronic inflammatory bowel disease. <i>Scandinavian Journal of Gastroenterology</i> . 2006; Supplement.(243):55-58.	Narrative review
61. Ward B, Shah S, Eaden JA, Mayberry JF. Patients with inflammatory bowel disease: their response to information leaflets about medical therapy in particular azathioprine. <i>Arquivos De Gastroenterologia</i> . 1998; 35(4):264-266.	Not question of interest
62. Westwood N, Travis SP. Review article: what do patients with inflammatory bowel disease want for their clinical management? <i>Alimentary Pharmacology and Therapeutics</i> . 2008; 27 Suppl 1:1-8.	Ulcerative colitis
63. Zutshi M, Hull TL, Hammel J. Crohn's disease: a patient's perspective. <i>International Journal of Colorectal Disease</i> . 2007; 22(12):1437-1444.	No information needs

1.8 Reruns

Excluded Papers	Reason for exclusion
1. Bewtra M, Lewis JD. Update on the risk of lymphoma following immunosuppressive therapy for inflammatory bowel disease. <i>Expert Review of Clinical Immunology</i> . 2010; 6(4):621-631.	Narrative summary
2. Borowiec AM, Fedorak RN. Predicting, treating and preventing postoperative recurrence of Crohn's disease: the state of the field. <i>Canadian Journal of Gastroenterology</i> . 2011; 25(3):140-146.	Narrative review
3. Buisson A, Chevaux JB, Allen PB, Bommelaer G, Peyrin-Biroulet L. Review article: the natural history of postoperative Crohn's disease recurrence. <i>Alimentary Pharmacology and Therapeutics</i> . 2012; 35(6):625-633.	Does not report distal ileum since year 2000
4. Chande N, Abdelgadir I, Gregor J. The safety and tolerability of methotrexate for treating patients with Crohns disease. <i>Journal of Clinical Gastroenterology</i> . 2011; 45(7):599-601.	No serious adverse events reported
5. Collins CA, Potru R, Green J. A review of postoperative crohn's disease. <i>Practical Gastroenterology</i> . 2011; 35(5):20-30.	Not RCT
6. Critch J, Day AS, Otley A, King-Moore C, Teitelbaum JE, Shashidhar H. Use of enteral nutrition for the control of intestinal inflammation in pediatric crohn disease. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2012; 54(2):298-305.	Review and guidelines; summarised for GDG as a quality assurance exercise
7. Doherty G, Moss AC. 5-aminosalicylates to prevent relapse of Crohn's disease after surgery. <i>American Journal of Gastroenterology</i> . 2012; 107(3):487.	Letter to the editor
8. Dotan I, Werner L, Vigodman S, Agarwal S, Pfeffer J, Horowitz N, Malter L, Abreu M, Ullman T, Guzner-Gur H, Halpern Z, Mayer L. Normal response to vaccines in inflammatory bowel disease patients treated with thiopurines. <i>Inflammatory Bowel Diseases</i> . 2012; 18(2):261-268.	Not question of interest
9. Duffy CM, Wells GA, Russell AS, Haraoui B. Quality of life issues in pediatric immune-mediated inflammatory disease. <i>Journal of Rheumatology</i> . 2011; 38(SUPPL. 88):20-25.	Summarised and reported to GDG. No new information
10. Ehteshami-Afshar S, Nikfar S, Rezaie A, Abdollahi M. A systematic review and meta-analysis of the effects of infliximab on the rate of colectomy and post-operative complications in patients with inflammatory bowel disease. <i>Archives of Medical Science</i> . 2011; 7(6):1000-1012.	Not question of interest
11. Ford AC, Khan KJ, Talley NJ, Moayyedi P. 5-aminosalicylates prevent relapse of Crohn's disease after surgically induced remission: Systematic review and meta-analysis. <i>American Journal of Gastroenterology</i> . 2011; 106(3):413-420.	Systematic review used for quality assurance
12. French H, Mark DA, Srinivasan R, El-Matary W. Relapse rate following azathioprine withdrawal in maintaining remission for Crohn's disease: A meta-analysis. <i>Digestive Diseases and Sciences</i> . 2011;	Withdrawal from AZA – not question of interest

Excluded studies

Excluded Papers	Reason for exclusion
56(7):1929-1936.	
13. Habal FM, Huang VW. Review article: a decision-making algorithm for the management of pregnancy in the inflammatory bowel disease patient. <i>Alimentary Pharmacology and Therapeutics</i> . 2012; 35(5):501-515.	Review article
14. Jakobsen C, Bartek J, Wewer V, Vind I, Munkholm P, Groen R, Paerregaard A. Differences in phenotype and disease course in adult and paediatric inflammatory bowel disease—a population-based study. <i>Alimentary Pharmacology and Therapeutics</i> . 2011; 34(10):1217-1224.	Not question of interest
15. Johnson T, Macdonald S, Hill SM, Thomas A, Murphy MS. Treatment of active Crohn's disease in children using partial enteral nutrition with liquid formula: a randomised controlled trial. <i>Gut</i> . 2006; 55(3):356-361.	Not question of interest
16. Levine A, Turner D. Combined azithromycin and metronidazole therapy is effective in inducing remission in pediatric Crohn's disease. <i>Journal of Crohn's and Colitis</i> . 2011; 5(3):222-226.	Not RCT
17. Lowe W, Kenwright D, Wyeth J, Blair N. Crohn Disease: Effect on Children's Lifestyles. <i>Journal of Pediatric Gastroenterology and Nutrition</i> . 2012; 54(3):397-400.	No results of interest
18. Riello L, Talbotec C, Garnier-Lengline H, Pigneur B, Svahn J, Canioni D, Goulet O, Schmitz J, Ruemmele FM. Tolerance and efficacy of azathioprine in pediatric Crohn's disease. <i>Inflammatory Bowel Diseases</i> . 2011; 17(10):2138-2143.	Not RCT
19. Setshedi M, Epstein D, Winter TA, Myer L, Watermeyer G, Hift R. Use of thiopurines in the treatment of inflammatory bowel disease is associated with an increased risk of non-melanoma skin cancer in an at-risk population: A cohort study. <i>Journal of Gastroenterology and Hepatology</i> . 2012; 27(2):385-389.	CD not reported separately
20. Siddhi S, Mowat C. Service standards for IBD supported by updated BSG guideline. <i>Guidelines in Practice</i> . 2011; 14(11):11.	Service standards
21. Siegel CA, Finlayson SRG, Sands BE, Tosteson ANA. Adverse events do not outweigh benefits of combination therapy for crohn's disease in a decision analytic model. <i>Clinical Gastroenterology and Hepatology</i> . 2012; 10(1):46-51.	Not drug combination of interest
22. Watanabe O, Ando T, Ishiguro K, Takahashi H, Ishikawa D, Miyake N, Kato T, Hibi S, Mimura S, Nakamura M, Miyahara R, Ohmiya N, Niwa Y, Goto H. Enteral nutrition decreases hospitalization rate in patients with Crohn's disease. <i>Journal of Gastroenterology and Hepatology</i> . 2010; 25 Suppl 1:S134-S137.	Not RCT
23. Zappa M, Stefanescu C, Cazals-Hatem D, Bretagnol F, Deschamps L, Attar A, Larroque B, Treton X, Panis Y, Vilgrain V, Bouhnik Y. Which magnetic resonance imaging findings accurately evaluate inflammation in small bowel Crohn's disease? A retrospective	Correlation study. Not question asked by GDG

Excluded studies

Excluded Papers	Reason for exclusion
comparison with surgical pathologic analysis. <i>Inflammatory Bowel Diseases</i> . 2011; 17(4):984-993.	