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CLINICAL REVIEW

Ulcerative colitis

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Ulcerative colitis is an inflammatory disorder of the gastrointestinal tract that affects the colorectum. It often presents in young adulthood and is more common in developed nations. The diagnosis is reached after lower gastrointestinal investigation confirms diffuse, continuous, and superficial inflammation in the large bowel and biopsies show changes in keeping with the disorder. There is no single known unifying cause, and the pathogenesis probably relates to a change in colonic environment in a genetically susceptible person. It is a chronic lifelong condition that, untreated, has a relapsing and remitting course. Medical treatment aims to induce remission and prevent relapse of disease activity once this has been achieved, thereby minimising the impact on quality of life and preventing long term sequelae. We summarise recent guidelines, systematic reviews, meta-analyses, and randomised controlled trials (RCTs) to provide the general reader with an update on how this disorder can be effectively identified and managed.

What is ulcerative colitis and who gets it?

Ulcerative colitis is an idiopathic inflammatory bowel disease (IBD), which affects the colon in a diffuse, continuous, and superficial pattern. Inflammation, which can be detected at lower gastrointestinal endoscopy, extends from the anorectal verge to a variable proximal extent. The epidemiology of ulcerative colitis varies considerably worldwide. The highest incidence and prevalence rates are in the developed world, but incidence is increasing in developing countries. It has been proposed that this is the result of improved hygiene and sanitation, which have led to reduced exposure to enteric infections and immaturity of the immune system.

In a recent systematic review of population based studies, incidence varied from 0.6 to more than 20 people per 100 000 person years in Europe and North America, compared with 0.1 to 6.3 per 100 000 person years in Asia and the Middle East.[1] Overall, incidence appeared to be on the rise worldwide. Peak incidence occurred in the second to fourth decade of life, although a modest rise was also seen in later life. Prevalence was estimated at 5-500 people per 100 000 worldwide. No consistent difference was seen between the sexes. Smoking protects against developing ulcerative colitis. Risk is eight times higher in first degree relatives of people with the disorder compared with first degree relatives of healthy controls,[2] although this is not completely explained by known genetic risk factors.

What are the clinical features and associated conditions?

Because the rectum is inevitably affected, the presenting symptoms are usually rectal bleeding, urgency, and tenesmus, with diarrhoea depending on the proximal extent and severity of inflammation. The current Montreal classification system for ulcerative colitis is based on the severity of symptoms and the extent of inflammation of the colorectum (table⇓).[3] However, the extent of disease may change in 50% of patients during follow-up.[4]

About 30% of patients exhibit immune mediated inflammatory disorders of other organs.[5] The liver is affected in 5% of patients (primary sclerosing cholangitis and autoimmune liver disease), joints in 20% (seronegative arthritis of the large joints, sacroiliitis, and ankylosing spondylitis), eye in around 5% (scleritis, episcleritis, and anterior uveitis), and skin in 5% (erythema nodosum and pyoderma gangrenosum).

What is the underlying pathophysiology of ulcerative colitis?

The exact pathophysiology is unknown, but the condition is probably caused by an inappropriate immune response to an unknown environmental stimulus within the colon.[6] Genome-wide association studies have shown that defects in genes integral to the preservation of the colonic epithelial barrier are implicated in the pathogenesis.[7] Mucin depletion and dysregulated tight junctions are thought to contribute to a disrupted epithelial architecture, which allows normal commensal bacteria to be sampled by dendritic cells. These then act as antigen presenting cells and induce inappropriate

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Summary points

- Ulcerative colitis affects one in 200 people in developed nations
- The condition commonly presents in young adults
- Most people with ulcerative colitis will have a normal life expectancy
- 5-aminosalicylates and thiopurines are effective at preventing relapse of disease activity
- Patients are at increased risk of colorectal cancer and should undergo regular surveillance colonoscopy
- Bone densitometry is recommended in patients who need repeated courses of glucocorticosteroids and those at high risk of osteoporosis
- Most drugs used to treat ulcerative colitis are safe during pregnancy

Sources and selection criteria

We searched Medline, Embase, the Cochrane Database of Systematic Reviews, and Clinical Evidence online using the term "ulcerative colitis". We limited studies to those conducted in adults and focused on systematic reviews, meta-analyses, and high quality randomised controlled trials published within the past five years.

activation of the host immune system, leading to an aberrant T cell driven inflammatory response. It is unclear what triggers this inflammatory cascade, although imbalances in intestinal flora have been implicated.

How is ulcerative colitis diagnosed?

The condition is usually diagnosed when a patient with typical symptoms undergoes endoscopic examination of the lower gastrointestinal tract, after infectious causes of the symptoms have been excluded by stool examination. The diagnosis is secured if inflammation of the colorectum is confirmed and colorectal epithelial biopsies show chronic changes, including crypt distortion, along with acute inflammatory changes of cryptitis, crypt abscesses, and a plasma-lymphocytoid cell infiltrate in the lamina propria. However, an exact diagnosis at initial presentation may prove elusive, and more than 40% of those thought to have IBD unclassified (indeterminate colitis) may later be found to have ulcerative colitis.[8] Conversely, a small proportion (probably <5%) of patients initially thought to have ulcerative colitis may later be reclassified as having Crohn's disease. [8] Correct diagnosis at presentation is important because disease course, complications, and treatments differ.

What is the prognosis?

Recent data suggest that less than 10% of patients will need colectomy within the first 10 years of diagnosis[9]; more extensive disease, raised inflammatory markers, and age less than 50 years at diagnosis are associated with colectomy. Modifiable risk factors associated with relapse of disease activity are uncertain but may include diet, cessation of smoking, stressful life events, and poor adherence to drugs. The disease may be associated with a modest increase in mortality in the community, although this effect seems to be attenuating in more contemporary cohorts of patients,[10] perhaps because of earlier diagnosis and improved treatment.

What are the treatment options?

Ulcerative colitis is a chronic lifelong disorder. One in five patients will require sickness related absence from work or school, which impacts adversely on quality of life.[11] About 50% of affected people are in remission at any one time, but 90% will experience a relapsing and remitting course.[12] As a result, no one treatment modality will entirely control symptoms throughout a lifetime of disease (box). It may therefore be useful to categorise treatments according to severity of disease activity (table) and tailor therapy accordingly. Although cessation of symptoms has traditionally been the aim of treatment, in the past 10 years endoscopic mucosal healing has increasingly been used as an endpoint in RCTs because of accumulating evidence that it is associated with a lower likelihood of disease relapse or colectomy.[13]

Induction of remission in mildly to moderately active disease

Mild to moderate flares of disease activity (table) are often treated with oral or topical 5-aminosalicylates or oral glucocorticosteroids. These drugs inhibit production of cytokines and other inflammatory mediators, although the exact mechanisms underlying their beneficial effects in ulcerative colitis are unknown. Glucocorticosteroids usually act within days, whereas 5-aminosalicylates may take up to four weeks to have any benefit. If there is no response to 5-aminosalicylates within two weeks, consider switching to oral glucocorticosteroids.

Glucocorticosteroids

A recent meta-analysis on the efficacy of glucocorticosteroids in active disease identified five RCTs comparing the efficacy of glucocorticosteroids with placebo.[14] Remission rates with active treatment in individual trials varied from 13% to 80%. The likelihood of not achieving remission was significantly lower with glucocorticosteroids (relative risk 0.65, 95% confidence interval 0.45 to 0.93), with a number needed to treat (NNT) of 3. Potential side effects of glucocorticosteroids include infections, weight gain, hyperglycaemia, acne, hirsutism, and hypertension, although these were no more common in patients assigned to active treatment in trials that reported these data. Bone loss occurs within the first six months of treatment and warrants supplementation with calcium and vitamin D.

Oral 5-aminosalicylates

Two systematic reviews and meta-analyses of RCTs show that 5-aminosalicylates can induce remission in mildly to moderately active disease. A recently updated Cochrane review reported that these drugs were more effective than placebo for inducing clinical remission in eight trials (relative risk of not achieving remission 0.86, 0.81 to 0.91).[15] A second meta-analysis of data from 11 RCTs found a similar relative risk, with remission rates with active treatment varying from 11% to 70%. The NNT to prevent one patient not achieving remission was 6.[16] Overall, the best evidence was for the use of mesalazine, which was studied in seven trials. It is unclear which preparations of oral

Discussing ulcerative colitis and its treatment with patients

- Explain that ulcerative colitis is a lifelong disorder but that the symptoms come and go
- Explain that the cause is incompletely understood
- Explain that 5-aminosalicylates are effective for inducing remission of mild to moderate exacerbations and for preventing relapse of disease activity
- Stress to pregnant women that 5-aminosalicylates and thiopurines are not detrimental to the fetus and that the priority is to maintain remission

mesalazine are most effective because of a paucity of trials comparing equivalent doses of the available preparations.

The most common side effects of 5-aminosalicylates are headache, abdominal pain, nausea, vomiting, skin rash, and diarrhoea. However, overall, 5-aminosalicylates were safe and well tolerated, with no significant difference in adverse events compared with placebo. The second meta-analysis also studied the effect of total dose used on rates of remission.[16] Overall, failure to achieve remission was significantly reduced with total daily doses of 2 g or more mesalazine, compared with doses under 2 g, with an NNT of 11, and no significant difference in adverse events.

Topical 5-aminosalicylates

Topical 5-aminosalicylates are prescribed in the form of suppositories or retention suspensions (enemas). This route of administration is useful for patients whose disease is confined to the rectum or distal colon. A Cochrane review studied their efficacy in inducing remission of mildly to moderately active ulcerative colitis.[17] The authors concluded that topical 5-aminosalicylates were more effective than placebo. They were superior for clinical, endoscopic, and histological remission, and safety and tolerability were excellent. The pooled odds ratio for remission was 8.3 (4.3 to 16.1); remission rates with active treatment in individual trials varied from 40% to 80%.

A more recent meta-analysis compared the efficacy of topical and oral 5-aminosalicylates for induction of remission in mildly to moderately active disease.[18] No significant difference in remission rates was detected (relative risk 0.82, 0.52 to 1.28). Despite these findings, and the fact that European guidelines recommend topical treatment as first line in patients with mildly to moderately active ulcerative proctitis,[19] patient preference and its impact on adherence to treatment dictate how 5-aminosalicylates are administered. There is limited evidence to suggest that patients prefer oral 5-aminosalicylates,[20] although more studies are needed.

Combined oral and topical 5-aminosalicylates

Some patients with difficult to control disease may benefit from combined oral and topical 5-aminosalicylates. National and international guidelines recommend such an approach for mild to moderate flares of disease activity in left sided colitis.[19 21 22] A meta-analysis published in 2012 identified four RCTs comparing combined treatment with oral 5-aminosalicylates alone in active disease.[18] Combined treatment seemed to be better, with a relative risk of not achieving remission of 0.65 (0.47 to 0.91) and an NNT of 5. However, no trials have looked at adherence to combination treatment, particularly in the long term.

Induction of remission in severely active disease

Severe exacerbations (table), characterised by the passage of at least six bloody stools a day (often with nocturnal symptoms), with systemic signs, anaemia, or raised inflammatory markers usually require admission to hospital for intravenous glucocorticosteroids. If these drugs do not work, infliximab or ciclosporin are used as rescue therapy, in an attempt to avoid surgery. In this setting, response to intravenous glucocorticosteroids should be judged at three to five days, and a decision made on whether rescue therapy is needed. Success of treatment with ciclosporin or infliximab should be judged within five to seven days of treatment.

Glucocorticosteroids

The only study in the meta-analysis to recruit patients with a severe flare of activity showed a significant benefit of glucocorticosteroids.[14] Despite considerable evidence from routine clinical practice that intravenous glucocorticosteroids are effective in acute severe ulcerative colitis, evidence from RCTs to support this is sparse.

Anti-tumour necrosis factor α biological agents

Infliximab and adalimumab are monoclonal antibodies that are directed against tumour necrosis factor α (TNF-α). Five placebo controlled trials have studied the efficacy of infliximab in moderately to severely active ulcerative colitis[23-26]; three recruited inpatients[23 24 26] and two recruited ambulatory outpatients.[24] Trials conducted in inpatients found no significant improvement in outcomes with infliximab,[23 24 26] whereas both trials of outpatients found a benefit.[w11] A meta-analysis of all five RCTs found a significant effect of infliximab over placebo in moderately to severely active disease,[27] with a relative risk of remission not being achieved of 0.72 (0.57 to 0.91) and an NNT of 4. Remission rates with active treatment in individual trials varied from 25% to 60%. In the United Kingdom, the use of infliximab is restricted to three dose induction therapy for acute severe exacerbations.[28] More recent RCTs, that enrolled similarly refractory outpatient populations, have shown that adalimumab is significantly superior to placebo,[29 30] although absolute differences in remission rates were modest (7-9%).The meta-analysis of RCTs of infliximab found no significant difference in adverse event rates.[27] Common side effects of anti-TNF-α agents include infusion or injection site reactions, headache, nausea, vomiting, arthralgia, and myalgia. More serious adverse events are rare but include increased risk of certain infections,[31] such as reactivation of latent tuberculosis, and increased risk of lymphoma, particularly if combined with other immunosuppressants.[32]

Ciclosporin

Ciclosporin is a fungally derived calcineurin inhibitor that reduces T cell activation. In a small but pivotal trial, which recruited 20 patients with severely active glucocorticosteroid refractory disease,[33] none of the nine patients randomised to placebo showed a clinical response at seven days, compared with nine of 11 given ciclosporin. The results of this study led to the widespread use of ciclosporin in this setting. More recently, an open label RCT that compared infliximab and ciclosporin head to head for the treatment of acute severe

glucocorticosteroid refractory ulcerative colitis found that both treatments were similarly effective, with no response to treatment occurring in 54% and 60% respectively.[34]

Preventing relapse of quiescent disease

Once remission has been achieved, oral or topical 5-aminosalicylates form the mainstay of medical treatment. Patients who experience repeated flares of disease activity, despite optimising this treatment, may need an immunosuppressant drug, such as a thiopurine. Because of their side effects, glucocorticosteroids should not be used long term to maintain remission.

Oral 5-aminosalicylates

A recently updated Cochrane review and another meta-analysis examined maintenance treatment with 5-aminosalicylates.[16 35] The Cochrane review identified seven placebo controlled trials and reported that the risk of relapse was significantly lower with 5-aminosalicylates (relative risk 0.69, 0.62 to 0.77).[35] The second meta-analysis identified 11 RCTs, and reported a similar effect in favour of 5-aminosalicylates after six to 12 months of treatment, with an NNT to prevent one relapse of only 4, and relapse rates with active treatment in individual trials of 0% to 63%.[16] Adverse events were no higher with 5-aminosalicylates. This meta-analysis also examined the effect of total daily dose of 5-aminosalicylate on likelihood of relapse. Doses of 2 g/day or more were more effective than doses of less than 2 g/day (NNT 10), with no increase in adverse events.[16]

Despite oral 5-aminosalicylates being highly efficacious in preventing disease relapse, evidence suggests that less than 50% of patients adhere to treatment.[36] This may be due to the inconvenience of divided dosing schedules,[37] which stem from a desire to minimise the side effects of sulfasalazine. Non-sulfa containing mesalazine formulations are better tolerated, so adherence may be improved if once daily, rather than two or three times daily, dosing schedules are used. A meta-analysis identified seven RCTs (>2700 patients) that compared once daily schedules with conventional ones.[38] It found that relapse rates were no higher with once daily dosing (relative risk of relapse 0.94, 0.82 to 1.08) and adverse events were no more common. However, adherence rates were not significantly different (relative risk of non-adherence 0.87, 0.46 to 1.66).

Topical 5-aminosalicylates

In terms of preventing relapse of disease activity, a recent meta-analysis identified seven trials of topical 5-aminosalicylates (555 patients).[39] All trials compared topical mesalazine with placebo, and in three treatment was intermittent (two or three times a week). The duration of treatment ranged from six to 24 months, and the relative risk of relapse was 0.60 (0.49 to 0.73), with relapse rates with active treatment in individual trials varying from 20% to 55%. The NNT to prevent one patient relapsing was 3, and no significant difference in adverse events was detected.

Thiopurines

Azathioprine, and its metabolite mercaptopurine, are the most commonly used immunosuppressants in ulcerative colitis. They are usually used in an attempt to maintain glucocorticosteroid induced remission, where 5-aminosalicylates have failed. Despite their widespread use, the evidence base to support their efficacy is not strong. A recent systematic review and meta-analysis identified only three RCTs of 127 patients.[40] When data were pooled, the relative risk of relapse was significantly reduced with azathioprine compared with placebo (0.60, 0.37 to 0.95), and the NNT to prevent one relapse was 4. Relapse rates with active treatment in individual trials varied from 45% to 80%. Adverse event rates were incompletely reported by all trials. However, potentially serious adverse events include myelosuppression and associated opportunistic infections, acute and chronic effects on liver function, and hypersensitivity reactions, including pancreatitis. Long term use may be associated with an increased risk of lymphoproliferative disorders and non-melanoma skin cancer.

Treatment of refractory disease

Patients who have frequent relapses despite optimal conventional medical treatments have few options other than surgery. However, some investigators have reported success with other immunosuppressant drugs such as tacrolimus, a macrolide derived from soil bacteria. Other emerging treatments include golimumab, another anti-TNF-α agent; vedolizumab, a monoclonal antibody directed against integrin $\alpha_4\beta_7$; and phosphatidylcholine, a class of phospholipid thought to be deficient in the colonic mucus in ulcerative colitis.

When should surgery be considered?

Colectomy is an option for patients who do not respond to, or are intolerant of, medical treatment, or in those with complications such as colorectal neoplasia. Because ulcerative colitis is confined to the colorectum, colectomy is curative, and the usual approach is a restorative proctocolectomy with ileal pouch-anal anastomosis. A systematic review of 33 case series suggested that the quality of life of patients 12 months after the procedure was similar to that seen in the general population.[41]

The main complication related to this procedure is pouchitis, which can occur in 30% of cases, and presents with increased stool frequency, urgency, incontinence, and nocturnal seepage. This can be treated medically, most often using antibiotics, including metronidazole and ciprofloxacin, or probiotics, such as VSL#3, but it can become chronic in 5% of cases, which leads to pouch failure.[42] In this situation the only option is pouch excision with a permanent ileostomy. Other concerns with surgery are reduced fertility in women, with a systematic review suggesting a 3.9 (2.1 to 7.4) relative risk of infertility after pouch surgery,[43] and pre-operative misdiagnosis of Crohn's disease as ulcerative colitis, which can lead to Crohn's of the pouch and loss of the pouch in some patients.

Overall management of ulcerative colitis

There are a wealth of RCT data on individual treatments for inducing and maintaining remission in ulcerative colitis, but a paucity of data on overall disease management.[44] Patients who remain well for long periods on 5-aminosalicylates may be referred back to the community and told to continue maintenance treatment but to contact a specialist if they develop a flare of disease activity.[45] Those with frequent relapses (more than once a year) can benefit from specialist supervision and potential escalation to immunosuppressive or biological therapy.[21 22] Aggressive medical management of those with frequent relapses may explain why the rate of surgery in ulcerative colitis patients is falling.[46]

Monitoring of drug therapy in ulcerative colitis

Interstitial nephritis is a serious complication of 5-aminosalicylate treatment that is estimated to occur in less

than one in 500 people treated. Patients should therefore have their renal function monitored three months after starting the drug, and yearly thereafter (*BNF*). Vaccinate patients against preventable communicable diseases, including varicella zoster, hepatitis B, influenza, pneumococcus, and human papillomavirus, before starting immunosuppressants (glucocorticosteroids, thiopurines, biologicals, or ciclosporin). Exclude exposure to tuberculosis using skin tests or interferon based assays.

Patients receiving glucocorticosteroids require monitoring of blood pressure, blood glucose, and bone mineral density. Thiopurines can cause bone marrow suppression. Before starting these drugs, check the patient's thiopurine methyltransferase (TPMT) activity. This enzyme metabolises mercaptopurine to its active metabolite thioguanine. Patients with low TPMT activity have an increased risk of myelosuppression, and thiopurines should be avoided, or used with extreme caution. Even in patients with normal TPMT activity, thiopurines need to be monitored closely. Monitor patients' full blood count weekly for the first month of treatment, then monthly for the next six months or so, and three monthly thereafter. Observe patients on immunosuppressive treatments for evidence of opportunistic infection, and routinely check those on long term treatment for non-melanoma skin cancers.

Colorectal cancer screening in ulcerative colitis

A meta-analysis of population based studies found that patients with ulcerative colitis have about double the incidence of colorectal cancer than people without the disorder.[47] However, recent population based data suggest that the overall risk of colorectal cancer may be comparable to the general population, although patients with disease diagnosed in childhood and adolescence, a longer disease duration, or coexistent primary sclerosing cholangitis seem to be at higher risk.[48] In the UK, colonoscopic surveillance is recommended for all patients, starting about 10 years after the onset of symptoms, except for those with ulcerative proctitis that is documented on two consecutive endoscopic examinations, who do not require surveillance.[49] The surveillance interval depends on the extent of disease (figure⇓).

Osteoporosis in ulcerative colitis

Doctors should aim to minimise the use of glucocorticosteroids by optimising 5-aminosalicylate treatment and introducing thiopurines early in the disease course if 5-aminosalicylates do not control disease activity. In the UK, guidelines recommend bisphosphonate prophylaxis in patients over 65 years who need glucocorticosteroids.[50] In patients under 65 years who need more than three months of glucocorticosteroids, bone densitometry measurement is recommended, and a bisphosphonate started if the T score is 1.5 or less.

Pregnancy and breast feeding

Patients with ulcerative colitis are often young and the disease has serious implications for pregnancy. Patients with active disease at the time of conception may have an increased risk of spontaneous abortion. Rates of preterm delivery, low birth weight, and congenital anomalies, such as limb deficiencies and urinary obstruction, may be increased.[51] One in five pregnancies in patients with ulcerative colitis ends with caesarean section.[52] Relapse of disease activity during pregnancy may increase rates of low birth weight and preterm birth.[53]

A recent meta-analysis of seven studies (2200 pregnant women) found no significant association between 5-aminosalicylate use and rates of spontaneous abortion, preterm delivery, low birth weight, congenital abnormalities, or stillbirth.[54] Thiopurines pose a hypothetical risk to the fetus. A study that recruited more than 470 women who used azathioprine early in pregnancy, most of whom had IBD, found a higher rate of congenital malformations in these women compared with women with IBD not taking azathioprine (odds ratio 1.42, 0.93 to 2.18), although the increase was not significant.[55] Despite these theoretical risks, most experts recommend continuing these drugs throughout pregnancy because of the risks posed to the mother and fetus from an exacerbation of ulcerative colitis. Biologicals cross the placenta in the third trimester of pregnancy and should therefore be discontinued at this stage.

5-aminosalicylates are considered safe to take when breast feeding. Although small amounts of thiopurine may be secreted in breast milk,[56] long term follow-up of a small number of children exposed to the drug during breast feeding found no impairments in mental or physical development.[57] Secretion of biologicals in breast milk is limited, and these drugs are probably safe in this setting.

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Tips for non-specialists

- Most patients with ulcerative colitis should be cared for jointly with a gastroenterologist, except for those in long term remission
- Oral glucocorticosteroids or high dose oral, topical, or combined oral and topical 5-aminosalicylates are first line treatment for mild to moderate exacerbations of disease activity
- Patients with more severe exacerbations should be admitted to hospital for intravenous glucocorticosteroids and may require treatment with ciclosporin or anti-tumour necrosis factor α drugs
- Oral or topical 5-aminosalicylates are the main drugs used to prevent relapse
- Avoid repeated courses of glucocorticosteroids in patients who cannot be kept in remission with 5-aminosalicylates, and start treatment with thiopurine at an early stage

Additional educational resources

Resources for healthcare professionals

- Feagan BG, MacDonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochrane Database Syst Rev* 2012;10:CD000543
- Marshall JK, Thabane M, Steinhart AH, Newman JR, Anand A, Irvine EJ. Rectal 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochrane Database Syst Rev* 2010;1:CD004115

Resources for patients

These two websites are a source of reliable balanced information for people with ulcerative colitis, their families, and friends

- Crohn's and Colitis UK. www.nacc.org.uk
- Crohn's & Colitis Foundation of America. www.ccfa.org/

Questions for future research

- Do patients with ulcerative colitis prefer oral or topical 5-aminosalicylates to prevent relapse of disease activity?
- Does surveillance colonoscopy reduce mortality from colorectal cancer?
- Does screening for and treating osteoporosis reduce the risk of osteoporotic fracture?

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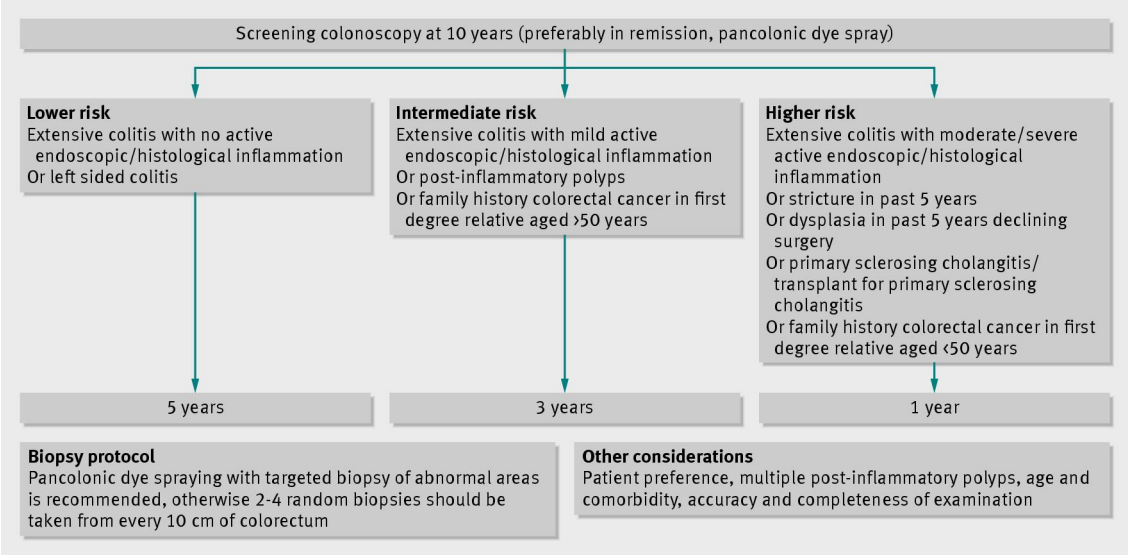
Table

Table 1| Montreal classification of extent and severity of ulcerative colitis[3]

Extent	Anatomy	Severity	Definition
E1: Ulcerative proctitis	Limited to the rectum	S0: Clinical remission	Asymptomatic
E2: Left sided (distal) ulcerative colitis	Limited to a proportion of the colorectum distal to the splenic flexure	S1: Mild	≤4 stools/day (with or without blood), absence of systemic illness, and normal inflammatory markers
E3: Extensive (pancolitis) ulcerative colitis	Extends proximally to the splenic flexure	S2: Moderate	>4 stools/day but minimal signs of systemic toxicity
		S3: Severe	≥6 bloody stools/day, pulse ≥90 beats/min, temperature ≥37.5ºC, haemoglobin <105 g/L, and erythrocyte sedimentation rate ≥30 mm in the first hour

Figure



Surveillance recommendations from the British Society of Gastroenterology for detection of colorectal cancer in ulcerative colitis[49]