

## British Society of Gastroenterology (BSG) advice for management of inflammatory bowel diseases during the COVID-19 pandemic

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### Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), is a condition in which the gastrointestinal immune system responds inappropriately. It is therefore often treated with immune suppression medications to control inflammation and to prevent 'flares', a worsening in symptoms, which may be unpredictable.

It is known that 0.8% of people in the UK (approx. 524,000 patients) currently have IBD, but only 44% have been to a clinic in the last 3 years<sup>1,2</sup>. There will be many patients who will be worried about the effect of the Coronavirus pandemic (SARS-CoV-2 or COVID-19 disease) on their IBD and vice versa.

During the COVID-19 outbreak we will do everything we can to keep our IBD patients safe. The biggest risks are related not only to the infection itself, but also the emergency reorganisation of hospital and general practice services to deal with the pandemic, meaning routine IBD services will be significantly affected. A combined approach covering both primary and secondary care is therefore required to keep vulnerable IBD patients out of hospital as much as possible.

Insights from Hubei, China and from Italy suggest hospital admission for non-COVID-19 illness will provide a reservoir for further spread of infection. However, alterations to the way we deliver IBD care in the UK must be balanced against the risks of undertreated, active IBD. Importantly, patients with active IBD are likely to have a higher risk of infection both in the community and during inpatient care, even in the absence of immunosuppressant treatment<sup>3</sup>. Therefore, it is of paramount importance to control the intestinal inflammation in IBD to prevent adverse outcomes.

### 1) COVID-19 disease and IBD

The impact of immunosuppression on the severity of COVID-19 disease remains unclear. Data reported thus far of 1099 patients from China did not observe immunomodulator use as a risk factor for severe disease (Guan et al.). The currently understood factors associated with poorer COVID-19 outcomes are older age (OR 1.1; 95% CI 1.03-1.17 per year increase) and comorbidity (Guan et al. Zhou et al.). NSAID use, given its association with adverse outcome in other viral respiratory infections and in precipitating IBD flare, should be avoided<sup>5</sup>.

‘Social distancing<sup>a</sup>’, and ‘shielding<sup>b</sup>’ are measures to reduce spread within a population and to protect high risk groups. These are also an understandable source of anxiety for patients with IBD.

On behalf of the British Society of Gastroenterology (BSG) a UK-wide COVID-19 working group has been established and has defined patient risk into highest, moderate and lowest for COVID-19 related poor outcome (see Table 1 and below for justification of groupings). Patients classified as at highest risk correspond to Group 5 in the UK Government’s instruction to undergo active ‘shielding’, the most stringent version of isolation. Note that all patients should still attend for infusions of biologics no matter what category they are in.

There will be a pragmatic approach to identification of groups. The UK Department of Health has requested patient contact details from local secondary care IBD services for those that meet the highest risk by Wednesday 25<sup>th</sup> March. This request currently applies to NHS England only, with clarification for devolved nations awaited.

To meet this request, we propose mobilising the following methods for patient identification

1. Where feasible, national datasets will be interrogated to identify higher risk patients
2. Communications direct to patients via BSG and Crohn’s & Colitis UK
3. Patients should also self-identify as to which group they belong and to contact local IBD team ideally by e-mail / phone
5. List to NHS England by 25th March 2020

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<sup>a</sup> <https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults>

<sup>b</sup> <https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19>

Table 1: Highest, moderate and lowest risk defined by the BSG IBD COVID-19 working group

| Highest Risk<br>'Shielding'  | Moderate risk<br>'Stringent <u>social distancing</u> '   | Lowest risk<br>'Social distancing'  |
|--|--|---|
| <ol style="list-style-type: none"> <li>1. IBD patients who <b>either</b> have a co-morbidity (respiratory, cardiac, hypertension or diabetes mellitus) <b>and/or</b> are <math>\geq 70</math> years old <b>and*</b> are on any therapy for IBD (per middle column) except 5ASA, budesonide, beclometasone or rectal therapies</li> <li>2. IBD patients of any age regardless of co-morbidity and who meet one or more of the following criteria:               <ul style="list-style-type: none"> <li>○ on oral or intravenous prednisolone <math>\geq 20</math> mg per day (only while on this dose)</li> <li>○ new induction therapy with combo therapy (starting biologic within previous 6 weeks)</li> <li>○ moderate-to-severely active disease despite immunosuppression/ biologics</li> <li>○ short gut syndrome requiring nutritional support</li> <li>○ requirement for parenteral nutrition</li> </ul> </li> </ol> | <p>Patients on the following medications:</p> <ul style="list-style-type: none"> <li>• Ustekinumab</li> <li>• Vedolizumab</li> <li>• Methotrexate</li> <li>• Anti-TNF alpha monotherapy (infliximab, adalimumab, golimumab)</li> <li>• Thiopurines (azathioprine, mercaptopurine, tioguanine)</li> <li>• Calcineurin inhibitors (tacrolimus or ciclosporin)</li> <li>• Janus kinase (JAK) inhibition (tofacitinib)</li> <li>• Combination therapy in stable patients**</li> <li>• Immunosuppressive/biologic trial medication</li> </ul> | <p>Patients on the following medications:</p> <ul style="list-style-type: none"> <li>• 5ASA</li> <li>• Rectal therapies</li> <li>• Orally administered topically acting steroids (budesonide or beclometasone)</li> <li>• Therapies for bile acid diarrhoea (colestyramine, colesevelam, colestipol)</li> <li>• Anti-diarrhoeals (e.g. loperamide)</li> <li>• Antibiotics for bacterial overgrowth or perianal disease</li> </ul> |
| <p>No specific recommendations are being made regarding IBD and pregnancy, and pregnant women with IBD are encouraged to follow the guidance available from the UK government for pregnant women in the general population.</p>  |  |   |
| <p>* i.e. at least one of (comorbidity or age<math>\geq 70</math>) plus at least one therapy from the middle column</p>  |  |   |
| <p>** Combination therapy may increase risk over monotherapy but there is no specific evidence for this situation</p>  |  |   |

Most IBD patients will fall into the moderate or lowest risk groups. Defining a 'highest-risk' group is not exact; the grouping has been determined following extensive discussion amongst UK IBD specialists with input from international colleagues. Based on the current evidence, we know increasing age, heart disease, diabetes and hypertension are the biggest risk factors for poor outcome in COVID-19 (Zhou et al. Guan et al.). As such priority has been given to these factors rather than medications other than individuals on high dose steroids (see below). Where risk is primarily determined by IBD (patient and treatment factors) we recognise this is a dynamic process; i.e. patients may move between risk categories over time.

Highest risk group 1. IBD patients who have a co-morbidity and / or are  $\geq 70$  years old AND are on any immune suppressing therapy for IBD (see Table 1 for details). It is accepted that in many cases physicians will need to use their clinical judgement to decide whether the severity of the co-morbidity merits shielding.

Highest risk group 2. IBD patients regardless of co-morbidity and who meet one or more of the following criteria:

- currently on prednisolone doses of 20mg daily or more (once dose drops below 20mg then the patient moves to moderate risk);
- patients recently started on biologic therapy in combination with an immunomodulator (azathioprine, mercaptopurine, thioguanine, tacrolimus or methotrexate);
- patients who have moderate to severely active disease despite biologics / immunosuppressants – this group captures the patients who despite best medical efforts still have significant on-going inflammation.

We wish to stress in the strongest possible terms;

- Patients should continue their current medications
- Access to injectable treatment (infliximab, vedolizumab, ustekinumab, adalimumab and golimumab) will be maintained irrespective of risk category and distancing/isolation recommendations
- Infusion suite services (with appropriate social distancing methods) should be maintained as a priority area to prevent treatment flare, admission and increased risk of immunogenicity.

## 2) Changes to current primary and secondary care practices

Hospital services are being reorganised in order to better deal with severe COVID-19 infections. Elective work is being suspended to maximise staffing and space for acute admissions. We also need to be very careful that rapid institution of telemedicine services does not adversely impact on primary care (e.g. phlebotomy and drug prescribing).

Consideration should be given to reorganising services to support well staff working from home when possible in order to minimise their own viral exposure. Staff sickness is likely to become a major factor during this pandemic and so efforts should be made to minimise this from the earliest stages.

Pre-symptomatic transmission has been reported, though estimated rates vary between studies. Face-to-face meetings between staff, particularly in confined spaces, should be minimised and, where necessary, should avoid people being in close proximity if possible. Services such as WebEx (<https://www.webex.com>), Zoom (<https://zoom.us>) and Microsoft Teams (<https://teams.microsoft.com>) can be used to facilitate virtual meetings. See also <https://www.ecdc.europa.eu/sites/default/files/documents/RRA-sixth-update-Outbreak-of-novel-coronavirus-disease-2019-COVID-19.pdf>.

**IBD nurse phone and email helpline.** To manage and support patients with IBD when outpatient clinics are being converted to telephone review, the minimum service provision needs to include a telephone/ email helpline to support patients having disease flares and to answer queries regarding immunosuppressant / biologics management. Ideally provision should be made for one member of the nursing team to work from home to ensure this is maintained, with appropriate senior review to support the clinical decision-making process. This would reduce burden on both primary and secondary care, in particular A&E. This should be supported with capacity for patients to have urgent review if needed in a 'safe clinic'.

## Box 2. Top 10 tips for everyone with IBD

1. We will do everything we can to keep you safe and well during the COVID-19 pandemic
- \*Note that hospitals are undergoing massive reorganisation to prepare to care for those with serious infection*
2. Don't stop your medication; preventing disease flares is a priority
- \*We want to keep you out of hospital if possible, but if you are unwell, we will be there for you*
3. Ensure you have a good supply of medication should you need to self-isolate or shield yourself
- \*Do not take steroids (prednisolone) from your GP without discussing with your local IBD team*
4. Contact your local IBD team via the phone or email helpline if you are experiencing a flare
  5. Wash your hands frequently and avoid touching your face; this goes for everyone
  6. Work from home if possible, avoid non-essential travel & contact with people who are currently unwell
  7. Quit smoking as this increases the risk and severity of COVID19 infection & avoid NSAIDs (e.g. ibuprofen)
  8. Government guidelines on self-isolation and social distancing are changing rapidly so please visit [www.gov.uk](http://www.gov.uk) and [www.nhs.uk](http://www.nhs.uk) to keep up to date. (If you are unclear on your level of risk, contact your local IBD helpline for further advice)
  9. If you develop a cough, fever or flu-like symptoms you should follow the government's recommendations about self-isolation and household quarantine. If you feel you cannot cope with your symptoms at home, or your condition gets worse, or your symptoms do not get better after 7 days, then use the NHS 111 online coronavirus service. If you do not have internet access, call NHS 111. For a medical emergency dial 999
  10. Take care of yourself but also be kind and considerate to others in these difficult times

Patients are being asked to keep taking their usual IBD therapy. If patients stop taking their medications without discussing it with their clinical team first, there is a risk of disease flare. **Active disease is associated with an increased risk of infection, exposure to steroids (increased risk from infection), hospitalisation and major surgery<sup>4,6</sup>.**

**Outpatient clinics.** Conduct clinical appointments by telephone or a formal telemedicine system where possible. Routine bloods may be deferred until the situation has improved, depending on local capacity. Access to faecal calprotectin (FC) testing, a potential alternative to endoscopy, may become limited due to the presence of virus in the stool. If accessible, consider introduction of point of care (POC) calprotectin testing. FC POC kits could be most effectively issued to high-risk patients at a new patient / flare clinic or on discharge from

hospital (sampling every 2-3 months depending on capacity). Given the limited access to endoscopic disease assessment, the combination of FC and clinical disease scores (Partial Mayo / SCCAI, PUCAI {UC}, HBI and wPCDAI) may help to guide treatment decisions more objectively.

**New IBD patients.** In line with the BSG endoscopy guidance released 16/3/20, careful case-case discussion will need to be given to decide timing of diagnostic endoscopy and imaging, with perhaps deferment of patients presenting with mild symptoms and borderline biomarkers. If centres experience delays in reviewing new IBD patients, a telephone triage system should be adopted to assess clinical urgency.

**Urgent outpatient review.** Patients who may need hospitalisation will need to continue to be assessed in a timely manner. Consider the most appropriate location to do this i.e. away from COVID-19 assessment areas. Daily flare-clinics with limited numbers of patients who are at high risk of imminent hospitalisation should be considered. Where possible limit visits to hospital and limit the patient journey around the hospital geographically.

### 3) General considerations regarding IBD medications

- Balance the risk of immune modifying drugs with the risk associated with active disease.
- Patients are advised not to stop or reduce their medication without discussing with the IBD Team, due to risk of flare leading to a need for steroids or other additional immunosuppression or hospitalisation.
- Immune suppressive effects of medications may persist for many weeks or months after treatment cessation.
- Identified experienced/senior person to oversee blood tests, initiation of biologics, prescribing of biologics and support the patients accordingly. Reduce any therapy-associated monitoring blood tests to minimum safe frequency.
- Administrative support should be identified to ensure prescriptions for subcutaneous biologics are forwarded to homecare in a timely manner.
- Patients should be given helpline number to arrange contact for advice regarding delayed deliveries.
- Maintaining a functional infusion service throughout the pandemic, should be a priority.

### 4) Therapy-specific considerations

Given the paucity of data regarding the effects of IBD medications on the course of COVID-19, contributing confirmed cases to the international registry (IBD secure) is encouraged.

- **Corticosteroids**
  - Should be avoided if possible but will still be necessary for some who should then observe 'shielding' while prednisolone dose is  $\geq 20$  mg daily.
  - Rapid tapering (10mg/week) should be considered where possible. This must be balanced against the risks of extending steroid exposure overall by decreasing dose too quickly.
  - Should not be stopped suddenly without advice

- Consider using budesonide MMX (9 mg/day 8 weeks) or beclometasone (5mg/day 4 weeks) for flaring UC patients (important to assess after 2 weeks)
- Consider using exclusive enteral nutrition (EEN) for flaring CD patients
- Consider budesonide (Entocort, Budenofalk) 9 mg/day 8 weeks) for active small bowel and ileo-caecal CD
- **Immunomodulators (azathioprine, mercaptopurine, thioguanine, methotrexate)**
  - No evidence of increased risk of COVID-19 infection
  - Initiation of monotherapy is not advised.
  - Combination therapy with biologics should be made on careful discussion of risk and benefit on a case-case basis.
  - Older patients (>65 years) or those with significant comorbidity who are in sustained remission on thiopurines should consider stopping after appropriate discussion with their IBD team
- **Anti-TNF therapy (adalimumab, infliximab, golimumab)**
  - No evidence of increased risk of COVID-19 infection
  - Consider initiation with monotherapy (therefore consider adalimumab to promote home care and lower risk of immunogenicity relative to infliximab)
  - Use early therapeutic drug monitoring (TDM) where possible, highlighting those appropriate for later combination immunosuppression where necessary
  - Enforced IV to S/C switching is not recommended
- **Anti-IL-12/23p40 therapy (ustekinumab)**
  - No evidence of increased risk of COVID-19 infection
  - One advantage of ustekinumab is one-off IV induction dose followed by S/C maintenance dosing (minimal impact on infusion suite)
- **Anti- $\alpha$ 4 $\beta$ 7 integrin therapy (vedolizumab)**
  - No evidence of increased risk of COVID-19 infection
  - Unlikely to increase risk of COVID-19 complications, though caution should be exercised in applying existing trial data to COVID-19
- **Janus Kinase inhibitors (tofacitinib)**
  - No evidence of increased risk of COVID-19 infection
- **5-Aminosalicylate acid derivatives (mesalazine etc.)**
  - No evidence of increased risk of COVID-19 infection
  - In UC patients with uncontrolled symptoms, oral 5ASA dose should be optimised +/- addition of topical (rectal) 5ASA

## 5) Service considerations

**The infusion service** is a priority area. Consider moving off-site to a 'clean' area possible. Visitors should no longer be permitted. Patients should not attend for infusion if they are symptomatic for COVID-19 and where possible should be screened on arrival for symptoms and pyrexia. 2m spacing should be employed between patients, and there should be a dedicated separate waiting area if possible. A strict hand washing policy on arrival should be enforced. Infusion chairs should be appropriately cleaned between patients. Parenteral electrolyte and iron replacement services should be reserved for urgent cases only. If capacity is reduced due to staff shortages, daily / weekly triage of infusions should take place.

**Endoscopy.** The BSG have provided separate guidance on endoscopy and COVID-19 (<https://www.bsg.org.uk/covid-19-advice/endoscopy-activity-and-covid-19-bsg-and-jag-guidance/>). IBD surveillance procedures should be deferred. IBD disease assessment scopes will need to be carefully assessed for priority. Alternative methods of disease assessment, including the use of biomarkers, radiology and capsule endoscopy should be considered

**Imaging.** The capacity for out-patient imaging may be reduced. However, this should be discussed within individual hospitals; access to different imaging modalities may vary during the pandemic and this may influence the choice of investigation for patients with IBD.

**Surgery.** Routine elective operations have been deferred in most centres. Where possible, urgent management of perianal sepsis should be undertaken as a day-case procedure. Complex IBD surgery should be deferred where possible and its timing should be reviewed regularly at MDT meetings. Emergency procedures (e.g. subtotal colectomy in acute severe UC, intestinal resection to control penetrating disease in CD) will continue as part of routine care. As with active disease, the choice of post-operative therapy to prevent recurrence will need to be considered in the context of the COVID-19 pandemic.

**Clinical trials** The NIHR and CSO have produced guidance on the management of clinical trials which will be updated regularly (NIHR <https://www.nihr.ac.uk/news/dhsc-issues-guidance-on-the-impact-on-covid-19-on-research-funded-or-supported-by-nihr/24469> ; CSO Link <http://www.nhsresearchscotland.co.uk/news/covid-19---guidance-for-sponsors-sites-and-researchers>). Many trials will have already been paused by their sponsors.

Where this has not happened participant screening and recruitment and continuation (for participants already recruited) should be reviewed at local level for appropriateness in the current clinical situation. The benefits of avoiding surgery and/or corticosteroids on trial medication that may not be otherwise available must be balanced against the risk of face to face visits and the unknown effects of the investigational medicinal products on the course of COVID-19 . Where possible, trial visits should occur virtually and investigations that require hospital attendance should be postponed unless clinically important. Protocol amendments should be made to the relevant regulatory bodies, and advice should be sought from RD Directors to protect participants immediately as formal approval may be significantly delayed. Blinded trials pose a particular concern where the participant may be on a placebo medication that does not require self-isolation or social distancing. In this situation principal investigators should be prepared to unblind participants where the information will influence the participant's treatment or when assessment and management of coronavirus being considered. Sponsors should consider minimising the burden of administrative tasks whilst healthcare teams are stretched; many members of the research team are already being redeployed into direct clinical care.

#### **Advice for NHS staff with IBD**

Frontline staff with IBD should follow the same precautions as other IBD patients. However, given the likely high exposure of frontline staff to COVID-19 it would be advisable that hospital teams consider utilising team members with IBD in roles where exposure is limited (i.e. telephone clinics as opposed to endoscopy lists and ward work), especially if that individual is 'moderate' risk or has other co-morbidity.

## References

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