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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

This online publication has been corrected. The corrected version first appeared at thelancet.com/gastrohep on March 11, 2021.

Supplement to: Sebastian S, Walker GJ, Kennedy NA, et al. Assessment, endoscopy, and treatment in patients with acute severe ulcerative colitis during the COVID-19 pandemic (PROTECT-ASUC): a multicentre, observational, case-control study. *Lancet Gastroenterol Hepatol* 2021; **6**: 271–81.

Supplement

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Supplementary Table 1: PROTECT-ASUC study contributors and institutions

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Blackpool Teaching Hospitals NHS Foundation Trust	Rhys Butcher Tom Riley Aye Mya Htun
Bolton NHS Foundation Trust	Salil Singh Kelly Chatten Ruth Tunney
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Leeds Teaching Hospitals NHS Trust	Christian Selinger Elaine Ong Ming San Konstantina Rosiou
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Torbay and South Devon NHS Foundation Trust	Gareth Walker Yuen-Hui Lim James Gulliver
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Supplementary Table 2: Disease severity indicators

Disease Severity Markers Median (IQR) ^a	N	COVID-19 pandemic period cohort (n = 398)	Historical control cohort (n = 384)	Significance P value
Day 1				
Day 1 stool frequency	613	10.0 (8.0 - 15.0)	10.0 (8.0 - 15.0)	0.57
Day 1 CRP	707	52.0 (17.0 - 120.0)	54.0 (23.0 - 110.0)	0.86
Day 1 haemoglobin	706	123.0 (106.0 - 136.0)	123.0 (109.0 - 137.0)	0.28
Day 1 albumin	666	35.0 (29.0 - 39.0)	37.0 (31.0 - 41.0)	0.0036
Day 1 CRP/albumin ratio	662	1.6 (0.5 - 3.6)	1.6 (0.6 - 3.3)	0.70
Day 3				
Day 3 stool frequency	450	7.0 (4.0 - 10.0)	6.0 (4.0 - 9.0)	0.21
Day 3 CRP	613	31.9 (11.0 - 72.0)	31.0 (14.5 - 60.0)	0.70
Day 3 haemoglobin	617	112.0 (98.0 - 125.0)	116.0 (101.0 - 128.2)	0.12
Day 3 albumin	527	31.0 (26.0 - 35.5)	33.0 (29.0 - 37.2)	0.0048
Day 3 CRP/albumin ratio	519	1.1 (0.3 - 2.7)	1.0 (0.4 - 2.2)	0.25
Day 5				
Day 5 stool frequency	438	5.0 (3.0 - 8.0)	4.0 (3.0 - 8.0)	0.72
Day 5 CRP	570	14.0 (5.0 - 35.0)	15.0 (6.0 - 31.5)	0.82
Day 5 haemoglobin	577	110.0 (97.8 - 125.0)	115.0 (100.0 - 127.0)	0.063
Day 5 albumin	499	31.0 (25.0 - 35.0)	32.0 (28.0 - 36.0)	0.028
Day 5 CRP/albumin ratio	493	0.5 (0.2 - 1.4)	0.5 (0.2 - 1.0)	0.60
Endoscopic assessment				
Flexible sigmoidoscopy	758	75.5% (289/383)	79.2% (297/375)	0.23
Day of endoscopic assessment median (IQR)	568	1.0 (0.0 - 3.0)	2.0 (0.0 - 3.0)	0.10
Endoscopic Severity % (n/N)	541			0.50
Mayo 1		4.9% (13/265)	6.2% (17/276)	
Mayo 2		33.2% (88/265)	36.6% (101/276)	
Mayo 3		61.9% (164/265)	56.9% (157/276)	

All values median (interquartile range) unless otherwise stated. IQR = interquartile range; CRP = C- Reactive Protein. P value = Fisher's exact test or Mann-Whitney U test for discrete and continuous variables continuous, respectively.

^a Units for variables: CRP - mg/L; albumin - g/L; haemoglobin - g/L; stool frequency - stools per 24 hours.

Supplementary Table 3: Table of post-operative complications

Variable	N	COVID-19 pandemic period cohort (n= 398)	Historic control cohort (n= 384)	Significance P value
Required emergency surgery for ASUC	764	16.5% (64/389)	13.3% (50/375)	0.26
Post-operative ITU stay required	102	31.6% (18/57)	31.1% (14/45)	1.0
Post-operative complications?	107	37.3% (22/59)	29.2% (14/48)	0.42
Gastrointestinal complication(s)	782	2.0% (8/398)	1.8% (7/384)	1.0
Wound complication(s)	782	1.3% (5/398)	0.0% (0/384)	0.062
Infective complication(s)	782	2.3% (9/398)	1.3% (5/384)	0.42
Renal and Endocrine complication(s)	782	0.3% (1/398)	0.0% (0/384)	1.0
Cardiovascular disorder(s)	782	0.0% (0/398)	0.0% (0/384)	NA
Pulmonary complication(s)	782	0.5% (2/398)	0.3% (1/384)	1.0
Neurological disorder(s)	782	0.3% (1/398)	0.0% (0/384)	1.0
Small bowel obstruction	782	0.3% (1/398)	0.0% (0/384)	1.0
Anastomotic stricture (includes peritoneal adhesions)	782	0.0% (0/398)	0.0% (0/384)	NA
Pouch leak/Pouch failure	782	0.3% (1/398)	0.0% (0/384)	1.0
Bowel perforation	782	0.3% (1/398)	0.0% (0/384)	1.0
Ileus	782	0.8% (3/398)	0.8% (3/384)	1.0
Ischaemic bowel	782	0.0% (0/398)	0.0% (0/384)	NA
GI bleeding	782	0.0% (0/398)	0.3% (1/384)	0.49
Ileostomy / colostomy complication or malfunction	782	0.3% (1/398)	0.8% (3/384)	0.37
Digestive organ disorders (includes acute hepatic failure and acute pancreatitis)	782	0.0% (0/398)	0.0% (0/384)	NA
Fistula	782	0.0% (0/398)	0.0% (0/384)	NA
Hematoma/seroma	782	0.0% (0/398)	0.0% (0/384)	NA
Wound dehiscence and Delayed wound healing	782	1.3% (5/398)	0.0% (0/384)	0.062
Iatrogenic injuries (includes foreign body accidentally left during procedure)	782	0.0% (0/398)	0.0% (0/384)	NA
Sepsis and bacteraemia	782	1.3% (5/398)	0.8% (3/384)	0.73
Abscess	782	1.0% (4/398)	0.8% (3/384)	1.0
Wound infection	782	0.3% (1/398)	0.0% (0/384)	1.0
Urinary tract infection	782	0.0% (0/398)	0.0% (0/384)	NA
Pneumonia and empyema	782	0.8% (3/398)	0.0% (0/384)	0.25
Acute renal failure	782	0.0% (0/398)	0.0% (0/384)	NA
Fluid and electrolyte disorders (includes hypokalaemia)	782	0.0% (0/398)	0.0% (0/384)	NA
Severe endocrine disorders (includes adrenal disorders, hypoglycaemic coma)	782	0.3% (1/398)	0.0% (0/384)	1.0
Retention of urine	782	0.0% (0/398)	0.0% (0/384)	NA
Thrombosis/embolism	782	0.0% (0/398)	0.0% (0/384)	NA
Myocardial infarction	782	0.0% (0/398)	0.0% (0/384)	NA
Cardiac arrest	782	0.0% (0/398)	0.0% (0/384)	NA
Hypotension or shock	782	0.0% (0/398)	0.0% (0/384)	NA
Cardiac arrhythmias (excludes tachycardia)	782	0.0% (0/398)	0.0% (0/384)	NA
Heart failure	782	0.0% (0/398)	0.0% (0/384)	NA
Bleeding	782	1.0% (4/398)	0.3% (1/384)	0.37
Haematoma	782	0.3% (1/398)	0.0% (0/384)	1.0
Infection	782	3.5% (14/398)	1.3% (5/384)	0.061
Intestinal leak	782	0.3% (1/398)	0.5% (2/384)	0.62
Rectal stump blow out	782	0.5% (2/398)	0.0% (0/384)	0.50
Ileus	782	1.3% (5/398)	0.8% (3/384)	0.73
Thromboembolism (deep vein thrombosis or pulmonary embolus)	769	0.3% (1/385)	0.0% (0/384)	1
High stoma output	769	0.5% (2/385)	0.5% (2/384)	1

Supplementary Table 4: UVA and MVA for composite endpoint of rescue therapy (including primary induction) or surgery using Day 1 and Day 3 variables

Term	Day 1 variables UVA			Day 1 variables MVA			Day 3 variables UVA			Day 3 variables MVA		
	OR	OR 95%CI	P value	OR	OR 95%CI	P value	OR	OR 95%CI	P value	OR	OR 95%CI	P value
Cohort type: historic cohort	0.60	0.43 to 0.82	0.0015	0.63	0.44 to 0.89	0.0083	0.60	0.43 to 0.82	0.0015	0.72	0.45 to 1.16	0.18
Stool frequency	1.04	1.01 to 1.07	0.017	1.04	1.00 to 1.07	0.034	1.19	1.13 to 1.26	<0.0001	1.19	1.11 to 1.27	<0.0001
Log[CRP]	1.08	0.95 to 1.22	0.23	0.95	0.77 to 1.16	0.59	1.17	1.03 to 1.34	0.020	1.04	0.81 to 1.38	0.81
Haemoglobin	1.01	1.00 to 1.01	0.10	1.01	1.00 to 1.02	0.016	1.00	1.00 to 1.01	0.30	1.02	1.01 to 1.04	0.0085
Albumin	0.96	0.94 to 0.99	0.0035	0.96	0.93 to 0.99	0.023	0.95	0.92 to 0.97	0.00029	0.93	0.89 to 0.97	0.0023
CRP/albumin	1.11	1.04 to 1.18	0.0026	1.09	0.98 to 1.22	0.14	1.00	0.96 to 1.02	0.69	0.96	0.82 to 1.01	0.55

MVA = multivariable analysis; UVA = univariable analysis; OR = odds ratio; OR 95% = 95% confidence interval for odds ratio
 Units for variables: CRP - mg/L; albumin – g/L; haemoglobin - g/L; stool frequency - stools per 24 hours

Supplementary Table 5: Details of ASUC patients testing positive for COVID-19 during or within 3 months of presentation

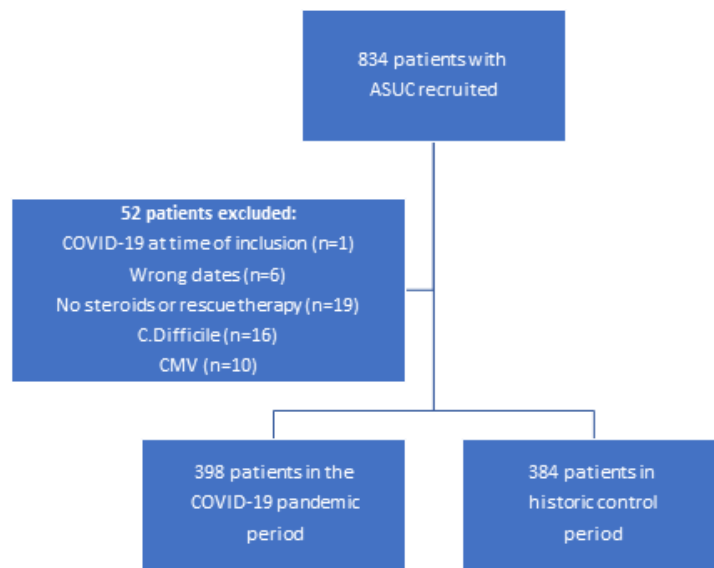
Age, gender, ethnicity	Co-morbidity	Baseline medications	Treatments for ASUC	Rescue therapy	COVID-19 PCR days from index admission, imaging changes, outcomes	Treatment during follow up
30 years, Male, Black	None	5-ASA oral 5-ASA topical	IV steroids, Oral 5-ASA	Nil	1 day, No imaging changes, No serious outcomes	Oral steroids, Azathioprine
53 years, Male, Asian	Current malignancy	No prior treatment	Oral 5-ASA, Rectal 5-ASA, IV steroids	Infliximab	1 day, No imaging changes, No serious outcomes	5-ASAs, Infliximab, Steroids
75 years, Female, White	Diabetes	No prior treatment	Oral 5-ASA, Rectal 5-ASA, IV steroids	Nil	7 days, No imaging changes, No serious outcomes	Oral steroids, Oral 5-ASAs
66 years, Female, White	Diabetes	No prior treatment	IV steroids, Oral -ASAs	Infliximab	2 days, No imaging changes, No serious outcomes	Oral 5-ASAs, Oral Steroids, Infliximab
37 years, Female White	Asthma	Oral 5-ASA Azathioprine Infliximab	IV steroids	Tofacitinib	1 day No imaging changes, No serious outcomes	Colectomy 31 days after index admission
75 years, Male, White	COPD, CVD, HTN, Obesity	Oral 5-ASA	IV steroids, Oral 5-ASA	Nil	28 days (12 days post discharge), Imaging changes, No serious outcomes	Oral steroids, Oral 5-ASAs
60 years, Male Asian	HTN Diabetes	Oral 5-ASA Azathioprine	IV steroids Oral 5-ASA	Nil	17 days (5 days post discharge) Imaging changes, No serious outcomes	Oral steroids Oral 5- ASA Infliximab

5-ASA = 5- aminosalicylic acid; COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; HTN = hypertension

Supplementary Table 6: Pre-ASUC and post-ASUC COVID-19 shielding and risk assessment

Variable	COVID-19 pandemic period cohort (N = 398)
Social distancing measures pre-ASUC	
No social distancing measures	12.6% (49/388)
Social distancing	23.7% (92/388)
Stringent social distancing	9.8% (38/388)
Shielding	20.6% (80/388)
Unknown	33.2% (129/388)
COVID-19 risk according to British Society of Gastroenterology risk grid	
Lowest	34.3% (133/388)
Moderate	26.3% (102/388)
Highest	39.4% (153/388)
Shielding in the 3-month follow up period after ASUC	
No	10.6% (31/292)
Advised to shield - unclear whether advice followed	34.9% (102/292)
Yes, confirmed to have shielded	17.5% (51/292)
Unsure	37.0% (108/292)

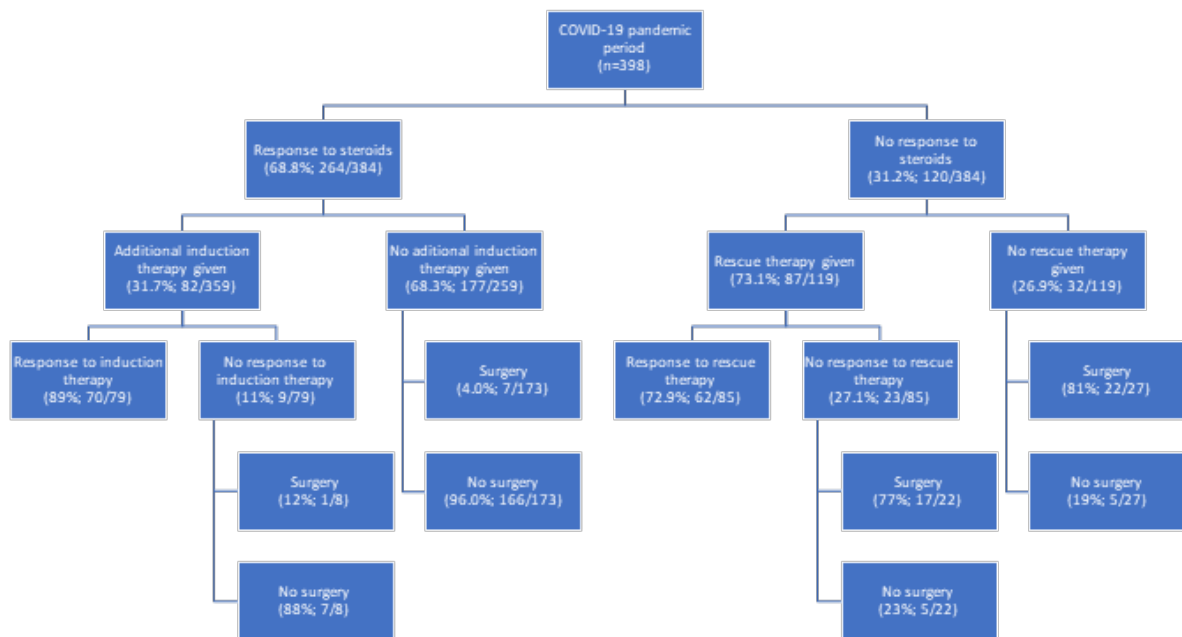
Supplementary Figure 1: Study cohorts



C. difficile = Clostridium difficile
CMV IgM positive and IgG negative inferred as acute CMV infection

Supplementary Figure 2: A. Outcomes in COVID-19 pandemic cohort and B. Historical control cohort

A



B

