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ECCO-EFCCA Patient Guidelines on Ulcerative Colitis (UC)

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Introduction

The European Crohn's and Colitis Organization is the largest association comprising Inflammatory Bowel Disease (IBD) specialists in the world. In addition to education and research, generation of new knowledge is included between its objectives. By development of practical guidelines related to IBD, ECCO assembles the expertise of the best specialist in different disciplines to generate these referential documents in a cooperative and consensual way.
In 2006, ECCO published its first guidelines covering diagnosis and management of Crohn's Disease[1,2]. Since that time, following a continuous interest to promote a common European perspective referred to IBD, a total amount of fifteen ECCO Guidelines have already been published, covering different subjects related to Ulcerative Colitis (UC) from general management[3] to very specific topics like paediatric UC[4].
Collaterally and since its foundation, European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) main's objective has been to improve patients quality of life by dissemination of good practices for patients and their families including educational

interventions, raising public awareness, encouraging research and development of new tools for medical treatment.

Through an initiative to improve the impact that consensuses on IBD have, ECCO and EFCCA have made synergistic efforts to deliver the following guidelines for patients suffering Ulcerative Colitis.
The recommendations included in this document are a collection of the most valuable statements for diagnosis and treatment of UC. The purpose of these guidelines is to provide a better understanding of how UC is diagnosed and treated by medical professionals. The guidelines have been divided in 5 main thematic blocks related to: Diagnosis, active disease, remission, surgery, colo-rectal cancer and extra intestinal complications. A glossary has been located at the end of the document for a better comprehension of the used terminology. In addition, to achieve a higher number of patient readers and an easy comprehension from them, these guidelines has been adapted in a patient's friendly format.

Diagnosis of Ulcerative Colitis (UC)

How much of your colon is affected (i.e. disease extent) will help decide which treatment you should have. The treatment type depends on how much the disease is extended and helps the doctor or nurse decide whether you should have oral and/or topical treatment. Disease extent affects when the surveillance of your disease should begin and how often it should occur. Therefore, your UC is grouped based on how much of your colon is diseased.
The preferred way to group UC is determined by endoscopy that allows confirming the degree of inflammation in your bowel. UC can be grouped into proctitis, left-sided colitis, and extensive colitis.

Experts agree that the best method to classify UC is by colonoscopy. UC should be divided into proctitis, left-sided colitis and extensive colitis (beyond the splenic flexure).
There are two broad reasons why patients with UC should be classified according to disease extent; 1. It influences the treatment type and 2. It determines the amount of surveillance a person receives. In terms of treatment, the first line of treatment for proctitis is often suppositories. Enemas are used for left-sided colitis and oral therapy (often combined with topical therapy) for extensive colitis.
Regarding surveillance, disease extent is important for predicting who may develop colorectal cancer. Patients with proctitis do not need surveillance colonoscopy but those with left-sided colitis or extensive colitis do.

It is useful for doctors to group UC based on how severe it is. Such grouping helps the doctor decide the best treatment. Severity has an effect on whether the treatment should be topical, systemic, surgical, or if it starts at all. Disease severity indices have not been validated yet properly. Clinical, laboratory, imaging and endoscopic measures, including biopsies, help doctors decide what is the best treatment. The definition of remission has not been fully agreed upon yet. Remission is best defined using a mixture of clinical measures (i.e. number of bowel motions ≤3 per day with no bleeding) and no signs of disease at endoscopy. Absence of signs of acute inflammation at biopsy is also helpful.

Management of the patient is in part determined by how severe the disease is. The severity of the inflammation determines if the patient receives no treatment, oral treatment, intravenous treatment or surgery. Many disease severity indices have been proposed but none have been validated (i.e. proven to be accurate and useful) yet. It is generally agreed that a combination of clinical features, laboratory findings (C-reactive protein blood levels or Faecal Calprotectin stool tests), imaging (e.g., X-Ray,) techniques,

and endoscopic findings (including biopsies) assist physicians in their patients' management.
The definition of remission is still to be fully agreed by experts. Nowadays, the best definition of remission combines the patient symptoms and the findings from colonoscopy. Those patients considered in remission will have three or less stools per day with no bleeding and will have no inflammation seen on their colonoscopy. Preferably, they should also not have any microscopic inflammation in their biopsies.

Symptoms of UC

UC symptoms depend on how much of the colon is inflamed and how severe the disease is. Blood in stools, diarrhoea, rectal bleeding, tenesmus and/or needing to rush to the toilet are the most common symptoms. UC patients also often need to open the bowels at night-time. Feeling generally unwell, losses of appetite or fever are signs that you are having a severe attack.

Severe UC symptoms generally coincide with severe inflammation of the colon and how much of the colon is affected; inflammation of the colon is measured using colonoscopy and biopsy.
The most common symptom showed by UC patients is visible blood in the stools. More than 90% of patients report this. ***Patients with extensive and active UC*** show chronic diarrhoea usually with rectal bleeding, or at least visible blood in the stools. Patients have also reported urgency to pass stools, tenesmus, passing mucous or blood, the need to open their bowels at night-time, crampy abdominal pain or ache (often the left side of the lower abdomen) prior to and relieved by defaecation. Moreover, if a person has severe inflammation, they often have fever, fast heartbeat, weight-loss, abdominal swelling or reduced bowel sounds. In contrast, ***patients with proctitis*** usually report rectal bleeding, urgency, tenesmus, and occasionally severe constipation.

Patient history

A full medical history should include many questions. For example, the doctor should ask about when the symptoms began and which type of symptoms. Such symptoms include:
- blood in stools
- urgency
- stool consistency and frequency
- tenesmus
- abdominal pain
- lack of bowel control
- needing to go to the toilet at night-time
- some symptoms not directly related to the bowels (e.g., joint pain).

The doctor should also ask about:
- recent travel
- contact with infectious illnesses that can affect the bowels
- medication (e.g., antibiotics and NSAIDs)
- smoking habits
- sexual practice
- having a family member with CD, UC, or bowel cancer
- previous appendectomy.

The diagnosis of UC should be suspected from clinical symptoms, such as blood in stool, urgency, frequency, tenesmus, abdominal pain, lack of bowel control, and needing to go to the toilet at night-time. The doctor or nurse should enquire about the family history of both IBD and bowel cancer. The patient should be asked about eye, mouth, joint or skin

symptoms. Infectious (e.g. bacteria from overseas travel) or drug induced (e.g. NSAIDs like ibuprofen) colitis need to be considered and excluded.

Appendectomy for confirmed appendicitis has been shown to decrease the risk of getting UC later in life. It also makes the UC less severe if performed for 'true' appendicitis at a younger age.
If you have a family member with CD or UC, you are higher risk to get UC yourself.

Studies have shown that in case a person had an appendectomy for confirmed appendicitis at an early age they are less likely to get UC; this risk reduction is reported to be as high as 69%. In addition, if you get UC after an appendectomy, it is less likely to be severe. It should be noted that appendectomy does not prevent the development of PSC. It is currently unknown if appendectomy after developing UC affects the disease course.
First degree relatives of people with UC are 10-15 times more likely to develop UC themselves. However, because the risk is so low to begin with, a first degree relative has a 2% increased risk of developing UC. Therefore this increased risk should not be significantly influential on a patient with UC deciding whether or not to have children.

Physical examination

A physical check-up should include a range of things:
- general well-being
- heart rate
- body temperature
- blood pressure
- weight
- height
- abdominal exam for swelling and soreness
- ano-rectal examination

When a doctor or nurse carries out a physical examination, findings will depend on how severe the UC is and the extension of the disease. If a person has mild or moderate disease activity, their examination will usually not reveal much apart from blood from the ano-rectal examination. If a person has severe inflammation, they may have a fever, fast heart rate, weight-loss, tenderness in their colon, abdominal swelling, or reduced bowel sounds.

Diagnostic tests

Early tests should include a full blood count, serum urea, creatinine, electrolytes, liver enzymes, Vitamin D levels, iron studies, and CRP. Faecal calprotectin is an accurate marker of presence of inflammation in the colon. CRP and ESR are useful for measuring the response to treatment in severe disease. The doctor should test for infectious diarrhoea, including Clostridium difficile. The doctor should find out whether the patient has been immunized against many viral diseases or has tuberculosis.

Ideally at diagnosis, every patient should have a full blood count, inflammatory markers (CRP or ESR), electrolytes, liver function tests, and stool sample tests carried out. Faecal calprotectin, obtained by a stool test, will accurately measure whether there is inflammation in the colon. However, tests measuring inflammation may be normal in mild or moderate left-sided UC. The full blood count may reveal (a) high platelet levels as a result of persistent inflammation, (b) Anemia and low iron levels indicating disease chronicity or severity, and (c) increased white blood cell count raising the possibility of infection being present.

Other than proctitis, CRP levels tend to be higher when a patient has severe symptoms. A high CRP level will usually coincide with high ESR, lower iron, and low albumin levels. These markers can also be used to see whether a person with acute severe colitis needs surgery. When raised, CRP and ESR can also represent the presence of infection. This means that they should not be used alone for distinguishing UC from other causes of symptoms. Therefore, the doctor or nurse should also rule out other possible causes, such as bacteria (e.g. Clostridium difficile, Campylobacter, or E. coli) or parasites (e.g. amoebae).

Colonoscopy

When UC is suspected, colonoscopy (preferably with ileoscopy) and biopsies in many places in the bowel (including the rectum) are the best methods to confirm diagnosis and severity. In case of a severe attack, abdominal X-rays should be performed and active disease confirmed by sigmoidoscopy as a first line method.

Immediate admission to hospital is warranted for all patients fulfilling criteria for severe colitis to prevent delayed decision making, which may lead to increased perioperative morbidity and mortality.

Colonoscopy with intubation into the small bowel, along with many biopsies is the best method to confirm a suspected diagnosis of UC. This allows the doctor or nurse to observe more of the colon and may be more effective than a sigmoidoscopy. However, the availability of resources as well as the severity of the suspected disease needs to be considered. Colonoscopy and bowel preparation should be avoided in patients with severe colitis because of the potential loss of time and the risk of perforation of the colon.
When a patient with suspected UC has severe disease, a plain abdominal radiography can be initially used, although it does not guarantee a diagnosis. Sigmoidoscopy as opposed to colonoscopy can then be used to confirm this.

If UC is inactive, findings at endoscopy can help predict the future of the disease. Repetition of the endoscopy is useful if and when UC becomes active again. It is also useful if the patient needs to take steroids to stay in remission or cannot get into remission even when taking steroids. Lastly, endoscopy is useful if colectomy is considered.

Studies have shown that in case there is no sign of inflammation during the colonoscopy, a patient is less likely to relapse or need colectomy in the future. They are also more likely to be symptom free for the year following the colonoscopy. Disease location, determined using colonoscopy, is also important for predicting future outcomes, assessing the risk of cancer, and determining what treatment should be applied. However, despite the apparent/seeming importance of colonoscopy for determining disease location, there has never been a study investigating routine colonoscopies after the initial colonoscopy at diagnosis.

In presence of stenosis (i.e. narrowing) of the colon, the doctor should rule out cancer as the cause of it. Many biopsies should be taken from the colon and surgery can be considered. Sometimes endoscopic intubation of the whole colon is not possible. In these cases, imaging procedures, such as double contrast barium enema, or colonography may be used.

In longstanding Ulcerative Colitis, a colonic stenosis (i.e. stricture/narrowing) is a potential sign of a bowel cancer tumour and requires careful assessment using

colonoscopy and biopsies. If colonoscopy is incomplete due to a stenosis, double or single contrast barium enema can be used to assess the narrowing and the colon adjacent to it. CT colonography can assess the tissue pattern near to a colonic stenosis, as well as extra-intestinal (i.e. tissue that is not in the intestine) pathology and is therefore becoming the investigation of choice in this situation.

The term indeterminate colitis (IC) should only be used for resection samples. If the doctor does not know whether you have CD or UC after all possible tests have been done, then it should be called IBD unclassified (IBDU).

IBD unclassified is the term best suited for cases where a definitive distinction between Ulcerative Colitis, Crohn's Disease, or other causes of colitis cannot be made. This term is applied when the distinction cannot be made even after the medical history, endoscopic appearance, histopathology of multiple mucosal biopsies and appropriate radiology have been taken into account. Indeterminate colitis is a term reserved for pathologists to describe a colectomy sample which has overlapping features of UC and CD.

Medical therapy of active Ulcerative Colitis

Proctitis

5-ASA 1g suppository once per day is the preferred early treatment for mild or moderate proctitis. 5-ASA foam enemas can also be used. Suppositories may get more of the drug to the rectum and patients seem to prefer them over enemas. Combining topical 5-ASA with oral 5-ASA or a topical steroid is better at treating the disease than either alone. Oral 5-ASA alone is not as good as combined for treating the disease. More resistant proctitis may need treatment with immunosuppressants and/or anti-TNFs.

If a person has proctitis, topical 5-ASA is the best treatment; this has been demonstrated in numerous studies which reported 5-ASA reducing symptoms and improving the findings in colonoscopy and biopsy. In addition, suppositories are more effective than enemas as they target the site of inflammation and are detected in the rectum of more patients after 4 hours (40% versus 10%). No increase in effectiveness of 5-ASA is found beyond one gram per day and having it once per day is as effective as many times per day.
Multiple studies have shown topical mesalazine is more effective than topical steroids in terms of reducing symptoms as well as improving the findings in colonoscopy and biopsy. Topical steroids should be reserved to people who are intolerant to topical 5-ASA.
Topical 5-ASA is more effective than oral 5-ASA alone for proctitis. Combining topical and oral 5-ASA, meanwhile, seems to be more effective than either alone, in case the patient has disease extending less than 50cm from the anal verge. Combining topical 5-ASA with topical steroids also helps. If the combination of oral or topical 5-ASA with topical corticosteroids does not successfully treat it, oral prednisolone should be added. If all else fails, immunosuppressant or anti-TNF treatment should be used.

Left sided colitis

Early in treatment, active mild-moderate left-sided colitis should be treated with 1g of an aminosalicylate enema per day combined with more than 2,4g of oral mesalazine per day. Combined treatment with oral plus topical 5-ASA treatment is better than using topical steroids or aminosalicylates alone. It is also better than oral aminosalycilates alone. Topical 5-ASA is better at treating the disease than topical steroids. Taking 5-ASA doses once daily is just as good as taking 5-ASA in divided doses. Systemic

corticosteroids can be used if 5-ASA does not work. When the disease is severe then the patient should be admitted to the hospital for intensive treatment.

There is clear evidence from studies that both oral and topical 5-ASA are effective for left-sided UC. Therefore, first line treatment for mild to moderately active left sided colitis is combined oral and topical 5-ASA; it is shown to be more effective than either applied separately combining oral and topical treatment is both more effective and works quicker than either alone. Results from multiple studies have shown rectal 5-ASA to be more effective than rectal corticosteroids, although several studies have shown that rectal beclomethasone dipropionate (a steroid medication) is as effective as rectal 5-ASA.
Several studies have shown that there is no advantage to divide the dose and so 5-ASAs can be taken once daily. However, increasing the dose has been shown to lead to better outcomes for patients and the minimum recommended dose for left-sided colitis is 2.4 grams per day.
Sometimes when 5-ASA is not effective or tolerated well in patients with left-sided UC, oral corticosteroids should be considered. Oral steroids may work more quickly but have the potential to cause more side effects. 5-ASAs take an average of 9-16 days to work and response will be more rapid with combination treatment, compared to oral treatment alone. If a patient on 5-ASA deteriorates in terms of symptoms, has rectal bleeding beyond 10-14 days of commencing treatment, or does not have relief from all symptoms within 40 days, additional therapy (usually oral corticosteroids) should be started.

Extensive colitis

Early in treatment, extensive colitis of mild-moderate severity should be treated with more than 2,4g of oral 5-ASA per day. This should be combined with topical 5-ASA, if tolerated, to increase the chance to stay in remission. Taking 5-ASA doses once daily is just as good as taking 5-ASA in divided doses. Systemic corticosteroids should be given if one does not respond to 5-ASA. Severe Extensive colitis needs hospitalization for intensive treatment.

Oral 5-ASA is effective for the induction of remission of mild to moderately active extensive UC. In addition, the combination of oral and topical 5-ASA is more effective than oral 5-ASA alone; a clinical trial showed combined treatment to achieve remission in 64% of patients compared to 43% who were taking oral 5-ASA alone. Once daily 5-ASA is as effective as divided doses in patients with extensive colitis.
Oral steroids should be started if mild or moderately active disease does not respond to 5-ASA. Similarly, if a patient is already on more than 2 grams per day of 5-ASA or immunomodulators as maintenance therapy and has a relapse, they should start steroids. Steroids have been shown to be valuable in inducing remission in at least two studies. If a person has severe extensive UC, they should be hospitalized because this is potentially life-threatening condition.

Severe colitis

In the presence of bloody diarrhoea, more than six times per day and any signs of systemic toxicity (i.e. a heartbeat of more than 90 beats per minute, a fever of more than 37.8°C, haemoglobin levels of less than 10.5g/dL, or an ESR more than 30mm/hr or a CRP level higher than 30mg/l), the patient has severe UC and should be admitted to hospital for intensive treatment.

Around one in every six UC patients has a severe flare at some point in their disease course. Severe UC needs to be treated seriously. Despite advances made in treatment in the past century, 2.9% of patients admitted in the UK with acute severe UC die although

less than 1% will die in specialist centres. Due to the risk of death from severe UC, it is important to recognise when a severe flare is happening. A severe UC flare is happening when the patient has six or more bloody stools per day in addition to one of the following: (a) a fast heartbeat (more than 90 beats per minute), (b) fever, (c) anaemia, or (d) high ESR or CRP levels.
All patients who are having a severe flare need to be admitted to hospital for intensive treatment that will initially include IV corticosteroids and then graduate to ciclosporin, tacrolimus, or infliximab if the patient does not respond to the IV corticosteroids within three days. In cases where the patient does not respond to medical treatment, they will require surgery. Decisions regarding high intensity medical treatment and surgery need to be made quickly but also carefully. If surgery is delayed too long, more complications during surgery can occur.

Severe active UC should be treated with IV steroids. One can use IV ciclosporin by itself. Low molecular weight heparin should be given to reduce the risk of blood clots. A joint team of a gastroenterologist and colorectal surgeon should take care of the patient.

The response to IV steroids is best assessed using medical tests around the third day. In case of severely active UC not responding to IV steroids, other treatment options should be discussed, including surgery. Ciclosporin, *or* infliximab *or* tacrolimus may be suitable as second line treatment. If there is no improvement within 4-7 days of salvage therapy, colectomy is recommended.

Deciding when to recommend/advise colectomy to a UC patient is one of the most difficult decisions that a gastroenterologist has to make. However, the gastroenterologist in collaboration with the surgeon needs to be as decisive as possible and not have their judgment clouded by the patient's understandable reluctance to delay surgery. If surgery is delayed too long, this can increase the chances of complications or even death during colectomy.
Objective measures (i.e. measures not influenced by the emotions of the patient or doctor) are needed to aid the gastroenterologist in important decision making regarding whether to treat the severe UC with colectomy or medications such as ciclosporin, infliximab or tacrolimus. Clinical (e.g. high stool frequency), biochemical (e.g. high CRP levels), and radiological (e.g. colonic dilatation) markers are objective measures that can be used to assist in the decision making process. It is also important to consider the patient's individual circumstances when making a decision. For example, intravenous ciclosporin should be avoided in patients with low cholesterol or magnesium due to the increased risk of neurological side effects in this patient group.

Medical treatment to maintain remission

The choice of maintenance treatment is informed by many factors:
- how much of the bowel is diseased (i.e. disease extent)
- how often flares occur
- whether prior maintenance treatment failed
- how severe the most recent flare was
- what treatment was used to gain remission during the most recent flare
- the safety of maintenance treatment
- cancer prevention.

Selection of the right treatment to keep patients in remission depends on a range of factors. Those patients with proctitis are more likely to only need topical treatment

whereas those with left-sided or extensive UC will require oral therapy. Moreover, if a person has a history of short periods between flares, they will benefit more from more intense therapy because this may increase the time between flares. If a medication has not worked for maintenance in the past, it should not be tried again. If a recent flare was more severe, more intense therapy should be undertaken. Severity of a present flare will predict the likelihood of a future flare. If a patient needs steroids to gain remission, they are more likely to need an intensive therapy to maintain remission. Side effects of the medications should be weighed up with their benefits in terms of flare and cancer prevention.

Amino salicylic acid

Oral 5-ASAs are the first line maintenance treatment if patients respond to 5-ASA or steroids (oral or rectal). Rectal 5-ASA is the first line maintenance treatment for proctitis and can be used for left-sided colitis. Oral and rectal 5-ASA combined can be used as a second line maintenance treatment.

Many studies have demonstrated that oral 5-ASAs are effective for maintaining remission. In addition, two studies have reported the use of rectal 5-ASA to successfully maintain remission in those patients with left-sided UC. Treatment with both oral 5-ASA and 5-ASA enemas has been shown to be more effective than oral 5-ASA alone for maintaining remission. A survey of UK patients reported that 80% preferred oral treatment alone; so it seems that oral treatment is more acceptable to patients than rectal treatment.

Oral 5-ASA does not work below a dose of 1.2g per day. For rectal treatment, 3g per week in divided doses is enough to maintain remission. The dose can be altered/changed based on how much it works. In some cases higher doses with or without topical 5-ASA are useful. You will not have more side effects from taking 5-ASA once daily. Other oral 5-ASA medicines are preferred over sulfasalazine (even though sulfasalazine may be slightly more effective) because they have fewer side effects. All available oral 5-ASAs are effective. There is no strong evidence that any 5-ASA is better than the others for maintenance treatment.

The minimum effective dose for oral 5-ASA is 1.2 g per day. Considering that there is no increase in side effects with higher doses of 5-ASA, higher doses should be given in certain cases. It also makes no difference whether you take the 5-ASA once per day or several times per day. Once per day is preferred because it improves adherence. While oral 5-ASAs have comparable effectiveness to sulfasalazine, 5-ASAs are preferred because they cause fewer side effects. Overall, there is no strong evidence that any particular 5-ASA is the better than the others.

Long term 5-ASA maintenance treatment is recommended because it may reduce the risk of getting bowel cancer.

A study has shown that regular 5-ASA treatment reduces the risk of getting bowel cancer by 75%. Therefore, it should be seriously considered as a maintenance treatment.

Thiopurines

If steroids are needed to stay in remission, the patient should be treated with a thiopurine.

Azathioprine is more effective than 5-ASA for reducing symptoms and inflammation (as seen in colonoscopy) in patients who need steroids to stay in remission. Moreover, about

half of steroid dependent patients on azathioprine will maintain steroid free remission for three years. Therefore, people who flare when they wean off steroids should start taking azathioprine.

Patients with moderately active UC who do not respond to thiopurines, should be treated with anti-TNF therapy or tacrolimus. Treatments that are not working should be stopped and surgery should also be an option.

Patients with steroid dependent UC who do not respond to thiopurines should ideally be reassessed by colonoscopy and biopsy to confirm the diagnosis and make sure other complications are not occurring. A treatment strategy with the goal of getting off steroids should be discussed with the patient and anti-TNF therapy should be considered. There is solid evidence that anti-TNF therapy is effective for moderate to severe UC that does not respond to corticosteroids or immunomodulators. Tacrolimus can also be considered but the evidence for this treatment is less convincing.
If the UC fails to respond or stops responding to any of these treatments, surgery needs to be taken into consideration. Colectomy, while not without risk, has the capability of removing the diseased colon and thus "curing" the UC. Treatment with immunosupressors or immunomodulatory therapy is pointless and irrational if the disease is not improving because the increased risk to get complications during and after surgery due to the delay.

All patients should have a maintenance treatment. It is possible to have treatment on an as needed basis only if you have disease of limited extent (e.g. proctitis).

It is important to remain on your medication even if you feel better. This is because those who are adherent to their medication are far less likely to flare than those who are not. In fact, adherence appears to be the most important factor for determining whether a person stays in remission or not. For example, one study showed that people who collected less than 80% of their prescriptions for maintenance 5-ASA were five times more likely to relapse than those who collected more than 80% of their prescriptions.

Thiopurines can be used in case of mild to moderate disease activity with early or frequent relapse while taking 5-ASA at optimal dose, in case of intolerance to 5ASA, in case steroids are needed to stay in remission, or when remission is gained from ciclosporin (or tacrolimus). Once responding to anti-TNF treatment, one has two options to stay in remission. The first is to take one of the thiopurines. The second option is to stay on anti-TNF treatment with or without thiopurines. If you have severe colitis which responds to IV steroids, ciclosporin, or infliximab, one should consider thiopurines for maintenance treatment. However, if you respond to infliximab it is also appropriate to continue infliximab. If thiopurines did not work for you in the past, you should try to stay in remission using anti-TNF treatment. In thiopurine-naïve patients with severe colitis responding to steroids, ciclosporin or tacrolimus, thiopurines are appropriate to maintain remission.

Several studies have demonstrated that thiopurines are effective for keeping UC patients in remission, although the evidence for their use in UC is weaker than for CD. A recent study has shown that azathioprine was better for maintaining steroid-free remission at six months than 5-ASAs (53% stayed in remission in azathioprine versus 21% on 5-ASA). Moreover, thiopurines can be used after remission is gained from ciclosporin (or tacrolimus); doing so can reduce the chances of needing colectomy both in the short term (i.e. 1 year) and long term (i.e. 5 years).
There is also the option of having anti-TNF treatment. Studies have shown that the use of infliximab helps the patient to gain and maintain remission as well as get them off

steroids; it also probably helps prevent colectomy. Adalimumab has also been shown to help patients with moderate-to-severe UC to gain and maintain remission, reduce symptoms, reduce inflammation in the colon, and get off steroids.
Another option is to combine thiopurines with anti-TNF treatment. This can decrease the chance of the anti-TNF reacting badly or losing its effectiveness when anti-TNF antibodies are produced. A study has reported that combining infliximab with azathioprine was more effective at getting people off steroids than using either alone. Combining the two also probably helps prevent colectomy. Moreover, it is possible that azathioprine can be stopped after the first six months of combination therapy because the antibodies that prevent infliximab from working and that are inhibited by thiopurines tend to occur in the first few months of anti-TNF treatment.

Surgery for UC

Surgical complications are more likely to occur when surgery is delayed.
A staged procedure (colectomy first) should be carried out in the acute case when there is no response to medical treatment, or in case the patient has been taking 20mg daily or more of prednisolone for more than six weeks.
If available, the patient may benefit from having the surgery done by a surgeon with laparoscopic skills.

In cases of acute severe UC, it is important that senior surgeons and gastroenterologists work together to ensure its safe management. Whilst it is important to try medical therapy before moving onto considering surgery, it is equally important that the decision is not unnecessarily delayed. Delaying surgery when it is needed will often lead to worse outcomes during and after surgery. Therefore, when medical therapy has failed, the patient should move on to having surgery.
The surgery should be done in two to three stages (i.e. colectomy and ileostomy first) when the patient has acute severe UC or has received many steroids. This is because it will remove the diseased colon, thus allowing them to regain health and start eating properly again. After the colectomy, the patient can then consider whether they want to have an IPAA or continue with an ileostomy. Having the colectomy first also allows the diagnosis of Crohn's Disease to be excluded; if Crohn's Disease is found in the colon specimen, this will mean an IPAA is not appropriate. Finally, there can be an advantage of having the colectomy done laparoscopically because it may lead to a faster recovery and less complications.

IPAAs should be done in specialist referral centres, with experience of carrying out this procedure. This seems to be the result of reduced complications and being better able to rescue the IPAA when complications do occur.

IPAA is a very complex surgery. Therefore, surgeons and hospitals who perform many of them tend to produce better outcomes and less complications than those who only perform few of them. In addition, more experienced surgeons and hospitals manage complications better and are more likely to "rescue" the IPAA if serious complications occur. Hence, it is better having IPAA performed in specialist centres that do many IPAAs than those that do not do many.

Fertile female patients should discuss other surgical options with both a gastroenterologist and a colorectal surgeon, because there is a risk of not being able to have children after IPAA. Such other options include subtotal colectomy and end ileostomy, or ileo-rectal anastomosis.

One in two females who have IPAA surgery become unable to have children and IPAA triples the risk of infertility compared to medically managing the UC (infertility rate 48% in IPAA surgery recipients versus 15% in medically managed UC patients). This is probably because the fallopian tubes get adhesions from the surgery. Therefore, alternative options should be sought by women hoping to conceive, such as permanent ileostomy or an ileo-rectal anastomosis. The advantage of ileo-rectal anastomosis is that it does not seem to decrease fertility. The disadvantage is that inflamed colon remains (and the associated risk of bowel cancer).

Ileorectal anastomosis should be considered in special cases. If it is performed, the retained rectum should be monitored by your gastroenterologist.

The ileorectal anastomosis is generally not a good option because it does not eliminate the UC and so UC symptoms are likely to remain due to the retained rectum. Nevertheless, one in two people who have ileorectal anastomosis will still have it after ten years and the quality of life is acceptable relative to IPAA. Therefore, it can be considered by certain UC patients, especially women hoping to conceive in the future. However, the rectum will need monitoring due to the risk of bowel cancer in the retained rectum.

Taking 20mg or more per day of prednisolone (or equivalent) for more than six weeks increases the risk of surgical complications. Therefore, corticosteroids dose should be weaned before surgery if possible.

Many studies have shown that patients who take 20mg or more per day of prednisone for more than six weeks are more likely to experience surgical complications. Therefore, steroids should be weaned before surgery if possible.
Moreover, when steroids are being weaned post-surgery it is important not to cause steroid withdrawal crisis which is characterised by low blood pressure, and low sodium and low blood sugar levels.

Taking thiopurines or ciclosporin before surgery does not increase the risk of complications after surgery. Taking infliximab before surgery may increase the risk of having complications after surgery.

Taking thiopurines or ciclosporin before surgery do not appear to increase the risk of post-operative complications after colectomy. Some studies have shown infliximab does seem to increase the risk of having complications immediately after surgery and it is likely that these complications are related to an increased risk of infection from immunosuppression. On the other hand, several other studies have not shown infliximab to increase the risk of post-operative complications and so this is not certain. It is not known whether tacrolimus increases the risk of post-operative complications, due to a lack of studies investigating this.

Surgical complications - Pouchitis

The diagnosis of pouchitis includes symptoms as well as certain endoscopic and histological abnormalities. Pouchitis is more frequent if more of the colon was diseased before surgery or if there was disease outside the bowels (i.e. PSC), the patient is a non-smoker, has p-ANCA positive serology, or used NSAIDs.

Symptoms related to pouchitis include increased stool frequency, liquid stools, abdominal cramping, urgency, tenesmus and pelvic discomfort. Rectal bleeding, fever, or extra-intestinal manifestations may occur. Symptoms alone do not determine that it is pouchitis. For example, cuffitis, which is inflammation of the remaining rectal cuff, can

cause similar symptoms. Similarly, Crohn's Disease of the pouch and irritable pouch syndrome (which is tantamount to irritable bowel syndrome) can cause similar symptoms. Therefore, pouchoscopy, which is an endoscopy of the IPAA, should be used to confirm the diagnosis. Inflammation from pouchitis looks different from inflammation from UC because it is a different disease. Biopsies should be taken during the pouchoscopy to make sure it is pouchitis and not something else like Crohn's Disease or *C. diff*.
Certain risk factors are associated with getting pouchitis. Having more extensive UC before surgery, backwash ileitis (i.e. inflammation of the terminal ileum), disease outside the bowel (especially PSC), being a non-smoker, and regular use of NSAIDs increase the probability of getting pouchitis. While these risk factors should not stop the person from going ahead with the IPAA, they should be included in the discussion with the patient.

The most frequent symptoms of pouchitis are increased number of liquid stools, urgency, abdominal cramping and pelvic (i.e. around the lower abdomen and anus) discomfort. Fever and bleeding are rare. Pouchoscopy is not needed when there are no symptoms.

Pouchitis symptoms include increased stool frequency, liquid stools, abdominal cramping, urgency, tenesmus and pelvic discomfort. Rectal bleeding, fever, or extra-intestinal manifestations may occur. Rectal bleeding is more often related to inflammation of the rectal cuff, than to pouchitis. Faecal incontinence may occur in the absence of pouchitis after IPAA, but is more common in patients with pouchitis.

Metronidazole or ciprofloxacin work for most of the patients with pouchitis, although the best method of treatment is not clear. Ciprofloxacin causes fewer side effects. Antidiarrheal drugs (e.g. loperamide) may reduce the number of liquid stools (in presence or absence of pouchitis).

Antibiotics are the most effective way to treat pouchitis. Metronidazole and ciprofloxacin are the most common antibiotics used. It appears ciprofloxacin is most effective in reducing symptoms, improving pouchoscopy findings, and causing less side effects. Antidiarrheal drugs (e.g. loperamide) should also be considered in IPAA patients because they can significantly reduce the number of liquid stools, irrespective of whether the person has pouchitis.

When remission of pouchitis is induced by antibiotics, VSL#3 can help maintain remission. VSL#3 may also prevent onset of pouchitis, when started as soon as IPAA surgery has been completed.

Once remission has been obtained in chronic pouchitis, treatment with the concentrated probiotic mixture VSL#3 helps maintain remission. It has been shown that pre-emptive use of VSL#3 can prevent the first onset of acute pouchitis in the first year after surgery with only 10% of patients who took VSL#3 getting pouchitis compared to 40% who took a placebo. It is largely unknown why VSL#3 works but it is thought it may work by increasing bacterial diversity and decreasing fungal diversity in the IPAA.

Complications - Colorectal cancer

Patients with long term and extensive UC are more prone to get bowel cancer.

The risk of a UC patient getting bowel cancer is 2% at 10 years, 8% at 20 years, and 18% at 30 years. Moreover, those with pancolitis have the greatest risk, those with left-sided colitis have a medium risk and those with proctitis have no increased risk. Therefore, the longer a person has had UC and the more of their bowel is/gets diseased, the more likely they are to get bowel cancer.

Some UC patients are more prone to get bowel cancer than others:
Patients with:
- PSC
- post-inflammatory polyps
- family members who have or had bowel cancer
- more severe or persistent inflammation.

The most consistent risk factors for bowel cancer reported are primary sclerosing cholangitis (PSC), and histological or clinical disease activity. PSC patients have a lifetime risk of bowel cancer of up to 31%. Post-inflammatory polyps have also been found to be strong risk factors although it is possible that this increased risk may be caused by dysplastic lesions being mistaken for post-inflammatory polyps. A family history of bowel cancer is associated with an increased risk, although not consistently across the studies.

The doctor should work out the risk of bowel cancer at the screening colonoscopy or at the first surveillance colonoscopy six to eight years after first signs of UC. Level of risk mainly depends on how much of the colon is affected and how severe the inflammation is.

The bowel cancer risk level of the patient can be determined at the screening colonoscopy or at the first surveillance colonoscopy eight years after disease onset. The risk factors are (a) pancolitis, (b) endoscopic and/or histological inflammation, (c) pseudopolyps and (d) family history of CRC; if a person has three or more of these risk factors they are at high risk while if they have two or less they are at low risk.
If a person is at high risk and has extensive or left-sided UC, they should have a colonoscopy every 1-2 years from the eighth year after diagnosis onwards but if they are low risk they should have a colonoscopy every 3-4 years. If there are no microscopic signs of cancer or endoscopic and/or histological inflammation in two consecutive surveillance colonoscopies the surveillance interval may be increased (e.g. from every 1–2 years to every 3–4 years).

5-ASAs may reduce the risk of getting bowel cancer. In presence of PSC, ursodeoxycholic acid should be given to reduce the risk of getting bowel cancer. It is unknown whether thiopurines can or should be used for reducing bowel cancer risk.

Chemopreventive agents are used to inhibit, delay or reverse cancer formation and progression. 5-ASAs are an example of a chemopreventive agent in UC. Multiple studies have shown 5-ASAs reduce the risk of bowel cancer in UC patients; the risk may even be halved by taking 5-ASAs. On the other hand, folic acid supplements, calcium, multivitamins, or statins do not reduce the risk of bowel cancer in UC while it is unknown whether thiopurines are effective in this regard.
Sometimes UC patients also have PSC and these patients have a far greater risk of developing bowel cancer; the lifetime risk to these patients may be as high as 31%. Fortunately, ursodeoxycholic acid has been shown to reduce the incidence of bowel cancer in those with UC and PSC and so should be used routinely in these patients.

Other complications

Psychological factors may affect the course of UC. Patients who suffer from stress or depression, may have an increased risk of relapse of the disease. Those who are often depressed have a low health-related quality of life and those who have anxiety are less likely to follow their treatment.

Multiple studies with UC patients have demonstrated that psychological stress and disease activity coincide with each other. Studies have shown that high perceived stress,

anxiety, and depression can precipitate flares although one study has shown that those with depression are not more likely to relapse. Therefore, the evidence in this regard is somewhat mixed. Nevertheless depression and neuroticism (a personality trait characterised by emotional instability, anxiety, fear, and worry) have been shown to be linked with having a lower quality of life. Anxiety and changes in low mood seem to be associated with not following medical treatment for UC.

Psychosocial effects of the disease and health-related quality of life should be discussed between the patient and doctor. Tailored (i.e. individualised) information and explanation about UC should be given. Combining self-management and patient-centred appointments may improve control of UC.

Health perceptions impact on the patient's experience of the illness. Psychologically distressed patients may have difficulty in processing important information about their disease. Raising awareness of this may lead to improved communication between the patient and doctor or nurse/professionals. It is important that patients are informed about their condition individually and are given emotional support. This is because patients who have a lesser understanding of the illness tend to have greater concerns and worries.
Healthcare utilization is strongly related to psychosocial factors. Non-adherence to medical advice has been reported in over 40% of patients and is a situation in which the relationship between the patient and doctor or nurse is key. Self-management guidebooks together with patient-centred consultations improve patients' disease control. Educational booklets on their own do not seem to be helpful and may worsen the outcomes for patients. In addition, patient education programmes seem to have little or no influence on the course of their illness or their psychological wellbeing.

Extra-intestinal complications-bone and joints

In UC, arthritis (i.e. joint pain with swelling) can sometimes occur in the joints of the arms and legs (called "peripheral arthritis") or in the lower back (called "axial arthritis"). When arthritis occurs in the large joints of the arms and legs, treating the UC usually relieves the symptoms. If the symptoms persist when the symptoms of UC go away, NSAIDs can be used in the short-term. Local steroid injections and physiotherapy are also useful for treating peripheral arthritis. If the peripheral arthritis persists, sulfasalazine can be taken. There is better evidence that intensive physiotherapy with NSAIDs can be used to treat arthritis of the lower back. However, NSAIDs are best avoided due to a lack of safety. In axial arthritis, Sulfasalazine, methotrexate and azathioprine usually do not work, or only work slightly. Anti-TNFs are a good treatment for ankylosing spondylitis and when patients cannot tolerate or do not respond to NSAIDs.

Recommendations for the treatment of UC-related arthropathy (i.e. joint disease) are based on studies in spondyloarthropathy (i.e. joint disease), predominantly ankylosing spondylitis (i.e. arthritis in the spine). No well-designed studies have been performed in the domain of IBD and so the recommendations are inferred from other disease areas.
In peripheral arthritis, the treatment of the underlying UC using corticosteroids, immunomodulators, and anti-TNFs should resolve the peripheral arthritis. If treating the underlying UC does not alleviate the joint pain then the patient should consider taking NSAIDs short term; while NSAIDS can potentially aggravate the underlying UC, the risk of this seems to be low. Physiotherapy can provide symptom relief. The use of COX-2 inhibitors (e.g. etoricoxib and celocoxib) appears safer with a lower risk of disease flare than conventional NSAIDs. Sulfasalazine can be beneficial for large joint arthropathy. Infliximab can also have a beneficial effect on peripheral arthritis.

Regarding axial arthropathy in UC, most of the treatments are based on evidence from studies of ankylosing spondylitis. Intensive physiotherapy and NSAIDs can be used although NSAIDs should be avoided in the long term. Local corticosteroid injections can be considered. Sulfasalazine, methotrexate and azathioprine are not effective for ankylosing spondylitis with axial symptoms. In patients with active ankylosing spondylitis that do not respond to or cannot tolerate NSAIDs, anti-TNF agents are recommended. Adalimumab and infliximab are both proven to be sufficiently safe and effective for treating ankylosing spondylitis.

Osteopenia may help predict future osteoporosis, but presents little direct risk. However, if a certain criterion is met (i.e. the T score is less than -1.5), calcium and vitamin D should be given. Osteoporosis should be treated in case of previous fracture (even if T scores are normal).

Treatment with calcium 500–1000 mg/day and vitamin D (800–1000 IU/day) increases bone density in patients with IBD although it has not been studied whether they prevent fractures in IBD patients. Therefore, a general recommendation of treatment with bisphosphonates on the basis of reduced bone density is not feasible. That being said, postmenopausal women or those with steroid-induced osteoporosis will benefit from them. Overall, in individual patients with low bone density and additional risk factors treatment should be considered.
The strongest predictor of future fracture is a prior vertebral fracture including in those with normal bone density. Therefore, all patients with previous fractures should be treated accordingly.

Skin

Anti-TNF treatment can cause skin inflammation. This usually disappears once the drug is stopped to be administered. When it is unclear which is the source causing the skin inflammation, the patient should be referred to a dermatologist. Related to this, the treatment to be used is mostly based on what has happened in other chronic diseases. These treatments can include topical steroids, topical keratolytic agents, vitamin D, methotrexate, or switching or stopping anti-TNF treatment.

Anti-TNF treatment of UC patients can sometimes cause skin abnormalities called psoriasis and eczema; approximately 22% of patients on anti-TNF will experience these abnormalities. Skin lesions did not coincide with IBD symptoms but were more common in females. Topical therapy with corticosteroids, keratolytics (e.g. salicylic acid, urea), emollients, vitamin D analogues and ultraviolet (UV) therapy (UVA or narrow band UVB) resulted in partial or total remission in almost half of the patients. Overall, 34% of people with skin problems had to ultimately stop taking anti-TNFs because they could not get the skin problems under control. Fortunately, skin problems will usually go away once the anti-TNF is stopped.

Eyes

A patient with eye problems, should be referred to an ophthalmologist. Episcleritis (i.e. inflammation in the eye), may not require systemic treatment and will usually respond to topical steroids or NSAIDs. Uveitis is treated with steroids, either topical or systemic. Immunomodulators, including anti-TNFs, may be helpful in more persistent cases.

Uveitis and episcleritis are the most common symptoms related to the eye caused by IBD. Episcleritis may be painless, presenting simply with red eyes, but itching and a burning sensation may also occur. The inflammation may heal by itself without treatment

but will usually respond to topical steroids, NSAIDs, or simple analgesics alongside the treatment of the underlying UC.
Uveitis (i.e. inflammation of the uvea) is less common but has potentially more severe consequences. When related to UC it frequently happens in both eyes, is insidious in onset and is long-lasting. Patients complain of eye pain, blurred vision, sensitivity to light and headaches. Because it is serious and can cause loss of vision, the person with uveitis should visit an ophthalmologist (i.e. medical eye specialist) immediately. The treatment will usually consist of both topical and systemic steroids. Azathioprine, methotrexate, infliximab and adalimumab have all been reported to be valuable in resistant cases.

Liver and gallbladder

Sometimes disorders of the liver, gallbladder, bile ducts, or bile happen with UC; these are called hepatobiliary disorders. In case of abnormal liver function tests, the doctor should check for these. Ultrasound scanning and serology are used to look for auto-immune and infective causes. One possible hepatobiliary disorder is PSC and the best way of diagnosing this is MRCP. People with PSC are more likely to get cancer.

Liver test abnormalities are common in IBD. PSC is the most common condition causing liver abnormalities in IBD patients although some other conditions (e.g. cirrhosis, gallstones, and chronic hepatitis) also co-occur in IBD. Some medications (e.g., azathioprine) used for IBD can also cause liver test abnormalities. Usually the liver abnormalities will appear in routine tests before symptoms occur.
If ultrasound scanning is normal, drug side effects have been thought unlikely, serological tests for other primary liver disease are negative, then it is likely to be PSC causing the abnormal liver tests. The usual diagnostic test for PSC is MRCP; if PSC is present this will show irregular bile ducts with areas of both narrowing and dilatation. If MRCP still reveals nothing then a liver biopsy should be done. It is important to make sure whether PSC is present because it increases the risk of a UC patient developing bowel cancer. Therefore, those with PSC need closer monitoring.

Blood and Coagulation

The risk of blood clots and deaths related to blood clots is doubled in patients with UC compared to people without UC. In the presence risk for blood clots in the blood vessels, prevention can be done mechanically (e.g. compression stockings) and using medicine (e.g. heparin). Treatment of blood clots in UC should follow established blood thinning treatment options taking into account the potentially increased risk of bleeding.

For largely unknown reasons, patients with UC have an increased risk for blood clots, called venous thromboembolism, in the veins. These are important to treat because they can lead to complications or even death. Such blood clots should be diagnosed using appropriate imaging techniques, such as ultrasound and venography.
In terms of treatment, blood thinning medications (called anticoagulants) should be used to treat blood clots. If a person has a second episode of blood clots they should consider having long-term treatment. Whether IBD patients have more bleeding complications from blood thinners than people without IBD is unclear. UC patients should be wary of long distance travel as well as oral contraceptives as these further increases the risk of blood clots.

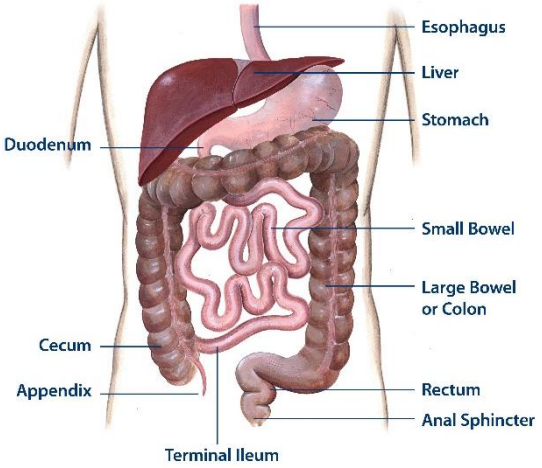
Iron supplements are needed in case of iron deficiency anaemia. They should also be considered if there is iron deficiency without anaemia. IV iron works better and is better tolerated than oral iron pills. In presence of severe anaemia, intolerance to oral iron, or

no good response to oral iron, IV iron should be given. When fast results are needed, IV iron should be used jointly with an erythropoietic agent.

If anaemia is present and iron deficiency is proven, iron supplementation should be commenced. In cases of iron deficiency without anaemia, an individualised approach should be undertaken. The main goal of therapy for iron deficiency anaemia is to supply sufficient iron to increase haemoglobin. Ideally haemoglobin levels should be increased by more than 2 g/dL or to normal values within 4 weeks, iron stores replenished (transferrin saturation more than 30%), relieve anaemia-related symptoms, and to improve quality of life. Transferrin saturation levels of more than 50% and ferritin levels of greater than 800 g/L are considered toxic and should be avoided.
Iron supplementation can be administered orally, intramuscularly or intravenously; which method is used is determined by symptoms, causes, severity, and whether other conditions aside from UC exist in the patient. Oral therapy, despite traditionally being preferred by gastroenterologists, frequently leads to gastrointestinal symptoms like nausea, flatulence, and diarrhoea. In addition, 90% of the iron does not get absorbed and so can lead to exacerbation of IBD. Therefore, IV iron infusions are gaining popularity although are still not mainstream despite being as effective, delivering faster results and being safer than oral iron. Overall, patients who should take IV iron are those who cannot tolerate or respond to oral iron, with severe anaemia, with high inflammation, and who are on medications to stimulate the production of red blood cells.

Glossary

Anatomical illustration of gastrointestinal tract



Term	What the term is related to	Definition
5-ASA or 5-aminosalicylic acid or mesalazine	Medication	This is a topical medication used to treat IBD, preferably UC and under certain conditions also CD. It can also be called mesalazine and can be taken orally or rectally as enema, foam or suppository.
6-TGN	Medication	The active metabolite of azathioprine or mercaptopurine.
Abscess	Complicatio n of CD	An abscess is an enclosed collection of liquefied tissue, known as pus, somewhere in the body. It is the result of the body's defensive reaction to foreign material.
Adalimumab	Medication	Anti-TNF medication commonly used for IBD treatment, belonging to the group of biological (biotechnologically produced) drugs. Injected under the skin (subcutaneous) by the patient or by a nurse.
Adhesions	Complicatio n of surgery	Parts of the bowel glued together by inflammatory reactions. May cause obstruction and pain.
Aminosalicylate	Medication	This is a medication used to treat IBD, also called 5-ASA.
Anaemia	Disease	A condition, in which you do not have enough healthy red blood cells or haemoglobin. Having anaemia may make you feel tired and weak.
Anaemia of chronic disease	Disease related to	This is anaemia that results from a chronic disease such as IBD or other inflammatory processes.

	IBD or inflammatory conditions	
Ankylosing spondylitis	Disease related to IBD	Is a form of arthritis characterized by chronic inflammation that primarily affects the spine, causing pain and stiffness of the back, progressing to the chest and neck.
Anti-TNF medication	Medication	Biological (biotechnologically produced) drugs commonly used to treat Inflammatory Bowel Disease. The most common ones are infliximab, adalimumab, certolizumab and golimumab.
Antibiotics	Medication	Medications used to treat infections caused by bacteria. They are ineffective against viruses.
Antidiarrheal	Medication	A medication that provides relief from the symptoms of diarrhoea. The most common one is loperamide.
Appendectomy	Surgery	The removal of the appendix by a surgeon. Usually done for appendicitis.
Appendicitis	Disease	The inflammation of the appendix which is an extension of the colon. Among other things, appendicitis can cause pain, loss of appetite, and fever or perforation.
Arthritis	Disease related to IBD	Inflammation of joint(s) that causes joint pain and swelling.
Arthropathy		Any disease or abnormal condition affecting a joint.
Auto-immune	Disease descriptor	An auto-immune disease is a disease wherein the immune system attacks healthy cells in the body.
Axial arthritis	Disease related to IBD	Disease of joint(s), can affect the spine and hips.
Azathioprine	Medication	See thiopurines
Biological drugs	Medication	Usually IG (Immunoglobulin) proteins that are made by genetically modified cells, e.g. anti-TNF agents or vedolizumab.
Barium (contrast)	Diagnostic Test	A substance used in certain radiological studies to enhance visualization of anatomical structures.
Biopsy, biopsies	Diagnostic Test	A biopsy is a sample of tissue taken from the body in order to examine it more closely. Biopsies are taken from the bowel wall during colonoscopy.
Bisphosphonates	Medication	Compounds that slow bone loss and increase bone density.
Bowel cancer	Disease related to CD/UC or treatment	This can also be called colorectal cancer. It is cancer of the bowel that IBD patients are at increased risk of getting. Among other things, it can cause symptoms like blood in stools, change in bowel habit, abdominal pain, lumps in the abdomen, and weight loss.
Budesonide	Medication	A drug that belongs to the group of corticosteroids. Budesonide has anti-inflammatory power and it is used to treat acute flares in patients with ileocecal

		CD and UC with the involvement of the end of the colon as enemas. Corticosteroids are also hormones naturally produced by the adrenal glands of our body.
Calcineurin inhibitors	Medication	Immunosuppressant agents which is used to treat IBD and to prevent of organ rejection in transplant patients.
Cervical dysplasia	Disease	Abnormal tissue development of the uterine cervix.
CD or Crohn's Disease	Disease descriptor	This is an Inflammatory Bowel Disease. Crohn's Disease can affect all parts of the gastrointestinal tract including frequently the small intestine whereas UC does not.
Chronic diseases	Disease descriptor	These are diseases that a person has for a long time (usually for life). IBD are chronic diseases.
Ciclosporin	Medication related to UC	Calcineurin inhibitor that is a drug used to slow down the immune system and therefore can be used for treating UC.
Ciprofloxacin	Medication	An antibiotic also used to treat IBD and pouchitis.
Clostridium difficile	Disease	A bacterium that can cause IBD-like symptoms.
Colectomy	Surgery	Removal of the colon by a surgeon. It precedes the IPAA surgery in UC patients.
Colon (see picture)	Body part	This can also be called the large bowel or large intestine.
Colonography	Test	This can be done using a CT or MRI machine. It is a method for gaining a view of the inside of the colon without needing to use an endoscope.
Colonoscopy	Test	This is a test wherein an endoscope with a camera is inserted into the rectum and the whole colon in order to investigate the disease activity and take biopsies.
Colorectal surgeon	Other	This is a surgeon who specialises in surgery of the rectum, anus, and colon.
Corticosteroids (or steroids)	Medication	A group of medications that mimic the effects of hormones naturally produced by the adrenal glands and act as immunosuppressant. Hydrocortisone and prednisolone are two commonly used in IBD treatment.
COX-2 inhibitors	Medication	This is a more specific NSAID with fewer side effects and better tolerated in IBD.
Creatinine	Test	A creatinine blood test helps determine how well the kidneys are functioning.
CRP (C-reactive protein)	Test	Blood test done to measure inflammation in the body. It is useful to detect inflammation in the body, however a high CRP-level does not necessarily mean that the inflammation is in the bowel. Therefore, other tests should also be performed to see whether the origin of inflammation is in the bowel of the IBD patient.
CT (computed tomography)	Test	This is a form of X-ray performed in a scanning machine.

Device-assisted enteroscopy	Test	Examination of the small bowel with a special endoscope.
Disease extent	Disease descriptor	This refers to how much of the colon is affected by UC or CD. This is not to be confused with severity which refers to how deep and extensive the inflammation is. Disease extent is useful for grouping UC into proctitis, left-sided colitis, and extensive colitis, similar for CD with small bowel, large bowel, and upper GI tract involvement.
Disease severity indices	Test	A disease severity index is a way of measuring the severity of disease based on a patients symptoms and certain tests (e.g., how the bowel looks in an endoscopy). Usually, more severe disease is represented by higher scores. One example of this is the Ulcerative Colitis Disease Activity Index (UCDAI) or Crohn' disease activity index (CDAI).
Double contrast barium enema	Test	This is a procedure in which x-rays of the colon and rectum are taken after a liquid containing barium is put into the rectum. The barium outlines the colon and rectum on an x-ray and thus helps to show abnormalities.
Electrolytes	Test	Tested via the blood, these are minerals (e.g., sodium, potassium, and chloride) in your blood and other body fluids that carry an electric charge. IBD can cause abnormal electrolyte levels.
End ileostomy	Surgery	This is when the end of the small intestine is divided and brought out through the abdomen and stitched to the skin to form a stoma. A person with an end ileostomy wears a bag on her/his belly to collect their stool.
Endoscopic	Test	This is the adverb of endoscopy.
Endoscopic intubation	Test	This is the insertion of a tube into the body using an endoscope.
Endoscopy	Test	A procedure wherein a camera on the end of a long tube is inserted into the body to look directly at the organs being examined. The most common endoscopy for IBD patients is (ileo) colonoscopy.
Enema	Medication	This is a fluid injected into the lower bowel by way of the rectum. This can be done to help the doctor perform tests or as a medication route.
Erythema nodosum	Disease related to IBD	Inflammatory condition of the skin.
Erythropoietic agent	Medication	This is a drug that stimulates red blood cell production.
ESR or erythrocyte sedimentation rate	Test	A blood test used to measure the degree of inflammation in the body, similar to CRP.
Extensive colitis	Disease descriptor	This is UC that affects the whole colon.
Extent (disease	Disease	Disease extent refers to how much of the intestine

extent)	descriptor	is affected by an IBD.
Faecal calprotectin	Test	Protein that is released into the bowel when it is inflamed. Faecal calprotectin levels only rise for bowel inflammation, thus making faecal calprotectin better for measuring inflammation than CRP or ESR. Not specific for IBD. The patient has to provide a stool sample for it to be measured.
Fertile	Other	A fertile person is a person who is physically able to have children.
Fistula, fistulae	Complicatio n of CD	An ulcer extending through the intestinal wall, creating an abnormal passage between the intestine and skin, or between intestine and another organ. Single fistulae consist of a single tract; complex fistulae have multiple tracts. Fistulizing CD is a form of CD.
Fistulography	Test	An X-ray examination of a fistula.
Fistulotomy	Surgery	Surgical opening of a fistula.
Flare or relapse	Disease descriptor	This is a state of active disease and is the opposite of the disease being in remission. A person who is in a flare will experience symptoms and have inflammation.
Fracture	Other	This is a break in the bone either caused by a single event or continual stress on the bone.
Gastroenterologis t	Other	This is a doctor who specialises in treating gastrointestinal diseases like IBD.
Haemoglobin levels	Test	Haemoglobin levels measure how much haemoglobin is in your blood. Haemoglobin carries oxygen in the blood. Low levels indicate anaemia.
Histological	Test	Histological examination occurs when cell tissue from biopsies gets examined under a microscope.
IBD	Disease	Short for Inflammatory Bowel Disease, this is a collective term for Crohn's Disease and Ulcerative Colitis.
IBDU or IBD unclassified	Disease descriptor	If it cannot be decided whether a person has CD or UC after all tests have been performed, the term IBDU should be used.
IC or indeterminate colitis	Disease descriptor	In cases where it is not possible to tell whether a person has CD or UC, it can be called IC. However, IC should only be used for resection samples.
Ileocolonoscopy	Test	Endoscopy to look at the colon and the ileum.
Ileorectal anastomosis	Surgery	This is a surgery wherein the rectum is preserved and the ileum is attached to the rectum. This is in contrast to the IPAA wherein the rectum is not preserved.
Ileoscopy	Test	This is using an endoscopy to look at the ileum which is the lowest part of the small bowel.
Imaging	Test	Production of a picture or image of a body part using any of a variety of techniques such as x-rays, ultrasound, CT or MRI. Imaging techniques are often needed to assess, which part of the body

		is affected by IBD.
Immunized	Other	A person is immunized if he/she has been made immune to an infection. Common immunizations are for measles, mumps, and tetanus but there are many others.
Immunomodulator	Medication	Immunomodulators weaken or stimulate the activity of the immune system. Immunosuppressants are a common immunomodulator used in IBD treatment because it is thought that IBD is at least partly caused by an overactive immune system.
Immunosuppressant	Medication	A group of drugs used to slow down the immune system, including steroids, thiopurines, methotrexate, anti-TNF medications, and vedolizumab. Because IBD may be caused by an overactive immune system, immunosuppressants can be useful for its treatment.
Infliximab	Medication	Anti-TNF biological medication commonly used for IBD treatment. It is given to the patient through a drip straight into the bloodstream.
IPAA or ileal pouch anal anastomosis	Surgery	This is a surgery often performed for UC patients wherein the end of small intestine is re-structured as a pouch and does the job the large intestine used to do before it was removed.
Iron deficiency	Disease	This is when there is not enough iron in the blood.
Iron deficiency anaemia	Disease	This is a condition in which blood lacks red blood cells due to iron deficiency.
Iron deficiency without anaemia	Disease	This is a condition where iron is depleted but not to such an extent that anaemia happens.
Irritable bowel syndrome (IBS)	Disease	A common condition with IBD-like symptoms, but without inflammation.
IV or Intravenous	Medication	This is medication taken through the veins into the blood stream.
Keratolytic agent	Medication	This is a medication used to remove warts and other lesions.
Laparoscopic	Surgery	Laparascopic surgery is a way of doing surgery wherein small incisions are made into the patient and cameras are inserted to view the surgical site. Due to the smaller incisions, it usually leads to a quicker recovery than usual surgery.
Lactoferrin	Test	Protein that is released into the bowel when it is inflamed. The patient has to provide a stool sample for it to be measured.
Left-sided colitis	Disease descriptor	This is UC that happens up to, but not beyond the left side of the colon and can be effectively treated with topical treatment
Loperamide	Medication	A typical anti-diarrheal drug, see antidiarrheal.
Low molecular weight heparin	Medication	This is a medication commonly used to prevent blood clots.
Localized disease	Disease descriptor	Disease confined to one organ system or a localized area of the bowel.

Lymphoproliferative disorders (LPDs)	Disease	A group of diseases in which lymphocytes (white blood cells) are produced excessively. LPDs include different leukemias and lymphomas.
Maintenance treatment	Medication	This is treatment used to keep the patient in remission.
Malabsorption	Complication of CD	Abnormal absorption of food nutrients in the gastrointestinal tract.
Malnutrition	Complication of CD	Lack of proper nutrition resulting from, for example, not being able to eat enough, not eating enough of the right things, or malabsorption (see Malabsorption).
Mesalazine	Medication	A drug used to treat IBD. It can be taken orally or rectally.
Methotrexate	Medication	Drug, belongs to the group of immunosuppressants, commonly used for CD treatment. Not as effective for Ulcerative Colitis.
Metronidazole	Medication	This is an antibiotic commonly used to treat pouchitis and fistulising CD.
MR (Magnetic Resonance) Enterography	Test	A test that uses magnetic waves to take diagnostic images of the small bowel with the help of an oral contrast dye. Radiation is not used.
MRCP or Magnetic resonance cholangiography	Test	This is a special test using an MRI machine to check for hepatobiliary disorders.
MRI or Magnetic Resonance Imaging	Test	A test that uses magnetic waves to take diagnostic images of various parts of the body. Radiation is not used.
NSAIDs or non-steroidal anti-inflammatory drugs	Medication	These drugs can provide pain relief and also reduce fever and non-gut inflammation. The most common ones are ibuprofen and aspirin and are best avoided by IBD patients, as they may increase the risk of a flare.
Obstruction, obstructive	Complication of CD	An obstruction is when the CD inflammation thickens the intestinal wall, causing the intestine to narrow, or when parts of the intestine develop adhesions and the flow of digestive contents is blocked.
Oral	Medication	Oral medication is medication taken via the mouth.
Osteopenia	Disease	This is weakening of the bones that is not significant enough to be considered osteoporosis.
Osteoporosis	Disease	This is a medical condition wherein the bones become weak and puts the person at a higher risk of getting a fracture.
p-ANCA	Test	p-ANCA stands for Perinuclear Anti-Neutrophil Cytoplasmic Antibodies. They are detected in the blood.
Patient-centred	Other	Patient-centred care involves ensuring that the individual needs of the patient are respected and responded to and that the patient values guide all clinical decisions.
Peripheral	Disease	Joint inflammation usually affecting the large joints

arthritis		of the limbs.
Pouchitis	Complicatio n	Inflammation of the ileal pouch (see IPAA).
Pyoderma gangrenosum	Disease	Inflammation of the skin resulting in painful ulcerations caused by autoimmune mechanisms and not by infection, sometimes seen in IBD patients
Rectal	Body part	Something that is rectal relates to the end of the colon, which is called a rectum. For example, a medication that is inserted into the rectum through the anus is called a rectal medication.
Rectum	Body part	This is the final section of the colon. It ends at the anus.
Relapse	Disease descriptor	Reactivation of the illness.
Remission	Disease descriptor	Remission is when a person has no active disease; this is in contrast to the terms "flare" or "relapse" which are used to describe when a person does have active disease.
Resection	Surgery	Surgically removing all or part of an organ or other body structure.
Sacroiliitis	Disease	Inflammation of the joint between sacrum and ileal pelvic bones.
Salvage therapy	Treatment	Salvage therapy is a treatment that is used when all conventional treatments have failed and is used as a last effort to get the disease under control.
Serological	Test	Serology studies serum and other body fluids. Usually it is used to diagnose antibodies in the serum.
Serology	Test	This is testing of serum or other bodily fluids.
Serum ferritin level	Test	This is a test that measures the amount of iron stored in the body.
Serum urea	Test	Urea is a substance normally cleared from the blood by the kidneys into the urine. Serum urea levels are important to test because abnormal readings can indicate whether the kidneys are affected or if the patient is dehydrated.
Seton	Surgery	A thread that is used to keep a fistula tract open and to avoid collection of pus in an abscess.
Side effects	Medication	Undesired (harmful) effect of a medication or intervention.
Sigmoidoscopy	Test	This is similar to a colonoscopy, except it only looks at the last part of the colon as opposed to the whole colon.
Small bowel capsule endoscopy (SBCE)	Test	A test in which the patient swallows a capsule that contains a tiny camera. The camera records images of the gastrointestinal tract.
Stenosis	Disease	This is a narrowing that is significant enough to cause the patient discomfort.
Steroids	Medication	Steroids are commonly used to treat IBD and work

		by immunosuppression. They can be topical or systemic. Due to their multiple side effects, their use should be limited as much as possible.
Stricture	Disease of CD	This is a narrowing that is significant enough to cause the patient discomfort.
Stool or stools	Other	A stool is a bowel motion or faeces.
Subtotal colectomy	Surgery	In contrast to a colectomy, this is a colectomy which involves removal of part of the colon, not the whole colon.
Sulfasalazine	Medication	Sulfasalazine is a drug used to treat IBD. Sulfasalazine consists of two parts, 5-ASA, the active part, and an antibiotic, sulfapyridine. Sulfasalazine is split by bacteria in the colon and delivers 5-ASA.
Suppositories or suppository	Medication	This is a drug that is inserted into the rectum and then melts and covers the bowel lining to treat inflammation.
Surveillance	Test	Surveillance happens when the doctor regularly checks the IBD patient, often with an endoscope, to see whether bowel cancer has developed. Surveillance is important because IBD patients are at an increased risk of getting bowel cancer.
Systemic	Medication	A systemic drug that affects the whole body. This in contrast with a topical drug that does not go throughout the body.
T-score	Test	A T-score is a measure of bone density.
Tacrolimus	Medication	This is an immunosuppressant similar to cyclosporine that can be used orally to treat UC.
Tenesmus	Disease descriptor	Painful spasm or cramp in the rectum/anus, usually accompanied by involuntary straining efforts and urgent desire to evacuate without real product.
Thiopurines	Medication	These drugs are immunosuppressants. Azathioprine and mercaptopurine are the most commonly used ones for treatment of IBD.
thrombocytosis	Test	Increased number of platelets (thrombocytes).
Topical	Medication	This is a drug that treats the inflammation directly without being absorbed by the body.
Transferrin saturation	Test	This is a measure of the iron binding capacity in the body and levels of lower than 16% indicate iron deficiency.
Tuberculosis	Disease	This is an infectious disease that affects the lungs and other parts of the body caused by mycobacterium tuberculosis.
UC or Ulcerative Colitis	Disease descriptor	UC is one of the Inflammatory Bowel Diseases.
Ultrasound	Test	An imaging method that uses sound waves to evaluate organs in the body.
Ursodeoxycholic acid	treatment	This is an oral medication that can be given to patients with PSC (Primary sclerosing cholangitis, a chronic liver disease characterised by inflammation

		and fibrosis of the bile ducts inside and outside the liver.) to protect the liver and prevent bowel cancer
Uveitis	Disease	This is inflammation of the uvea in the eye.
Validated	Test	If something has been validated, it means it has been proven to be an accurate measure of what it claims to be measuring. For example, a disease severity index will be validated once it is proven to be measuring disease severity accurately.
Vedolizumab	Medication	A biological (biotechnologically produced) drug used to treat IBD. It is given to the patient through a drip straight into the bloodstream.
VSL#3	Medication	This is a probiotic (live microorganisms which when administered in adequate amounts confer a health benefit on the host) which has shown promise for treating pouchitis.
Weaned	Medication	If a medication is weaned, it is taken off gradually and not suddenly. This has to be done in the case of steroids because sudden stopping of steroids can have serious side effects.

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The ECCO-EFCCA Patient Guidelines are based on the ECCO Clinical Guidelines on Crohn's Disease and Ulcerative Colitis. For access to the ECCO Clinical Guidelines, please follow this link: https://www.ecco-ibd.eu/index.php/publications/ecco-guidelines-science.html
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