Ulcerative Colitis (update)

Consultation on draft guideline - Stakeholder comments table
18/12/2019 to 22/01/2019

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

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British Association for Behavioural and Cognitive Psychotherapies (BABCP)	Guideline	22	17	In the discussion of ulcerative colitis in the section: context, it is noted that ulcerative colitis is a lifelong disease that can affect a person's social and psychological wellbeing, particularly if poorly controlled. Empirical evidence suggest this is also the case for people with Crohn's disease, yet neither guideline includes a recommendation for the assessment or measurement of psychological wellbeing or the consideration of psychological treatment for people with UC or CD who are identified as experiencing persistent disturbance to mood.	Thank you for your comment. This guideline update only considered pharmacological treatments for inducing remission in mild-to-moderate ulcerative colitis. Assessment of social and psychological wellbeing and the evaluation of psychological treatments were not within the scope of this update and therefore we are unable to make changes to recommendations in this area. NICE has produced guidelines on recognising and managing depression in people with chronic physical health problems. We will pass your comment on to the surveillance team for their consideration at the next update.
British Association for Behavioural and Cognitive Psychotherapies (BABCP)	Guidelines	25	1	Given the established association between anxiety, low mood and disease activity and the potential impact that CBT may have on improving these outcomes, it is advisable to recommend the consideration of the role of mood on the course of UC and CD in the guidelines for inducing remission in UC and CD. Symptoms of anxiety, depression and quality of life could potentially be assessed through self-report measures and monitored throughout treatment. This may be of particular importance for people who are experiencing prolonged periods of disease activity. Referrals to psychological services for potential treatment could be facilitated for those people found to be experiencing persistent disturbance to mood. Early identification and management of psychological distress could prevent disturbances in mood and quality of life from negatively influencing outcomes for people with IBD.	Thank you for your comment. This guideline update only considered pharmacological treatments for inducing remission in mild-to-moderate ulcerative colitis. Monitoring of social and psychological wellbeing was not within the scope of this update and therefore we are unable to make changes to this area. NICE has produced guidelines on recognising and managing depression in people with chronic physical health problems. We will pass your comment on to the surveillance team for their consideration at the next update. .
British Association for Behaviour	Evidence Review	43	17	Although the review is considering medication use to induce remission. We would like to draw the committee's attention to the important role of psychosocial factors.	Thank you for your comment. This guideline update only considered pharmacological treatments for inducing remission in mild-to-moderate ulcerative colitis. Quality of life was

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al and Cognitive Psychotherapies (BABCP)				Ulcerative Colitis (UC) and Crohn's disease (CD) pose numerous challenges for both physical and psychosocial functioning. Adults with UC & CD experience unpleasant and unpredictable symptoms and aggressive treatment regimes. In addition they face psychosocial consequences including disruptions to their life goals, employment, and social and leisure activities (Kemp et al 2012). Psychosocial difficulties are common in UC and CD when compared to both non-clinical (Kovac et al, 2007) and other chronic disease populations (Fillpovic et al, 2007). The empirical evidence demonstrates the life time prevalence rates of anxiety and depression to be 35.8% for people with UC and CD (Walker et al, 2008). The presence of mood disturbance has been established as being an independent risk factor for earlier and more active disease (Mittermaier et al, 2004, Graff et al, 2006, Mikocka –Walus et al, 2016) and is associated with poorer clinical outcome and increased healthcare utilization in patients with UC and CD (Mickocka-Walus et al, 2012). Although disease related factors such as remission status, frequency of relapse, pain severity, and extra intestinal manifestations have been linked to emotional distress and poor quality of life in UC & CD, evidence suggests that psychological factors have a comparable influence (Jordan et al, 2016). A recent systematic review found that emotion focused coping strategies, extreme perceptions of the illness and of being stressed were significantly associated with worse mental health outcomes, and this was maintained when controlling for the influence of clinical factors (Jordan et al, 2016). Disease activity and psychological functioning are likely to be interrelated and bidirectional. • Qualitative studies exploring the burden of living with IBD from the patients' perspective have described symptoms of anxiety as linked to a fear of embarrassing symptoms occurring in public. This has been reported to lead to range of behavioural responses intended to minimise the probability of this occurring such as always knowing the whereabouts of toilets. Low mood has been liked to a perceived lack of understanding of IBD from others and to feeling stigmatised which has been reported to lead to behavioural withdrawal (Kemp et al, 2012, Jordan et al, 2018). Qualitative studies exploring the burden of living with IBD from the patients' perspective have described symptoms of anxiety as linked to a fear of embarrassing symptoms occurring in public. This has been reported to lead to range of behavioural responses intended to minimise the probability of this occurring such as always knowing the whereabouts of toilets. Low mood has been liked to a perceived lack of understanding of IBD from others and to feeling stigmatised	listed as an outcome of interest in the protocol for the evidence review of pharmacological treatments. Psychological interventions were not within the scope of this update and therefore we did not review the evidence and are unable to make changes to recommendations in this area. We have passed your comment on to the surveillance team for consideration in future updates.

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				which has been reported to lead to behavioural withdrawal (Kemp et al, 2012, Jordan et al, 2018). Cognitive and behavioural responses are potentially modifiable factors which it is possible to address in a psychological intervention and people with UC and CD have been found to state a desire for psychological support. The findings of qualitative studies suggest a strong preference for this to be delivered by a compassionate practitioner who can draw on specialised knowledge of the key symptoms of IBD and their impact on functioning and mental health, with a focus on building coping strategies (Jordan et al, 2018). A meta-analysis conducted by Timmer and colleagues (2011) concluded that there was no evidence that psychological interventions in general enhance emotional states, HRQOL and disease activity for adults with IBD. However, there are limitations to this review. The authors combined stress management, psychodynamic psychotherapy and cognitive behaviour therapy (CBT) studies as "psychotherapy" in the meta–analysis, therefore any differential efficacy between these theoretically distinct approaches could not be evaluated. When considered independently, a more recent review found promising evidence that CBT improved mental health in patients with IBD, both immediately following the intervention and at 6 months follow up (Knowles et al, 2013). In addition both reviews have included studies where the majority of participants have sub clinical levels of anxiety and depression which is likely to have reduced treatment effects. Several studies carried out since the above mentioned reviews have identified improvements in disease activity, anxiety, depression, quality of life, and coping when cognitive-behavioural therapy (CBT) was provided to patients with clinically significant anxiety and depression. For example ; Jordan et al, 2018, investigated the clinical benefits of a non-randomised uncontrolled trial of clinic based cognitive behaviour therapy (CBT) for adults with IBD who had moderate to severe levels of anxiety and low mood and compared the results to a previous randomised controlled trial of CBT in this population. Previous randomised controlled trials had found no evidence that psychological interventions enhanced outcomes for people with IBD but had recruited patients without distress (Timmer et al, 2011). The results of this study identified statistically significant improvements to mood, quality of life and symptomatic disease activity and uncontrolled effect sizes were superior to those of the RCT. This suggested that CBT may have benefits for those with moderate to severe disturbances to	

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				mood and that the effect sizes of RCT's could be improved by targeting those with distress. Mikocka-Walus et al 2012, investigated the impact of implementing a biopsychosocial model of care for IBD in a hospital-based cohort of patients. This included the provision of CBT for patients with UC & CD identified as experiencing moderate to severe anxiety and depression. This study found that patients with documented psychological comorbidities were more likely to be hospitalized than those without (odds ratio [OR] ¼ 4.13, 95% confidence interval [CI]: 1.25, 13.61). Improvements in disease activity, anxiety, depression, quality of life, and coping were found when cognitive-behavioural therapy (CBT) was provided to patients. A drop in the use of opiates (P ¼ 0.037) and hospitalization rates (from 48% to 30%) in IBD patients were noted as a result of introduction of the changed model of care. In addition, the mean total cost of inpatient care was lower for IBD patients than controls (US$12,857.48 [US$15,236.79] vs. US$ 30,467.78 [US$ 53,760.20], P ¼ 0.005). Given the established association between anxiety, low mood and disease activity and the potential impact that CBT may have on improving these outcomes, it is advisable to recommend the consideration of the role of mood on the course of UC and CD in the guidelines for inducing remission in UC and CD. Symptoms of anxiety, depression and quality of life could potentially be assessed through self-report measures and monitored throughout treatment. This may be of particular importance for people who are experiencing prolonged periods of disease activity. Referrals to psychological services for potential treatment could be facilitated for those people found to be experiencing persistent disturbance to mood. Early identification and management of psychological distress could prevent disturbances in mood and quality of life from negatively influencing outcomes for people with IBD. References: Filipović B R., Filipović B F., Kerkez M., Milinić N., Randelović T. (2007).Depression and anxiety levels in therapy-naive patients with inflammatory bowel disease and cancer of the colon. World J Gastroenterology. 13(3), pp 438-43. Graff, L. A., Walker, J., Lix, R., Clara, L., Rawsthorne, I., Rogala, P., Miller, L., Jakul, N., McPhail, L., Ediger, C., Bernstein, J. (2006). The Relationship of Inflammatory Bowel Disease Type and Activity to Psychological Functioning and Quality of Life. Clinical Gastroenterology and Hepatology 4 (12), pp1491-1501. Jordan, C., Sin, J., Fear, N.T. & Chalder, T. (2016) A systematic review of the psychological correlates of adjustment outcomes in adults with inflammatory bowel disease. Clinical Psychology Review.	

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				Jordan C., Ohlsen R., Hayee B., Chalder T. (2017). A qualitative study exploring the experience of people with IBD and elevated symptoms of anxiety and low mood and the type of psychological help they would like, Psychology & Health, pp 1-18. Cheryl Jordan, Bu 'Hussain Hayee & Trudie Chalder, (2018). Cognitive behaviour therapy for distress in people with Inflammatory Bowel Disease: A bench marking study. Clinical psychology and psychotherapy. Kemp K., Griffiths J., Lovell, K. (2012). Understanding the health and social care needs of people living with IBD: a meta-synthesis of the evidence. World J gastroenterol. 18(43), pp6240-6249. Knowles, S., Monshat, K., Castle, D., 2013. The Efficacy and Methodological Challenges of Psychotherapy for Adults with Inflammatory Bowel Disease: A Review. Inflammatory Bowel Diseases, 19(12) pp2704-2715. Mikocka-Walus A, Pittet V., Rossel JB., Von Känel R; Swiss IBD Cohort Study Group. (2016). Symptoms of Depression and Anxiety Are Independently Associated With Clinical Recurrence of Inflammatory Bowel Disease. Clin Gastroenterol Hepatol. 2016 Jun;14(6):829-835.e1 Mikocka-Walus AA[1], Turnbull D, Holtmann G, Andrews JM. An integrated model of care for inflammatory bowel disease sufferers in Australia: development and the effects of its implementation. Inflamm Bowel Dis. 2012 Aug;18(8):1573-81. doi: 10.1002/ibd.22850. Epub 2011 Dec 16. Mittermaier, C., Dejaco, C., Waldhoer, T., Oefferlauber-Ernst, A., Miehsler, W., Beier, M., Tillinger, W., Gangl, A., Moser, G. (2004). Impact of depressive mood on relapse in patients with inflammatory bowel disease: A prospective 18-month follow-up study. Psychosomatic Medicine 66(1), pp 79-84. Timmer, A., Preiss, J. C., Motschall, E., Rücker G., Jantschek G., Moser G. (2011). Psychological interventions for treatment of inflammatory bowel disease (Review). The Cochrane Library (8). Walker JR., Ediger JP., Graff LA., Greenfeld JM., Clara I., Lix L., Rawsthorne P., Miller N., Rogala L., McPhail CM., Bernstein CN., (2008). The Manitoba IBD cohort study: a population-based study of the prevalence of lifetime and 12-month anxiety and mood disorders. Am J Gastroenterol. Aug; 103(8)	
British Dietetic Association (BDA)	Guideline UC management			Diet is not mentioned in the management of mild-moderate UC and in this patient group there may be overlap with functional bowel symptoms. There is a small amount of evidence that a low FODMAP diet is beneficial in patients with UC in remission and it may be worth including a research recommendation for mild-moderate disease. We would recommend the following question: What are the benefits, risk and cost effectiveness of using diet in the management of mild-moderate UC?	Thank you for your comment. Diet was not considered as part of this guideline and therefore we are unable to make research recommendations related to this area.
British Society for		General	General	No comments	Thank you for your response.

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Antimicrobial Chemotherapy					
British Society of Gastroenterology	Guideline	General	General	We have serious concerns that this guideline update, as drafted, does not reflect current practice or the comprehensive and evidence-based British Society of Gastroenterologists (BSG) Inflammatory Bowel Disease (IBD) guidelines and consensus-based IBD Standards, which have been collaboratively developed by 17 professional and patient organisations, both of which are very soon to be published and have been developed in alignment with each other. We strongly believe that the next stage of the guideline update should be delayed enabling full consideration of and alignment with the BSG IBD guidelines and IBD Standards. Without this, the delivery of high-quality treatment and care for people with Crohn's Disease and Ulcerative Colitis could be impeded. Alternatively, NICE guidelines that support and align with the BSG guidelines and IBD Standards will significantly enhance this.	**NICE is aware of the forthcoming BSG IBD guideline. NICE and the BSG have met to discuss the synergies and overlaps in the 2 organisations' portfolios for gastroenterology topics. For this particular guideline the update covers only the induction of remission in mild-moderate ulcerative colitis. Following the publication of the BSG guideline NICE will consider the impact on the ulcerative colitis guideline**
British Society of Gastroenterology	Guideline	8	1	We are concerned about the recommendation that strongly supports the use of cyclosporine as treatment for steroid failures in acute severe ulcerative colitis. This is in contrast to current practice in the UK at the moment where most gastroenterologists are using infliximab.	Thank you for your comment. Use of ciclosporin in moderate-to-severe ulcerative colitis was not considered as part of this guideline update, which only updated the section on inducing remission in mild-to-moderate ulcerative colitis, and therefore we are unable to make changes to this area.
British Society of Gastroenterology	Guideline	General	General	This recommendation is presumably based on cost. However it is likely that this is based on a cost model of Remicade in 2008 with no mention of the impact of biosimilars which have reduced drug costs by over 50%. In addition, there is no acknowledgement of the difficulties in accurately monitoring a Ciclosporin infusion in a District General Hospital (DGH) where there may be little or no access to therapeutic monitoring and drug levels.	Thank you for your comment. This guideline update only reviewed evidence on treatments for inducing remission in people with mild-to-moderate ulcerative colitis. Recommendations for treating acute severe ulcerative colitis are from the 2013 guideline or cross-refer to relevant NICE technology appraisals. They were not part of the current update and therefore we are not able to address comments on them or alter the recommendations.
British Society of Gastroenterology	Guideline	General	General	Topical 5-ASA only for first line treatment for left sided disease runs the risk of undertreating inflammation in the descending colon. We would favour a combination of oral and rectal therapy for patients with this disease distribution.	Thank you for your comment. In this guideline update, the committee agreed to stratify extent of disease into 3 categories: 1) proctitis, 2) proctosigmoiditis and left-sided disease and 3) extensive disease.

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					The results of the network meta-analyses showed that for proctosigmoiditis and left-sided disease, topical aminosalicylates were the most effective treatment for inducing remission. This is consistent with the committee's clinical experience that enemas are able to reach the descending colon. Strategies that start with a topical aminosalicylate alone were also the most cost effective in proctosigmoiditis and left-sided disease. Following consultation, the committee discussed the time frame for assessing response to first-line treatment with a topical aminosalicylate. They agreed to amend the recommendation for proctosigmoiditis and left-sided disease to specify that if remission is not achieved with a topical aminosalicylate alone *within 4 weeks*, consider adding a high-dose oral aminosalicylate to the topical aminosalicylate or switching to a high-dose oral aminosalicylate and topical corticosteroid. For extensive disease affecting the colon proximal to the splenic flexure (with or without left-sided involvement), the committee recommended the combination of a topical aminosalicylate and high-dose oral aminosaliyclate as first-line treatment.
British Society of Gastroenterology				We have a similar comment to the Crohn`s section in terms of steroid sparing drugs. We suggest that these should be used when more than a single course of steroids is needed in a calendar year. The section on pregnancy is too short and general. There is a lack of advice on when to choose which biologic or Tofacitinib; but a recommendation of ciclosporin for acute severe ulcerative colitis.	Thank you for your comment. This guideline update only reviewed evidence on treatments for inducing remission in people with mild-to-moderate ulcerative colitis. Pregnancy and the issue of which biologic agent to use for acute severe ulcerative colitis are beyond the scope of the current update and therefore we are not able to address comments on them.
British Society of Gastroenterology	Guideline	General	General	Suggest you might mention use of synthetic steroids in UC too (cortiment and clipper). These can be important treatment options in some patients with UC	Thank you for your comment. These steroids are included under the class 'corticosteroids'. Guidance on the use of oral corticosteroids is provided in recommendations 1.2.8, 1.2.9, 1.2.10,

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					1.2.12 and 1.2.13.
British Society of Gastroenterology	Guideline	General	General	Suggest there should be mention of the role of aTNFs in induction and maintenance of remission in UC as well as the role of dose escalation of these drugs. The reference to 2015 guidelines is not adequate.	Thank you for your comment. Anti-TNF drugs were not included in the scope of this guidline update, which was specific to the induction of remission of mild-to-moderate ulcerative colitis. We have not reviewed the evidence for these drugs as part of the current update and are unable to make changes to these recommendations. However, links have been updated to cross-refer to relevant NICE technology appraisals that have been published since the last guideline.
British Society of Gastroenterology				It is of note that the British Society of Gastroenterology has just finished an updated treatment guideline for IBD. This is an exceptionally detailed and well researched document. It is with the clinical services committee and will be published as a supplement to Gut later this year. Ideally there should be some synergy between these key UK guidance documents. I would be happy to discuss this further if this would be of help.	NICE is aware of the forthcoming BSG IBD guideline. NICE and the BSG have met to discuss the synergies and overlaps in the 2 organisations' portfolios for gastroenterology topics. For this particular guideline the update covers only the induction of remission in mild-moderate ulcerative colitis. Following the publication of the BSG guideline NICE will consider the impact on the ulcerative colitis guideline.
British Society of Gastrointestinal & Abdominal Radiology	1.2.23			Suggest update to "imaging showing colonic dilatation" as may get CT etc first line if severe	Thank you for your comment. Assessing likelihood of needing surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.
British Society of Paediatric gastroenterology Hepatology and nutrition (BSPGHAN)	Guideline	5	General	In children oral 5-ASA is tried before trying rectal 5-ASA preparation because of better acceptance from patients and parents. Could this point be highlighted in the guidelines please?	Thank you for your comment. The evidence showed that topical aminosalicylates are more effective and cost effective compared to oral aminosalicylates as first-line treatment for proctitis so the committee agreed that topical aminosalicylates should be tried first. However, the committee noted that there may be an issue of acceptance of topical preparations in children and in some adults. They therefore included a separate recommendation consider an oral aminosalicylate as first-line treatment for those who decline a topical aminosalicylate, noting that it should be explained that oral

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					aminosalicylates are not as effective as topical aminosalicylates.
Crohn's & Colitis UK	General	General	General	We have serious concerns that this guideline update, as drafted, does not reflect current practice or the comprehensive and evidence-based British Society of Gastroenterology (BSG) Inflammatory Bowel Disease (IBD) guidelines and consensus-based IBD Standards, which have been collaboratively developed by 17 professional and patient organisations, both of which are very soon to be published and have been developed in alignment with each other. We strongly believe that the next stage of the guideline update should be delayed enabling full consideration of and alignment with the BSG IBD guidelines and IBD Standards. Without this, the delivery of high-quality treatment and care for people with Crohn's Disease and Ulcerative Colitis could be impeded. Alternatively, NICE guidelines that support and align with the BSG guidelines and IBD Standards will significantly enhance this. *The position above is shared by Crohn's & Colitis UK and the British Society of Gastroenterology* In Spring 2019 IBD UK will be launching a refreshed version of the IBD Standards. The IBD Standards are collaboratively developed between 17 professional and patient organisations, following the Delphi consensus method, in alignment with BSG guidelines. The Standards cover the IBD Service, Pre-Diagnosis, Flare Management, Surgery, Inpatient Care and Ongoing Care. A newly launched national patient survey and benchmarking tool will enable IBD services to benchmark their care against the IBD Standards, informed by the experience of patients using their service. The BSG will also be launching a new version of the BSG IBD guidelines. The BSG IBD guidelines are based on an extensive literature review, widespread involvement across all relevant professional disciplines, including patient and patient organisation involvement and input and a robust consensus process.	**NICE is aware of the forthcoming BSG IBD guideline. NICE and the BSG have met to discuss the synergies and overlaps in the 2 organisations' portfolios for gastroenterology topics. For this particular guideline the update covers only the induction of remission in mild-moderate ulcerative colitis. Following the publication of the BSG guideline NICE will consider the impact on the ulcerative colitis guideline.**Your feedback on the timeline for the consultation process have been passed to the relevant team in NICE for consideration.

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				Crohn's & Colitis UK also want to share some concerns that have arisen regarding the consultation process itself. The deadline given to respond to two significant consultations over the Christmas period has inhibited our organisation's ability to respond effectively, and to engage with members and stakeholders. We are concerned that this element of the guideline review has not been given sufficient time, with limited meaningful proactive stakeholder engagement. We also wish to note that we have been disappointed by the Committee secretariat's lack of communication and response to enquiries.	
Crohn's & Colitis UK	Guideline /Algorithm	General	General	There are a number of areas - aligned with pathways and the patient journey - that are unclear or omitted (as currently drafted): - Identification and referral pathway (pre-diagnosis), see page 1, sentence 6 - Preventing and managing a flare/relapse (picking up on the link between primary and secondary care) - The role of the IBD nurse and multidisciplinary team - Personalised care planning	Thank you for your comment. This guideline update only considered pharmacological treatments for inducing remission in mild-to-moderate ulcerative colitis. Only the areas of the pathway that are affected by this guideline update will be changed. We will pass your comment to our surveillance team for consideration in future updates.
Crohn's & Colitis UK	Guideline	1	6	We are concerned that the guideline as currently drafted does not include 'self-management' as part of its main specified aims. Given the Government's emphasis on the importance of self-management (NHS Long-Term Plan, 2020 Vision and Healthier Wales) and the important role that supported self-management plays in patient experience and clinical outcomes, we believe it should be a clear aim of the guideline and subsequent guidance. Crohn's & Colitis UK's position on self-management can be supplied on request.	Thank you for your comment. Self-management was not considered as part of this guideline update and therefore we are unable to make changes to this area. We will pass your comment to our surveillance team for consideration in future updates...
Crohn's & Colitis UK	Guideline	1	6	We would strongly suggest adding a reference to the NICE quality standard for inflammatory bowel disease QS81 both in the introduction and throughout the document. We would also suggest specifying how the updated guideline and quality standard correlate to each other in terms that members of the general public will understand.	Thank you for your comment. The NICE Quality standard QS81 will be linked to from the main webpage of this guideline.
Crohn's & Colitis UK	Guideline	4	1	We suggest revising this section. In line with the IBD Standards, patients should be supported to make informed, shared decisions about their treatment and care to ensure these take their preferences and goals fully into account. Patients should be given timely, clear information which is appropriate to their needs, age and level of understanding, and the right support to decide the acceptability and benefits and risks of treatment options, including potential complications and in order that they	Thank you for your comment. The 'Patient information and support' section was not considered as part of this guideline update and therefore we are unable to make changes to this area.. NICE is currently producing a guideline on shared decision making, and you would be welcome to register as a stakeholder for that

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				may have realistic expectations and understand possible (and optimal) outcomes. As such, shared decision making is very important and we would suggest that it is referenced clearly in this document, rather than signposted to on other pages of the NICE website. The guideline as currently written assumes greater understanding of shared decision making than should be expected of the general public, especially children and young people.	guideline on the NICE website.
Crohn's & Colitis UK	Guideline	4	4	This section does not align with the Crohn's Disease guideline and is weaker. We would ask the Committee to revisit this section and provide the same level of information and guidance. In line with the IBD Standards, we suggest adding that *patients should be provided with information in a format and language they can easily understand which is made available at every point of their journey*. Regarding the latter point, the guidelines should seek to reflect that information provided at the time of diagnosis may be different to further along in their journey. Information will need to be revisited, explained and reissued with changes to treatment, understanding and practice. In line with the IBD Standards, rapid access to specialist advice should be available to patients who are experiencing a flare, including access to a telephone/email advice line with response by the end of the next working day. The 'Providing information and support' section should also *extend to providing information and support about the IBD service itself*, and not limited to just the condition. The IBD Standards state: *All IBD patients should have information describing the IBD service and how it can be accessed. This should include information on how patients who have concerns about their condition or their care can request discussion of their case at the IBD team meeting or request a second opinion. It should also explain how patients can give feedback on the care they receive or participate actively in service development.* Furthermore, all patients should be provided with a point of contact, and clear information about pathways and timescales while awaiting the outcome of tests and investigations.	Thank you for your comment. The ' Patient information and support' section was not considered as part of this guideline update and therefore we are unable to make changes to this area. NICE is currently producing a guideline on shared decision making, and you would be welcome to register as a stakeholder for that guideline on the NICE website.
Crohn's & Colitis UK	Guideline	4	14	Signpost: • patients to information on shared decision making	Thank you for your comment. The 'Patient information and support' section was not

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				• health professionals and commissioners to examples of good practice	considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	4	15	To bring this into line with the IBD Standards and BSG IBD guidelines, we would strongly urge the committee to revisit this section to recommend a clear local and shared (with primary and secondary care) protocol for colorectal cancer surveillance in line with national guidance. This protocol should be clearly communicated to patients and be included in their notes and personalised care plan.	Thank you for your comment. The 'Patient information and support' section was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	4	11	The evidence suggests that regular 5-ASA therapy reduce cancer risk. Patients should be advised of this. https://www.ncbi.nlm.nih.gov/pubmed/10651654	Thank you for your comment. The 'Patient information and support' section was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	5	1	We recommend revisiting this recommendation to bring it in line with the IBD Standards and ensure that newly diagnosed outpatients start treatment rapidly, given the established and accepted implications of delayed treatment (poorer prognosis, increased use of surgery and use of more expensive drug treatments). We would recommend, based on current good practice, that a treatment plan be started within 48 hours for moderate to severe symptoms and within two weeks for mild symptoms.	Thank you for your comment. This guideline update only considered pharmacological treamtents for the induction of remission in mild-to-moderate ulcerative colitis. Optimal timing for initiating treatment in newly diagnosed patients was not covered in this guideline update and therefore we are unable to make changes to this recommendation. We will pass your comment to our surveillance team for consideration in future updates.
Crohn's & Colitis UK	Guideline	5 6	15-17 9-11 and 16-18	This section should make it clearer that oral corticosteroids, for reasons including their side effects and safety profile, are not recommended for long-term use in line with ECCO guidelines and NICE CKS. https://www.ncbi.nlm.nih.gov/pubmed/29336432 We would also ask the Committee to include a recommendation that would direct clinicians to counsel on their side effects, the risks associated with long-term use/repeated courses without intervals (on bone formation, for example) and to recommend the prescribing of calcium and vitamin D for bone protection during a course(s) of treatment(s).	Thank you for your comment. The recommendations for oral corticosteroids (recommendations 1.2.3, 1.2.4, 1.2.5, 1.2.8, 1.2.9, 1.2.10, 1.2.12, 1.2.13) have been amended to specify a time-limited course of treatment. This is to highlight that most corticosteroids are normally offered as a course of 4 to 8 weeks. The committee believe that this will reduce variability in prescribing practice and ensure that long-term corticosteroid courses are not offered. Recommendations for monitoring bone health are covered in section 1.6. The guideline includes a recommendation (1.6.1) to refer to NICE guideline osteoporosis: assessing the risk of fragility fracture. The recommendations in this section

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					were from the 2013 guideline and have not changed as they were out of scope of the current update.
Crohn's & Colitis UK	Guideline	7	4	This section, as currently drafted, does not give enough information on which to support patients to make an informed decision between biological drug treatments. In line with the BSG we would ask the Committee to revisit this section and consider the role of aTNFs in induction and maintenance of remission in UC, as well as the role of dose escalation of these drugs. Furthermore, the lack of information is not consistent with the Crohn's Disease guideline. Additionally, in line with the IBD Standards and BSG IBD guidelines, we would recommend revisiting this recommendation to direct healthcare professionals and commissioners to have protocols in place for pre-treatment tests, vaccinations, prescribing, administration and monitoring of biological therapies. We would ask that the Committee consider directing healthcare professionals and commissioners to record and audit the use of biologics through the IBD Registry, which is currently part of the Quality Accounts and would bring this section into line with the IBD Standards. Information on NICE Technology Appraisal Guidance on tofacitinib TA547 has been omitted and should be added.	Thank you for your comment. This guideline update only considered pharmacological treatments for the induction of remission in mild-to-moderate ulcerative colitis. AntiTNF and biological treatments were not considered as part of this guideline update and therefore we are only able to link to the relevant technology appraisal guidance. A cross-reference to the technology appraisal for tofactinib has been added. Thank you for pointing this omission out.
Crohn's & Colitis UK	Guideline	7 7	9 12	We would ask the Committee to revisit this section as the recommendation does not reflect current evidence-based practice. Patients presenting with acute severe colitis should: • be treated at a centre with medical and surgical expertise in managing IBD which is available at all times • have infectious causes of colitis excluded on admission • have daily monitoring of electrolytes, liver function, and full blood count in addition to regular measurement of C-reactive protein and serum albumin • limited flexible sigmoidoscopy, when indicated, should be performed without bowel preparation by an experienced endoscopist Those not settling on intravenous steroids should be assessed by a consultant colorectal surgeon on day three and a decision made with the patient and gastroenterologist to escalate to rescue therapy or undertake a colectomy	Thank you for your comment. Acute severe colitis was not considered part of this guideline update and therefore we are unable to make changes to this area.

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				Children should have daily joint review by a consultant paediatric gastroenterologist and a paediatric surgeon with experience of IBD.	
Crohn's & Colitis UK	Guideline	8	14	It is our understanding that the use of infliximab only if ciclosporin is contraindicated does not reflect current practice. We would urge the Committee to seek advice on the recommendation from the BSG.	Thank you for your comment. Use of infliximab or ciclosporin was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	9	4	The recommendation, as currently written, will not support or promote the implementation of good practice in the prescribing, management and monitoring of drugs between primary and secondary care. As currently worded, it does not reflect current practice or the fact that shared care is the reality for significant numbers of patients and this will only increase in line with the current shift towards moving care closer to home and transforming outpatient services (as set out in the NHS Long-Term Plan). We would also query why this section is not higher up in the document. To further understand the role of primary care in the management of people with IBD we would recommend the RCGP and Crohn's & Colitis IBD Toolkit. The IBD toolkit contains information for GPs and commissioners to help diagnosis, flare management, pathway development and support patients, as well as information for managing medications, contraception and IBD in pregnancy. www.rcgp.org.uk/ibd. We would strongly urge the Committee to revisit this guideline (and the Crohn's Disease guideline) with this in mind to ensure that this recommendation promotes and reinforces, in line with IBD Standards and BSG guidelines, clear shared care protocols which are clearly communicated to patients (and implemented with their agreement). Examples of good practice include: • South East London CCG	Thank you for your comment. Neither monitoring treatment, nor the increasing role of primary care were considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	10	2	We strongly urge the Committee to take action to align this guideline with the NICE Quality Standard on Inflammatory Bowel Disease. *Standard statement 3 states:* *People having surgery for inflammatory bowel disease have it undertaken by a colorectal surgeon who is a core member of the inflammatory bowel disease multidisciplinary team.*	Thank you for you comment. This guideline update only reviewed evidence on treatments for inducing remission in people with mild-to-moderate ulcerative colitis. Surgery was not considered as part of the current update and therefore we are unable to make changes to this area.

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				We would ask the Committee to revisit this section and in doing so align the current recommendations with the IBD Standards which promote good practice, which include: • Elective IBD surgery should be performed by a recognised colorectal surgeon • The surgeon should be a member of the IBD team • The unit should undertake these kinds of operations regularly. In the absence of relevant local expertise, complex surgery should be referred to a specialist unit. • Patients should have access to age appropriate expertise and advice • There should be regular combined or parallel clinics bringing together medical and surgical teams	The NICE Quality standard QS81 will not be updated because none of the new recommendations affect the quality statements.
Crohn's & Colitis UK	Guideline	10	2	Information when considering surgery Information should be offered in a written, audio-visual or web-based format, language and level patients can easily access and understand (especially for children and young adults). To align with the IBD Standards, all patients considering elective surgery should receive not just information, but opportunities to: • receive specialist counselling • access specialist opinion regarding reconstructive surgery • to meet with people (and families) of a similar age who have experienced surgery (particularly pouch and ileostomy patients) • discuss the impact on fertility (especially for women) and consider options regarding future fertility such as laparoscopic techniques or delaying surgery until they have had a family • give informed consent. It is important that patients are empowered to make informed decisions at all stages of their care, for example giving access to information on the outcome and complication rates of the different services can support patients to make a more informed judgement about their care • optimise their treatment and physical condition (including nutritional assessment) ahead of surgery	Thank you for your comment. Information about treatment options for people who are considering surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	10	19	Add: • fertility and pregnancy	Thank you for your comment. Information about treatment options for people who are considering surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.

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Crohn's & Colitis UK	Guideline	10	25	As currently written this recommendation does not promote a two-way dialogue between patient and clinician, which aims bring out an individual's preferences and life goals or facilitate shared decision making. We would ask the Committee to revisit this section, and the guidelines overall with this approach in mind. Where appropriate, the stoma nurse should have paediatric experience.	Thank you for your comment. Information about treatment options for people who are considering surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	11	2	Information post-surgery Current best practice directs healthcare professionals to • discharge with clear instructions relating to follow up care, wound management and prescribed medications. Any and all information should be shared with the patient's GP and IBD clinical team within 48 hours • offer counselling, in particular, for those considering reconstructive surgery • take steps to reduce the risk of VTE • provide long-term follow up (and data collection) to Ileoanal pouch patients • ensure pathways for rapid access for diagnosis and treatment of suspected pouchitis Add link to NICE guidance on *Transition between inpatient hospital settings and community or care home settings for adults with social care needs* https://www.nice.org.uk/guidance/ng27	Thank you for your comment. Information provided for people after surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Crohn's & Colitis UK	Guideline	13	6	This section does not adequately reflect current practice and thinking in relation to supporting those living with Crohn's Disease who wish to conceive or are pregnant. Additional information to include: • the impact of surgery on fertility. For female patients requiring sub-total colectomy and ileostomy, decisions regarding protectomy and ileoanal pouch reconstruction should be discussed because of the potential for impaired fertility. Decisions should be personalised, including use of laparoscopic techniques, and the option of delaying until after completion of the family. • medications to avoid when trying to conceive (e.g. methotrexate) • the impact and use of medications in pregnancy (e.g. biologics) • the method of delivery (possible caesarean section) for those with active perianal Crohn's Disease, an ileo-anal pouch or vulvul Crohn's disease - multidisciplinary working is key in these circumstances, drawing in the patient and obstetrician to enable shared and informed decision making) • action to reduce risk of VTE prophylaxis after a caesarian section. • treatment that is available to support fertility	Thank you for your comment. Treatment of ulcerative colitis in pregnant women was not considered as part of this guideline update and therefore we are unable to make changes to this area.

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				• breastfeeding and medication • increasing folic acid supplements where a person with Crohn's disease has had surgery or are taking certain medications • neonatal vaccinations after exposure to biologics • managing a stoma when pregnant • the risks of a child having Crohn's Disease Crohn's and Colitis UK's resources on pregnancy and fertility can be read here. Research on the transition to motherhood for people with Crohn's and Colitis can be read here.	
Crohn's & Colitis UK	Guideline	13	17	This section does not make clear enough to members of the general public what the specific links between bone health and ulcerative colitis are or recommended actions to take. Prolonged corticosteroid use is a risk factor for osteoporosis in IBD. The BSG IBD guideline recommends patients prescribed a course of steroids should be first assessed for risk of osteoporosis and prescribed vitamin D and calcium supplement as part of their treatment course. Patients on long courses of corticosteroids should be tested regularly (bone densitometry). More general risk factors also include malnutrition, inflammation, smoking and lack of weight-bearing exercise, all of which should be screened for and addressed. We would ask that this recommendation be revised and bought in line with the IBD Standards which states that following diagnosis that all patients should have full assessment of bone health (in addition to assessment of their disease, nutritional status, mental health and baseline infection screen) and that this information is recorded in their personalised care plan. In line with good practice and evidence-based approaches (as set out in the Royal College of General Practitioners and Crohn's & Colitis UK IBD toolkit www.rcgp.org.uk/ibd), healthcare professionals should be directed to: • Measure bone mineral density (BMD) to assess fracture risk in people aged under 40 years who have a major risk factor, such as history of multiple fragility fracture, major osteoporotic fracture, or current or recent use of high-dose oral or high-dose systemic glucocorticoids (more than 7.5 mg prednisolone or equivalent per day for 3 months or longer). • Bone-protective treatment should be started at the onset of glucocorticoid	Thank you for your comment. Monitoring bone health was not considered as part of this guideline update and therefore we are unable to make changes to this area. It is impossible for NICE guidelines to cover every eventuality and it is expected that prescribers understand their responsibilities.

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				therapy in individuals at high risk of fracture, including some premenopausal women and younger men, particularly in individuals with a previous history of fracture or receiving high doses of glucocorticoids.	
Crohn's & Colitis UK	General	23	2	Unclear where the statistics are from. References would be welcome.	Thank you for your comment. We have amended the statistics and added a hyperlink to the source of the reference..
Crohn's & Colitis UK	General	23		We would recommend revisiting how Ulcerative Colitis is described in this section: https://www.crohnsandcolitis.org.uk/about-inflammatory-bowel-disease/ulcerative-colitis	Thank you for your comment. The context section is only intended to provide a very brief overview of the condition.
Crohn's & Colitis UK	General	23	5	Crohn's & Colitis UK usually refer to: • the genes you are born with, • plus an abnormal reaction of your immune system to certain bacteria in your intestines, • along with an unknown trigger that could include viruses, bacteria, diet, smoking, stress or something else in the environment.	Thank you for your comment. The context section is only intended to provide a very brief overview of the condition..
Crohn's in Childhood Research Association	guideline	22	8 + 9	a note should be inserted about extensive disease being more prevalent in children at presentation, and the importance of disease activity scores (PUCAI) and escalation of treatment if the patient is not responding	Thank you for your comment. The context section is only intended to provide a very brief overview of the condition.
Department of Health and Social Care		General	General	I wish to confirm that the Department of Health and Social Care has no substantive comments to make, regarding this consultation.	Thank you for your comment.
Intensive Care Society.	Guideline	General	General	This document, especially in the section relating to post-surgery, could include a statement on when to discuss patients to Critical Care.	Thank you for your comment. Information provided for people after surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Janssen UK	Guideline	7	7	The Guideline does not make it clear that moderate to severe patients can have multiple biologic treatments, as per TA547, which could lead to sub-optimal patient outcomes. We suggest the following sentences could be added to section 1.2.14:	Thank you for your comment. Biologic treatments and treatments for moderately to severely active ulcerative colitis were not considered as part of this guideline update and therefore we are unable

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				For patients who have had an inadequate response with, lost response to or were intolerant to conventional therapy (or have medical contraindications to such therapies) a biological therapy should be considered. For patients who have had an inadequate response with, lost response to or were intolerant to a biologic therapy (or the therapy is medically contraindicated) then a subsequent biological therapy should be considered. The 2019 draft guideline provides an opportunity for NICE to reiterate clinical management options that have become available since 2013, with the aim of encouraging better outcomes if initial therapies prove ineffective. We suggest the following sentence could be added to section 1.2.14: Patients should be routinely assessed for clinical response, and for patients who have had an inadequate response with, lost response to or were intolerant to a biological therapy (or the therapy is medically contraindicated) then a subsequent biological therapy should be considered.	to make changes to this area. The purpose of the recommendation you referred to is to signpost relevant technology appraisal guidance on the use of drugs for moderately to severely active ulcerative colitis.
Janssen UK	Guideline	General	General	There appears to be confusion on the definition of mild, moderate and severe disease in the guidelines and what populations these refer to. It would be useful to make it clear at the start of the guideline what population is being referred to and how the severity of the population has been categorised (what scales/scores have been used).	Thank you for your comment. The categories mild, moderate and severe are described in the section 'Terms used in this guideline.' Subheadings have been used to specify which recommendations relate to the different severities of disease.
Janssen UK	Guideline	General	General	A summary table detailing what treatments are recommended for which populations could be added at the end of the document to improve the clarity of the guideline recommendations.	Thank you for your comment. This update is only addressing a small part of the guideline and therefore we are not able to produce a summary table for the whole guideline. Most ofthe evidence is summarised in the NICE pathway associated with this guideline.
Janssen UK	Guideline	15	12	We are concerned that the use of the Truelove and Witt severity index may not be the most clinically relevant measure, and that another system which is commonly used in clinical practice (such as the partial Mayo score) may be more informative for clinicians accessing this guideline.	Thank you for your comment. Comparison of severity indices was not within the remit of this update. For consistency, we continued using the same scales as the rest of the guideline. We will pass your comment to our surveillance team for consideration in future updates.
MSD	Evidence	236	10	Table 65 reports the dose and cost of biological therapies. Within the maintenance column of the table only the 50mg dose is reported. In accordance with the golimumab dose optimisation label change accepted by the EMA in July 2018 , MSD request the	Thank you for your comment. The 100mg dose for golimumab has been added to the maintenance column.

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				inclusion for golimumab 100mg in the maintenance column.	
Napp Pharmaceuticals Limited	Evidence Review	General And page 236	General And Table 65	Thank you for the opportunity to contribute to the guideline consultation. Biosimilar infliximab became available in February 2015, the NHS list price for Remsima® is £377.66 per 100 mg vial as shown in the BNF. However, biosimilars and the originator are subject to the tendering process for procurement in the NHS. The launch of a number of biosimilars of infliximab has led to a drop in the real price paid by the NHS since 2015. The lower prices will of course have an effect on the ICERs. We suggest that the ERG may wish to take this into account through price sensitivity analysis using prices based on discounts on the NHS price for Remicade® (originator infliximab) of £419.62 per 100mg vial. We suggest that the discounts should be in the range of 75% to 90% of the Remicade price. The induction cost for biosimilar infliximab in Table 65 may therefore be overestimated by the ERG. The lower cost of biosimilars will also contribute to lower treatment costs for those patients who require maintenance treatment and we also suggest that these prices should be included in any calculation of the cost effectiveness of maintenance treatment.	Thank you for your comment. In accordance with our methods manual, public list prices for medicines are used in the reference-case analysis. Analyses based on price reductions for the NHS will be considered when the reduced prices are transparent and can be consistently available across the NHS. We checked for nationally available price reductions for infliximab in eMIT but no information was available and therefore the list price from the BNF was used. In the economic model, biologics are not one of the comparators in the decision space for the induction of remission of mild-to-moderate ulcerative colitis but contribute to a weighted estimate of the overall cost of rescue therapy that affects all strategies and has a limited impact on incremental results. For example, scenario analyses were run in which the assumption about the duration (cost) of maintenance treatment with biologics was varied and did not change the overall conclusions.
National Ankylosing Spondylitis Society (NASS)	Guideline	13	18	Extra articular manifestations should be considered in people with ulcerative colitis. 7% of people with axial spondyloarthritis including ankylosing spondylitis have inflammatory bowel disease. Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis, Carmen Stolwijk, Astrid van Tubergen, José Dionisio Castillo-Ortiz, Annelies Boonen, Annals of the Rheumatic Diseases 2015, 74:65–73	Thank you for your comment. Monitoring bone health was not considered as part of this guideline update and therefore we are unable to make changes to this area. We have passed your comment on to the surveillance team for consideration in future updates.
Pfizer Ltd	Draft Guideline	7 of 29	2	Section 1.2.14 refers to technologies to be considered for "all extents of disease" citing TA329 (infliximab, adalimumab and golimumab for moderately to severely active ulcerative colitis) and TA342 (vedolizumab for treating moderately to severely active ulcerative colitis). NICE has also recently appraised and recommended tofacitinib in ulcerative colitis; TA547 (tofacitinib for moderately to severely active ulcerative colitis). Tofacitinib is a small molecule, not a biologic, and has a different mode of action to currently recommended biologic in ulcerative colitis. In order to reflect the recent guidance within the current CG166 guidance, Pfizer recommends changing section 1.2.14 to:	Thank you for your comment. We have added a reference to the technology appraisal TA547 for tofactinib.

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				1.2.14 For guidance on biologics and small molecules for treating moderately to severely active ulcerative colitis, see the NICE technology appraisal guidance on: • infliximab, adalimumab and golimumab for moderately to severely active ulcerative colitis • vedolizumab for treating moderately to severely active ulcerative colitis [2019] • tofacitinib for moderately to severely active ulcerative colitis. [2019]	
Pharma UK Ltd	Guideline	5	5	With reference to the general comment made above, this would be clearer if it stated '…offer a rectal (topical) aminosalicylate…'	Thank you for your comment. To remain consistent with other parts of the guideline the committee decided to retain 'topical' in the updated recommendations. The committee agreed that topical was still the term in common use.
Pharma UK Ltd	Guideline	6	6	There is evidence that switching to an alternative delivery/release formulation of an aminosalicylate may be beneficial before using a high-dose oral aminosalicylate with the topical aminosalicylate – Taylor K, Irving P. Optimization of conventional therapy in patients with IBD. *Nat. Rev. Gastroenterol. Hepatol.* 8, 646–656 (2011)	Thank you for your comment. There was no strong evidence to suggest any meaningful differences in achieving remission between various formulations of topical aminosalicylates in proctosigmoiditis and left-sided disease and we did not identify any randomised controlled trials that compared switching between different topical formulations to the use of an oral aminosalicylate and a topical aminosalicylate. .
Pharma UK Ltd	Guideline	6	24	A topical steroid should be offered first.	Thank you for your comment. In spite of extensive literature searching, no evidence was identified for topical corticosteroids in extensive mild-to-moderate ulcerative colitis.
Primary Care Society for Gastroenterology	Guideline	General	General	The new BSG IBD Guidance has been submitted for publication. This should be published in the Spring of 2019. It would seem sensible to await this publication so that the NICE Guidance can be updates to reflect the detailed and comprehensive work that has gone into this document, and to ensure that proper alignment of the recommendations can take place	NICE is aware of the forthcoming BSG IBD guideline. NICE and the BSG have met to discuss the synergies and overlaps in the 2 organisations' portfolios for gastroenterology topics. For this particular guideline the update covers only the induction of remission in mild-moderate ulcerative colitis. Following the publication of the BSG guideline NICE will consider the impact on the ulcerative colitis guideline..
Primary Care Society for Gastroenterology	Guidance	General	General	The review lacks clarity on the diagnostic pathway, and communication between primary and secondary care. It would more complete if this could be added.	Thank you for your comment. Diagnosis and communication between primary and secondary care were not considered as part of this guideline update and therefore we are unable to make changes to this area. future updates.

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Primary Care Society for Gastroenterology	Guidance	General	General	Identification and initial management of flare is also missing. Primary care and patients would benefit greatly from having a simple algorithm for this, as it can be difficult to recognise when a flare is occurring, when to use self-care, and when to seek further advice. A care plan provided by secondary care to primary care and the patient can form an essential part of this.	Thank you for your comment. Identification and initial management were not considered as part of this guideline update and therefore we are unable to make changes to this area.
Primary Care Society for Gastroenterology	Guidance	General	General	The role of the clinical nurse specialist/IBD nurse does not have a high enough profile in this review. Areas that have a high proportion of IBD nurses (https://www.nice.org.uk/guidance/qs81) often have a lower admission rate and shorter length of stay.	Thank you. This update focussed on the pharmacological treamtents for induction of remission in mild-to-moderate ulcerative colitis and therefore the role of different health professionals was outside of the scope of this update.
Royal College of General Practitioners	Guideline	General	General	The new BSG IBD Guidance has been submitted for publication. This should be published in the Spring of 2019. It would seem sensible to await this publication so that the NICE Guidance can be updates to reflect the detailed and comprehensive work that has gone into this document, and to ensure that proper alignment of the recommendations can take place	NICE is aware of the forthcoming BSG IBD guideline. NICE and the BSG have met to discuss the synergies and overlaps in the 2 organisations' portfolios for gastroenterology topics. For this particular guideline the update covers only the induction of remission in mild-moderate ulcerative colitis. Following the publication of the BSG guideline NICE will consider the impact on the ulcerative colitis guideline.
Royal College of General Practitioners	Guidance	General	General	The review lacks clarity on the diagnostic pathway, and communication between primary and secondary care. It would more complete if this could be added.	Thank you for your comment. Diagnosis and communication between primary and secondary care were not considered as part of this guideline update and therefore we are unable to make changes to this area.
Royal College of General Practitioners	Guidance	General	General	Identification and initial management of flare is also missing. Primary care and patients would benefit greatly from having a simple algorithm for this, as it can be difficult to recognise when a flare is occurring, when to use self-care, and when to seek further advice. A care plan provided by secondary care to primary care and the patient can form an essential part of this.	Thank you for your comment. Identification and initial management were not considered as part of this guideline update and therefore we are unable to make changes to this area.
Royal College of General Practitioners	Guidance	General	General	The role of the clinical nurse specialist/IBD nurse does not have a high enough profile in this review. Areas that have a high proportion of IBD nurses (https://www.nice.org.uk/guidance/qs81) often have a lower admission rate and shorter length of stay.	Thank you for your comment. This update focussed on the pharmacological treamtents for induction of remission in mild-to-moderate ulcerative colitis and therefore the role of different health professionals was outside of the scope of

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					this update
[Royal College of Nursing]	General	General	General	The Royal College of Nursing (RCN) welcomes proposals to update the NICE Ulcerative Colitis guideline. The RCN invited members who care for people with this condition to review the draft consultation document on its behalf. The comments below reflect the views of our reviewers.	Thank you for your comments.
[Royal College of Nursing]	Guideline	6	24	Add: "If remission is not achieved after 4 weeks". The ground for the amendment is for this recommendation to be equitable with the recommendation in section 1.2.4 Line 11 of the draft document.	Thank you for your comment. The committee agreed that this was a useful addition and included this in the recommendation.
Royal College of Paediatrics and Child Health				The reviewer was pleased with the documents	Thank you for your comment.
Royal College of Physicians		General	General	We would like to endorse the responses submitted by the British Society of Gastroenterology (BSG).	Thank you for your comment.
South Worcestershire CCG	Guideline	5-7	General	The mainstay of recommended treatment for inducing remission appears to be topical and oral aminosalicylate and corticosteroids but for use of biologics (referenced separately and not included) initiation is recommended "in adults whose disease has responded inadequately to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who cannot tolerate, or have medical contraindications for, such therapies." Where does the role of mercaptopurine and azathioprine fall within this management guideline? There is some reference in the subsequent section for maintaining remission but this is not entirely clear in terms of the management pathway.	Thank you for your comment. This guideline update considered pharmacological treatments for the induction of remission in mild-to-moderate ulcerative colitis. Azathioprine and mercaptopurine were excluded from this guideline update as the committee ageed that both of these treatments would not be considered for induction of remission. Both of these treatments are considered within the recommendations relating to maintenance of remission (recommendations 1.4.4 and 1.4.5): 1.4.4 Consider oral azathioprine or oral mercaptopurine8 to maintain remission: • after 2 or more inflammatory exacerbations in 12 months that require treatment with systemic corticosteroids or • if remission is not maintained by

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					aminosalicylates. [2013] 1.4.5 To maintain remission after a single episode of acute severe ulcerative colitis: • consider oral azathioprine or oral mercaptopurine • consider oral aminosalicylates if azathioprine and/or mercaptopurine are contraindicated or the person cannot tolerate them. [2013].
South Worcestershire CCG	Guideline	7	2-7	• It would be more helpful if the detail for the NICE technology appraisals was included in this guideline. • Tofacitinib for moderately to severely active ulcerative colitis (TA547) should also be referenced here as it is now published. • There is a lack of clarity in related technology appraisals with regard to the sequential use of these agents (including how many?). If no advice in relation to sequential use is to be provided then it would be helpful if the guideline acknowledges local pathways of care that might better inform use of biologics. • There is no mention on the role of add-on treatment with biologic therapies; however as UC is managed very similarly to CD I suspect that this is undertaken and if there is no evidence for this it would be helpful to state that. • Further definition of "disease response" and "stable clinical remission" (as per TA guidance) would better inform use of biologics. • Local clinicians have suggested that a "trial withdrawal" may not be appropriate for the following patient groups: - Short duration of remission (ideally require at least 12 months and possibly up to 3-4 years) - Lack of available alternative options either biologics or DMARDs (specifically azathioprine or mercaptopurine) due to either prior lack of response or contra-indication - Risk of antibody development if treatment stopped and subsequent lack of response when restarted - Disease severity/history concern	Thank you for your comments. Technology appraisals for infliximab, adalimumab, golimumab, vedolizumab and tofacitnib are still current and will be updated as necessary Therefore, a link has been inserted to cross-refer to the recommendations in the technology appraisal so that any updates are reflected. Where technology appraisals have been moved to a static list (ie they will no longer be updated) they are incorporated as text within the guideline. We have added a link to the technology appraisal TA547 for tofacitinib. The use of biologics and Janus kinase inhibitors for moderately to severely active ulcerative colitis is outside of the remit of the current update. We have not reviewed the evidence in relation to these drugs and are unable to make any recommendations in this area.
South Worcestershire CCG	Guideline	8	1 and 7	There is clinical reluctance to use ciclosporin due to the side effect profile, potential for longer hospital stay and issues with drug level monitoring. This results in earlier use of infliximab citing that ciclosporin is "clinically inappropriate". Clarification of the appropriateness of this would be welcomed particularly in relation to the stated concerns.	Thank you for your comment. Use of ciclosporin and infliximab was not considered as part of this guideline update and therefore we are unable to make changes to this area.
South Worcestershire CCG	Guideline	8	14 and 21	Patients initiated on infliximab often continue to receive it long-term for fear of further flares; this would be patients who fail prior management options. Is this appropriate and can it be included within the guideline?	Thank you for your comment. Use of infliximab was not considered as part of this guideline update and therefore we are unable to make changes to this area.

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South Worcestershire CCG	Guideline	11	12 general	This section does not address whether there is a role for maintaining remission with biologics in patients who received them to induce remission. Further clarity would be helpful. Also need to clarify the role of azathioprine and mercaptopurine (as in comment 1)	Thank you for your comment. Maintenance of remission was not considered as part of this guideline update, which considered induction of remission.
South Worcestershire CCG	Guideline	9 - 11	General	It would also be helpful to advise: i. If ongoing biologic treatment is ever appropriate following surgical intervention ii. what circumstances would support a patient re-starting biological treatment post-surgery and where in the pathway a patient would sit; do they reconvene in the same place ie. as a second line biologic treatment or do they recommence as a 1st line treatment as it could be considered new disease?	Thank you for your comment. Use of biologics was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Surrey Downs Clinical Commissioning Group	Guidance	7	1.2.12	The NICE guideline referred to does not make specific the place in therapy of each biologic, including sequential use, dose escalation and / or tofacitinib i.e. which is the preferred option, and when it would be used, and when it could be replaced with an alternative, and how many alternatives should be used sequentially. It would be useful if this CG could be more directive.	Thank you for your comment. Biologics were not considered as part of this guideline update and therefore we are unable to make recommendations in these areas.
Takeda UK Ltd	Evidence review	82	General	In relation to comment 1 above, the evidence base for mucosal healing appears to come purely from clinical papers examining the use of budesonide. There is a wider evidence base for mucosal healing as explored in the STRIDE paper and ECCO guidelines referenced above and we feel this evidence should be considered.	Thank you for your comment. Mucosal healing was not included as an outcome in this guideline update and therefore the evidence pertaining to it was not identified or reviewed. However, clinical remission, as reported by the author, was included as an outcome. This guideline update did not define how clinical remission should be assessed in clinical practice.
Takeda UK Ltd	Guideline	10	20	We feel that one of the most important considerations for patients considering surgery is the potential impact on fertility. Although it could be considered that this is covered under sexual functioning this is not clear and we therefore feel that fertility should be specifically cited as an example.	Thank you for your comment. Surgery was not considered as part of this guideline update and therefore we are unable to make changes to this area.
Tillotts Pharma UK Ltd	Draft guidance	7	2	The guideline should include reference to other factors which might affect prescribing decisions and we recommend a statement such as: "The treatment used should be selected based on lowest acquisition cost. The licensed posology varies between mesalazine products and individual product SPCs should be consulted by prescribers."	Thank you for your comment. The committee chose not to recommend specific preparations of mesalazine to allow healthcare professionals and people with mild-to-moderate ulcerative colitis to choose the most appropriate treatment, depending on patient preference, availability and acquisition cost. Clinicians are expected to consult the BNF for dosing and cost information.
Tillotts	Evidence	11	Table	We are concerned by the ambiguity with which the criteria "high dose" and "standard	Thank you for your comment. We have re-labelled

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<tr><td>Pharma UK Ltd</td><td>review</td><td></td><td>2</td><td>dose" are applied to mesalazine products, as they do not adequately reflect the information in the various mesalazine product SPCs, nor the findings of the latest Cochrane meta-analysis on 5-ASAs in the induction of remission of ulcerative colitis (Wang et al, 2016).

The term "high dose" is applied equally to Asacol and Octasa at 4.8g/day, Pentasa at 4g/day and Salofalk granules at 3g/day, a range from 3 to 4.8g/day. The term "standard dose" is applied equally to Asacol and Octasa at 2.4 to <4.8g/day, Pentasa at up to 2g/day and Salofalk granules at up to 1.5g/day, a range of 1.5 to <4.8g/day). This is confusing for the prescriber and may lead to inconsistent treatment of patients.

The latest Cochrane meta-analysis concludes that all 5-ASAs are equally effective at equimolar doses. Therefore, all reference to mesalazine product names should be removed from Table 2, which should instead recommend that high doses of mesalazine are those over 3g/day and standard doses are those up to 3g/day. This definition is applied by Nguyen et al in their recent network meta-analysis (Nguyen et al, 2018). This is consistent with all other product classes described in the table and the NICE guidance itself, which does not specify brand names.

The prescriber may then prescribe any product with the confidence that they are providing their patient with an effective dose of mesalazine, irrespective of the product used. However, the information in product SPCs must be respected as maximum doses differ between products and this might be explained in a footnote to the table.

The mesalazine row in Table 2 would then appear as follows:

<table>
<tr><td></td><td>Standard dose</td><td>High dose</td></tr>
<tr><td>Mesalazine</td><td>Up to 3g/day</td><td>Over 3g/day</td></tr>
</table>

References
Wang Y, Parker CE, Bhanji T, Feagan BG, MacDonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis (Review). Cochrane Database of Systematic Reviews. 2016, Issue 4, Art No.: CD000543.

Nghia H Nguyen, Mathurin Fumery, Parambir S Dulai, Larry J Prokop, William J Sandborn, Mohammad Hassan Murad and Siddharth Singh. Comparative efficacy and tolerability of pharmacological agents for management of mild to moderate ulcerative colitis: a systematic review and network meta-analyses. Lancet Gastroenterol Hepatol. 2018; August: 1-12</td><td>Table 2 to make it clear that the doses listed here were defined by the committee for the purpose of classifying RCT evidence in the review. The classification was based on committee consensus about what would constitute a standard vs. a high dose in clinical practice. It was necessary to refer to the brand names in this table because there are multiple preparations of e.g., granules given in different doses.

Clinicians are expected to consult relevant sources (BNF, SPC) for dosing information when prescribing mesalazine products.</td></tr>
</table>

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Tillotts Pharma UK Ltd	Evidence review	232	Table 57	The products in the table should be listed in alphabetical order. The table should not be split by a page break.	Thank you for your comment. Products are now listed in alphabetical order. Every attempt has been made to avoid splitting tables across pages but sometimes this can still happen in the final stages when documents are edited.
Tillotts Pharma UK Ltd	Evidence review	232	Table 57	There are a number of errors in the data in the table: Cost per week of Pentasa Gran Sach 1g M/R (2g dose) should be £8.61 (not £6.46 as shown) Cost per week of Salofalk Gran Sach G/R 500mg M/R (1.5g dose) should be £6.80 (not £5.70 as shown) Cost per week of Salofalk Tab G/R 500mg (1.5g dose) should be £6.04 (not £6.80 as shown) The cost per week is calculated by dividing the daily dose by the product strength to give the number of tablets/sachets required. The number of tablets/sachets is then multiplied by the cost per tablet/sachet to give the cost per day. The cost per day is multiplied by 7 to give the cost per week. For example, for Pentasa Gran Sach 1g M/R (at a dose of 2g): The daily dose (2g) divided by the strength of the sachet (1g) = 2 sachets per day The cost per sachet (£0.61) multiplied by 2 = £1.23 per day The cost per day multiplied by 7 = £8.61 per week There is no clarity about how a dose is defined as low dose in Table 57 of the evidence review and there is significant overlap with the "standard" dose (as discussed in Table 2). Please consider these errors and whether they have consequences in other calculations within the evidence review and hence the draft guideline.	Thank you for your comment. The cost per week of Pentasa Gran Sach 1g M/R (2g dose) has been corrected to £8.61. The error was because the incorrect daily dose (1.5g) had been assumed for this preparation. The cost per week of Salofalk Gran Sach G/R 500mg M/R (1.5g dose) was checked and according to our calculations this should be £6.04 per week (£28.74/100 x 1.5/0.5 x 7). This has been updated. The cost per week of Salofalk Tab G/R 500mg (1.5g dose) was checked and according to our calculations this should be £6.80 per week (£32.38/100 x 1.5/0.5 x7). No change was made to the table. A sentence has been added to the text to clarify that the doses correspond to most common dose across the clinical trials included in the evidence review and, in the event of any discrepancies, to the lower limit (low dose) and upper limit (high dose) of the treatment dose ranges specified for each preparation in the BNF. The analyses have be re-run and results updated in the evidence report. These changes did not have any meaningful impact on the conclusions of the cost-effectiveness analysis and subsequent recommendations.
Tillotts Pharma	Evidence review	233	Table 58	The products in the table should be listed in alphabetical order.	Thank you for your comment. Products are now listed in alphabetical order.

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UK Ltd					
Tillotts Pharma UK Ltd	Evidence review	233	Table 58	There are a number of errors in the data in the table, which should be corrected: • Asacol 400mg should not be included in this table, as the maximum licensed dose is 2.4g and therefore high doses may not be achieved. • The cost per week of Pentasa Gran Sach 1g M/R (3g dose) should be costed at a dose of 4g per day for the comparison to be accurate and consistent with the product SPC. • The cost per week of Pentasa Gran Sach 4g M/R (3g dose) is impossible to achieve with a 4g sachet. Only a dose of 4g can be achieved with this preparation. There is no clarity about how a dose is defined as high dose in Table 58 of the evidence review and there is significant overlap with the "standard" dose (as discussed in Table 2).	Thank you for your comment. Tables 57 and 58 have now been updated to assume that Asacol 400mg, mesalazine 400mg and Octasa 400mg would generally be prescribed for the low daily dose (2.4g) and Asacol 800mg, mesalazine 800mg and Octasa 800mg would generally be prescribed for the high daiy dose (4.8g) to minimise the number of pills per day. The cost per week for Pentasa Gran Sach 1g M/R and Pentasa Gran Sach 4g M/R have been corrected assuming a dose of 4g per day. A sentence has been added to the text to clarify that the doses correspond to most common dose across the clinical trials included in the evidence review and, in the event of any discrepancies, to the lower limit (low dose) and upper limit (high dose) of the treatment dose ranges specified for each preparation in the BNF.