National Clinical Guideline Centre

Ulcerative colitis

Appendices A-F

Scope, declarations of interest, review protocols, search strategies, study selection flowcharts and excluded studies

Ulcerative colitis

Clinical guideline

June 2013

NICE's original guidance on Ulcerative colitis: management in adults, children and young people was published in June 2013 and has undergone an 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 2013 replaced by the 2019 update.

Final version

Commissioned by the National Institute for Health and Care Excellence

Royal College of Physicians
Royal College of Nursing
RCGP Royal College of General Practitioners
The Royal College of Surgeons of England
NICE accredited www.nice.org.uk/accreditation

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Funding
National Institute for Health and Care Excellence

Contents

1 Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

SCOPE

Clinical guideline title: Ulcerative colitis: the management of ulcerative colitis

Quality standard title: Ulcerative colitis: the management of ulcerative colitis

1 Introduction

1.1 Clinical guidelines

Clinical guidelines are recommendations by NICE on the appropriate treatment and care of people with specific diseases and conditions in the NHS. They are based on the best available evidence.

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

1.2 Quality standards

Quality standards are a set of specific, concise quality statements and measures that act as markers of high-quality, cost-effective patient care, covering the treatment and prevention of diseases and conditions.

For this topic a NICE quality standard will be produced based on the guideline recommendations. The clinical guideline and the quality standard will be published at the same time.

This scope defines the areas of care for which specific quality statements and measures will (and will not) be developed.

The guideline and quality standard development processes are described in detail on the NICE website (see section 7).

2 Need for guidance

2.1 Epidemiology

a) Ulcerative colitis is an idiopathic chronic inflammatory disorder of the colon that has a relapsing remitting pattern. It is the most common type of inflammatory disease of the bowel, with an incidence of 10 per 100,000 people annually, and a prevalence of 243 per 100,000. This amounts to approximately 146,000 patients in the UK with a diagnosis of ulcerative colitis.

b) Ulcerative colitis can present at any age but tends to have highest incidence in a bimodal distribution, with peaks between the ages of 15 and 25 years and between 55 and 65 years.

c) Ulcerative colitis is a lifelong disease associated with significant morbidity, and the potential for social and psychological sequelae particularly if poorly controlled. An estimated 30–60% of people with ulcerative colitis will have at least one relapse per year. About 80% of these are mild to moderate and about 20% are severe. Symptoms of relapse include bloody diarrhoea, abdominal pain, anorexia, and weight loss.

d) Approximately 25% of people with ulcerative colitis will have one or more episodes of acute severe colitis in their lifetime. Of these, 20% will need a colectomy on their first admission and 40% on their next admission. Although mortality rates have improved steadily over the past 30 years, acute severe colitis still has a mortality rate of up to 2%. Mortality is directly influenced by the timing of interventions, including medical therapy and colectomy.

e) Elective pan-proctocolectomy can be an effective treatment for eliminating the symptoms of severe ulcerative colitis. However postoperative morbidity is associated with stoma care and ileoanal pouch use. Complications of pan-proctocolectomy include: decrease in female fertility, male impotency, pouchitis and small

bowel obstruction. Problems with urgency, leakage and nocturnal soiling may persist after surgery, and some patients may need a permanent ileostomy if ileal pouch anastomosis fails. Even in expert centres, pan-proctocolectomy has an operative mortality of between 1 and 4%, and postoperative lifelong morbidity of up to 15%.

f) Ulcerative colitis has a well documented association with the development of colorectal cancer, with greatest risk in long-standing and extensive disease. Overall lifetime risk of colorectal cancer in people with ulcerative colitis is approximately 2.7%, with an annual incidence of dysplasia or cancer between 3.7 and 5.7%. Moreover, degree of colonic inflammation in ulcerative colitis is a predictor of dysplasia or cancer development. This emphasises the importance of adequate and effective control of disease activity to reduce the risk of colorectal cancer.

2.2 Current practice

a) Current medical management centres on treating active disease and maintaining remission in an attempt to reduce both morbidity and mortality.

b) Treatment of relapse may depend on the clinical severity, extent of disease and patient's preference and may include the use of aminosalicylates or corticosteroids. Preparations of aminosalicylates and corticosteroids are usually administered orally or per rectum; corticosteroids may be administered intravenously in acute severe disease.

c) Most patients receive maintenance therapy with aminosalicylates. There may be variation in the doses of aminosalicylates and in whether a combination of treatment routes is used.

d) People needing two or more courses of corticosteroids in a year may be started on second-line immunosuppressants such as

azathioprine or mercaptopurine unless contraindicated. It appears that azathioprine and mercaptopurine are increasingly used to maintain remission and reduce inflammation in people with long-standing ulcerative colitis.

e) Some people may need 'rescue' therapy with intravenous ciclosporin if an acute severe colitis flare-up does not respond to standard first-line management with intravenous corticosteroids. Response rate is variable but an estimated 50% of patients at this stage will need either emergency colectomy, or semi-elective colectomy in the subsequent 6 months.

f) Anti-TNF agents have been used as an alternative to ciclosporin for managing acute severe colitis over the past few years.

g) The resulting wide choice of agents and dosing regimens has produced widespread heterogeneity in management across the UK, and emphasises the importance of comprehensive guidelines to help healthcare professionals provide consistent high quality care.

3 Clinical guideline

3.1 Population

3.1.1 Groups that will be covered

a) Adults (18 years and older), young people and children with a diagnosis of ulcerative colitis.

b) Consideration will be given to specific needs, if any, of:

- children and young people (including transition between paediatric and adult services and puberty)
- pregnant women.

3.1.2 Groups that will not be covered

a) People with indeterminate colitis.

3.2 Healthcare settings

a) NHS settings in which treatment for ulcerative colitis is delivered.

3.3 Management

3.3.1 Key issues that will be covered

a) Drug therapy for the induction of remission for mild, moderate and severe active ulcerative colitis, and maintenance of remission, including the following drug categories:

- aminosalicylates
- corticosteroids
- immunomodulators – azathioprine, mercaptopurine, methotrexate, ciclosporin and tacrolimus.

Guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

b) Indications and timing of surgical management, specifically, ileoanal pouch surgery or total colectomy for acute severe colitis, recurrent relapses or continuous uncontrolled symptoms.

c) Monitoring of bone health.

d) Monitoring of growth in children.

e) Information, education and support for people with ulcerative colitis and their families and carers.

3.3.2 Key issues that will not be covered

a) Diagnosis.

b) Treatment of extraintestinal manifestations of ulcerative colitis.

c) Surgical techniques (except those listed in section 3.3.1 b).

d) Reconstruction after previous surgery.

e) Pouchitis.

f) Management with:

- antibiotics
- fish oil
- helminths
- heparin as a primary treatment
- leukapheresis
- nicotine
- probiotics.

3.4 Main outcomes

a) Mortality.

b) Remission and relapse.

c) Health-related quality of life.

d) Growth in children.

e) Onset of puberty or pubertal development.

f) Adverse events, including effects of treatment on fertility.

g) Admissions to hospital (including length of stay).

h) Surgery, specifically colectomy.

Outcomes for both paediatric and adult practice will be included if data is available.

3.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative

interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see section 7).

4 Quality standard

Information on the NICE quality standards development process is available on the NICE website, see section 7.

4.1 Areas of care

The areas of care in a patient's journey that will inform the development of the quality statements are set out below. The content of the final quality standard may differ after consultation with stakeholders.

4.1.1 Areas of care that will be considered

a) Treatment

- Drug therapy for the induction of remission
- Drug therapy for the management of acute and severe exacerbations of ulcerative colitis.

b) Ongoing management

- Drug therapy for the maintenance of remission
- Nutrition support. See:
  - Nutrition support in adults. NICE clinical guideline 32 (2006). Available from www.nice.org.uk/guidance/CG32

c) Indications and timing of surgical management

d) Identification and management of risks and complications

- Fertility and pregnancy
- Growth

- Monitoring of bone health
- Risk of colorectal cancer. See:
  - Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas. NICE clinical guideline 118 (2011). Available from www.nice.org.uk/guidance/CG118
  - Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/guidance/CG27 and scheduled for an update.

f) Information, education and support for people with ulcerative colitis and their families and carers.

4.1.2 Areas of care that will not be considered

a) Diagnosis.

4.2 Economic aspects

Developers will take into account both clinical and cost effectiveness when prioritising the quality statements to be included in the quality standard. The economic evidence will be considered, and the cost and commissioning impact of implementing the quality standard will be assessed.

5 Status

5.1 Scope

This is the final scope.

5.2 Timings

The development of the guideline recommendations and the quality standard will begin in September 2011.

6 Related NICE guidance

Published

- Infliximab for acute exacerbations of ulcerative colitis. NICE technology appraisal guidance 163 (2008). Available from www.nice.org.uk/guidance/TA163
- Infliximab for subacute manifestations of ulcerative colitis. NICE technology appraisal guidance 140 (2008). Available from www.nice.org.uk/guidance/TA140
  (These two technology appraisals will be cross-referred to in the guideline as appropriate)
- Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn's disease or adenomas. NICE clinical guideline 118 (2011). Available from www.nice.org.uk/guidance/CG118
- Medicines adherence. NICE clinical guideline 76 (2009). Available from www.nice.org.uk/guidance/CG76
- Irritable bowel syndrome in adults. NICE clinical guideline 61 (2008). Available from www.nice.org.uk/guidance/CG61
- Faecal incontinence. NICE clinical guidance 49 (2007). Available from www.nice.org.uk/guidance/CG49
- Injectable bulking agents for faecal incontinence. NICE interventional procedure guidance 210 (2007). Available from www.nice.org.uk/guidance/IPG210
- Nutrition support in adults. NICE clinical guideline 32 (2006). Available from www.nice.org.uk/guidance/CG32
- Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/guidance/CG27
- Leukapheresis for inflammatory bowel disease. NICE interventional procedure guidance 126 (2005). Available from www.nice.org.uk/guidance/IPG126
- Fertility. NICE clinical guidance 11 (2004). Available from www.nice.org.uk/guidance/CG11

NICE guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Colorectal cancer. NICE clinical guideline. Publication expected October 2011
- Crohn's disease. NICE clinical guideline. Publication expected December 2012
- Adalimumab for second-line treatment of moderate to severe ulcerative colitis. NICE technology appraisal. Publication date to be confirmed.
- Patient experience in generic terms. NICE clinical guideline. Publication expected October 2011

7 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'
- 'Developing NICE quality standards: interim process guide'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual and www.nice.org.uk/aboutnice/qualitystandards). Information on the progress of the guideline and quality standards is also available from the NICE website (www.nice.org.uk).

2 Appendix B: Declarations of interest

Alan Lobo (Chair)

GDG meeting	Declaration of Interests	Action taken
On appointment 28.1.11	Personal pecuniary interest: P&G Pharmaceuticals (now Warner Chilcott) - payment for work in establishing Yorkshire and Humber IBD network; £500 24.7.09: no work specific to this or any company's product. Participation in 'IBD Ahead' meeting, 17.6.10, sponsored by Abbott Pharmaceuticals discussing questions relating to management of inflammatory bowel disease. Only travel expenses paid. Travel expenses for attendance at American Gastroenterology Association meeting, May 2010. Abbott Pharmaceuticals. I will speak at the Yorkshire and Humber IBD Network symposium on 16.6.11. This event is sponsored by four pharmaceutical companies: Biohit, Abbott, MSD and Warner Chilcott. I will not receive payment and the pharmaceutical companies have no input into the content of the programme and the talks.	Declare and participate.
First GDG meeting 27.9.11	Personal pecuniary interest: I attended the American Gastroenterology Association meeting in June 2010, sponsored by Abbott, manufacturers of the anti-TNF agent, adalimumab. This covered hotel and travel costs (economy flights) and registration at the meeting (page 7, section 3.3 of the Code of Practice). Non-personal pecuniary interest: Chairing Yorkshire and Humber IBD Network meeting sponsored by Abbott, Biohit, MSD and Warner Chilcott June 16, 2011. No personal payment received. 8 CPD points approved by the RCP - on the basis of it being an independent meeting. Approval was given to one individual on behalf of the Yorkshire and Humber IBD network, not to any company. Attending pre-meeting dinner (15 June 2011) to welcome international speakers. Will not receive sponsorship for this. The department have been considering use of an IBD database - and have met with companies for two systems. One would be funded by Ferring and the other by Warner Chilcott - both manufacturers of 5 aminosalicyclic acids. We have not made a decision about whether we will use one of these - or neither. The Ferring database is in use in the other hospital in the Trust, but I do not work there, except on-call, do not use the	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
	system and had no role in its procurement or implementation. I am involved in the running of the Yorkshire and Humber IBD network, the logistic arrangements for which (so far, hire of a room only) are made by a representative for Warner Chilcott. I have taken no fee for this since that declared to NICE for Crohn's GDG in June 2011. (originally declared June 2009) Personal non-pecuniary interest: Invited commentary on paper mesalazine granules vs tablets for Alimentary Pharmacology and therapeutics - submitted September 2011. Manuscript emailed.	
Second GDG Meeting 10.11.11	Personal pecuniary interest: Attended European Digestive Diseases week, London, October 2009. Sponsored by Proctor and Gamble pharmaceuticals (now Warner Chilcott). Travel, hotel and conference registration covered. P+G Pharmaceuticals - Payment for work in establishing Yorkshire and Humber IBD network; £500 24/07/09; no work specific to this or any company's product. Attended the American Gastroenterology Association meeting in June 2010, sponsored by Abbott, manufacturers of the anti-TNF agent, adalimumab. This covered hotel and travel costs (economy flights) and registration at the meeting, (see page 7, section 3.3 of the Code of Practice) Non -personal pecuniary interest: as per GDG1 entry Personal non-pecuniary: Invited commentary: Brooks AJ, Lobo AJ. Are mesalazine granules superior to Eudragit-L coated mesalazine tablets for induction of remission in distal ulcerative colitis? Aliment Pharmacol Ther 2011 (in press) Participation in “IBD Ahead” meeting, 17/06/10, sponsored by Abbott Pharmaceuticals discussing questions relating to management of inflammatory bowel disease. Travel expenses only. Main contribution on use of corticosteroids. Participation in discussion relating to management of inflammatory bowel disease. Travel expenses only. Main contribution on use of corticosteroids. Particpation in discussion relating to other treatments. Copy	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
	of document produced emailed to NCGC previously. Previous publications on treatment of inflammatory bowel disease.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	Non-personal pecuniary: Relating to the Yorkshire and Humber IBD network of which I am co-chair/mentor – previously declared. £1000 has been paid by Warner Chilcott into the "Treasurers account Yorkshire and Humber IBD network" for setting up and running of the Yorkshire and IBD network. I think the date was 9th May 2012, but I can't see it on the invoice. I have no personal access to this account. Personal non-pecuniary: One of my colleagues has run two meetings for General Practitioners in Sheffield. Sponsorship was received to run the meeting from a number of companies (Warner Chilcott, Ferring, Shire, Pfizer, AstraZeneca, Dr Schar, Abbott, Dr Falk) There was no input to the content of the meeting from anyone other than the speakers and chairs. I spoke at both of these, and co-chaired one. There was no payment to me. Talk on management of an IBD flare, received by body not manager for.	Declare and participate.
Ninth GDG	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
Meeting 20.7.12		
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

David Bartolo

GDG meeting	Declaration of Interests	Action taken
On appointment 22.6.11	Personal pecuniary interest: I advise Atlantic Health Care who are developing Alicaforsin for the treatment of pouchitis.	Declare and participate.
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
14.3.12		
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	Personal pecuniary interest: Attended lectures on IBD at an evening with food sponsored by makers of Pentas.	Declare and participate.
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Nick Bishop

GDG meeting	Declaration of Interests	Action taken
On appointment 7.11.12		
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Assad Butt

GDG meeting	Declaration of Interests	Action taken

GDG meeting	Declaration of Interests	Action taken
On appointment 22.8.11	Personal non-pecuniary interest: I am a member of the 'British Society of Paediatric Gastroenterology, Hepatology and Nutrition' (BSPGHN), which is a national professional organisation and advocacy society for children and young people with gastrointestinal and nutritional conditions in the U.K.	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
20.7.12		
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Sarah Cripps

GDG meeting	Declaration of Interests	Action taken
On appointment 22.7.11	None	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	Personal pecuniary interest: speaker at UKCPA autumn symposium on 16 November 2012 sponsored by various drug companies: Napp; Sanofi; Pfizer; RPS; Hameln. Conference fees, accommodation and travel were paid for.	Declare and participate.
Thirteenth GDG Meeting 15.3.13		

Valda Forbes

GDG meeting	Declaration of Interests	Action taken
On appointment 24.8.11	None	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
10.11.11		
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	Personal pecuniary interest: Nutricia - paid a train fare to annual winter meeting. Warner Chilcott - sponsor RCN IBD quarterly meetings in Birmingham - funded venue and travel.	Declare and participate.
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting	Personal pecuniary interest: Abbott advisory board meeting in Birmingham 26-27	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
15.3.13	November 2012. Paid reasonable travel and accommodation to attend the Ferring national IBD nurse symposium in Birmingham 20 November 2012.	

Poonam Gulia

GDG meeting	Declaration of Interests	Action taken
On appointment 28.1.11	None	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Adam Harris

GDG meeting	Declaration of Interests	Action taken
On appointment 27.6.11	None	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	Personal pecuniary interest: I will be attending European Crohn's and Colitis Organisation (ECCO) meeting in Barcelona 16-18 February 2012. Abbott will be paying for my return flights (Easyjet) and 2 nights' accommodation and breakfast in a standard hotel. I will not be speaking for Abbott nor attending any Abbott-sponsored meetings.	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Parastoo Karimi

GDG meeting	Declaration of Interests	Action taken
On appointment 26.7.11	None	
First GDG meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
27.9.11		
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
24.10.12		
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Jeremy Nightingale

GDG meeting	Declaration of Interests	Action taken
On appointment 8.7.11	None	
First GDG meeting 27.9.11	Personal pecuniary interest: 1. Contribution from Abbott to attend BSG 2011 2. Attended speciality advisory board for Vifor 2011 (1 day meeting) - intravenous iron 3. Speaker at Falk symposium Sep 2011 (payment 9 Sept 2011).	Declare and withdraw from discussing evidence and formulating recommendations for steroids and ASAs.
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	Personal pecuniary interest: I shall be speaking at a Baxter Nutrition meeting in May 2012 on fluid balance and refeeding syndrome. There is likely to be an honorarium.	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	Personal pecuniary interest: Attending United European Gastroenterology meeting in October 2012 sponsored by Abbott. Flight, hotel and registration fee was paid for to attend.	Declare and participate.
Twelfth GDG Meeting 24.10.12	Personal pecuniary interest: will be paid in November 2012 for speaking at lecture on nutrition sponsored by Abbott.	Declare and participate.
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Kerry Robinson

GDG meeting	Declaration of Interests	Action taken
On appointment 4.8.11	None	
First GDG meeting 27.9.11	Personal pecuniary interest: attended quarterly RCN IBD nurse meetings - room, lunch and travel expenses covered by Warner Chilcott. Attend Yorkshire and the Humber IBD network meetings - room and lunch sponsored by Warner Chilcott. Attend Yorkshire and the Humber IBD nurse meetings - room and lunch sponsored jointly by Warner Chilcott, Ferring, Abbott, MSD, Dr Falk, Shire.	Declare and participate.
Second GDG Meeting 10.11.11	Personal pecuniary interest: I have been offered sponsorship to attend the European Crohn's and Colitis Organisation National Conference in Barcelona, February 2012 by Abbott pharmaceuticals. This includes travel, accommodation and meals. Abbott promotes adalimumab which is not licensed for use in ulcerative colitis and will not be reviewed by	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
	this GDG.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting	Personal pecuniary interest: I attended the European Crohn's and Colitis organisation conference in Vienna 14-16 February 2013,	Declare and participate.

GDG meeting	Declaration of Interests	Action taken
15.3.13	sponsored by Abbvie pharmaceuticals. This included food and travel expenses only.	

Eshan Senanayake

GDG meeting	Declaration of Interests	Action taken
On appointment 4.6.11	None	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
20.7.12		
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Julian Stern

GDG meeting	Declaration of Interests	Action taken
On appointment 28.1.11	Personal pecuniary interest: have received payments from a number of pharmaceutical and medical appliance companies whilst lecturing at events on the "Psychology of IBD", or "Psychological problems in patients with ulcerative colitis", or "Psychology and stomas". These include: Warner Chilcott; Shire Pharmaceuticals; Coloplast and Dansac (latter 2 companies involved in the production of stoma equipment). Coloplast have also paid for teaching, to my research funds at St Mark's hospital. Non-personal pecuniary interest: Coloplast have paid for teaching that I have done, to my research funds at St Mark's hospital.	Declare and participate.
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

Nigel Westwood

GDG meeting	Declaration of Interests	Action taken

GDG meeting	Declaration of Interests	Action taken
On appointment 3.8.11	Personal pecuniary interest: Have received travel expenses and attendance fees from a number of pharmaceuticals (Abbott, Proctor and Gamble, Kinetic Concepts Inc (KCI) and Warner Chilcott) over the last 5 or 6 years as a speaker on patient experience to pharmaceutical staff, trainee medical professionals and specialist registrars.	Declare and withdraw from discussing the evidence and formulating recommendations for ASAs.
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting 3.2.12	No change to declarations of interest.	
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting	Personal pecuniary interest: Pharmacy Management Ltd is preparing a "Toolkit on Ulcerative Colitis" which will include a	Declare and withdraw from discussing the evidence and formulating recommendations for ASAs.

GDG meeting	Declaration of Interests	Action taken
20.7.12	patient's perspective chapter. I am being interviewed on Monday 16 July by phone and will review the chapter before publication. The toolkit is sponsored by Tillotts Pharma but I have had no contact with them.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	Personal pecuniary interest: I spoke at the Faculty of Medical Leadership and Management's inaugural annual conference in Manchester to an audience of 150 trainee doctors on the patient experience. They are paying me travel expenses only.	Declare and withdraw from discussing the evidence and formulating recommendations for ASAs.
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

NCGC members

GDG meeting	Declaration of Interests	Action taken
On appointment	In receipt of NICE commissions.	
First GDG meeting 27.9.11	No change to declarations of interest.	
Second GDG Meeting 10.11.11	No change to declarations of interest.	
Third GDG Meeting 15.12.11	No change to declarations of interest.	
Fourth GDG Meeting 2.2.12	No change to declarations of interest.	
Fifth GDG Meeting	No change to declarations of interest.	

GDG meeting	Declaration of Interests	Action taken
3.2.12		
Sixth GDG Meeting 14.3.12	No change to declarations of interest.	
Seventh GDG Meeting 24.4.12	No change to declarations of interest.	
Eighth GDG Meeting 6.6.12	No change to declarations of interest.	
Ninth GDG Meeting 20.7.12	No change to declarations of interest.	
Tenth GDG Meeting 21.8.12	No change to declarations of interest.	
Eleventh GDG Meeting 25.9.12	No change to declarations of interest.	
Twelfth GDG Meeting 24.10.12	No change to declarations of interest.	
Thirteenth GDG Meeting 15.3.13	No change to declarations of interest.	

3 Appendix C: Review protocols

3.1 Induction of remission

R question	Please note that evidence on treatments for inducing remission in people with mild-to-moderate ulcerative colitis was reviewed in 2019. The updated evidence review and full current recommendations can be found on the NICE website.
Objectives	To assess the clinical and cost effectiveness of corticosteroids, aminosalicylates & immunomodulators vs. placebo and each other for the induction of remission in ulcerative colitis and to develop a recommended sequence strategy for drug treatment in induction of remission in ulcerative colitis.
Criteria	**Population:** Included: Adults (18 years and older), young people and children with a diagnosis of mild to moderate (according to Truelove and Witts criteria or equivalent) ulcerative colitis. Excluded: Mixed IBD populations where the results are not displayed separately for ulcerative colitis. People with indeterminate or idiopathic colitis. Chronic active ulcerative colitis. Greater than 10% of the study population has severe ulcerative colitis. The following groups will be considered separately if data are present: Pregnant women. **Settings:** • Primary Care • Secondary Care • Tertiary Care • Community settings in which NHS care is delivered **Population size and directness:** • No limitations on sample size **Intervention and comparisons:** • Aminosalicylates: dose, formulation, regimen, mode of delivery, interclass comparison • Conventional corticosteroids: dose, formulation, regimen, mode of delivery, interclass comparison • Immunomodulators: methotrexate, tacrolimus, mercaptopurine, azathioprine (oral, IM or S/C as appropriate): dose, formulation, regimen, mode of delivery, interclass comparison • Combinations of the above: dose, formulation, regimen, mode of delivery, interclass comparison • Placebo compared to class effect for aminosalicylates and corticosteroids The doses included are those considered effective for inducing remission for an acute exacerbation of ulcerative colitis. Only drug treatments and preparations available in the UK are included. **Outcomes:** HRs will be used for outcomes considered as time-to-event data

	Critical outcomes • Clinical remission; absence of clinical symptoms (author defined) • Clinical improvement ((author defined)) • Health-related quality of life (any validated indexes) Important outcomes • Endoscopic remission; mucosal healing (author defined) • Clinical and endoscopic remission (author defined) • Adverse events • Serious adverse events (author defined) • Colectomy • Hospitalisations Ideally all the studies would have used the same validated index to define remission and improvement. This is not the case, numerous indexes are used and most are not validated. The GDG considered the impact of choosing one or only validated indexes which would result in a sparse evidence base. Using different indexes and author's definitions would include more studies but introduce a higher risk of bias. The GDG decided as the majority of the authors and indexes defined remission and improvement in a similar way it was reasonable to use the author defined definitions. Studies were excluded if there was not a definition stated of remission. A trial duration limit of 12 weeks was applied. It was thought that any drug taking longer than 12 weeks to have an effect would not be suitable for the induction of remission and more likely to be a maintenance treatment. The GDG considered the time taken to achieve remission or clinical improvement was important. The GDG considered the following time interval important ≤ 2weeks, 2-≤ 4 weeks, 4-≤ 6 weeks 6-≤ 8weeks and >8 weeks.
Search	• The databases to be searched are Medline, Embase, The Cochrane Library • Type of studies included: randomised controlled trials (RCTs) • Studies will be restricted to English language only • Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question or included in a Cochrane review. • Phase I and II (non randomised) • Cross-over studies are excluded unless results are presented for the first part of the trial. • No date restriction will be applied. • No trial duration minimum limit. Maximum duration of 12 weeks.
Review strategy	• Cochrane Reviews will be quality assessed and presented where appropriate • Further meta-analyses will be conducted as appropriate If there is heterogeneity the following subgroups will be analysed separately: • Disease extent: proctitis, proctosigmoiditis, left-sided ulcerative colitis, extensive ulcerative colitis • Disease severity: mild and moderate • Age (adults, children and young people) • Formulation (foam, enema, suppository, tablet, capsule, granules) • Mechanism of release

3.2 Induction of remission NMA (baseline)

Study design	Only published RCTs Phase II or III would be included. Exclusion: • Trial arms that used aminosalicylates or corticosteroids (oral/rectal) preparations

	(which are not currently available in the United Kingdom (Rowasa, Claversal, Mesasal, Predocol)) • (Rectal preparations as a single treatment. It was felt that only giving a rectal treatment for the induction of remission in people with left sided/extensive disease would not be appropriate and does not reflect current clinical practice for the combined group. It is also not included in the health economic model. Rectal preparations in combination with oral treatment will be included) • (Preparation, volume or regimen comparisons for example once versus more than once a day etc. It was established in the clinical review that there was no clinically relevant difference for these groups of comparisons. In addition, these comparisons are not included in the health economic model) • (RCTs that only compared different types of mesalazine, for example Asacol versus Ipocol. The NMA will analyse the different mesalazine formulations as a group due to complexity and lack of data to do this separately.) • (4.8g mesalazine (mezavant XL) has been excluded from the NMA as it did not demonstrate a dose effect in the clinical review and was thought to have the same effect as 2.4g mesalazine (mezavant XL) at a greater cost and risk of more adverse events) • (RCTs only comparing different doses for oral corticosteroids. We are not looking at increasing the dose of oral corticosteroids in the health economic model) • (RCTs where the population does not include patients with left sided/ extensive disease for example; proctitis or proctosigmoiditis populations. See below for a detailed inclusion criteria) • (Trial arms containing immunomodulators have been excluded from the NMA as they are not included in the treatment sequences in the health economic model. In addition, they have only been compared to placebo in trials and so they would not add much power to the NMA if they were to be included)
Subjects	(Adults with mild/ moderate left sided or extensive ulcerative colitis) (Definition of the extent of disease: In the first instance extent is author defined. If it is not specified or given in cm, the GDG definition of extent was the following:) (Proctitis: <15cm) (Proctosigmoiditis: up to 30-40cm) (Left sided: Up to 50 cm) (Therefore left sided or extensive is >30-40cm. Populations with only proctitis or proctosigmoiditis or <50% of the population have left sided or extensive disease will be excluded. If the extent of disease is not described or unable to be calculated in the paper, it will be included.)
Interventions	(Oral aminosalicylates (mesalazine, olsalazine, balsalazide, sulphasalazine) (Oral corticosteroids (prednisolone, budesonide [not mezavant XL as not licenced in the UK], beclometasone)) (Rectal aminosalicylates (mesalazine) or corticosteroids (hydrocortisone, budesonide) in combination with oral treatments) (Placebo)
Outcome measures/ Networks	(Trials would only be included if they report 1 or more of the following outcomes in ≤ 12 weeks. For the induction of remission in adults with left sided/ extensive ulcerative colitis:) • (Network 1: Proportion of people achieving clinical remission by the end of the trial) • (Network 2: Proportion of people achieving clinical improvement by the end of the trial) • (Network 3: Proportion of people who withdrew from the study due to adverse events (drug and non-drug related) by the end of the trial)
Date of publication	(No limits will be used.)

Language	Only English
Methodological considerations	A random effects model will be used as it is assumed that the relative effects are different in each trial but that they are from a single common distribution. The distribution is common across all sets of trials. Studies were included under the following assumptions: • The doses for the aminosalicylates were split into the following groups for analysis:

Type of 5-ASA	Lower dose of range stated in the BNF	Higher dose of the range stated in the BNF
Mesalazine	≥1.6-2.4g	>2.4g
Sulphasalazine	4-6g	>6g
Balsalazide	≥ 6≤6.75*g	
Olsalazine	1-<1.5g	≥1.5g

*The Balsalazide dose ranges from ≥ 6≤6.75g in order to include a study using a dose of 6.6g; this was considered to be likely to have a similar efficacy to 6.75g.

- Oral steroids have not been separated by dose on the assumption that it will reflect current clinical practice dosing (40mg) and we are not looking at the effect of increasing their doses in the health economic model
- There may be some differences in dose effect between the different mesalazines. In the NMA they have been grouped together to strengthen the data.
- A sensitivity analysis will be performed:

  1. Trial duration as per the clinical review (≥2≤4 weeks, >4≤6 weeks, >6≤8 weeks, >8 weeks)
- Inconsistency will be explored by comparing the indirect comparison point estimate (median relative risk) with the direct comparison results when available. In the event of inconsistency, the individual studies' PICO (Population, intervention, comparison, outcome definition) will be looked at to determine possible reasons to explain this. Further analyses will then be carried out using subgroups.
- The model will be checked for goodness of fit by comparing a random and fixed effects model.

3.3 Induction of remission NMA (combined aminosalicylates)

Study design	Only published RCTs Phase II or III would be included. Exclusion: • Trial arms that used aminosalicylates or corticosteroids (oral/rectal) preparations which are not currently available in the United Kingdom (Rowasa, Claversal, Mesasal, Predocol) • Rectal preparations as a single treatment. It was felt that only giving a rectal treatment for the induction of remission in people with left sided/extensive disease would not be appropriate and does not reflect current clinical practice for the combined group. It is also not included in the health economic model. Rectal preparations in combination with oral treatment will be included • Preparation, volume or regimen comparisons for example once versus more than once a day etc. It was established in the clinical review that there was no clinically relevant difference for these groups of comparisons. In addition, these comparisons are not included in the health economic model • RCTs that only compared different types of mesalazine, for example Asacol versus Ipocol. The NMA will analyse the different mesalazine formulations as a group due to complexity and lack of data to do this separately. • 4.8g mesalazine (mezavant XL) has been excluded from the NMA as it did not demonstrate a dose effect in the clinical review and was thought to have the same effect as 2.4g mesalazine (mezavant XL) at a greater cost and risk of more adverse events

	• RCTs only comparing different doses for oral corticosteroids. We are not looking at increasing the dose of oral corticosteroids in the health economic model • RCTs where the population does not include patients with left sided/ extensive disease for example; proctitis or proctosigmoiditis populations. See below for a detailed inclusion criteria • Trial arms containing immunomodulators have been excluded from the NMA as they are not included in the treatment sequences in the health economic model. In addition, they have only been compared to placebo in trials and so they would not add much power to the NMA if they were to be included
Subjects	Adults with mild/ moderate left sided or extensive ulcerative colitis Definition of the extent of disease: In the first instance extent is author defined. If it is not specified or given in cm, the GDG definition of extent was the following: Proctitis: <15cm Proctosigmoiditis: up to 30-40cm Left sided: Up to 50 cm Therefore left sided or extensive is >30-40cm. Populations with only proctitis or proctosigmoiditis or <50% of the population have left sided or extensive disease will be excluded. If the extent of disease is not described or unable to be calculated in the paper, it will be included.
Interventions	Oral aminosalicylates (mesalazine, olsalazine, balsalazide, sulphasalazine) Oral corticosteroids (prednisolone, budesonide [not mezavant XL as not licenced in the UK], beclometasone) Rectal aminosalicylates (mesalazine) or corticosteroids (hydrocortisone, budesonide) in combination with oral treatments Placebo
Outcome measures/ Networks	Trials would only be included if they report 1 or more of the following outcomes in ≤ 12 weeks. For the induction of remission in adults with left sided/ extensive ulcerative colitis: • Network 1: Proportion of people achieving clinical remission by the end of the trial • Network 2: Proportion of people who withdrew from the study due to adverse events (drug and non-drug related) by the end of the trial
Date of publication	No limits will be used.
Language	Only English
Methodological considerations	A random effects model will be used as it is assumed that the relative effects are different in each trial but that they are from a single common distribution. The distribution is common across all sets of trials. Studies were included under the following assumptions: • The doses for the aminosalicylates were split into the following groups for analysis:

Drug treatment	Lower dose of range stated in the BNF	Higher dose of the range stated in the BNF
Aminosalicylates	Mesalazine (≥1.6-2.4g), sulphasalazine (4-6g), olsalazine (1-<1.5g)	Mesalazine (>2.4g), sulphasalazine (>6g), balsalazide (≥ 6≤6.75*g), olsalazine (≥1.5g)

*The Balsalazide dose ranges from ≥ 6≤6.75g in order to include a study using a dose of 6.6g; this was considered to be likely to have a similar efficacy to 6.75g.

• Oral steroids have not been separated by dose on the assumption that it will reflect current clinical practice dosing (40mg) and we are not looking at the effect of increasing their doses in the health economic model
• There may be some differences in dose effect between the different mesalazines. In the NMA they have been grouped together to strengthen the data.

	• Inconsistency will be explored by comparing the indirect comparison point estimate (median relative risk) with the direct comparison results when available. In the event of inconsistency, the individual studies' PICO (Population, intervention, comparison, outcome definition) will be looked at to determine possible reasons to explain this. Further analyses will then be carried out using subgroups. • The model will be checked for goodness of fit by comparing a random and fixed effects model.

3.4 Maintenance of remission

Review question	In adults, children and young people with ulcerative colitis in remission, what is the clinical and cost-effectiveness of corticosteroids, aminosalicylates, immunomodulators (mercaptopurine, azathioprine, methotrexate and tacrolimus) for the maintenance of remission compared to themselves (different preparations and doses), each other, combinations of preparations (oral and topical) and placebo?
Objectives	To assess the clinical and cost effectiveness of corticosteroids, aminosalicylates & immunomodulators vs. placebo and each other for the maintenance of remission in ulcerative colitis and to develop a recommended sequence strategy for drug treatment in the maintenance of remission in ulcerative colitis.
Criteria	**Population:** Included: Adults (18 years and older), young people and children with a diagnosis of ulcerative colitis in remission. Excluded: Mixed IBD populations where the results are not displayed separately for ulcerative colitis. People with indeterminate or idiopathic colitis. Chronic active ulcerative colitis. The following groups will be considered separately if data are present: Pregnant women **Settings:** • Primary Care • Secondary Care • Tertiary Care • Community settings in which NHS care is delivered **Population size and directness:** • No limitations on sample size **Intervention and comparisons:** • Aminosalicylates: dose, formulation, regimen, mode of delivery, interclass comparison • Conventional corticosteroids: dose, formulation, regimen, mode of delivery, interclass comparison • Immunomodulators: methotrexate, tacrolimus, mercaptopurine, azathioprine (oral, IM or S/C as appropriate): dose, formulation, regimen, mode of delivery, interclass comparison • Combinations of the above: dose, formulation, regimen, mode of delivery, interclass comparison • Placebo compared to class effect for aminosalicylates and corticosteroids The doses included are those considered effective for maintaining remission. Only drug treatments and preparations available in the UK are included. **Outcomes:**

	HRs will be used for outcomes considered as time-to-event data Critical outcomes • Relapse (author defined) • Health-related quality of life (any validated indexes) Important outcomes • Adverse events • Serious adverse events (author defined) • Colectomy • Hospitalisations Ideally all the studies would have used the same validated index to define relapse. This is not the case, numerous indexes are used and most are not validated. The GDG considered the impact of choosing one or only validated indexes which would result in a sparse evidence base. Using different indexes and author's definitions would include more studies but introduce a higher risk of bias. The GDG decided as the majority of the authors and indexes defined relapse in a similar way it was reasonable to use the author defined definitions. Studies were excluded if there was no definition stated of relapse. A minimum trial duration of 6 months was applied. The GDG considered the time taken to achieve relapse was important. The GDG considered the following time interval important 6, 12 and 18 months.
Search	• The databases to be searched are Medline, Embase, The Cochrane Library • Type of studies included: randomised controlled trials (RCTs) • Studies will be restricted to English language only • Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question or included in a Cochrane review. • Phase I and II (non randomised) • Cross-over studies are excluded unless results are presented for the first part of the trial. • No date restriction will be applied.
Review strategy	• Cochrane Reviews will be quality assessed and presented where appropriate • Further meta-analyses will be conducted as appropriate The following strata • Severity of previous relapse (mild/moderate/severe) • Frequency of relapses • Current use of immunomodulators prior to the trial. If there is heterogeneity the following subgroups will be analysed separately: • Disease extent: proctitis, proctosigmoiditis, left-sided ulcerative colitis, extensive ulcerative colitis • Age (adults, children and young people) • Mechanism of release

3.5 Maintenance of remission NMA (baseline)

Study design	Only published RCTs Phase II or III would be included. Exclusion: • Rectal preparations as a single treatment. It was felt that only giving a rectal treatment for the maintenance of remission in people with left sided/extensive disease would not be appropriate and does not reflect current clinical practice for the combined group. It is also not being included in the health economic model.

<table>
<tr><td></td><td>

Preparation, volume or regimen comparisons (including weekly frequencies of treatment and once versus twice a day etc.). These comparisons are not included in the health economic model
The use of corticosteroids in the maintenance of remission has been excluded as it is not deemed a suitable treatment for use in the long term due to its adverse events.
RCTs where the population does not include patients with left sided/ extensive disease for example; proctitis or proctosigmoiditis populations. See below for a detailed inclusion criteria

</td></tr>
<tr><td>Subjects</td><td>Adults in remission who have previously had a mild to moderate inflammatory exacerbation of left sided or extensive ulcerative colitis.
Definition of the extent of disease: In the first instance extent is author defined. If it is not specified or given in cm, the GDG definition of extent was the following:
Proctitis: <15cm
Proctosigmoiditis: up to 30-40cm
Left sided: Up to 50 cm
Therefore left sided or extensive is >30-40cm. Populations with only proctitis or proctosigmoiditis or <50% of the population have left sided or extensive disease will be excluded. If the extent of disease is not described or unable to be calculated in the paper, it will be included.</td></tr>
<tr><td>Interventions</td><td>Oral aminosalicylates (mesalazine (Pentasa, Asacol, Salofalk, mezavant XL), olsalazine, balsalazide, sulphasalazine)
Placebo</td></tr>
<tr><td>Outcome measures/ Networks</td><td>Trials would only be included if they report 1 or more of the following outcomes. For the maintenance of remission in adults with left sided/ extensive ulcerative colitis:

Network 1: Rate of people relapsing by the end of the trial
Network 2: Proportion of people who withdrew from the study (excluding relapses) by the end of the trial

</td></tr>
<tr><td>Date of publication</td><td>No limits will be used.</td></tr>
<tr><td>Language</td><td>Only English</td></tr>
<tr><td>Methodological considerations</td><td>A multi-statistic evidence synthesis will be conducted by combining hazard ratios and relative risks from trials reporting relapse. A random effects model will be used as it is assumed that the relative effects are different in each trial but that they are from a single common distribution. The distribution is common across all sets of trials.
Studies were included under the following assumptions:

The doses for the aminosalicylates were split into the following groups for analysis:

<table>
<tr><td>Type of 5-ASA</td><td>Lower dose of the range in the BNF</td><td>Higher dose of the range in the BNF</td></tr>
<tr><td>Mesalazine</td><td>≤1.5g</td><td>>1.5g</td></tr>
<tr><td>Salofalk</td><td>≤1.5g</td><td>>1.5g</td></tr>
<tr><td>Pentasa</td><td>≤2g</td><td>>2g</td></tr>
<tr><td>Asacol</td><td>≤1.2g</td><td>>1.2g</td></tr>
<tr><td>Olsalazine</td><td>≤1g</td><td>>1g</td></tr>
<tr><td>Balsalazide</td><td>≤3g</td><td>>3g</td></tr>
<tr><td>Sulfasalazine</td><td>≤2g</td><td>>2g</td></tr>
</table>

ITT has been used for the withdrawals data. As the relapses are conditional on not

</td></tr>
</table>

	withdrawing, for studies that report count statistics, the number of people who relapse excludes those who withdrew from the study. • Inconsistency will be explored by comparing the indirect comparison point estimate (median hazard ratio) with the direct comparison results when available. In the event of inconsistency, the individual studies' PICO (Population, intervention, comparison, outcome definition) will be looked at to determine possible reasons to explain this. Further analyses will then be carried out using subgroups. The model will be checked for goodness of fit by comparing a random and fixed effects model.

3.6 Maintenance of remission NMA (combined aminosalicylates)

Study design	Only published RCTs Phase II or III would be included. Exclusion: • Rectal preparations as a single treatment. It was felt that only giving a rectal treatment for the maintenance of remission in people with left sided/extensive disease would not be appropriate and does not reflect current clinical practice for the combined group. It is also not being included in the health economic model. • Preparation, volume or regimen comparisons (including weekly frequencies of treatment and once versus twice a day etc.). These comparisons are not included in the health economic model • The use of corticosteroids in the maintenance of remission has been excluded as it is not deemed a suitable treatment for use in the long term due to its adverse events. • RCTs where the population does not include patients with left sided/ extensive disease for example; proctitis or proctosigmoiditis populations. See below for a detailed inclusion criteria
Subjects	Adults in remission who have previously had a mild to moderate inflammatory exacerbation of left sided or extensive ulcerative colitis. Definition of the extent of disease: In the first instance extent is author defined. If it is not specified or given in cm, the GDG definition of extent was the following: Proctitis: <15cm Proctosigmoiditis: up to 30-40cm Left sided: Up to 50 cm Therefore left sided or extensive is >30-40cm. Populations with only proctitis or proctosigmoiditis or <50% of the population have left sided or extensive disease will be excluded. If the extent of disease is not described or unable to be calculated in the paper, it will be included.
Interventions	Oral aminosalicylates (mesalazine (Pentasa, Asacol, Salofalk, mezavant XL), olsalazine, balsalazide, sulphasalazine) Placebo
Outcome measures/ Networks	Trials would only be included if they report 1 or more of the following outcomes. For the maintenance of remission in adults with left sided/ extensive ulcerative colitis: • Network 1: Rate of people relapsing by the end of the trial • Network 2: Proportion of people who withdrew from the study (excluding relapses) by the end of the trial
Date of publication	No limits will be used.
Language	Only English
Methodological considerations	A multi-statistic evidence synthesis will be conducted by combining hazard ratios and relative risks from trials reporting relapse. A random effects model will be used as it is assumed that the relative effects are different in each trial but that they are from a single common distribution. The distribution is common across all sets of trials.

Studies were included under the following assumptions:

- The doses for the aminosalicylates were split into the following groups for analysis:

Type of 5-ASA	Lower dose oral ASAs	Higher dose oral ASAs
Mesalazine	≤1.5g	>1.5g
Salofalk	≤1.5g	>1.5g
Pentasa	≤2g	>2g
Asacol	≤1.2g	>1.2g
Olsalazine	≤1g	>1g
Balsalazide	≤3g	>3g
Sulfasalazine	≤2g	>2g

- ITT has been used for the withdrawals data. As the relapses are conditional on not withdrawing, for studies that report count statistics, the number of people who relapse excludes those who withdrew from the study.
- Inconsistency will be explored by comparing the indirect comparison point estimate (median hazard ratio) with the direct comparison results when available. In the event of inconsistency, the individual studies' PICO (Population, intervention, comparison, outcome definition) will be looked at to determine possible reasons to explain this. Further analyses will then be carried out using subgroups. The model will be checked for goodness of fit by comparing a random and fixed effects model.

3.7 Acute severe ulcerative colitis

Review question	In adults, children and young people with acute severe ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids and ciclosporin compared to each other and their combination (corticosteroids and ciclosporin) for the induction of remission?
Objectives	Assess the clinical and cost effectiveness of corticosteroids and ciclosporin for the induction of remission in Ulcerative Colitis disease and to develop a recommended sequence strategy for drug treatment in induction of remission in acute severe Ulcerative Colitis disease.
Criteria	**Population:** Included: Adults (18 years and older), young people and children with a diagnosis of acute severe ulcerative colitis (Truelove & Witts criteria or equivalent) that are receiving inpatient treatment. Excluded: Mixed IBD populations where the results are not displayed separately for Ulcerative Colitis. People with indeterminate or idiopathic colitis. The following groups will be considered separately if data are present: Pregnant women **Intervention/comparison:** • Ciclosporin (Oral or IV) • Corticosteroids (Oral or IV) • Ciclosporin and corticosteroids • Placebo Only drug treatments and preparations available in the UK are included. **Outcomes:**

	HRs will be used for outcomes considered as time-to-event data Critical outcomes • Mortality • Clinical remission; absence of clinical symptoms (author defined) • Clinical improvement ((author defined)) • Health-related quality of life (any validated indexes) Important outcomes • Endoscopic remission; mucosal healing (author defined) • Clinical and endoscopic remission (author defined) • Adverse events • serious adverse events (author defined) • Colectomy • Hospitalisations Ideally all the studies would have used the same validated index to define remission and improvement. This is not the case. Numerous indexes are used and most are not validated. The GDG considered the impact of choosing one or only validated indexes which would result in a sparse evidence base. Using different indexes and author's definitions would include more studies but introduce a higher risk of bias. The GDG decided as the majority of the authors and indexes defined remission and improvement in a similar way it was reasonable to use the author defined definitions. Studies were excluded if there was no definition stated of remission. A trial duration limit of 4weeks was applied. It was thought that any drug taking longer than 4 weeks to have an effect would not be suitable for the induction of remission in this population. The GDG considered the time taken to achieve remission or clinical improvement was important. The GDG considered the following time interval important ≤ 2weeks and 2-≤ 4 weeks **Settings:** • Secondary Care • Tertiary Care **Population size and directness:** • No limitations on sample size
Search	• The databases to be searched are Medline, Embase, The Cochrane Library • Type of studies included: randomised controlled trials (RCTs) • Studies will be restricted to English language only • Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question • Phase I and II (non randomised) and cross-over studies are excluded • No date restriction will be applied. • No trial duration minimum limit. Maximum duration of 4weeks (analysed as 0≤2 and 2≤4 weeks)
Review strategy	• Cochrane Reviews will be quality assessed and presented • Further meta-analyses will be conducted as appropriate If there is heterogeneity the following subgroups will be analysed separately: • Age (adults and children)

3.8 Timing of surgery

Review question	**Which validated tools are the most predictive of the likelihood of surgery in people with acute severe ulcerative colitis?**

Objectives	To determine if any validated tools for acute severe ulcerative colitis predict colectomy in at risk patients
Criteria	**Population:** Adults, young people and children with acute severe ulcerative colitis (according to the Truelove & Witts criteria or equivalent). If patients are hospitalized for ulcerative colitis, it is considered to be severe for this question. Excluded: Mixed IBD populations, indeterminate colitis The following groups will be considered separately if data are present: Pregnant women **Intervention:** Validated risk scores for acute severe UC to predict the risk of surgery (colectomy). If there are less than 3 validated risk scores, then un-validated risk scores will also be reviewed. The risk scores needed to have a derivation study and could be internally or externally validated. **Comparison:** Not applicable. **Outcomes:** Statistical measures of discrimination and calibration including Area Under the Curve (AUC)
Search	The databases to be searched are Medline, Embase, the Cochrane Library and CINAHL. Studies will be restricted to the English language only. No study design filters will be applied. If no validated score found then a search will be done for prospective cohort studies designed to look at the risk factors for surgery.
Review strategy	**Criteria for individual studies:** • Multivariate analysis (exclude if variables have not been controlled for in the analysis depending on the quantity and quality of the papers found) **Hierarchy of evidence:** • IPD meta-analysis (Gold standard) • Meta-analysis/ systematic reviews • Prospective cohort studies **Strata:** Adults, young people and children

3.9 Pregnancy

Review question	**What are the consequences of using drug treatments for the induction and maintenance of remission in pregnant women?**
Objectives	To determine whether there are any drug treatments for the induction and maintenance of remission that are not appropriate for use in pregnant women with ulcerative colitis
Criteria	**Population:** Included: Pregnant women with a diagnosis of ulcerative colitis Excluded: Mixed IBD populations where the results are not displayed separately for Ulcerative Colitis patients People with indeterminate or idiopathic colitis **Intervention/comparisons:** • Aminosalicylates • Corticosteroids • Immunomodulators (ciclosporin, tacrolimus, azathioprine, mercaptopurine) **Note: methotrexate has not been included as it is contraindicated in pregnancy** • No treatment

	Oral/rectal/IV as appropriate. In addition to the outcomes stated in the protocols x and y (induction and maintenance) this outcomes were included. **Critical outcomes:** Stillbirth Congenital abnormalities Spontaneous abortion Premature births (<37 weeks gestation) Low birth weight (<2.5kg) Maternal mortality **Important outcomes:** Normal birth (Term (≥37 weeks)with no abnormalities) Quality of Life **Strata:** Disease activity (active, inactive) **Settings:** • No setting restrictions **Population size and directness:** • No limitations on sample size • Studies with indirect populations will not be considered
Search	• The databases to be searched are Medline, Embase, The Cochrane Library • Type of studies included: randomised controlled trials (RCTs), cohort studies, case series, cross- sectional • Studies will be restricted to English language only • Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question • No date restriction will be applied. • No trial duration limit.
Review strategy	• Cochrane Reviews will be quality assessed and presented • Further meta-analyses will be conducted as appropriate **Hierarchy of evidence:** • Multivariate analysis • Uni-variate analysis

3.10 Bone health

Review question	**In children and young people with ulcerative colitis, are disease activity, systemic corticosteroid use, total vitamin D and malnutrition, risk factors for poor bone health?**
Objectives	To determine whether the following are risk factors for poor bone health; disease activity; steroid use; total vitamin D and malnutrition
Criteria	**Population:** Included: Young people and children with a diagnosis of ulcerative colitis Excluded: Mixed IBD populations where the results are not displayed separately for Ulcerative Colitis patients or where the diagnosis has not been controlled for in the multivariate analysis. People with indeterminate or idiopathic colitis **Risk factors** • Disease activity (active versus inactive disease) • Systemic corticosteroid use: Current high dose use versus current low dose use, frequent use (>2 times/year) versus infrequent use (≤2 times/year), cumulative dose • Total vitamin D (25-hydroxycholecalciferol) • Malnutrition (reduction by 2 centiles in weight)

	Outcomes: **Critical outcomes** • Incidence of fractures (validated by medical records/ radiological reports) • Osteoporosis /osteopenia as indicated by Bone mineral density z score • Reduction in Bone mineral density score **Important outcomes** • Epiphyseal fusion (normal, delayed) • Bone age (wrist x-ray, delayed, normal or advanced)
Search	• The databases to be searched are Medline, Embase, The Cochrane Library • Type of studies included: meta-analysis, randomised controlled trials (RCTs), cohort studies, cross-sectional studies • Studies will be restricted to English language only • Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question • No date restriction will be applied. • No trial duration limit.
Review strategy	• Cochrane Reviews will be quality assessed and presented • Further meta-analyses will be conducted as appropriate **Potential confounders:** • Age • Sex • Ethnicity • Co-prescription of vitamin D • Tanner staging • Any of the risk factors listed above • Family history • Chronic diseases associated with osteoporosis (coeliacs, thyrotoxicosis, liver disease) • Diet (vegetarian, vegan etc.) **Criteria for individual studies:** • Multivariate analysis **Hierarchy of evidence:** • IPD meta-analysis (Gold standard) • Meta-analysis/ systematic reviews • Cohort studies • Cross-sectional studies

3.11 Growth and development

Review question	In children and young people with ulcerative colitis, what are the optimal strategies (timing, location) for monitoring growth?
Objectives	To determine how frequently children and young people with ulcerative colitis should be monitored for growth. To determine where children should be monitored To determine if pubertal assessment can be done by self assessment
Criteria	**Population** Included: Young people and children with a diagnosis of ulcerative colitis Excluded: Mixed IBD populations where the results are not displayed separately for Ulcerative

	Colitis. People with indeterminate or idiopathic colitis Strata: severity of disease, corticosteroid use ,location of assessment,self assessment and healthcare professional assessment **Interventions** Measuring growth with ≥ 1of the following indicators: • Linear height (growth velocity) • Weight • Tanner staging (pubertal development) • Bone age (wrist x-ray) • Quality of life at different time intervals **Comparisons** • Different time intervals **Outcomes** **Critical outcomes** • Deviation from normal/baseline linear height (growth velocity) as measured on the centile chart trajectory • Deviation from Tanner staging (pubertal development) • Younger /older? Bone age (wrist x-rays) **Important outcomes** • Deviation from normal weight as measured on the centile weight trajectory? **Population size and directness:** • No limitations on sample size • Studies with indirect populations will not be considered
Search	The databases to be searched are Medline, Embase, The Cochrane Library Type of studies included: randomised controlled trials (RCTs), cohort studies, cross-sectional studies, prospective case series Studies will be restricted to English language only Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question No date restriction will be applied. No trial duration limit.
Review strategy	Cochrane Reviews will be quality assessed and presented Further meta-analyses will be conducted as appropriate

3.12 Information for patients relating to the outcomes of elective surgery

Review question	**For adults, children and young people with ulcerative colitis considering surgery, what information on short and long term outcomes should be offered to patients and their carers by healthcare professionals?**
Objectives	To determine what short and long term outcomes patients would like to have known/ found important to know about, who have undergone surgical interventions as a treatment for ulcerative colitis.
Criteria	**Population** Included: Adults (18 years and older), young people and children with a diagnosis of ulcerative

	colitis who have had surgical interventions (elective) as treatment for their ulcerative colitis. Mixed IBD populations will be included if there is very limited evidence but downgraded as an indirect population if the results for the ulcerative colitis patients are not separated out. Excluded: Mixed IBD and non IBD populations where the results are not displayed separately for Ulcerative Colitis patients. People with indeterminate or idiopathic colitis **Intervention** • Information that patients were given on the long and short term outcomes of surgery for ulcerative colitis (prior to surgery) • Information that patients would like to have known prior to surgery for the treatment of ulcerative colitis (post surgery) **Comparison** No comparison **Outcomes** Any outcomes that are identified by the participants This will be broken down into: • Short term outcomes (biological, physical/ interference with daily activities, psychological) • Long term outcomes(biological, physical/ interference with daily activities, psychological)
Search	• The databases to be searched are Medline, Embase, The Cochrane Library • Type of studies included: randomised controlled trials (RCTs), cohort studies, cross-sectional studies, survey studies, qualitative studies (interviews, focus groups) • Studies will be restricted to English language only • Abstracts will be excluded unless there are no other studies available for a particular outcome or clinical question • No date restriction will be applied. • No trial duration limit. • A call for evidence to identify any unpublished data.
Review strategy	• Cochrane Reviews will be quality assessed and presented • Further meta-analyses will be conducted as appropriate • Analysis of the data will be appropriate to the design of the studies identified.

3.13 Health economic review protocol for all questions

Review question	All questions – health economic evidence
Objectives	To identify economic studies relevant to the review questions set out above.
Criteria	Populations, interventions and comparators as specified in the individual review protocols above. Must be a relevant economic study design (cost-utility analysis, cost-benefit analysis, cost-effectiveness analysis, cost-consequence analysis, comparative cost analysis).
Search strategy	An economic study search was undertaken using population specific terms and an economic study filter – see Appendix D.
Review strategy	Each study is assessed using the NICE economic evaluation checklist – NICE (2009) Guidelines Manual. **Inclusion/exclusion criteria** • If a study is rated as both 'Directly applicable' and 'Minor limitations' (using the NICE economic evaluation checklist) then it should be included in the guideline. An evidence table should be completed and it should be included in the economic profile. • If a study is rated as either 'Not applicable' or 'Very serious limitations' then it should be

	excluded from the guideline. It should not be included in the economic profile and there is no need to include an evidence table. • If a study is rated as 'Partially applicable' and/or 'Potentially serious limitations' then there is discretion over whether it should be included. The health economist should make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim being to include studies that are helpful for decision making in the context of the guideline and current NHS setting. Where exclusions occur on this basis, this should be noted in the relevant section of the guideline with references. Also exclude: • unpublished reports unless submitted as part of a call for evidence • abstract-only studies • letters • editorials • reviews of economic evaluations[(a)] • foreign language articles **Where there is discretion** The health economist should be guided by the following hierarchies. *Setting:* • UK NHS • OECD countries with predominantly public health insurance systems (e.g. France, Germany, Sweden) • OECD countries with predominantly private health insurance systems (e.g. USA, Switzerland) • Non-OECD settings (always 'Not applicable') *Economic study type:* • Cost-utility analysis • Other type of full economic evaluation (cost-benefit analysis, cost-effectiveness analysis, cost-consequence analysis) • Comparative cost analysis • Non-comparative cost analyses including cost of illness studies (always 'Not applicable') *Year of analysis:* • The more recent the study, the more applicable it is *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the effectiveness data used in the economic analysis matches with the studies included for the clinical review the more useful the analysis will be to decision making for the guideline.

(a) Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.

4 Appendix D: Literature search strategies

4.1 Contents

4.2 Introduction

Search strategies used for the ulcerative colitis guideline are outlined below and were run in accordance with the methodology in the NICE Guidelines Manual 2009.[284]

All searches were run up to 15th November 2012 unless otherwise stated. Any studies added to the databases after this date were not included unless specifically stated in the text. Searches were run for the dates shown in table 1 below. Where possible searches were limited to retrieve material published in English.

Table 1: Database date parameters

Database	Dates searched
Medline	1946 – 15th November 2012
Embase	1980 – 15th November 2012
The Cochrane Library	Cochrane Reviews to 2012 Issue 11 CENTRAL to 2012 Issue 11 DARE to 2012 Issue 4 HTA and NHSEED to 2012 Issue 4

Database	Dates searched
	Methods Studies to 2012 Issue 4

Clinical searches

Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID), and the Cochrane Library (Wiley). Usually, searches were constructed in the following way:

- A PICO format was used for **intervention** searches where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

- A PEO format was used for **prognosis** searches where population (P) terms were combined with exposure (E) terms and sometimes outcomes (O). Search filters were added to the search where appropriate.

Economic searches

Searches for the **health economic reviews** were run in Medline (OVID), Embase (OVID), the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). HTA and NHSEED searches were carried out via the Centre for Reviews and Dissemination (CRD) interface. The HEED database was accessed via the Wiley interface. Searches in these three databases were constructed using population terms only. For Medline and Embase a health economic filter (instead of a study type filter) was added to the standard population search strategy.

4.3 Population search strategies

4.3.1 Standard population search strategy

This population was used for all except one question (D.3.6: Which validated tools are the most predictive of the likelihood of surgery in people with acute severe ulcerative colitis?)

Medline search terms

1.	colitis, ulcerative/
2.	exp proctitis/
3.	exp inflammatory bowel diseases/
4.	(inflamm* adj2 (colon* or bowel)).ti,ab.
5.	(ulcer* adj2 colitis).ti,ab.
6.	(pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-colitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis).ti,ab.
7.	((total or sub-total or subtotal or extensive or left-sided or universal) adj colitis).ti,ab.
8.	or/1-7

Embase search terms

1.	ulcerative colitis/
2.	proctocolitis/
3.	proctitis/
4.	(inflamm* adj2 (colon* or bowel)).ti,ab.
5.	(ulcer* adj colitis).ti,ab.

6.	(pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-colitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis).ti,ab.
7.	((total or sub-total or subtotal or extensive or left-sided or universal) adj colitis).ti,ab.
8.	or/1-7

Cochrane search terms

#1.	MeSH descriptor Inflammatory Bowel Diseases explode all trees
#2.	MeSH descriptor Proctitis explode all trees
#3.	MeSH descriptor Colitis, Ulcerative explode all trees
#4.	(ulcer* near/2 colitis):ti,ab,kw
#5.	(inflamm* near/2 (colon* or bowel)):ti,ab,kw
#6.	(pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-colitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis):ti,ab,kw
#7.	((total or sub-total or subtotal or extensive or left-sided or universal) near colitis):ti,ab,kw
#8.	(#1 or #2 or #3 or #4 or #5 or #6 or #7)

4.3.2 Paediatrics filter

The following terms were used to limit retrieval by age group for questions relating to children and young people only.

Medline search terms

#1.	exp child/
#2.	child*.tw.
#3.	exp infant/
#4.	infan*.tw.
#5.	(baby or babies).tw.
#6.	"adolescent"/
#7.	(pediatric*1 or paediatric*1).tw.
#8.	or/1-7

Embase search terms

#1.	exp child/
#2.	child*.tw.
#3.	childhood/
#4.	infancy/
#5.	infan*.tw.
#6.	(baby or babies).tw.
#7.	exp adolescent/
#8.	(pediatric*1 or paediatric*1).tw.
#9.	or/1-8

Cochrane search terms

#1.	child*:ti,ab,kw
#2.	infan*:ti,ab,kw
#3.	(baby or babies):ti,ab,kw
#4.	adolescen*:ti,ab,kw

#5.	(pediatric? or paediatric?):ti,ab,kw
#6.	(#1 or #2 or #3 or #4 or #5)

4.4 Study filter search terms

4.4.1 Systematic review (SR)

Medline search terms

1.	meta-analysis/
2.	meta-analysis as topic/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	cochrane.jw.
10.	or/1-9

Embase search terms

1.	systematic review/
2.	meta-analysis/
3.	(meta analy* or metanaly* or metaanaly*).ti,ab.
4.	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
5.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7.	(search* adj4 literature).ab.
8.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9.	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10.	cochrane.jw.
11.	or/1-10

4.4.2 Randomised controlled trials (RCT)

Medline search terms

1.	randomized controlled trial.pt.
2.	controlled clinical trial.pt.
3.	randomi#ed.ab.
4.	placebo.ab.
5.	randomly.ab.
6.	clinical trials as topic.sh.
7.	trial.ti.
8.	or/1-7

Embase search terms

1.	random*.ti,ab.

2.	factorial*.ti,ab.
3.	(crossover* or cross over*).ti,ab.
4.	((doubl* or singl*) adj blind*).ti,ab.
5.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6.	crossover procedure/
7.	double blind procedure/
8.	single blind procedure/
9.	randomized controlled trial/
10.	or/1-9

4.4.3 Health economic studies

Medline search terms

1.	economics/
2.	value of life/
3.	exp "costs and cost analysis"/
4.	exp economics, hospital/
5.	exp economics, medical/
6.	economics, nursing/
7.	economics, pharmaceutical/
8.	exp "fees and charges"/
9.	exp budgets/
10.	budget*.ti,ab.
11.	cost*.ti.
12.	(economic* or pharmaco?economic*).ti.
13.	(price* or pricing*).ti,ab.
14.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15.	(financ* or fee or fees).ti,ab.
16.	(value adj2 (money or monetary)).ti,ab.
17.	or/1-16

Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/
4.	exp fee/
5.	budget/
6.	funding/
7.	budget*.ti,ab.
8.	cost*.ti.
9.	(economic* or pharmaco?economic*).ti.
10.	(price* or pricing*).ti,ab.
11.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12.	(financ* or fee or fees).ti,ab.
13.	(value adj2 (money or monetary)).ti,ab.
14.	or/1-13

4.4.4 Quality of life studies

Medline search terms

1.	quality-adjusted life years/
2.	sickness impact profile/
3.	(quality adj2 (wellbeing or well-being)).ti,ab.
4.	sickness impact profile.ti,ab.
5.	disability adjusted life.ti,ab.
6.	(qal* or qtime* or qwb* or daly*).ti,ab.
7.	(euroqol* or eq5d* or eq 5d*).ti,ab.
8.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
9.	(health utility* or utility score* or disutilit*).ti,ab.
10.	(hui or hui1 or hui2 or hui3).ti,ab.
11.	health* year* equivalent*.ti,ab.
12.	(hye or hyes).ti,ab.
13.	rosser.ti,ab.
14.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
15.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
16.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
17.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
18.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
19.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
20.	or/1-19

Embase search terms

1.	quality adjusted life year/
2.	"quality of life index"/
3.	short form 12/ or short form 20/ or short form 36/ or short form 8/
4.	sickness impact profile/
5.	(quality adj2 (wellbeing or well-being)).ti,ab.
6.	sickness impact profile.ti,ab.
7.	disability adjusted life.ti,ab.
8.	(qal* or qtime* or qwb* or daly*).ti,ab.
9.	(euroqol* or eq5d* or eq 5d*).ti,ab.
10.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
11.	(health utility* or utility score* or disutilit*).ti,ab.
12.	(hui or hui1 or hui2 or hui3).ti,ab.
13.	health* year* equivalent*.ti,ab.
14.	(hye or hyes).ti,ab.
15.	rosser.ti,ab.
16.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
17.	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
18.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
19.	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
20.	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
21.	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.

22.	or/1-21

4.4.5 Excluded study designs and publication types

The following study designs and publication types were removed from retrieved results using the NOT operator.

Medline search terms

1.	letter/
2.	editorial/
3.	news/
4.	exp historical article/
5.	anecdotes as topic/
6.	comment/
7.	case report/
8.	(letter or comment*).ti.
9.	or/1-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animals/ not humans/
13.	exp animals, laboratory/
14.	exp animal experimentation/
15.	exp models, animal/
16.	exp rodentia/
17.	(rat or rats or mouse or mice).ti.
18.	or/11-17

Embase search terms

1.	letter.pt. or letter/
2.	note.pt.
3.	editorial.pt.
4.	case report/ or case study/
5.	(letter or comment*).ti.
6.	or/1-5
7.	randomized controlled trial/ or random*.ti,ab.
8.	6 not 7
9.	animal/ not human/
10.	nonhuman/
11.	exp animal experiment/
12.	exp experimental animal/
13.	animal model/
14.	exp rodent/
15.	(rat or rats or mouse or mice).ti.
16.	or/8-15

4.5 Searches for specific questions

4.5.1 Induction and maintenance of remission

Searches for the following three questions were run as one search:

1. In adults, children and young people with mild to moderate ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids, aminosalicylates and immunomodulators (mercaptopurine, azathioprine, methotrexate and tacrolimus) for the induction of remission compared to themselves (different preparations and doses), each other, combinations of preparations (oral and topical) and placebo?
2. In adults, children and young people with ulcerative colitis in remission, what is the clinical and cost-effectiveness of corticosteroids, aminosalicylates, immunomodulators (mercaptopurine, azathioprine, methotrexate and tacrolimus) for the maintenance of remission compared to themselves (different preparations and doses), each other, combinations of preparations (oral and topical) and placebo?
3. In adults, children and young people with acute severe ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids and ciclosporin compared to each other and their combination (corticosteroids and ciclosporin) for the induction of remission?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults, children and young people diagnosed with ulcerative colitis / acute severe ulcerative colitis	Corticosteroids, aminosalicylates, immunomodulators (mercaptopurine, azathioprine, methotrexate & tacrolimus) and ciclosporin	None	SR, RCT and exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	exp glucocorticoids/
2.	cortisone/
3.	hydrocortisone/
4.	(beclomethasone or betamethasone or budesonide or budenofalk or cortisone or deflazacort or depomedrone or depo-medrone or desoximetasone or dexamethasone or diflucortolone or efcortesol or entocort or hydrocortisone or kenalog or medrone or melengestrol acetate or methylprednisolone or methylprednisone or prednisolone or prednisone or solucortel or solu-cortel or solumedrone or solu-medrone or triamcinolone).ti,ab.
5.	methotrexate/
6.	methotrexate.ti,ab.
7.	6-mercaptopurine/
8.	mercaptopurine.ti,ab.
9.	azathioprine/
10.	(azathioprine or imuran).ti,ab.
11.	tacrolimus/
12.	(prograf* or FK506 or FK 506).ti,ab.
13.	cyclosporine/
14.	(ciclosporin* or cyclosporin* or sandimmun* or neoral).ti,ab.

15.	mesalamine/
16.	sulfasalazine/
17.	(aminosalicyl* or 5-aminosalicyl* or 5-ASA or 5ASA or 5aminosalicyl* or pentasa or mesalazine or mesalamine or asacol or mezavant or ipocol or mesren or salofalk).ti,ab.
18.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab.
19.	(olsalazine or balsalazide or dipentum or colazide or balsalazine).ti,ab.
20.	or/1-19

Embase search terms

1.	exp glucocorticoid/
2.	(beclomethasone or betamethasone or budesonide or budenofalk or cortisone or deflazacort or depomedrone or depo-medrone or desoximetasone or dexamethasone or diflucortolone or efcortesol or entocort or hydrocortisone or kenalog or medrone or melengestrol acetate or methylprednisolone or methylprednisone or prednisolone or prednisone or solucortel or solu-cortel or solumedrone or solu-medrone or triamcinolone).ti,ab.
3.	methotrexate/
4.	methotrexate.ti,ab.
5.	mercaptopurine/
6.	mercaptopurine.ti,ab.
7.	azathioprine/
8.	(azathioprine or imuran).ti,ab.
9.	tacrolimus/
10.	(prograf* or FK506 or FK 506).ti,ab.
11.	cyclosporin/
12.	(ciclosporin* or cyclosporin* or sandimmun* or neoral).ti,ab.
13.	mesalazine/
14.	salazosulfapyridine/
15.	(aminosalicyl* or 5-aminosalicyl* or 5-ASA or 5ASA or 5aminosalicyl* or pentasa or mesalazine or mesalamine or asacol or mezavant or ipocol or mesren or salofalk).ti,ab.
16.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab.
17.	(olsalazine or balsalazide or dipentum or colazide or balsalazine).ti,ab.
18.	or/1-17

Cochrane search terms

#1.	(beclomethasone or betamethasone or budesonide or budenofalk or cortisone or deflazacort or depomedrone or depo-medrone or desoximetasone or dexamethasone or diflucortolone or efcortesol or entocort or hydrocortisone or kenalog or medrone or melengestrol acetate or methylprednisolone or methylprednisone or prednisolone or prednisone or solucortel or solu-cortel or solumedrone or solu-medrone or triamcinolone):ti,ab,kw
#2.	MeSH descriptor Glucocorticoids explode all trees
#3.	(glucocorticoid* or corticosteroid*):ti,ab,kw
#4.	(methotrexate or mercaptopurine or azathioprine or imuran or tacrolimus or prograf* or FK 506 or FK506 or cyclosporin* or ciclosporin* or sandimmun* or neoral):ti,ab,kw
#5.	(aminosalicyl* or 5-aminosalicyl* or 5-ASA or 5ASA or 5aminosalicyl* or pentasa or mesalazine or mesalamine or asacol or mezavant or ipocol or mesren or salofalk):ti,ab,kw
#6.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*):ti,ab,kw

#7.	(olsalazine or balsalazide or dipentum or colazide or balsalazine):ti,ab,kw
#8.	(#1 or #2 or #3 or #4 or #5 or #6 or #7)

4.5.2 Risk factors for poor bone health in children

In children and young people with ulcerative colitis, are disease activity, systemic corticosteroid use, total vitamin D and malnutrition, risk factors for poor bone health?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Outcome	Comparison	Study filter used	Date parameters
Children and young people diagnosed with ulcerative colitis	Poor bone health, fracture	None	Exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	bone.hw. or bone*.ti,ab.
2.	(osteopor* or osteomal*).ti,ab.
3.	exp osteoporosis/
4.	osteomalacia/
5.	osteoporotic fractures/
6.	fracture*.ti,ab.
7.	fractures, cartilage/ or exp fractures, bone/
8.	or/1-7

Embase search terms

1.	bone.hw. or bone*.ti,ab.
2.	(osteopor* or osteomal*).ti,ab.
3.	fracture*.ti,ab.
4.	osteoporotic fractures/
5.	exp fracture/
6.	exp osteoporosis/
7.	exp osteomalacia/
8.	or/1-7

Cochrane search terms

#1.	(bone* or osteomal* or osteopor* or fracture*):ti,ab,kw

4.5.3 Growth and development in children and young people

In children and young people with ulcerative colitis, what are the optimal strategies (timing, location) for monitoring growth?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Children and young people diagnosed with ulcerative colitis	Monitoring of growth / development	None	Exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	growth/
2.	growth retardation/
3.	failure to thrive/
4.	growth disorder/
5.	child growth/
6.	exp puberty/
7.	delayed puberty/
8.	child development/
9.	adolescent development/
10.	body height/
11.	body weight/
12.	((growth or pubert*) adj2 (impair* or delay* or disorder* or retard*)).ti,ab.
13.	linear growth.ti,ab.
14.	((height or growth) adj2 velocity).ti,ab.
15.	bone age.ti,ab.
16.	bone development/
17.	bone density/
18.	exp growth hormone/
19.	or/1-18

Embase search terms

1.	growth/
2.	growth retardation/
3.	failure to thrive/
4.	growth disorder/
5.	child growth/
6.	exp puberty/
7.	delayed puberty/
8.	child development/
9.	adolescent development/
10.	body height/
11.	body weight/
12.	((growth or pubert*) adj2 (impair* or delay* or disorder* or retard*)).ti,ab.
13.	linear growth.ti,ab.
14.	((height or growth) adj2 velocity).ti,ab.
15.	bone age.ti,ab.
16.	growth rate/
17.	growth hormone/
18.	human growth hormone/
19.	bone density/
20.	bone development/
21.	or/1-20

Cochrane search terms

#1.	MeSH descriptor Puberty explode all trees

#2.	MeSH descriptor Growth explode all trees
#3.	MeSH descriptor Growth Disorders explode all trees
#4.	MeSH descriptor Puberty, Delayed explode all trees
#5.	MeSH descriptor Adolescent Development explode all trees
#6.	MeSH descriptor Child Development explode all trees
#7.	MeSH descriptor Body Weight explode all trees
#8.	MeSH descriptor Body Height explode all trees
#9.	MeSH descriptor Failure to Thrive explode all trees
#10.	((growth or pubert*) near/2 (impair* or delay* or disorder* or retard*)):ti,ab,kw
#11.	linear growth:ti,ab,kw
#12.	((height or growth) near/2 velocity):ti,ab,kw
#13.	bone age:ti,ab,kw
#14.	MeSH descriptor Bone Density, this term only
#15.	MeSH descriptor Bone Development, this term only
#16.	MeSH descriptor Growth Hormone explode all trees
#17.	(bone next (develop* or density)):ti,ab,kw
#18.	growth hormone*:ti,ab,kw
#19.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18)

4.5.4 Information for patients relating to the outcomes of elective surgery

For adults, children and young people with ulcerative colitis considering surgery, what information on short and long term outcomes should be offered to patients and their carers by healthcare professionals?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults, children and young people diagnosed with ulcerative colitis	Patient information on surgery for ulcerative colitis	None	Exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	ileostomy/
2.	colonic pouches/
3.	exp colectomy/
4.	ileostomy.ti,ab.
5.	colectomy.ti,ab.
6.	(proctocolectomy or procto-colectomy).ti,ab.
7.	IPAA.ti,ab.
8.	((J or S or W or kock or pelvic) adj2 pouch).ti,ab.
9.	((ileal or ileoanal or ileo-anal or anal or ileum or anus or rectal or rectum) adj2 (pouch* or reservoir*)).ti,ab.
10.	((ileal or pouch or ileoanal or ileo-anal or anal or ileum or anus or rectal or rectum) adj2 anastomos*).ti,ab.
11.	su.fs.
12.	or/1-11

13.	((client* or patient* or user* or carer* or consumer* or customer*) adj3 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience* or opinion*)).mp.
14.	(information adj need*).mp.
15.	(information adj requirement*).mp.
16.	(information adj support*).mp.
17.	(patient* adj information*).mp.
18.	(service* adj2 acceptab*).mp.
19.	(service* adj2 unacceptab*).mp.
20.	psycho?social.mp.
21.	(patient* adj (complian* or adheren* or concordan*)).mp.
22.	patient education as topic/
23.	exp attitude to health/
24.	exp patient acceptance of health care/
25.	patient preference/
26.	or/13-25
27.	12 and 26

Embase search terms

1.	continent ileostomy/
2.	ileostomy/
3.	colon pouch/
4.	exp colon resection/
5.	proctocolectomy/
6.	ileoanal anastomosis/
7.	ileostomy.ti,ab.
8.	colectomy.ti,ab.
9.	(proctocolectomy or procto-colectomy).ti,ab.
10.	IPAA.ti,ab.
11.	((J or S or W or kock or pelvic) adj2 pouch).ti,ab.
12.	((ileal or ileoanal or ileo-anal or anal or ileum or anus or rectal or rectum) adj2 (pouch* or reservoir*)).ti,ab.
13.	((ileal or pouch or ileoanal or ileo-anal or anal or ileum or anus or rectal or rectum) adj2 anastomos*).ti,ab.
14.	su.fs.
15.	or/1-14
16.	((client* or patient* or user* or carer* or consumer* or customer*) adj3 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience* or opinion*)).mp.
17.	(information adj need*).mp.
18.	(information adj requirement*).mp.
19.	(information adj support*).mp.
20.	(patient* adj information*).mp.
21.	(service* adj2 acceptab*).mp.
22.	(service* adj2 unacceptab*).mp.
23.	psycho?social.mp.
24.	(patient* adj (complian* or adheren* or concordan*)).mp.

25.	patient education/
26.	exp attitude/
27.	exp patient attitude/
28.	patient preference/
29.	patient information/
30.	or/16-29
31.	15 and 30

Cochrane search terms

#1.	((client* or patient* or user* or carer* or consumer* or customer*) near/3 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience* or opinion*)):ti,ab,kw
#2.	(information near need*):ti,ab,kw
#3.	(information near requirement*):ti,ab,kw
#4.	(information near support*):ti,ab,kw
#5.	(patient* near information*):ti,ab,kw
#6.	(service* near/2 acceptab*):ti,ab,kw
#7.	(service* near/2 unacceptab*):ti,ab,kw
#8.	(psychosocial or psycho-social):ti,ab,kw
#9.	(patient* near (complian* or adheren* or concordan*)):ti,ab,kw
#10.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9)

4.5.5 Induction and maintenance of remission in pregnant women

What are the consequences of using drug treatments for the induction and maintenance of remission in pregnant women?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Pregnant women with ulcerative colitis	Corticosteroids, aminosalicylates, immunomodulators (mercaptopurine, azathioprine, methotrexate & tacrolimus) and ciclosporin	None	Exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	exp pregnancy/
2.	exp pregnancy complications/
3.	birth weight/
4.	pregnant women/
5.	prenatal care/
6.	(pregnant or pregnanc*).ti,ab.
7.	or/1-6
8.	exp glucocorticoids/
9.	cortisone/
10.	hydrocortisone/

11.	(beclomethasone or betamethasone or budesonide or budenofalk or cortisone or deflazacort or depomedrone or depo-medrone or desoximetasone or dexamethasone or diflucortolone or efcortesol or entocort or hydrocortisone or kenalog or medrone or melengestrol acetate or methylprednisolone or methylprednisone or prednisolone or prednisone or solucortel or solu-cortel or solumedrone or solu-medrone or triamcinolone).ti,ab.
12.	methotrexate/
13.	methotrexate.ti,ab.
14.	6-mercaptopurine/
15.	mercaptopurine.ti,ab.
16.	azathioprine/
17.	(azathioprine or imuran).ti,ab.
18.	tacrolimus/
19.	(prograf* or FK506 or FK 506).ti,ab.
20.	cyclosporine/
21.	(ciclosporin* or cyclosporin* or sandimmun* or neoral).ti,ab.
22.	mesalamine/
23.	sulfasalazine/
24.	(aminosalicyl* or 5-aminosalicyl* or 5-ASA or 5ASA or 5aminosalicyl* or pentasa or mesalazine or mesalamine or asacol or mezavant or ipocol or mesren or salofalk).ti,ab.
25.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab.
26.	(olsalazine or balsalazide or dipentum or colazide or balsalazine).ti,ab.
27.	or/8-26
28.	7 and 27

Embase search terms

1.	exp pregnancy/
2.	exp pregnancy complication/
3.	pregnancy outcome/
4.	exp birth weight/
5.	pregnant woman/
6.	exp prenatal care/
7.	(pregnant or pregnanc*).ti,ab.
8.	or/1-7
9.	exp glucocorticoid/
10.	(beclomethasone or betamethasone or budesonide or budenofalk or cortisone or deflazacort or depomedrone or depo-medrone or desoximetasone or dexamethasone or diflucortolone or efcortesol or entocort or hydrocortisone or kenalog or medrone or melengestrol acetate or methylprednisolone or methylprednisone or prednisolone or prednisone or solucortel or solu-cortel or solumedrone or solu-medrone or triamcinolone).ti,ab.
11.	methotrexate/
12.	methotrexate.ti,ab.
13.	mercaptopurine/
14.	mercaptopurine.ti,ab.
15.	azathioprine/
16.	(azathioprine or imuran).ti,ab.
17.	tacrolimus/
18.	(prograf* or FK506 or FK 506).ti,ab.

19.	cyclosporin/
20.	(ciclosporin* or cyclosporin* or sandimmun* or neoral).ti,ab.
21.	mesalazine/
22.	salazosulfapyridine/
23.	(aminosalicyl* or 5-aminosalicyl* or 5-ASA or 5ASA or 5aminosalicyl* or pentasa or mesalazine or mesalamine or asacol or mezavant or ipocol or mesren or salofalk).ti,ab.
24.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab.
25.	(olsalazine or balsalazide or dipentum or colazide or balsalazine).ti,ab.
26.	or/9-25
27.	8 and 26

Cochrane search terms

#1.	(pregnan* or "birth weight" or birthweight or pre-natal or ante-natal or prenatal or antenatal):ti,ab,kw

4.5.6 Tools for predicting likelihood of surgery in people with acute severe ulcerative colitis

Searches for this question used a slightly different population which is included in full in the following tables.

Which validated tools are the most predictive of the likelihood of surgery in people with acute severe ulcerative colitis?

Search constructed by combining the columns in the following table using the AND Boolean operator

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults children and young people with acute severe ulcerative colitis	Validated prediction tools	None	Exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	colitis, ulcerative/
2.	exp proctitis/
3.	exp inflammatory bowel diseases/
4.	(inflamm* adj2 (colon* or bowel)).ti,ab.
5.	(ulcer* adj2 colitis).ti,ab.
6.	(pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-colitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis).ti,ab.
7.	((total or sub-total or subtotal or extensive or left-sided or universal) adj colitis).ti,ab.
8.	megacolon, toxic/
9.	megacolon.ti,ab.
10.	or/1-9
11.	((decision or predict* or assess* or screen* or score* or scoring or stratif*) adj4 (tool* or rule* or instrument*1 or index* or test* or technique* or analys* or criteria or course)).ti,ab.
12.	risk assessment/
13.	or/11-12
14.	incidence/

15.	exp mortality/
16.	follow-up studies/
17.	prognos*.tw.
18.	predict*.tw.
19.	course*.tw.
20.	prognosis/
21.	or/14-20
22.	10 and 13 and 21

Embase search terms

1.	ulcerative colitis/
2.	proctocolitis/
3.	proctitis/
4.	(inflamm* adj2 (colon* or bowel)).ti,ab.
5.	(ulcer* adj colitis).ti,ab.
6.	(pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-colitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis).ti,ab.
7.	((total or sub-total or subtotal or extensive or left-sided or universal) adj colitis).ti,ab.
8.	toxic megacolon/
9.	megacolon.ti,ab.
10.	or/1-9
11.	((decision or predict* or assess* or screen* or score* or scoring or stratif*) adj4 (tool* or rule* or instrument*1 or index* or test* or technique* or analys* or criteria or course)).ti,ab.
12.	risk assessment/
13.	or/11-12
14.	incidence/
15.	exp mortality/
16.	follow-up studies/
17.	prognos*.tw.
18.	predict*.tw.
19.	course*.tw.
20.	prognosis/
21.	or/14-20
22.	10 and 13 and 21

Cochrane search terms

#1.	MeSH descriptor Inflammatory Bowel Diseases explode all trees
#2.	MeSH descriptor Proctitis explode all trees
#3.	MeSH descriptor Colitis, Ulcerative explode all trees
#4.	(ulcer* near/2 colitis):ti,ab,kw
#5.	(inflamm* near/2 (colon* or bowel)):ti,ab,kw
#6.	(pancolitis or rectitis or proctocolitis or procto-colitis or colorectitis or rectocolitis or recto-colitis or recto-sigmoiditis or rectosigmoiditis or procto-sigmoiditis or proctosigmoiditis or proctitis):ti,ab,kw
#7.	((total or sub-total or subtotal or extensive or left-sided or universal) near colitis):ti,ab,kw
#8.	megacolon:ti,ab,kw

#9.	(#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8)
#10.	((decision or predict* or assess* or screen* or score* or scoring or stratif*) near/4 (tool* or rule* or instrument* or index* or test* or technique* or analys* or criteria or course)):ti,ab,kw
#11.	(risk* near/2 assessment*):ti,ab,kw
#12.	(#10 or #11)
#13.	(prognos* or predict* or course*):ti,ab,kw
#14.	(incidence or mortality or follow-up or followup or follow up):ti,ab,kw
#15.	(#13 or #14)
#16.	(#9 and #12 and #15)

4.6 Economic searches

4.6.1 Economic reviews

Economic searches were conducted in Medline and Embase using the standard population terms and an economic filter. Search terms used in HEED and CRD (NHS EED and HTA) are below.

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults, children and young people diagnosed with ulcerative colitis	None	None	Economic (Medline and Embase only)	Medline and Embase 2010-15th Nov 2012 CRD EED and HTA to 15th Nov 2012

CRD search terms

#1	MeSH Colitis, Ulcerative explode 1 2 3 4
#2	MeSH Proctocolitis explode 1 2 3 4 5
#3	MeSH Inflammatory Bowel Diseases explode 1 2
#4	inflamm* near bowel
#5	inflamm* near colon
#6	((ulcer* or hemorrhagic or haemorrhagic) and (colitis or colon*))
#7	(pancolitis or rectitis or proctocolitis or colorectitis or rectocolitis or rectosigmoiditis or proctosigmoiditis or proctitis or procto-colitis or colo-rectitis or recto-colitis or recto-sigmoiditis or procto-sigmoiditis)
#8	#1 or #2 or #3 or #4 or #5 or #6 or #7

HEED search terms

1	AX=(inflamm* and colon) or (inflamm* and bowel)
2	AX=ulcer* and colitis
3	AX=ulcer* and colon
4	AX=pancolitis or rectitis or proctocolitis or colorectitis or rectocolitis or rectosigmoiditis or proctosigmoiditis or procto-colitis or colo-rectitis or recto-colitis or recto-sigmoiditis or procto-sigmoiditis or proctitis
5	CS=1 or 2 or 3 or 4

4.6.2 Quality of life reviews

These searches were carried out on Medline and Embase only

Population	Intervention / exposure	Comparison	Study filter used	Date parameters

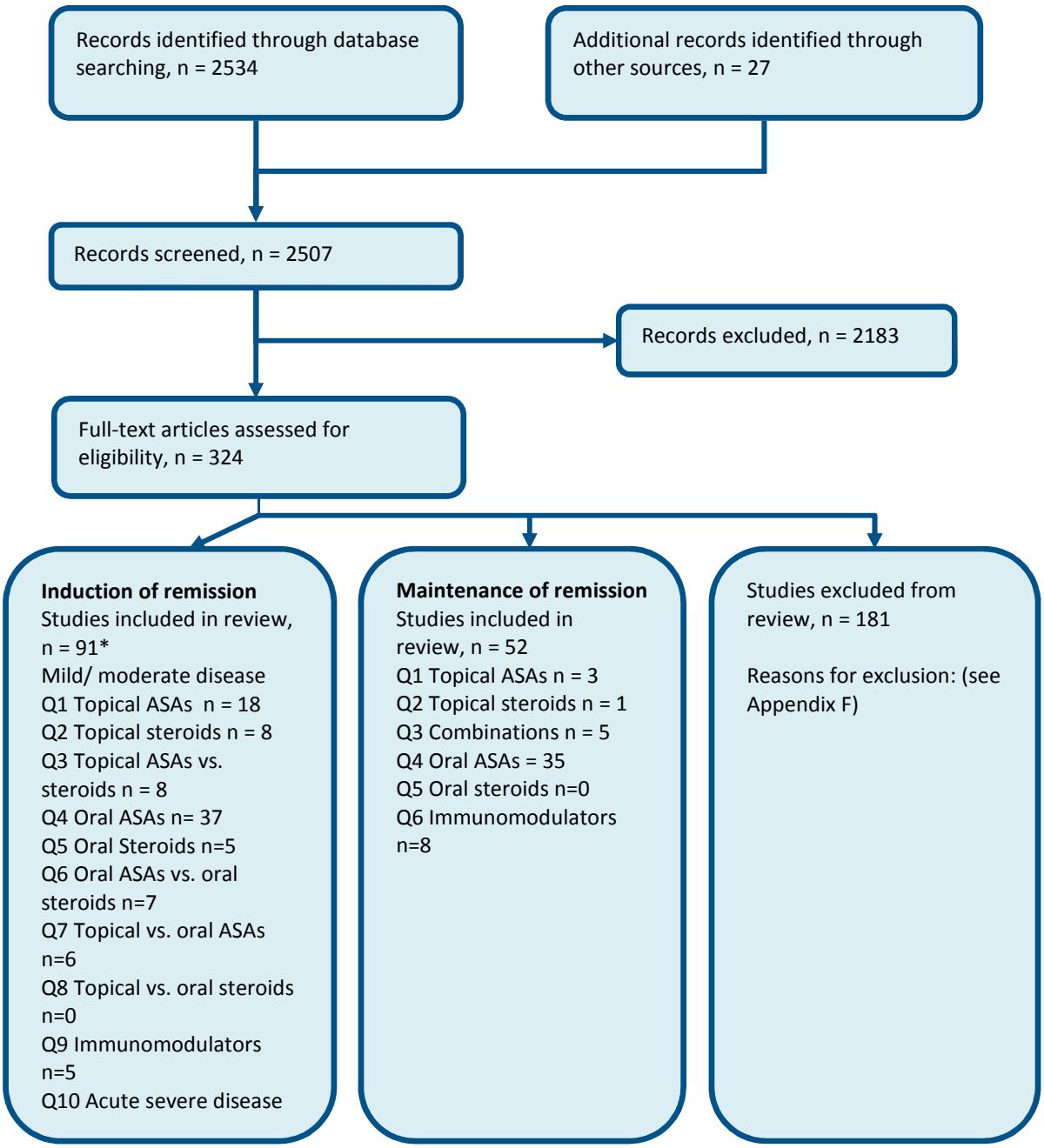
Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults, children and young people diagnosed with ulcerative colitis	None	None	Quality of life, exclusions (Medline and Embase only)	Medline and Embase to May 2011

5 Appendix E: Study selection flowcharts

5.1 Clinical reviews

5.1.1 Induction and maintenance of remission

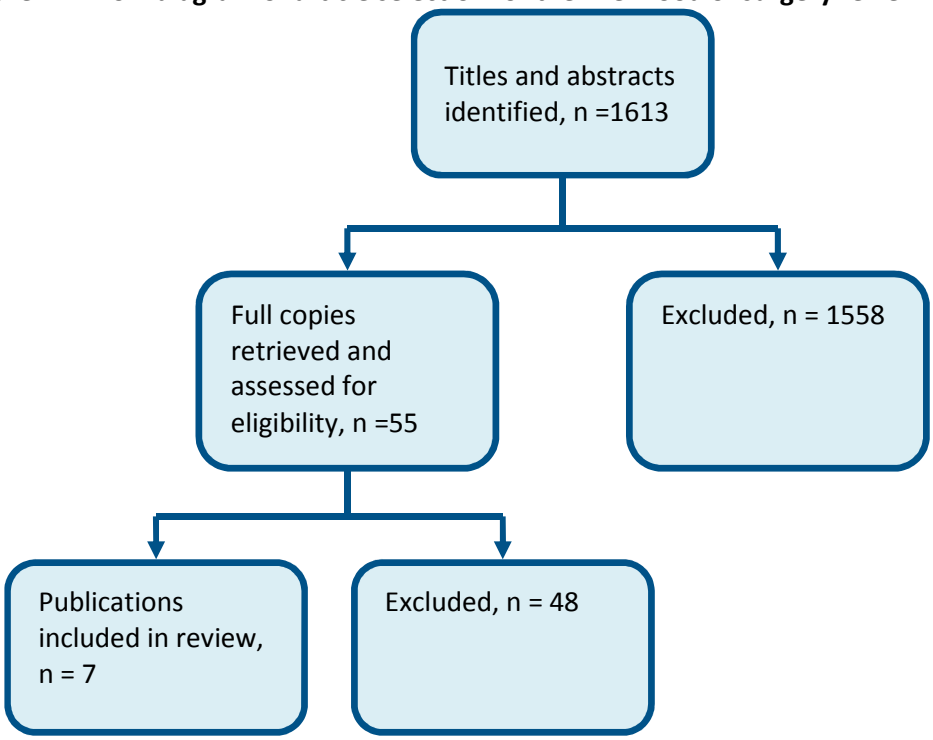
Figure 1: Flow diagram of article selection for the induction and maintenance of remission review



*Note: *Some papers appear in more than one clinical review question*

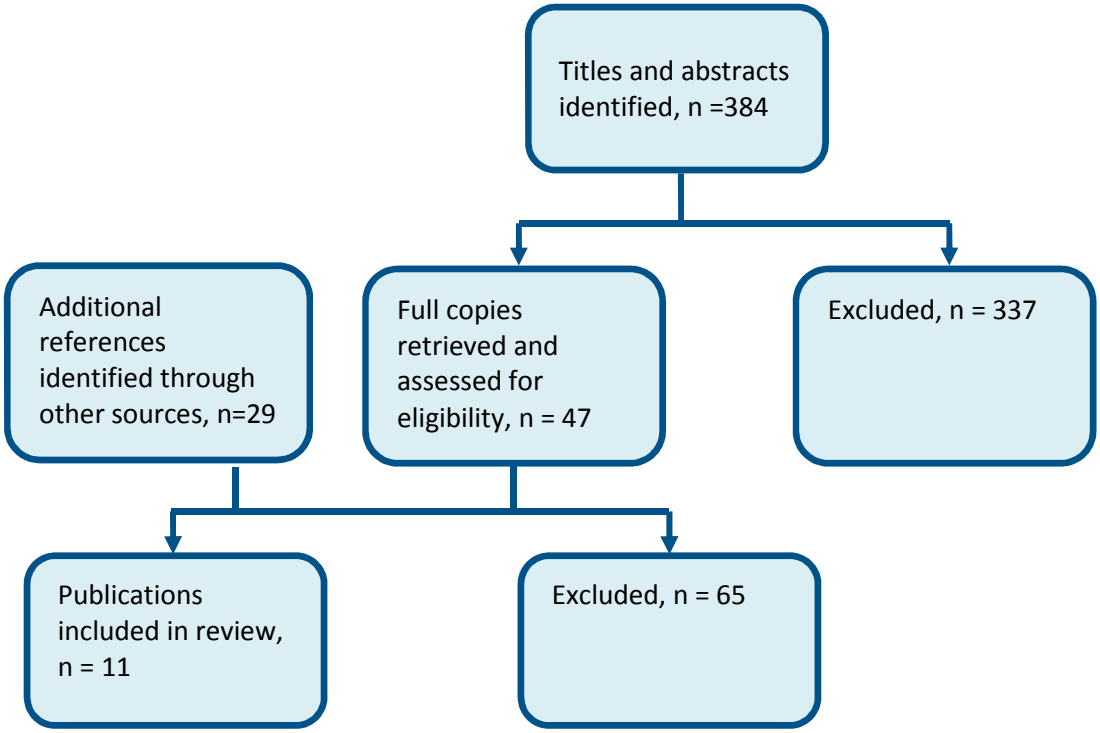
5.1.2 Likelihood of surgery

Figure 2: Flow diagram of article selection for the likelihood of surgery review



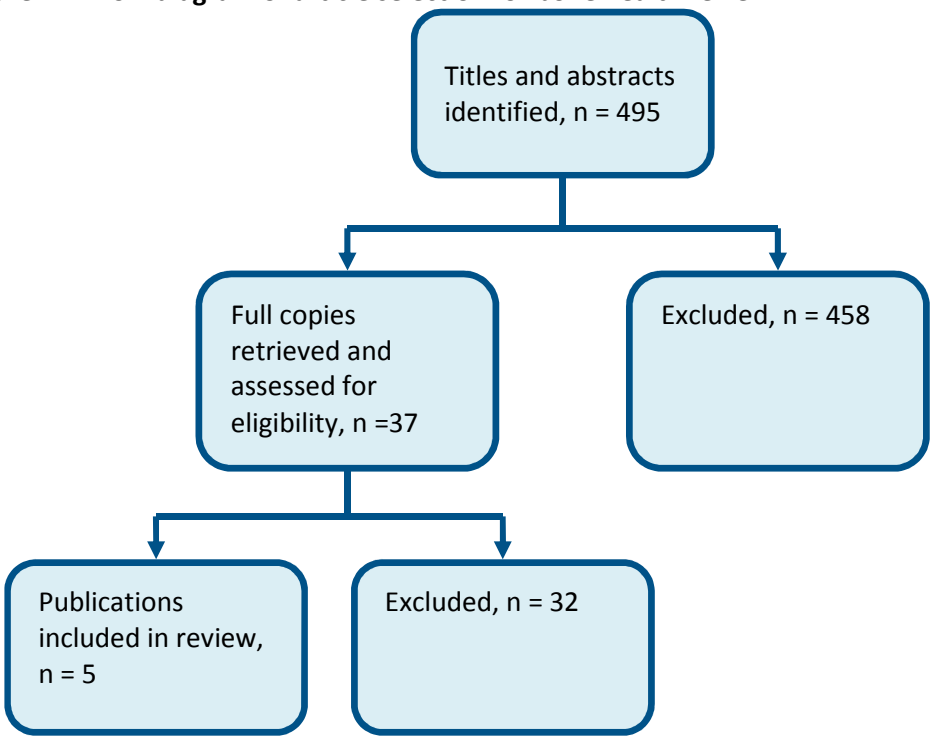
5.1.3 Pregnancy

Figure 3: Flow diagram of article selection for the pregnancy review



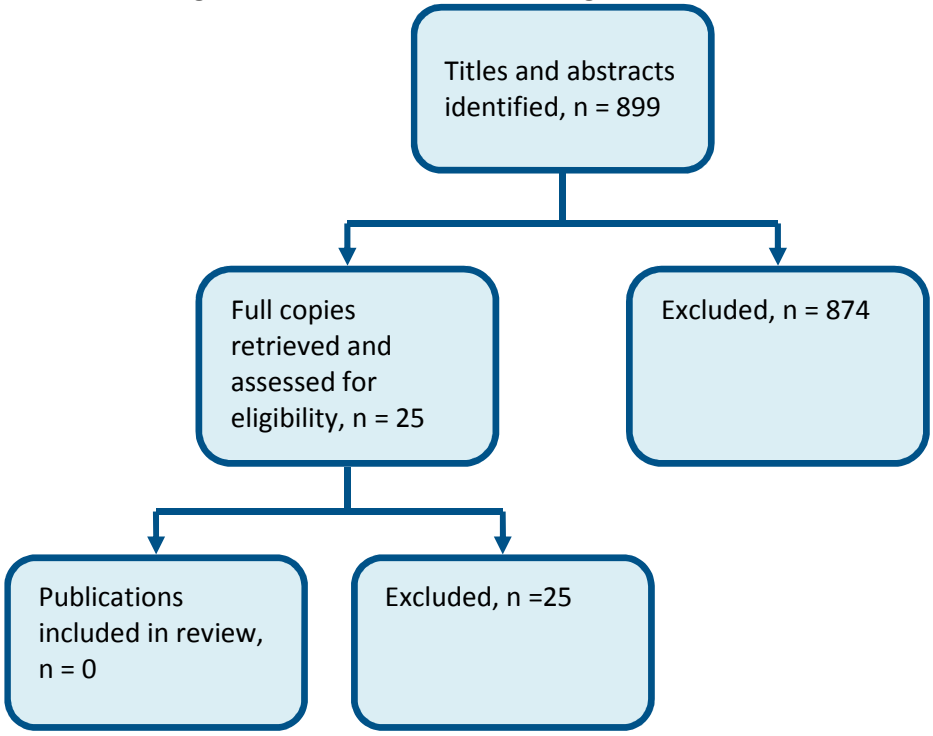
5.1.4 Monitoring – Bone health

Figure 4: Flow diagram of article selection for bone health review



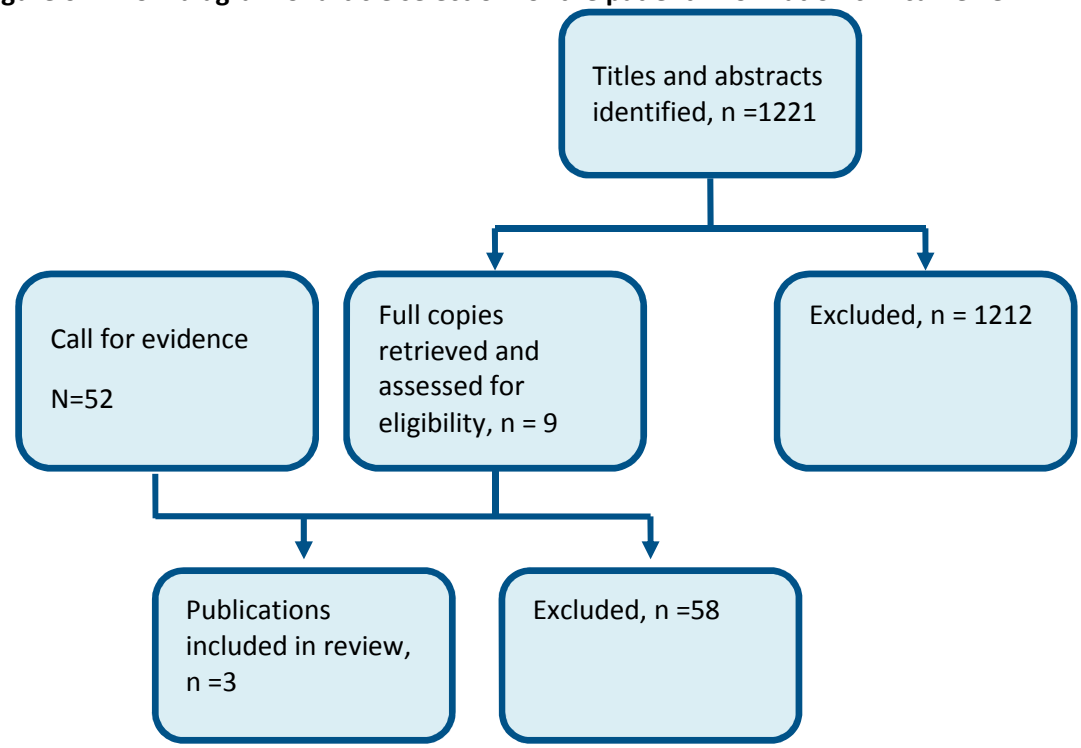
5.1.5 Monitoring – Growth in children

Figure 5: Flow diagram of article selection for the growth in children review



5.1.6 Patient information – Long and short term outcomes of surgery

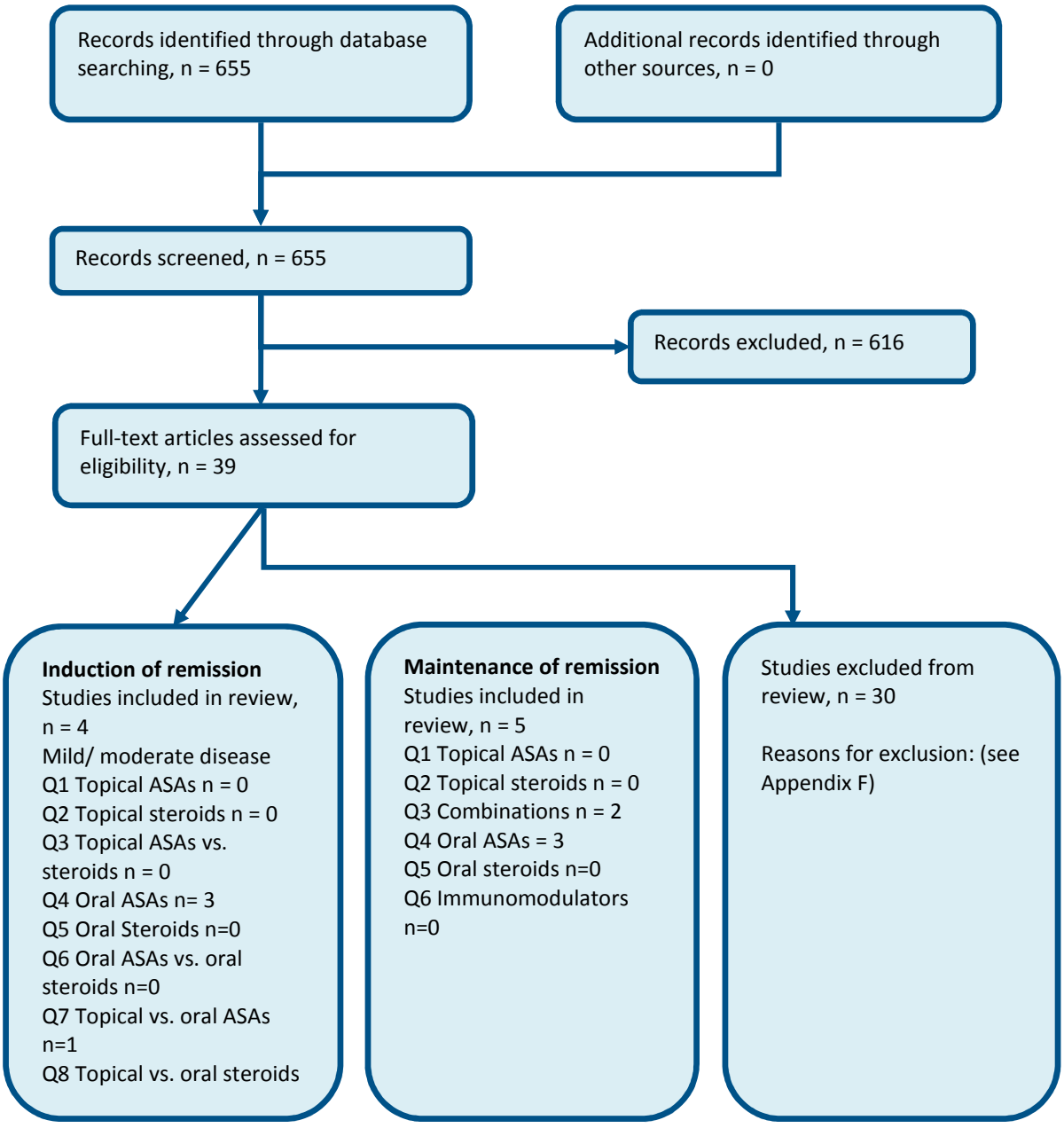
Figure 6: Flow diagram of article selection for the patient information clinical review



5.2 Economic reviews

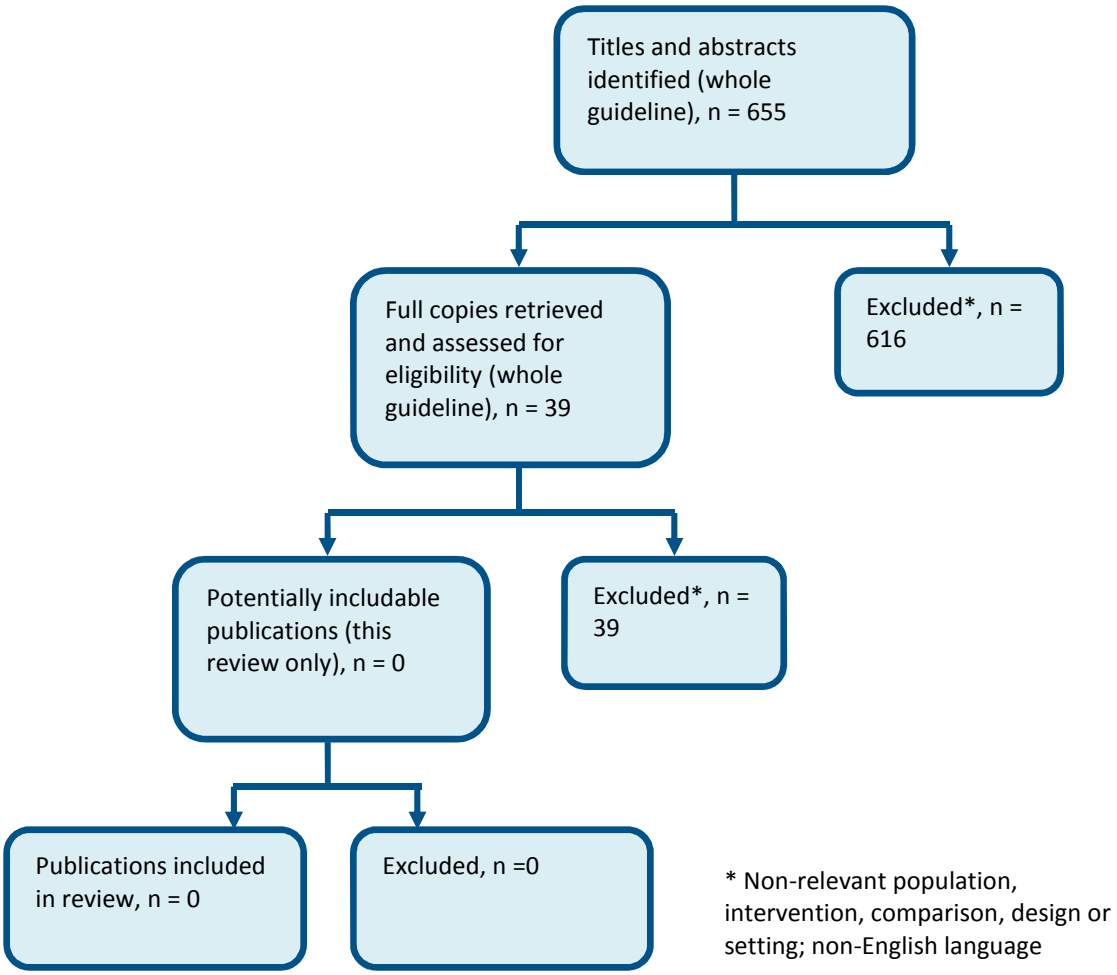
5.2.1 Induction and maintenance of remission

Figure 7: Flow diagram of article selection for the induction and maintenance of remission economic review



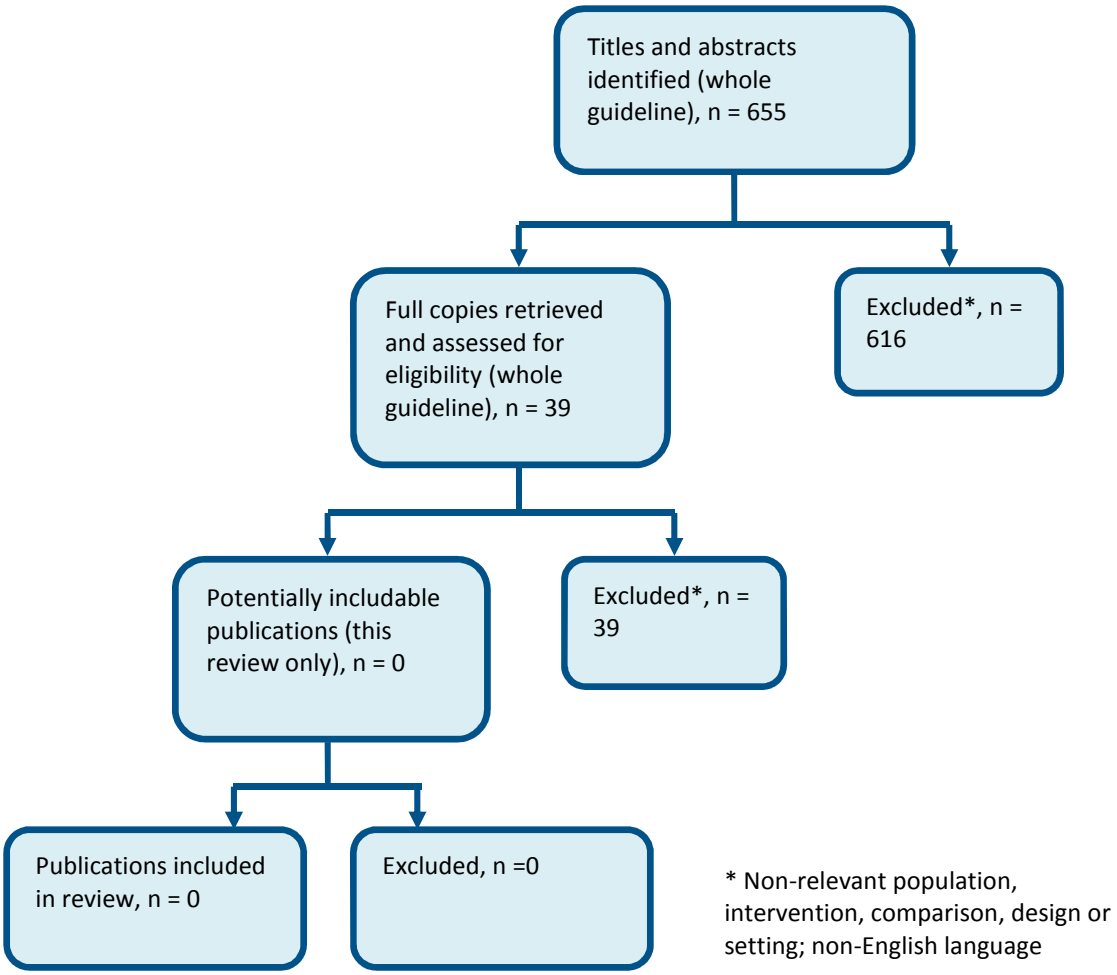
5.2.2 Likelihood of surgery

Figure 8: Flow diagram of article selection for the likelihood of surgery economic review



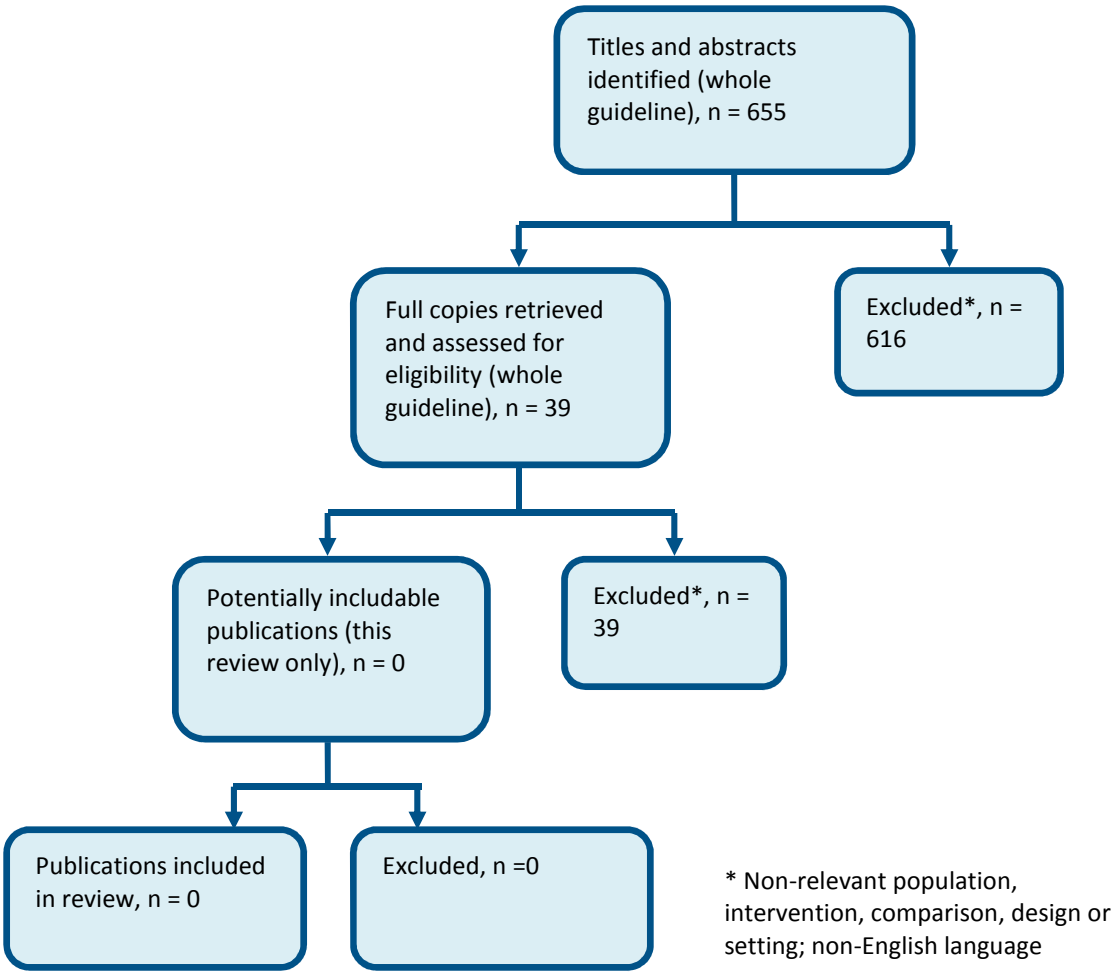
5.2.3 Pregnancy

Figure 9: Flow diagram of article selection for the pregnancy economic review



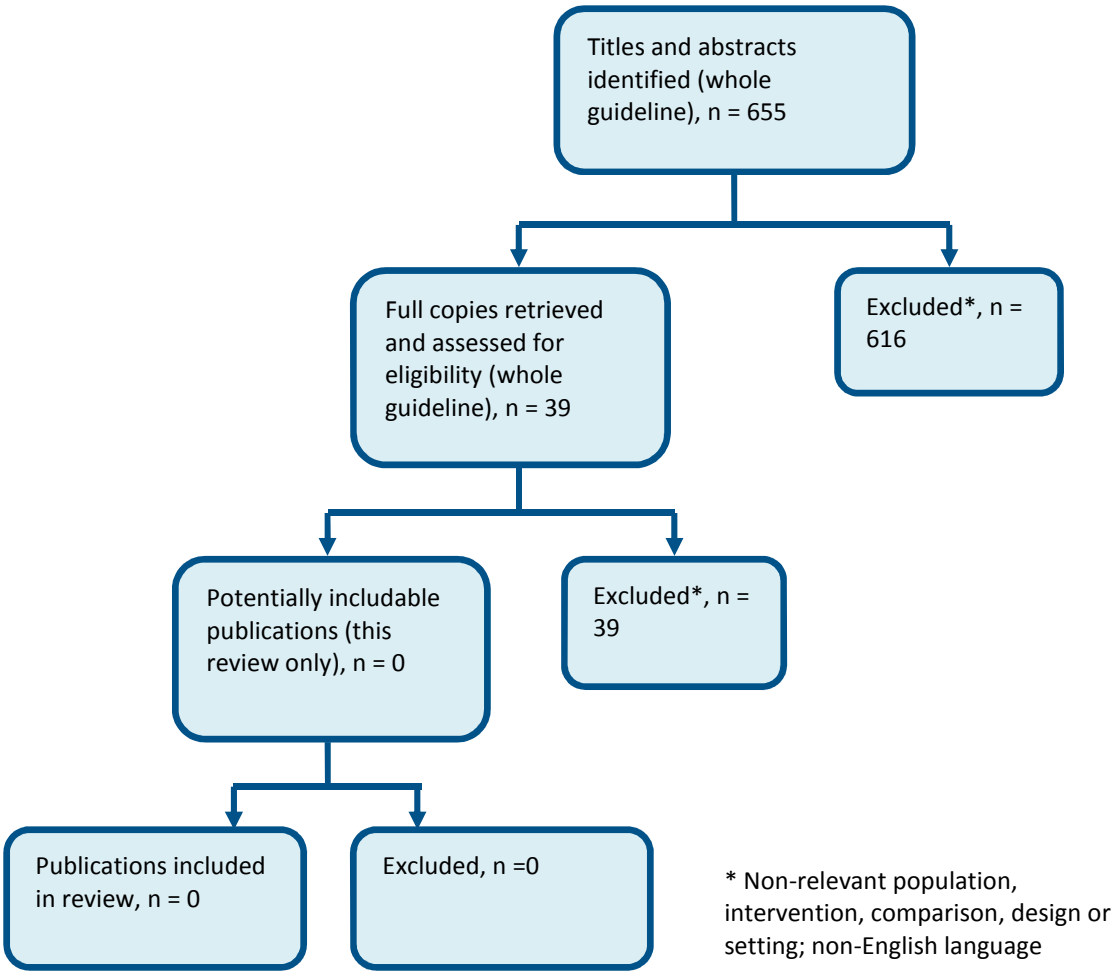
5.2.4 Monitoring – Bone health

Figure 10: Flow diagram of article selection for bone health economic review



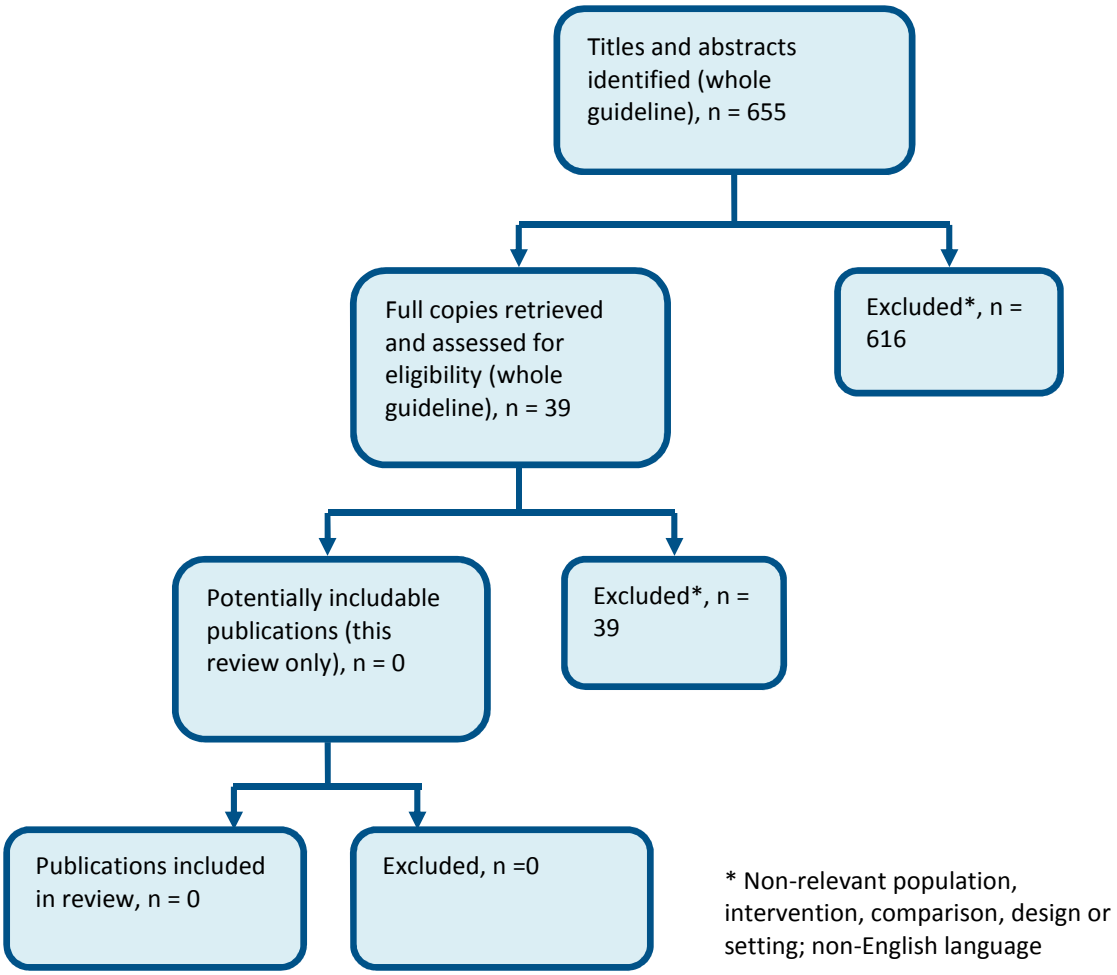
5.2.5 Monitoring – Growth in children

Figure 11: Flow diagram of article selection for the growth in children economic review



5.2.6 Patient information – Likelihood of surgery

Figure 12: Flow diagram of article selection for the patient information economic review



6 Appendix F: Excluded studies

6.1 Excluded clinical studies

Table 2: Studies excluded from the clinical review

Reference	Reason for exclusion
AKBARI2012[5]	Does not separate out for the UC population for the relationship between medication and birth outcome.
ALEXANDER2003[6]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
ALSTEAD1990[7]	Only 2 UC cases in the cohort (GDG exclusion).
ANDREOLI1987[8]	Dose used was below BNF recommended dosing.
ANGELBERGER2006[9]	Case report.
ANGELBERGER2011[10]	No separate results for UC.
ANGUS1992[11]	Fluticasone propionate is not available orally in the UK.
ANON1971[1]	Comparator not available in the UK (betamethasone 17-valerate enema).
ANON2007[4]	Not a systematic review.
ARDIZZONE1995[13]	Mesalazine used in the trial is Claversal which is not available in the UK.
ARDIZZONE2006[12]	No results given for the first 12 weeks of the trial.
AWAD1993[15]	Does not look at what information patients wanted to know about/ or prior to surgery. Reports lifestyle activities affected by ileostomy.
AZADKHAN1977[16]	None of the specified outcomes were reported. No definition given for clinical improvement.
BACH2007[17]	Not a systematic review. Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
BADALYAN2011[18]	Abstract. Cross-sectional study. Does not separate out UC from Crohn's patients.
BAIOCCO1984[19]	Large number of participants were excluded and reasons for exclusion do not seem justified. Findings are not generalisable (GDG exclusion).
BAIRD1990[20]	No information on medication taken during pregnancy.
BALDASSANO2002[21]	Background paper. Consensus recommendations.
BANSKY1987[22]	Re-entry of patients into the trial and unable to separate them from the analysis.
BARDEN1989[23]	Not an RCT.
BARON1962A[24]	Dose used was below BNF recommended dosing.

BARRENA2011[25]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
BARTON1989[26]	Measured whether height and weight were recorded by paediatricians and gastroenterologists. Does not study how often it should be done.
BASILISCO1987[27]	Sulphasalazine is not available as a liquid enema in the UK.
BATRA2010[28]	Abstract. Does not separate out UC from Crohn's patients.
BAUMGART2008[29]	Cochrane review on Tacrolimus for the induction of remission.
BEATTIE1996[30]	Not an RCT.
BECKER2009[31]	Not a systematic review.
BEEKEN1997[32]	Wrong comparison (4ASA).
BENIADA2005[33]	Paper not in English.
BENKOV1994[34]	Not an RCT.
BERGER1975[35]	Does not look at when to monitor growth. Looks at relationship between steroid use and surgery and growth.
BERGMAN2006[36]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
BERTSCHINGER1995[37]	Letter.
BIANCHIPORRO1995[38]	Chronic intermittent ulcerative colitis.
BIDDLE1988[39]	Re-entry of patients was permitted.
BISCHOFF1997[40]	No multivariate analysis.
BONDESEN1986[42]	No drug comparison. Not an RCT.
BORTOLI2007[43]	Does not separate out for the UC population for the relationship between medication and birth outcome.
BOSSA2008[44]	Wrong comparator (Erythrocyte mediated delivery of dexamethasone).
BRESCI1990[45]	Dose used was below BNF recommended dosing.
BRMS2009[46]	Does not report our outcomes. Authors contacted but no further data was provided.
BROWN2012[47]	Poster presentation abstract.
BUSH2004[49]	Does not look at the relationship of medication on birth outcome.
CAI2001[50]	Chinese. Although included in the Cochrane, insufficient information available; no details on extent of disease, trial duration and clinical improvement definition.
CAMPBELL1976[51]	Use the same participants as Jewell & Truelove, 1974 trial. Additional outcomes reported are not relevant to the scope.
CAMPIERI1980[52]	Trial duration of 3 weeks.
CAMPIERI1981[59]	Abstract.

CAMPIERI1981A[56]	No definition of remission given. No other specified outcomes reported.
CAMPIERI1984[57]	Wrong comparison (4ASA).
CAMPIERI1985[58]	Letter.
CAMPIERI1987[55]	Not randomised.
CAMPIERI1989[53]	Abstract symposium.
CAMPIERI1998[54]	Comparator not available in the UK (beclometasone dipropionate enemas).
CAPRILLI1975[60]	Idiopathic proctocolitis. Unclear if it is definitely ulcerative colitis. Unclear if the study is randomised. 35% severe UC population.
CARPENTER1964[61]	No additional data from the Dick et al. study was found.
CASANOVA2011[62]	Abstract. No separate results for UC.
CEBALLOS2008[63]	Does not look at when to monitor growth. Prevalence of growth failure and look its pattern over time.
CHANDE2007[64]	Cochrane review on Methotrexate.
CHAPMAN1986[65]	Wrong comparator (IV metronidazole).
CHEY2000[66]	Abstract. Infliximab is not included as a comparator.
CHRISTENSEN1993[67]	Wrong population (healthy children).
CHRISTENSEN1994[68]	Unclear what type of IBD the population has.
CLARKE1982[69]	Not an RCT.
CLEARY2009[70]	No separate results for UC.
COBDEN1991[71]	Rectal drips are no longer used. No definitions given for outcomes. Does not report any other outcomes.
COCCO1967[72]	Not randomised.
COELHO2009[74]	Abstract. Does not separate out for the UC population for the relationship between medication and birth outcome.
COELHO2011[73]	Only one case can be extracted from the CESAME study (GDG exclusion).
COHEN2000[75]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
COHRAN2008[76]	Cross-sectional study. Unclear if ulcerative colitis patients and unable to separate them out.
COLOMBEL1994[77]	Wrong population; Crohn's disease.
COLWELL2001[78]	Does not look at what information patients wanted to know about/ or prior to surgery. Reports complications.
CORNISH2007[79]	No separate results for UC.
COWAN1997[80]	Does not separate out UC from Crohn's patients.
DAGATA1994[81]	Not a systematic review.
DAGATA1996[84]	Not an RCT.

DALUZ2010[83]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.
DANIELSSON1992[85]	No definition of improvement given. No other specified outcomes were reported.
DAPERNO2002[86]	Not a systematic review.
DAPERNO2004[87]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.
DAS1975[88]	Not an RCT or systematic review.
DAVIS1994[89]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
DE2011[91]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Reports post operative complications.
DE2012[92]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Reviews the complications of surgery.
DECASSAN2012[90]	Systematic review. Checked included papers. They also included non RCTs.
DEW1982[94]	Abstract.
DEW1983[93]	Randomisation methods unclear.
DHAENS2010[82]	Budesonide-mezavant XL is not available in the UK.
DIAVCITRIN1998[95]	No separate results for UC.
DICKINSON1985[96]	Rescue therapy study.
DINCA1999[97]	Adult population.
DOMINITZ2002[98]	No information on medication taken during pregnancy.
DUDLEYBROWN2012[99]	Does not look at surgery. Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.
DURNO1998[100]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
EBELL1998[101]	Paper not available from UK sources.
ECKHOFF1994[102]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
EGAN1999[103]	Results are not separated out for UC and Crohn's patients.
EIDELWEIN2005[104]	Not an RCT. Infliximab is not an included comparator.

ELBAZ2005[106]	Does not separate out for the UC population for the relationship between medication and birth outcome.
ELIAKIM2007[107]	Aminosalicylate not available in the UK (Claversal).
ELMATARY2009[105]	Cochrane review. Methotrexate.
EWE1988[109]	Cross over trial. Results only given at the end of the trial.
EWE1996[108]	Paper unavailable.
FAURE1998[110]	Unclear whether they are a UC population and there are no separate results for the rectocolitis.
FEAGAN2012[111]	Systematic review has different outcomes to those used in our protocol.
FERRARI2010[112]	Abstract. Does not separate out UC from Crohn's patients.
FEURLE1988[113]	Same paper as FEURLE1989. Paper not ordered.
FISCHER1983[114]	Cross-over trial.
FISHMAN2010[115]	Self management questions; does not cover self assessment.
FISHMAN2010[115]	No relevant growth outcomes.
FLEIG1988[116]	Comparator is not available in the UK (Benzalazine).
FLORES2010[117]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
FLOURIE2012[118]	Abstract.
FOCKENS1995[119]	Dose used was below BNF recommended dosing.
FONKALARUD1996[120]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
FORD2011[122]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
FORD2011A[121]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
FORD2011D[125]	Different definition of outcomes used. Systematic review. Different protocol to the clinical review. Checked for all included papers.
FORD2012[124]	Systematic review. Checked for all included papers.
FORD2012A[123]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
FRANCELL1996[126]	Abstract. No separate results for UC.
FRANCELLA2003[127]	No separate results for UC.
FRASER2010[128]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.

FREI2006[129]	Unclear population age range. Does not separate out results for children and young people.
FRIEDMAN1986A[130]	Not a systematic review.
FRHMORGEN1980[132]	Methods are described in another paper which is in German.
FRIERI1999[131]	Patients were in remission and active UC. The results were not split. None of our specified outcomes were reported.
GANDOLFO1987[133]	Wrong comparator (4ASA).
GARASSINO2011[134]	Abstract.
GHOSH1998[136]	No separate results for ulcerative colitis patients. Decade later follow on from the BARTON1989 study.
GHOSHI1994[135]	No multivariate analysis.
GIAFFER1992[137]	Dose used was below BNF recommended dosing.
GINSBERG1988[138]	Wrong comparator (4ASA).
GINSBERG1992[139]	Wrong comparator (4ASA).
GINSBURG2006[140]	Not a systematic review.
GIONCHETT1996[141]	Cross over study. Only 7 days long for each treatment arm.
GIONCHETTI1997[144]	Aminosalicylate not available in the UK (Claversal).
GIONCHETTI1999[142]	Gel enemas are not available in the UK.
GIONCHETTI2005[143]	Comparator not available in the UK (beclometasone dipropionate enema).
GISBERT2009[145]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
GLAZIER2005[146]	Unclear if the pregnant women had UC or Crohn's disease.
GOKHALE1998[147]	Unable to separate out UC from Crohn's patients. Diagnosis not included in multivariate analysis. Does not look at when to monitor growth.
GOOD1992[148]	Abstract. Comparator not available in the UK (Rowasa).
GRAY2012[149]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
GREEN2002[150]	Dose used was below BNF recommended dosing.
GRIFFITHS2009[151]	Consensus recommendations.
GUPTA2004[152]	Does not look at risk factors. No multivariate analysis.
HABAL2012[153]	No separate results for UC.
HAHNLOSER2007[154]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.

HAIT2007[156]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
HAIT2009[155]	Does not look at when to monitor growth only reports confidence in the ability to deal with development issues.
HALPERN1991[157]	Re-entry of patients. Data presented as number of attacks.
HAMILTON1984[158]	None of the specified outcomes were reported.
HAMMOND2004[159]	Comparator not available in the UK (betamethasone).
HANAN1998[160]	Not a systematic review.
HANAUER1999[162]	Abstract.
HANAUER2000[161]	Rowasa is not available in the UK.
HANAUER2009[163]	Pooled data from other studies. It is not reported separately. Original studies are included.
HAWTHORNE1993[164]	Fluticasone propionate is not available orally in the UK.
HAWTHORNE2002[165]	Not an RCT. Abstract.
HEETUN2007[166]	Systematic review is presented for IBD patients overall. Does not separate out for the UC population.
HEIKENS2012[167]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Reports quality of life.
HERMANOWICZ1985[168]	No outcomes reported in the first 12 weeks of the study.
HETZEL1988[169]	Same study as HETZEL1986.
HEUSCHKEL2008[170]	Clinical guidelines. Consensus recommendations.
HILDEBRAND1994[171]	Does not look at when to monitor growth. Looks at height velocity and weight for height at different ages.
HILL2009[172]	Does not look at when to monitor growth. Looks at the relationship between bone age and chronological age.
HOES2009[173]	Systematic review included other chronic diseases.
HOOD2011[174]	Does not look at when to monitor growth. Compares general population to an IBD one.
HUETING2004[175]	Does not look at what information patients wanted to know about/ or prior to surgery. Reports complications.
HUSAIN2004[176]	Does not cover surgery.
HYAMS2006[177]	Not an RCT.
INCE2011[179]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.
INGRAM2005[180]	Cross-over trial.

ISMAIL2012[181]	Does not separate out UC from Crohn's patients or control for diagnosis in the multivariate analysis.
ITO2010[182]	Abstract.
JARNEROT1980[184]	Paper not in English.
JARNEROT1981[185]	No separate results for UC.
JARNEROT1981A[183]	No separate results for UC.
JARNEROT1985[186]	Not an RCT.
JAYAPRAKASH2004[187]	Case report.
JEWELL1988[188]	Paper unavailable.
JHARAP2012[189]	Abstract. No separate results for UC.
JOHNSON2004[190]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Female fertility after a surgical procedure.
KAM1996[191]	Comparator not available in the UK (Rowasa enemas).
KAMM2009A[192]	Not an RCT.
KANE2012[193]	Not an RCT.
KAPPELMAN2011A[194]	Cross-sectional study. No UC separation for relationship with steroids. No multivariate analysis.
KARAMANOLIS1996[195]	Cross over study. Only 7 days long for each treatment arm.
KELLER1997[196]	Not an RCT.
KERNER2011[197]	Abstract.
KHAN2011[198]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
KIRK1982[199]	Chronic active ulcerative colitis. Not clear that it was randomised.
KLOTZ1980[200]	Mixed Crohn's and UC patients. Results only split for remission but there is no clear definition of remission given. It does not use a UC index.
KOIVUSALO2007[202]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
KOIVUSALO2009[201]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
KORNFIELD1997[203]	No separate results for UC. Does not look at relationship with medication.
KRUIS1998[204]	Comparator not available in the UK (Claversal).
KRZESLEK2006[205]	No multivariate analysis.
KUMANA1981[206]	Paper is not available.
KUMANA1982[207]	No definition of remission. Comparator not available in the UK (beclometasone dipropionate

	enemas).
LAAKSO2012[208]	No multivariate analysis.
LAMAH2002[209]	Background paper ordered.
LAMERS1999[210]	Not a systematic review.
LANGAGERAARD2007[211]	Only 6 ulcerative colitis cases in a cohort.
LAURITSEN1988[212]	Randomisation based on PGE levels.
LECHIN1985[213]	Wrong population (severe ulcerative colitis only).
LEICKLY1986[214]	Not an RCT.
LEIFELD2011[215]	No additional data identified from original studies.
LEIGHTON2001[216]	Comment on a study.
LEIGHTON2010[217]	Abstract.
LENNARDJONES1962[218]	Wrong population (idiopathic proctitis).
LEOWARDI2010[219]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.
LEVIN2011[220]	Does not separate out the UC patients from those with unclassified IBD.
LEWIS1985[221]	Not a systematic review.
LICHTENSTEIN2008[223]	Pooled data from two RCTs which have already been included. There is subgroup analysis but the studies are not reported separately.
LICHTENSTEIN2010[222]	Mesalamine granules were Apriso which are not available in the UK yet.
LICHTIGER2009[224]	Not a systematic review.
LILLEHEI2009[225]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
LILLEHEI2010[226]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
LIN2010[227]	No information on medication taken during pregnancy.
LIU2011[228]	In Chinese.
LOFTBERG1996[229]	Budesonide preparation is not available in the UK.
LOFTUS2003[230]	Does not separate out results for children and young people.
LOPES2008[231]	Unable to separate out UC from Crohn's patients. Diagnosis not included in multivariate analysis.
LUCIDARME1997[232]	Included patients with Crohn's and idiopathic proctosigmoiditis.
MAHADEVAN2000[234]	Not randomised.
MAHADEVAN2010[233]	Abstract. Unclear if the population is only UC patients.

MAHMUD2002[235]	Mesalazine used in the trial is Asacolon which is only available in Ireland.
MAIER1985[236]	Dose used was below BNF recommended dosing.
MALCHOW2002[237]	Claversal foam is not available in the UK.
MALGARINOS2007[238]	Paper not in English.
MAMULA2002[239]	Infliximab is not an included comparator.
MANGUSO2007[240]	Comparator not available in the UK (beclometasone dipropionate enema).
MANSFIELD2002[241]	Dose used was below BNF recommended dosing.
MARION1996[242]	Abstract. No individual outcome data. No separate results for UC.
MARION1998[243]	Conference paper/ abstract.
MARKEL2008[244]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
MARKOWITZ1993[245]	Does not look at when to monitor growth. Looks at different methods of measuring growth failure and relationship with steroid use.
MARSHALL2010[247]	Cochrane review. Rectal aminosalicylates.
MARTEAU1998A[249]	Risk of double counting. Unable to categorise study type.
MARTEAU2000[248]	Mixed population of UC, Crohn's and non-specific proctitis. Results are not separated.
MARUTHACHALAM2011[251]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
MASON2011[253]	Does not look at when to monitor growth. Looks at pubertal growth over time.
MASON2011A[252]	Abstract. No risk factors reported.
MASON2012[254]	Abstract. No multivariate analysis.
MATTIOLI2011[255]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
MATZEN1991[256]	None of the specified outcomes were reported. No definition of remission given.
MCGOVERN2003[257]	Not a systematic review.
MCINTYRE1985[258]	Not randomised.
MCINTYRE1988[259]	Dose used was below BNF recommended dosing.
MEHTA2011[260]	Abstract. Does not look at when to monitor growth. Relationship with BMI and height over time.
MEIER2007[261]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.

MILLER1986[262]	Not a systematic review.
MINER2006[263]	Alicaforsen is not included in the scope.
MOCCIARO2012[264]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Compares ciclosporin and infliximab for rescue therapy.
MOGADAM1980[265]	Abstract. Does not separate out for the UC population for the relationship between medication and birth outcome.
MOGADAM1981[266]	Survey of gastroenterologists. Wrong study design.
MOLLER1978[267]	Sulphasalazine is not available as a liquid enema and at 3g.
MOLNAR2010[268]	Unclear analysis methods.
MORTELLARO2011[269]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
MOSKOVITZ2004[270]	No separate results for UC.
MOTIL1993[271]	Does not look at when to monitor growth. Relationship with disease severity, steroids and growth.
MOUNTFIELD2010[272]	Does not separate out for the UC population for the relationship between medication and birth outcome.
MULDER1988[274]	Dose used was below BNF recommended dosing.
MULDER1989[273]	Comparator not available in the UK (beclometasone dipropionate enemas).
MULDER1996[275]	Comparator not available in the UK (beclometasone dipropionate enemas).
MUNAKATA1995[276]	Dose used was below BNF recommended dosing.
MUNKHOLM2000[277]	Not a systematic review.
NAGANUMA2011[279]	Unclear population used when the relationship between medication and birth outcome were examined.
NAGY1989[280]	Cross-over trial. Wrong comparator (4ASA).
NEUMANN2012[285]	Does not look at what information patients wanted to know about/ or prior to surgery. Only looked at preference of timing of the surgery.
NEWBY2008[286]	Does not look at when to monitor growth. Looks at relationship between delay in diagnosis and growth. 1 UC patient.
NG2011[287]	Not a systematic review. Checked included papers.
NORGARD2001[288]	No separate results for UC.
NORGARD2003[290]	No separate results for UC.
NORGARD2003B[289]	Only one UC case using azathioprine.
NULMAN2011[291]	Abstract. No separate results for UC.
ODERDA1986[293]	In Spanish.
ODES1997[294]	Trial duration of 56 days.

ODONNELL1992[292]	Wrong comparator (4ASA).
ODZE1993[295]	None of the specified outcomes were reported.
ORCHARD2011[296]	Reports pooled data of ASCEND I and II trials at week 2 for moderate disease patients but only for some symptoms (not the specified outcomes). No additional data identified.
ORDING2002[297]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports female fecundity.
OSHITANI1995[298]	Reports two studies. First one reports none of our selected outcomes. The second study does not appear randomised.
PACINI1996[299]	Abstract.
PAKARINEN2009[300]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
PALMER1981[301]	Sulphasalazine is not available as a liquid enema and at 3g.
PAOLUZI2002[303]	Only compares duration of therapy.
PAPPA2006[305]	Outcome is vitamin D in the multivariate analysis and not looked at as a predictor. No multivariate analysis was carried out for UC patients due to the sample size.
PAPPA2011[304]	Recommendations for practice. Not a systematic review. No references given to support recommendations.
PAPPA2011B[306]	No relevant outcomes reported. Multivariate analysis looking at the effect of diagnosis, ESR and albumin on serum 25OHD concentration.
PATTON2010[307]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
PERRIN2012[308]	Mixed UC and Familial adenomatous polyposis population. No information given on what information the patients would have liked to have known.
PEYRINBIROULET2011[309]	Systematic review has different inclusion to the protocol. RCTs included were checked.
PHILIPS1985[310]	Does not look at what information patients wanted to know about/ or prior to surgery. Review of stomatherapy service.
PIERIK2012[311]	Abstract.
PIMPO2010[312]	Trial duration too short.
PORTER1986[314]	Does not report birth outcomes by medication subgroups.
POWELLTUCK1981[315]	3 month cross over (3 months with oral Prednisolone on alternate days, 3 months placebo). Excluded due to too short trial duration.
POWELLTUCK1986[316]	20mg dose of cortisone is not current clinical

	practice.
QIAN2004[322]	In Chinese. Dose used was below BNF recommended dosing.
QUIROS2009[323]	Includes patients with indeterminate colitis and the results are not separated.
RAATTKAINEN2011[324]	Does not separate out for the UC population for the relationship between medication and birth outcome.
RACHMILEWITZ1989[325]	Dose used was below BNF recommended dosing.
RAHIMI2008[326]	Systematic review analyses Crohn's and UC patients together.
RAMAKRISHNA1996[327]	Not an RCT.
RAO1987[329]	Not randomised.
RAO1988[328]	Abstract.
RAO1989[330]	Dose used was below BNF recommended dosing.
REINDL2007[331]	Case report.
REINISCH2012[332]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Consensus recommendations on the use of infliximab.
RHODES2008[333]	Predcol is not available in the UK.
RIIS1979[334]	Comparator is not available in the UK (Methylsulphasalazine).
RILEY1988[336]	Dose used was below BNF recommended dosing.
RILEY1989[335]	Wrong comparator (sucralfate).
RINTALA2002[337]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
ROBB2003[338]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
ROBINSON1994[339]	Same study as HANAUER1993 and has no additional outcomes. Invalidated quality of life measure.
ROBINSON1998[340]	Population includes indeterminate colitis and the results are not separated.
ROMANOS1996[341]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
ROSENBAUM2010[342]	Abstract. Does not separate out UC from Crohn's patients.
ROSENBERG1975[343]	6 month trial. None of the specified outcomes were reported in the first 12 weeks. Chronic ulcerative colitis.
RUDDELL1980[345]	None of the specified outcomes were reported.
RUSSELL2004[346]	Infliximab is not an included comparator.

RUTGEERTS1989[347]	Mesalazine used in the trial is Claversal which is not available in the UK.
RYAN2011[349]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
SAFDI1997[350]	Comparator is not available in the UK (Rowasa enema).
SAGAR2003[351]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
SAHA1998[352]	Does not look at when to monitor growth. Looks at relationship between steroid use, severity of disease and height velocity.
SAKLANI2011[354]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
SAKO2006[355]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
SALEHI2011[356]	Abstract.
SANDBERGGERTZEN1988[357]	Long term follow up of SANDBERGGERTZEN1986. Would be excluded due to trial duration.
SANDBORN1994[360]	Cyclosporin enema was used which is not included in the protocol.
SANDBORN2011[359]	Abstract. Budesonide mezavant XL is not available in the UK.
SANDBORN2011A[358]	Both included studies use Rowasa which is not available in the UK.
SANDS2001[361]	Infliximab is not included as a comparator.
SATHYANARAYANA2004[362]	Not a systematic review.
SCHADE1984[363]	No comparator data for relationship of birth outcomes and medical treatment.
SCHREIBER2008[364]	Abstract.
SCHREIBER2008A[365]	Abstract.
SELBY1984[367]	Wrong comparator (4ASA).
SELBY1985[366]	Olsalazine is no longer available in a rectal preparation.
SENAGORE1992[368]	Included patients with idiopathic proctosigmoiditis.
SHAMBERGER1999[370]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
SHARMA1992[371]	Wrong comparator (4ASA).
SHERLOCK2010[372]	Cochrane review. Budesonide.
SHIBOLET2005[374]	Cochrane review. Cyclosporin.

SHIM2011[375]	No separate results for UC.
SOLOMON2012A[376]	Data not based on RCTs.
SOMERVILLE1985[377]	Abstract.
STAVLO2003[379]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
SUBRAMANIAN2006[380]	Background paper.
SUTHERLAND1987[383]	Comparator is not available in the UK (Rowasa).
SUTHERLAND1987A[381]	Comparator is not available in the UK (Rowasa).
SUTHERLAND1987B[382]	Thought to be a pilot study and includes the same patients as SUTHERLAND1987.
SUTHERLAND1990[384]	Comparator is not available in the UK (Rowasa).
SWINBURN2011/12[385,386]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Reports quality of life.
SYLVESTER2007[387]	No multivariate analysis.
SZUMERA2009[388]	Abstract. Unclear age range. Does not separate out UC from Crohn's patients. Does not look like any multivariate analysis has been done.
TAKAO1998[389]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
TALLEY2011[390]	Systematic review. Different protocol to the clinical review. Checked for all included papers. No meta-analysis.
THOMSEN1994[391]	None of our selected outcomes were reported. AEs are said not to be significantly different but there is no data to support this.
TIMMER2012[392]	Cochrane review. Azathioprine and mercaptopurine.
TOLIA1989[393]	Not an RCT.
TOMITA2012[394]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
TONG2010[395]	Wrong comparator (Chinese medicine).
TOTTRUP2012[396]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery.
TRALLORI1995A[398]	Paper not in English.
TREEM1995[399]	Not an RCT.
TRIANTAFILLIDIS2007[400]	No separate results for UC.
TRUELOVE1955[404]	Cortisone 100mg not available in the UK.
TRUELOVE1958[402]	Unclear methods. Unable to calculate the hazard ratio. No other outcomes reported.
TRUELOVE1960[401]	Re-entry of patients into the trial.

TRUELOVE1962[403]	Hydrocortisone rectal drips are not used/ available in the UK. Only comes in a foam enema.
TULCHINSKY2010[406]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the functional outcomes and quality of life post surgical procedures.
TURNER2007[408]	Systematic review includes non RCTs. Different protocol to the clinical review. Checked for all included papers.
TURNER2011[407]	Systematic review includes non RCTs. Different protocol to the clinical review. Checked for all included papers.
TURSI2004[409]	Dose used was below BNF recommended dosing.
TZIVRAS1997[410]	Correspondence/ abstract.
VANDERHEIDE1988[411]	Comparator not available in the UK (beclometasone dipropionate).
VANDIEREN2009[412]	Phase 1 study.
VANHEES1980[413]	Wrong population (idiopathic proctitis).
VANHOGEZAND1988[414]	Wrong population (idiopathic proctitis).
VANSCHAIK2008[415]	Does not separate out results for children and young people.
VANTONGEREN1980[416]	Abstract.
VERNIA2000[418]	Wrong comparator (sodium butyrate).
VERNIA2003[417]	Wrong comparator (fatty acid in combination with an ASA).
VIHINEN2008A[419]	Does not separate out UC from Crohn's patients.
VONSCHEVEN2006[420]	Does not separate out UC from Crohn's patients.
WALTHER2006[421]	For the relationship with steroids use, does not separate out UC from Crohn's patients.
WATKINSON1958[422]	Re-entry of patients.
WEWER2005[423]	Does not report what long/short term outcomes the patient's wished they had known/ been told about prior to surgery. Only reports the outcomes of surgical procedures.
WIERSMA2004[424]	Not an RCT.
WILLOUGHBY1980[427]	None of the specified outcomes were reported
WILLOUGHBY1980A[428]	Inclusion criteria were married women, introducing selection bias. Results not generalisable.
WILLOUGHBY1988[426]	Dose used was below BNF recommended dosing.
WILSON2010[429]	Systematic review. Different protocol to the clinical review. Checked for all included papers.
WINTER1997[430]	Letter.
WISKIN2010[431]	Does not look at when to monitor growth. Focus is on relationship of lean mass and ulcerative colitis. Abstract.

WISKIN2011[432]	Does not look at when to monitor growth. Looks at relationship of height, weight and body composition of IBD patients.
WITTS1954[433]	Not in English.
WONG2010[434]	Does not look at when to monitor growth. Looks at relationship between insulin like growth factor and growth.
WRIGHT1999[435]	Wrong comparator (sucralfate).
YARLAS2011[437]	Abstract.
ZAITOUN1991[438]	None of our specified outcomes were reported.
ZALI2006[439]	Adult population (17-75 years).

6.2 Excluded economic studies

Reference	Reason for exclusion
ANON2000[2]	Non relevant comparator.
ANON2000A[3]	Non relevant comparator.
ASSASI2009[14]	Non relevant comparator.
BODGER1996[41]	Review.
BRYAN2008[48]	Non relevant comparator.
HYDE2009[178]	Non relevant comparator.
MARSHALL1997[246]	Not economic study.
MARTIN1983[250]	Non relevant comparator.
MUNKHOLM2010[278]	Not economic study.
NATIONALHORIZONSCANNINGCENTRE2009[281]	Non relevant comparator.
NATIONALINSTITUTEFORHEALTHANDCLINICALEXCELLENCE2008[282]	Non relevant comparator.
NATIONALINSTITUTEFORHEALTHANDCLINICALEXCELLENCE2008A[283]	Non relevant comparator.
PANES2007[302]	Non relevant comparator.
PORITZ2005[313]	Not economic study.
PRENZLER2011[317]	The model structure and all inputs except costs are based on the Brereton study (included in the economic review). The costs in the model are specific to the German health system. Therefore excluded because similar UK study available.
PRIEST2006[318]	Not economic study.
PROVENZALE1998[320]	Non relevant comparator.
PROVENZALE2001[319]	Non relevant comparator.
PUNEKAR2010[321]	Non relevant comparator.
RUBENSTEIN2009[344]	Non relevant comparator.
RUTTER2006[348]	Non relevant comparator.
SAINI2012[353]	Analysis includes comparator that is not reviewed in this guideline.

Reference	Reason for exclusion
	An original economic analysis has been conducted for this guideline which has greater applicability due to resource use and cost data based on the UK health system.
SHAH2011[369]	Not economic study.
SHERLOCK1996[373]	Non relevant comparator.
SONU2010[378]	Not economic study.
TRALLORI1995[397]	Not full economic evaluation.
TSAI2008[405]	Non relevant comparator.
WILLIAMS2000[425]	Non relevant comparator.
XIE2009[436]	Non relevant comparator.
ZISMAN2007[440]	Non relevant comparator.

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