

British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic

Nicholas A. Kennedy^{1,2*}, Gareth-R. Jones^{3,4*}, Christopher A. Lamb^{5,6*}, Richard Appleby⁷, Ian Arnott⁴, R. Mark Beattie⁸, Stuart Bloom⁹, Alenka J. Brooks¹⁰, Rachel Cooney^{11,12}, Robin J. Dart^{13,14}, Cathryn Edwards¹⁵, Aileen Fraser¹⁶, Daniel R. Gaya¹⁷, Subrata Ghosh^{11,12}, Kay Greveson¹⁴, Richard Hansen¹⁸, Ailsa Hart¹⁹, A. Barney Hawthorne²⁰, Bu'Hussain Hayee^{13,21}, Jimmy K. Limdi²², Charles D. Murray¹⁴, Gareth C. Parkes^{23,24}, Miles Parkes²⁵, Kamal Patel²⁶, Richard Pollok^{26,27}, Nick Powell^{28,29}, Chris Probert^{30,31}, Tim Raine²⁵, Shaji Sebastian³², Christian P. Selinger³³, Philip J Smith³⁰, Catherine Stansfield³⁴, Lisa Younge³⁵, James O. Lindsay^{23,24}, Peter M. Irving^{36,37}, Charlie W. Lees^{3,4}.

*Denotes equal contribution

Word count: 4159 words

Corresponding author email: charlie.lees@ed.ac.uk

Twitter: @charlie_lees

Address: Institute of Genetics & Molecular Medicine, University of Edinburgh

Crewe Road, Edinburgh EH4 2XU

Tel: +44 131 651 8500

Institutions

1. Royal Devon and Exeter NHS Foundation Trust, Exeter, EX2 5DW, UK
2. University of Exeter, Exeter, EX4 4QL, UK
3. University of Edinburgh, Edinburgh, EH16 4SB, UK
4. Western General Hospital, Edinburgh, EH4 2XU, UK
5. Newcastle University, Newcastle upon Tyne, NE2 4HH, UK
6. Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, NE1 4LP, UK
7. Chelsea and Westminster Hospital NHS Foundation Trust, London, SW10 9NH, UK
8. Southampton Children's Hospital, University Hospital Southampton NHS Foundation Trust
9. University College London Hospitals NHS Foundation Trust, NW1 2BU, UK
10. Sheffield Teaching Hospitals NHS Foundation Trust, S10 2JF, UK
11. Queen Elizabeth Hospital Birmingham NHS Foundation Trust, Birmingham, B15 2TH, UK
12. University of Birmingham, Birmingham, B15 2TT, UK
13. King's College London, London, SE1 9NH, UK
14. The Royal Free Hospital, London, NW3 2QG
15. Torbay & South Devon NHS Foundation Trust, TQ2 7AA, UK
16. University Hospitals Bristol NHS Foundation Trust, Bristol, BS1 3NU, UK
17. Glasgow Royal Infirmary, Glasgow, G4 0SF
18. Royal Hospital for Children, Glasgow, G51 4TF, UK
19. St Mark's Hospital, Harrow, HA1 3UJ, UK
20. University Hospital of Wales, Cardiff, CF14 4XW, UK
21. King's College Hospital NHS Foundation Trust, London, SE5 9RS, UK
22. The Pennine Acute Hospitals NHS Trust, Manchester, M8 5RB, UK
23. The Royal London Hospital, Barts Health NHS Trust, London, E1 1BB, UK
24. Barts and the London School of Medicine and Dentistry, London, E1 2AT, UK
25. Cambridge University Hospitals NHS Foundation Trust, Cambridge, CB2 0QQ, UK
26. St George's University Hospitals NHS Foundation Trust, London, SW17 0QT, UK
27. St George's, University of London, London, SW17 0RE, UK
28. Imperial College Healthcare NHS Trust, London, W2 1NY, UK

29. Imperial College London, London, SW7 2AZ, UK
30. Royal Liverpool, Liverpool University Hospitals NHS Foundation Trusts, L7 8XP, UK
31. University of Liverpool, Liverpool, L69 3BX
32. Hull University Teaching Hospitals NHS Trust HU3 2JZ
33. Leeds Teaching Hospitals NHS Trust, LS1 3EX, UK
34. Salford Royal NHS Foundation Trust, Salford, M6 8HD, UK
35. Crohn's & Colitis UK, Hatfield, AL10 9NE, UK
36. Guy's and St Thomas' NHS Foundation Trust, London, SE1 9RT, UK
37. School of Immunology and Microbial Sciences, King's College, London, London, SE1 9RT, UK

ORCID iDs

Nicholas A. Kennedy: <https://orcid.org/0000-0003-4368-1961>
Gareth R. Jones: <http://orcid.org/0000-0001-7355-2357>
Christopher A. Lamb: <https://orcid.org/0000-0002-7271-4956>
Richard Appleby: <https://orcid.org/0000-0001-5887-8922>
Ian Arnott: <https://orcid.org/0000-0003-3352-9253>
R. Mark Beattie: <https://orcid.org/0000-0003-4721-0577>
Stuart Bloom: <https://orcid.org/0000-0002-6361-4662>
Alenka Brooks: <https://orcid.org/0000-0001-7162-7845>
Rachel Cooney: <https://orcid.org/0000-0003-3710-157X>
Robin Dart: <https://orcid.org/0000-0003-3470-8210>
Cathryn Edwards: <https://orcid.org/0000-0002-5550-9184>
Aileen Fraser: <https://orcid.org/0000-0001-6462-5091>
Daniel R. Gaya: <https://orcid.org/0000-0003-1942-7568>
Subrata Ghosh: <https://orcid.org/0000-0002-1713-7797>
Kay Greveson: <https://orcid.org/0000-0003-4713-7306>
Richard Hansen: <https://orcid.org/0000-0002-3944-6646>
Bu'Hussain Hayee: <https://orcid.org/0000-0003-1670-8815>
Ailsa Hart: <https://orcid.org/0000-0002-7141-6076>
A. Barney Hawthorne: <https://orcid.org/0000-0002-8768-4550>
Jimmy K. Limdi: <https://orcid.org/0000-0002-1039-6251>
Charles Murray: <https://orcid.org/0000-0001-6736-1546>
Gareth C. Parkes: <https://orcid.org/0000-0002-5285-7714>
Miles Parkes: <https://orcid.org/0000-0002-6467-0631>
Kamal Patel
Richard Pollok: <https://orcid.org/0000-0001-6452-6763>
Nicholas Powell: <https://orcid.org/0000-0003-3231-6950>
Chris Probert: <https://orcid.org/0000-0003-0477-6714>
Tim Raine: <https://orcid.org/0000-0002-5855-9873>
Shaji Sebastian : <https://orcid.org/0000-0002-3670-6545>
Christian P. Selinger: <https://orcid.org/0000-0003-2022-5859>
Catherine Stansfield: <https://orcid.org/0000-0002-7775-2337>
Philip J Smith: <https://orcid.org/0000-0003-1568-3978>
Lisa Younge: <https://orcid.org/0000-0002-3436-9696>
James O. Lindsay: <https://orcid.org/0000-0003-3353-9590>
Peter Irving: <https://orcid.org/0000-0003-0972-8148>
Charlie W. Lees: <https://orcid.org/0000-0002-0732-8215>

Abbreviations:

5-ASA: 5-aminosalicylate; BSG: British Society of Gastroenterology; CI: confidence interval; COVID-19: Coronavirus Disease 2019; CSO: Chief Scientist Office; ECCO: European Crohn's and Colitis Organisation; EEN: exclusive enteral nutrition; HBI: Harvey Bradshaw Index; IBD: inflammatory bowel disease; IL: interleukin; IV: intravenous; MDT: multidisciplinary team; MMX: Multi Matrix; NHS: national health service; NIHR: National Institute for Health Research; NSAID: non-steroidal anti-inflammatory drug; OR: odds ratio; PUCAI: paediatric ulcerative colitis activity index; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SCCAI: Simple Clinical Colitis Activity Index; S/C: subcutaneous; SOFA: sequential organ failure assessment; TDM: therapeutic drug monitoring; TNF: tumour necrosis factor; UC: ulcerative colitis; UK: United Kingdom; wPCDAI: weighted Paediatric Crohn's Disease Activity Index.

Keywords:

COVID-19, coronavirus, SARS-CoV-2, shielding, social distancing, public health, Ulcerative colitis, UC, colitis, Crohn's disease, CD, ileitis, perianal, inflammatory bowel disease, IBD, guideline, diagnosis, endoscopy, endoscopic, colonoscopy, sigmoidoscopy, biomarker, calprotectin, management, therapy, surgery, suppository, enema, 5-aminosalicylate, 5-ASA, mesalazine, corticosteroid, budesonide, prednisolone, hydrocortisone, methylprednisolone, thiopurine, azathioprine, mercaptopurine, ciclosporin, cyclosporine, anti-TNF, infliximab, adalimumab, integrin, vedolizumab, ustekinumab, JAK, janus kinase inhibitor, tofacitinib, therapeutic drug monitoring, probiotic, antibiotic, faecal microbial transplant, telephone clinic, virtual clinic.

Abstract

The COVID-19 pandemic is putting unprecedented pressures on healthcare systems globally. Early insights have been made possible by rapid sharing of data from China and Italy. In the UK we have rapidly mobilised inflammatory bowel disease (IBD) centres in order that preparations can be made to protect our patients and the clinical services they rely on. This is a novel coronavirus; much is unknown as to how it will affect people with IBD. We also lack information about the impact of different immunosuppressive medications. To address this uncertainty the British Society of Gastroenterology (BSG) COVID-19 IBD Working Group have used the best available data and expert opinion to generate a risk grid that groups patients into highest, moderate and lowest risk groupings. This grid allows patients to be instructed to follow the UK Government's advice for shielding, stringent and standard advice regarding social distancing respectively. Further considerations are given to service provision, medical and surgical therapy, endoscopy, imaging and clinical trials.

Introduction

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

Whilst it is known that 0.8% of people in the UK currently have IBD (approximately 524,000 patients), only 44% have been to a clinic in the last 3 years^{1,2}. 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, many of whom will be unknown to secondary care.

During the COVID-19 outbreak we will do everything we can to keep our IBD patients safe. The biggest risks relate not only to the infection itself, but also the emergency reorganisation of hospital and general practice services to deal with the pandemic. This will result in significant changes to routine IBD services. 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 attendance for non-COVID-19 illness may 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 immunosuppressive treatment³. Therefore, it is of paramount importance to control 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 from 1,099 Chinese patients with COVID-19 did not observe immunodeficiency as a risk factor for severe disease (defined as per American Thoracic

Society guidelines for community acquired pneumonia)⁴. The currently understood predictors associated with COVID-19 mortality at the time of hospital admission are older age (OR 1.1; 95% CI 1.03-1.17 per year increase), higher sequential organ failure assessment (SOFA) score (OR 5.65; 95% CI 2.61-12.23) and d-dimer >1µg/ml (OR 18.42; 95% CI, 2.64-128.55)⁵. However, smoking, comorbidity, particularly hypertension, vascular disease, diabetes and male sex have been associated with poor outcome⁴⁻⁹. Prolonged illness and complications from respiratory infection are perhaps more common when NSAIDs are used, however no data in COVID-19 currently exist^{10,11}. Given NSAIDs have also been implicated in IBD flare, paracetamol is advocated as first line analgesia / antipyretic ¹².

At the time of writing, the Surveillance Epidemiology of Coronavirus Under Research Exclusion (SECURE)-IBD registry has reported 239 (54% male) cases of COVID-19 in IBD patients (137 CD, 94 UC, 5 IBD-U), of which 64 were hospitalised and 11 patients died¹³. Seven patients were ventilated. Among the 11 patients that died, a range of medications were seen. Five patients were on mesalazine alone or no therapy, though all were aged 69 years or older. Four were on steroids alone or in combination. The youngest patient who died was 33 and was on combination therapy with adalimumab, azathioprine and prednisolone.¹³ The BSG, in line with the international Organization for the Study of IBD (IOIBD) and the European Crohn's and Colitis Organisation (ECCO) recommend that patients with IBD do not routinely stop their medication to prevent infection or adverse outcome with COVID-19.^{14,15}

'Social distancing^a', and 'shielding^b' are measures to reduce spread within the population and to protect high risk groups. These are also an understandable source of anxiety for patients with IBD¹⁶.

On behalf of the British Society of Gastroenterology (BSG) a UK-wide IBD 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 'shielding', the most stringent form of isolation. The moderate group are recommended to be even stricter at following the government's instructions regarding social distancing. Note that all patients should still attend for infusions of biologics irrespective of risk stratification.

The UK Department of Health has requested patient contact details from local secondary care IBD services for those that meet the highest risk. A pragmatic approach to identify individuals within the highest-risk group has been adopted:

^a <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>

^b <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>

1. Where feasible, national datasets are being interrogated to identify 'highest-risk' patients.
2. Direct communication with patients via BSG and Crohn's & Colitis UK workflows.
3. Patients may self-identify into risk group (<https://www.ibdregistry.org.uk/covid-19>) and/or contact their local IBD team (ideally by e-mail).
4. Secondary care IBD teams will then provide patient details to NHS.

The self-identification tool (point 3 above) was developed using the information in Table 1 in partnership with the IBD Registry as a pragmatic solution to obtain up-to-date information from UK patients with IBD and maximise the ability to identify patients in the highest risk group. Indeed, early identification and intervention (shielding education) to 318 Chinese IBD patients in Hubei at risk of COVID-19 was well received by patients and may have protected them from infection, with none of them reporting infection as of 28th February 2020¹⁷.

At the time of writing, there is a lot of activity at UK government level around the wearing of masks by the general population in public spaces and hospitals. The BSG recommend members of the public to follow the most up-to-date advice from the Government with respect to this.

Table 1: BSG IBD COVID-19 risk grid: Stratification of IBD patients' risk of serious COVID-19 disease into highest, moderate and lowest risk categories.

Highest Risk 'Shielding'	Moderate risk 'Stringent social distancing ' ⁱ	Lowest risk 'Social distancing'
<p>1. IBD patients who either have a comorbidity (respiratory, cardiac, hypertension or diabetes mellitus) and/or are ≥70 years old</p> <p>and* are on any 'moderate risk' therapy for IBD (per middle column) and/or have moderate-to severely active disease</p> <p>2. IBD patients of any age regardless of comorbidity and who meet one or more of the following criteria:</p> <ul style="list-style-type: none"> • Intravenous or oral steroids ≥20 mg prednisolone or equivalent per day (only while on this dose) • Commencement of biologic plus immunomodulator or systemic steroids within previous 6 weeks** • Moderate-to-severely active disease*** not controlled by 'moderate risk' treatments • Short gut syndrome requiring nutritional support • Requirement for parenteral nutrition 	<p>1. Patients on the following medications****:</p> <ul style="list-style-type: none"> • Anti-TNF (infliximab, adalimumab, golimumab, certolizumab) monotherapy • Biologic plus immunomodulator** in stable patients • Ustekinumab • Vedolizumab • Thiopurines (azathioprine, mercaptopurine, tioguanine) • Methotrexate • Calcineurin inhibitors (tacrolimus or ciclosporin) • Janus kinase (JAK) inhibitors (tofacitinib) • Immunosuppressive trial medication • Mycophenolate mofetil • Thalidomide • Prednisolone <20 mg or equivalent per day <p>2. Patients with moderate-to-severely active disease*** who are not on any of the medications in this column</p>	<p>Patients on the following medications:</p> <ul style="list-style-type: none"> • 5-ASA • Rectal therapies • Orally administered topically acting steroids (budesonide or beclometasone) • Therapies for bile acid diarrhoea (colestyramine, colesevelam, colestipol) • Anti-diarrhoeals (e.g. loperamide) • Antibiotics for bacterial overgrowth or perianal disease

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.

ⁱThe UK government advises those at increased risk, but not reaching the highest risk, of severe illness from coronavirus (COVID-19) to be particularly stringent when applying social distancing recommendations.

* i.e. **at least one of** (comorbidity listed above or age ≥ 70 years) plus **at least one of** (therapy from middle column or moderate-to-severely active disease).

** Patients should be categorised as highest risk (requiring shielding) within 6 weeks of starting biologic if they are on concomitant immunomodulator treatment or systemic steroids, whether started simultaneously or prior to the biologic. After 6 weeks they may enter the 'moderate' risk category provided not meeting other highest risk criteria e.g. moderate-severe disease not controlled by treatment. Biologic plus immunomodulator in stable patients may increase risk over monotherapy but there is no specific evidence for this situation.

*** As adjudged by clinical team responsible for patient care.

**** Patients who have stopped biologics or immunomodulators should remain within their pre-treatment cessation risk category for 3 months; for drugs with a much shorter half-life (e.g. tofacitinib) we advise clinician discretion.

These guidelines were last updated by the UK IBD COVID-19 working group on 02/04/2020 and were based on expert opinion and the available evidence at the time.

Most IBD patients will fall into the moderate or lowest risk groups. Defining a 'highest-risk' group is not exact, with little or no evidence specific to COVID-19. The grouping has therefore been determined following extensive discussion amongst UK IBD specialists with input from international colleagues. Based on the current evidence, we understand increasing age, heart disease, diabetes and hypertension are the amongst the biggest risk factors for poor outcome in COVID-19⁴⁻⁹. As such priority has been given to these factors alongside medications, other than individuals on high dose steroids (*Table 1* and 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 the duration of the pandemic.

This will be a very busy time for clinical teams with redeployment in order to manage the COVID-19 pandemic. We have therefore aimed for simple clear messages wherever possible. For this reason, we have deliberately not provided a drug by drug description of clearance and recommend it is 3 months after cessation of a drug therapy before a patient changes risk category. In part this is to discourage practice of stopping drugs purely to switch risk category. The exception is steroids which is covered explicitly in the grid. As a working group we have had some discussion about tofacitinib which has a much shorter half-life; in this case we advise clinician discretion regarding the timepoint at which cessation impacts on risk categorisation.

We wish to strongly emphasise;

- Patients should continue their current medications.
- Access to injectable treatment (infliximab, vedolizumab, ustekinumab, adalimumab, certolizumab and golimumab) should 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.
- Homecare provision of sub-cutaneous medicines should be maintained as a priority for IBD patients.

General advice for all IBD patients is provided in Box 1.

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 Microsoft Teams (<https://teams.microsoft.com>) WebEx (<https://www.webex.com>) and Zoom (<https://zoom.us>) 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 1: Top 10 tips for everyone with IBD during the COVID-19 pandemic

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. Stop smoking as this increases the risk and severity of COVID-19 infection & avoid NSAIDs (e.g. ibuprofen).
8. Government guidelines on self-isolation and social distancing are changing rapidly so please visit www.gov.uk and 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, or a household member, develop a continuous cough, flu-like symptoms OR fever you should
 - a. Follow the government's recommendations about self-isolation and household quarantine.
 - b. If you test positive for COVID-19 you should contact your IBD team.
 - c. Stop taking medicines seen in the middle column of *Table 1*. Steroids should be tapered with advice from the IBD team and not stopped abruptly. Fourteen days after your symptoms have resolved, or if a house-hold member is affected the household quarantine period ends, contact your local IBD team for advice regarding restarting your medication.
 - d. 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***^{3,18}.

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 (e.g. Partial Mayo / SCCAI, PUCAI, HBI or wPCDAI) may help to guide treatment decisions more objectively.

New IBD patients. In line with the JAG/BSG endoscopy guidance released 26/3/20, all non-emergency endoscopy should stop immediately. Careful case-by-case discussion will need to be given to decide timing of diagnostic endoscopy for the most urgent suspected new IBD cases. If centres are delayed in assessing new IBD patients, a telephone triage system should be adopted to assess clinical urgency.

Urgent outpatient review. Patients who may require 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' (virtual where possible) 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.
- Immunosuppressive effects of medications may persist for many weeks or months after treatment cessation.
- Identify an 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 details 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 (SECURE-IBD, <https://covidibd.org>) is encouraged.

- **Corticosteroids**
 - Should be avoided if possible but will still be necessary for some who should then observe 'shielding' while prednisolone dose is ≥ 20 mg daily.
 - High dose steroids are an established risk factor for respiratory tract infection and opportunistic infection in IBD and septicaemia^{19,20}.
 - Rapid tapering (10 mg/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 (5 mg/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, tioguanine, methotrexate, tacrolimus, mycophenolate mofetil)**
 - No current evidence of increased risk of COVID-19 infection.
 - Initiation of monotherapy may not be appropriate.
 - Combination therapy with biologics should be made on careful discussion of risk and benefit on a case-by-case basis.
 - Older patients (>60 years) or those with significant comorbidity who are in sustained remission on thiopurines may wish to consider stopping after appropriate discussion with their IBD team.
- **Anti-TNF therapy (adalimumab, infliximab, golimumab, certolizumab)**
 - No current 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 current 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 current 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 current evidence of increased risk of COVID-19 infection.
- **5-Aminosalicylate acid derivatives (mesalazine)**

- No current evidence of increased risk of COVID-19 infection.
- In UC patients with uncontrolled symptoms, oral 5-ASA dose should be optimised +/- addition of topical (rectal) 5-ASA.

5) Service considerations

Remote monitoring of disease activity can be achieved through virtual clinics using blood test taken at sites remote to the hospital (e.g. satellite facilities or via GP) with faecal calprotectin testing where available or point of care remote faecal calprotectin monitoring where available.

The infusion service is a priority area. Consider moving off-site to a 'clean' area if possible or facility with alternative access avoiding the need to pass through the main hospital. 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. Two metre 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/>). 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. If surgery is required for sub-acute obstructive symptoms it may be possible to avoid or delay surgery by using partial or entirely enteral nutrition (EEN) regimes.²¹

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 <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, recruitment and continuation (for participants already recruited) should be reviewed at the local level for appropriateness in the current clinical situation. The benefits of avoiding surgery and / or corticosteroids by receiving 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 product 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 R&D Directors promptly to protect participants, as formal approval may be significantly delayed. Blinded trials pose a particular concern; principal investigators should be prepared to unblind participants where the information will influence the participant's treatment or when assessment and management of coronavirus is being considered. In addition, patients who may be on a placebo medication that does not require self-isolation or social distancing should have this highlighted to them in case they wish to withdraw from a study. 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 high risk of exposure of frontline staff to SARS-CoV-2 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 comorbidity, in which case they should be supported in working from home if possible. If it is essential for them to work in a hospital environment, they should ensure they avoid close contact with other staff members and can maintain social distancing.

Conclusion

The COVID-19 pandemic has posed unprecedented challenges to healthcare providers across the globe. The IBD community must continue to demonstrate adaptability in this rapidly moving field. Collaborative working is vital to ensure we gather as much knowledge as possible collectively, sharing ideas to provide the best outcomes for our patients as new evidence emerges.

Contributions

CWL, NAK, GRJ and CAL led the writing group. All authors contributed to either or both discussion regarding guidance set out in this manuscript and editing of the final document.

Conflicts of interest:

For details of conflicts of interest see Supplementary Table 1

Acknowledgements

This guideline has been developed by the British Society of Gastroenterology UK COVID-19 IBD working group and we are grateful for all of the input from contributors within the group. The British Society of Gastroenterology UK COVID-19 IBD working group are thankful

for the support of Crohn's & Colitis UK in developing a patient-friendly version of these guidelines and to the UK IBD Registry for supporting development of a patient self-identification tool implementing the guidelines. Working with these organisations, and real time, valuable feedback from patients engaging with the IBD Registry and Crohn's and Colitis UK tools, as well as previous versions of this guidance on the BSG website, has helped clarify ambiguities in the original risk stratification grid. This has provided a powerful and unique mechanism for rapid patient-clinician co-development of this clinical guideline.

References

- 1 Jones GR, Lyons M, Plevris N, et al. IBD prevalence in Lothian, Scotland, derived by capture-recapture methodology. *Gut* 2019;68:1953-60.
- 2 Jones GR, Lyons M, Plevris N et al. A capture-recapture study of all-age IBD point prevalence *Gut* 2019;68:A63-A64; DOI: 10.1136/gutjnl-2019-BSGAbstracts.125
- 3 Lichtenstein GR, Feagan BG, Cohen RD, et al. Serious infection and mortality in patients with Crohn's disease: more than 5 years of follow-up in the TREAT registry. *Am J Gastroenterol* 2012;107:1409-22.
- 4 Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020. DOI: 10.1056/NEJMoa2002032
- 5 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. DOI: 10.1016/S0140-6736(20)30566-3
- 6 Integrated surveillance of COVID-19 in Italy (Published: 27th February 2020). https://www.epicentro.iss.it/coronavirus/bollettino/Infografica_19marzo%20ENG.pdf: The COVID-19 Task force of the Department of Infectious Diseases and the IT Service Istituto Superiore di Sanità, (Date accessed: 24th March 2020).
- 7 Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis* Published Online First: 17th March 2020. doi: 10.1016/j.ijid.2020.03.017
- 8 Vardavas CI, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. *Tob Induc Dis* 2020;18:20.
- 9 Wenham C, Smith J, Morgan R, et al. COVID-19: the gendered impacts of the outbreak. *Lancet* 2020;395:846-8.
- 10 Little P, Moore M, Kelly J, et al. Ibuprofen, paracetamol, and steam for patients with respiratory tract infections in primary care: pragmatic randomised factorial trial. *BMJ* 2013;347:f6041.
- 11 Little P, Stuart B, Andreou P, et al. Primary care randomised controlled trial of a tailored interactive website for the self-management of respiratory infections (Internet Doctor). *BMJ Open* 2016;6:e009769.
- 12 Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019;68:s1-s106.
- 13 SECURE-IBD Registry: Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion (Published: 27th March 2020). <https://covidibd.org/current-data/>: SECURE-IBD Registry, (Date accessed: 27th March 2020).
- 14 IOIBD Update on COVID19 for Patients with Crohn's Disease and Ulcerative Colitis (Published: 26th March 2020). <https://www.ioibd.org/ioibd-update-on-covid19-for-patients-with-crohns-disease-and-ulcerative-colitis/>: International Organization for the Study of Inflammatory Bowel Disease, (Date accessed: 27th March 2020).

- 15 1st Interview COVID-19 ECCO Taskforce (Published: 13th March 2020). https://ecco-ibd.eu/images/6_Publication/6_8_Surveys/1st_interview_COVID-19%20ECCOTaskforce_published.pdf: European Crohn's and Colitis Organisation, (Date accessed: 27th March 2020).
- 16 Mao R, Liang J, Shen J, et al. Implications of COVID-19 for patients with pre-existing digestive diseases. *Lancet Gastroenterol Hepatol* Published Online First: 15th March 2020. doi: 10.1016/S2468-1253(20)30076-5
- 17 An P, Ji M, Ren H et al. Protection of 318 Inflammatory Bowel Disease Patients from the Outbreak and Rapid Spread of COVID-19 Infection in Wuhan, China. Published Online First 27th February 2020. Available at SSRN: <https://ssrn.com/abstract=3543590> or doi: 10.2139/ssrn.3543590
- 18 Wisniewski A, Kirchgesner J, Seksik P, et al. Increased incidence of systemic serious viral infections in patients with inflammatory bowel disease associates with active disease and use of thiopurines. *United European Gastroenterology Journal* 2019. DOI: 10.1177/2050640619889763
- 19 Naganuma M, Kunisaki R, Yoshimura N, et al. A prospective analysis of the incidence of and risk factors for opportunistic infections in patients with inflammatory bowel disease. *J Gastroenterol* 2013;48:595-600.
- 20 Fardet L, Petersen I, Nazareth I. Common Infections in Patients Prescribed Systemic Glucocorticoids in Primary Care: A Population-Based Cohort Study. *PLoS Med* 2016;13:e1002024.
- 21 Heerasing N, Thompson B, Hendy P, et al. Exclusive enteral nutrition provides an effective bridge to safer interval elective surgery for adults with Crohn's disease. *Aliment Pharmacol Ther* 2017;45:660-9.