



King's Research Portal

Document Version
Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Din, S., Kent, A., Pollok, R. C., Meade, S., Kennedy, N. A., Arnott, I., Beattie, M. R., Chua, F., Cooney, R., Dart, R., Galloway, J., Gaya, D. R., Ghosh, S., Griffiths, M., Hancock, L., Hansen, R., Hart, A., Lamb, C. A., Lees, C. W., ... Irving, P. (2020). Adaptation of the British Society of Gastroenterology guidelines on the management of acute severe ulcerative colitis in the context of the COVID-19 pandemic: a RAND appropriateness panel. *Gut*.

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Adaptations to the British Society of Gastroenterology guidelines on the management of acute severe ulcerative colitis in the context of the COVID-19 pandemic: a RAND appropriateness panel

Authors

1. Shahida Din (Department of Gastroenterology, Western General Hospital, Edinburgh, UK)*
2. Alexandra Kent (Department of Gastroenterology, King's College Hospital NHS Foundation Trust, London, UK) *
3. Richard C Pollok (Department of Gastroenterology, St Georges University Hospitals NHS Foundation Trust, London, UK) *
4. Susanna Meade (Department of Gastroenterology, Guy's and St Thomas' NHS Foundation Trust, London, UK) *
5. Nicholas A Kennedy (Department of Gastroenterology, Royal Devon and Exeter NHS Foundation Trust, Exeter, UK)
6. Ian Arnott (Department of Gastroenterology, Western General Hospital, Edinburgh, UK)
7. R Mark Beattie (Department of Paediatric Gastroenterology, Southampton Children's Hospital, Southampton, UK)
8. Felix Chua (Interstitial Lung Disease Unit, Department of Respiratory Medicine, Royal Brompton Hospital, Royal Brompton and Harefield NHS Foundation Trust, London)
9. Rachel Cooney (Queen Elizabeth Hospital Birmingham NHS Foundation Trust, Birmingham, UK)

- 1
2
3 10. Robin J. Dart (Department of Gastroenterology, Royal Free London NHS
4 Foundation Trust, London, UK)
- 5
6
7 11. James Galloway (Department of Rheumatology, King's College Hospital NHS
8 Foundation Trust, London, UK)
- 9
10
11 12. Daniel R Gaya (Gastroenterology Unit, Glasgow Royal Infirmary, Castle Street,
12 Glasgow, UK)
- 13
14 13. Subrata Ghosh (Queen Elizabeth Hospital Birmingham NHS Foundation Trust,
15 Birmingham, UK)
- 16
17 14. Mark Griffiths (Peri-operative medicine, St Bartholomew's Hospital, London,
18 UK)
- 19
20 15. Laura Hancock (Manchester University Foundation Trust, Manchester, UK)
- 21
22 16. Richard Hansen (Glasgow Royal Infirmary, Glasgow, UK and University of
23 Glasgow, Glasgow, UK)
- 24
25 17. Ailsa Hart (IBD Unit, St Mark's Hospital, London, UK)
- 26
27 18. Christopher A Lamb (Department of Gastroenterology, Newcastle upon Tyne
28 Hospitals NHS Foundation Trust, Newcastle, UK)
- 29
30 19. Charlie W Lees (Department of Gastroenterology, Western General Hospital,
31 Edinburgh, UK)
- 32
33 20. Jimmy K Limdi (Department of Gastroenterology, The Pennine Acute
34 Hospitals NHS Trust, Manchester, UK)
- 35
36 21. James O Lindsay (Department of Gastroenterology, The Royal London
37 Hospital, Barts Health NHS Trust, London, UK)
- 38
39 22. Charlie D Murray (Department of Gastroenterology, Royal Free London NHS
40 Foundation Trust, London, UK)
- 41
42 23. Kamal Patel (Department of Gastroenterology, St Georges University
43 Hospitals NHS Foundation Trust, London, UK)
- 44
45 24. Nick Powell (Department of Gastroenterology, Imperial College Healthcare
46 NHS Trust, London, UK)
- 47
48 25. Chris Probert (Gastroenterology Research Unit, Department of Cellular and
49 Molecular Physiology, Institute of Translational Medicine, University of
50 Liverpool, Liverpool, UK)
- 51
52
53
54
55
56
57
58
59
60

- 1
2
3 26. Tim Raine (Department of Gastroenterology, Cambridge University Hospitals
4 NHS Foundation Trust, Cambridge, UK)
5
6
7 27. Christian Selinger (Department of Gastroenterology, Leeds Teaching
8 Hospitals, NHS Trust, Leeds, UK)
9
10 28. Shaji Sebastian (IBD Unit, Hull University Teaching Hospitals NHS Trust, Hull,
11 UK)
12
13
14 29. Philip J Smith (Department of Gastroenterology, Royal Liverpool Hospital,
15 Liverpool, UK)
16
17
18 30. Phil Tozer (IBD Unit, St Mark's Hospital, London, UK)
19
20 31. Andrew Ustianowski (Dept of Infectious Disease, North Manchester General
21 Hospital, Manchester, UK)
22
23
24 32. Lisa Younge (IBD Unit, St Mark's Hospital, London UK)
25
26 33. Mark A Samaan (Department of Gastroenterology, Guy's and St Thomas' NHS
27 Foundation Trust, London UK)
28
29 34. Peter M Irving (School of Immunology and Microbial Sciences, King's College
30 London, UK)
31
32

33
34 * Joint first authors
35
36

37 Corresponding Author:
38
39

40
41 Peter M Irving, College House, St Thomas' Hospital, Westminster Bridge Road,
42 London, SE1 7EH, UK.
43
44

45
46 E: Peter.irving@gstt.nhs.uk
47
48

49
50 T: +44 207 188 2491
51
52

53
54 F: +44 207 188 2484
55
56

57 **Key words:** Ulcerative colitis, clinical decision making, IBD clinical
58
59
60

Abbreviations:

Acute severe ulcerative colitis (ASUC)

Novel coronavirus 2019 (COVID-19)

British Society of Gastroenterology (BSG)

RAND/UCLA (Research and Development/University of California, Los Angeles)

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)

Disagreement index (DI)

Inflammatory bowel disease (IBD)

World Health Organisation (WHO)

Physician response to disease flares and patient adaptation in response to events in inflammatory bowel disease during the COVID-19 pandemic (PREPARE IBD)

5-aminosalicylic acid (5-ASA)

Computed tomography (CT)

Anti-tumour necrosis factor (anti-TNF)

International Organisation For the Study of Inflammatory Bowel Disease (IOIBD)

Middle Eastern Respiratory Syndrome (MERS)

Chest x-ray (CXR)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Venous thromboembolism (VTE)

Clinical Research Group (CRG)

MMX (multi-matrix).

Word count: 4408

Confidential: For Review Only

Abstract

Objective

Management of acute severe ulcerative colitis (ASUC) during the novel coronavirus 2019 (COVID-19) pandemic presents significant dilemmas. We aimed to provide COVID-19-specific guidance using current British Society of Gastroenterology (BSG) guidelines as a reference point.

Design

We convened a RAND appropriateness panel comprising 14 gastroenterologists and an IBD nurse consultant supplemented by surgical and COVID-19 experts. Panellists rated the appropriateness of interventions for ASUC in the context of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Median scores and disagreement index (DI) were calculated. Results were discussed at a moderated meeting prior to a second survey.

Results

Panellists recommended that patients with ASUC should be isolated throughout their hospital stay and should have a SARS-CoV-2 swab performed on admission. Patients with a positive swab should be discussed with COVID-19 specialists.

As per BSG guidance, intravenous hydrocortisone was considered appropriate as initial management; only in patients with COVID-19 pneumonia was their use deemed uncertain. In patients requiring rescue therapy, infliximab with continuing steroids was recommended. Delaying colectomy because of COVID-19 was deemed inappropriate.

Steroid tapering as per BSG guidance, was deemed appropriate for all patients apart from those with COVID-19 pneumonia in whom a 4-6-week taper was preferred. Post-

1
2
3 ASUC maintenance therapy was dependent on SARS-CoV-2 status but, in general,
4 biologics were more likely to be deemed appropriate than azathioprine or tofacitinib.
5
6 Panellists deemed prophylactic anticoagulation post-discharge to be appropriate in
7
8 patients with a positive SARS-CoV-2 swab.
9

10 11 12 **Conclusion**

13
14
15 We have suggested COVID-19-specific adaptations to the BSG ASUC guideline using a
16
17 RAND Panel.
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Significance of the Study

What is already known on this subject?

- The BSG has published evidence-based guidelines for management of patients with ASUC, but it is unknown whether these are appropriate in the setting of SARS-CoV-2.
- Currently there are limited data to inform clinicians in this area and there is no published guidance for the management of ASUC in the setting of the COVID-19 pandemic.

What are the new findings?

- The current BSG IBD guidelines provide a management pathway which remains largely appropriate during the COVID-19 pandemic.
- However, some treatment options were deemed uncertain or inappropriate in patients with established COVID-19 pneumonia.
- It is appropriate to involve COVID-19 specialists in decision-making for ASUC patients who are SARS-CoV-2 positive.
- Steroid tapering as per BSG guidance, was deemed appropriate for all patients apart from those with COVID-19 pneumonia in whom a 4-6-week taper was preferred.
- Prophylactic anticoagulation post-discharge is appropriate in patients with a positive SARS-CoV-2 swab

How might it impact on clinical practice in the foreseeable future?

- This paper summarises available evidence and provides expert opinion for the appropriate management of patients with ASUC during the COVID-19 pandemic.

- 1
2
3 ➤ It also highlights areas of uncertainty which may help direct areas of future
4 research.
5
6
7
8
9
10

Contributors

11
12
13
14
15 All authors approved the final version. Study concept and design: SD, RP, AK, MS, PI.
16 Development of questionnaire: SD, RP, AK, SM, PI, MS, NK. Data Analysis: PI, MS, SM.
17 Interpretation of data and drafting of manuscript: SD, RP, AK, SM, MS, NK, PI.
18 Panellists, experts and moderators: SD, AK, RP, SM, NK, JOL, CAL, JKL, CP, CS, SS, DRG,
19 TR, RD, AH, LY, CWL, IA, FC, JG, AU, MG, PT, LH, MS, SM, PI Contributions to literature
20 review and critical revision of the manuscript for important intellectual content: All
21 authors
22
23
24
25
26
27
28
29

ORCID iDs

30
31
32
33 SD 0000-0003-2855-3400
34
35

36
37 AK 0000-0003-0577-6177
38
39

40
41 RP 0000-0001-6452-6763
42
43

44
45 SM 0000-0002-8283-6148
46
47

48
49 NK 0000-0003-4368-1961
50
51

52
53 IA 0000-0003-3352-925
54
55

56
57 MB 0000-0003-4721-0577
58
59

60
FC 0000-0001-7845-0173

1
2
3 RC 0000-0003-3710-157X
4
5

6
7 RD 0000-0003-3470-8210
8
9

10 JG 0000-0002-1230-2781
11
12

13
14 DRG 0000-0003-1942-7568
15
16

17 SG 0000-0002-1713-7797
18
19

20 MG 0000-0002-1615-1896
21
22

23
24 LH 0000-0002-8399-6646
25
26

27
28 RH 0000-0002-3944-6646
29
30

31 AH 0000-0002-7141-6076
32
33

34
35 CAL 0000-0002-7271-4956
36
37

38
39 CWL 0000-0002-0732-8215
40
41

42
43 JKL 0000-0002-1039-6251
44
45

46
47 JOL 0000-0003-3353-9590
48
49

50
51 KP 0000-0003-2611-4260
52
53

54
55 NP 0000-0003-3231-6950
56
57

58
59 CM 0000-0001-6736-1546
60

CP 0000-0003-0477-6714

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

TR 0000-0002-5855-9873

CS 0000-0003-2022-5859

SS 0000-0002-3670-6545

PJS 0000-0003-1568-3978

PT 0000-0002-2532-7267

LY 0000-0002-3436-9696

MAS 0000-0002-4057-9200

PMI 0000-0003-0972-8148

Confidential: For Review Only

Introduction

The novel coronavirus severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was first reported in December 2019 and its spread led to the declaration of a pandemic by the World Health Organisation (WHO) on 11th March 2020. Infection varies in severity from asymptomatic carriage to an acute respiratory illness which, at its most severe, results in acute respiratory distress syndrome with hyperinflammation and cytokine storm syndrome.[1] By mid-May 2020, there have been nearly 5 million cases reported worldwide with over 300,000 deaths.[2] Risk factors associated with more severe coronavirus disease 2019 (COVID-19) include older age, male sex, hypertension, cardiovascular disease, respiratory disease, diabetes, renal failure, and ethnicity.[3] Neither an effective medical therapy nor a vaccine has yet been described, although numerous candidates are under evaluation.

Acute severe ulcerative colitis (ASUC) occurs in up to 25% of patients with UC and is associated with a mortality of approximately 1%.[4,5] The management of ASUC is particularly challenging in the context of SARS-CoV-2 as the typical presenting features of ASUC, namely diarrhoea with raised inflammatory markers, often in association with a fever, may mimic those of COVID-19. ASUC is managed with high dose parenteral corticosteroids, progressing to rescue therapy and/or surgery in those who fail to respond adequately.[6] The safety of all of these interventions in the context of COVID-19 infection is unclear. For example, there are concerns that corticosteroids may increase the risk of acquiring SARS-CoV-2 infection and/or worsen the severity of COVID-19 disease.[7] In addition, the commonly used rescue therapies, infliximab and ciclosporin are associated with an increased risk of infection, particularly if used in combination with immunomodulators such as thiopurines, or steroids.[8] Finally, individuals in whom corticosteroids and rescue therapy fail require urgent colectomy which is associated with high morbidity and mortality in patients infected with SARS-CoV-2.[9] However, withholding treatment in ASUC is clearly not an option in view of the high mortality (in excess of 20%) associated with such an approach.[10]

1
2
3 Whilst national and international registries continue to collate data regarding IBD
4 patients with COVID-19, very few cases relate to the management of ASUC. The
5 PREPARE IBD study (www.prepareibd.org) is collecting data from patients with
6 inflammatory bowel disease (IBD) who are admitted to hospital during the pandemic,
7 as well as from those who develop confirmed or suspected SARS-CoV-2 infection. As
8 of 8th May 2020, 19 patients with severe active UC including four with suspected or
9 confirmed COVID-19 had been identified (personal communication, manuscript
10 submitted). The Surveillance Epidemiology of Coronavirus Under Research Exclusion
11 (SECURE)-IBD registry (<https://covidibd.org/>) is collating data on IBD patients with
12 confirmed coronavirus, with 1074 patients included to date, the majority of whom
13 have Crohn's disease; details of how many in the cohort have ASUC are not yet
14 available.[11] Finally, in case series from Italy and Spain, 4 of 79 and 1 of 40 patients
15 respectively had COVID-19 in conjunction with ASUC [12,13] (the number of ASUC
16 patients in the Italian case series was provided on request from authors).
17
18
19
20
21
22
23
24
25
26
27
28
29

30 Treatment of ASUC during the COVID-19 pandemic presents substantial management
31 dilemmas in the absence of a high-quality evidence base to guide clinicians. We
32 therefore aimed to address this deficit of informed guidance by convening a RAND
33 appropriateness panel. Current BSG guidelines were used as a reference point to
34 highlight differences to current management.[6]
35
36
37
38
39
40

41 **Methods**

42 **Study Overview**

43
44
45 The RAND/UCLA (University of California, Los Angeles) appropriateness method uses
46 a modified Delphi panel approach and combines expert opinion with the best available
47 evidence to determine the appropriateness of specific practices in certain clinical
48 situations.[14] It is particularly useful in areas of uncertainty in which evidence is
49 insufficient to guide day-to-day clinical practice, such as in the COVID-19
50 pandemic.[15]
51
52
53
54
55
56
57
58
59
60

1
2
3 The aim of this RAND panel was to provide clarity on the management of ASUC, as
4 defined by Truelove and Witts criteria, in the context of the COVID-19 pandemic.[10]
5
6 The panel sought to identify areas where it was appropriate to deviate from current
7 BSG ASUC guidance and consider alternative strategies.
8
9

10
11
12 We assembled a 15-person panel comprising representatives from the BSG IBD
13 Section Committee, the BSG IBD Clinical Research Group (CRG) and other
14 gastroenterologists, each from different IBD centres across the UK, as well as an IBD
15 nurse consultant (supplementary Table 1). A web-based questionnaire was created
16 and iteratively improved before being completed by all panellists prior to a moderated
17 online meeting. We circulated a list of relevant publications with the questionnaire,
18 comprising the current BSG guidelines on the management of ASUC[6] along with up
19 to date publications about COVID-19 in general and specifically in relation to IBD. Due
20 to the rapid growth of available data, the panel used a range of instant messaging
21 services to disseminate publications that were not available at the time of the initial
22 literature review.
23
24
25
26
27
28
29
30
31

32
33
34 Panellists rated the appropriateness of management options at five different time
35 points during the course of admission for ASUC (admission, first line therapy, rescue
36 therapy, continued medical therapy and surgery) in the context of absence of, or
37 varying severity of SARS-CoV-2 infection. They were asked to grade the
38 appropriateness of specific interventions on a scale of 1-9 (where 1-3 is inappropriate,
39 4-6 is uncertain and 7-9 is appropriate). The responses were summarised and
40 anonymised before being presented at a virtual meeting in May 2020 with the aim of
41 allowing discussion which ensured a common understanding of the questions and
42 which focussed on areas of disagreement, without trying to force consensus. Also
43 present at the meeting were non-voting specialists who provided expert opinion with
44 regards to IBD surgery (PT, LH), rheumatology (JG), intensive care (MG), respiratory
45 medicine (FC) and infectious diseases (AU). In practice, several specialities may
46 provide expert opinion in COVID-19 management, including intensivists, respiratory
47 physicians and infectious disease physicians. We, therefore, used the encompassing
48 term "COVID-19 specialist" to represent this group. Finally, the Chairs of the BSG IBD
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Section Committee (IA) and the BSG IBD Clinical Research Group (CL) were also
4 present. The moderators (PI, MS) neither expressed opinions on management nor
5 voted, but were experts both in RAND panels and in the management of IBD. After the
6 meeting, a second online survey comprising 91 questions, which had been slightly
7 modified from the initial questionnaire following discussion at the meeting, was
8 circulated for completion.
9
10
11
12
13

14
15
16 Several assumptions were made for clarity. First, patients were assumed to have a
17 confirmed diagnosis of UC with intercurrent gastrointestinal infection having been
18 excluded. Second, if this was not an index presentation, patients were assumed to
19 have received optimised 5-aminosalicylic acid (5-ASA) therapy prior to admission and
20 were also presumed to be biologic-naïve. In addition, where ciclosporin was suggested
21 as an option, it was assumed that the patient was thiopurine-naïve. Third, other than
22 those areas addressed in the survey, the management of ASUC was assumed to be in
23 line with BSG guidance.[6] Finally, where steroid weaning or discontinuation was
24 considered, it was assumed that patients could safely stop steroids without the risk of
25 Addisonian crisis.
26
27
28
29
30
31
32
33
34
35

36 In addition, in the section about first line medical therapy, panellists assumed patients
37 were not steroid refractory. For the rescue therapy section, patients were assumed to
38 have ongoing acute severe colitis despite 3 days of intravenous corticosteroid therapy
39 and had reached standard criteria for rescue therapy.[16] For the continuing medical
40 therapy section, patients were assumed to have responded to intravenous
41 corticosteroids sufficiently to switch to oral prednisolone and were ready to be
42 discharged from hospital. Lastly, as per RAND methodology, respondents were
43 advised to make decisions without considering local availability of treatments or cost.
44
45
46
47
48
49
50
51

52 Analysis

53
54

55 For each scenario, median scores were calculated with a score of <3.5 being
56 considered inappropriate, ≥3.5 but <6.5 uncertain, and ≥6.5 appropriate. We used the
57 validated RAND disagreement index (DI) to define disagreement amongst panellists
58
59
60

1
2
3 using the equation outlined below.[14] A $DI \geq 1$ denotes disagreement. Any scenario
4 in which disagreement was found was scored as uncertain, regardless of the median
5 score.
6
7
8
9

$$DI = \frac{70\%ile - 30\%ile}{2.35 + \left(1.5 \times \text{abs}\left(5 - \frac{70\%ile + 30\%ile}{2}\right)\right)}$$

17 Results

20 Overall Results

21
22
23 Of the 91 clinical scenarios, panellists rated 28 as appropriate, 19 as uncertain and 44
24 as inappropriate. After the second round of voting, agreement was present for all
25 scenarios ($DI < 1$). The key findings are summarised below and their relationship to
26 current BSG guidance is highlighted in figure 1. A detailed list of all scenarios,
27 complete with median score, appropriateness rating and DI can be found in
28 supplementary Table 2.
29
30
31
32
33
34
35

36 Indications for investigations, inpatient isolation and specialist referral

37 (Table 1)

38
39
40 The panellists agreed that all patients admitted to hospital with ASUC should have a
41 SARS-CoV-2 swab performed on admission. If the result was negative it was deemed
42 appropriate to repeat the swab at the point of requiring rescue therapy and/or surgery
43 to exclude subclinical infection. It was also considered appropriate to isolate all
44 patients throughout their hospital stay, irrespective of their COVID-19 status.
45
46
47
48
49
50

51 It was rated appropriate to perform a flexible sigmoidoscopy within 24 hours of
52 admission. If a patient had not had a flexible sigmoidoscopy on admission, it was
53 considered appropriate that one should be performed prior to rescue therapy or
54 colectomy. Repeating this test at these timepoints was deemed unnecessary in
55 patients who had already had a flexible sigmoidoscopy performed.
56
57
58
59
60

1
2
3 Routine computed tomography (CT) scanning of the abdomen/pelvis on admission (in
4 addition to abdominal X-ray) was deemed inappropriate. However, the
5 appropriateness of routine chest CT on admission was rated as uncertain. The one
6 scenario in which a CT scan of the chest was felt to be appropriate for all patients
7 irrespective of COVID-19 status was in the context of patients requiring colectomy.
8
9
10
11

12
13
14 Throughout the scenarios, the panellists considered the appropriateness of discussion
15 with COVID-19 specialists. In patients without symptoms or signs of COVID-19 and
16 with a negative swab this was deemed inappropriate if receiving first line therapy but
17 uncertain in patients requiring rescue therapy. However, it was considered
18 appropriate in all patients with a positive swab, irrespective of the presence of
19 symptoms or signs of COVID-19.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

	On admission	Prior to Rescue therapy	Prior to colectomy
Inpatient Isolation	All patients		
SARS-CoV-2 swab	Perform in all patients	Repeat swab if initial swab negative	Repeat swab if initial swab negative
Flexible sigmoidoscopy	≤24h admission	If not performed	If not performed
		If already performed	If already performed
CT chest	Perform in all patients		Perform in all patients
CT abdomen & pelvis	Perform in all patients		

Table 1. Appropriateness of patient isolation and investigation in patients admitted with acute severe ulcerative colitis in the context of the COVID-19 pandemic. (Green is considered appropriate, yellow uncertain and red inappropriate).

Initial Treatment of ASUC (Table 2)

As per BSG guidance, intravenous hydrocortisone, 100mg, four times per day (or equivalent) was rated appropriate as the initial management of patients presenting with ASUC in the absence of symptoms and signs of COVID-19 pneumonia. In patients with COVID-19 pneumonia, use of hydrocortisone was deemed uncertain. Other possible treatments (poorly bioavailable oral steroids e.g. budesonide multi-matrix (MMX) and beclometasone modified release, infliximab either with or without steroids, ciclosporin or tofacitinib) were considered inappropriate. The exception was infliximab (without steroids) which was considered uncertain in patients with a positive swab for SARS-CoV-2, either with or without signs of COVID-pneumonia. Ambulatory outpatient management with daily intravenous methylprednisolone was rated as inappropriate in all patients with ASUC regardless of SARS-CoV-2 status, as was management by immediate colectomy unless complications mandating emergency surgery were present such as toxic megacolon, perforation or severe haemorrhage.

	First line medical therapy				
Negative COVID swab WITHOUT respiratory symptoms	*Inpatient IV steroids	❖ Poorly bioavailable steroids	IFX alone	Tofacitinib	^Discussion with COVID-19 specialist
	**Ambulatory IV steroids	IV steroids* + IFX	Ciclosporin	Colectomy	
Positive COVID swab WITHOUT respiratory symptoms or signs of COVID pneumonia	*Inpatient IV steroids	❖ Poorly bioavailable steroids	IFX alone	Tofacitinib	^Discussion with COVID-19 specialist
	**Ambulatory IV steroids	IV steroids* + IFX	Ciclosporin	Colectomy	
Positive COVID swab WITH symptoms or signs of COVID pneumonia	*Inpatient IV steroids	❖ Poorly bioavailable steroids	IFX alone	Tofacitinib	^Discussion with COVID-19 specialist
	**Ambulatory IV steroids	IV steroids* + IFX	Ciclosporin	Colectomy	

Table 2. Appropriateness of treatment options in acute severe ulcerative colitis in the context of the COVID-19 pandemic: First line medical therapy. (Green is considered appropriate, yellow uncertain and red inappropriate). *Steroids, intravenous (IV) hydrocortisone 100mg QDS or IV methylprednisolone 60mg daily as an inpatient; **IV Methylprednisolone 60mg daily as an outpatient; ❖Budesonide MMX 9 mg/beclometasone 5 mg OD PO as an inpatient; IFX, Infliximab (either 5mg/kg or 10mg/kg); ^Discussion with appropriate COVID-19 specialist as per local availability.

Rescue therapy (Table 3)

In patients meeting criteria for escalation of management at day 3, it was considered inappropriate to avoid rescue therapy by continuing monotherapy with intravenous corticosteroids, irrespective of COVID status. Instead, the panellists deemed that following standard BSG guidance by initiating infliximab and continuing steroids was appropriate, whereas treatment with infliximab in conjunction with immediate steroid withdrawal was deemed uncertain. The BSG guidelines also recommend ciclosporin as an alternative rescue therapy. However, the RAND panel voted that ciclosporin, either with or without ongoing steroids, was inappropriate in all scenarios other than in patients with a negative SARS-CoV-2 swab in whom it was rated uncertain. Finally, colectomy without rescue therapy was deemed inappropriate in all of the scenarios considered by the panel. However, once colectomy became necessary, for example where rescue therapy had failed or when complications had occurred, it was deemed inappropriate to delay surgery, even in patients with COVID-19 pneumonia.

	Rescue therapy				Failure of Rescue Therapy
Negative COVID swab WITHOUT respiratory symptoms	Continue IV steroids alone	IFX + steroids	IV ciclosporin + steroids	Colectomy	Delay surgery
		IFX, stop steroids	IV ciclosporin, stop steroids	^Discussion with COVID-19 specialist	
Positive COVID swab WITHOUT respiratory symptoms or signs of COVID pneumonia	Continue IV steroids alone	IFX + steroids	IV ciclosporin + steroids	Colectomy	
		IFX, stop steroids	IV ciclosporin, stop steroids	^Discussion with COVID-19 specialist	
Positive COVID swab WITH symptoms or signs of COVID pneumonia	Continue IV steroids alone	IFX + steroids	IV ciclosporin + steroids	Colectomy	
		IFX, stop steroids	IV ciclosporin, stop steroids	^Discussion with COVID-19 specialist	

Table 3. Appropriateness of treatment options in acute severe ulcerative colitis in the context of the COVID-19 pandemic: Rescue therapy. (Green is considered appropriate, yellow uncertain and red inappropriate). Steroids, Intravenous (IV) hydrocortisone 100mg QDS or IV methylprednisolone 60mg daily as an inpatient; IFX: Infliximab (either 5mg/kg or 10mg/kg); ^Discussion with appropriate COVID-19 specialist as per local availability.

Continuing medical therapy (Table 4)

The ongoing management of patients who had responded to intravenous corticosteroids and were ready for discharge on oral steroids was also considered. In patients with a negative SARS-CoV-2 swab, or with a positive swab but without signs or symptoms of pneumonia, steroid tapering over 6-8 weeks as per BSG guidance was deemed appropriate. However, in patients with COVID-19 pneumonia it was rated uncertain. Accelerated steroid withdrawal over 4-6 weeks was rated appropriate regardless of COVID-19 status. More rapid withdrawal over 4 weeks was deemed inappropriate except in patients with COVID-19 pneumonia, in whom it was rated uncertain. The use of poorly bioavailable oral steroids as an alternative to a standard steroid taper was rated as inappropriate in all scenarios

Initiation of additional therapy prior to, or soon after discharge to prevent relapse was also considered. Following BSG guidance by initiating a thiopurine was rated uncertain in SARS-CoV-2 swab-negative patients, and inappropriate in swab-positive patients. Use of biological therapy (anti-tumour necrosis factor (TNF), ustekinumab or vedolizumab) was deemed appropriate in swab-negative patients. In all other patients, the appropriateness of biological therapy was uncertain, except for anti-TNF therapy in patients with a positive swab but without pneumonia in whom treatment was rated as appropriate. Tofacitinib was generally rated as inappropriate except in swab-negative patients in whom it was rated uncertain.

Finally, panellists were asked whether patients should be discharged with a period of ongoing prophylactic anticoagulation. This was deemed appropriate in patients who had a positive SARS-CoV-2 swab regardless of whether they had pneumonia but was rated uncertain in those who had negative swabs.

	Continuing medical therapy [∞]				
Negative COVID swab WITHOUT respiratory symptoms	Standard steroid taper	Accelerated steroid taper <4 weeks	°Thiopurine	°Ustekinumab	°Tofacitinib
	Accelerated steroid taper 4-6 weeks	◆Poorly bioavailable steroids	°Anti-TNF	°Vedolizumab	⊙Thromboprophylaxis
Positive COVID swab WITHOUT respiratory symptoms or signs of COVID pneumonia	Standard steroid taper	Accelerated steroid taper <4 weeks	°Thiopurine	°Ustekinumab	°Tofacitinib
	Accelerated steroid taper 4-6 weeks	◆Poorly bioavailable steroids	°Anti-TNF	°Vedolizumab	⊙Thromboprophylaxis
Positive COVID swab WITH symptoms or signs of COVID pneumonia	Standard steroid taper	Accelerated steroid taper <4 weeks	°Thiopurine	°Ustekinumab	°Tofacitinib
	Accelerated steroid taper 4-6 weeks	◆Poorly bioavailable steroids	°Anti-TNF	°Vedolizumab	⊙Thromboprophylaxis

Table 4. Appropriateness of treatment options in acute severe ulcerative colitis in the context of the COVID-19 pandemic: Continuing medical therapy. (Green is considered appropriate, yellow uncertain and red inappropriate). [∞]Patient has responded to intravenous steroid therapy; ◆Switch from corticosteroids to budesonide MMX 9 mg daily/beclometasone 5 mg daily; °Steroid taper and start additional therapy at or soon after discharge; ⊙Continue for a period after discharge.

Discussion

General Considerations

The recent International Organisation For the Study of Inflammatory Bowel Disease (IOIBD) RAND appropriateness panel addressing the use of medications to treat IBD in the COVID-19 era did not specifically address the management of patients with ASUC.[17] To date, there has been no consensus on how to manage this condition during the COVID-19 pandemic; in the context of a limited, although rapidly evolving evidence base, this is perhaps unsurprising.[18] Thus, there is an urgent need for guidance on how best to manage ASUC in the current setting. Several areas need consideration in this regard including: the effect of SARS-CoV-2 on the activity and course of IBD; the effect of IBD and its activity on the risk of being infected with SARS-CoV-2 and the progression to COVID-19; the interaction of SARS-CoV-2/COVID-19 with the drugs used to treat IBD; and the possible effects of treatments for COVID-19 on IBD.

SARS-CoV-2 is found in the gut and RNA is measurable in the stool significantly longer than in serum or respiratory samples [19] although the significance of this is unclear. The effects of the virus on the intestinal mucosa remain undefined, as does its interaction with inflamed tissue.[20] Gastrointestinal symptoms including diarrhoea occur in around 30% of patients and have been associated with worse outcome [21,22] and a single report describes a possible case of COVID-19 colitis.[23]

Currently, it is not clear whether IBD-specific factors lead to worse outcomes in patients who develop COVID-19. In the Italian series of 79 patients with IBD and COVID-19, active disease was associated with the risk of COVID-19 pneumonia even after controlling for other risk factors.[12] Furthermore, active IBD was also significantly associated with increased hospitalisation, the need for respiratory support and death. In contrast, in Bergamo, Northern Italy, an observational study reported no cases of COVID-19 in 522 patients with IBD.[24] Whilst there are data that

1
2
3 suggest that active IBD increases the risk of some viral infections,[25] it is difficult to
4 draw firm conclusions with regard to SARS-CoV-2 infection given the limited data
5 available.
6
7
8
9

10 Of concern to most clinicians caring for patients with IBD is the possible risk of the
11 drugs used to manage ASUC in the context of the COVID-19 pandemic. Intravenous
12 corticosteroids remain the most widely used induction therapy in ASUC [26], but it is
13 uncertain how they may influence outcome in patients with SARS-CoV-2 infection and
14 COVID-19. Corticosteroids are known to increase the risk of sepsis and respiratory
15 tract infections and may also increase viral replication and susceptibility to SARS-CoV-
16 2.[27,28] There is also evidence that steroids may increase morbidity and/or mortality
17 from some respiratory viruses such as influenza, Middle Eastern Respiratory
18 Syndrome (MERS) and SARS-CoV,[27,29–31] although steroids have an established
19 role in the management of ARDS.[32] Beyond corticosteroids, immunomodulators
20 such as thiopurines, biologics and tofacitinib are frequently used at various stages of
21 the management of ASUC and there is also a lack of data regarding their safety in the
22 context of the SARS-CoV-2 pandemic. Finally, it is important to consider the possible
23 effects of drugs used to manage COVID-19 on IBD. For example, interleukin-6
24 inhibitors are being tested in patients with COVID-19 (ClinicalTrials.gov Identifier:
25 NCT04315298) but have been associated with intestinal perforation in IBD.
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

41 We used an established methodology, a RAND appropriateness panel, to produce
42 guidance in this challenging clinical area. Regarding initial management, there was
43 agreement that all patients with ASUC should be managed as inpatients. Ambulatory
44 care was considered inappropriate, since patients with ASUC need regular monitoring
45 and involvement of a multi-disciplinary team, this type of complex care being difficult
46 to deliver in the out-patient setting. Whilst there was some support for ambulatory
47 management to avoid patients being admitted, thereby decreasing the risk of
48 nosocomial acquisition of SARS-CoV-2, the risks of managing ASUC as an outpatient
49 were considered to outweigh this possible benefit. Furthermore, in scenarios in which
50 patients had confirmed SARS-CoV-2 infection, no such benefit existed. Nevertheless,
51 in view of the acknowledged risk of contracting SARS-CoV-2 infection in hospital, it is
52
53
54
55
56
57
58
59
60

perhaps unsurprising that the panel considered it appropriate to isolate patients with ASUC in a side room wherever possible.

The panel deemed it uncertain whether a CT chest should be performed in all patients on admission. While a CT chest is more sensitive than a chest x-ray (CXR) in detecting signs of early or limited infection, the COVID-19 specialists advised that a CXR would suffice in asymptomatic patients on admission. However, The Royal College of Radiologists has advised a low dose CT chest should be performed in patients who are having a CT abdomen as part of the investigation of an abdominal emergency.[33–35]

It was considered appropriate to involve a COVID-19 specialist in all scenarios in the presence of a positive SARS-CoV-2 swab, regardless of signs or symptoms of COVID-19 pneumonia. The panel was uncertain whether this was required in patients with a negative SARS-CoV-2 swab who required rescue therapy. During the meeting, concern was expressed by some panellists about the possible effects of corticosteroids and rescue therapies on SARS-CoV-2 infection and COVID-19 pneumonia driving the need to seek clarification from COVID experts and highlighting the need for further research.

First Line Therapy

It was considered appropriate to follow the BSG guidelines on the initial management of ASUC in patients without signs or symptoms of COVID-19, regardless of SARS-CoV-2 swab results. Only in patients with COVID-19 pneumonia was there uncertainty amongst the panel regarding the appropriateness of conventional therapy with intravenous corticosteroids, largely driven by concerns of possible harm. However, it should be noted that in this challenging condition in which there is scant experience and almost no published data in relation to COVID-19, of all suggested treatments, intravenous corticosteroids were given the highest median score by the panel. Regarding the ongoing uncertainty about the benefits or harms of corticosteroids in patients with COVID-19 pneumonia and the inconclusive data emerging from the current coronavirus pandemic, the results of the adaptive trial, RECOVERY, which

1
2
3 includes a dexamethasone arm, are eagerly awaited.[1] Nevertheless, leaving ASUC
4 untreated is associated with a high risk of death, mortality being at least 24% in the
5 days before the use of corticosteroids.[26] The expert advisers supported the WHO
6 position that steroid use should not be avoided because of theoretical risks in patients
7 with COVID-19.[36]
8
9
10
11

12
13
14 The panel was uncertain whether infliximab, without concurrent corticosteroids,
15 should be used as a first line therapy in patients who are SARS-CoV-2 positive,
16 regardless of whether they had COVID-19. As with corticosteroids, the risk of anti-TNF
17 in the context of the pandemic is unknown. In addition, there is no high-quality
18 evidence for infliximab in ASUC other than as a rescue therapy following corticosteroid
19 failure. Anti-TNF agents are known to increase the risk of respiratory tract and other
20 opportunistic infections,[37] particularly when used in association with thiopurines
21 and corticosteroids.[38] However, anti-TNF therapies are currently being evaluated in
22 clinical trials [39] as a potential treatment for COVID-19-induced cytokine 'storm'
23 [40,41]. In view of the uncertainty of the effects of corticosteroids and infliximab on
24 SARS-CoV-2 infection, it was considered appropriate that all patients with a positive
25 swab should be discussed with a COVID-19 specialist to guide decision making.
26
27
28
29
30
31
32
33
34
35
36
37

38 Rescue Therapy

39
40 Up to half of patients with ASUC fail first line medical therapy with corticosteroids.[6]
41 In all scenarios, it was considered inappropriate to continue this treatment alone in
42 the face of non-response at day 3, consistent with current BSG guidelines.[6] Similarly,
43 in line with BSG guidance, it was considered appropriate to commence infliximab
44 whilst continuing corticosteroids regardless of SARS-CoV-2 status. Discontinuation of
45 corticosteroids at the point of commencing infliximab rescue therapy was considered
46 of uncertain appropriateness across all scenarios, as it may result in worsening colitis,
47 whilst acknowledging the potential risks of combining the two drugs. Ciclosporin
48 rescue therapy was generally considered inappropriate, due in part to concerns about
49 the risks of drug-induced nephrotoxicity given the frequency of acute kidney injury in
50 SARS-CoV-2 infection.[42] In addition, the infusion regimen requires frequent
51
52
53
54
55
56
57
58
59
60

1
2
3 healthcare worker-patient contact which could, in theory, increase the risk of
4 transmission. The panel did not explore its use in settings in which infliximab may be
5 relatively contraindicated, such as previous loss of response to infliximab, drug
6 immunogenicity or when relevant co-morbidities exist, such as multiple sclerosis.
7 Similarly, the panel did not specifically address the question of whether infliximab was
8 used as a monotherapy or in combination with an immunomodulator.
9
10
11
12
13
14
15

16 There is little evidence regarding the risks of surgical management in patients with
17 COVID-19. Preliminary data demonstrate a substantial increase in morbidity and
18 mortality amongst SARS-CoV-2-infected patients undergoing surgery (*personal
19 communication, submitted for publication*). In one report, 34 patients underwent
20 elective surgery in Wuhan, China with all developing COVID-pneumonia, 7 of whom
21 (20%) died.[9] Accordingly, the risks of surgery drove the rating of colectomy as first
22 line therapy, or as an alternative to rescue therapy, as being inappropriate. However,
23 in patients failing medical therapy, there was consensus that delaying surgery would
24 be inappropriate.
25
26
27
28
29
30
31
32
33

34 Continuing Medical Therapy

35
36 The BSG IBD guidelines recommend corticosteroid tapering over 6-8 weeks which was
37 considered appropriate by the panel, except in the context of COVID-19 pneumonia
38 where an accelerated taper over 4-6 weeks was considered appropriate instead. A
39 more accelerated taper, over fewer than 4 weeks, was generally deemed
40 inappropriate due to the high risk of relapse in this cohort.[6] Regarding initiation of
41 maintenance therapy either before or shortly after discharge from hospital, it was
42 considered appropriate to start anti-TNF, vedolizumab or ustekinumab in patients
43 with negative swabs. However, in scenarios in which patients had positive swabs, with
44 or without evidence of COVID-19 pneumonia, there was uncertainty about the risk:
45 benefit ratio of biologic therapy, driven by the lack of evidence. Thus, biologic use in
46 this situation was deemed uncertain in nearly all scenarios.
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Thiopurines and tofacitinib were not considered appropriate at any stage during the
4 scenarios. This is despite the BSG recommendation that thiopurines should be
5 initiated at or soon after discharge following successful treatment of ASUC.[6]
6
7 Azathioprine therapy was in part considered inappropriate due to possible side effects
8 such as pancreatitis, which could result in readmission to hospital, and drug
9 hypersensitivity, which can manifest as a flu-like syndrome which may potentially be
10 confused with COVID-19.[43] Azathioprine can also induce significant lymphopaenia
11 [43] which may mimic the lymphopaenia seen in SARS-CoV-2 infection. How this
12 affects outcome of COVID-19 is unclear; some reports even suggest a theoretical
13 benefit of thiopurines.[44,45] The additional monitoring required when azathioprine
14 is initiated may also be a challenge with COVID-19-related service reconfiguration and
15 antecedent risks of SARS-CoV-2 acquisition posed by the requirement for face-to-face
16 contact from laboratory monitoring.
17
18
19
20
21
22
23
24
25
26
27

28 Tofacitinib is a non-selective Janus kinase (JAK) inhibitor which is associated with
29 herpes zoster viral reactivation and, like COVID-19, is also associated with an increased
30 risk of deep vein thrombosis.[46] There is also very limited evidence for its use in the
31 setting of ASUC.[47] For these reasons, the panel considered its use inappropriate in
32 nearly all settings although it was noted that its rapid offset of action could be of
33 theoretical benefit.
34
35
36
37
38
39
40

41 Anticoagulation

42
43
44 Prophylactic anticoagulation was considered appropriate beyond discharge amongst
45 patients with a positive SARS-CoV-2 swab, although this strategy was deemed
46 uncertain in people with negative swabs. Like ASUC, COVID-19 is strongly linked to a
47 hypercoagulable state with substantially increased risk of microthrombi and venous
48 thromboembolism (VTE).[48] It is notable that the British Thoracic Society
49 recommends doubling the dose of anticoagulation and/or prescribing VTE prophylaxis
50 (low molecular weight heparin or direct oral anticoagulant) for up to 4 weeks following
51 discharge in high risk patients with COVID-19.[49]
52
53
54
55
56
57
58
59
60

Strengths & Limitations

The strengths of our study include the inclusion of a diverse group of IBD experts drawn from a wide range of UK centres as well as non-gastroenterology specialists with experience in managing patients with COVID-19. In addition, we used the RAND methodology which is a validated technique to guide decision making in the absence of a robust evidence base. It is not necessarily an attempt to reach consensus but rather to guide clinicians as to the appropriateness or inappropriateness of interventions, whilst accepting that uncertainty is also a valid outcome, which was highly appropriate in this setting. It was impossible for our scenarios to encompass fully all cases encountered in clinical practice. We, therefore, focussed on principles that may help to guide decision making in most cases of ASUC in the context of COVID-19. We appreciate that by doing so, this guidance may not be directly applicable to more nuanced cases where decision making may be influenced by a myriad of factors. Nor was every aspect of care considered; for example, the question of repeating testing for *Clostridium difficile* prior to colectomy in view of higher exposure to antibiotics in the COVID-19 era, was not addressed. The outcomes should, therefore, be considered an adjunct to multidisciplinary decision-making rather than a replacement. Finally, knowledge within the field remains fast moving such that it will be important to stay abreast of new developments as they arise.

Implications and concluding remarks

By combining clinical expertise from the BSG CRG and IBD Section Committee in conjunction with other medical and surgical IBD and COVID-19 experts, we have provided guidance to clinicians regarding the appropriate management of ASUC during the COVID-19 pandemic, highlighting where current BSG guidance may need adaptation. Population-based studies are needed to clarify the risks and benefits of interventions used in the management of ASUC during the pandemic. Until then, we consider the results of the panel, which largely support following the well-established and evidence-based BSG guideline, will help guide clinicians in this challenging and evolving area.

Acknowledgments

The authors would like to acknowledge the input of Professor Jon Rhodes for his helpful comments and suggestions.

Funding The authors have declared no funding for this research

Competing interests Please see supplementary table 3

References

- 1 Huang C, Wang Y, Li X, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;**395**:497–506.
doi:10.1016/S0140-6736(20)30183-5
- 2 Johns Hopkins University. Johns Hopkins Coronavirus Resource Center. 2020.<https://coronavirus.jhu.edu/> (accessed 8 May 2020).
- 3 The OpenSAFELY Collaborative, Williamson E, Walker AJ, *et al.* OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *medRxiv* Published Online First: 7 May 2020. doi:10.1101/2020.05.06.20092999
- 4 Turner D, Walsh CM, Steinhart AH, *et al.* Response to Corticosteroids in Severe Ulcerative Colitis: A Systematic Review of the Literature and a Meta-Regression. *Clin Gastroenterol Hepatol* 2007;**5**:103–10.
doi:10.1016/j.cgh.2006.09.033
- 5 Seah D, De Cruz P. Review article: the practical management of acute severe

- 1
2
3 ulcerative colitis. *Aliment Pharmacol Ther* 2016;**43**:482–513.
4
5 doi:10.1111/apt.13491
6
7
8
9 6 Lamb CA, Kennedy NA, Raine T, *et al.* British Society of Gastroenterology
10 consensus guidelines on the management of inflammatory bowel disease in
11 adults. *Gut* 2019;**68**:s1–106. doi:10.1136/gutjnl-2019-318484
12
13
14
15
16 7 Rubin DT, Abreu MT, Rai V, *et al.* Management of Patients with Crohn’s
17 Disease and Ulcerative Colitis During the COVID-19 Pandemic: Results of an
18 International Meeting. *Gastroenterology* Published Online First: April 2020.
19
20
21
22
23
24
25 8 Kirchgerner J, Lemaitre M, Carrat F, *et al.* Risk of Serious and Opportunistic
26 Infections Associated With Treatment of Inflammatory Bowel Diseases.
27
28
29
30
31
32 9 Lei S, Jiang F, Su W, *et al.* Clinical characteristics and outcomes of patients
33 undergoing surgeries during the incubation period of COVID-19 infection.
34
35
36
37
38
39
40 10 Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a
41 therapeutic trial. *Br Med J* 1955;**2**:1041–8.
42
43
44
45 11 SECURE-IBD. SECURE-IBD Registry: Surveillance Epidemiology of Coronavirus
46 (COVID-19) Under Research Exclusion. 2020.[https://covidibd.org/updates-](https://covidibd.org/updates-and-data/)
47
48
49
50
51
52 12 Bezzio C, Saibeni S, Variola A, *et al.* Outcomes of COVID-19 in 79 patients with
53 IBD in Italy: an IG-IBD study. *Gut* Published Online First: 30 April 2020.
54
55
56
57
58
59 13 Rodríguez-Lago I, Ramírez de la Piscina P, Elorza A, *et al.* Characteristics and
60

- 1
2
3 prognosis of patients with inflammatory bowel disease during the SARS-CoV-2
4 pandemic in the Basque Country (Spain). *Gastroenterology* 2020;**0**.
5
6 doi:10.1053/j.gastro.2020.04.043
7
8
9
- 10
11 14 Fitch K, Bernstein María SJ, Aguilar D, *et al*. The RAND/UCLA Appropriateness
12 Method User's Manual. 2001.
13
14
15
16 15 Coulter I, Elfenbaum P, Jain S, *et al*. SEaRCH™ expert panel process:
17 streamlining the link between evidence and practice. *BMC Res Notes*
18 2016;**9**:16. doi:10.1186/s13104-015-1802-8
19
20
21
22
23 16 Travis SP, Farrant JM, Ricketts C, *et al*. Predicting outcome in severe ulcerative
24 colitis. *Gut* 1996;**38**:905–10. doi:10.1016/j.dld.2004.03.002
25
26
27
28 17 Rubin DT, Abreu MT, Rai V, *et al*. Management of Patients with Crohn's
29 Disease and Ulcerative Colitis During the COVID-19 Pandemic: Results of an
30 International Meeting. *Gastroenterology* Published Online First: April 2020.
31
32 doi:10.1053/j.gastro.2020.04.002
33
34
35
36
37 18 Al-Ani A, Prentice R, Rentsch C, *et al*. Review Article: Prevention, Diagnosis
38 and Management of COVID-19 in the Inflammatory Bowel Disease Patient.
39 *Aliment Pharmacol Ther* Published Online First: 29 April 2020.
40
41 doi:10.1111/apt.15779
42
43
44
45
46 19 Zheng S, Fan J, Yu F, *et al*. Viral load dynamics and disease severity in patients
47 infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020:
48 retrospective cohort study. *BMJ* 2020;;m1443. doi:10.1136/bmj.m1443
49
50
51
52
53 20 Ding S, Liang TJ. Journal Pre-proof Is SARS-CoV-2 Also an Enteric Pathogen
54 with Potential Fecal-Oral Transmission: A COVID-19 Virological and Clinical
55 Review. *Gastroenterology* Published Online First: 2020.
56
57 doi:10.1053/j.gastro.2020.04.052
58
59
60

- 1
2
3 21 Pan L, Mu M, Yang P, *et al.* Clinical Characteristics of COVID-19 Patients With
4 Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional,
5 Multicenter Study. *Am J Gastroenterol* 2020;**115**:766–73.
6
7 doi:10.14309/ajg.0000000000000620
8
9
10
11
12 22 Mao R, Qiu Y, He J-S, *et al.* Manifestations and prognosis of gastrointestinal
13 and liver involvement in patients with COVID-19: a systematic review and
14 meta-analysis. *Lancet Gastroenterol Hepatol* Published Online First: May 2020.
15
16 doi:10.1016/S2468-1253(20)30126-6
17
18
19
20
21 23 Carvalho A, Alqusairi R, Adams A, *et al.* SARS-CoV-2 Gastrointestinal Infection
22 Causing Hemorrhagic Colitis. *Am J Gastroenterol* 2020;:1.
23
24 doi:10.14309/ajg.0000000000000667
25
26
27
28 24 Norsa L, Indriolo A, Sansotta N, *et al.* Uneventful course in IBD patients during
29 SARS-CoV-2 outbreak in northern Italy. *Gastroenterology* Published Online
30 First: April 2020. doi:10.1053/j.gastro.2020.03.062
31
32
33
34
35 25 Wisniewski A, Kirchgesner J, Seksik P, *et al.* Increased incidence of systemic
36 serious viral infections in patients with inflammatory bowel disease associates
37 with active disease and use of thiopurines. *United Eur Gastroenterol J*
38 Published Online First: 2019. doi:10.1177/2050640619889763
39
40
41
42
43
44 26 Truelove SC, Witts LJ. Cortisone in Ulcerative Colitis. *BMJ* 1955;**2**:1041–8.
45
46 doi:10.1136/bmj.2.4947.1041
47
48
49
50 27 Van Kerkhove MD, Vandemaele KAH, Shinde V, *et al.* Risk Factors for Severe
51 Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled
52 Analysis. *PLoS Med* 2011;**8**:e1001053. doi:10.1371/journal.pmed.1001053
53
54
55
56
57 28 Lee N, Allen Chan KC, Hui DS, *et al.* Effects of early corticosteroid treatment on
58 plasma SARS-associated Coronavirus RNA concentrations in adult patients. *J*
59
60

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- Clin Virol* 2004;**31**:304–9. doi:10.1016/j.jcv.2004.07.006
- 29 Arabi YM, Mandourah Y, Al-Hameed F, *et al.* Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med* 2018;**197**:757–67. doi:10.1164/rccm.201706-1172OC
- 30 Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet* 2020;**395**:473–5. doi:10.1016/S0140-6736(20)30317-2
- 31 Lansbury LE, Rodrigo C, Leonardi-Bee J, *et al.* Corticosteroids as Adjunctive Therapy in the Treatment of Influenza. *Crit Care Med* 2020;**48**:e98–106. doi:10.1097/CCM.0000000000004093
- 32 Lewis SR, Pritchard MW, Thomas CM, *et al.* Pharmacological agents for adults with acute respiratory distress syndrome. *Cochrane Database Syst Rev* Published Online First: 23 July 2019. doi:10.1002/14651858.CD004477.pub3
- 33 The Royal College of Radiologists. Statement on use of CT chest to screen for COVID-19 in pre-operative patients. 2020.<https://www.rcr.ac.uk/college/coronavirus-covid-19-what-rcr-doing/clinical-information/statement-use-ct-chest-screen-covid> (accessed 8 May 2020).
- 34 Royal College of Surgeons. Updated Intercollegiate General Surgery Guidance on COVID-19. 2020.<https://www.rcseng.ac.uk/coronavirus/joint-guidance-for-surgeons-v2/> (accessed 8 May 2020).
- 35 Ai T, Yang Z, Hou H, *et al.* Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology* 2020;**200642**. doi:10.1148/radiol.2020200642

- 1
2
3 36 World Health Organization. Clinical management of severe acute respiratory
4 infection (SARI) when COVID-19 disease is suspected.
5
6 2020.[https://www.who.int/publications-detail/home-care-for-patients-with-](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-)
7
8
9
10
11
12 37 Shah ED, Farida JP, Siegel CA, *et al.* Risk for Overall Infection with Anti-TNF and
13 Anti-integrin Agents Used in IBD. *Inflamm Bowel Dis* 2017;**23**:570–7.
14
15 doi:10.1097/MIB.0000000000001049
16
17
18
19 38 Singh S, Facciorusso A, Dulai PS, *et al.* Comparative Risk of Serious Infections
20 With Biologic and/or Immunosuppressive Therapy in Patients With
21 Inflammatory Bowel Diseases: A Systematic Review and Meta-Analysis. *Clin*
22
23
24
25
26
27
28 39 Zhou L, Xu H. A clinical study for the efficacy and safety of Adalimumab
29 Injection in the treatment of patients with severe novel coronavirus
30 pneumonia (COVID-19). Chinese Clin. Trial Regist.
31
32 2020.<http://www.chictr.org.cn/showprojen.aspx?proj=49889> (accessed 13
33
34
35
36
37
38
39 40 Feldmann M, Maini RN, Woody JN, *et al.* Trials of anti-tumour necrosis factor
40 therapy for COVID-19 are urgently needed. *Lancet* 2020;**395**:1407–9.
41
42
43
44
45
46 41 Mehta P, McAuley DF, Brown M, *et al.* COVID-19: consider cytokine storm
47 syndromes and immunosuppression. *Lancet.* 2020;**395**:1033–4.
48
49
50
51
52
53 42 Fanelli V, Fiorentino M, Cantaluppi V, *et al.* Acute kidney injury in SARS-CoV-2
54
55
56
57
58
59 43 Chaparro M, Ordás I, Cabré E, *et al.* Safety of Thiopurine Therapy in
60

- 1
2
3 Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2013;**19**:1404–10.
4 doi:10.1097/MIB.0b013e318281f28f
5
6
7
8
9 44 Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated With Acute Respiratory
10 Distress Syndrome and Death in Patients With Coronavirus Disease 2019
11 Pneumonia in Wuhan, China. *JAMA Intern Med* Published Online First: 13
12 March 2020. doi:10.1001/jamainternmed.2020.0994
13
14
15
16
17 45 Tan L, Wang Q, Zhang D, *et al.* Lymphopenia predicts disease severity of
18 COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther*
19 2020;**5**:33. doi:10.1038/s41392-020-0148-4
20
21
22
23
24 46 Sandborn WJ, Su C, Sands BE, *et al.* Tofacitinib as Induction and Maintenance
25 Therapy for Ulcerative Colitis. *N Engl J Med* 2017;**376**:1723–36.
26 doi:10.1056/NEJMoa1606910
27
28
29
30
31 47 Kotwani P, Terdiman J, Lewin S. Tofacitinib for rescue therapy in acute severe
32 ulcerative colitis: a real-world experience. *J Crohn's Colitis* Published Online
33 First: 5 February 2020. doi:10.1093/ecco-jcc/jjaa018
34
35
36
37
38 48 Middeldorp S, Coppens M, van Haaps TF, *et al.* Incidence of venous
39 thromboembolism in hospitalized patients with COVID-19. *Preprints.org*
40 Published Online First: 2020. doi:10.20944/preprints202004.0345.v1
41
42
43
44
45 49 British Thoracic Society. BTS Guidance on Venous Thromboembolic Disease in
46 patients with COVID-19. Br. Thorac. Soc. 2020.[https://www.brit-](https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/)
47 [thoracic.org.uk/document-library/quality-improvement/covid-19/bts-](https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/)
48 [guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/](https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/)
49 (accessed 8 May 2020).
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Confidential: For Review Only

Day 0

ASUC as defined by Truelove and Witt Criteria^a

Refer to Paediatrics for ESPGHAN/ECCO flowchart

Isolate
1Send SARS-CoV-2 swab
2Discuss all +ve cases
3with a COVID-19
4specialist
5Routine CT is not
6required^b
7
8Daily review and
9investigations
10throughout stay^a

Patient ≥16 years
Presenting to adult setting with
acute severe colitis

Patient <16 years
Presenting to adult setting
with acute severe colitis

Baseline Investigations including
stool cultures and *C. difficile*^a

Commence treatment without delay:
IV hydrocortisone 100 mg 6 hourly
OR IV methylprednisolone 60 mg daily (inpatient only)
AND LMW heparin prophylaxis
Consider withholding 5-ASA

Sigmoidoscopy within 24
hours^c including CMV
screen^a

Uncertain: SARS-CoV-2+ with pneumonia → IV
steroids SARS-CoV-2+ irrespective of symptoms →
Infliximab without steroids

Repeat SARS-CoV-2 swab if -ve first swab. Discuss all +ve cases with COVID-19 specialist

Day 3

>6 bowel movements per day
OR
3-8 bowel movements per day AND
CRP >45 mg/l

No

<4 bowel movements per day
for 2 days
AND no rectal bleeding

Yes

Sigmoidoscopy if not performed^c

Yes

Surgical review: colectomy required?

No

Uncertain: Start infliximab
and discontinue steroids^d

No

Continue IV steroids
for 3-5 additional days

23CT chest and
24sigmoidoscopy
25if not performed

31Delay
32colectomy
Emergency
Colectomy

Continue IV steroids
Commence second-line therapy: Infliximab 5 mg/kg^d
OR IV ciclosporin 2 mg/kg (unless failed thiopurine)^e

Day 6-8

<4 bowel movements per day
for 2 days
AND no rectal bleeding

Yes

<4 bowel movements per day
for 2 days
AND no rectal bleeding

Yes

34CT chest and
35sigmoidoscopy^c
36if not performed

Surgical review: Colectomy
required?

No

Continue IV steroids. If received infliximab -
Accelerated dosing^d: Repeat infliximab 5mg/
kg

Continue IV steroids
Commence second-line therapy:
Infliximab 5 mg/kg^d OR
IV ciclosporin 2 mg/kg^e (unless failed
thiopurine)

No

37

38

39

40

41

42

43

44

<4 bowel movements per day
for 2 days AND no rectal bleeding

No

Yes

Day 13-15

The above guideline is adapted from the original BSG guideline for the management of acute severe colitis⁶.

Additional Notes - RAND panel outcome (green is considered appropriate, yellow uncertain and red inappropriate):

- a. See BSG guidelines for standard recommendations⁶.
 - b. At the time of admission, the appropriateness of routine CT chest is uncertain and routine CT abdomen inappropriate.
 - c. If not performed on admission, sigmoidoscopy should be arranged prior to treatment escalation or colectomy.
 - d. Infliximab rescue therapy with steroids: appropriate. Infliximab rescue therapy without steroids: uncertain (irrespective of SARS-COV-2 status).
 - e. Ciclosporin with steroids: uncertain in SARS-CoV-2 negative patients. Ciclosporin without steroids: inappropriate (irrespective of SARS-CoV-2 status).
 - f. Standard and accelerated steroid taper over 6-8 or 4-6 weeks, respectively: appropriate in SARS-CoV-2 negative, or positive patients without pneumonia.
 - g. In patients with SARS-CoV-2 pneumonia: an accelerated taper over 4-6 weeks was considered appropriate and a standard taper uncertain.
 - h. Thiopurines: uncertain if SARS-CoV-2 negative and inappropriate if SARS-CoV-2 positive.
- In SARS-CoV-2 negative or SARS-CoV-2 positive patients without pneumonia: consider anti-TNF, vedolizumab or ustekinumab at or soon after discharge. In SARS-CoV-2 pneumonia the appropriateness of these agents are uncertain.

Supplementary Table 1: RAND Panel members

RAND Panellists	Affiliation
Shahida Din*	Western General Hospital, Edinburgh
Alex Kent	King's College Hospital NHS Foundation Trust, London
Richard Pollok*	St Georges University Hospitals NHS Foundation Trust, London
Nick Kennedy^	Royal Devon and Exeter NHS Foundation Trust, Exeter
Robin Dart	Royal Free London NHS Foundation Trust
Daniel Gaya*	Glasgow Royal Infirmary, NHS Greater Glasgow and Clyde
Ailsa Hart^	St Mark's Hospital North West University Healthcare NHS Trust, London
Chris Lamb	Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle
Jimmy Limdi	The Pennine Acute Hospitals NHS Trust, Manchester
James Lindsey^	The Royal London Hospital, Barts Health NHS trust, London
Chris Probert	University of Liverpool
Tim Raine^	Cambridge University Hospitals NHS Foundation Trust
Christian Selinger*	Leeds Teaching Hospitals, NHS Trust, Leeds
Shaji Sebastian*^	Hull University Teaching Hospitals NHS Trust
Lisa Younge	St Mark's Hospital, North West University Healthcare NHS Trust, London

*Denotes British Society of Gastroenterology Inflammatory Bowel Disease Section Committee member

^Denotes British Society of Gastroenterology Inflammatory Bowel Disease Clinical Research Group member

Supplementary Table 2. Final Assessment of Statements by RAND Panel: Appropriateness of management in acute severe ulcerative colitis (ASUC) in the context of COVID19

91 Statements	Median	Disagreement Index	Standard Deviation	Category
Admission				
All patients admitted with ASUC				
Perform a SARS-CoV-2 swab on admission	8	0.13*	0.51	Appropriate
Perform a CT chest within 24 hours of admission	4	0.52	1.39	Uncertain
Perform a CT abdomen, in addition to AXR, within 24 hours of admission	3	0.45	2.09	Inappropriate
Isolate them in a side room throughout their admission regardless of COVID status	8	0.23	1.21	Appropriate
Perform a flexible sigmoidoscopy				
Within 24 hours of admission in all patients admitted with ASUC (as per BSG guidance)	8	0.00	1.96	Appropriate
In all patients failing IV corticosteroids who have not had a flexible sigmoidoscopy on admission	9	0.13*	0.64	Appropriate
In all patients failing intravenous corticosteroid therapy who have already had a flexible sigmoidoscopy on admission	3	0.00	0.88	Inappropriate
In all patients being referred for colectomy who have not had a flexible sigmoidoscopy on admission, to confirm the diagnosis prior to surgery (excluding patients who have toxic megacolon or perforation)	8	0.23*	0.85	Appropriate
In all patients being referred for colectomy who have already had a flexible sigmoidoscopy on admission, to assess the degree of ongoing inflammation (excluding patients who have toxic megacolon or perforation)	2	0.16	0.94	Inappropriate
First line medical therapy				
Negative swab and no respiratory symptoms				
Follow standard BSG guidelines and start intravenous hydrocortisone/methylprednisolone	9	0.10	0.92	Appropriate

1	Start IV methylprednisolone 60 mg daily				
2	as an outpatient (with daily specialist				
3	review, once daily observations and	3	0.30	2.18	Inappropriate
4	access to x-ray and bloods as required)				
5					
6	Start budesonide MMX 9 mg or				
7	beclometasone 5 mg daily PO (as an	1	0.13*	0.74	Inappropriate
8	inpatient)				
9					
10	Start IV steroids concurrently with				
11	infliximab	3	0.13	2.06	Inappropriate
12					
13	Start infliximab without steroids	3	0.33	1.83	Inappropriate
14					
15	Start ciclosporin monotherapy as a bridge				
16	to another therapy	2	0.16	1.41	Inappropriate
17					
18	Start tofacitinib 10 mg bd	2	0.13	1.64	Inappropriate
19					
20	Colectomy	1	0.10*	0.74	Inappropriate
21					
22	Discuss with COVID-19 specialist	3	0.16	0.92	Inappropriate
23					
24	Positive swab but no symptoms or signs of COVID-19 pneumonia				
25	Follow standard BSG guidelines and start				
26	intravenous	7	0.13	0.80	Appropriate
27	hydrocortisone/methylprednisolone				
28					
29	Start IV methylprednisolone 60 mg daily				
30	as an outpatient (with daily specialist	2	0.29	2.13	Inappropriate
31	review, once daily observations and				
32	access to x-ray and bloods as required)				
33					
34	Start budesonide MMX 9 mg or				
35	beclometasone 5 mg daily PO (as an	1	0.10*	0.63	Inappropriate
36	inpatient)				
37					
38	Start IV steroids concurrently with				
39	infliximab	2	0.16	1.58	Inappropriate
40					
41	Start infliximab without steroids	4	0.52	1.94	Uncertain
42					
43	Start ciclosporin monotherapy as a bridge				
44	to another therapy	2	0.16	1.36	Inappropriate
45					
46	Start tofacitinib 10 mg bd	1	0.13	1.10	Inappropriate
47					
48	Colectomy	1	0.13*	0.64	Inappropriate
49					
50	Discuss with COVID-19 specialist	7	0.13	1.41	Appropriate
51					
52	Positive swab with symptoms or signs of COVID-19 pneumonia				
53	Follow standard BSG guidelines and start				
54	intravenous	6	0.45	1.42	Uncertain
55	hydrocortisone/methylprednisolone				
56					
57	Start IV methylprednisolone 60 mg daily				
58	as an outpatient (with daily specialist	1	0.00*	0.72	Inappropriate
59	review, once daily observations and				
60	access to x-ray and bloods as required)				

Start budesonide MMX 9 mg or beclometasone 5 mg daily PO (as an inpatient)	1	0.00	2.07	Inappropriate
Start IV steroids concurrently with infliximab	2	0.29	1.98	Inappropriate
Start infliximab without steroids	5	0.49	1.95	Uncertain
Start ciclosporin monotherapy as a bridge to another therapy	1	0.13	1.39	Inappropriate
Start tofacitinib 10 mg bd	1	0.10*	0.49	Inappropriate
Colectomy	1	0.13*	0.74	Inappropriate
Discuss with COVID-19 specialist	9	0.00*	0.59	Appropriate
Rescue Therapy				
Repeat a SARS-CoV-2 swab in patients with a negative first swab	7	0.22	2.03	Appropriate
Negative swab and no respiratory symptoms				
Continue intravenous steroids alone	1	0.00*	0.74	Inappropriate
Start infliximab and continue steroids	8	0.23*	0.85	Appropriate
Start infliximab and discontinue steroids	4	0.52	1.59	Uncertain
Start intravenous ciclosporin therapy with steroids (unless failed thiopurine)	5	0.95	2.02	Uncertain
Start intravenous ciclosporin and discontinue steroids (unless failed thiopurine)	3	0.22	1.59	Inappropriate
Colectomy	3	0.33	1.79	Inappropriate
Discuss with COVID-19 specialist	5	0.95	1.85	Uncertain
Positive swab but no symptoms or signs of COVID-19 pneumonia				
Continue intravenous steroids alone	1	0.00*	0.62	Inappropriate
Start infliximab therapy with steroids	7	0.16	1.05	Appropriate
Start infliximab and discontinue steroids	6	0.52	1.59	Uncertain
Start intravenous ciclosporin therapy with steroids (unless failed thiopurine)	3	0.22	1.29	Inappropriate
Start intravenous ciclosporin and discontinue steroids (unless failed thiopurine)	3	0.16	1.25	Inappropriate
Colectomy	2	0.33	1.74	Inappropriate
Discuss with COVID-19 specialist	8	0.26*	0.88	Appropriate
Positive swab with symptoms or signs of COVID-19 pneumonia				
Continue intravenous steroids alone	1	0.00	0.92	Inappropriate
Start infliximab with steroids	7	0.17	1.06	Appropriate
Start infliximab and discontinue steroids	5	0.52	1.54	Uncertain

1	Start intravenous ciclosporin therapy with steroids (unless failed thiopurine)	2	0.27	1.46	Inappropriate
2					
3					
4	Start intravenous ciclosporin and discontinue steroids (unless failed thiopurine)	2	0.29	2.07	Inappropriate
5					
6					
7					
8	Colectomy	2	0.29	1.64	Inappropriate
9					
10	Discuss with COVID-19 specialist	9	0.10*	0.74	Appropriate
11					
12					
13	Continuing medical therapy				
14	Negative swab and no respiratory symptoms				
15					
16	Follow standard BSG guidelines for tapering oral steroids over 6-8 weeks	8	0.16	1.06	Appropriate
17					
18	Use an accelerated steroid taper over 4-6 weeks	7	0.13	1.03	Appropriate
19					
20					
21	Use an accelerated steroid taper over fewer than 4 weeks	3	0.30	1.55	Inappropriate
22					
23					
24	Switch to budesonide MMX 9 mg or beclomethasone 5 mg daily PO	3	0.16	0.83	Inappropriate
25					
26	Taper steroids and follow standard BSG guidelines initiating thiopurine therapy at or soon after discharge	4	0.45	1.77	Uncertain
27					
28	Taper steroids and initiate anti-TNF therapy at or soon after discharge	7	0.00	0.64	Appropriate
29					
30					
31	Taper steroids and initiate ustekinumab at or soon after discharge	7	0.00	1.76	Appropriate
32					
33	Taper steroids and initiate vedolizumab at or soon after discharge	7	0.22	1.72	Appropriate
34					
35					
36	Taper steroids and initiate tofacitinib at or soon after discharge	4	0.86	1.92	Uncertain
37					
38					
39	Continue prophylactic anticoagulation for a period after discharge	5	0.95	1.98	Uncertain
40					
41					
42					
43					
44	Positive swab but no symptoms or signs of COVID-19 pneumonia				
45	Follow standard BSG guidelines for tapering oral steroids over 6-8 weeks	7	0.45	1.58	Appropriate
46					
47	Use an accelerated steroid taper over 4-6 weeks	7	0.16	0.70	Appropriate
48					
49					
50	Use an accelerated steroid taper over fewer than 4 weeks	3	0.45	1.82	Inappropriate
51					
52					
53	Switch to budesonide MMX 9 mg or beclomethasone 5 mg daily PO	3	0.16	1.35	Inappropriate
54					
55					
56	Taper steroids and follow standard BSG guidelines initiating thiopurine therapy at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	3	0.16	1.49	Inappropriate
57					
58					
59					
60					

1 2 3 4 5 6	Taper steroids and initiate anti-TNF therapy at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	7	0.22	1.21	Appropriate
7 8 9 10 11	Taper steroids and initiate ustekinumab at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	6	0.52	1.71	Uncertain
12 13 14 15 16	Taper steroids and initiate vedolizumab at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	6	0.52	1.73	Uncertain
17 18 19 20 21	Taper steroids and initiate tofacitinib at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	3	0.00	0.83	Inappropriate
22 23 24	Continue prophylactic anticoagulation for a period after discharge	7	0.00	1.31	Appropriate
25	Positive swab with symptoms or signs of COVID-19 pneumonia				
26 27 28	Follow standard BSG guidelines for tapering oral steroids over 6-8 weeks	6	0.84	1.92	Uncertain
29 30 31	Use an accelerated steroid over 4-6 weeks	7	0.13	0.88	Appropriate
32 33	Use an accelerated steroid taper over fewer than 4 weeks	4	0.52	2.15	Uncertain
34 35 36	Switch to budesonide MMX 9 mg or beclomethasone 5 mg daily PO	2	0.27	1.55	Inappropriate
37 38 39 40 41 42	Taper steroids and follow standard BSG guidelines initiating thiopurine therapy at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	3	0.16	1.29	Inappropriate
43 44 45 46 47	Taper steroids and initiate anti-TNF therapy at or soon after discharge (but within the period of potential ongoing SARS-CoV2 infection)	6	0.45	1.56	Uncertain
48 49 50 51 52	Taper steroids and initiate ustekinumab at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	6	0.49	1.94	Uncertain
53 54 55 56 57 58	Taper steroids and initiate vedolizumab at or soon after discharge (but within the period of potential ongoing SARS-CoV-2 infection)	5	0.52	1.68	Uncertain
59 60	Taper steroids and initiate tofacitinib at or soon after discharge (but within the period of potential ongoing SARS-CoV-2	3	0.27	1.30	Inappropriate

infection)				
Continue prophylactic anticoagulation for a period after discharge	8	0.13*	0.83	Appropriate
Surgery				
In patients with a SARS-CoV-2 positive swab who have failed medical therapy, surgery should be delayed	3	0.17	1.29	Inappropriate
Patients with a negative swab on admission should have a repeat swab	8	0.16	1.51	Appropriate
Patients should have a CT chest prior to surgery regardless of swab status, respiratory symptoms examination findings and observations	8	0.16	0.92	Appropriate

* Denotes questions where all panelists voted the same appropriateness category as the final outcome category (i.e. level of appropriateness was agreed unanimously)

Supplementary Table 3: Conflicts of interests declared by authors of manuscript *Adaptation of British Society of Gastroenterology guidelines on the management of acute severe ulcerative colitis in the context of the COVID-19 pandemic: a RAND appropriateness panel*

Q1: Do you, your partner (if applicable) or any member of your immediate family have any commercial interest (including personal shares, sponsorship or paid consultancy work) in any companies that are, or could be, involved in the above-named guideline?

Q2: Does your department or unit receive financial support from any commercial organisations that are, or could be, involved in the above-named guideline?

Q3: Are you a consultant to or a member of any national body, charity or pressure group whose work is related to the above-named guideline?

Q4: Do you receive editorial fees for commissioned articles for publication (in any format) or are you paid for editorial work for any publication related to the above-named guideline?

Q5: Do you or your department hold a patent (existing or pending) related to the above-named guideline?

First name or initial	Preferred name or middle initial	Family name	Q1 response	Q2 response	Q3 response	Q4 response	Q5 response
Shahida		Din	Speaker fees/educational support AbbVie, Dr Falk, Takeda	No	BSG IBD Committee Member 2019-2022 BSG Member 2010	No	No
Alexandra	J	Kent	Consultancy to Abbvie, and speaker fees with Pfizer, Janssen and Takeda.	No	No	No	No
Richard		Pollok	No	Dr Falk: Fee for advisory board, 2018	BSG IBD Section Member: BSG is an organisation for Gastroenterologists	No	No
Susanna		Meade	No	No	No	No	No
Nick	A	Kennedy	Janssen: Speaker fees, from 2019-	AbbVie: Research support,	ECCO: Member, from 2011-	No	No

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

			2020. Takeda: Speaker fees, from 2019-2020. Falk: Speaker fees, from 2015-2020	from 2013-2020. Celltrion: Research support, from 2015-2020. Celgene: Research support. From 2018-2020	2020. BSG: Member, from 2011-2020		
Ian		Arnott	No	No	BSG IBD section committee chair	No	No
R	Mark	Beattie	No	No	No	No	No
Felix		Chua	No	No	No	No	No
Rachel		Cooney	No	No	No	No	No
Robin	J	Dart	Takeda: Consultancy, from April 2019 to May 2019	No	No	No	No
James		Galloway	No	No	No	No	No
Daniel	R	Gaya	Abbvie, Ferring, Vifor, Janssen, Pfizer: Speaker fees &/or travel grants, from 2015 to 2020	No	BSG IBD Committee: Secretary from 2019 to 2022	No	No
Subrata		Ghosh	AbbVie: International steering committee, from 2016 to present. Janssen: International steering committee, from 2013 to 2017. Takeda: Consultancy, from 2015 to present. Pfizer: International steering committee, from 2007 to 2013	AbbVie: Research grant, from 2019 to 2020	No	No	No
Mark		Griffiths	No	No	No	No	No
Laura		Hancock	No	No	No	No	No
Richard		Hansen	4D Pharma: Consultancy fees and meeting expenses, from 2014 to 2019. Nutricia: Consultancy fees and meeting expenses, from 2014 to 2019	No	CiCRA: Honorary Medical Director from March 2017 to present	No	No
Ailsa		Hart	AbbVie, Celltrion, Falk, Ferring, Janssen, MSD,	No	Crohn's and Colitis UK: Scientific	No	No

			Napp Pharmaceuticals, Pfizer, Shire and Takeda: Advisory Boards Lecture Fees. Within last 5 years		Research Committee, last 5 years		
Chris	A	Lamb	Janssen, Takeda, Abbvie, AstraZeneca, Eli Lilly, Orion, Pfizer, Roche, Sanofi Aventis, Ferring, UCB and Biogen: Research support and/or fees for development and delivery of non-promotional education, from October 2019 to present. Genentech Inc: Research support, from October 2012 to present	See Q1	British Society of Gastroenterology: IBD Section Committee Member, from June 2018 to present British Society of Gastroenterology: Society member, from 2008 to present	No	No
Charlie	W	Lees	Takeda, Abbvie, Gilead, Pfizer, GSK, Janssen, Vifor, and Ferring: Consultancy and Lecture fees, from 2018 - 2021	Gilead, Ferring and Janssen: Unrestricted research grant, from 2019-2021	BSG IBD Clinical Research Group Chair	No	No
Jimmy	K	Limdi	AbbVie: Consultancy and speaker fees, from 2014-2019. Janssen: Consultancy and speaker fees, from 2017 to present.	Takeda: Consultancy and speaker fees, from 2018 to present. Research support.	MSD: Speaker fees, from Jan 2020 to Jan 2020 only. Pfizer: Speaker fees, from June 2019-present	No	No
James	O	Lindsey	Abbvie, Ferring, GSK, Janssen, Takeda, Pfizer, Napp, Shire, Celltrion, Celgene and Gilead: I have received honoraria for advisory Boards and for lectures from January 2018 to March 2020	Abbvie, Gilead, (Jan 2020 ongoing), Takeda (Jan 2017 to Jan 2020), Abbvie (Jan 2019 ongoing): Research grant support for investigator Led translational research. UK National led for Upadacitinib and Risankizumab phase III program	No	No	No
Charlie	D	Murray	No	No	No	No	No
Kamal		Patel	Abbvie, Janssen, Takeda, T, illots	No	No	No	No

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

			Dr Falk, Ferring: Honoraria received for educational meetings and speaker fees from all listed companies. Advisory board fees from Janssen and Abbvie. 2017 to date				
Nick		Powell	BMS: Consultant, from 2019 to current. AbbVie: Consultant, from 2018 to current. Celgene: Consultant, from 2018 to current. Allergan: Consultant, from 2018 to current. Eli-Lilly: Consultant, from 2018 to current	Takeda: Honoraria for talks, from 2018 to current. Allergan: Honoraria for talks, from 2018 to current. Janssen: Honoraria for talks, from 2018 to current. Tillotts: Honoraria for talks, from 2018 to current. BMS: Honoraria for talks, from 2018 to current	No	No	No
Chris		Probert	My pharma work (within last 2 years) is in relation to disease areas unrelated to IBD	No	Crohn's & Colitis UK: Former committee member, now Research Panel member From 2009 To 2023. BSG: Former Section Lead, Council Member and Trustee From 2011 to 2018	No	No
Tim		Raine	Abbvie, BMS, Celgene, Ferring, Gilead, GSK, LabGenius, Janssen, Mylan, MSD, Novartis, Pfizer, Sandoz, Takeda and UCB: Research/educational grants and/or speaker/consultation fees, from 2017 to present	Unrestricted educational grant from Abbvie	No	No	No
Christian	P	Selinger	Dr Falk: Speaker from 2015	Janssen: Unrestricted	BSG IBD section committee	No	No

			to ongoing. AbbVie: Speaker and consultancy from 2015 to ongoing. Takeda: Speaker and consultancy from 2015 to ongoing. Fresenius Kabi: Consultancy from 2019 to ongoing. Janssen: Speaker and consultancy from 2017 to ongoing. Pfizer: Speaker from 2019 to ongoing	research grants from 2019 to ongoing. AbbVie: Unrestricted research grants from 2015 to ongoing. Takeda: Unrestricted research grants from 2017 to ongoing	member.		
Shaji		Sebastian	No	No	No	No	No
Phil	J	Smith	No	No	CICRA, Guts UK and IBD Passport Trustee: I am a trustee of these Gastro/IBD charities. BSG IBD section committee member	No	No
Phil		Tozer	No	No	No	No	No
Andrew		Ustianowski	Served as a speaker for UCB, Biogen	Our Research Unit has participated in study programmes with: Abbvie, Alios, BMS, Gilead, Janssen, MSD, Roche, ViiV	No	No	No
Lisa		Younge	No	No	No	No	No
Mark	A	Samaan	Served as a speaker, a consultant and/or an advisory board member for Sandoz, Janssen, Takeda, MSD, Falk, Samsung Bioepis.	No	No	No	No
Peter	M	Irving	AbbVie, Celgene, Falk Pharma, Ferring MSD, Janssen, Pfizer, Takeda, Tillotts, Sandoz, Shire, Warner Chilcott: Speaking/education, intermittent -	No	No	No	No

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

			last 3 years. MSD, Pfizer, Takeda: Research, intermittent - last 3 years. AbbVie, Arena, Genentech, Gilead, Hospira, Janssen, Lilly, MSD, Pfizer, Pharmacosmos, Prometheus, Roche, Sandoz, Samsung Bioepis, Takeda, Topivert, VH2, Vifor Pharma: Advisory fees, intermittent - last 3 years				
--	--	--	---	--	--	--	--

Confidential: For Review Only

Adaptations to the British Society of Gastroenterology guidelines on the management of acute severe ulcerative colitis in the context of the COVID-19 pandemic: a RAND appropriateness panel

Authors

1. Shahida Din (Department of Gastroenterology, Western General Hospital, Edinburgh, UK)*
2. Alexandra Kent (Department of Gastroenterology, King's College Hospital NHS Foundation Trust, London, UK) *
3. Richard C Pollok (Department of Gastroenterology, St Georges University Hospitals NHS Foundation Trust, London, UK) *
4. Susanna Meade (Department of Gastroenterology, Guy's and St Thomas' NHS Foundation Trust, London, UK) *
5. Nicholas A Kennedy (Department of Gastroenterology, Royal Devon and Exeter NHS Foundation Trust, Exeter, UK)
6. Ian Arnott (Department of Gastroenterology, Western General Hospital, Edinburgh, UK)
7. R Mark Beattie (Department of Paediatric Gastroenterology, Southampton Children's Hospital, Southampton, UK)
8. Felix Chua (Interstitial Lung Disease Unit, Department of Respiratory Medicine, Royal Brompton Hospital, Royal Brompton and Harefield NHS Foundation Trust, London)
9. Rachel Cooney (Queen Elizabeth Hospital Birmingham NHS Foundation Trust, Birmingham, UK)

- 1
 - 2
 - 3
 - 4
 - 5
 - 6
 - 7
 - 8
 - 9
 - 10
 - 11
 - 12
 - 13
 - 14
 - 15
 - 16
 - 17
 - 18
 - 19
 - 20
 - 21
 - 22
 - 23
 - 24
 - 25
 - 26
 - 27
 - 28
 - 29
 - 30
 - 31
 - 32
 - 33
 - 34
 - 35
 - 36
 - 37
 - 38
 - 39
 - 40
 - 41
 - 42
 - 43
 - 44
 - 45
 - 46
 - 47
 - 48
 - 49
 - 50
 - 51
 - 52
 - 53
 - 54
 - 55
 - 56
 - 57
 - 58
 - 59
 - 60
10. Robin J. Dart (Department of Gastroenterology, Royal Free London NHS Foundation Trust, London, UK)
 11. James Galloway (Department of Rheumatology, King's College Hospital NHS Foundation Trust, London, UK)
 12. Daniel R Gaya (Gastroenterology Unit, Glasgow Royal Infirmary, Castle Street, Glasgow, UK)
 13. Subrata Ghosh (Queen Elizabeth Hospital Birmingham NHS Foundation Trust, Birmingham, UK)
 14. Mark Griffiths (Peri-operative medicine, St Bartholomew's Hospital, London, UK)
 15. Laura Hancock (Manchester University Foundation Trust, Manchester, UK)
 16. Richard Hansen (Glasgow Royal Infirmary, Glasgow, UK and University of Glasgow, Glasgow, UK)
 17. Ailsa Hart (IBD Unit, St Mark's Hospital, London, UK)
 18. Christopher A Lamb (Department of Gastroenterology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK)
 19. Charlie W Lees (Department of Gastroenterology, Western General Hospital, Edinburgh, UK)
 20. Jimmy K Limdi (Department of Gastroenterology, The Pennine Acute Hospitals NHS Trust, Manchester, UK)
 21. James O Lindsay (Department of Gastroenterology, The Royal London Hospital, Barts Health NHS Trust, London, UK)
 22. Charlie D Murray (Department of Gastroenterology, Royal Free London NHS Foundation Trust, London, UK)
 23. Kamal Patel (Department of Gastroenterology, St Georges University Hospitals NHS Foundation Trust, London, UK)
 24. Nick Powell (Department of Gastroenterology, Imperial College Healthcare NHS Trust, London, UK)
 25. Chris Probert (Gastroenterology Research Unit, Department of Cellular and Molecular Physiology, Institute of Translational Medicine, University of Liverpool, Liverpool, UK)

- 1
2
3 26. Tim Raine (Department of Gastroenterology, Cambridge University Hospitals
4 NHS Foundation Trust, Cambridge, UK)
5
6
7 27. Christian Selinger (Department of Gastroenterology, Leeds Teaching
8 Hospitals, NHS Trust, Leeds, UK)
9
10 28. Shaji Sebastian (IBD Unit, Hull University Teaching Hospitals NHS Trust, Hull,
11 UK)
12
13 29. Philip J Smith (Department of Gastroenterology, Royal Liverpool Hospital,
14 Liverpool, UK)
15
16 30. Phil Tozer (IBD Unit, St Mark's Hospital, London, UK)
17
18 31. Andrew Ustianowski (Dept of Infectious Disease, North Manchester General
19 Hospital, Manchester, UK)
20
21 32. Lisa Younge (IBD Unit, St Mark's Hospital, London UK)
22
23 33. Mark A Samaan (Department of Gastroenterology, Guy's and St Thomas' NHS
24 Foundation Trust, London UK)
25
26 34. Peter M Irving (School of Immunology and Microbial Sciences, King's College
27 London, UK)
28
29
30
31
32
33

34 * Joint first authors
35
36
37

38 Corresponding Author:
39
40

41 Peter M Irving, College House, St Thomas' Hospital, Westminster Bridge Road,
42 London, SE1 7EH, UK.
43
44

45
46 **E:** Peter.irving@gstt.nhs.uk
47
48

49
50 **T:** [+44 207 188 2491](tel:+442071882491)
51
52

53
54 **F:** [+44 207 188 2484](tel:+442071882484)
55
56

57 **Key words:** Ulcerative colitis, clinical decision making, IBD clinical
58
59
60

1
2
3 **Abbreviations:**
4

5
6
7 Acute severe ulcerative colitis (ASUC)
8

9
10 Novel coronavirus 2019 (COVID-19)
11

12
13 British Society of Gastroenterology (BSG)
14

15
16
17 RAND/UCLA (Research and Development/University of California, Los Angeles)
18

19
20
21 Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)
22

23
24 Disagreement index (DI)
25

26
27 Inflammatory bowel disease (IBD)
28

29
30
31 World Health Organisation (WHO)
32

33
34
35 Physician response to disease flares and patient adaptation in response to events in
36 inflammatory bowel disease during the COVID-19 pandemic (PREPARE IBD)
37

38
39
40 5-aminosalicylic acid (5-ASA)
41

42
43 Computed tomography (CT)
44

45
46
47 Anti-tumour necrosis factor (anti-TNF)
48

49
50
51 International Organisation For the Study of Inflammatory Bowel Disease (IOIBD)
52

53
54 Middle Eastern Respiratory Syndrome (MERS)
55

56
57 Chest x-ray (CXR)
58
59
60

1
2
3 Venous thromboembolism (VTE)
4
5

6 Clinical Research Group (CRG)
7
8
9

10 MMX (multi-matrix).
11
12
13
14
15
16
17
18
19

20 Word count: 4408
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Confidential: For Review Only

Abstract

Objective

Management of acute severe ulcerative colitis (ASUC) during the novel coronavirus 2019 (COVID-19) pandemic presents significant dilemmas. We aimed to provide COVID-19-specific guidance using current British Society of Gastroenterology (BSG) guidelines as a reference point.

Design

We convened a RAND appropriateness panel comprising 14 gastroenterologists and an IBD nurse consultant supplemented by surgical and COVID-19 experts. Panellists ~~completed a survey rating~~ rated the appropriateness of interventions for ASUC in the context of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Median scores and disagreement index (DI) were calculated. Results were ~~presented and~~ discussed at a moderated meeting prior to a second survey.

Results

Panellists recommended that patients with ASUC should be isolated throughout their hospital stay and should have a SARS-CoV-2 swab performed on admission. Patients with a positive swab should be discussed with COVID-19 specialists.

As per BSG guidance, intravenous hydrocortisone was considered appropriate as initial management; only in patients with COVID-19 pneumonia was their use deemed uncertain. In patients requiring rescue therapy, infliximab with continuing steroids was recommended. Delaying colectomy because of COVID-19 was deemed inappropriate.

Steroid tapering as per BSG guidance, was deemed appropriate for all patients apart from those with COVID-19 pneumonia in whom a 4-6-week taper was preferred. Post-

1
2
3 ASUC maintenance therapy was dependent on SARS-CoV-2 status but, in general,
4 biologics were more likely to be deemed appropriate than azathioprine or tofacitinib.
5
6 Panellists deemed prophylactic anticoagulation post-discharge to be appropriate in
7
8 patients with a positive SARS-CoV-2 swab.
9

10 11 12 **Conclusion**

13
14
15 We have suggested COVID-19-specific adaptations to the BSG ASUC guideline using a
16
17 RAND Panel.
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Significance of the Study

What is already known on this subject?

- The BSG has published evidence-based guidelines for management of patients with ASUC, but it is unknown whether these are appropriate in the setting of SARS-CoV-2.
- Currently there are limited data to inform clinicians in this area and there is no published guidance for the management of ASUC in the setting of the COVID-19 pandemic.

What are the new findings?

- The current BSG IBD guidelines provide a management pathway which remains largely appropriate during the COVID-19 pandemic.
- However, some treatment options were deemed uncertain or inappropriate in patients with established COVID-19 pneumonia.
- It is appropriate to involve COVID-19 specialists in decision-making for ASUC patients who are SARS-CoV-2 positive.
- Steroid tapering as per BSG guidance, was deemed appropriate for all patients apart from those with COVID-19 pneumonia in whom a 4-6-week taper was preferred.
- Prophylactic anticoagulation post-discharge is appropriate in patients with a positive SARS-CoV-2 swab

How might it impact on clinical practice in the foreseeable future?

- This paper summarises available evidence and provides expert opinion for the appropriate management of patients with ASUC during the COVID-19 pandemic.

- 1
2
3 ➤ It also highlights areas of uncertainty which may help direct areas of future
4 research.
5
6
7
8
9
10

11 **Contributors**

12
13
14
15 All authors approved the final version. Study concept and design: SD, RP, AK, MS, PI.
16 Development of questionnaire: SD, RP, AK, SM, PI, MS, NK. Data Analysis: PI, MS, SM.
17 Interpretation of data and drafting of manuscript: SD, RP, AK, SM, MS, NK, PI.
18 Panellists, experts and moderators: SD, AK, RP, SM, NK, JOL, CAL, JKL, CP, CS, SS, DRG,
19 TR, RD, AH, LY, CWL, IA, FC, JG, AU, MG, PT, LH, MS, SM, PI Contributions to literature
20 review and critical revision of the manuscript for important intellectual content: All
21 authors
22
23
24
25
26
27
28
29

30 **ORCID iDs**

31
32
33 SD 0000-0003-2855-3400
34

35
36
37 AK 0000-0003-0577-6177
38

39
40
41 RP 0000-0001-6452-6763
42

43
44
45 SM 0000-0002-8283-6148
46

47
48
49 NK 0000-0003-4368-1961
50

51
52
53 IA 0000-0003-3352-925
54

55
56
57 MB 0000-0003-4721-0577
58

59
60
FC 0000-0001-7845-0173

1
2
3 RC 0000-0003-3710-157X
4
5

6
7 RD 0000-0003-3470-8210
8
9

10 JG 0000-0002-1230-2781
11
12

13
14 DRG 0000-0003-1942-7568
15
16

17 SG 0000-0002-1713-7797
18
19

20 MG 0000-0002-1615-1896
21
22

23
24 LH 0000-0002-8399-6646
25
26

27 RH 0000-0002-3944-6646
28
29

30
31 AH 0000-0002-7141-6076
32
33

34 CAL 0000-0002-7271-4956
35
36

37
38 CWL 0000-0002-0732-8215
39
40

41 JKL 0000-0002-1039-6251
42
43

44
45 JOL 0000-0003-3353-9590
46
47

48 KP 0000-0003-2611-4260
49
50

51 NP 0000-0003-3231-6950
52
53

54
55 CM 0000-0001-6736-1546
56
57

58
59 CP 0000-0003-0477-6714
60

1
2
3 TR 0000-0002-5855-9873
4
5

6 CS 0000-0003-2022-5859
7
8

9
10 SS 0000-0002-3670-6545
11

12
13
14 PJS 0000-0003-1568-3978
15

16
17 PT 0000-0002-2532-7267
18

19
20 LY 0000-0002-3436-9696
21

22
23
24 MAS 0000-0002-4057-9200
25

26
27
28 PMI 0000-0003-0972-8148
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

The novel coronavirus severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) was first reported in December 2019 and its spread led to the declaration of a pandemic by the World Health Organisation (WHO) on 11th March 2020. Infection varies in severity from asymptomatic carriage to an acute respiratory illness which, at its most severe, results in acute respiratory distress syndrome with hyperinflammation and cytokine storm syndrome.[1] By mid-May 2020, there have been nearly 5 million cases reported worldwide with over 300,000 deaths.[2] Risk factors associated with more severe coronavirus disease 2019 (COVID-19) include older age, male sex, hypertension, cardiovascular disease, respiratory disease, diabetes, renal failure, and ethnicity.[3] Neither an effective medical therapy nor a vaccine has yet been described, although numerous candidates are under evaluation.

Acute severe ulcerative colitis (ASUC) occurs in up to 25% of patients with UC and is associated with a mortality of approximately 1%.[4,5] The management of ASUC is particularly challenging in the context of SARS-CoV-2 as the typical presenting features of ASUC, namely diarrhoea with raised inflammatory markers, often in association with a fever, may mimic those of COVID-19. ASUC is managed with high dose parenteral corticosteroids, progressing to rescue therapy and/or surgery in those who fail to respond adequately.[6] The safety of all of these interventions in the context of COVID-19 infection is unclear. For example, there are concerns that corticosteroids may increase the risk of acquiring SARS-CoV-2 infection and/or worsen the severity of COVID-19 disease.[7] In addition, the commonly used rescue therapies, infliximab and ciclosporin are associated with an increased risk of infection, particularly if used in combination with immunomodulators such as thiopurines, or steroids.[8] Finally, individuals in whom corticosteroids and rescue therapy fail require urgent colectomy which is associated with high morbidity and mortality in patients infected with SARS-CoV-2.[9] However, withholding treatment in ASUC is clearly not an option in view of the high mortality (in excess of 20%) associated with such an approach.[10]

1
2
3 Whilst national and international registries continue to collate data regarding IBD
4 patients with COVID-19, very few cases relate to the management of ASUC. The
5 PREPARE IBD study (www.prepareibd.org) is collecting data from patients with
6 inflammatory bowel disease (IBD) who are admitted to hospital during the pandemic,
7 as well as from those who develop confirmed or suspected SARS-CoV-2 infection. As
8 of 8th May 2020, 19 patients with severe active UC including four with suspected or
9 confirmed COVID-19 had been identified (personal communication, manuscript
10 submitted). The Surveillance Epidemiology of Coronavirus Under Research Exclusion
11 (SECURE)-IBD registry (<https://covidibd.org/>) is collating data on IBD patients with
12 confirmed coronavirus, with 1074 patients included to date, the majority of whom
13 have Crohn's disease; details of how many in the cohort have ASUC are not yet
14 available.[11] Finally, in case series from Italy and Spain, 4 of 79 and 1 of 40 patients
15 respectively had COVID-19 in conjunction with ASUC [12,13] (the number of ASUC
16 patients in the Italian case series was provided on request from authors).
17
18
19
20
21
22
23
24
25
26
27
28
29

30 Treatment of ASUC during the COVID-19 pandemic presents substantial management
31 dilemmas in the absence of a high-quality evidence base to guide clinicians. We
32 therefore aimed to address this deficit of informed guidance by convening a RAND
33 appropriateness panel. Current BSG guidelines were used as a reference point to
34 highlight differences to current management.[6]
35
36
37
38
39
40

41 **Methods**

42 **Study Overview**

43
44
45 The RAND/UCLA (University of California, Los Angeles) appropriateness method uses
46 a modified Delphi panel approach and combines expert opinion with the best available
47 evidence to determine the appropriateness of specific practices in certain clinical
48 situations.[14] It is particularly useful in areas of uncertainty in which evidence is
49 insufficient to guide day-to-day clinical practice, such as in the COVID-19
50 pandemic.[15]
51
52
53
54
55
56
57
58
59
60

1
2
3 The aim of this RAND panel was to provide clarity on the management of ASUC, as
4 defined by Truelove and Witts criteria, in the context of the COVID-19 pandemic.[10]
5
6 The panel sought to identify areas where it was appropriate to deviate from current
7 BSG ASUC guidance and consider alternative strategies.
8
9

10
11
12 We assembled a 15-person panel comprising representatives from the BSG IBD
13 Section Committee, the BSG IBD Clinical Research Group (CRG) and other
14 gastroenterologists, each from different IBD centres across the UK, as well as an IBD
15 nurse consultant (supplementary Table 1). A web-based questionnaire was created
16 and iteratively improved before being completed by all panellists prior to a moderated
17 online meeting. We circulated a list of relevant publications with the questionnaire,
18 comprising the current BSG guidelines on the management of ASUC[6] along with up
19 to date publications about COVID-19 in general and specifically in relation to IBD. Due
20 to the rapid growth of available data, the panel used a range of instant messaging
21 services to disseminate publications that were not available at the time of the initial
22 literature review.
23
24
25
26
27
28
29
30
31

32
33
34 Panellists rated the appropriateness of management options at five different time
35 points during the course of admission for ASUC (admission, first line therapy, rescue
36 therapy, continued medical therapy and surgery) in the context of absence of, or
37 varying severity of SARS-CoV-2 infection. They were asked to grade the
38 appropriateness of specific interventions on a scale of 1-9 (where 1-3 is inappropriate,
39 4-6 is uncertain and 7-9 is appropriate). The responses were summarised and
40 anonymised before being presented at a virtual meeting in May 2020 with the aim of
41 allowing discussion which ensured a common understanding of the questions and
42 which focussed on areas of disagreement, without trying to force consensus. Also
43 present at the meeting were non-voting specialists who provided expert opinion with
44 regards to IBD surgery (PT, LH), rheumatology (JG), intensive care (MG), respiratory
45 medicine (FC) and infectious diseases (AU). In practice, several specialities may
46 provide expert opinion in COVID-19 management, including intensivists, respiratory
47 physicians and infectious disease physicians. We, therefore, used the encompassing
48 term "COVID-19 specialist" to represent this group. Finally, the Chairs of the BSG IBD
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Section Committee (IA) and the BSG IBD Clinical Research Group (CL) were also
4 present. The moderators (PI, MS) neither expressed opinions on management nor
5 voted, but were experts both in RAND panels and in the management of IBD. After the
6 meeting, a second online survey comprising 91 questions, which had been slightly
7 modified from the initial questionnaire following discussion at the meeting, was
8 circulated for completion.
9
10
11
12
13

14
15
16 Several assumptions were made for clarity. First, patients were assumed to have a
17 confirmed diagnosis of UC with intercurrent gastrointestinal infection having been
18 excluded. Second, if this was not an index presentation, patients were assumed to
19 have received optimised 5-aminosalicylic acid (5-ASA) therapy prior to admission and
20 were also presumed to be biologic-naïve. In addition, where ciclosporin was suggested
21 as an option, it was assumed that the patient was thiopurine-naïve. Third, other than
22 those areas addressed in the survey, the management of ASUC was assumed to be in
23 line with BSG guidance.[6] Finally, where steroid weaning or discontinuation was
24 considered, it was assumed that patients could safely stop steroids without the risk of
25 Addisonian crisis.
26
27
28
29
30
31
32
33
34
35

36 In addition, in the section about first line medical therapy, panellists assumed patients
37 were not steroid refractory. For the rescue therapy section, patients were assumed to
38 have ongoing acute severe colitis despite 3 days of intravenous corticosteroid therapy
39 and had reached standard criteria for rescue therapy.[16] For the continuing medical
40 therapy section, patients were assumed to have responded to intravenous
41 corticosteroids sufficiently to switch to oral prednisolone and were ready to be
42 discharged from hospital. Lastly, as per RAND methodology, respondents were
43 advised to make decisions without considering local availability of treatments or cost.
44
45
46
47
48
49
50
51

52 Analysis

53
54
55 For each scenario, median scores were calculated with a score of <3.5 being
56 considered inappropriate, ≥3.5 but <6.5 uncertain, and ≥6.5 appropriate. We used the
57 validated RAND disagreement index (DI) to define disagreement amongst panellists
58
59
60

using the equation outlined below.[14] A $DI \geq 1$ denotes disagreement. Any scenario in which disagreement was found was scored as uncertain, regardless of the median score.

$$DI = \frac{70\%ile - 30\%ile}{2.35 + \left(1.5 \times \text{abs}\left(5 - \frac{70\%ile + 30\%ile}{2}\right)\right)}$$

Results

Overall Results

Of the 91 clinical scenarios, panellists rated 28 as appropriate, 19 as uncertain and 44 as inappropriate. After the second round of voting, agreement was present for all scenarios ($DI < 1$). The key findings are summarised below and their relationship to current BSG guidance is highlighted in figure 1. A detailed list of all scenarios, complete with median score, appropriateness rating and DI can be found in supplementary Table 2.

Indications for investigations, inpatient isolation and specialist referral

(Table 1)

The panellists agreed that all patients admitted to hospital with ASUC should have a SARS-CoV-2 swab performed on admission. If the result was negative it was deemed appropriate to repeat the swab at the point of requiring rescue therapy and/or surgery to exclude subclinical infection. It was also considered appropriate to isolate all patients throughout their hospital stay, irrespective of their COVID-19 status.

It was rated appropriate to perform a flexible sigmoidoscopy within 24 hours of admission. If a patient had not had a flexible sigmoidoscopy on admission, it was considered appropriate that one should be performed prior to rescue therapy or colectomy. Repeating this test at these timepoints was deemed unnecessary in patients who had already had a flexible sigmoidoscopy performed.

1
2
3 Routine computed tomography (CT) scanning of the abdomen/pelvis on admission (in
4 addition to abdominal X-ray) was deemed inappropriate. However, the
5 appropriateness of routine chest CT on admission was rated as uncertain. The one
6 scenario in which a CT scan of the chest was felt to be appropriate for all patients
7 irrespective of COVID-19 status was in the context of patients requiring colectomy.
8
9

10
11
12
13
14 Throughout the scenarios, the panellists considered the appropriateness of discussion
15 with COVID-19 specialists. In patients without symptoms or signs of COVID-19 and
16 with a negative swab this was deemed inappropriate if receiving first line therapy but
17 uncertain in patients requiring rescue therapy. However, it was considered
18 appropriate in all patients with a positive swab, irrespective of the presence of
19 symptoms or signs of COVID-19.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

	On admission	Prior to Rescue therapy	Prior to colectomy
Inpatient Isolation	All patients		
SARS-CoV-2 swab	Perform in all patients	Repeat swab if initial swab negative	Repeat swab if initial swab negative
Flexible sigmoidoscopy	≤24h admission	If not performed	If not performed
		If already performed	If already performed
CT chest	Perform in all patients		Perform in all patients
CT abdomen & pelvis	Perform in all patients		

Table 1. Appropriateness of patient isolation and investigation in patients admitted with acute severe ulcerative colitis in the context of the COVID-19 pandemic. (Green is considered appropriate, yellow uncertain and red inappropriate).

Initial Treatment of ASUC (Table 2)

As per BSG guidance, intravenous hydrocortisone, 100mg, four times per day (or equivalent) was rated appropriate as the initial management of patients presenting with ASUC in the absence of symptoms and signs of COVID-19 pneumonia. In patients with COVID-19 pneumonia, use of hydrocortisone was deemed uncertain. Other possible treatments (poorly bioavailable oral steroids e.g. budesonide multi-matrix (MMX) and beclometasone modified release, infliximab either with or without steroids, ciclosporin or tofacitinib) were considered inappropriate. The exception was infliximab (without steroids) which was considered uncertain in patients with a positive swab for SARS-CoV-2, either with or without signs of COVID-pneumonia. Ambulatory outpatient management with daily intravenous methylprednisolone was rated as inappropriate in all patients with ASUC regardless of SARS-CoV-2 status, as was management by immediate colectomy unless complications mandating emergency surgery were present such as toxic megacolon, perforation or severe haemorrhage.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

	First line medical therapy				
Negative COVID swab WITHOUT respiratory symptoms	*Inpatient IV steroids	❖ Poorly bioavailable steroids	IFX alone	Tofacitinib	^Discussion with COVID-19 specialist
	**Ambulatory IV steroids	IV steroids* + IFX	Ciclosporin	Colectomy	
Positive COVID swab WITHOUT respiratory symptoms or signs of COVID pneumonia	*Inpatient IV steroids	❖ Poorly bioavailable steroids	IFX alone	Tofacitinib	^Discussion with COVID-19 specialist
	**Ambulatory IV steroids	IV steroids* + IFX	Ciclosporin	Colectomy	
Positive COVID swab WITH symptoms or signs of COVID pneumonia	*Inpatient IV steroids	❖ Poorly bioavailable steroids	IFX alone	Tofacitinib	^Discussion with COVID-19 specialist
	**Ambulatory IV steroids	IV steroids* + IFX	Ciclosporin	Colectomy	

Table 2. Appropriateness of treatment options in acute severe ulcerative colitis in the context of the COVID-19 pandemic: First line medical therapy. (Green is considered appropriate, yellow uncertain and red inappropriate). *Steroids, intravenous (IV) hydrocortisone 100mg QDS or IV methylprednisolone 60mg daily as an inpatient; **IV Methylprednisolone 60mg daily as an outpatient; ❖Budesonide MMX 9 mg/beclometasone 5 mg OD PO as an inpatient; IFX, Infliximab (either 5mg/kg or 10mg/kg); ^Discussion with appropriate COVID-19 specialist as per local availability.

Rescue therapy (Table 3)

In patients meeting criteria for escalation of management at day 3, it was considered inappropriate to avoid rescue therapy by continuing monotherapy with intravenous corticosteroids, irrespective of COVID status. Instead, the panellists deemed that following standard BSG guidance by initiating infliximab and continuing steroids was appropriate, whereas treatment with infliximab in conjunction with immediate steroid withdrawal was deemed uncertain. The BSG guidelines also recommend ciclosporin as an alternative rescue therapy. However, the RAND panel voted that ciclosporin, either with or without ongoing steroids, was inappropriate in all scenarios other than in patients with a negative SARS-CoV-2 swab in whom it was rated uncertain. Finally, colectomy without rescue therapy was deemed inappropriate in all of the scenarios considered by the panel. However, once colectomy became necessary, for example where rescue therapy had failed or when complications had occurred, it was deemed inappropriate to delay surgery, even in patients with COVID-19 pneumonia.

	Rescue therapy				Failure of Rescue Therapy
Negative COVID swab WITHOUT respiratory symptoms	Continue IV steroids alone	IFX + steroids	IV ciclosporin + steroids	Colectomy	Delay surgery
		IFX, stop steroids	IV ciclosporin, stop steroids	^Discussion with COVID-19 specialist	
Positive COVID swab WITHOUT respiratory symptoms or signs of COVID pneumonia	Continue IV steroids alone	IFX + steroids	IV ciclosporin + steroids	Colectomy	
		IFX, stop steroids	IV ciclosporin, stop steroids	^Discussion with COVID-19 specialist	
Positive COVID swab WITH symptoms or signs of COVID pneumonia	Continue IV steroids alone	IFX + steroids	IV ciclosporin + steroids	Colectomy	
		IFX, stop steroids	IV ciclosporin, stop steroids	^Discussion with COVID-19 specialist	

Table 3. Appropriateness of treatment options in acute severe ulcerative colitis in the context of the COVID-19 pandemic: Rescue therapy. (Green is considered appropriate, yellow uncertain and red inappropriate). Steroids, Intravenous (IV) hydrocortisone 100mg QDS or IV methylprednisolone 60mg daily as an inpatient; IFX: Infliximab (either 5mg/kg or 10mg/kg); ^Discussion with appropriate COVID-19 specialist as per local availability.

Continuing medical therapy (Table 4)

The ongoing management of patients who had responded to intravenous corticosteroids and were ready for discharge on oral steroids was also considered. In patients with a negative SARS-CoV-2 swab, or with a positive swab but without signs or symptoms of pneumonia, steroid tapering over 6-8 weeks as per BSG guidance was deemed appropriate. However, in patients with COVID-19 pneumonia it was rated uncertain. Accelerated steroid withdrawal over 4-6 weeks was rated appropriate regardless of COVID-19 status. More rapid withdrawal over 4 weeks was deemed inappropriate except in patients with COVID-19 pneumonia, in whom it was rated uncertain. The use of poorly bioavailable oral steroids as an alternative to a standard steroid taper was rated as inappropriate in all scenarios

Initiation of additional therapy prior to, or soon after discharge to prevent relapse was also considered. Following BSG guidance by initiating a thiopurine was rated uncertain in SARS-CoV-2 swab-negative patients, and inappropriate in swab-positive patients. Use of biological therapy (anti-tumour necrosis factor (TNF), ustekinumab or vedolizumab) was deemed appropriate in swab-negative patients. In all other patients, the appropriateness of biological therapy was uncertain, except for anti-TNF therapy in patients with a positive swab but without pneumonia in whom treatment was rated as appropriate. Tofacitinib was generally rated as inappropriate except in swab-negative patients in whom it was rated uncertain.

Finally, panellists were asked whether patients should be discharged with a period of ongoing prophylactic anticoagulation. This was deemed appropriate in patients who had a positive SARS-CoV-2 swab regardless of whether they had pneumonia but was rated uncertain in those who had negative swabs.

	Continuing medical therapy [∞]				
Negative COVID swab WITHOUT respiratory symptoms	Standard steroid taper	Accelerated steroid taper <4 weeks	°Thiopurine	°Ustekinumab	°Tofacitinib
	Accelerated steroid taper 4-6 weeks	◆Poorly bioavailable steroids	°Anti-TNF	°Vedolizumab	⊙Thromboprophylaxis
Positive COVID swab WITHOUT respiratory symptoms or signs of COVID pneumonia	Standard steroid taper	Accelerated steroid taper <4 weeks	°Thiopurine	°Ustekinumab	°Tofacitinib
	Accelerated steroid taper 4-6 weeks	◆Poorly bioavailable steroids	°Anti-TNF	°Vedolizumab	⊙Thromboprophylaxis
Positive COVID swab WITH symptoms or signs of COVID pneumonia	Standard steroid taper	Accelerated steroid taper <4 weeks	°Thiopurine	°Ustekinumab	°Tofacitinib
	Accelerated steroid taper 4-6 weeks	◆Poorly bioavailable steroids	°Anti-TNF	°Vedolizumab	⊙Thromboprophylaxis

Table 4. Appropriateness of treatment options in acute severe ulcerative colitis in the context of the COVID-19 pandemic: Continuing medical therapy. (Green is considered appropriate, yellow uncertain and red inappropriate). [∞]Patient has responded to intravenous steroid therapy; ◆Switch from corticosteroids to budesonide MMX 9 mg daily/beclometasone 5 mg daily; °Steroid taper and start additional therapy at or soon after discharge; ⊙Continue for a period after discharge.

Discussion

General Considerations

The recent International Organisation For the Study of Inflammatory Bowel Disease (IOIBD) RAND appropriateness panel addressing the use of medications to treat IBD in the COVID-19 era did not specifically address the management of patients with ASUC.[17] To date, there has been no consensus on how to manage this condition during the COVID-19 pandemic; in the context of a limited, although rapidly evolving evidence base, this is perhaps unsurprising.[18] Thus, there is an urgent need for guidance on how best to manage ASUC in the current setting. Several areas need consideration in this regard including: the effect of SARS-CoV-2 on the activity and course of IBD; the effect of IBD and its activity on the risk of being infected with SARS-CoV-2 and the progression to COVID-19; the interaction of SARS-CoV-2/COVID-19 with the drugs used to treat IBD; and the possible effects of treatments for COVID-19 on IBD.

SARS-CoV-2 is found in the gut and RNA is measurable in the stool significantly longer than in serum or respiratory samples [19] although the significance of this is unclear. The effects of the virus on the intestinal mucosa remain undefined, as does its interaction with inflamed tissue.[20] Gastrointestinal symptoms including diarrhoea occur in around 30% of patients and have been associated with worse outcome [21,22] and a single report describes a possible case of COVID-19 colitis.[23]

Currently, it is not clear whether IBD-specific factors lead to worse outcomes in patients who develop COVID-19. In the Italian series of 79 patients with IBD and COVID-19, active disease was associated with the risk of COVID-19 pneumonia even after controlling for other risk factors.[12] Furthermore, active IBD was also significantly associated with increased hospitalisation, the need for respiratory support and death. In contrast, in Bergamo, Northern Italy, an observational study reported no cases of COVID-19 in 522 patients with IBD.[24] Whilst there are data that

1
2
3 suggest that active IBD increases the risk of some viral infections,[25] it is difficult to
4 draw firm conclusions with regard to SARS-CoV-2 infection given the limited data
5 available.
6
7
8
9

10 Of concern to most clinicians caring for patients with IBD is the possible risk of the
11 drugs used to manage ASUC in the context of the COVID-19 pandemic. Intravenous
12 corticosteroids remain the most widely used induction therapy in ASUC [26], but it is
13 uncertain how they may influence outcome in patients with SARS-CoV-2 infection and
14 COVID-19. Corticosteroids are known to increase the risk of sepsis and respiratory
15 tract infections and may also increase viral replication and susceptibility to SARS-CoV-
16 2.[27,28] There is also evidence that steroids may increase morbidity and/or mortality
17 from some respiratory viruses such as influenza, Middle Eastern Respiratory
18 Syndrome (MERS) and SARS-CoV,[27,29–31] although steroids have an established
19 role in the management of ARDS.[32] Beyond corticosteroids, immunomodulators
20 such as thiopurines, biologics and tofacitinib are frequently used at various stages of
21 the management of ASUC and there is also a lack of data regarding their safety in the
22 context of the SARS-CoV-2 pandemic. Finally, it is important to consider the possible
23 effects of drugs used to manage COVID-19 on IBD. For example, interleukin-6
24 inhibitors are being tested in patients with COVID-19 (ClinicalTrials.gov Identifier:
25 NCT04315298) but have been associated with intestinal perforation in IBD.
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

41 We used an established methodology, a RAND appropriateness panel, to produce
42 guidance in this challenging clinical area. Regarding initial management, there was
43 agreement that all patients with ASUC should be managed as inpatients. Ambulatory
44 care was considered inappropriate, since patients with ASUC need regular monitoring
45 and involvement of a multi-disciplinary team, this type of complex care being difficult
46 to deliver in the out-patient setting. Whilst there was some support for ambulatory
47 management to avoid patients being admitted, thereby decreasing the risk of
48 nosocomial acquisition of SARS-CoV-2, the risks of managing ASUC as an outpatient
49 were considered to outweigh this possible benefit. Furthermore, in scenarios in which
50 patients had confirmed SARS-CoV-2 infection, no such benefit existed. Nevertheless,
51 in view of the acknowledged risk of contracting SARS-CoV-2 infection in hospital, it is
52
53
54
55
56
57
58
59
60

perhaps unsurprising that the panel considered it appropriate to isolate patients with ASUC in a side room wherever possible.

The panel deemed it uncertain whether a CT chest should be performed in all patients on admission. While a CT chest is more sensitive than a chest x-ray (CXR) in detecting signs of early or limited infection, the COVID-19 specialists advised that a CXR would suffice in asymptomatic patients on admission. However, The Royal College of Radiologists has advised a low dose CT chest should be performed in patients who are having a CT abdomen as part of the investigation of an abdominal emergency.[33–35]

It was considered appropriate to involve a COVID-19 specialist in all scenarios in the presence of a positive SARS-CoV-2 swab, regardless of signs or symptoms of COVID-19 pneumonia. The panel was uncertain whether this was required in patients with a negative SARS-CoV-2 swab who required rescue therapy. During the meeting, concern was expressed by some panellists about the possible effects of corticosteroids and rescue therapies on SARS-CoV-2 infection and COVID-19 pneumonia driving the need to seek clarification from COVID experts and highlighting the need for further research.

First Line Therapy

It was considered appropriate to follow the BSG guidelines on the initial management of ASUC in patients without signs or symptoms of COVID-19, regardless of SARS-CoV-2 swab results. Only in patients with COVID-19 pneumonia was there uncertainty amongst the panel regarding the appropriateness of conventional therapy with intravenous corticosteroids, largely driven by concerns of possible harm. However, it should be noted that in this challenging condition in which there is scant experience and almost no published data in relation to COVID-19, of all suggested treatments, intravenous corticosteroids were given the highest median score by the panel. Regarding the ongoing uncertainty about the benefits or harms of corticosteroids in patients with COVID-19 pneumonia and the inconclusive data emerging from the current coronavirus pandemic, the results of the adaptive trial, RECOVERY, which

1
2
3 includes a dexamethasone arm, are eagerly awaited.[1] Nevertheless, leaving ASUC
4 untreated is associated with a high risk of death, mortality being at least 24% in the
5 days before the use of corticosteroids.[26] The expert advisers supported the WHO
6 position that steroid use should not be avoided because of theoretical risks in patients
7 with COVID-19.[36]
8
9
10
11

12
13
14 The panel was uncertain whether infliximab, without concurrent corticosteroids,
15 should be used as a first line therapy in patients who are SARS-CoV-2 positive,
16 regardless of whether they had COVID-19. As with corticosteroids, the risk of anti-TNF
17 in the context of the pandemic is unknown. In addition, there is no high-quality
18 evidence for infliximab in ASUC other than as a rescue therapy following corticosteroid
19 failure. Anti-TNF agents are known to increase the risk of respiratory tract and other
20 opportunistic infections,[37] particularly when used in association with thiopurines
21 and corticosteroids.[38] However, anti-TNF therapies are currently being evaluated in
22 clinical trials [39] as a potential treatment for COVID-19-induced cytokine 'storm'
23 [40,41]. In view of the uncertainty of the effects of corticosteroids and infliximab on
24 SARS-CoV-2 infection, it was considered appropriate that all patients with a positive
25 swab should be discussed with a COVID-19 specialist to guide decision making.
26
27
28
29
30
31
32
33
34
35
36
37

38 Rescue Therapy

39
40 Up to half of patients with ASUC fail first line medical therapy with corticosteroids.[6]
41 In all scenarios, it was considered inappropriate to continue this treatment alone in
42 the face of non-response at day 3, consistent with current BSG guidelines.[6] Similarly,
43 in line with BSG guidance, it was considered appropriate to commence infliximab
44 whilst continuing corticosteroids regardless of SARS-CoV-2 status. Discontinuation of
45 corticosteroids at the point of commencing infliximab rescue therapy was considered
46 of uncertain appropriateness across all scenarios, as it may result in worsening colitis,
47 whilst acknowledging the potential risks of combining the two drugs. Ciclosporin
48 rescue therapy was generally considered inappropriate, due in part to concerns about
49 the risks of drug-induced nephrotoxicity given the frequency of acute kidney injury in
50 SARS-CoV-2 infection.[42] In addition, the infusion regimen requires frequent
51
52
53
54
55
56
57
58
59
60

1
2
3 healthcare worker-patient contact which could, in theory, increase the risk of
4 transmission. The panel did not explore its use in settings in which infliximab may be
5 relatively contraindicated, such as previous loss of response to infliximab, drug
6 immunogenicity or when relevant co-morbidities exist, such as multiple sclerosis.
7 Similarly, the panel did not specifically address the question of whether infliximab was
8 used as a monotherapy or in combination with an immunomodulator.
9
10
11
12
13

14
15
16 There is little evidence regarding the risks of surgical management in patients with
17 COVID-19. Preliminary data demonstrate a substantial increase in morbidity and
18 mortality amongst SARS-CoV-2-infected patients undergoing surgery (*personal
19 communication, submitted for publication*). In one report, 34 patients underwent
20 elective surgery in Wuhan, China with all developing COVID-pneumonia, 7 of whom
21 (20%) died.[9] Accordingly, the risks of surgery drove the rating of colectomy as first
22 line therapy, or as an alternative to rescue therapy, as being inappropriate. However,
23 in patients failing medical therapy, there was consensus that delaying surgery would
24 be inappropriate.
25
26
27
28
29
30
31
32
33

34 Continuing Medical Therapy

35
36
37 The BSG IBD guidelines recommend corticosteroid tapering over 6-8 weeks which was
38 considered appropriate by the panel, except in the context of COVID-19 pneumonia
39 where an accelerated taper over 4-6 weeks was considered appropriate instead. A
40 more accelerated taper, over fewer than 4 weeks, was generally deemed
41 inappropriate due to the high risk of relapse in this cohort.[6] Regarding initiation of
42 maintenance therapy either before or shortly after discharge from hospital, it was
43 considered appropriate to start anti-TNF, vedolizumab or ustekinumab in patients
44 with negative swabs. However, in scenarios in which patients had positive swabs, with
45 or without evidence of COVID-19 pneumonia, there was uncertainty about the risk:
46 benefit ratio of biologic therapy, driven by the lack of evidence. Thus, biologic use in
47 this situation was deemed uncertain in nearly all scenarios.
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Thiopurines and tofacitinib were not considered appropriate at any stage during the
4 scenarios. This is despite the BSG recommendation that thiopurines should be
5 initiated at or soon after discharge following successful treatment of ASUC.[6]
6
7 Azathioprine therapy was in part considered inappropriate due to possible side effects
8 such as pancreatitis, which could result in readmission to hospital, and drug
9 hypersensitivity, which can manifest as a flu-like syndrome which may potentially be
10 confused with COVID-19.[43] Azathioprine can also induce significant lymphopaenia
11 [43] which may mimic the lymphopaenia seen in SARS-CoV-2 infection. How this
12 affects outcome of COVID-19 is unclear; some reports even suggest a theoretical
13 benefit of thiopurines.[44,45] The additional monitoring required when azathioprine
14 is initiated may also be a challenge with COVID-19-related service reconfiguration and
15 antecedent risks of SARS-CoV-2 acquisition posed by the requirement for face-to-face
16 contact from laboratory monitoring.
17
18
19
20
21
22
23
24
25
26
27
28

29 Tofacitinib is a non-selective Janus kinase (JAK) inhibitor which is associated with
30 herpes zoster viral reactivation and, like COVID-19, is also associated with an increased
31 risk of deep vein thrombosis.[46] There is also very limited evidence for its use in the
32 setting of ASUC.[47] For these reasons, the panel considered its use inappropriate in
33 nearly all settings although it was noted that its rapid offset of action could be of
34 theoretical benefit.
35
36
37
38
39
40

41 Anticoagulation

42
43
44 Prophylactic anticoagulation was considered appropriate beyond discharge amongst
45 patients with a positive SARS-CoV-2 swab, although this strategy was deemed
46 uncertain in people with negative swabs. Like ASUC, COVID-19 is strongly linked to a
47 hypercoagulable state with substantially increased risk of microthrombi and venous
48 thromboembolism (VTE).[48] It is notable that the British Thoracic Society
49 recommends doubling the dose of anticoagulation and/or prescribing VTE prophylaxis
50 (low molecular weight heparin or direct oral anticoagulant) for up to 4 weeks following
51 discharge in high risk patients with COVID-19.[49]
52
53
54
55
56
57
58
59
60

Strengths & Limitations

The strengths of our study include the inclusion of a diverse group of IBD experts drawn from a wide range of UK centres as well as non-gastroenterology specialists with experience in managing patients with COVID-19. In addition, we used the RAND methodology which is a validated technique to guide decision making in the absence of a robust evidence base. It is not necessarily an attempt to reach consensus but rather to guide clinicians as to the appropriateness or inappropriateness of interventions, whilst accepting that uncertainty is also a valid outcome, which was highly appropriate in this setting. It was impossible for our scenarios to encompass fully all cases encountered in clinical practice. We, therefore, focussed on principles that may help to guide decision making in most cases of ASUC in the context of COVID-19. We appreciate that by doing so, this guidance may not be directly applicable to more nuanced cases where decision making may be influenced by a myriad of factors. Nor was every aspect of care considered; for example, the question of repeating testing for Clostridium difficile prior to colectomy in view of higher exposure to antibiotics in the COVID-19 era, was not addressed. The outcomes should, therefore, be considered an adjunct to multidisciplinary decision-making rather than a replacement. Finally, knowledge within the field remains fast moving such that it will be important to stay abreast of new developments as they arise.

Implications and concluding remarks

By combining clinical expertise from the BSG CRG and IBD Section Committee in conjunction with other medical and surgical IBD and COVID-19 experts, we have provided guidance to clinicians regarding the appropriate management of ASUC during the COVID-19 pandemic, highlighting where current BSG guidance may need adaptation. Population-based studies are needed to clarify the risks and benefits of interventions used in the management of ASUC during the pandemic. Until then, we consider the results of the panel, which largely support following the well-established and evidence-based BSG guideline, will help guide clinicians in this challenging and evolving area.

Acknowledgments

The authors would like to acknowledge the input of Professor Jon Rhodes for his helpful comments and suggestions.

Funding The authors have declared no funding for this research

Competing interests Please see supplementary table 3

References

- 1 Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;**395**:497–506.
doi:10.1016/S0140-6736(20)30183-5
- 2 Johns Hopkins University. Johns Hopkins Coronavirus Resource Center. 2020.<https://coronavirus.jhu.edu/> (accessed 8 May 2020).
- 3 The OpenSAFELY Collaborative, Williamson E, Walker AJ, *et al*. OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *medRxiv* Published Online First: 7 May 2020. doi:10.1101/2020.05.06.20092999
- 4 Turner D, Walsh CM, Steinhart AH, *et al*. Response to Corticosteroids in Severe Ulcerative Colitis: A Systematic Review of the Literature and a Meta-Regression. *Clin Gastroenterol Hepatol* 2007;**5**:103–10.
doi:10.1016/j.cgh.2006.09.033
- 5 Seah D, De Cruz P. Review article: the practical management of acute severe

- 1
2
3 ulcerative colitis. *Aliment Pharmacol Ther* 2016;**43**:482–513.
4
5 doi:10.1111/apt.13491
6
7
8
9 6 Lamb CA, Kennedy NA, Raine T, *et al.* British Society of Gastroenterology
10 consensus guidelines on the management of inflammatory bowel disease in
11 adults. *Gut* 2019;**68**:s1–106. doi:10.1136/gutjnl-2019-318484
12
13
14
15
16 7 Rubin DT, Abreu MT, Rai V, *et al.* Management of Patients with Crohn’s
17 Disease and Ulcerative Colitis During the COVID-19 Pandemic: Results of an
18 International Meeting. *Gastroenterology* Published Online First: April 2020.
19
20
21
22
23
24
25 8 Kirchgesner J, Lemaitre M, Carrat F, *et al.* Risk of Serious and Opportunistic
26 Infections Associated With Treatment of Inflammatory Bowel Diseases.
27
28
29
30
31
32
33 9 Lei S, Jiang F, Su W, *et al.* Clinical characteristics and outcomes of patients
34 undergoing surgeries during the incubation period of COVID-19 infection.
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60 10 Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a
therapeutic trial. *Br Med J* 1955;**2**:1041–8.

11 SECURE-IBD. SECURE-IBD Registry: Surveillance Epidemiology of Coronavirus
(COVID-19) Under Research Exclusion. 2020.[https://covidibd.org/updates-
and-data/](https://covidibd.org/updates-and-data/)

12 Bezzio C, Saibeni S, Variola A, *et al.* Outcomes of COVID-19 in 79 patients with
IBD in Italy: an IG-IBD study. *Gut* Published Online First: 30 April 2020.
doi:10.1136/gutjnl-2020-321411

13 Rodríguez-Lago I, Ramírez de la Piscina P, Elorza A, *et al.* Characteristics and

- 1
2
3 prognosis of patients with inflammatory bowel disease during the SARS-CoV-2
4 pandemic in the Basque Country (Spain). *Gastroenterology* 2020;**0**.
5
6 doi:10.1053/j.gastro.2020.04.043
7
8
9
- 10
11 14 Fitch K, Bernstein María SJ, Aguilar D, *et al*. The RAND/UCLA Appropriateness
12 Method User's Manual. 2001.
13
14
- 15
16 15 Coulter I, Elfenbaum P, Jain S, *et al*. SEaRCH™ expert panel process:
17 streamlining the link between evidence and practice. *BMC Res Notes*
18 2016;**9**:16. doi:10.1186/s13104-015-1802-8
19
20
21
- 22
23 16 Travis SP, Farrant JM, Ricketts C, *et al*. Predicting outcome in severe ulcerative
24 colitis. *Gut* 1996;**38**:905–10. doi:10.1016/j.dld.2004.03.002
25
26
27
- 28
29 17 Rubin DT, Abreu MT, Rai V, *et al*. Management of Patients with Crohn's
30 Disease and Ulcerative Colitis During the COVID-19 Pandemic: Results of an
31 International Meeting. *Gastroenterology* Published Online First: April 2020.
32
33 doi:10.1053/j.gastro.2020.04.002
34
35
36
- 37
38 18 Al-Ani A, Prentice R, Rentsch C, *et al*. Review Article: Prevention, Diagnosis
39 and Management of COVID-19 in the Inflammatory Bowel Disease Patient.
40 *Aliment Pharmacol Ther* Published Online First: 29 April 2020.
41
42 doi:10.1111/apt.15779
43
44
45
- 46
47 19 Zheng S, Fan J, Yu F, *et al*. Viral load dynamics and disease severity in patients
48 infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020:
49 retrospective cohort study. *BMJ* 2020;;m1443. doi:10.1136/bmj.m1443
50
51
52
- 53
54 20 Ding S, Liang TJ. Journal Pre-proof Is SARS-CoV-2 Also an Enteric Pathogen
55 with Potential Fecal-Oral Transmission: A COVID-19 Virological and Clinical
56 Review. *Gastroenterology* Published Online First: 2020.
57
58 doi:10.1053/j.gastro.2020.04.052
59
60

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- 21 Pan L, Mu M, Yang P, *et al.* Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. *Am J Gastroenterol* 2020;**115**:766–73. doi:10.14309/ajg.0000000000000620
- 22 Mao R, Qiu Y, He J-S, *et al.* Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* Published Online First: May 2020. doi:10.1016/S2468-1253(20)30126-6
- 23 Carvalho A, Alqusairi R, Adams A, *et al.* SARS-CoV-2 Gastrointestinal Infection Causing Hemorrhagic Colitis. *Am J Gastroenterol* 2020;:1. doi:10.14309/ajg.0000000000000667
- 24 Norsa L, Indriolo A, Sansotta N, *et al.* Uneventful course in IBD patients during SARS-CoV-2 outbreak in northern Italy. *Gastroenterology* Published Online First: April 2020. doi:10.1053/j.gastro.2020.03.062
- 25 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 Eur Gastroenterol J* Published Online First: 2019. doi:10.1177/2050640619889763
- 26 Truelove SC, Witts LJ. Cortisone in Ulcerative Colitis. *BMJ* 1955;**2**:1041–8. doi:10.1136/bmj.2.4947.1041
- 27 Van Kerkhove MD, Vandemaele KAH, Shinde V, *et al.* Risk Factors for Severe Outcomes following 2009 Influenza A (H1N1) Infection: A Global Pooled Analysis. *PLoS Med* 2011;**8**:e1001053. doi:10.1371/journal.pmed.1001053
- 28 Lee N, Allen Chan KC, Hui DS, *et al.* Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients. *J*

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- Clin Virol* 2004;**31**:304–9. doi:10.1016/j.jcv.2004.07.006
- 29 Arabi YM, Mandourah Y, Al-Hameed F, *et al.* Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med* 2018;**197**:757–67. doi:10.1164/rccm.201706-1172OC
- 30 Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet* 2020;**395**:473–5. doi:10.1016/S0140-6736(20)30317-2
- 31 Lansbury LE, Rodrigo C, Leonardi-Bee J, *et al.* Corticosteroids as Adjunctive Therapy in the Treatment of Influenza. *Crit Care Med* 2020;**48**:e98–106. doi:10.1097/CCM.0000000000004093
- 32 Lewis SR, Pritchard MW, Thomas CM, *et al.* Pharmacological agents for adults with acute respiratory distress syndrome. *Cochrane Database Syst Rev* Published Online First: 23 July 2019. doi:10.1002/14651858.CD004477.pub3
- 33 The Royal College of Radiologists. Statement on use of CT chest to screen for COVID-19 in pre-operative patients. 2020.<https://www.rcr.ac.uk/college/coronavirus-covid-19-what-rcr-doing/clinical-information/statement-use-ct-chest-screen-covid> (accessed 8 May 2020).
- 34 Royal College of Surgeons. Updated Intercollegiate General Surgery Guidance on COVID-19. 2020.<https://www.rcseng.ac.uk/coronavirus/joint-guidance-for-surgeons-v2/> (accessed 8 May 2020).
- 35 Ai T, Yang Z, Hou H, *et al.* Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology* 2020;**200642**. doi:10.1148/radiol.2020200642

- 1
2
3 36 World Health Organization. Clinical management of severe acute respiratory
4 infection (SARI) when COVID-19 disease is suspected.
5
6 2020.[https://www.who.int/publications-detail/home-care-for-patients-with-](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-)
7
8
9
10
11
12 37 Shah ED, Farida JP, Siegel CA, *et al.* Risk for Overall Infection with Anti-TNF and
13 Anti-integrin Agents Used in IBD. *Inflamm Bowel Dis* 2017;**23**:570–7.
14
15 doi:10.1097/MIB.0000000000001049
16
17
18
19 38 Singh S, Facciorusso A, Dulai PS, *et al.* Comparative Risk of Serious Infections
20 With Biologic and/or Immunosuppressive Therapy in Patients With
21 Inflammatory Bowel Diseases: A Systematic Review and Meta-Analysis. *Clin*
22
23
24
25
26
27
28 39 Zhou L, Xu H. A clinical study for the efficacy and safety of Adalimumab
29 Injection in the treatment of patients with severe novel coronavirus
30 pneumonia (COVID-19). Chinese Clin. Trial Regist.
31
32 2020.<http://www.chictr.org.cn/showprojen.aspx?proj=49889> (accessed 13
33
34
35
36
37
38
39 40 Feldmann M, Maini RN, Woody JN, *et al.* Trials of anti-tumour necrosis factor
40 therapy for COVID-19 are urgently needed. *Lancet* 2020;**395**:1407–9.
41
42
43
44
45
46 41 Mehta P, McAuley DF, Brown M, *et al.* COVID-19: consider cytokine storm
47 syndromes and immunosuppression. *Lancet.* 2020;**395**:1033–4.
48
49
50
51
52
53 42 Fanelli V, Fiorentino M, Cantaluppi V, *et al.* Acute kidney injury in SARS-CoV-2
54
55
56
57
58
59 43 Chaparro M, Ordás I, Cabré E, *et al.* Safety of Thiopurine Therapy in
60

- 1
2
3 Inflammatory Bowel Disease. *Inflamm Bowel Dis* 2013;**19**:1404–10.
4 doi:10.1097/MIB.0b013e318281f28f
5
6
7
8
9 44 Wu C, Chen X, Cai Y, *et al.* Risk Factors Associated With Acute Respiratory
10 Distress Syndrome and Death in Patients With Coronavirus Disease 2019
11 Pneumonia in Wuhan, China. *JAMA Intern Med* Published Online First: 13
12 March 2020. doi:10.1001/jamainternmed.2020.0994
13
14
15
16
17 45 Tan L, Wang Q, Zhang D, *et al.* Lymphopenia predicts disease severity of
18 COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther*
19 2020;**5**:33. doi:10.1038/s41392-020-0148-4
20
21
22
23
24 46 Sandborn WJ, Su C, Sands BE, *et al.* Tofacitinib as Induction and Maintenance
25 Therapy for Ulcerative Colitis. *N Engl J Med* 2017;**376**:1723–36.
26 doi:10.1056/NEJMoa1606910
27
28
29
30
31 47 Kotwani P, Terdiman J, Lewin S. Tofacitinib for rescue therapy in acute severe
32 ulcerative colitis: a real-world experience. *J Crohn's Colitis* Published Online
33 First: 5 February 2020. doi:10.1093/ecco-jcc/jjaa018
34
35
36
37
38 48 Middeldorp S, Coppens M, van Haaps TF, *et al.* Incidence of venous
39 thromboembolism in hospitalized patients with COVID-19. *Preprints.org*
40 Published Online First: 2020. doi:10.20944/preprints202004.0345.v1
41
42
43
44
45 49 British Thoracic Society. BTS Guidance on Venous Thromboembolic Disease in
46 patients with COVID-19. Br. Thorac. Soc. 2020.[https://www.brit-](https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/)
47 [thoracic.org.uk/document-library/quality-improvement/covid-19/bts-](https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/)
48 [guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/](https://www.brit-thoracic.org.uk/document-library/quality-improvement/covid-19/bts-guidance-on-venous-thromboembolic-disease-in-patients-with-covid-19/)
49 (accessed 8 May 2020).
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Confidential: For Review Only