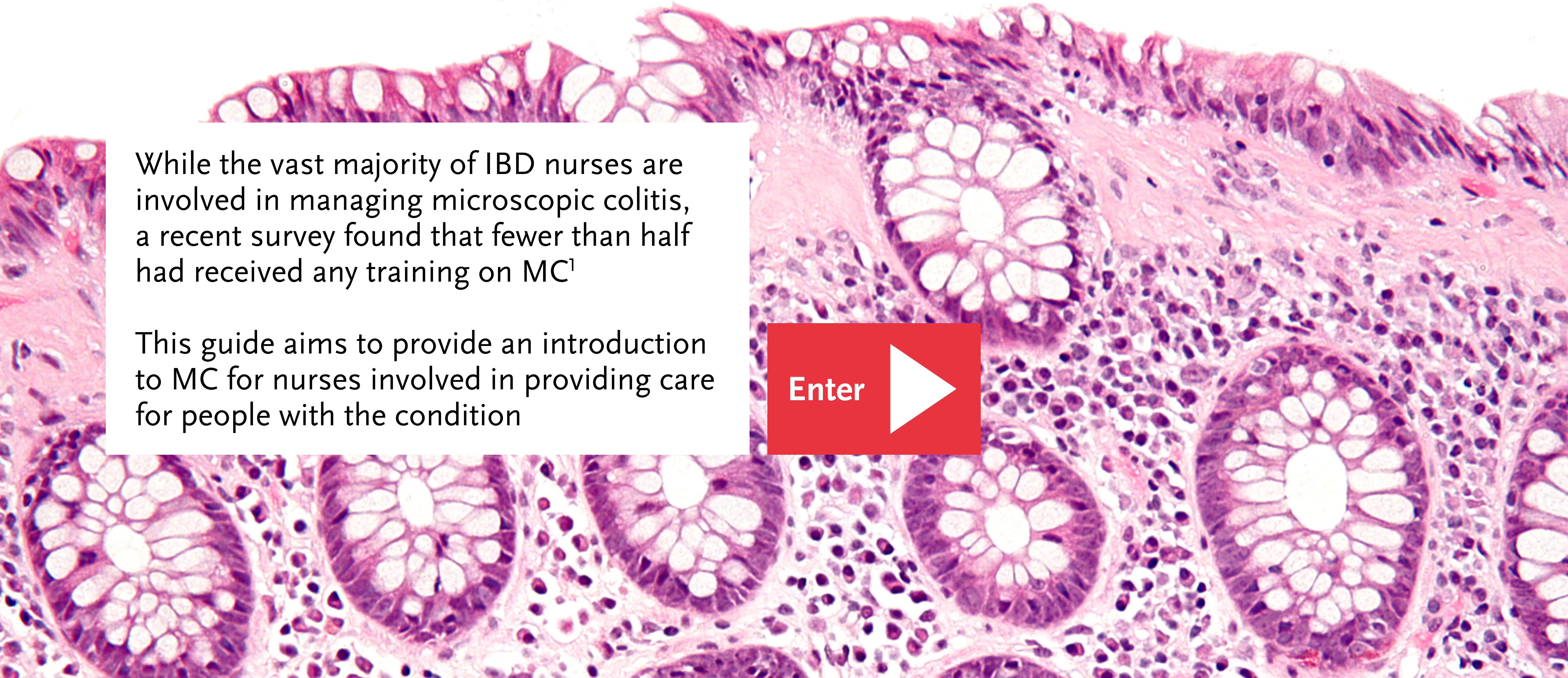


MICROSCOPIC COLITIS

M MADE C CLEAR

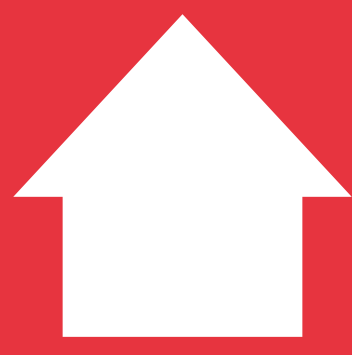


While the vast majority of IBD nurses are involved in managing microscopic colitis, a recent survey found that fewer than half had received any training on MC¹

This guide aims to provide an introduction to MC for nurses involved in providing care for people with the condition

Enter





Click on any of the sections below to find a menu screen with more information related to each topic

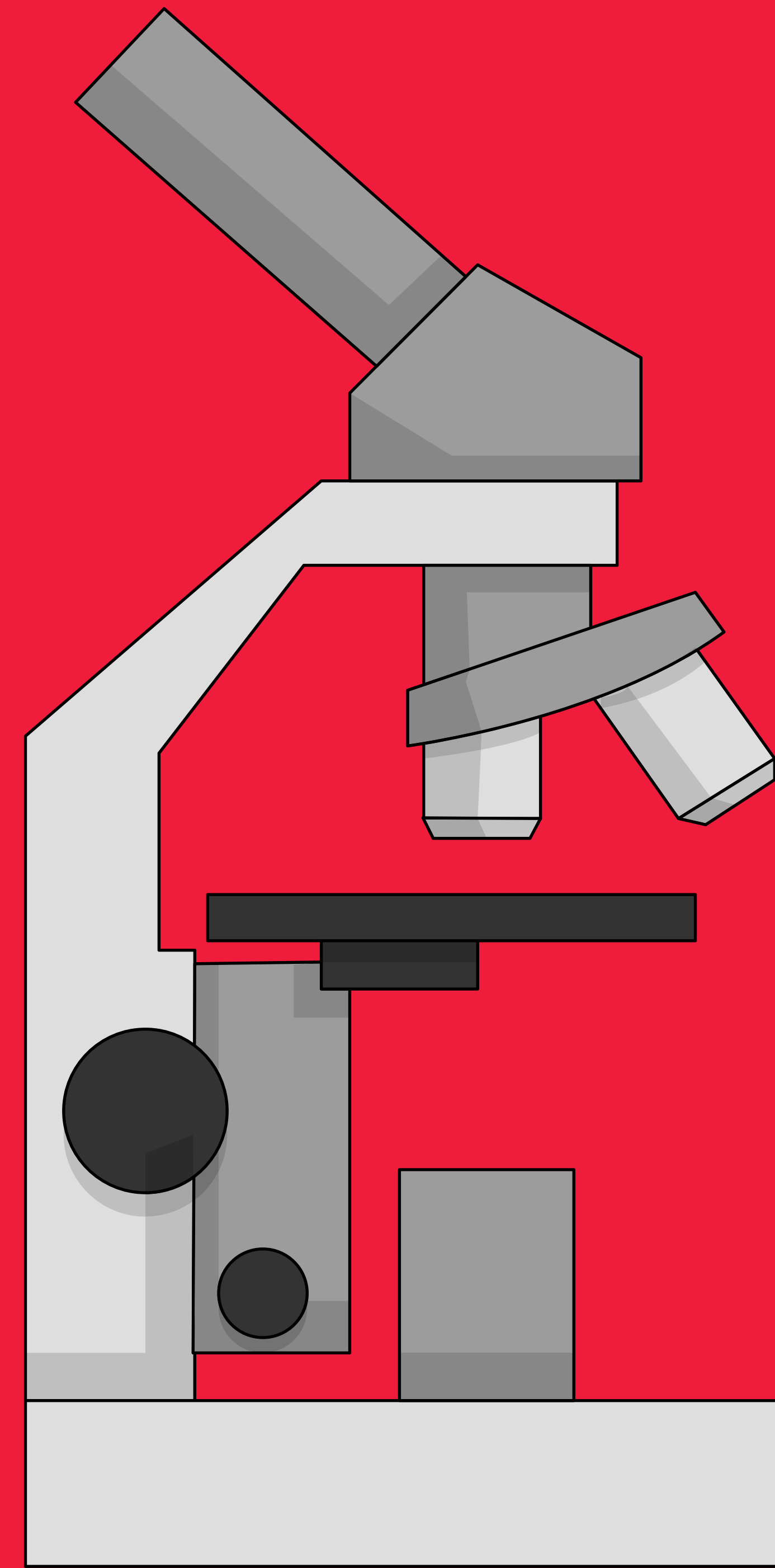
To get back to this main menu screen, you can click on the button in the top left-hand corner of each screen

MICROSCOPIC COLITIS

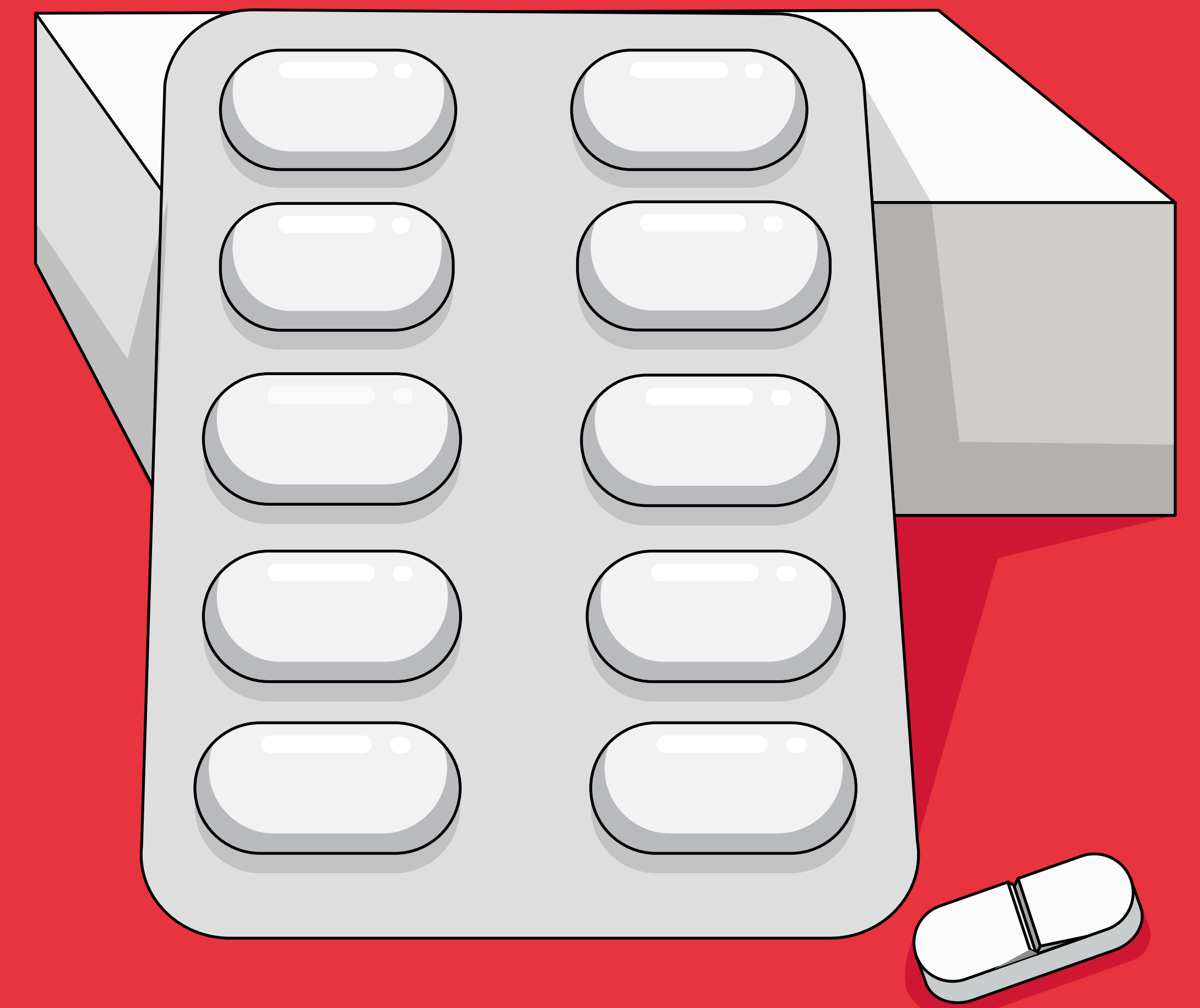
**MADE
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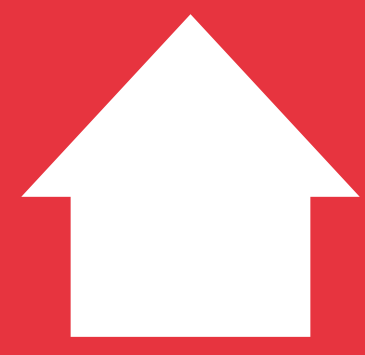
Finding It



Confirming It



Treating It



Finding It

1

What is MC?

2

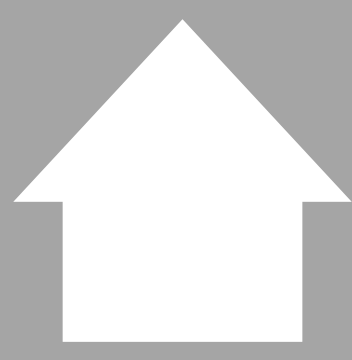
How common is MC?

3

What are the risk factors for MC?

4

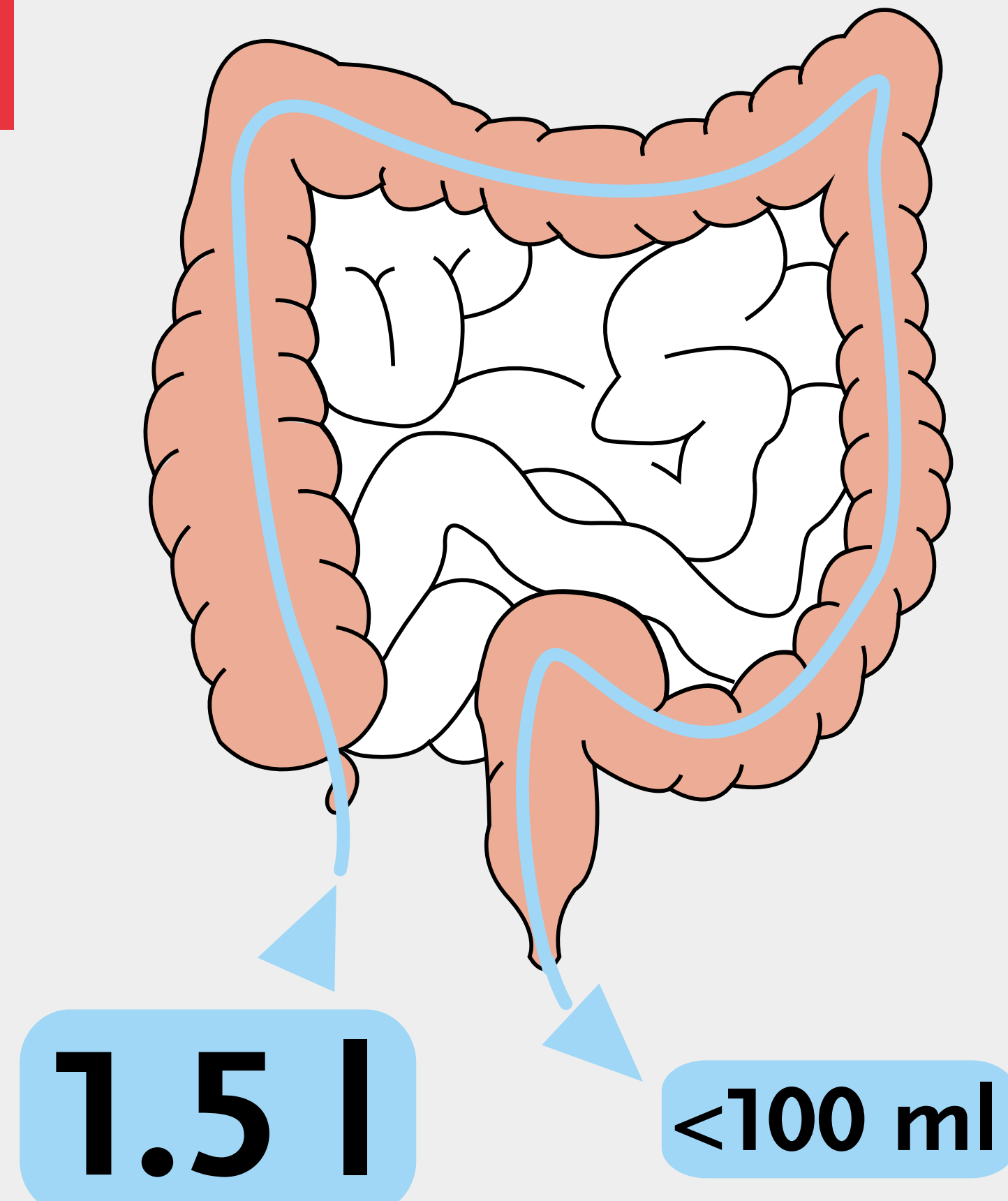
How does MC differ from IBS?



MC is a chronic inflammatory disease of the colon¹

The colon converts indigestible liquid food material (chyme) into semi-solid faeces²

Of the 1.5 l of fluid entering the colon every day, most is absorbed leaving <100 ml to pass out in the faeces²



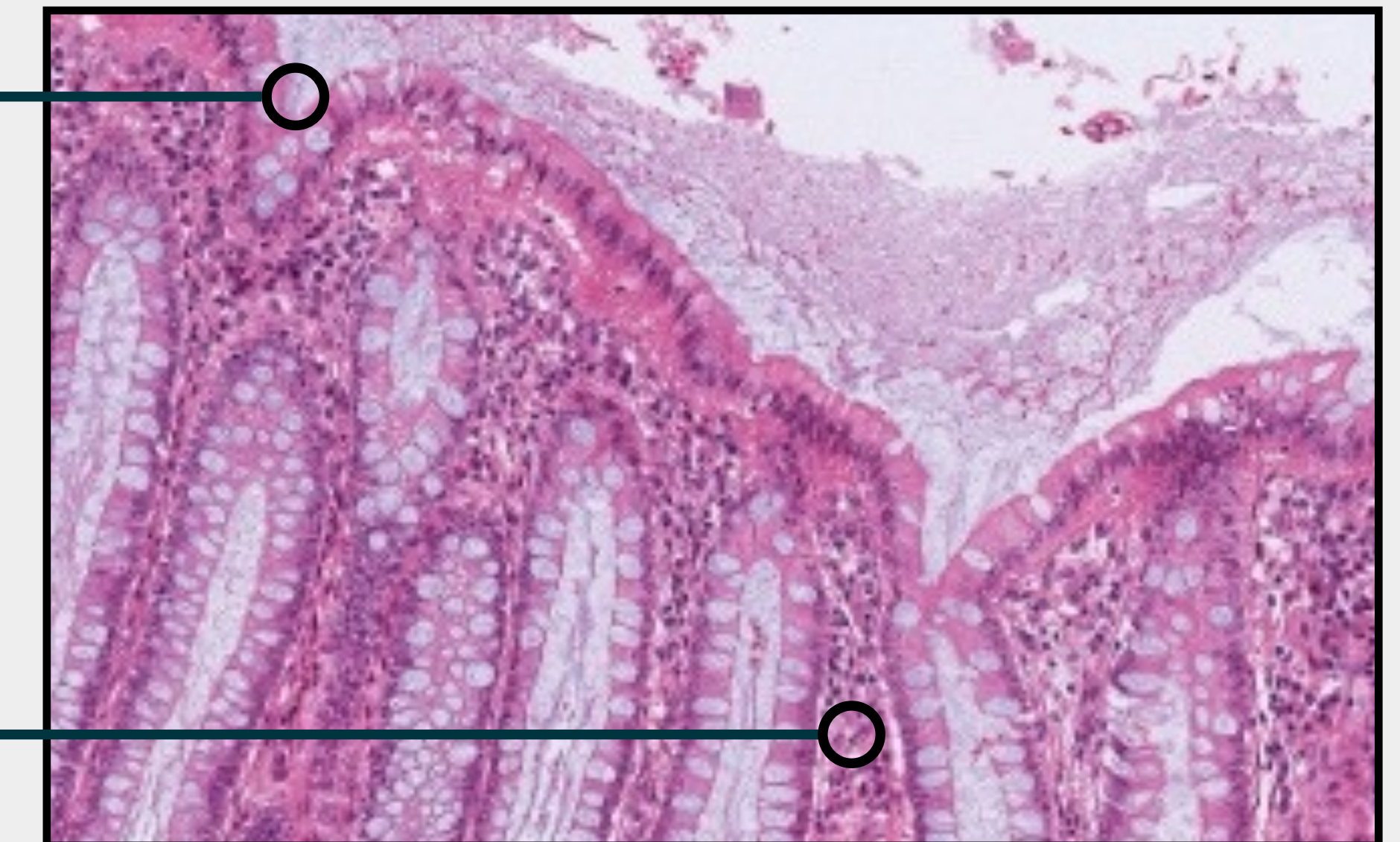
In MC, there are changes to the colonic mucosa⁵

Epithelium

- injuries to the surface epithelial cells
- subepithelial collagen deposition

Lamina propria

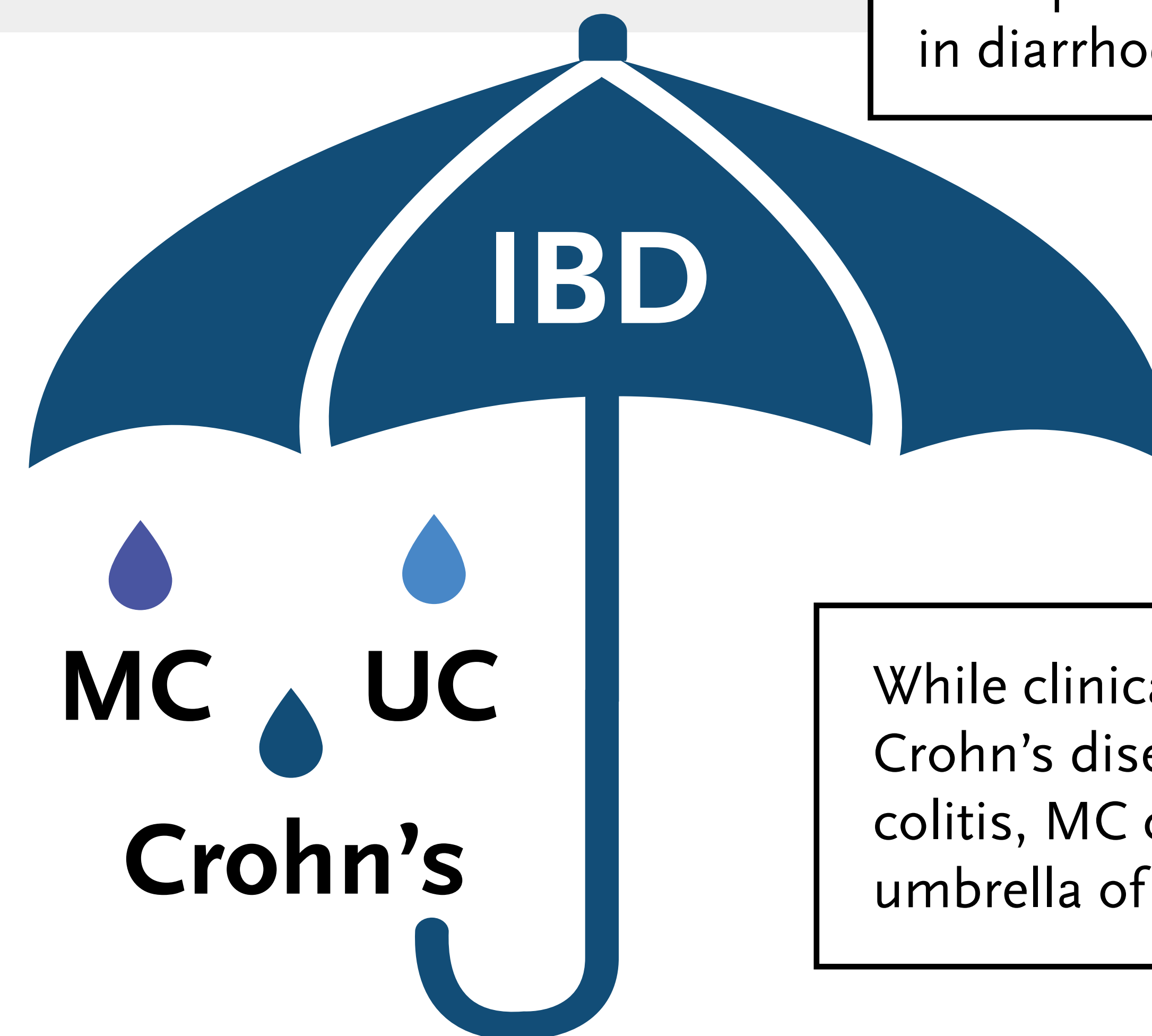
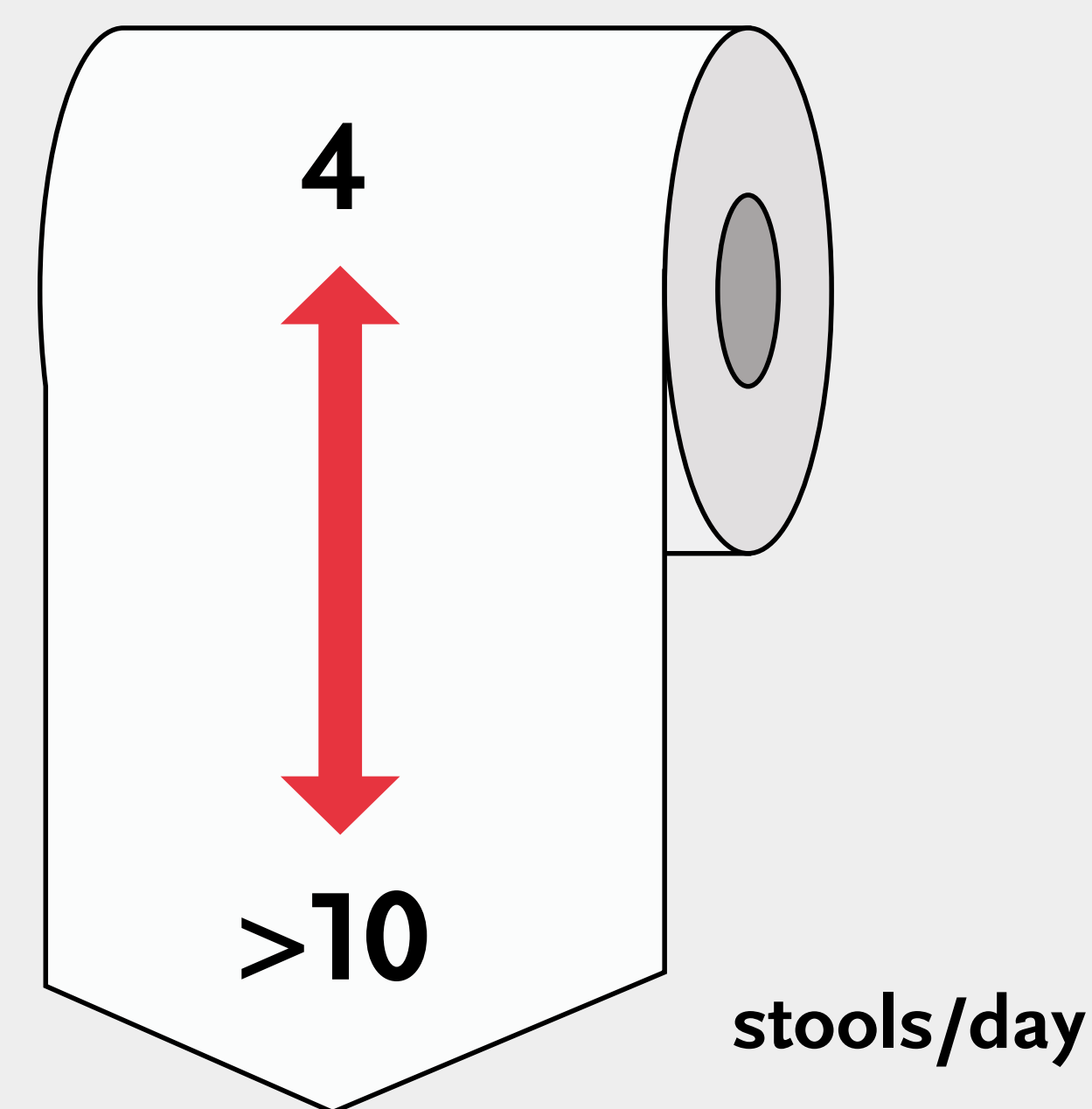
- increased number of inflammatory cells



The net result is decreased absorption of water resulting in diarrhoea⁶

The defining feature of MC is chronic or recurrent, non-bloody, watery diarrhoea with a normal or near-normal endoscopy³

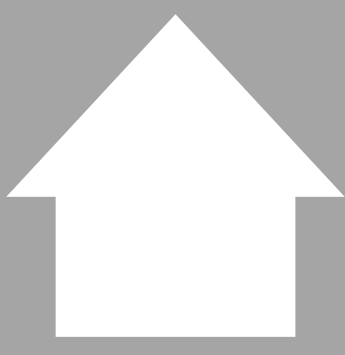
Stool frequency varies; commonly it is 4-9 stools/day, but it can often exceed 10 stools/day⁴



While clinically distinct from Crohn's disease and ulcerative colitis, MC comes under the umbrella of IBD⁵

1. Miehke S *et al.* Lancet Gastroenterol Hepatol 2019; 4(4): 305-14.
 2. Nigam Y *et al.* Nursing Times 2019; 115(10): 50-3.
 3. Münch A *et al.* Frontline Gastroenterol 2020; 11(3): 228-34.
 4. Townsend T *et al.* Frontline Gastroenterol 2019; 10(4): 388-93.
 5. Walsh C. Gastro Nurs 2021; 19(9): 20-6.
 5. Protic M *et al.* World J Gastroenterol 2005; 11(35): 5535-99.

MC: microscopic colitis
 IBD: inflammatory bowel disease
 UC: ulcerative colitis



MC is no longer considered to be a rare disease¹

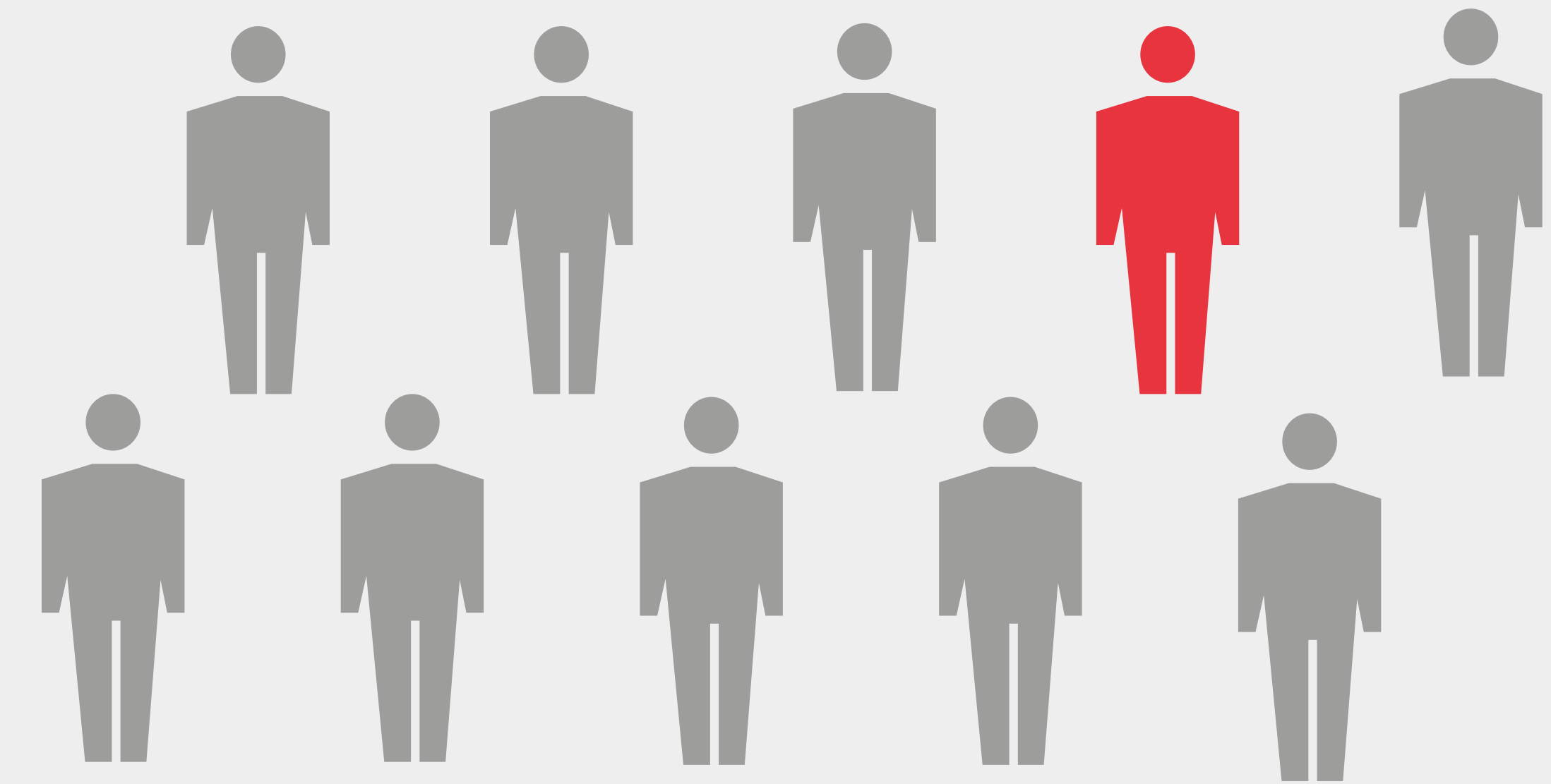
The data from five population-based MC studies conducted in Western countries were pooled to estimate the prevalence of MC²

The estimated number of cases of MC was

119
per 100,000

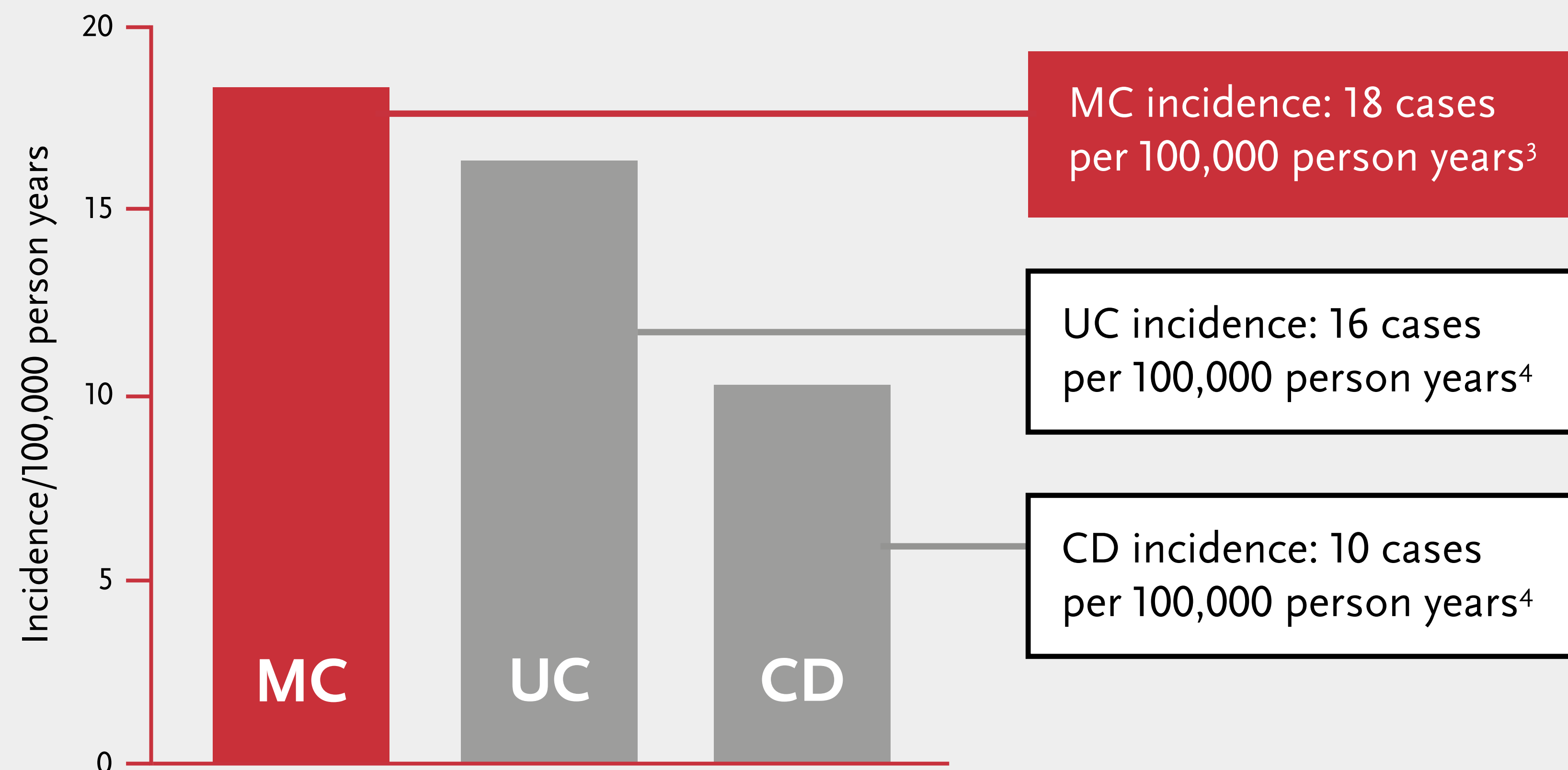
of the population²

Approximately 1 in 10 people who present with non-bloody diarrhoea will have MC²



In those ≥65 years of age, as many as 1 in 5 cases may be due to MC⁵

Recent UK studies suggest the number of new cases of MC appears to be comparable to that of UC and CD¹

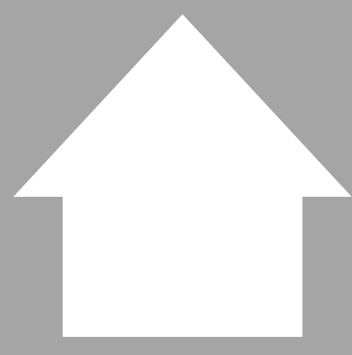


A large, hidden burden of undiagnosed and untreated MC likely exists in the UK population owing to systematic misdiagnosis of MC as IBS⁶

1. Walsh C. *Gastro Nurs* 2021; 19(9): 20-6.
 2. Miehke S *et al.* *United Eur Gastroenterol J* 2021; 9(1): 13-37.
 3. Lewis NR *et al.* *Gut* 2017; 66: A156.
 4. Pasvol TJ *et al.* *BMJ Open* 2020; 10: e036584.
 5. Burke KE *et al.* *Nat Rev Dis Primers* 2021; 7(1): 39.
 6. Münch A *et al.* *Frontline Gastroenterol* 2020; 11(3): 228-34.

CD: Crohn's disease
 MC: microscopic colitis
 IBS: irritable bowel syndrome
 UC: ulcerative colitis





What is MC?

How common is MC?

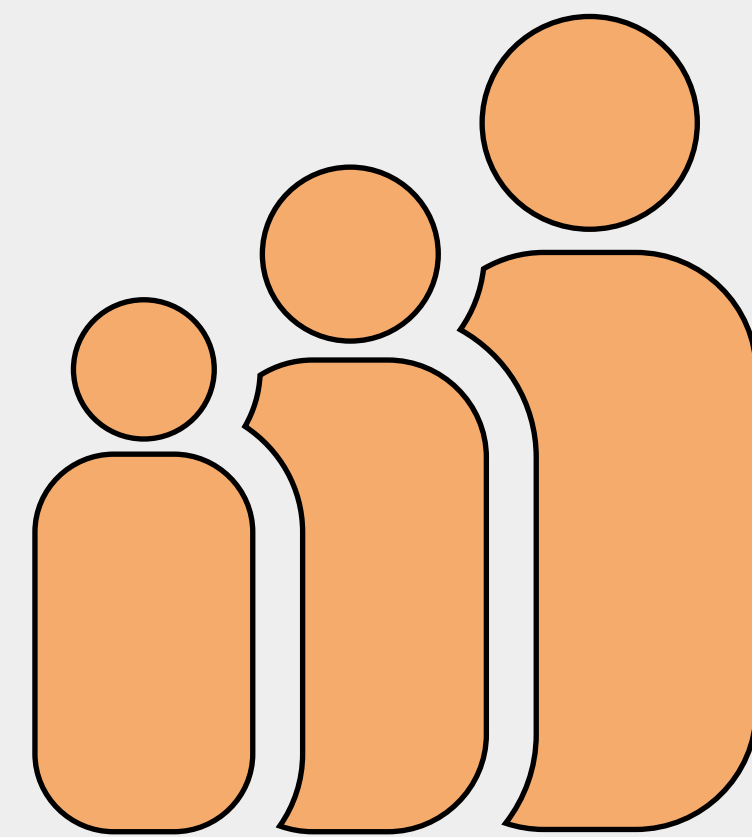
What are the risk factors for MC?

How does MC differ from IBS?

Increasing age

Those over 65 years of age are 5 times more likely to be diagnosed with MC than younger people¹

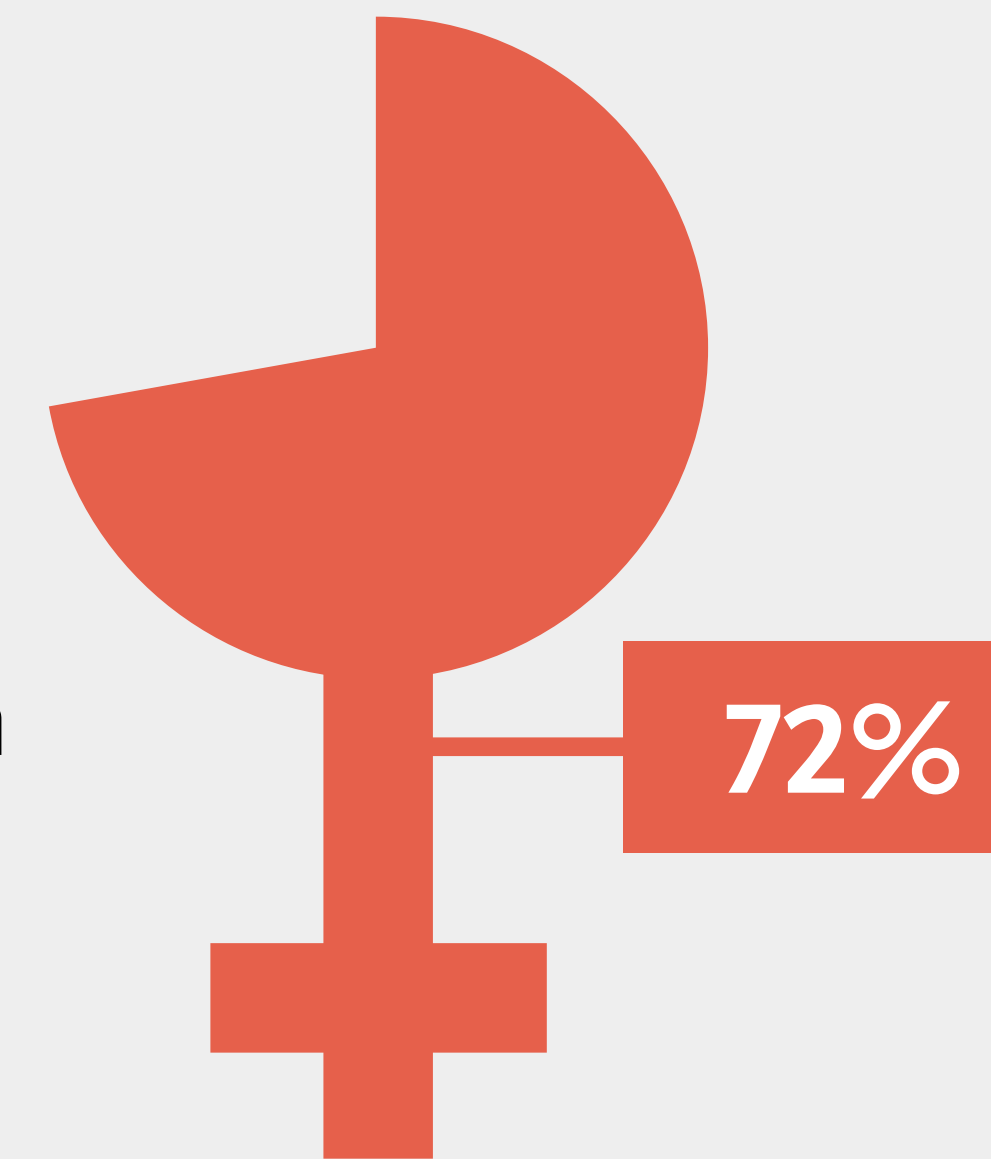
Not everyone with MC is, however, elderly; cases have even been described in children²



Female sex

The risk of developing MC is higher in women than in men²

Research has shown that 72% of people with MC were female²



Smoking

Smokers are more than 2 times as likely to develop MC as non-smokers³

Smoking may increase frequency of watery stools in MC, as well as the risk of persistent disease⁴



Use of some medications

Chronic or frequent use of PPIs, NSAIDs or SSRIs is associated with an increased risk of MC²

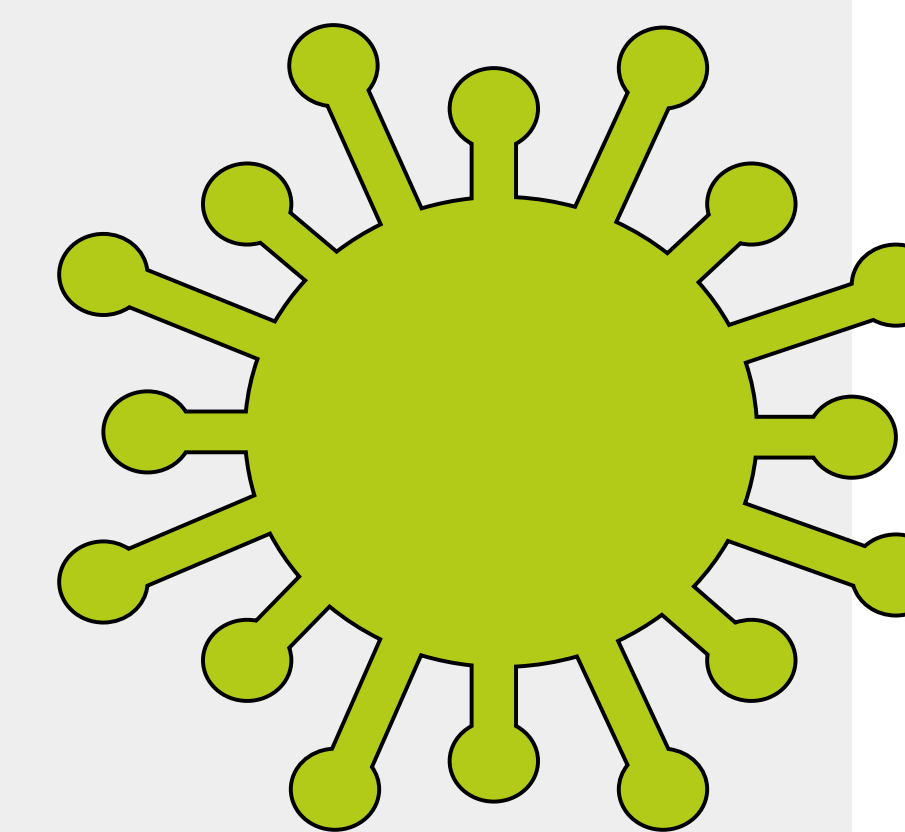
These drugs may not actually cause MC, but rather worsen diarrhoea and bring the diagnosis to attention⁵



Other autoimmune diseases

Rheumatoid arthritis, hypo/hyperthyroidism, coeliac disease, and type 1 diabetes mellitus among others have been linked to MC⁴

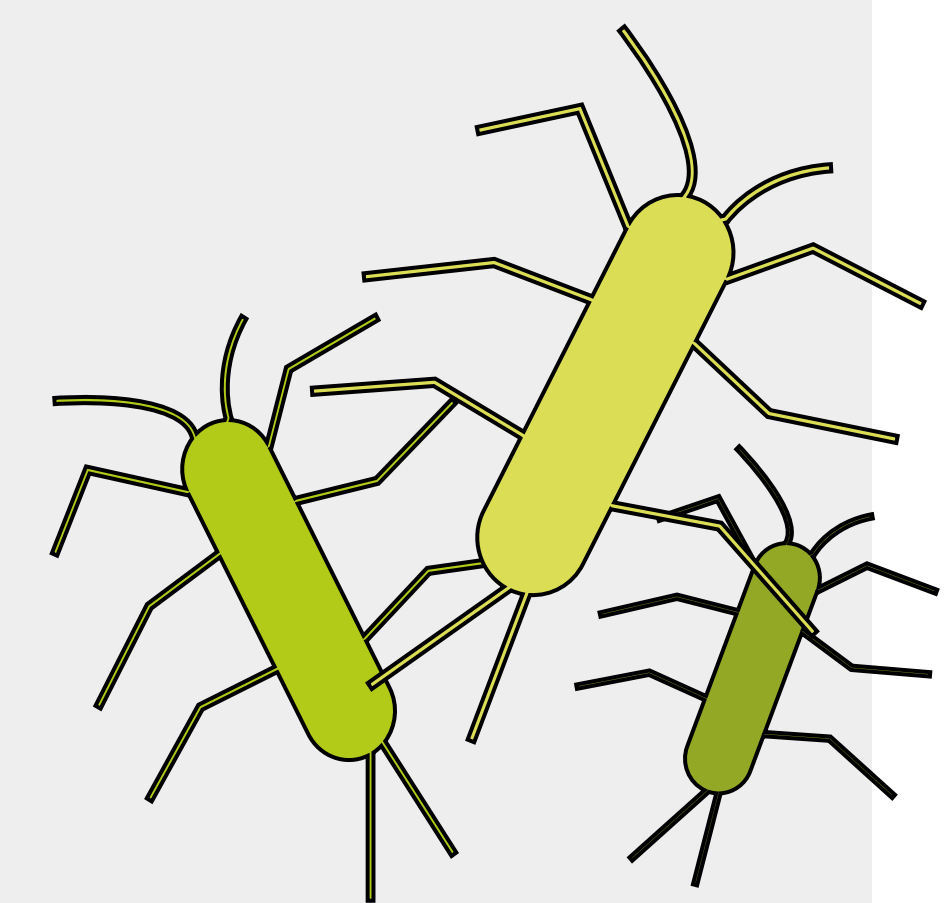
Patients with coeliac disease have a 50 to 70 times greater risk of MC⁴



Gastrointestinal infections

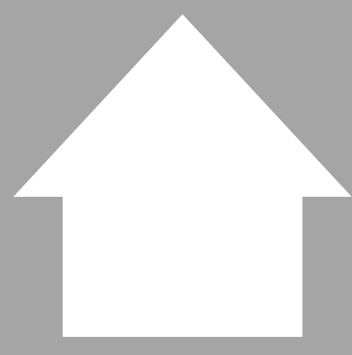
Gastrointestinal infections have been linked to changes in the gut microbiome and development of IBD⁵

7.5% of patients with MC in a recent Swedish study had a previously diagnosed gastrointestinal infection⁵



1. Fernández-Bañares F *et al.* J Crohns Colitis 2016; 10(7): 805-11.
 2. Miehke S *et al.* United Eur Gastroenterol J 2021; 9(1): 13-37.
 3. Burke KE *et al.* J Crohns Colitis 2018; 12(5): 559-67.
 4. Tome J *et al.* Mayo Clin Proc 2021; 96(5): 1302-8.
 5. Khalili H *et al.* Gastroenterology 2021; 160(5): 1599-1607.e5.

IBD: inflammatory bowel disease
 MC: microscopic colitis
 NSAID: nonsteroidal anti-inflammatory drug
 PPI: proton-pump inhibitor
 SSRI: selective serotonin reuptake inhibitor

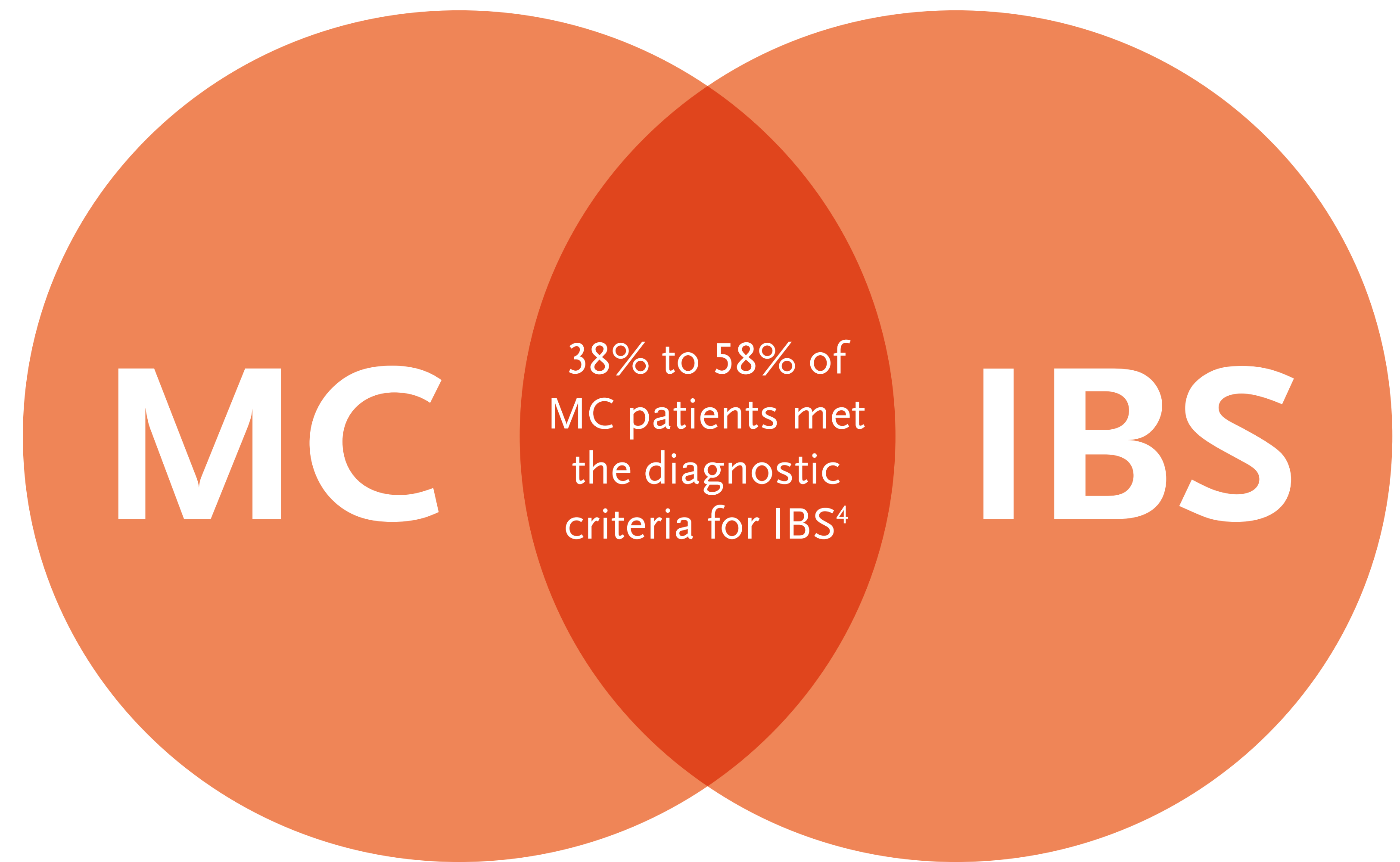


As GPs regularly diagnose IBS without specialist referral, MC can quite easily be missed^{1,2}

Besides diarrhoea, patients with MC can present with abdominal pain, even when they are in clinical remission which may lead to misdiagnosis as IBS²

A negative faecal calprotectin test rules out UC or CD, and typically indicates a diagnosis of IBS³

While faecal calprotectin levels can be slightly elevated with MC, results may be within relatively normal limits³



Differentiating IBS from MC with clinical history⁵

Patient history data	IBS	MC
Age of onset	Usually before 50 years of age	Mostly after 50 years of age
Stool consistency	Variable, alternating	Usually watery
Abdominal pain or discomfort	Obligatory	Variably present
Diarrhoea during night	Very rare	Possible
A feeling of inadequate bowel emptying	Common	Not present
Weight loss	Rare	Common
Faecal incontinence	Rare	Common
Bloating/a feeling of fullness	Common	Rare
Other immune-mediated disorders	Common	Common

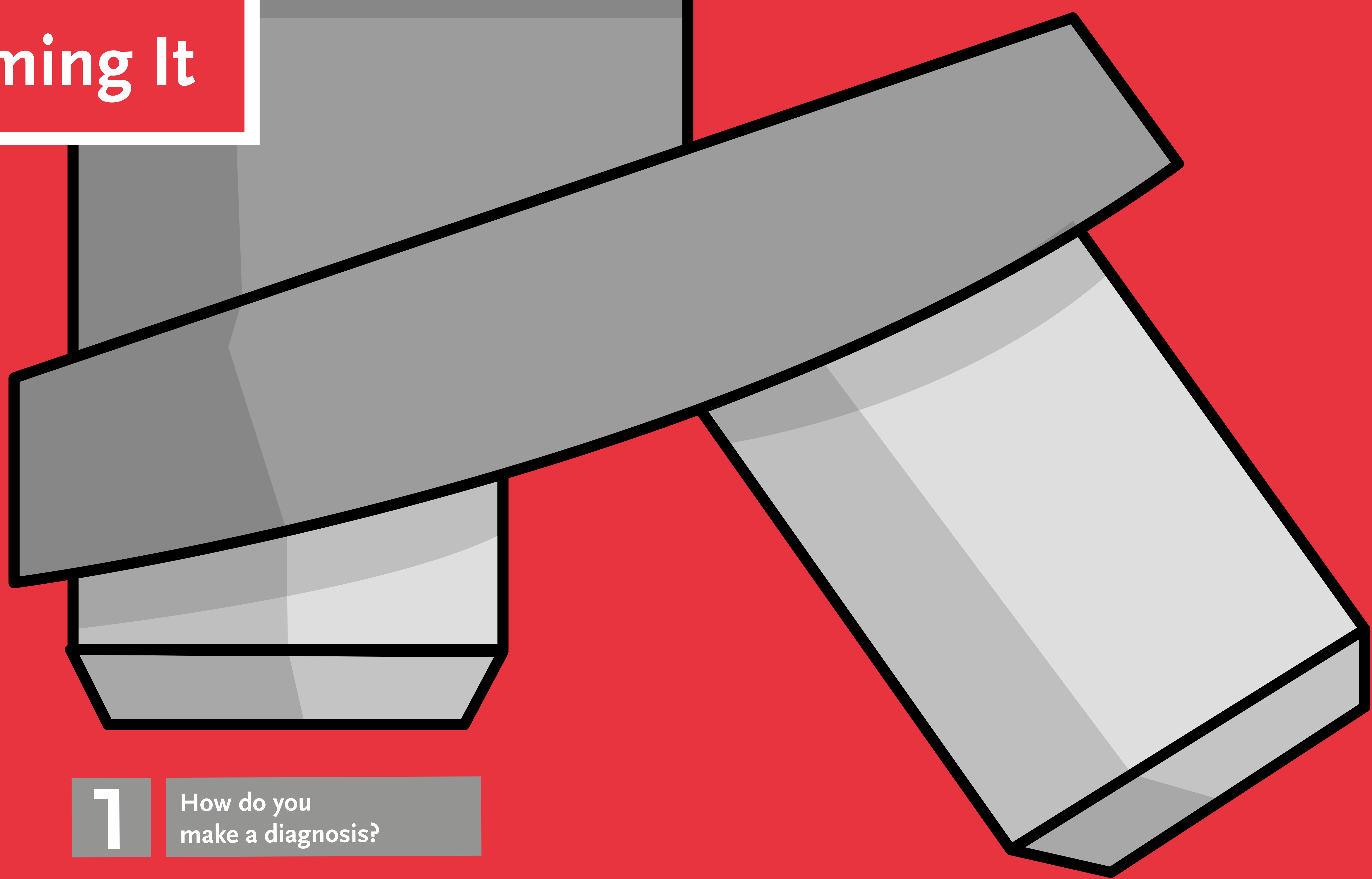
“ Given the high overall symptom burden and severely affected quality of life, diagnostic differentiation of patients with MC from those with IBS is crucial⁶ ”

1. Münch A *et al.* Frontline Gastroenterol 2020; 11(3): 228-34.
 2. Münch A. UEG Education 2021; 21: 10-3.
 3. Walsh C. Gastro Nurs 2021; 19(9): 20-6.
 4. Abboud R *et al.* Inflamm Bowel Dis 2013; 19(3): 550-3.
 5. Fedor I *et al.* Ther Adv Chronic Dis 2022; 13: 20406223221102821.
 6. Miehleke S *et al.* Lancet Gastroenterol Hepatol 2019; 4(4): 305-14.

CD: Crohn's disease
 GP: general practitioner
 IBS: irritable bowel syndrome
 MC: microscopic colitis
 UC: ulcerative colitis



Confirming It



1

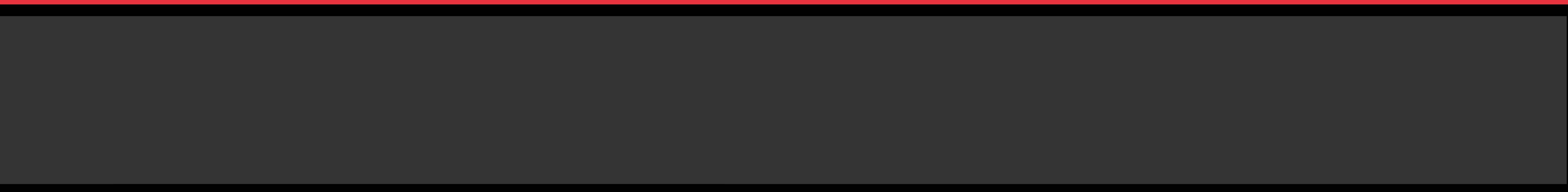
How do you make a diagnosis?

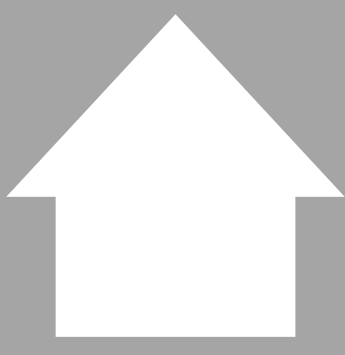
2

What histological criteria define MC?

3

What else causes chronic diarrhoea?





How do you make a diagnosis?

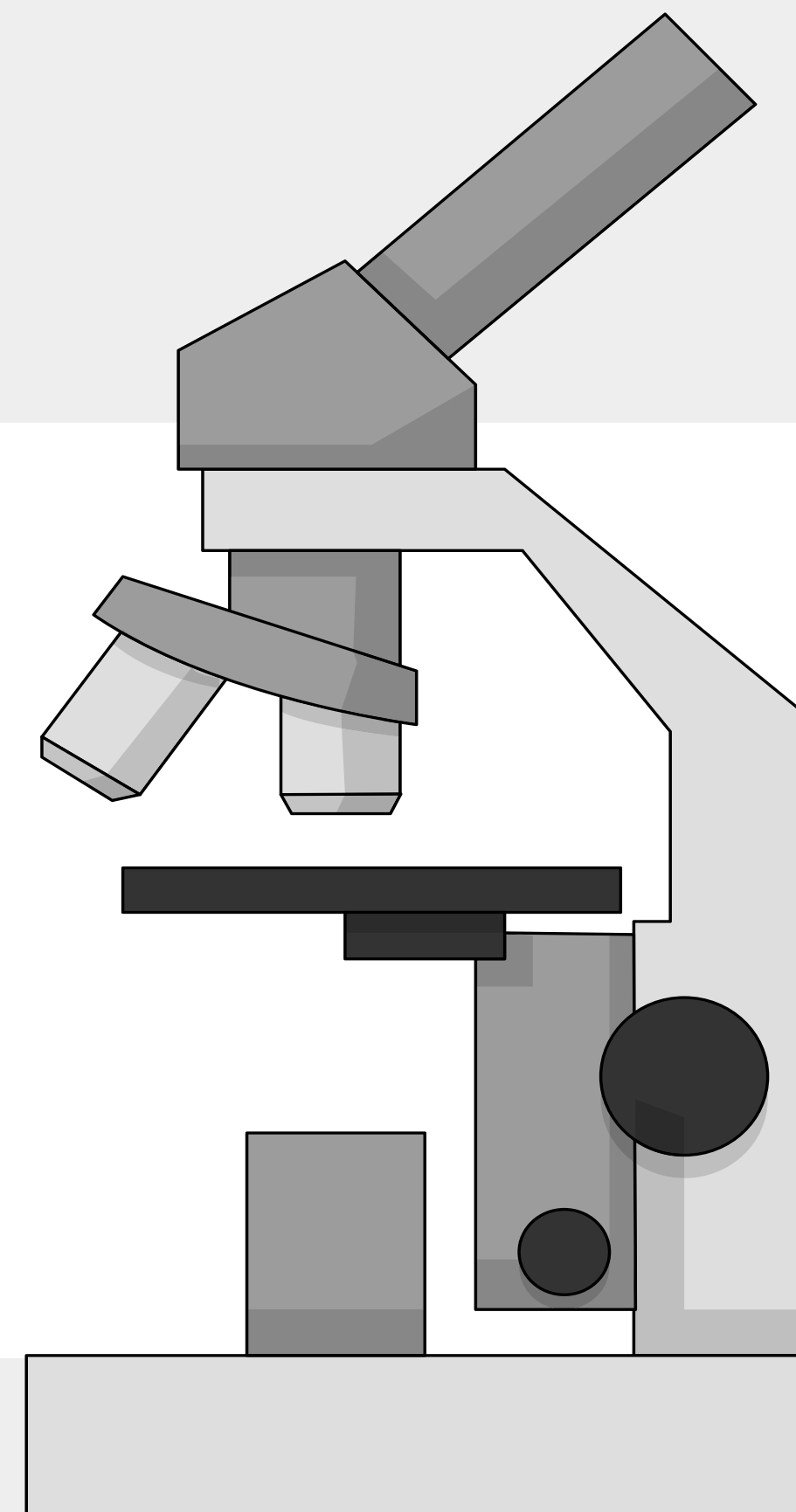
What histological criteria define MC?

What else causes chronic diarrhoea?

Numerous biomarkers for MC have been explored, but none are diagnostic¹

FBC, CRP and ESR testing (usually indicated for UC and CD) do not yield inflammatory abnormalities in 50% MC patients²

As the name implies, to diagnose MC, endoscopic imaging with histologic sampling is required³



The characteristic MC triad⁴

**CHRONIC
WATERY
DIARRHOEA**

**NORMAL
OR NEARLY
NORMAL
ENDOSCOPY**

**DISTINCT
HISTOLOGY**

Colonoscopy is preferred over flexible sigmoidoscopy, as it allows a more comprehensive investigation³

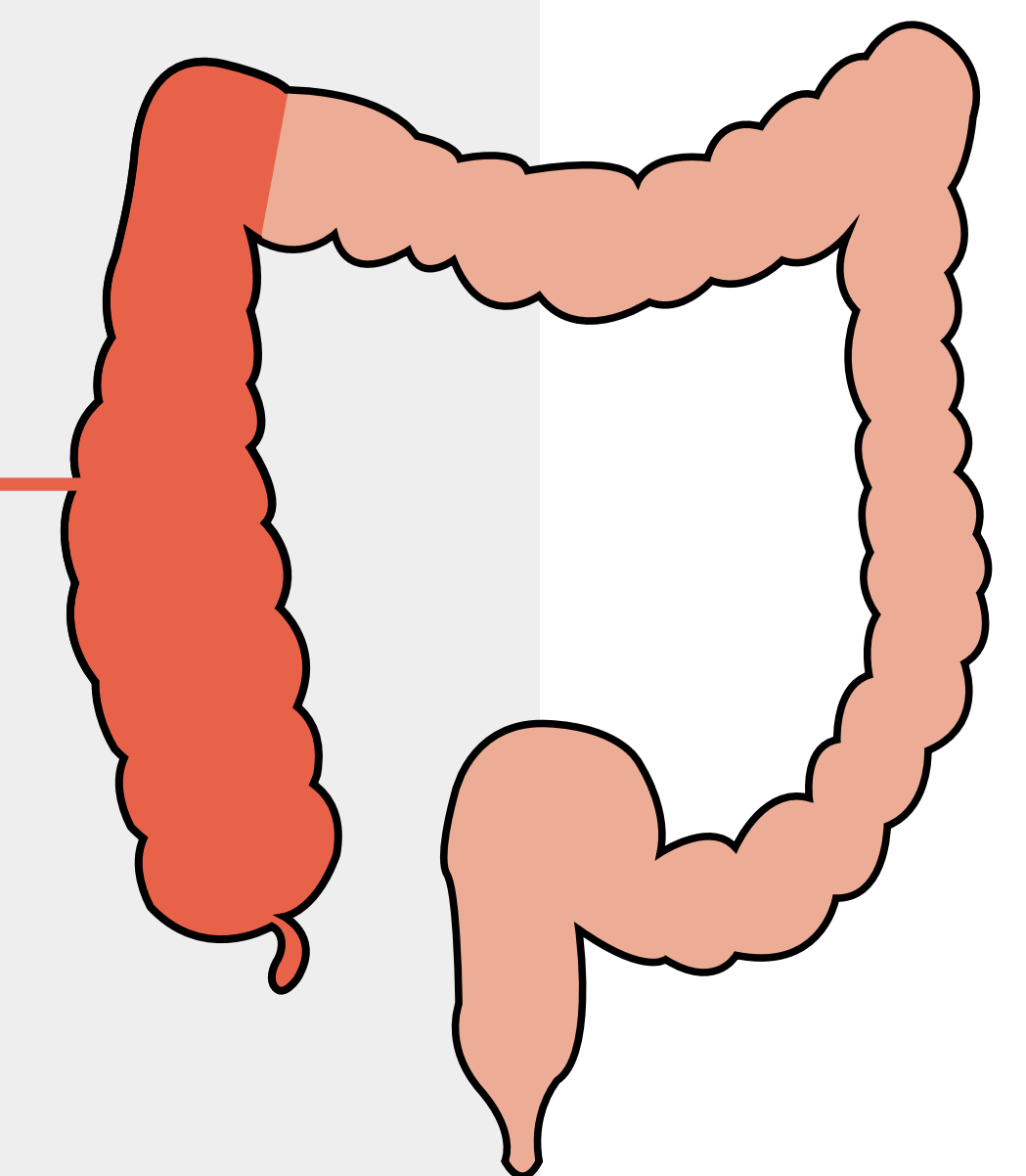
Visual changes such as erythema and oedema are seen in ~1 in 3 patients during endoscopy, but they are not specific to MC^{1,5}

Diagnosis therefore requires histological examination of colonic biopsies⁵

Biopsies should be taken from at least the right and left side of the colon, preferably in separate containers⁵

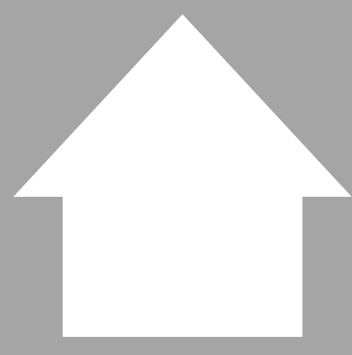
The number of inflammatory cells tends to be higher in the **right colon⁵**

Especially in borderline cases, it may help the pathologist to know where in the colon the biopsies are from⁵



1. Münch A *et al.* Frontline Gastroenterol 2020; 11(3): 228-34.
2. Walsh C. Gastro Nurs 2021; 19(9): 20-6.
3. Fedor I *et al.* Ther Adv Chronic Dis 2022; 13: 20406223221102821.
4. Miehle S *et al.* United Eur Gastroenterol J 2021; 9(1): 13-37.
5. Goudkade D *et al.* Ann Diagn Pathol 2020; 46: 151520.

CD: Crohn's disease
CRP: C-reactive protein
ESR: erythrocyte sedimentation rate
FBC: full blood count
MC: microscopic colitis
UC: ulcerative colitis



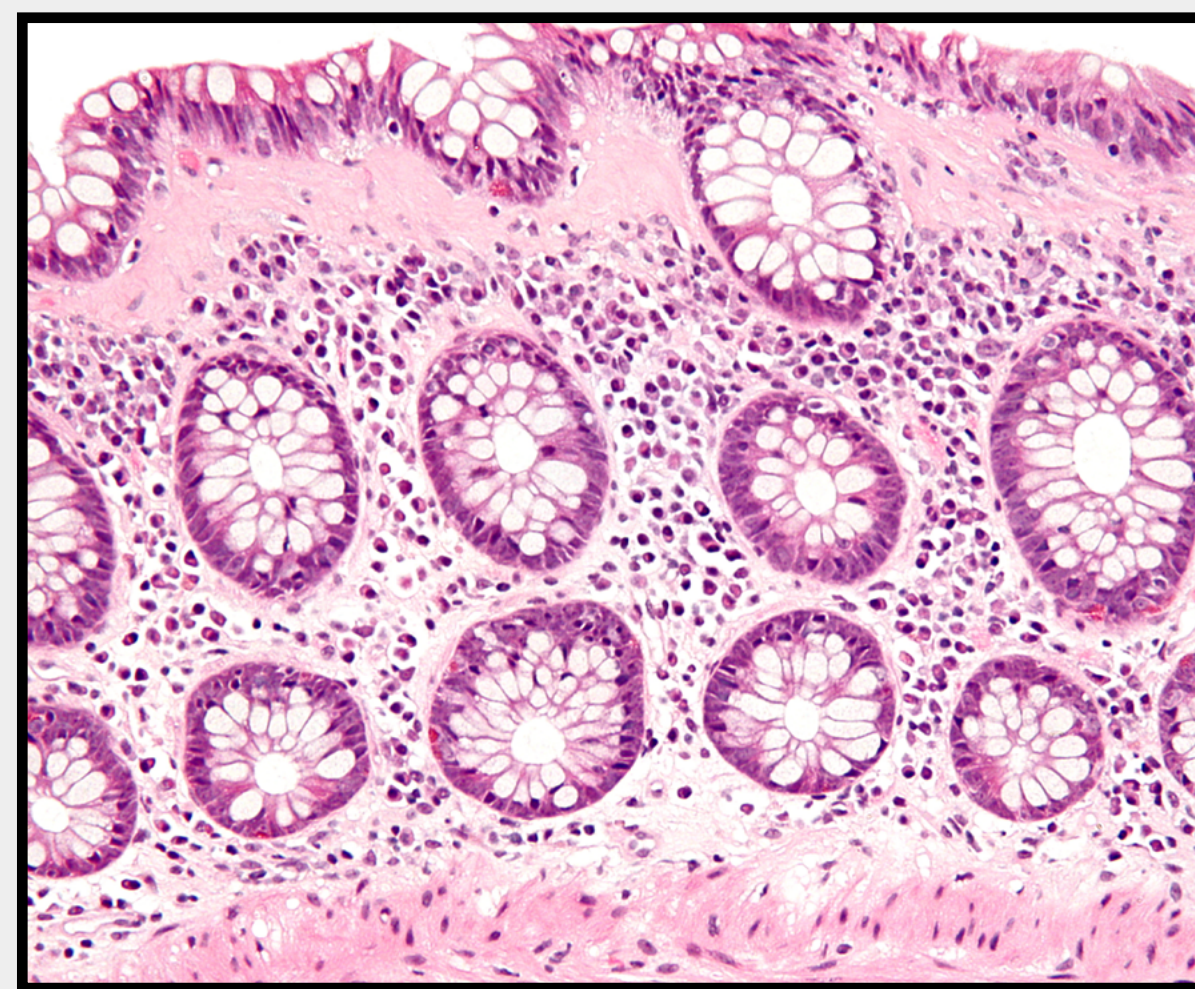
How do you make a diagnosis?

What histological criteria define MC?

What else causes chronic diarrhoea?

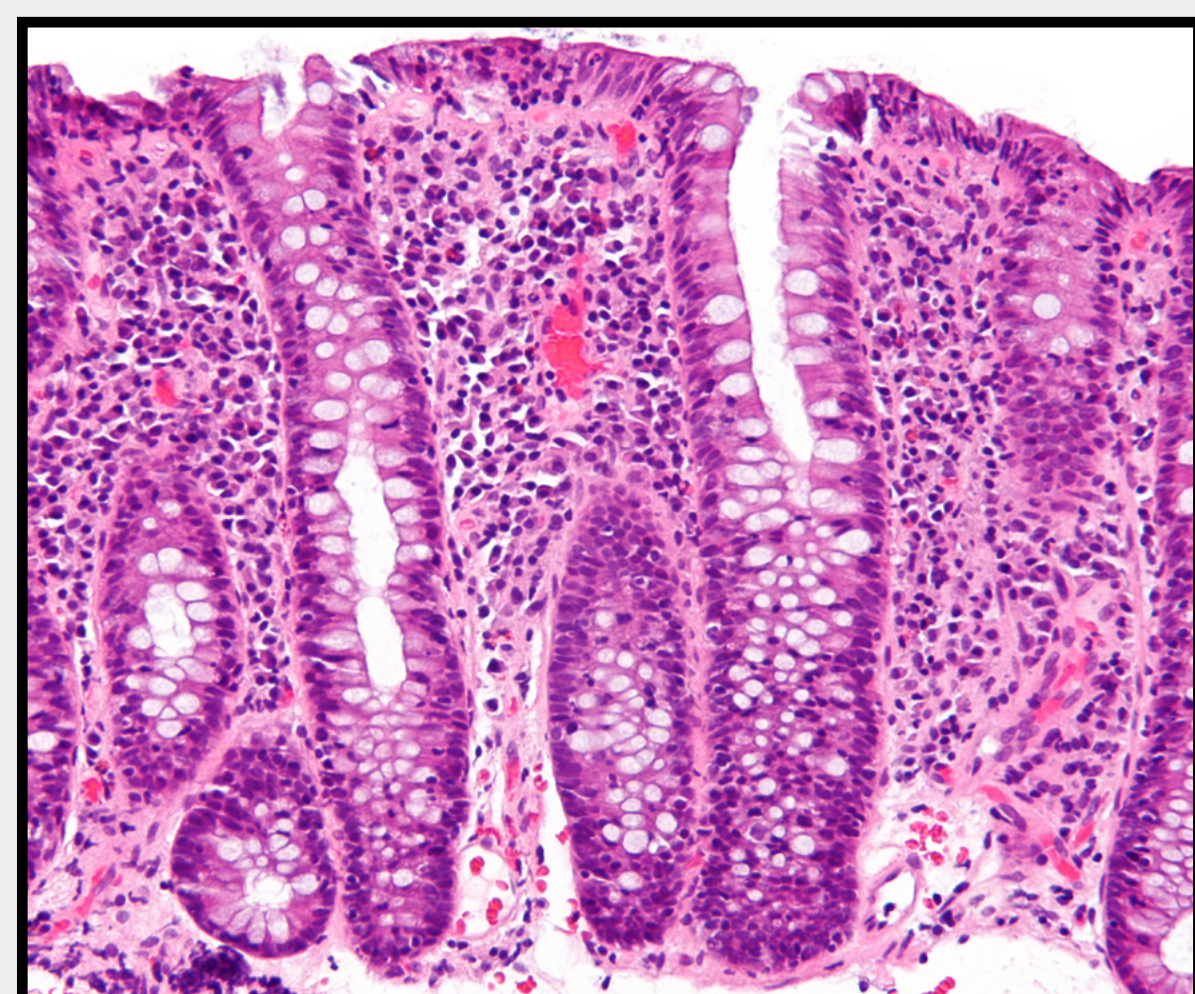
Histology can distinguish between two main types of MC: collagenous colitis and lymphocytic colitis¹

Histopathologic criteria of CC^{1,2}



- a thickened subepithelial collagen band (>10 µm) immediately underneath the surface epithelium
- an increased inflammatory infiltrate in the lamina propria

Histopathologic criteria of LC^{1,2}

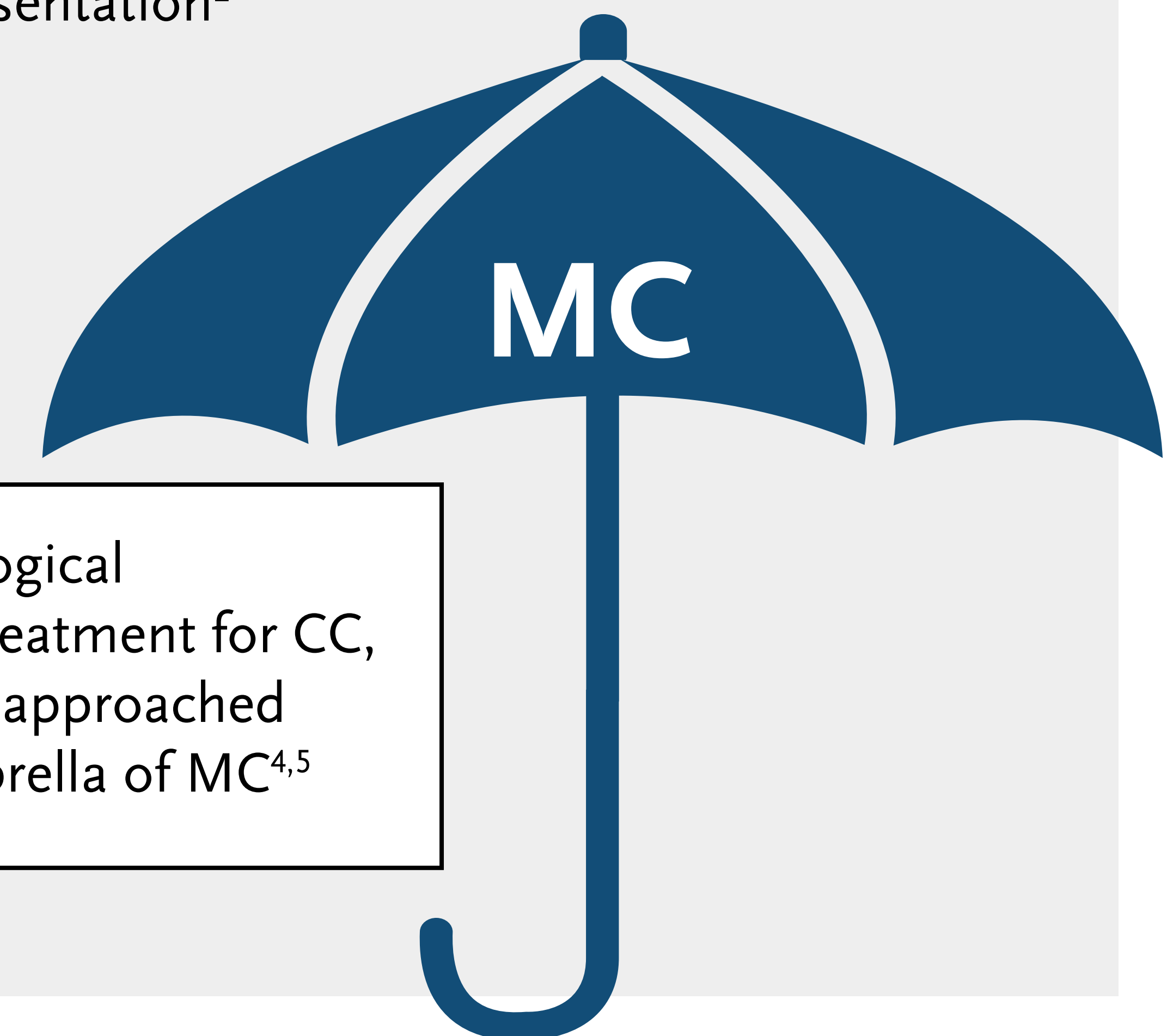


- an increased number of intraepithelial lymphocytes (≥20 per 100 epithelial cells)
- an increased inflammatory infiltrate in the lamina propria
- absence of a significantly thickened collagenous band

Incomplete MC describes patients who have histology that is not normal, but who fall short of fulfilling the classic criteria for MC:³

- a thickened collagen layer, >5 µm and <10 µm
- and/or IELs >5 and <20 per 100 epithelial cells
- inflammation in the lamina propria

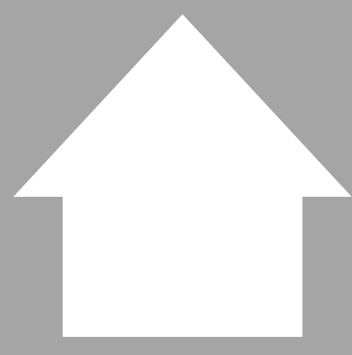
Patients with CC, LC and MCi cannot be distinguished from each other based on their demographic features, clinical characteristics, or symptom presentation²



Despite histological distinctions, treatment for CC, LC and MCi is approached under the umbrella of MC^{4,5}

1. Miehke S *et al.* United Eur Gastroenterol J 2021; 9(1): 13-37.
 2. Münch A *et al.* Frontline Gastroenterol 2020; 11(3): 228-34.
 3. Münch A. UEG Education 2021; 21: 10-3.
 4. Walsh C. Gastro Nurs 2021; 19(9): 20-6.
 5. Münch A *et al.* United Eur Gastroenterol J 2021; 9(7): 837-47.

CC: collagenous colitis
 IEL: intraepithelial lymphocyte
 LC: lymphocytic colitis
 MC: microscopic colitis
 MCi: incomplete MC




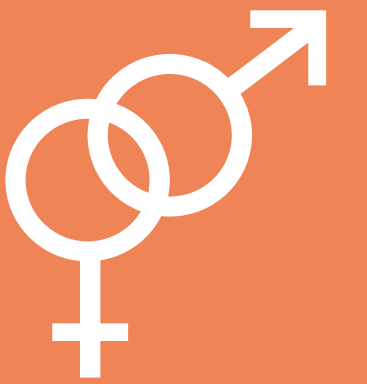




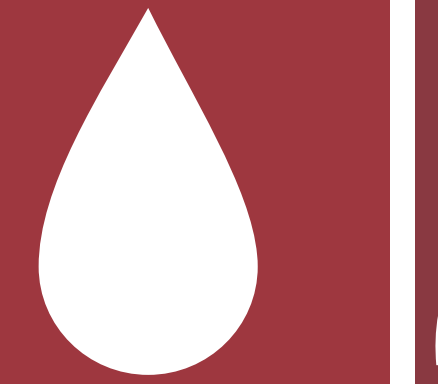
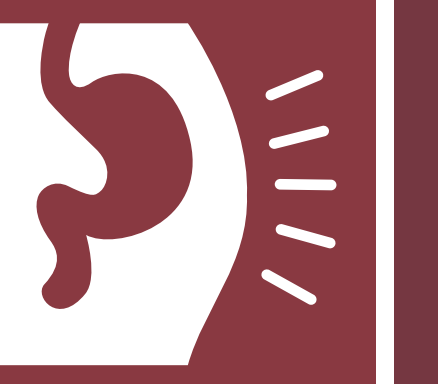


How do you make a diagnosis?

What histological criteria define MC?

What else causes chronic diarrhoea?

The broad range of conditions which lead to diarrhoea can make it difficult to be too prescriptive with regard to the investigative pathways that should be adopted¹

The table below offers a simple guide based on clinical symptoms and signs to help the differential diagnosis of patients with chronic diarrhoea²

	 Mean age	 Gender	 Stool consistency	 Nocturnal	 Incontinence	 Pain	 Blood	 Bloating	 Weight loss	 Diagnostic tests
MC	>50	F>M	Watery	Yes	Yes	Unusual	No	No	Possible	Serial colonic biopsies including right side
IBS	<40	F>M	Watery/Loose	No	Possible	Yes	No	Yes	No	Clinical history
IBD	<40	Equal	Loose	Possible	Yes	Possible	Possible	Possible	Yes	Colonoscopy, biopsies, imaging
Bile acid malabsorption	Any	F>M	Watery	Possible	Possible	No	No	No	No	SeHCAT
Coeliac disease	Any	Equal	Loose	No	No	No	No	Possible	Possible	IgA TTGAB
Colorectal cancer	More common >55	M>F	Variable*	Unlikely	Possible	Unlikely	Possible	Possible	Possible	Colonoscopy
Ischaemic colitis	Older	Equal	Variable*	No	No	Yes	Yes	No	Yes	CT, MRI, angiography

*diarrhoea may occur

1. Arasaradnam RP *et al.* Gut 2018; 67(8): 1380-99.
 2. Output of a round table discussion of UK physicians expert in the treatment of MC, supported by an educational grant from Dr Falk Pharma.

CT: computed tomography
 IBD: inflammatory bowel disease
 IBS: irritable bowel syndrome
 IgA: immunoglobulin A

MC: microscopic colitis
 MRI: magnetic resonance imaging
 SeHCAT: radioactive 75Selenium test
 TTGAB: tissue transglutaminase antibody



Treating It

1

What are the goals of MC treatment?

3

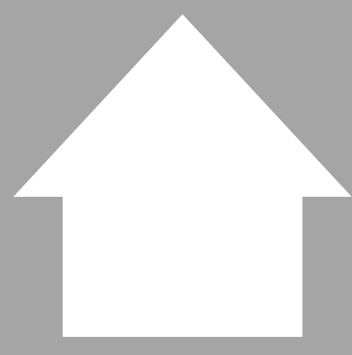
How does budesonide work?

2

What do guidelines recommend?

4

Will patients need maintenance therapy?



What are the goals of MC treatment?

What do guidelines recommend?

How does budesonide work?

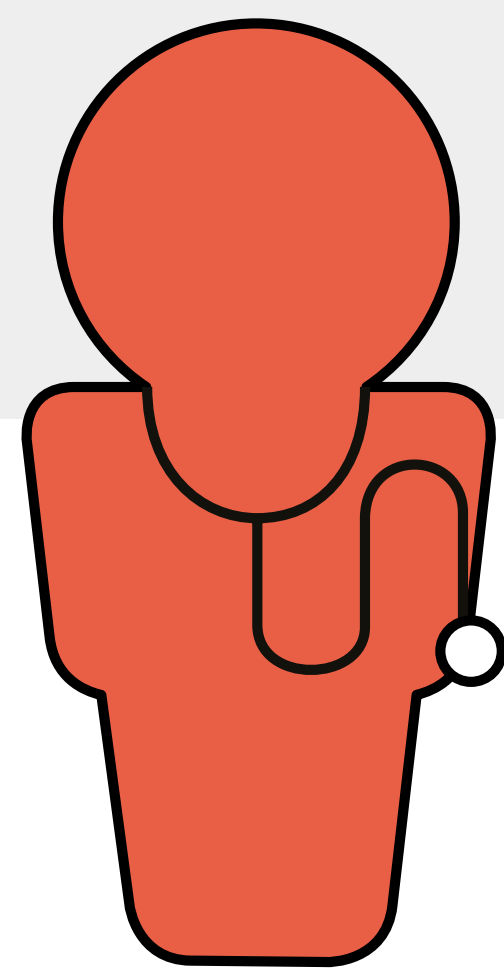
Will patients need maintenance therapy?

Given there is no increased risk of colon cancer or other serious complications with MC, it is, in a sense, a benign disease¹

However, MC can be a disabling life experience that impacts every aspect of a patient's life¹

" I don't live fully, there's always a little fear. If I have planned something, it's my stomach that decides, not me² "

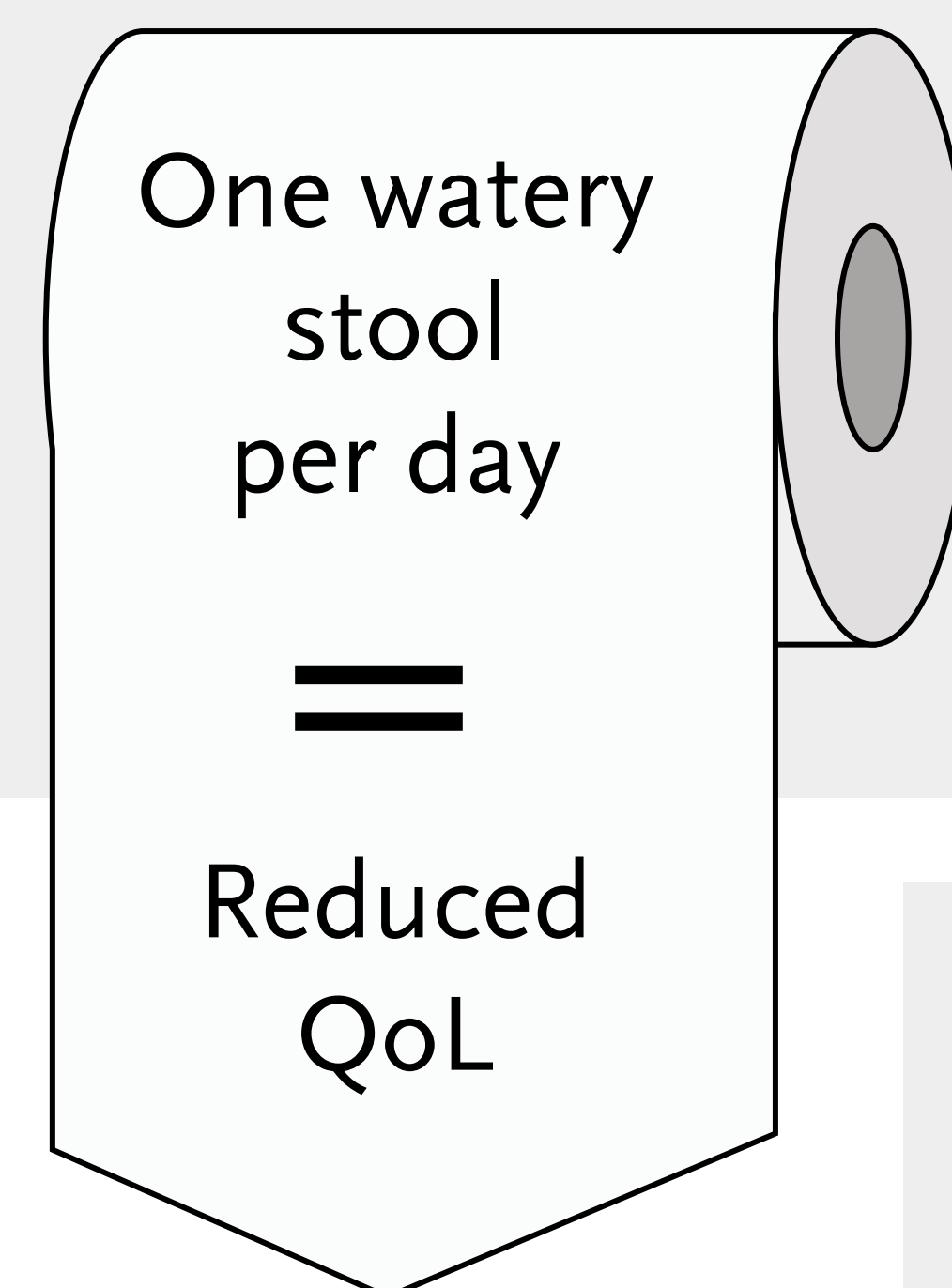
" It can be quite astonishing to discover how patients with MC have adapted to live with their symptoms or live in a state of isolation and neglect¹ "



The classic definition of chronic diarrhoea is ≥ 3 defecations/day for a duration of ≥ 4 weeks³

While easy to assess, stool frequency may have less impact on a patient's quality of life than stool consistency¹

Even one watery stool a day can mean patients suffer⁴



Management of MC should aim to reduce the impact of symptoms on quality of life⁵

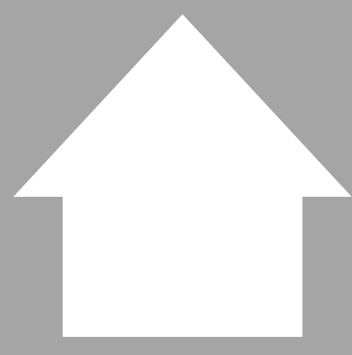
Disease activity can be assessed using the Hjortswang Criteria which considers both number of stools and number of watery stools^{4,6}

Average number of stools or watery stools per day recorded over a one week period⁴

	Stools per day		Watery stools per day
Clinical remission	<3	and	<1
Clinical activity	≥ 3	or	≥ 1

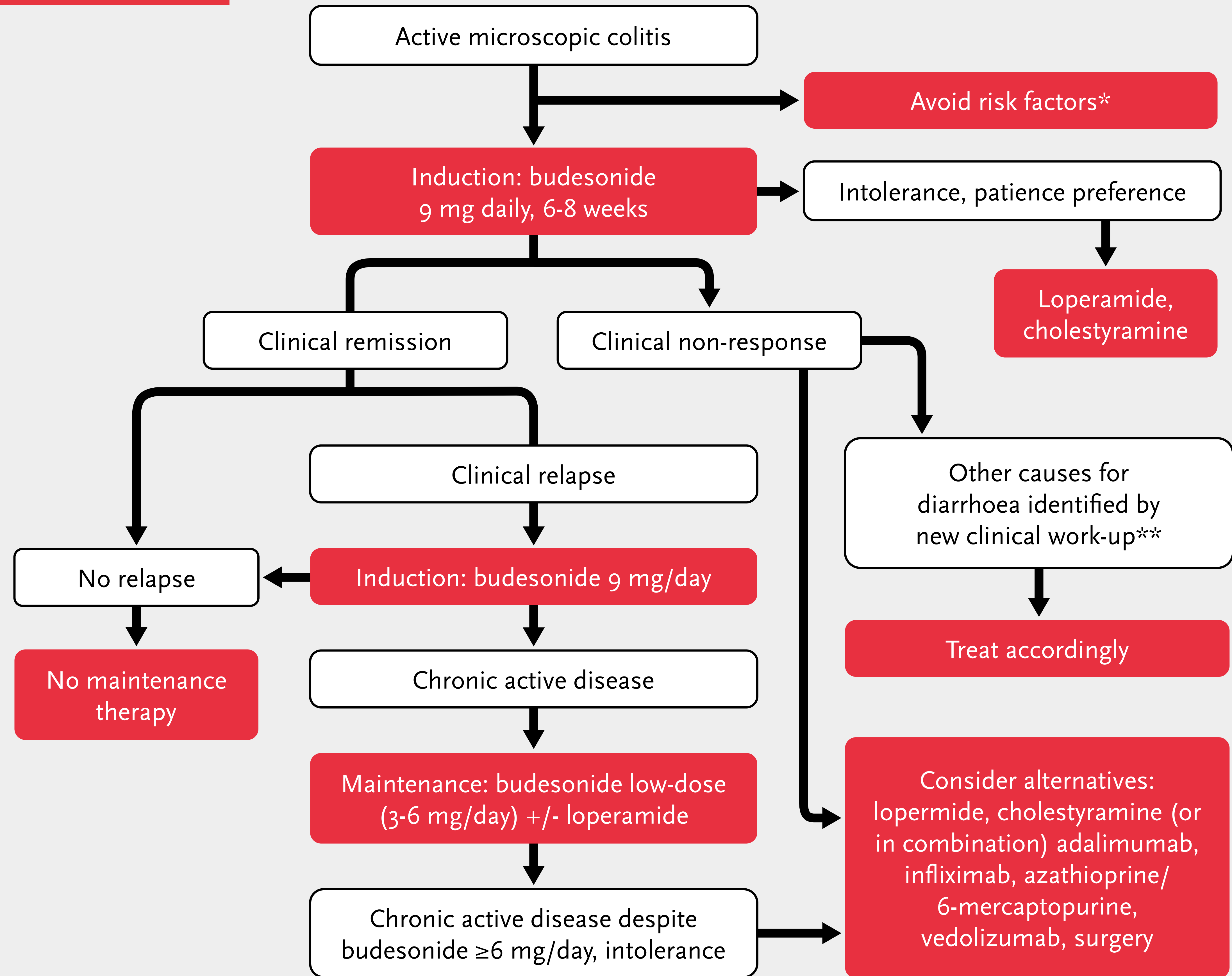
1. Münch A. UEG Education 2021; 21: 10-3.
 2. Pihl Lesnovska K *et al.* J Clin Nurs 2019; 28(19-20): 3408-15.
 3. Fine KD, Schiller LR. Gastroenterology 1999; 116(6): 1464-86.
 4. Hjortswang H *et al.* Inflamm Bowel Dis 2009; 15(12): 1875-81.
 5. Walsh C. Gastro Nurs 2021; 19(9): 20-6.
 6. Miehle S *et al.* United Eur Gastroenterol J 2021; 9(1): 13-37.

MC: microscopic colitis
 QoL: quality of life



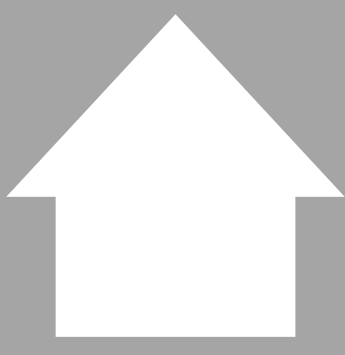
The management of MC¹

In their recently published guidelines, the European Microscopic Colitis Group and United European Gastroenterology included a treatment algorithm to guide health professionals on the MC treatment pathway¹



* Smoking, nonsteroidal anti-inflammatory drugs, proton-pump inhibitors

** For example, bile acid diarrhoea, coeliac disease



What are the goals of MC treatment?

What do guidelines recommend?

How does budesonide work?

Will patients need maintenance therapy?

While corticosteroids are very effective at treating inflammatory disease, glucocorticoid receptors are present in nearly all cell types^{1,2}

As a result, steroids are associated with a broad array of adverse effects on multiple body systems^{1,2}

e.g.	mood	bones
	skin	blood sugar
	weight	blood pressure
		eyes

Budesonide is a different type of steroid that selectively treats the gut and liver³

'Steroid-sparing' steroid⁴
Unlike prednisolone, ~90% of the dose is deactivated in the liver

A far smaller amount reaches the systemic circulation (prednisolone is 80-100% bioavailable⁵)

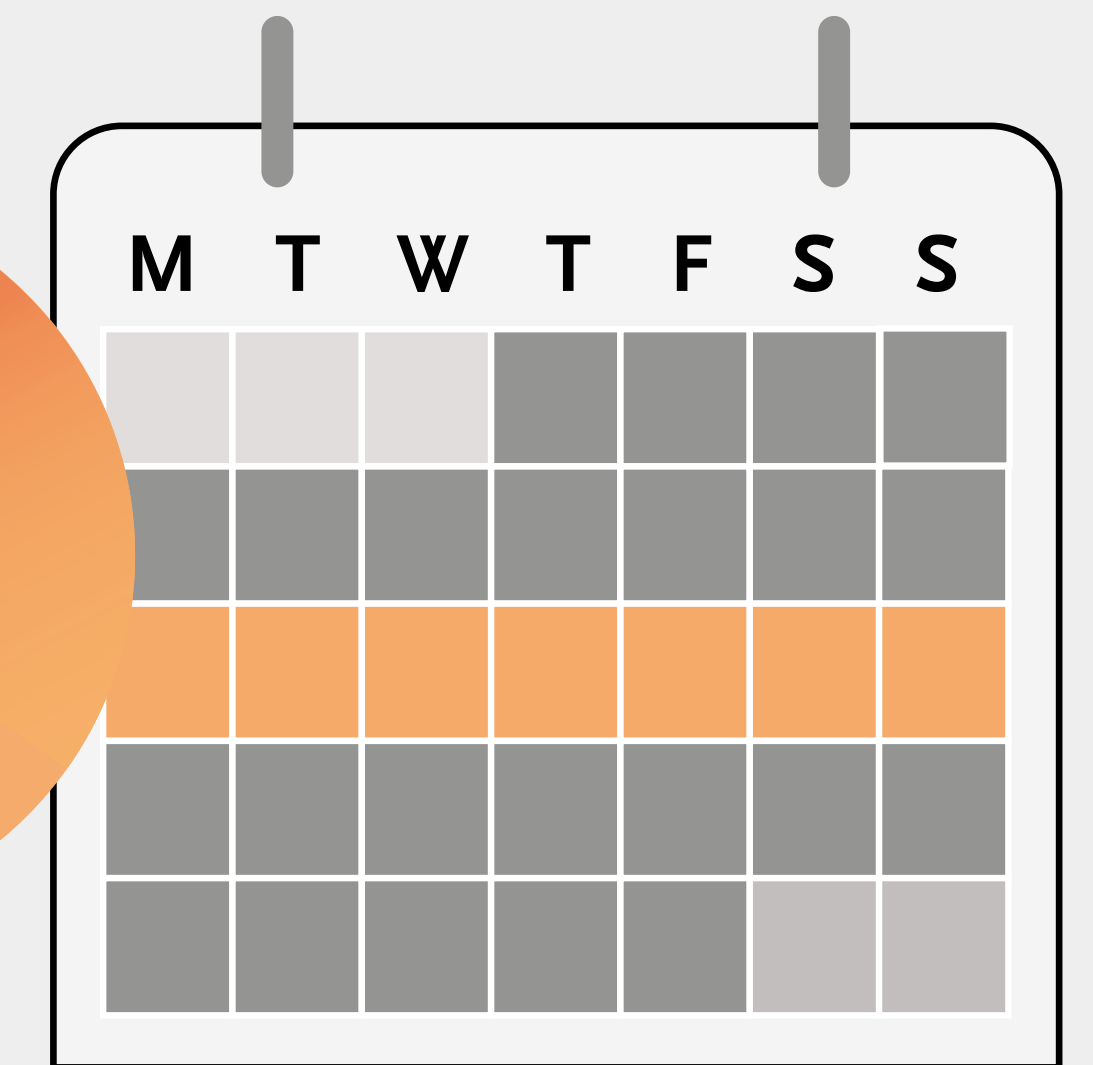
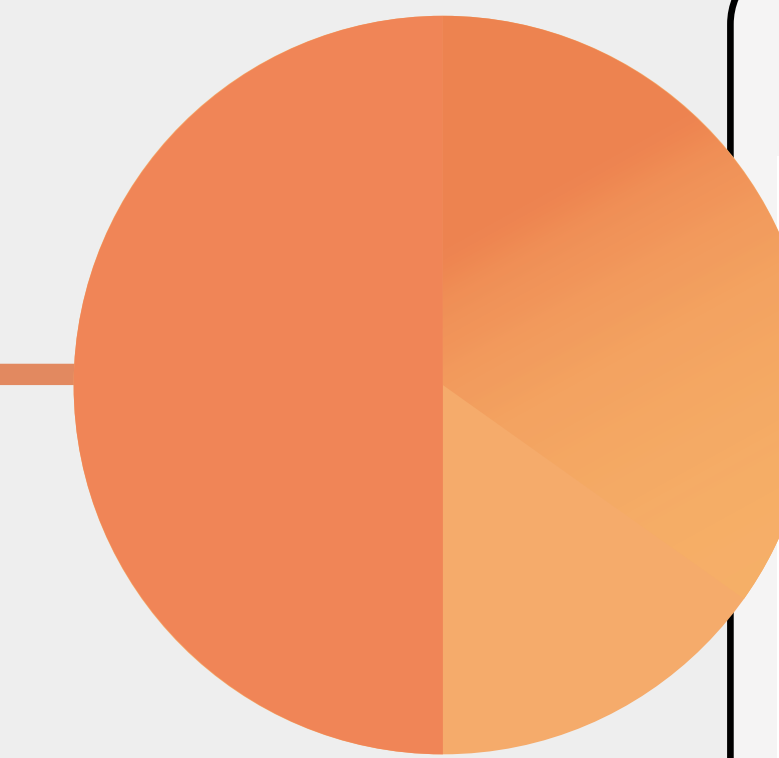
The risk of systemic side effects is reduced³



Budesonide has high receptor-binding affinity, providing strong topical effects in the GI tract⁶

Patients respond quickly

Over half of MC patients achieved remission within a week with budesonide^{7,8}



Meanwhile reduced systemic availability helps limit unwanted side effects⁶

Meta-analysis of 7 MC RCTs⁹

Withdrawal due to AEs:

budesonide

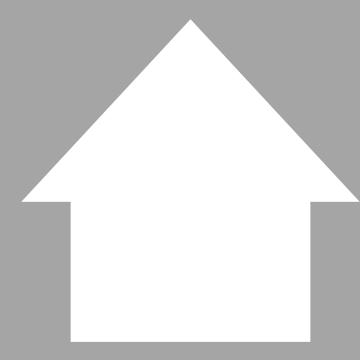
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placebo

1. Manson SC *et al.* Respir Med 2009; 103(7): 975-94.
 2. McMaster A, Ray DW. Exp Physiol 2007; 92(2): 299-309.
 3. Miehle S *et al.* J Gastroenterol Hepatol 2018; 33(9): 1574-81.
 4. Zandieh I *et al.* Can J Gastroenterol 2008; 22(4): 388-92.
 5. Bashar T *et al.* Dose Response 2018; 16(3): 1559325818783932.

6. Münch A. UEG Education 2021; 21: 10-13.
 7. Miehle S *et al.* Gastroenterology 2014; 146(5): 1222-30.
 8. Miehle S *et al.* Gastroenterology 2018; 155(6): 1795-1804.e3.
 9. Stewart MJ *et al.* Clin Gastroenterol Hepatol 2011; 9(10): 881-90.

AE: adverse event
 GI: gastrointestinal
 MC: microscopic colitis
 RCT: randomised controlled trial



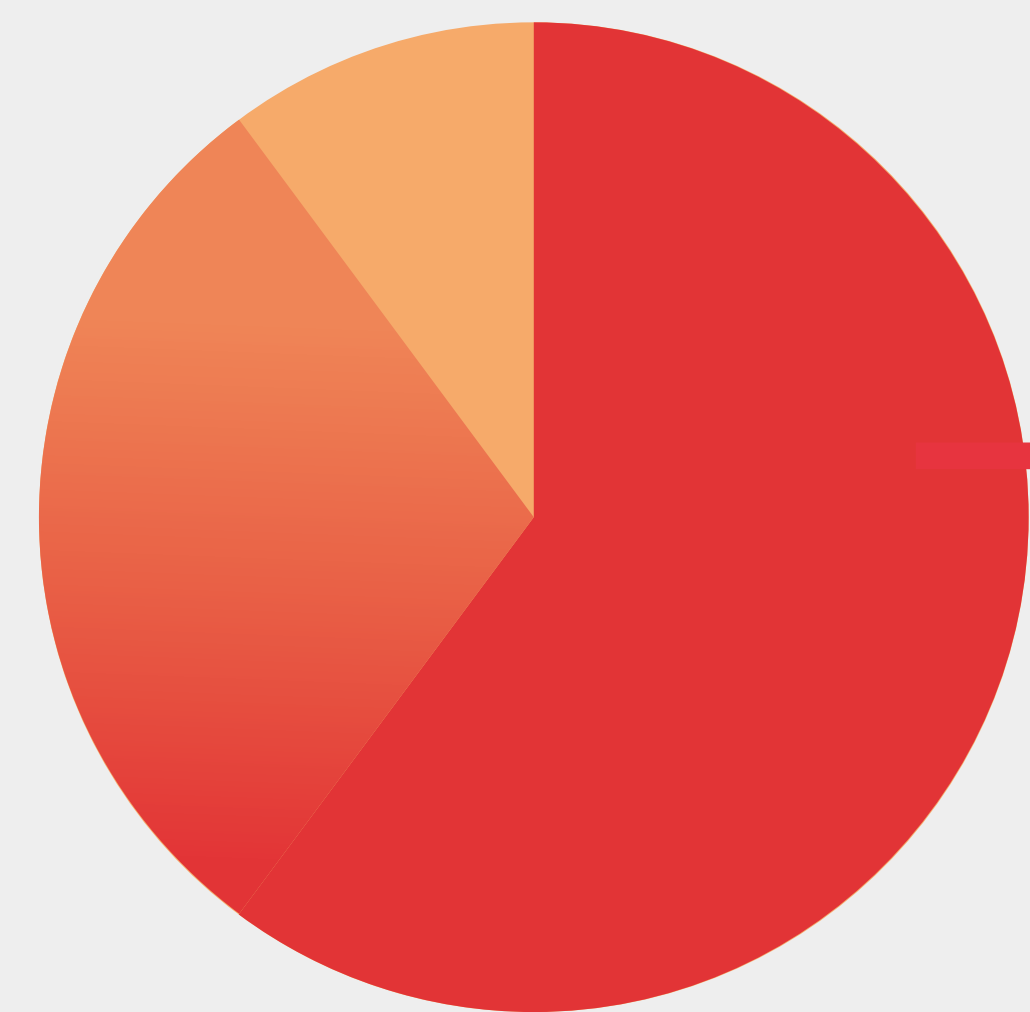
What are the goals of MC treatment?

What do guidelines recommend?

How does budesonide work?

Will patients need maintenance therapy?

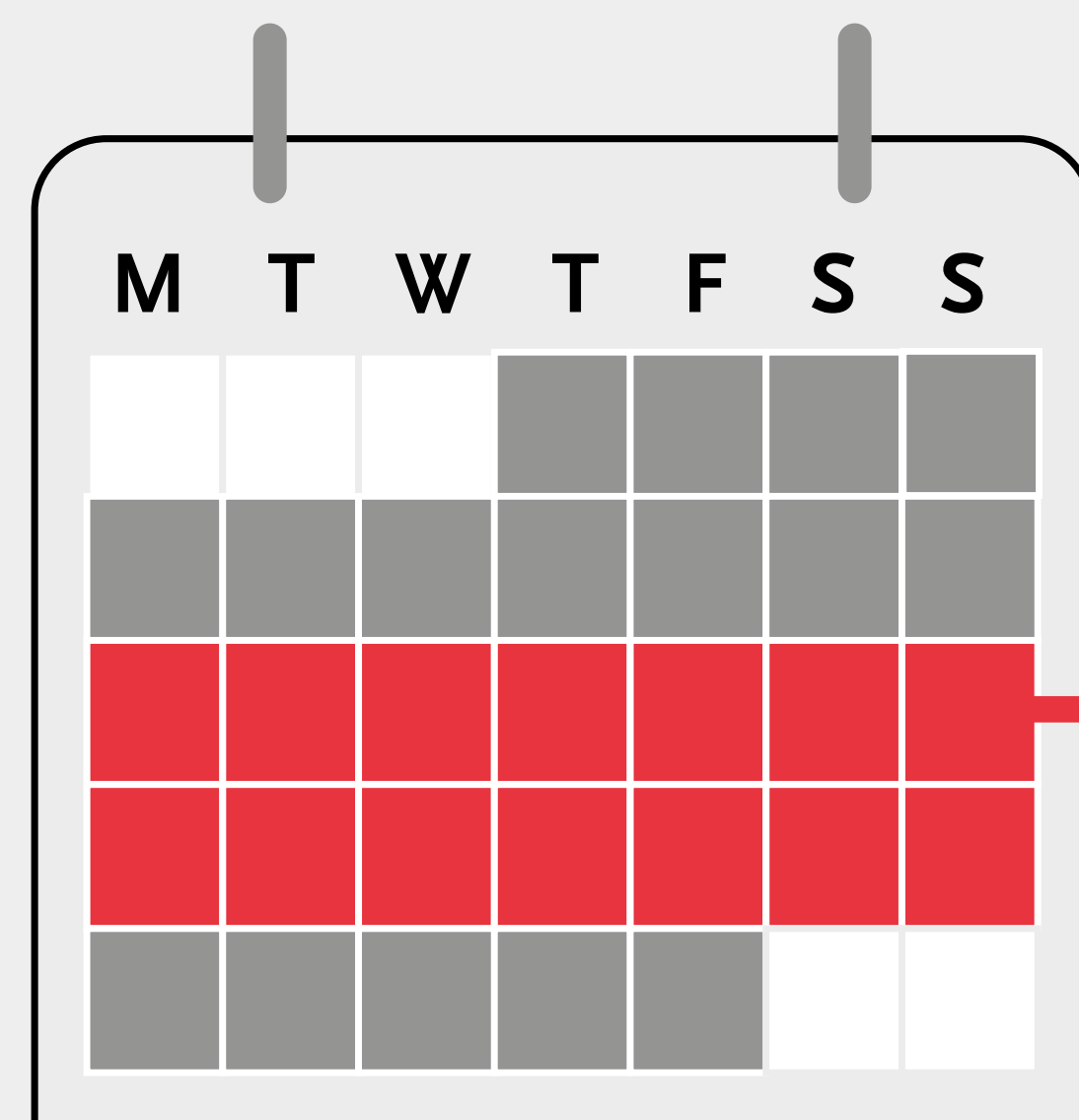
Recurrence after discontinuation of treatment is common¹



Relapse occurs in around

60%-90%

of patients after they finish budesonide therapy¹



Clinical relapse has been reported as soon as

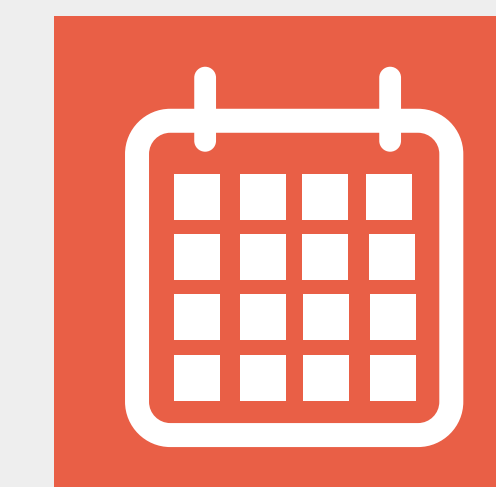
2 weeks

after withdrawal of budesonide²

Risk factors for relapse after the discontinuation of budesonide³



Older age



Longer duration of symptoms



High stool frequency on presentation

In chronic disease states, long-term maintenance on a lower dose of budesonide is advised⁴

Induction of remission:

Budesonide 9 mg daily

Maintenance of remission:

Budesonide 3-6 mg daily

The long-term disease course is not altered by maintenance therapy, as the risk of relapse after 24 weeks' budesonide therapy is similar to that observed after induction therapy¹

MC is highly treatable and has an excellent chance of improved outcomes... [it] should be considered as part of the growing role of the specialist IBD nurse, who is ideally placed to care for these patients⁵

1. Münch A *et al.* Gut 2016; 65(1): 47-56.

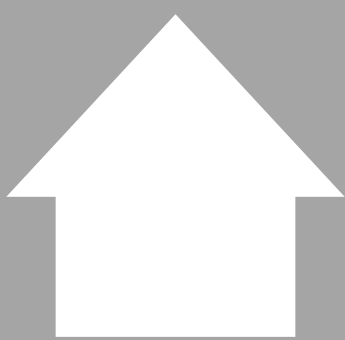
2. Boland K, Nguyen GC. Gastroenterol Hepatol (NY) 2017; 13(11): 671-7.

3. Tome J *et al.* Mayo Clin Proc 2021; 96(5): 1302-8.

4. Miehke S *et al.* United Eur Gastroenterol J 2021; 9(1): 13-37.

5. Walsh C. Gastro Nurs 2021; 19(9): 20-6.

MC: microscopic colitis
IBD: inflammatory bowel disease



Access resources from Dr Falk below by clicking on the titles or scanning the QR codes

Dr Falk Pharma UK website



MC Educational Booklet



MC Hub



MC Explained Atlas

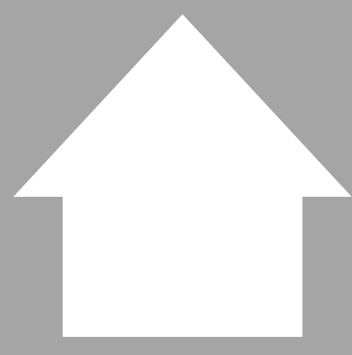


MC Patient Leaflet



MC Presentation by Professor Probert





<https://www.dralfk.co.uk/budenofalk-oral-preparations/>

Adverse events should be reported. Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk> or search for MHRA Yellow Card in the Google Play Apple App Store (UK residents) or at email: medsafety@hpra.ie or at <http://www.hpra.ie/homepage/aboutus/report-an-issue/human-adverse-reaction-form> (residents in Ireland). Adverse events should also be reported to Dr Falk Pharma UK Ltd at office@dralfkpharma.co.uk

