

Crohn's disease

Appendix D

Clinical Guideline <...>

Search strategies

10 October 2012

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

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

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1 Search strategies

1.1 Population search strategies

Medline search terms

1.	exp crohn disease/
2.	((crohn or crohn's or crohns) adj2 (disease* or colitis)).ti,ab,hw.
3.	((ileitis or enteritis) adj2 (terminal or regional)).ti,ab,hw.
4.	((colitis or enteritis) adj2 granuloma*).ti,ab,hw.
5.	ileocoli*.ti,ab,hw.
6.	(epithelioid adj2 granuloma*).ti,ab,hw.
7.	exp inflammatory bowel diseases/
8.	(inflamm* adj2 bowel).ti,ab,hw.
9.	or/1-8

Embase search terms

1.	exp crohn disease/
2.	((crohn or crohn's or crohns) adj2 (disease* or colitis)).ti,ab,hw.
3.	((ileitis or enteritis) adj2 (terminal or regional)).ti,ab,hw.
4.	((colitis or enteritis) adj2 granuloma*).ti,ab,hw.
5.	ileocoli*.ti,ab,hw.
6.	(epithelioid adj2 granuloma*).ti,ab,hw.
7.	(inflamm* adj2 bowel).ti,ab,hw.
8.	or/1-7

Cinahl search terms

S1.	(MH "Crohn Disease") or (MH "Ileitis+") or (MH "Inflammatory Bowel Diseases+")
S2.	crohn* or colitis
S3.	regional and (ileitis or enteritis)
S4.	terminal and (ileitis or enteritis)
S5.	colitis n2 granuloma*
S6.	enteritis n2 granuloma*
S7.	epithelioid n2 granuloma*
S8.	ileocoli*
S9.	inflamm* n2 bowel
S10.	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9

Cochrane search terms

#1.	MeSH descriptor Crohn Disease explode all trees
#2.	((crohn or crohn's or crohns) near/2 (disease* or colitis)):ti,ab,kw
#3.	((ileitis or enteritis) near/2 (terminal or regional)):ti,ab,kw
#4.	((colitis or enteritis) and granuloma*):ti,ab,kw
#5.	ileocoli*:ti,ab,kw
#6.	(epithelioid near/2 granuloma*):ti,ab,kw
#7.	MeSH descriptor Inflammatory Bowel Diseases explode all trees

#8.	(inflamm* near/2 bowel):ti,ab,kw
#9.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)

1.2 Study filter search terms

1.2.1 Systematic review (SR) search terms

Medline search terms

1.	review.pt. or review.ti. or "review"/
2.	(systematic* or evidence* or methodol* or quantitativ* or analys* or assessment*).ti,sh,ab.
3.	1 and 2
4.	meta-analysis.pt.
5.	meta-analysis/
6.	meta-analysis as topic/
7.	"systematic review"/
8.	(meta-analy* or metanaly* or metaanaly* or meta analy*).ti,ab.
9.	((systematic* or evidence* or methodol* or quantitativ*) adj5 (review* or survey* or overview*)).ti,ab,sh.
10.	((pool* or combined or combining) adj2 (data or trials or studies or results)).ti,ab.
11.	or/3-10

Embase search terms

1.	review.pt. or review.ti. or "review"/
2.	(systematic* or evidence* or methodol* or quantitativ* or analys* or assessment*).ti,sh,ab.
3.	1 and 2
4.	meta-analysis.pt.
5.	meta-analysis/
6.	meta-analysis as topic/
7.	"systematic review"/
8.	(meta-analy* or metanaly* or metaanaly* or meta analy*).ti,ab.
9.	((systematic* or evidence* or methodol* or quantitativ*) adj5 (review* or survey* or overview*)).ti,ab,sh.
10.	((pool* or combined or combining) adj2 (data or trials or studies or results)).ti,ab.
11.	or/3-10

1.2.2 Randomized controlled trial (RCT) search terms

Medline search terms

1.	randomized controlled trial*.pt,sh.
2.	clinical trial*.pt,sh.
3.	random allocation/
4.	double blind method/
5.	single blind method/
6.	((clin* or control*) adj5 trial*).ti,ab.
7.	((singl* or doubl* or trebl* or tripl*) adj25 (blind* or mask*)).ti,ab.
8.	placebos/
9.	placebo*.ti,ab.

10.	random*.ti,ab.
11.	(volunteer* or "control group" or controls or prospective*).ti,ab.
12.	research design/
13.	or/1-12

Embase search terms

1.	exp randomized controlled trial/
2.	(random* or placebo*).ti,ab.
3.	((singl* or doubl* or trebl* or tripl*) adj25 (blind* or mask*)).ti,ab.
4.	(clin* adj25 trial*).ti,ab.
5.	exp comparative study/
6.	exp evaluation/
7.	exp follow up/
8.	exp prospective study/
9.	(control* or prospective* or volunteer*).ti,ab.
10.	or/1-9

1.2.3 Combined RCT and observational studies search terms**Medline search terms**

1.	randomized controlled trial*.pt,sh.
2.	clinical trial*.pt,sh.
3.	random allocation/
4.	double blind method/
5.	single blind method/
6.	((clin* or control*) adj5 trial*).ti,ab.
7.	((singl* or doubl* or trebl* or tripl*) adj25 (blind* or mask*)).ti,ab.
8.	placebos/
9.	placebo*.ti,ab.
10.	random*.ti,ab.
11.	(volunteer* or "control group" or controls or prospective*).ti,ab.
12.	research design/ or comparative study/
13.	exp clinical trial/
14.	exp clinical trials as topic/
15.	exp evaluation studies/ or follow-up studies/ or prospective studies/
16.	exp epidemiological studies/
17.	cohort stud*.ti,ab.
18.	case control stud*.ti,ab.
19.	((crossover or cross-over or cross over) adj2 (design* or stud* or procedure* or trial*)).ti,ab.
20.	or/1-19

Embase search terms

1.	exp randomized controlled trial/ or controlled study/
2.	clinical study/ or major clinical study/ or clinical trial/ or phase 1 clinical trial/ or phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/
3.	placebo/ or "double blind procedure"/ or randomization/
4.	(random* or placebo*).ti,ab.

5.	((singl* or doubl* or trebl* or tripl*) adj25 (blind* or mask*)).ti,ab.
6.	(clin* adj25 trial*).ti,ab.
7.	exp comparative study/
8.	exp follow up/
9.	exp prospective study/
10.	exp Longitudinal Study/
11.	exp Cohort Analysis/
12.	cohort studies.ti,ab.
13.	(control* or prospective* or volunteer*).ti,ab.
14.	(cross adj2 over adj2 (study or design)).ti,ab.
15.	crossover procedure/
16.	or/1-15

1.2.4 Cohort studies search terms

Medline search terms

1.	exp cohort studies/
2.	cohort*.tw.
3.	controlled clinical trial.pt.
4.	epidemiologic studies/
5.	or/1-4

Embase search terms

1.	exp cohort analysis/
2.	exp longitudinal study/
3.	exp prospective study/
4.	exp follow up/
5.	cohort*.tw.
6.	or/1-5

1.2.5 Health economic search terms

Medline search terms

1.	exp "costs and cost analysis"/
2.	economics/
3.	exp economics, hospital/
4.	exp economics, medical/
5.	exp economics, nursing/
6.	exp economics, pharmaceutical/
7.	exp "fees and charges"/
8.	exp budgets/
9.	ec.fs.
10.	(economic* or pharmaco-economic* or price* or pricing* or cost* or budget*).ti,ab.
11.	(value adj2 (money or monetary)).ti,ab.
12.	(expenditure not energy).ti,ab.
13.	or/1-12
14.	((metabolic or energy or oxygen) adj1 cost*).ti,ab.

15.	13 not 14
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Embase search terms

1.	health economics/
2.	exp economic evaluation/
3.	exp health care cost/
4.	exp pharmacoeconomics/
5.	exp fee/
6.	budget/
7.	(economic* or pharmacoeconomic* or cost* or price* or pricing* or budget*).ti,ab.
8.	(value adj2 (money or monetary*)).ti,ab.
9.	(expenditure not energy).ti,ab.
10.	or/1-9
11.	((metabolic or energy or oxygen) adj1 cost*).ti,ab.
12.	10 not 11

1.2.6 Quality of life search terms**Medline search terms**

1.	exp quality-adjusted life years/
2.	quality adjusted life.tw.
3.	exp "quality of life"/
4.	value of life/
5.	(qaly* or qald* or qale* or qtime*).tw.
6.	disability adjusted life.tw.
7.	daly*.tw.
8.	health status indicators/
9.	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
10.	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
11.	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
12.	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
13.	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
14.	(euroqol or euro qol or eq5d or eq 5d).tw.
15.	(hql or hqol or h qol or hrqol or hr qol).tw.
16.	(hye or hyes).tw.
17.	health* year* equivalent*.tw.
18.	health utilit*.tw.
19.	(hui or hui1 or hui2 or hui3).tw.
20.	disutili*.tw.
21.	rosser.tw.
22.	quality of well?being.tw.
23.	qwb.tw.

24.	willingness to pay.tw.
25.	standard gamble*.tw.
26.	time trade off.tw.
27.	time tradeoff.tw.
28.	tto.tw.
29.	or/1-28

Embase search terms

1.	quality adjusted life year/
2.	quality of life/
3.	(qaly* or qald* or qale* or qtime*).tw.
4.	daly*.tw.
5.	quality adjusted life.tw.
6.	disability adjusted life.tw.
7.	(sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
8.	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
9.	(sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
10.	(sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
11.	(sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
12.	(euroqol or euro qol or eq5d or eq 5d).tw.
13.	(hql or hqol or h qol or hrqol or hr qol).tw.
14.	(hye or hyes).tw.
15.	health* year* equivalent*.tw.
16.	health utilit*.tw.
17.	(hui or hui1 or hui2 or hui3).tw.
18.	disutili*.tw.
19.	rosser.tw.
20.	quality of well?being.tw.
21.	qwb.tw.
22.	willingness to pay.tw.
23.	standard gamble*.tw.
24.	time trade off.tw.
25.	time tradeoff.tw.
26.	tto.tw.
27.	or/1-26

1.2.7 Excluded study designs and publication types search terms

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

Medline search terms

1.	letter.pt.
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2.	letter/
3.	letter*/
4.	editorial.pt.
5.	historical article.pt.
6.	anecdote.pt.
7.	commentary.pt.
8.	note.pt.
9.	case report/
10.	case report*.pt.
11.	case study/
12.	case study.pt.
13.	exp animal/ not human/
14.	nonhuman/
15.	exp animal studies/
16.	animals, laboratory/
17.	exp experimental animal/
18.	exp animal experiment/
19.	exp animal model/
20.	exp rodentia/
21.	exp rodents/
22.	exp rodent/
23.	or/1-22

Embase search terms

1.	letter.pt.
2.	letter/
3.	letter*/
4.	editorial.pt.
5.	historical article.pt.
6.	anecdote.pt.
7.	commentary.pt.
8.	note.pt.
9.	case report/
10.	case report*.pt.
11.	case study/
12.	case study.pt.
13.	exp animal/ not human/
14.	nonhuman/
15.	exp animal studies/
16.	animals, laboratory/
17.	exp experimental animal/
18.	exp animal experiment/
19.	exp animal model/
20.	exp rodentia/
21.	exp rodents/

22.	exp rodent/
23.	conference.pt.
24.	or/1-23

1.3 Searches for specific questions

1.3.1 Conventional glucocorticosteroid for induction and maintenance of remission

Q.1: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of conventional glucocorticosteroid treatment for induction of remission

1.1.1 compared with placebo?

1.1.2 compared with 5-aminosalicylate (5-ASA) treatment?

1.2 *plus* 5-ASA treatment compared with placebo?

This search was carried out to update a Cochrane review (Benchimol, 2008).

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 and children diagnosed with Crohn's disease	Conventional glucocorticosteroid	Placebo or 5-aminosalicylates	SRs, RCTs, standard exclusions (Embase only)	2008 to current

Medline search terms

1.	glucocorticoids/
2.	dexamethasone isonicotinate/ or dexamethasone/
3.	fluprednisolone/
4.	methylprednisolone hemisuccinate/ or methylprednisolone/
5.	prednisolone/
6.	prednisone/
7.	hydrocortisone/
8.	cortisone/
9.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
10.	(beclo methasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or flucortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone).ti,ab,hw.
11.	or/1-10
12.	exp placebos/ or (placebo* or sham* or dummy*).ti,ab,hw.
13.	exp mesalamine/ or ("5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicylate* or 5asa or pentasa or mesalamine or asacol).ti,ab,hw.
14.	exp sulfasalazine/ or (sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.

15.	or/12-14
16.	11 and 15

Embase search terms

1.	glucocorticoids/
2.	dexamethasone isonicotinate/ or dexamethasone/
3.	fluprednisolone/
4.	methylprednisolone hemisuccinate/ or methylprednisolone/
5.	prednisolone/
6.	prednisone/
7.	hydrocortisone/
8.	cortisone/
9.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
10.	or/1-9
11.	exp placebos/ or (placebo* or sham* or dummy*).ti,ab,hw.
12.	exp mesalamine/ or ("5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicylate* or 5asa or pentasa or mesalamine or asacol).ti,ab,hw.
13.	exp sulfasalazine/ or (sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.
14.	or/11-13
15.	10 and 14

Cinahl search terms

S1.	(mh "glucocorticoids+")
S2.	(mh "dexamethasone")
S3.	"dexamethasone isonicotinate"
S4.	"fluprednisolone"
S5.	"methylprednisolone hemisuccinate"
S6.	(mh "methylprednisolone")
S7.	(mh "prednisolone")
S8.	(mh "prednisone")
S9.	(mh "hydrocortisone")
S10.	(mh "cortisone")
S11.	methylprednisone
S12.	prednisolone n1 therapeutic
S13.	prednisone n1 therapeutic
S14.	cortisone n1 therapeutic
S15.	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14
S16.	(mh "placebos")
S17.	placebo* or sham* or dummy*
S18.	(mh "mesalamine")
S19.	"5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicylate* or 5asa or pentasa or mesalamine or asacol
S20.	(mh "sulfasalazine")
S21.	sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*
S22.	s16 or s17 or s18 or s19 or s20 or s21

S23.	s15 and s22
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Cochrane search terms

#1.	MeSH descriptor Glucocorticoids explode all trees
#2.	beclomethasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or flucortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone:ti,ab,kw
#3.	MeSH descriptor Dexamethasone explode all trees
#4.	MeSH descriptor Dexamethasone Isonicotinate explode all trees
#5.	MeSH descriptor Fluprednisolone explode all trees
#6.	MeSH descriptor Methylprednisolone explode all trees
#7.	MeSH descriptor Methylprednisolone Hemisuccinate explode all trees
#8.	MeSH descriptor Prednisone explode all trees
#9.	MeSH descriptor Prednisolone explode all trees
#10.	MeSH descriptor Hydrocortisone explode all trees
#11.	MeSH descriptor Cortisone explode all trees
#12.	(methylprednisone or ((prednisolone or prednisone or cortisone) near/1 therapeutic)):ti,ab,kw
#13.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14.	MeSH descriptor Placebos explode all trees
#15.	(placebo* or sham* or dummy*):ti,ab,kw
#16.	MeSH descriptor Mesalamine explode all trees
#17.	("5-aminosalicylic"* or "5-aminosalicylate"* or "5-ASA" or 5aminosalicylic* or 5aminosalicylate* or 5ASA or pentasa or mesalamine or asacol):ti,ab,kw
#18.	MeSH descriptor Sulfasalazine explode all trees
#19.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*):ti,ab,kw
#20.	(#14 OR #15 OR #16 OR #17 OR #18 OR #19)
#21.	(#13 AND #20)

Q.1 (cont): In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of conventional glucocorticosteroid treatment for induction of remission

- 1.3** compared with azathioprine or mercaptopurine (AZA/MP)?
- 1.4** *plus* azathioprine or mercaptopurine (AZA/MP) compared with conventional glucocorticosteroid treatment *plus* placebo?
- 1.5** compared with methotrexate?
- 1.6** *plus* methotrexate compared with conventional glucocorticosteroid treatment *plus* placebo?

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 and children	Conventional	Azathioprine,	SRs, RCTs	All available dates

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
diagnosed with Crohn's disease	glucocorticosteroid	mercaptopurine or methotrexate	(Embase only)	(see Table 1)

Medline search terms

1.	glucocorticoids/
2.	dexamethasone isonicotinate/ or dexamethasone/
3.	fluprednisolone/
4.	methylprednisolone hemisuccinate/ or methylprednisolone/
5.	prednisolone/
6.	prednisone/
7.	hydrocortisone/
8.	cortisone/
9.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
10.	(beclo methasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or flucortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone).ti,ab,hw.
11.	or/1-10
12.	methotrexate/
13.	methotrexate.ti,ab.
14.	6-mercaptopurine/
15.	mercaptopurine.ti,ab.
16.	azathioprine/
17.	(azathioprine or imuran).ti,ab.
18.	or/12-17
19.	11 and 18

Embase search terms

1.	glucocorticoids/
2.	dexamethasone isonicotinate/ or dexamethasone/
3.	fluprednisolone/
4.	methylprednisolone hemisuccinate/ or methylprednisolone/
5.	prednisolone/
6.	prednisone/
7.	hydrocortisone/
8.	cortisone/
9.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
10.	or/1-9
11.	methotrexate/
12.	methotrexate.ti,ab.
13.	mercaptopurine/

14.	mercaptapurine.ti,ab.
15.	azathioprine/
16.	(azathioprine or imuran).ti,ab.
17.	or/11-16
18.	10 and 17

Cinahl search terms

S1.	(mh "glucocorticoids+")
S2.	(mh "dexamethasone")
S3.	"dexamethasone isonicotinate"
S4.	"fluprednisolone"
S5.	"methylprednisolone hemisuccinate"
S6.	(mh "methylprednisolone")
S7.	(mh "prednisolone")
S8.	(mh "prednisone")
S9.	(mh "hydrocortisone")
S10.	(mh "cortisone")
S11.	methylprednisone
S12.	prednisolone n1 therapeutic
S13.	prednisone n1 therapeutic
S14.	cortisone n1 therapeutic
S15.	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14
S16.	methotrexate or mercaptopurine or azathioprine or imuran
S17.	s15 and s16

Cochrane search terms

#1.	MeSH descriptor Glucocorticoids explode all trees
#2.	beclomethasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone:ti,ab,kw
#3.	MeSH descriptor Dexamethasone explode all trees
#4.	MeSH descriptor Dexamethasone Isonicotinate explode all trees
#5.	MeSH descriptor Fluprednisolone explode all trees
#6.	MeSH descriptor Methylprednisolone explode all trees
#7.	MeSH descriptor Methylprednisolone Hemisuccinate explode all trees
#8.	MeSH descriptor Prednisone explode all trees
#9.	MeSH descriptor Prednisolone explode all trees
#10.	MeSH descriptor Hydrocortisone explode all trees
#11.	MeSH descriptor Cortisone explode all trees
#12.	(methylprednisone or ((prednisolone or prednisone or cortisone) near/1 therapeutic)):ti,ab,kw
#13.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
#14.	methotrexate or mercaptopurine or azathioprine or imuran:ti,ab,kw

#15.	(#13 AND #14)
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Q.7: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of conventional glucocorticosteroid treatment for maintenance of remission for 12 months or longer

- 7.1** compared with placebo?
- 7.2** compared with 5-aminosalicylate (5-ASA) treatment?
- 7.3** *plus* 5-ASA treatment with conventional glucocorticosteroid *plus* placebo ?
- 7.4** compared with azathioprine or mercaptopurine (AZA/MP)?
- 7.5** *plus* azathioprine or mercaptopurine compared with conventional glucocorticosteroid treatment *plus* placebo?
- 7.6** methotrexate?

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 and children diagnosed with Crohn's disease	Conventional glucocorticosteroid	None	SRs, RCTs, standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	glucocorticoids/
2.	dexamethasone isonicotinate/ or dexamethasone/
3.	fluprednisolone/
4.	methylprednisolone hemisuccinate/ or methylprednisolone/
5.	prednisolone/
6.	prednisone/
7.	hydrocortisone/
8.	cortisone/
9.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
10.	(beclomethasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone).ti,ab,hw.
11.	or/1-10

Embase search terms

1.	glucocorticoids/
2.	dexamethasone isonicotinate/ or dexamethasone/
3.	fluprednisolone/
4.	methylprednisolone hemisuccinate/ or methylprednisolone/
5.	prednisolone/
6.	prednisone/

7.	hydrocortisone/
8.	cortisone/
9.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
10.	(beclo­methasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or ef­cortisol or "solu-cortel" or solucortel or fludrocortisone).ti,ab,hw.
11.	or/1-10

Cinahl search terms

S1.	(mh "glucocorticoids+")
S2.	(mh "dexamethasone")
S3.	"dexamethasone isonicotinate"
S4.	"fluprednisolone"
S5.	"methylprednisolone hemisuccinate"
S6.	(mh "methylprednisolone")
S7.	(mh "prednisolone")
S8.	(mh "prednisone")
S9.	(mh "hydrocortisone")
S10.	(mh "cortisone")
S11.	methylprednisone
S12.	prednisolone n1 therapeutic
S13.	prednisone n1 therapeutic
S14.	cortisone n1 therapeutic
S15.	beclo­methasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or ef­cortisol or "solu-cortel" or solucortel or fludrocortisone
S16.	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9 or s10 or s11 or s12 or s13 or s14 or s15

Cochrane search terms

#1.	MeSH descriptor Glucocorticoids explode all trees
#2.	beclo­methasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or ef­cortisol or "solu-cortel" or solucortel or fludrocortisone:ti,ab,kw

#3.	MeSH descriptor Dexamethasone explode all trees
#4.	MeSH descriptor Dexamethasone Isonicotinate explode all trees
#5.	MeSH descriptor Fluprednisolone explode all trees
#6.	MeSH descriptor Methylprednisolone explode all trees
#7.	MeSH descriptor Methylprednisolone Hemisuccinate explode all trees
#8.	MeSH descriptor Prednisone explode all trees
#9.	MeSH descriptor Prednisolone explode all trees
#10.	MeSH descriptor Hydrocortisone explode all trees
#11.	MeSH descriptor Cortisone explode all trees
#12.	(methylprednisone or ((prednisolone or prednisone or cortisone) near/1 therapeutic)):ti,ab,kw
#13.	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)

1.3.2 Budesonide for induction and maintenance of remission

Q.2: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of low dose and high dose budesonide for induction of remission compared with

- 2.1 placebo?
- 2.2 conventional glucocorticosteroid treatment?
- 2.3 5-aminosalicylate (5-ASA) treatment?
- 2.4 azathioprine or mercaptopurine (AZA/MP)?
- 2.5 methotrexate?

Q.8: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of low dose and high dose budesonide for maintenance of remission for 12 months or longer compared with

- 8.1 placebo?
- 8.2 conventional glucocorticosteroid treatment?
- 8.3 5-aminosalicylate (5-ASA) treatment?
- 8.4 azathioprine or mercaptopurine (AZA/MP)?
- 8.5 methotrexate?

This search was carried out to update two Cochrane reviews (Seow, 2008; Benchimol 2009).

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 and children diagnosed with Crohn's disease	Budesonide	None	None	2008 to current

Medline search terms

1.	budesonide/
2.	budesonide.ti,ab.
3.	or/1-2

Embase search terms

1.	budesonide/
2.	budesonide.ti,ab.
3.	or/1-2

Cinahl search terms

S1.	budesonide
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Cochrane search terms

#1.	budesonide:ti,ab,kw
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1.3.3 5-aminosalicylates for induction and maintenance of remission

Q.3: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of 5-aminosalicylate (5-ASA) treatment for induction of remission compared with

3.1 placebo?

3.2 azathioprine or mercaptopurine (AZA/MP)?

3.3 methotrexate?

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 and children diagnosed with Crohn's disease	5-aminosalicylate	None	SRs, RCTs, standard exclusions (medline and embase only)	2008 to current

Medline search terms

1.	mesalamine/
2.	sulfasalazine/
3.	("5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicyclate* or 5asa or pentasa or mesalazine or mesalamine or asacol).ti,ab,hw.
4.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.
5.	or/1-4

Embase search terms

1.	mesalazine/
2.	salazosulfapyridine/
3.	("5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicyclate* or 5asa or pentasa or mesalazine or mesalamine or asacol).ti,ab,hw.
4.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.
5.	or/1-4

Cinahl search terms

S1.	(mh "sulfasalazine")
S2.	(mh "mesalamine")
S3.	("5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicyclate* or 5asa or pentasa or mesalamine or asacol or mesalazine)
S4.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*)
S5.	s1 or s2 or s3 or s4

Cochrane search terms

#1.	("5-aminosalicylic*" or "5-aminosalicylate*" or "5-ASA" or 5aminosalicylic* or 5aminosalicyclate* or 5ASA or pentasa or mesalamine or asacol or mesalazine):ti,ab,kw
#2.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*):ti,ab,kw
#3.	#1 OR #2

1.3.4 Azathioprine/mercaptopurine

Q.4: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of azathioprine or mercaptopurine (AZA/MP) for induction of remission compared with

4.1 placebo?

4.2 methotrexate?

Q.9: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of azathioprine or mercaptopurine (AZA/MP) for maintenance of remission for 12 months or longer

9.1 compared with placebo?

9.2 compared with methotrexate?

9.3 *plus* conventional glucocorticosteroid or 5-ASA treatment compared with placebo *plus* conventional glucocorticosteroid or 5-ASA treatment?

The Q.4 search was carried out to update a Cochrane review (Prefontaine, 2010).

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 and children diagnosed with Crohn's disease	Azathioprine or mercaptopurine	None	SRs, RCTs, standard exclusions (Medline and Embase only)	2008 to current (Q.4) All available dates (see Table 1) (Q.6)

Medline search terms

1.	6-mercaptopurine/
2.	mercaptopurine.ti,ab.
3.	azathioprine/
4.	(azathioprine or imuran).ti,ab.
5.	or/1-4

Embase search terms

1.	mercaptopurine/
2.	mercaptopurine.ti,ab.
3.	azathioprine/
4.	(azathioprine or imuran).ti,ab.
5.	or/1-4

Cinahl search terms

S1.	mercaptopurine or azathioprine or imuran
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Cochrane search terms

#1.	mercaptopurine or azathioprine or imuran:ti,ab,kw
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1.3.5 Thiopurine methyltransferase activity

Q.5: In individuals diagnosed with Crohn's disease what is the incidence of serious adverse events for the following subgroups:

- Individuals with normal blood TPMT activity, on a standard dose of azathioprine
- Individuals with low blood TPMT activity, on a low dose of azathioprine
- Individuals whose blood TPMT is unknown, on a standard dose of azathioprine?

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 and children diagnosed with Crohn's disease	TPMT monitoring in conjunction with use of azathioprine or mercaptopurine	None	Standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	(thiopurine methyltransferase or thiopurine s-methyltransferase or tpmt).ti,ab.
2.	methyltransferases/
3.	drug monitoring/
4.	or/1-3
5.	azathioprine/
6.	(azathioprine or imuran).ti,ab.
7.	6-mercaptopurine/
8.	mercaptopurine.ti,ab.
9.	or/5-8
10.	4 and 9

Embase search terms

1.	(thiopurine methyltransferase or thiopurine s-methyltransferase or tpmt).ti,ab.
2.	thiopurine methyltransferase/
3.	drug monitoring/
4.	or/1-3
5.	azathioprine/
6.	(azathioprine or imuran).ti,ab.
7.	mercaptopurine/
8.	mercaptopurine.ti,ab.
9.	or/5-8
10.	4 and 9

Cinahl search terms

S1.	thiopurine methyltransferase or thiopurine s-methyltransferase or tpmt
S2.	methyltransferase*
S3.	s1 or s2

Cochrane search terms

#1.	mercaptopurine or azathioprine or imuran:ti,ab,kw
#2.	(thiopurine methyltransferase or thiopurine S-methyltransferase or TPMT):ti,ab,kw
#3.	methyltransferase*:ti,ab,kw
#4.	#2 or #3
#5.	#1 and #4

1.3.6 Methotrexate for induction and maintenance of remission

- Q.6:** In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of methotrexate for induction of remission
- 6.1** compared with placebo?

6.2 *plus* conventional glucocorticosteroid treatment compared with placebo *plus* conventional glucocorticosteroid treatment for induction of remission?

Q.10: In individuals diagnosed with Crohn’s disease what is the clinical and cost effectiveness of methotrexate for maintenance of remission for 12 months or longer

10.1 compared with placebo?

10.2 *plus* conventional glucocorticosteroid treatment compared with placebo *plus* conventional glucocorticosteroid treatment?

The search was carried out to update two Cochrane reviews (Alfadhli Ahmad, 2004; Patel, 2009)

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 and children diagnosed with Crohn’s disease	Methotrexate	None	SRs, RCTs, standard exclusions (Medline and embase only)	2004 to current

Medline search terms

1.	methotrexate/
2.	methotrexate.ti,ab.
3.	or/1-2

Embase search terms

1.	methotrexate/
2.	methotrexate.ti,ab.
3.	or/1-2

Cinahl search terms

S1.	methotrexate
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Cochrane search terms

#1.	methotrexate:ti,ab,kw
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1.3.7 Post-surgical maintenance of remission

Please note that evidence on treatments for post-surgical maintenance of remission in Crohn's disease was reviewed in 2019. The updated evidence review and full current recommendations can be found on the NICE website.

- ⊖ budesonide
- ⊖ 5-aminosalicylate treatment
- ⊖ azathioprine
- ⊖ mercaptopurine
- ⊖ methotrexate
- ⊖ metronidazole or
- ⊖ combinations thereof
- ⊖ or nutritional treatment
- Versus**
- ⊖ placebo or
- ⊖ no treatment ?

The search was carried out to update a Cochrane review (Doherty, 2009). A supplementary search for nutritional treatments was conducted as these interventions were not in the Cochrane review (see below).

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 and children diagnosed with Crohn's disease	Post-surgical maintenance therapy	None	Standard exclusions (Medline and Embase only)	2009 to current

Medline search terms

1.	exp digestive system surgical procedures/
2.	recurrence/
3.	postoperative complications/
4.	postoperative period/
5.	su.fs.
6.	(post?surg* or post?operative).ti,ab.
7.	or/1-6
8.	glucocorticoids/
9.	dexamethasone isonicotinate/ or dexamethasone/
10.	fluprednisolone/
11.	methylprednisolone hemisuccinate/ or methylprednisolone/
12.	prednisolone/
13.	prednisone/
14.	hydrocortisone/
15.	cortisone/
16.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.
17.	(beclomethasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or fluocortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone).ti,ab,hw.
18.	methotrexate/
19.	methotrexate.ti,ab.
20.	6-mercaptopurine/
21.	mercaptopurine.ti,ab.
22.	azathioprine/
23.	(azathioprine or imuran).ti,ab.
24.	mesalamine/
25.	sulfasalazine/
26.	(aminosalicyl* or "5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicylate* or 5asa or pentasa or mesalazine or mesalamine or asacol).ti,ab,hw.
27.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.

28.	(olsalazine or balsalazide).ti,ab,hw.)
29.	enteral nutrition/
30.	food, formulated/
31.	exp food/
32.	exp diet/
33.	lactose/
34.	((polymeric or elemental or liquid or peptide or whole protein) adj (diet* or food* or formula*)).ti,ab)
35.	(formula* adj2 (diet* or food*)).ti,ab)
36.	((diet or nutrition) adj therapy).ti,ab)
37.	enteral nutrition.ti,ab)
38.	dh.fs.)
39.	exp anti-bacterial agents/
40.	exp nitroimidazoles/
41.	or/8-40)
42.	7 and 41)

Embase search terms

1.	exp abdominal surgery/
2.	recurrent disease/
3.	postoperative complication/
4.	postoperative period/
5.	(post?surg* or post?operative).ti,ab)
6.	su.fs.)
7.	or/1-6)
8.	glucocorticoids/
9.	dexamethasone isonicotinate/ or dexamethasone/
10.	fluprednisolone/
11.	methylprednisolone hemisuccinate/ or methylprednisolone/
12.	prednisolone/
13.	prednisone/
14.	hydrocortisone/
15.	cortisone/
16.	(methylprednisone or ((prednisolone or prednisone or cortisone) adj1 therapeutic)).ti,ab,hw.)
17.	((beclomethasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or flucortolone or fluorometholone or fluprednisolone or flurandrenolone or melengestrol acetate or methylprednisolone or medrone or "solu-medrone" or solumedrone or "depo-medrone" or depomedrone or methylprednisolone hemisuccinate or paramethasone or prednisolone or prednimustine or prednisone or triamcinolone or kenalog or triamcinolone acetonide or deflazacort or calcort or cortisone acetate or cortisone or hydrocortisone or efcortisol or "solu-cortel" or solucortel or fludrocortisone).ti,ab,hw.)
18.	methotrexate/
19.	methotrexate.ti,ab)
20.	mercaptopurine/
21.	mercaptopurine.ti,ab)

22.	azathioprine/
23.	(azathioprine or imuran).ti,ab.
24.	mesalazine/
25.	salazosulfapyridine/
26.	(aminosalicyl* or "5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicylate* or 5asa or pentasa or mesalazine or mesalamine or asacol).ti,ab,hw.
27.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.
28.	(olsalazine or balsalazide).ti,ab,hw.
29.	enteric feeding/
30.	elemental diet/
31.	exp food/
32.	exp diet/
33.	diet therapy/
34.	lactose/
35.	((polymeric or elemental or liquid or peptide or whole protein) adj (diet* or food* or formula*)).ti,ab.
36.	(formula* adj2 (diet* or food*)).ti,ab.
37.	((diet or nutrition) adj therapy).ti,ab.
38.	enteral nutrition.ti,ab.
39.	exp *antibiotic agent/
40.	exp *nitroimidazole derivative/
41.	or/8-40
42.	7 and 41

Cinahl search terms

S1.	(recurren* or prevent* or surg* or resection or remov* or excis*)
S2.	(post-surg* or postsurg* or post surg* or post-operative or postoperative or post operative)
S3.	S1 or S2

Cochrane search terms

#1.	(post-surg* or postsurg* or post surg* or post-operative or postoperative or post operative).ti,ab,kw
#2.	(recurren* or prevent* or surg* or resection or remov* or excis*):ti,ab,kw
#3.	(#1 or #2)
#4.	MeSH descriptor Glucocorticoids explode all trees
#5.	(beclomethasone or betnelan or betnesol or betamethasone or budesonide or clobetasol or desoximetasone or dexamethasone or dexamethasone isonicotinate or diflucortolone or flumethasone or fluocinolone acetonide or fluocinonide or flucortolone or fluorome
#6.	(methylprednisone or ((prednisolone or prednisone or cortisone) near/1 therapeutic)):ti,ab,kw
#7.	("5-aminosalicylic*" or "5-aminosalicylate*" or "5-ASA" or 5aminosalicylic* or 5aminosalicylate* or 5ASA or pentasa or mesalamine or asacol):ti,ab,kw
#8.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*):ti,ab,kw
#9.	(olsalazine or balsalazide):ti,ab,kw
#10.	methotrexate or mercaptopurine or azathioprine or imuran:ti,ab,kw
#11.	(food or diet or lactose or enteral nutrition):ti,ab,kw
#12.	((polymeric or elemental or liquid or peptide or whole protein) next (diet* or food* or

	(formula*):ti,ab,kw
#13.	(formula* near/2 (diet* or food*)):ti,ab,kw
#14.	((diet or nutrition) near/2 therapy):ti,ab,kw
#15.	MeSH descriptor Anti-Bacterial Agents explode all trees
#16.	MeSH descriptor Nitroimidazoles explode all trees
#17.	(metronidazole or ornidazole):ti,ab
#18.	(#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)
#19.	(#3 and #18)

A supplementary search for Q.11, on post-surgical nutritional treatments, was conducted for all available dates.

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 and children diagnosed with Crohn's disease	Post-surgical nutritional treatment	None	Standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	exp digestive system surgical procedures/
2.	recurrence/
3.	postoperative complications/
4.	postoperative period/
5.	su.fs.
6.	(post?surg* or post?operative).ti,ab.
7.	or/1-6
8.	enteral nutrition/
9.	food, formulated/
10.	exp food/
11.	exp diet/
12.	lactose/
13.	((polymeric or elemental or liquid or peptide or whole protein) adj (diet* or food* or formula*)):ti,ab.
14.	(formula* adj2 (diet* or food*)).ti,ab.
15.	((diet or nutrition) adj therapy).ti,ab.
16.	enteral nutrition.ti,ab.
17.	dh.fs.
18.	or/8-17
19.	7 and 18

Embase search terms

1.	exp abdominal surgery/
2.	recurrent disease/
3.	postoperative complication/
4.	postoperative period/
5.	(post?surg* or post?operative).ti,ab.
6.	su.fs.

7.	or/1-6
8.	enteric feeding/
9.	elemental diet/
10.	exp food/
11.	exp diet/
12.	diet therapy/
13.	lactose/
14.	((polymeric or elemental or liquid or peptide or whole protein) adj (diet* or food* or formula*)).ti,ab
15.	(formula* adj2 (diet* or food*)).ti,ab
16.	((diet or nutrition) adj therapy).ti,ab
17.	enteral nutrition.ti,ab
18.	or/8-17
19.	7 and 18

Cinahl search terms

s1.	(recurren* or prevent* or surg* or resection or remov* or excis*)
s2.	(post-surg* or postsurg* or post surg* or post-operative or postoperative or post operative)
s3.	s1 or s2
s4.	food or diet or lactose or enteral nutrition
s5.	((polymeric or elemental or liquid or peptide or whole protein) and (diet* or food* or formula*))
s6.	(formula* and (diet* or food*))
s7.	((diet or nutrition) and therapy)
s8.	s4 or s5 or s6 or s7
s9.	s3 and s8

Cochrane search terms

#1.	(post-surg* or postsurg* or post surg* or post-operative or postoperative or post operative):ti,ab,kw
#2.	(recurren* or prevent* or surg* or resection or remov* or excis*):ti,ab,kw
#3.	(#1 or #2)
#4.	(food or diet or lactose or enteral nutrition):ti,ab,kw
#5.	((polymeric or elemental or liquid or peptide or whole protein) next (diet* or food* or formula*)):ti,ab,kw
#6.	(formula* near/2 (diet* or food*)):ti,ab,kw
#7.	((diet or nutrition) near/2 therapy):ti,ab,kw
#8.	(#4 or #5 or #6 or #7)
#9.	(#3 and #8)

1.3.8 Surgery

Q.12: In individuals diagnosed with Crohn's disease limited to the distal ileum, what is the clinical and cost-effectiveness of surgical resection for induction and maintenance of remission compared with medical or nutritional treatment?

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

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
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Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults and children diagnosed with Crohn's disease	Surgical resection	None	SR, combined RCT and observational studies, standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	((terminal or distal) adj ile*).ti,ab.
2.	ileum/
3.	ileitis/
4.	ileal disease/
5.	cecum/
6.	colitis/
7.	(ileocec* or ileocolitis).ti,ab.
8.	typhlitis/
9.	(cectitis or caecitis or caecum or ileocaec*).ti,ab.
10.	or/1-9
11.	colectomy/
12.	hemicolectomy.ti,ab.
13.	(resection or remov* or excis*).ti,ab.
14.	or/11-13
15.	10 and 14

Embase search terms

1.	((terminal or distal) adj ile*).ti,ab.
2.	ileitis/
3.	ileum/
4.	ileum disease/
5.	cecum/
6.	colitis/
7.	typhlitis/
8.	(ileocec* or ileocolitis).ti,ab.
9.	(cectitis or caecitis or caecum or ileocaec*).ti,ab.
10.	or/1-9
11.	hemicolectomy/
12.	hemicolectomy.ti,ab.
13.	(resection or remov* or excis*).ti,ab.
14.	ileum resection/
15.	or/11-14
16.	10 and 15

Cinahl search terms

S1.	terminal ile* or distal ile*
S2.	ileum or ileitis or ileal or cecum or coli* or ileocec* or ileocoli* or typhlitis or cecitis or caecitis or caecum or ileocaec*
S3.	(mh "colectomy")
S4.	hemicolectomy

S5.	(resection or remov* or excis*)
S6.	s1 or s2
S7.	s3 or s4 or s5
S8.	s6 and s7

Cochrane search terms

#1.	((terminal or distal) near ile*):ti,ab
#2.	(ileum or ileitis or ileal or cecum or coli* or ileocec* or ileocoli* or typhlitis or cecitis or caecitis or caecum or ileocaec*):ti,ab,kw
#3.	(#1 OR #2)
#4.	colectomy:kw
#5.	hemicolectomy:ti,ab
#6.	(resection or remov* or excis*):ti,ab
#7.	(#4 OR #5 OR #6)
#8.	(#3 AND #7)

Q.13: In individuals diagnosed with Crohn's disease what is the clinical and cost effectiveness of surgical treatment of stricture compared with

- balloon dilation
- balloon dilation *plus* intralesional glucocorticosteroid injections,
- conservative management?

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 and children diagnosed with Crohn's disease	Surgical treatment of stricture	None	SR, combined RCT and observational studies, standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	(stricture* or stenosis*).ti,ab.
2.	intestinal obstruction/
3.	constriction, pathologic/
4.	or/1-3

Embase search terms

1.	gastrointestinal obstruction/
2.	"stenosis, occlusion and obstruction"/
3.	colon stenosis/
4.	stenosis/
5.	intestine stenosis/
6.	colon stenosis/ or duodenum stenosis/ or esophagus stenosis/ or intestine stenosis/ or stenosis/
7.	intestine obstruction/
8.	(stricture* or stenosis*).ti,ab.
9.	or/1-8

Cinahl search terms

S1.	stricture* or stenosis*
S2.	(mh "intestinal obstruction")
S3.	(mh "constriction, pathologic")
S4.	s1 or s2 or s3

Cochrane search terms

#1.	(obstruct* or constrict* or stricture* or stenosis*):ti,ab,kw
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1.3.9 Enteral nutrition for induction and maintenance of remission

Q.14.1: In adults and children diagnosed with Crohn's disease what is the clinical and cost effectiveness of enteral nutrition (elemental, semi-elemental and polymeric) as a sole source of nutrition for induction of remission compared with:

- usual diet
- conventional glucocorticosteroid treatment
- budesonide
- a combination of conventional glucocorticosteroid treatment *plus* 5-ASA treatment
- a combination of conventional glucocorticosteroid treatment *plus* azathioprine or mercaptopurine
- a combination of conventional glucocorticosteroid treatment *plus* methotrexate

Q.14.2: In adults and children diagnosed with Crohn's disease what is the clinical and cost effectiveness for induction of remission of enteral nutrition (elemental, semi-elemental and polymeric) plus medical therapy versus usual diet?

Q.15.1: What is the clinical and cost effectiveness of enteral nutrition (elemental, semi-elemental and polymeric) for maintenance of remission compared with:

- usual diet
- medical treatment
 - conventional glucocorticosteroid treatment
 - budesonide
 - 5-ASA treatment
 - azathioprine or mercaptopurine
 - methotrexate

Q.15.2: What is the clinical and cost effectiveness of enteral nutrition (elemental, semi-elemental and polymeric) for maintenance of remission in combination with:

- conventional glucocorticosteroid treatment
- budesonide
- 5-ASA treatment
- azathioprine or mercaptopurine
- methotrexate

compared with *any of the above?*

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 and children diagnosed with Crohn's disease	Enteral nutrition	None	SRs, RCTs, standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	enteral nutrition/
2.	food, formulated/
3.	exp food/
4.	exp diet/
5.	lactose/
6.	((polymeric or elemental or liquid or peptide or whole protein) adj (diet* or food* or formula*)).ti,ab.
7.	(formula* adj2 (diet* or food*)).ti,ab.
8.	((diet or nutrition) adj therapy).ti,ab.
9.	enteral nutrition.ti,ab.
10.	dh.fs.
11.	or/1-10

Embase search terms

1.	enteric feeding/
2.	elemental diet/
3.	exp food/
4.	exp diet/
5.	diet therapy/
6.	lactose/
7.	((polymeric or elemental or liquid or peptide or whole protein) adj (diet* or food* or formula*)).ti,ab.
8.	(formula* adj2 (diet* or food*)).ti,ab.
9.	((diet or nutrition) adj therapy).ti,ab.
10.	enteral nutrition.ti,ab.
11.	or/1-10

Cinahl search terms

S1.	(mh "enteral nutrition")
S2.	(mh "food, formulated")
S3.	(mh "food+")
S4.	(mh "diet+")
S5.	(mh "lactose")
S6.	((polymeric or elemental or liquid or peptide or whole protein) and (diet* or food* or formula*))
S7.	(formula* and (diet* or food*))
S8.	((diet or nutrition) and therapy)
S9.	enteral nutrition
S10.	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8 or s9

Cochrane search terms

#1.	(food or diet or lactose or enteral nutrition):ti,ab,kw
#2.	((polymeric or elemental or liquid or peptide or whole protein) next (diet* or food* or formula*)):ti,ab,kw
#3.	(formula* near/2 (diet* or food*)):ti,ab,kw
#4.	((diet or nutrition) near/2 therapy):ti,ab,kw
#5.	(#1 or #2 or #3 or #4)

1.3.10 Monitoring

Q.16: In adults and children diagnosed with Crohn's disease, what is the clinical and cost effectiveness of DEXA compared with no monitoring for changes in bone mineral density on patient outcomes (fracture rate)?

During development of this guideline a NICE guideline on osteoporosis was published. This work supersedes the question originally asked by the GDG. The osteoporosis guideline excludes people under the age of 18, hence a supplementary search was undertaken to retrieve information relating to fracture risk in children diagnosed with Crohn's disease (see section E.4.3)

Q.17: Does predicting early relapse through monitoring:

- Unintended weight loss
- CRP
- ESR
- MRI
- Calprotectin
- Colonoscopy or capsule endoscopy
- Growth in children

compared with standard care, improved patient outcomes (quality of life, future surgery, hospitalization)?

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 and children diagnosed with Crohn's disease	Monitoring unintended weight loss, CRP, ESR, MRI, faecal calprotectin, colonoscopy, capsule endoscopy and growth	None	Standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	recurrence/
2.	exp monitoring, physiologic/
3.	biological markers/
4.	*intestinal mucosa/
5.	or/1-4
6.	c-reactive protein/
7.	leukocyte I1 antigen complex/
8.	exp endoscopy, gastrointestinal/
9.	blood sedimentation/
10.	weight loss/
11.	exp magnetic resonance imaging/
12.	*growth/
13.	exp growth disorders/
14.	puberty, delayed/
15.	*endoscopy/
16.	or/6-15
17.	((marker* or monitor* or relapse* or recurrence* or indicator*) adj5 (crp or "c-reactive protein" or calprotectin or calgranulin or I1 antigen or I1 protein or erythrocyte sedimentation

	or esr or growth or height or weight or development or mri or magnetic resonance imaging or endoscop* or colonoscop* or duodenoscop* or gastroscop* or (mucosa* adj5 (relapse or healing or ulcer* or inflamm*))).ti,ab.
18.	(5 and 16) or 17

Embase search terms

1.	recurrent disease/
2.	relapse/
3.	deterioration/
4.	exp monitoring/
5.	biological marker/
6.	*intestine mucosa/
7.	or/1-6
8.	c reactive protein/
9.	calgranulin/
10.	exp gastrointestinal endoscopy/
11.	erythrocyte sedimentation rate/
12.	weight change/ or weight fluctuation/ or weight reduction/
13.	exp nuclear magnetic resonance imaging/
14.	*endoscopy/
15.	*growth/
16.	growth retardation/
17.	failure to thrive/
18.	growth disorder/
19.	child growth/
20.	delayed puberty/
21.	or/8-20
22.	((marker* or monitor* or relapse* or recurrence* or indicator*) adj5 (crp or "c-reactive protein" or calprotectin or calgranulin or I1 antigen or I1 protein or erythrocyte sedimentation or esr or growth or height or weight or development or mri or magnetic resonance imaging or endoscop* or colonoscop* or duodenoscop* or gastroscop* or (mucosa* adj5 (relapse or healing or ulcer* or inflamm*))).ti,ab.
23.	(7 and 21) or 22

Cinahl search terms

S1.	crp or "c-reactive protein" or calprotectin or calgranulin or I1 antigen or I1 protein or erythrocyte sedimentation or esr or growth or height or weight or development or mri or magnetic resonance imaging or endoscop* or colonoscop* or duodenoscop* or gastroscop*
S2.	mucosa* and (relapse or healing or ulcer* or inflamm*)
S3.	s1 or s2
S4.	marker* or monitor* or relapse* or recurrence* or indicator*
S5.	s3 and s4

Cochrane search terms

#1.	((marker* or monitor* or relapse* or recurrence* or indicator*) and (CRP or "c-reactive protein" or calprotectin or calgranulin or L1 antigen or L1 protein or erythrocyte sedimentation or ESR or growth or height or weight or development or MRI or magnetic resonance imaging or endoscop* or colonoscop* or duodenoscop* or gastroscop* or (mucosa* near/5 (relapse or healing or ulcer* or inflamm*))).ti,ab,kw
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1.3.11 Patient information and support

Q.18.1: What are the primary information needs of adults with Crohn's disease in the UK?

Q.18.2: What are the primary information needs of children and young people with Crohn's disease in the UK?

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 and children diagnosed with Crohn's disease	Information and support	None	Standard exclusions (Medline and Embase only)	All available dates (see Table 1)

Medline search terms

1.	(information adj need*).mp.
2.	(information adj requirement*).mp.
3.	(information adj support*).mp.
4.	*patient education as topic/
5.	((client* or patient* or user* or carer* or consumer* or customer*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience* or opinion*)).mp.
6.	or/1-5

Embase search terms

1.	(information adj need*).mp.
2.	(information adj requirement*).mp.
3.	(information adj support*).mp.
4.	*patient education/
5.	((client* or patient* or user* or carer* or consumer* or customer*) adj2 (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.
6.	or/1-5

Cinahl search terms

S1.	information n1 need*
S2.	information n1 requirement*
S3.	information n1 support*
S4.	((client* or patient* or user* or carer* or consumer* or customer*) and (attitud* or educat* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience* or opinion*))
S5.	s1 or s2 or s3 or s4

Cochrane search terms

#1.	(information next (need* or requirement* or support*)):ti,ab,kw
#2.	((client* or patient* or user* or carer* or consumer* or customer*) near/2 (attitud* or educat* 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
#3.	(#1 or #2)

1.4 Additional searches

Searches in this section were undertaken to retrieve supplementary material, i.e. not relating to specific clinical questions in the guideline.

1.4.1 Pregnancy and breastfeeding

This search was carried out to retrieve all studies relevant to pregnancy and breastfeeding in the Crohn's disease population.

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 and children diagnosed with Crohn's disease	Pregnancy /breastfeeding	None	Standard exclusions (embase only)	All available dates (see Table 1)

Medline search terms

1.	exp pregnancy/
2.	exp pregnancy complications/
3.	birth weight/
4.	abnormalities, drug-induced/
5.	teratogens/
6.	breast feeding/
7.	milk, human/
8.	or/1-7

Embase search terms

1.	exp pregnancy/
2.	exp pregnancy complication/
3.	pregnancy outcome/
4.	exp birth weight/
5.	exp congenital malformation/
6.	exp teratogenic agent/
7.	breast feeding/
8.	breast milk/
9.	or/1-8

Cinahl search terms

S1.	(mh "pregnancy+")
S2.	(mh "pregnancy complications+")
S3.	(mh "birth weight")
S4.	(mh "abnormalities+")
S5.	(mh "pregnancy outcomes")
S6.	(mh "teratogens")
S7.	(mh "breast feeding+")
S8.	(mh "milk, human")
S9.	s1 or s2 or s3 or s4 or s5 or s6 or s7 or s8

Cochrane search terms

#1.	(pregnan* or birthweight or "birth weight" or breastfeed* or "breast feed*" or breastfed or "breast fed" or "breast milk" or "human milk"):ti,ab,kw
#2.	((congenital or birth) and (defect* or malform* or anomal*)):ti,ab,kw
#3.	(abnormal* or teratogen* or fetotoxi* or foetotoxi* or embryotoxi*):ti,ab,kw
#4.	(#1 OR #2 OR #3)

1.4.2 Adverse events

An additional search was carried out to retrieve papers on adverse events associated with azathioprine, mercaptopurine and methotrexate in adults and children diagnosed with Crohn's disease.

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 and children diagnosed with Crohn's disease	Azathioprine, mercaptopurine and methotrexate	None	Cohorts only (Medline and Embase)	All available dates (see Table 1)

Medline search terms

1.	methotrexate/
2.	methotrexate.ti,ab.
3.	6-mercaptopurine/
4.	mercaptopurine.ti,ab.
5.	azathioprine/
6.	(azathioprine or imuran).ti,ab.
7.	or/1-6
8.	exp cohort studies/
9.	cohort\$.tw.
10.	controlled clinical trial.pt.
11.	epidemiologic studies/
12.	or/8-11
13.	7 and 12

Embase search terms

1.	methotrexate/
2.	methotrexate.ti,ab.
3.	mercaptopurine/
4.	mercaptopurine.ti,ab.
5.	azathioprine/
6.	(azathioprine or imuran).ti,ab.
7.	or/1-6
8.	exp cohort analysis/
9.	exp longitudinal study/
10.	exp prospective study/
11.	exp follow up/
12.	cohort\$.tw.
13.	or/8-12

14.	7 and 13
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Cinahl search terms

S1.	methotrexate or mercaptopurine or azathioprine or imuran
S2.	adverse* and (effect* or reaction* or event*)
S3.	side effect*
S4.	toxic*
S5.	drug* n2 safe*
S6.	complication* or tolerability
S7.	mw "adverse effects"
S8.	s2 or s3 or s4 or s5 or s6 or s7
S9.	s1 and s8

Cochrane search terms

#1.	methotrexate or mercaptopurine or azathioprine or imuran:ti,ab,kw
#2.	((adverse*) near/2 (effect* OR reaction* OR event*)):ti,ab,kw
#3.	side effect*:tw,ab,ti
#4.	toxic*:ti,ab,kw
#5.	drug* near/2 safe*:ti,ab,kw
#6.	(complication* or tolerability):ti,ab,kw
#7.	Any MeSH descriptor with qualifiers: AE,TO
#8.	(#2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9.	(#1 AND #8)

An additional search was carried out to retrieve papers on adverse events associated with 5-aminosalicylates in adults and children diagnosed with Crohn's disease.

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 and children diagnosed with Crohn's disease	5-aminosalicylates	None	Cohorts only (Medline and Embase)	All available dates (see Table 1)

Medline search terms

1.	mesalamine/
2.	sulfasalazine/
3.	(aminosalicyl* or "5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicyclate* or 5asa or pentasa or mesalazine or mesalamine or asacol).ti,ab,hw.
4.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.
5.	or/1-4
6.	exp cohort studies/
7.	cohort\$.tw.
8.	controlled clinical trial.pt.
9.	epidemiologic studies/
10.	or/6-9
11.	5 and 10

Embase search terms

1.	mesalazine/
2.	salazosulfapyridine/
3.	(aminosalicyl* or "5-aminosalicylic*" or "5-aminosalicylate*" or "5-asa" or 5aminosalicylic* or 5aminosalicyclate* or 5asa or pentasa or mesalazine or mesalamine or asacol).ti,ab,hw.
4.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*).ti,ab,hw.
5.	or/1-4
6.	exp cohort analysis/
7.	exp longitudinal study/
8.	exp prospective study/
9.	exp follow up/
10.	cohort\$.tw.
11.	or/6-10
12.	5 and 11

Cinahl search terms

S1.	(MH "Sulfasalazine")
S2.	(MH "Mesalamine")
S3.	(aminosalicyl* or "5-aminosalicylic*" or "5-aminosalicylate*" or "5-ASA" or 5aminosalicylic* or 5aminosalicyclate* or 5ASA or pentasa or mesalamine or asacol or mesalazine)
S4.	(sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*)
S5.	S1 or S2 or S3 or S4
S6.	adverse* and (effect* or reaction* or event*)
S7.	side effect*
S8.	toxic*
S9.	drug* n2 safe*
S10.	complication* or tolerability
S11.	mw "adverse effects"
S12.	S6 or S7 or S8 or S9 or s10 or s11
S13.	s5 and s12

Cochrane search terms

#1.	(aminosalicyl* or "5-aminosalicylic*" or "5-aminosalicylate*" or "5-ASA" or 5aminosalicylic* or 5aminosalicyclate* or 5ASA or pentasa or mesalamine or asacol or mesalazine or sulfasalazine* or salazopyrin* or salazosulfapyridine* or asulfidine* or azulfadine* or azulfidine*):ti,ab,kw
#2.	((adverse*) near/2 (effect* OR reaction* OR event*)):ti,ab,kw
#3.	side effect*:tw,ab,ti
#4.	toxic*:ti,ab,kw
#5.	drug* near/2 safe*:ti,ab,kw
#6.	(complication* or tolerability):ti,ab,kw
#7.	Any MeSH descriptor with qualifiers: AE,TO
#8.	(#2 OR #3 OR #4 OR #5 OR #6 OR #7)
#9.	(#1 AND #8)

1.4.3 Fracture risk in children diagnosed with Crohn's disease

An additional search was performed to retrieve information relating to fracture risk in children diagnosed with Crohn's disease. This was done in order to supplement recommendations from a NICE guideline on fracture risk (Osteoporosis: assessing the risk of fragility fracture due for publication July 2012) which covers adults only.

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 diagnosed with Crohn's disease	Fragility fracture	None	None	All available dates (see Table 1)

Medline search terms

1.	osteoporotic fractures/
2.	fracture*.ti,ab.
3.	fractures, cartilage/ or exp fractures, bone/
4.	or/1-3
5.	exp child/
6.	child*.tw.
7.	exp infant/
8.	infan*.tw.
9.	(baby or babies).tw.
10.	"adolescent"/
11.	(pediatric*1 or paediatric*1).tw.
12.	or/5-11
13.	4 and 12

Embase search terms

1.	osteoporotic fractures/
2.	exp fracture/
3.	fracture*.ti,ab.
4.	or/1-3
5.	exp child/
6.	child*.tw.
7.	childhood/
8.	infancy/
9.	infan*.tw.
10.	(baby or babies).tw.
11.	exp adolescent/
12.	(pediatric*1 or paediatric*1).tw.
13.	or/5-12
14.	4 and 13

Cinahl search terms

S1.	fracture*
S2.	(mh "fractures+")
S3.	s1 or s2
S4.	(mh "child+")

S5.	(mh "adolescence+")
S6.	pediatric or pediatrics or paediatrics or paediatrics or baby or babies or infan* or child*
S7.	s4 or s5 or s6
S8.	s3 and s7

Cochrane search terms

#1.	fracture*:kw,ti,ab
#2.	child*:ti,ab,kw
#3.	infan*:ti,ab,kw
#4.	(baby or babies):ti,ab,kw
#5.	adolescen*:ti,ab,kw
#6.	(pediatric? or paediatric?):ti,ab,kw
#7.	(#2 OR #3 OR #4 OR #5 OR #6)
#8.	#1 AND #7

1.5 Economics searches

1.5.1 Economic evaluations

Searches were conducted in Medline, Embase, HEED and CRD (for NHS EED and HTA). For Medline and Embase an economic filter was added to the standard population search strategy.

Population	Intervention / exposure	Study filter used	Date parameters
Adults and children diagnosed with Crohn's disease	None	Economic (Medline and Embase only)	<ul style="list-style-type: none"> Medline and Embase: 2009 to current CRD and HEED: all available dates

CRD search terms

#1.	MeSH Crohn Disease EXPLODE 1 2
#2.	(crohn OR crohn's OR crohns OR colitis)
#3.	(ileitis OR enteritis)
#4.	colitis
#5.	ileocoli*
#6.	epithelioid AND granuloma*
#7.	inflammatory AND bowel AND disease*
#8.	MeSH Inflammatory Bowel Diseases
#9.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

HEED search terms

1.	crohn* or colitis or ileitis or enteritis or ileocoli*
2.	inflammatory bowel
3.	1 or 2

1.5.2 Quality of life studies

Searches were conducted in Medline and Embase using a quality of life filter added to the standard population search strategy.

Population	Intervention / exposure	Comparison	Study filter used	Date parameters
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Population	Intervention / exposure	Comparison	Study filter used	Date parameters
Adults and children diagnosed with Crohn's disease	None	None	Quality of life	2009 to current