Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study

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Fig. S1 – Non-CLD cohort selection

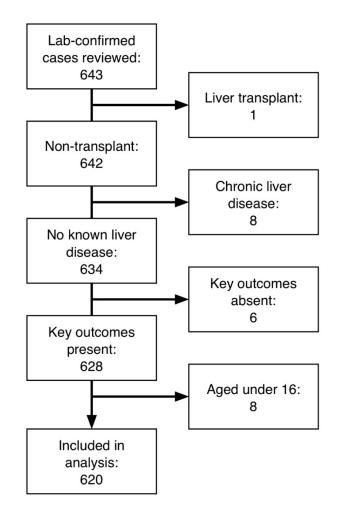


Fig. S1. Total submissions of consecutive patients testing positive for SARS-CoV-2 at Oxford University Hospitals NHS Foundation Trust and the number included in the final analysis after exclusions

Fig. S1 – Countries of origin of CLD cohort

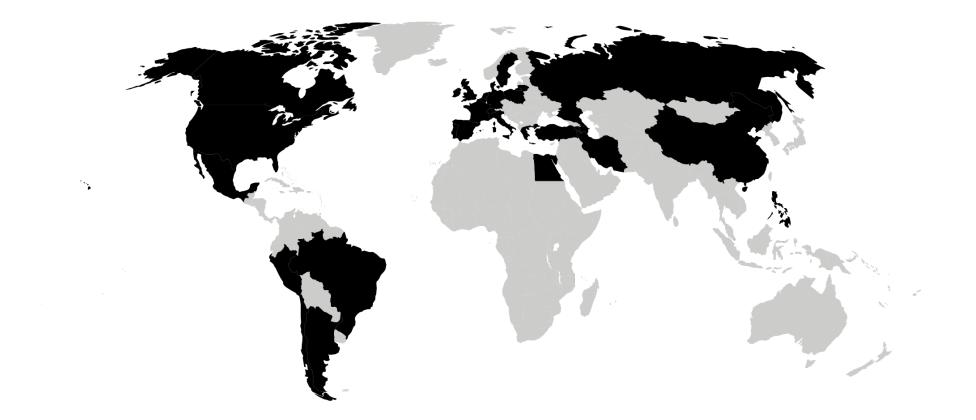


Fig. S2. World map showing countries contributing patients with CLD and SARS-CoV-2 infection between 25th March and 8th July 2020 which were included in the final analysis.

Fig. S3 – Accuracy of prognostic scores in predicting mortality in patients with cirrhosis

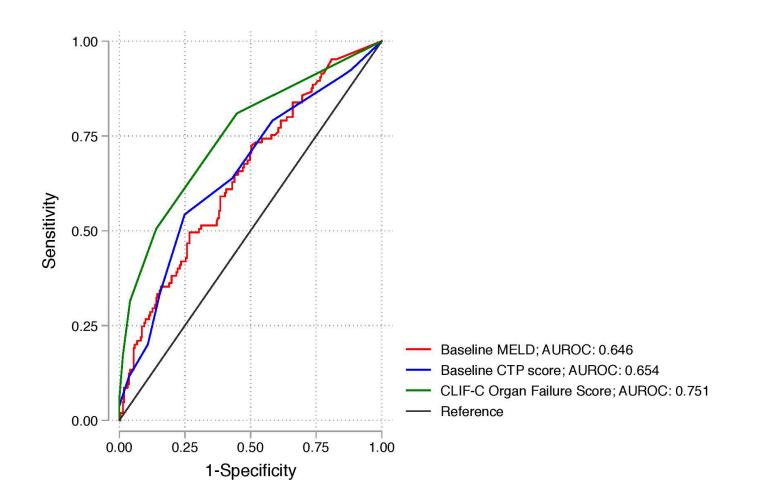


Fig. S3. Receiver operating characteristic (ROC) curves and the area under the curve (AUC) to determine the score accuracy of baseline CTP score, baseline MELD, and CLIF-C organ failure score as predictors of mortality following SARS-CoV-2 in patients with cirrhosis. AUC of baseline CTP score, baseline MELD, and CLIF-C organ failure score were 0.65, 0.64, and 0.75 respectively.

Table S1 – Submitting countries

Country	Submissions	Percentage
UK	184	24.7
USA	183	24.6
China	118	15.8
Spain	63	8.5
Singapore	30	4.0
Egypt	29	3.9
Mexico	27	3.6
Iran	18	2.4
Turkey	14	1.9
Italy	13	1.7
Sweden	11	1.5
Belgium	8	1.1
Germany	8	1.1
Canada	6	0.8
Azerbaijan	5	0.7
France	5	0.7
Peru	5	0.7
Lithuania	3	0.4
Argentina	2	0.3
Brazil	2	0.3
Ireland	2	0.3
Portugal	2	0.3
Armenia	1	0.1
Chile	1	0.1
Denmark	1	0.1
Greece	1	0.1
Philippines	1	0.1
Poland	1	0.1
Russia	1	0.1

Table S1. List of all countries contributing cases which were included in final analyses.

Table S2 – List of CLD aetiologies

Aetiology	Cases	Percentage
NAFLD	286	38.4
Alcohol	133	17.9
HBV	75	10.1
HCV	63	8.5
Other	43	5.8
AIH	42	5.6
Alcohol HCV	23	3.1
NAFLD Alcohol	15	2.0
NAFLD HBV	10	1.3
AIH PBC	7	0.9
PSC	7	0.9
HFE	6	0.8
PBC	5	0.7
Alcohol Other	4	0.5
NAFLD HCV	4	0.5
HCV HBV	3	0.4
AIH PSC	2	0.3
Alcohol HBV	2	0.3
HBV Other	2	0.3
NAFLD AIH	2	0.3
NAFLD Other	2	0.3
AIH PSC IGG4	1	0.1
Alcohol AIH	1	0.1
HCV HFE	1	0.1
HCV Other	1	0.1
NAFLD Alcohol Other	1	0.1
NAFLD HCV Other	1	0.1
NAFLD IGG4	1	0.1
PSC IGG4	1	0.1
Wilson	1	0.1

Table S2. List and relative proportions of CLD actiologies (and combination of actiologies) for cases included in the final analyses. NAFLD= non-alcoholic fatty liver disease; HBV = chronic hepatis B virus infection; HCV = chronic hepatitis C virus infection; AIH = autoimmunehepatitis; PSC = primary sclerosing cholangitis; HFE = HFE-related hereditary haeochromatosis; PBC = primary biliary cholangitis; IGG4= IgG4 related disease

Table S3 – Patient characteristics of the total CLD cohort co	ompared to the non-CLD cohort.
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	CLD	Non-CLD	p value
	n = 745	n = 620	•
Demographics			
Age (years)	59 (47-68)	73 (55-84)	<0.001
Sex (male)	465 (62%)	324 (52%)	<0.001
Ethnicity (white)	363 (49%)	426 (69%)	<0.001
Co-factors			
Smoker	51 (7%)	7 (1%)	<0.001
Obesity	207 (28%)	155 (25%)	0.268
Heart disease	146 (20%)	198 (32%)	<0.001
Diabetes mellitus	142 (23%)	274 (37%)	<0.001
Hypertension	303 (41%)	235 (38%)	0.317
COPD	56 (8%)	41 (7%)	0.528
Non HCC cancer	68 (11%)	42 (6%)	<0.001
нсс	48 (6%)	0 (0%)	<0.001
Creatinine (mg/dl)	0.9 (0.7-1.0)	0.9 (0.7-1.1)	0.021
Major outcomes			
Hospitalisation	668 (90%)	467 (75%)	<0.001
ICU requirement	235 (32%)	179 (29%)	0.288
ICU admission	177 (24%)	51 (8%)	<0.001
RRT	32 (4%)	2 (0%)	<0.001
Ventilation	132 (18%)	31 (5%)	<0.001
Death	150 (25%)	160 (26%)	0.014

Table S3. Demographics, co-factors and major outcomes for the total CLD and non-CLD cohorts. HCC = hepatocellular carcinoma; COPD= chronic obstructive pulmonary disease; ICU = intensive care unit; RRT = new requirement for renal replacement therapy.

Table S4 – Target antiviral treatments used in the CLD cohort.

	Total CLD cohort	CLD without cirrhosis	CLD with cirrhosis
Drug	n=745	n=359	n=386
Hydroxychloroquine	162 (22%)	78 (22%)	84 (22%)
Lopinovir/Ritonavir	114 (15%)	95 (26%)	19 (5%)
Interferon alpha	69 (9%)	64 (18%)	5 (1%)
Remdesivir	21 (3%)	8 (2%)	13 (3%)
Azithromycin	21 (3%)	15 (4%)	6 (2%)
Anti-IL6 therapy	17 (2%)	12 (3%)	5 (1%)
Umifenovir	16 (2%)	6 (2%)	10 (3%)
Oseltamivir	9 (1%)	1 (<1%)	8 (2%)
Corticosteroids	6 (1%)	6 (2%)	0
Convalescent plasma	6 (1%)	3 (1%)	3 (1%)
Favipiravir	6 (6%)	3 (1%)	3 (1%)
Ribavirin	3 (<1%)	2 (1%)	1 (<1%)
Interferon beta	3 (<1%)	3 (1%)	0
Darunavir/cobicistat	2 (<1%)	1 (<1%)	1 (<1%)
Dolutegravir	1 (<1%)	0	1 (<1%)
Anakinra	1 (<1%)	1 (<1%)	0
Any targeted COVID-19 treatment	315 (42%)	186 (52%)	129 (33%)

Table S4. List of all targeted antiviral treatments used in the total cohort of patients with CLD and laboratory proven SARS-CoV-2 infection separated into those with and without cirrhosis.

Table S5 – Patient characteristics separated by stage of liver disease

	CLD without			
	cirrhosis	CTP-A	СТР-В	CTP-C
	n=359	n=171	n=124	n=91
Demographics				
Age (years)	55 (43-66)	64 (54-73)	62 (54-68)	58 (48-63)
Sex (male)	216 (60%)	104 (61%)	84 (68%)	61 (67%)
Ethnicity (white)	124 (35%)	98 (57%)	80 (65%)	61 (67%)
Aetiology				
NAFLD	220 (62%)	55 (32%)	32 (26%)	15 (16%)
ALD	21 (6%)	46 (27%)	58 (47%)	54 (59%)
HBV	55 (15%)	27 (16%)	5 (4%)	5 (5%)
нси	24 (7%)	37 (22%)	25 (20%)	10 (11%)
Co-factors				
Smoker	15 (4%)	13 (8%)	11 (9%)	12 (13%)
Obesity	103 (29%)	48 (28%)	34 (27%)	22 (24%)
Heart disease	49 (14%)	49 (29%)	33 (27%)	15 (16%)
Diabetes mellitus	123 (34%)	76 (44%)	51 (41%)	24 (26%)
Hypertension	143 (40%)	75 (44%)	53 (43%)	32 (35%)
COPD	22 (6%)	12 (7%)	13 (10%)	9 (10%)
нсс	2 (1%)	30 (18%)	9 (7%)	7 (8%)
Non-HCC malignancy	15 (4%)	15 (9%)	8 (7%)	4 (4%)
Creatinine (mg/dl)	0.8 (0.7-1.0)	0.8 (0.6-1.0)	0.9 (0.7-1.4)	0.9 (0.7-1.2)
Major outcomes				
Hospitalisation	323 (90%)	150 (88%)	111 (90%)	84 (92%)
ICU requirement	80 (22%)	57 (33%)	48 (39%)	50 (55%)
ICU admission	69 (19%)	40 (23%)	34 (27%)	34 (37%)
RRT	11 (3%)	4 (2%)	6 (5%)	11 (12%)
Invasive ventilation	61 (17%)	27 (16%)	23 (19%)	21 (23%)
Death	27 (8%)	33 (19%)	44 (35%)	46 (51%)

Table S5. Demographics, liver disease aetiology, co-factors and major outcomes for all 745 CLD patients separated according to liver disease stage (CLD without cirrhosis, CTP-A, CTP-B and CTP-C cirrhosis). NAFLD = non-alcoholic fatty liver disease; ALD = alcohol related liver disease; HBV = chronic hepatis B virus infection; HCV = chronic hepatitis C virus infection; HCC = hepatocellular carcinoma; COPD = chronic obstructive pulmonary disease; RRT = new requirement for renal replacement therapy.

Table S6 – Patient	characteristics	of cirrhosis	cohort and	factors	associated	with	death	following	SARS-CoV-2
infection									

	Coho	rt	Surviv	ed	Diec	1	Univariable		Multivariabl	e 1	Multivariable 2	
	n=38	6	n=26	3	n=12	3						
Variable	n or median	% or IQR	n or median	% or IQR	n or median	% or IQR	OR (95%CI)	р	OR (95%CI)	р	OR (95%CI)	р
Age (years)	61	(53–70)	62	(50–70)	61	(54–71)	1.00 (0.99–1.02)	0.549	1.02 (0.99–1.04)	0.157	1.02 (0.99–1.04)	0.166
Sex (male)	239	59%	155	59%	84	68%	0.84 (0.54–1.31)	0.445	0.68 (0.40–1.15)	0.151	0.76 (0.44–1.29)	0.305
Ethnicity (white)	249	66%	173	66%	76	62%	0.84 (0.35–2.06)	0.708	1.31 (0.77–2.20)	0.317	1.39 (0.81–2.40)	0.238
СТР А	171	52%	138	52%	33	27%	1.00 (REF)	<0.001	1.00 (REF)	-	-	-
СТР В	124	30%	80	30%	44	36%	2.30 (1.36-3.90)	0.002	2.19 (1.21–3.96)	0.009	-	-
СТР С	91	17%	45	17%	46	37%	4.27 (2.44–7.48)	<0.001	4.60 (2.41–8.79)	<0.001	-	-
MELD	12	(8–19)	19	(7–17)	7	(9–23)	1.07 (1.03–1.10)	<0.001	-	-	1.07 (1.03–1.11)	<0.001
NAFLD	102	26%	69	26%	33	27%	1.03 (0.64–1.67)	0.902	0.99 (0.50–1.95)	0.966	0.81 (0.40–1.65)	0.570
ARLD	158	38%	99	38%	59	48%	1.53 (0.99–2.35)	0.055	1.51 (0.82–2.77)	0.184	1.41 (0.75–2.64)	0.281
HBV	72	21%	54	21%	18	15%	0.56 (0.25–1.27)	0.164	0.98 (0.36–2.69)	0.972	0.84 (0.31–2.27)	0.733
нсv	37	11%	29	11%	8	7%	0.66 (0.37–1.19)	0.168	0.84 (0.42–1.70)	0.631	0.75 (0.36–1.60)	0.463
Smoker	36	10%	27	10%	9	7%	0.69 (0.31–1.52)	0.355	0.60 (0.24–1.50)	0.278	0.71 (0.29–1.77)	0.467
Obesity	104	24%	64	24%	40	33%	1.50 (0.94–2.40)	0.092	1.54 (0.90–2.65)	0.116	1.55 (0.88–2.73)	0.129
Heart disease	97	26%	69	26%	28	23%	0.83 (0.50–1.37)	0.464	0.72 (0.39–1.32)	0.293	0.65 (0.34–1.23)	0.183
Diabetes mellitus	151	38%	100	38%	51	41%	1.15 (0.75–1.79)	0.519	1.23 (0.71–2.13)	0.456	1.27 (0.72–2.24)	0.418
Hypertension	160	40%	105	40%	55	45%	1.22 (0.79–1.88)	0.374	1.21 (0.71–2.06)	0.477	1.52 (0.88–2.64)	0.132
COPD	34	9%	24	9%	10	8%	0.88 (0.41–1.91)	0.748	0.79 (0.32–1.95)	0.612	0.71 (0.27–1.89)	0.496
Non-HCC cancer	70	18%	48	18%	22	18%	1.28 (0.57–2.89)	0.551	1.56 (0.64–3.82)	0.331	1.71 (0.69–4.19)	0.244
нсс	46	13%	33	13%	13	11%	0.82 (0.42–1.63)	0.577	1.21 (0.55–2.64)	0.638	1.13 (0.49–2.60)	0.774
Creatinine (mg/dl)	0.9	(0.7–1.1)	1.1	(0.7–1.1)	0.7	(0.7–1.3)	1.15 (0.95–1.37)	0.145	1.09 (0.89–1.34)	0.398	-	-

Table S6. Patient characteristics of patients with cirrhosis and laboratory-confirmed SARS-CoV-2 infection. Univariable associations with death and associated *p* values assessed by logistic regression. Multivariable analysis for association with death performed using logistic regression including all variables. Multivariable 1 includes CTP class, comparing with CTP-A as the reference. Multivariable 2 includes MELD and therefore excludes creatinine as an independent variable. No additional variables were significantly associated with death after

sensitivity analysis using stepwise backwards selection at p<0.2. CI = confidence interval; IQR = interquartile range; CTP = Child-Turcotte-Pugh; NAFLD = non-alcoholic fatty liver disease; ALD = Alcohol related liver disease; HBV = chronic hepatitis B virus infection; HCV = chronic hepatitis C virus infection; COPD = chronic obstructive pulmonary disease; HCC = hepatocellular carcinoma; MELD = model for end stage liver disease.

Table S7 - Patient characteristics after propensity score matching.

	Total cohort								
	CLD wi	thout cirrhosis	СТР	-A cirrhosis	СТР	-B cirrhosis	СТР	CTP-C cirrhosis	
	Disease	Matched non-CLD							
n	359	359	171	171	124	124	91	91	
Demographics									
Age (years)	55 (43–67)	54 (53–64)	64 (54–73)	61 (52–74)	62 (54–68)	60 (54–69)	58 (48–63)	58 (48–65)	
Sex (male)	216 (60%)	217 (60%)	104 (61%)	114 (67%)	84 (68%)	89 (72%)	61 (67%)	59 (65%)	
Ethnicity (white)	124 (35%)	202 (56%)	98 (57%)	110 (64%)	80 (65%)	75 (60%)	61 (67%)	52 (57%)	
Co-factors									
Smoker	15 (4%)	1 (0%)	13 (8%)	2 (1%)	11 (9%)	0 (0%)	12 (13%)	2 (2%)	
Obesity	103 (29%)	93 (26%)	48 (28%)	54 (32%)	34 (27%)	34 (27%)	22 (24%)	24 (26%)	
Heart disease	49 (14%)	39 (11%)	49 (29%)	49 (29%)	33 (27%)	30 (24%)	15 (16%)	14 (15%)	
Diabetes mellitus	123 (34%)	105 (29%)	76 (44%)	73 (43%)	51 (41%)	41 (33%)	24 (26%)	28 (31%)	
Hypertension	143 (40%)	113 (31%)	75 (44%)	60 (35%)	53 (43%)	33 (26%)	32 (35%)	35 (38%)	
COPD	22 (6%)	10 (3%)	12 (7%)	8 (5%)	13 (10%)	15 (12%)	9 (10%)	8 (9%)	
НСС	2 (1%)	0 (0%)	30 (18%)	0 (0%)	9 (7%)	0 (0%)	7 (8%)	0 (0%)	
Non-HCC cancer	15 (4%)	28 (8%)	15 (9%)	14 (8%)	8 (6%)	13 (10%)	4 (4%)	7 (7%)	
Creatinine (mg/dL)	0.8 (0.7–1.0)	0.8 (0.7–1.0)	0.8 (0.6–1.0)	0.9 (0.7–1.1)	0.9 (0.7–1.4)	0.9 (0.8–1.0)	0.9 (0.7–1.2)	0.9 (0.8–1.1)	

	UK cohort								
	CLD wi	thout cirrhosis	СТР	-A cirrhosis	СТР	-B cirrhosis	СТР	CTP-C cirrhosis	
	Disease	Matched non-CLD							
n	81	81	38	38	37	37	28	28	
Demographics									
Age (years)	62 (49–76)	61 (50–72)	63 (54–75)	64 (56–75)	66 (57–73)	65 (57–75)	58 (51–64)	59 (51–65)	
Sex (male)	44 (54%)	41 (51%)	23 (61%)	26 (68%)	24 (65%)	22 (59%)	21 (75%)	22 (79%)	
Ethnicity (white)	43 (53%)	53 (65%)	29 (79%)	24 (63%)	30 (81%)	22 (59%)	25 (89%)	14 (50%)	
Co-factors									
Smoker	3 (4%)	1 (1%)	5 (13%)	1 (3%)	5 (14%)	0 (0%)	4 (14%)	0 (0%)	
Obesity	20 (25%)	20 (25%)	13 (34%)	15 (39%)	11 (30%)	11 (30%)	6 (21%)	8 (29%)	
Heart disease	23 (28%)	17 (21%)	15 (39%)	18 (47%)	12 (32%)	10 (27%)	3 (11%)	4 (14%)	
Diabetes mellitus	37 (46%)	36 (44%)	21 (55%)	20 (53%)	15 (41%)	15 (41%)	6 (21%)	10 (36%)	
Hypertension	34 (42%)	28 (35%)	12 (32%)	16 (42%)	12 (32%)	13 (35%)	9 (32%)	11 (39%)	
COPD	10 (12%)	7 (9%)	5 (13%)	4 (11%)	3 (8%)	2 (5%)	5 (18%)	6 (21%)	
нсс	0 (0%)	0 (0%)	6 (16%)	0 (0%)	2 (5%)	0 (0%)	0 (0%)	0 (0%)	
Non-HCC cancer	3 (4%)	7 (9%)	4 (11%)	1 (3%)	3 (8%)	6 (16%)	1 (4%)	2 (7%)	
Creatinine (mg/dL)	0.9 (0.7–1.0)	0.8 (0.7–1.0)	0.9 (0.7–1.0)	0.9 (0.7–1.1)	1.0 (0.7–1.4)	0.9 (0.7–1.3)	0.8 (0.6–1.1)	0.9 (0.8–1.0)	

Table S7. Table shows the baseline patient characteristics for each liver disease stage after performing propensity score matching to non-CLD patients. Matching data is presented for both the total CLD cohort and when restricted to UK CLD cases. Variables selected for propensity score matching were age in years, interactions with age, sex, COPD, diabetes mellitus, and heart disease. HCC = hepatocellular carcinoma; COPD = chronic obstructive pulmonary disease; CTP = Child-Turcotte-Pugh

Table S8 – Full list of all contributing clinicians and centres of CLD patients included in final analysis

List of contributors, with thanks; (submitting clinician, responsible consultant, centre, country)

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Hannes Hagström & Annika Bergquist, Karolinska University Hospital, Sweden Heather Javaid & Jagadish Nagaraj, Morriston Hospital, Swansea, UK Hrishikesh Samant, Ochsner LSU Health Shreveport - Academic Medical Center, Louisiana, USA Iain Ewing & Cianan O'Sullivan, Homerton University Hospital, UK Iain Ewing, Homerton University Hospital, UK Ignacio García Juárez & Jesus a Camacho Escobedo, Hospital Almater, Mexicali, Mexico Ignacio García Juárez & Francisco i García-Juárez, Hospital Regional Lic. Adolfo López Mateos - ISSSTE, Mexico Ignacio García Juárez, El Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico Ignacio García Juárez & José a Avila Rojo, El Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico Ignacio García Juárez & Luis a Estrella Sato, El Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico Isaac Ruiz & Geneviève Huard, Centre Hospitalier de l'Université de Montréal (CHUM), Canada Isaac Ruiz & Hélène Castel, Centre Hospitalier de l'Université de Montréal (CHUM), Canada Isaac Ruiz & Julien Bissonnette, Centre Hospitalier de l'Université de Montréal (CHUM), Canada Isaac Ruiz & Marc Bilodeau, Centre Hospitalier de l'Université de Montréal (CHUM), Canada Isaac Ruiz & Catherine Vincent, Centre Hospitalier de l'Université de Montréal (CHUM), Canada James Esteban & Achutan Sourianarayanane, Froedtert and Medical College of Wisconsin, USA James Esteban & Aiman Ghufran, Froedtert and Medical College of Wisconsin, USA James Esteban & Kia Saeian, Froedtert and Medical College of Wisconsin, USA James Esteban & Syed Rizvi, Froedtert and Medical College of Wisconsin, USA James Esteban, Froedtert and Medical College of Wisconsin, USA Janisha Patel, University Hospital Southampton, UK Jihane Benhammou, University of California Los Angeles, USA Johnny Cash & Ian Cadden, Royal Victoria Hospital, Belfast, UK Jonathan Crisostomo & Arlinking Ong-Go, Metropolitan Medical Center, Philippines José Presa, Liver Unit – Centro Hospitalar Trás-os-Montes e Alto Douro, Portugal Judith Gomez Camarero & Belen Bernad Cabredo, Hospital Universitario de Burgos, Spain Judith Gomez Camarero & Cristina Fernandez Marcos, Hospital Universitario de Burgos, Spain Judith Gomez Camarero, Hospital Universitario de Burgos, Spain Juozas Kupcinskas, Lithuanian University of Health Sciences, Lithuania Justin Boike & Daniel Ganger, Northwestern Memorial Hospital, Chicago, Illinois, USA Justin Boike & Laura Kulik, Northwestern Memorial Hospital, Chicago, Illinois, USA

Justin Chin & Kosh Agarwal, King's College Hospital, London, UK Justin Chin & Vishal Patel, King's College Hospital, London, UK Kate Axe, Gwent Liver Unit, Royal Gwent Hospital, UK Katherine Marx & Maria-Andreea Catana, Beth Israel Deaconess Medical Center, USA Kevin Korenblat, Washington University School of Medicine, USA Konstantina Nikitopoulou & Andrew Johnston, Cambridge University Hospitals NHS Foundation Trust, UK Konstantina Nikitopoulou & George Mells, Cambridge University Hospitals NHS Foundation Trust, UK Konstantina Nikitopoulou & Joanna Leithead, Cambridge University Hospitals NHS Foundation Trust, UK Konstantina Nikitopoulou & Keval Naik, Cambridge University Hospitals NHS Foundation Trust, UK Konstantina Nikitopoulou & Michael Allison, Cambridge University Hospitals NHS Foundation Trust, UK Konstantina Nikitopoulou & Michalis Kostapanos, Cambridge University Hospitals NHS Foundation Trust, UK Konstantina Nikitopoulou & Victoria Snowdon, Cambridge University Hospitals NHS Foundation Trust, UK Kuldeep Cheent, Frimley Park Hospital, UK Lance Stein, Piedmont Atlanta Hospital, USA Leanne Stratton, Royal Victoria Hospital, Belfast, UK Logan Hobbs & Craig Lammert, Indiana University Hospital, USA Logan Hobbs & Archita Desai, Indiana University Hospital, USA Lorraine Blaise & Véronique Grando, Hepatology Unit Jean Verdier Hospital, Bondy, France Lorraine Blaise & Elia Gigante, Hepatology Unit Jean Verdier Hospital, Bondy, France Lorraine Blaise & Jean Charles Nault, Hepatology Unit Jean Verdier Hospital, Bondy, France Lorraine Blaise & Aurélie Walter, Hepatology Unit Jean Verdier Hospital, Bondy, France Maciej K Janik & Piotr Milkiewicz, Medical University of Warsaw, Poland Marcella Salzano & Joan Genescà, Hospital vall d'Hebron, Spain Marco Distefano, UOC Malattie Infettive, Italy Maria Fernanda Guerra Veloz, Hospital Universitario Virgen Macarena, Spain Maria Fernanda Guerra Veloz & Maria Jose Rios, Hospital Universitario Virgen Macarena, Spain Maria Fernanda Guerra Veloz & Patricia Cordero Ruiz, Hospital Universitario Virgen Macarena, Spain Maria Torrens & Joan Genescà, Hospital vall d'Hebron, Spain Maria-Andreea Catana & Afdhal Nezam, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Alan Bonder, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Zachary Fricker, Beth Israel Deaconess Medical Center, USA

Maria-Andreea Catana & Lau Daryl, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Michael Curry, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Michelle Lai, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Nezam Afdhal, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Patwardhan Vilas, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Raza Malik, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Tara Ghaziani, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana & Vilas Patwardhan, Beth Israel Deaconess Medical Center, USA Maria-Andreea Catana, Boston Medical Center, USA Maria-Andreea Catana, Cambridge Health Alliance, USA Maria-Andreea Catana & Kathleen Corey, Massachusetts General Hospital, USA Martin Prince, Manchester Royal Infirmary, UK Mary Kouba & Devina Bhasin, piedmont atlanta hospital, USA Matias Estevez Escobar & Cristina Vinolo Ubina, Hospital de Poniente, Spain Matias Estevez Escobar, Hospital de Poniente, Spain Matthew Armstrong, University Hospitals Birmingham, UK Matthew Armstrong & Fiona Thompson, University Hospitals Birmingham, UK Matthew McConnell & Cary Caldwell, Yale University, USA Mhairi C Donnelly & Mark Hudson, Newcastle Hospitals, UK Mhairi C Donnelly, Newcastle Hospitals, UK Ming-Hua Zheng, The First Affiliated Hospital of Wenzhou Medical University, China Mohamed Elfeki & Jason Kruse, Broadlawns Medical Center, USA Mohamed Elfeki & Donald Hillebrand, Iowa Methodist Medical Center, USA Mohamed Elfeki, Iowa Methodist Medical Center, USA Nancy Reau, Rush University Medical Center, USA Nicola Pugliese, Division of Internal Medicine and Hepatology, Department of Gastroenterology, Humanitas Clinical and Research Center IRCCS, Rozzano, Milan, Italy Nikolaos K Gatselis & George N Dalekos, University Hospital of Larissa, Greece Nneka Ufere & Lizabeth Cline, Boston Medical Center, USA Nneka Ufere & Panagiotis Trilianos, Boston Medical Center, USA

Nneka Ufere, Boston Medical Center, USA

Nneka Ufere & Stephen Zucker, Brigham and Women's Hospital, USA Nneka Ufere & Gary Trey, Cambridge Health Alliance, USA Nneka Ufere & Kathleen Corey, Massachusetts General Hospital, USA Nneka Ufere & Michael Thiim, Massachusetts General Hospital, USA Nneka Ufere & Tracey Simon, Massachusetts General Hospital, USA Nneka Ufere, Massachusetts General Hospital, USA Nneka Ufere & Connie Huang, North Shore Medical Center, Boston, USA Nneka Ufere & Karim Fawaz, CHA Somerville Hospital, USA Nuru Bayramov, Azerbaijan Medical University, Azerbaijan Nurun Tania & George Abouda, Hull University Teaching Hospitals, UK Patricia Jones & Arosemena, University of Miami, USA Patricia Jones, University of Miami, USA Patricia Jones & Molliner, University of Miami, USA Patricia Jones & O'Brien, University of Miami, USA Patricia Jones & P Martin, University of Miami, USA Patricia Jones & Shane, University of Miami, USA Pedro Montes, Hospital Nacional Daniel Alcides Carrion, Peru Ponni Perumalswami & Amon Asgharpour, Mount Sinai Hospital, USA Ponni Perumalswami & Charissa Chang, Mount Sinai Hospital, USA Ponni Perumalswami & Gene Im, Mount Sinai Hospital, USA Ponni Perumalswami & James Crismale, Mount Sinai Hospital, USA Ponni Perumalswami & Jawad Ahmad, Mount Sinai Hospital, USA Ponni Perumalswami & Jennifer Leong, Mount Sinai Hospital, USA Ponni Perumalswami & Joseph Odin, Mount Sinai Hospital, USA Ponni Perumalswami & Kamron Pourmand, Mount Sinai Hospital, USA Ponni Perumalswami & Linda Law, Mount Sinai Hospital, USA Ponni Perumalswami & Ritu Agarwal, Mount Sinai Hospital, USA Ponni Perumalswami & Thomas Schiano, Mount Sinai Hospital, USA Ponni Perumalswami, Mount Sinai Hospital, USA Rainer Guenther, Department of Internal Medicine/ Liver Unit, Universitätsklinikum Schleswig-Holstein, Kiel, Germany Rajiv Majithia, Rex Digestive Healthcare, USA

Raymond Rubin, Piedmont Atlanta hospital, USA Richard Parker, Leeds Liver Unit, UK Roger McCorry & Neil McDougall, Royal Victoria Hospital, Belfast, UK Rooshi Nathwani & William Howson, Charing Cross Hospital, UK Rooshi Nathwani & Ameet Dhar, St Mary's Hospital, UK Rooshi Nathwani & Heather Lewis, St Mary's Hospital, UK Rooshi Nathwani & Nowlan Selvapatt, St Mary's Hospital, UK Rooshi Nathwani & Pinelopi Manousou, St Mary's Hospital, UK Rooshi Nathwani & Lucia Possamai, St Mary's Hospital, UK Sarah Townsen & Jane Collier, Oxford University Hospitals, UK Sarang Thaker & Adam Mikolajczyk, University of Illinois, Chicago, USA Sarang Thaker & Sean Koppe, University of Illinois, Chicago, USA Sathish Subramanian, Massachusetts General Hospital, USA Sheila Eswaran, Rush University Medical Center, USA Sherief Abd-Elsalam, Tanta University, Egypt Sonia Blanco Sampascual & Castro, Hospital Universitario Basurto, Spain Sonia Blanco Sampascual & F Menendez, Hospital Universitario Basurto, Spain Sonia Blanco Sampascual, Hospital Universitario Basurto, Spain Stephen Barclay & Ewan Forrest, Glasgow Royal Infirmary, UK Stephen Barclay, Glasgow Royal Infirmary, UK Steven Masson, Newcastle Hospitals, UK Steven Masson & Stuart McPherson, Newcastle Hospitals, UK Teresa Broquetas, Hospital del Mar, Barcelona, Spain Thines Karunakaran & Chirag Oza, Broomfield Hospital, UK Thomas Marjot & Maheshi Ramasamy, Horton General Hospital, UK Upkar Gill & Aruna Dias, Newham University Hospital (Barts Health NHS Trust), UK Upkar Gill & Patrick Kennedy, Newham University Hospital (Barts Health NHS Trust), UK Upkar Gill & Vikram Sharma, Newham University Hospital (Barts Health NHS Trust), UK Upkar Gill & Paul Kooner, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & Graham Foster, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & Patrick Kennedy, Royal London Hospital (Barts Health NHS Trust), UK

Upkar Gill & Richard Marley, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & Sushma Saksena, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & Vikram Sharma, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & William Alazawi, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & Yiannis Kallis, Royal London Hospital (Barts Health NHS Trust), UK Upkar Gill & Janet Dearden, Whipps Cross University Hospital (Barts Health NHS Trust), UK Upkar Gill & Graham Foster, Whipps Cross University Hospital (Barts Health NHS Trust), UK Upkar Gill & Sudeep Tanwar, Whipps Cross University Hospital (Barts Health NHS Trust), UK Vanesa Bernal, Hospital Universitario Miguel Servet, Zaragoza, Spain Veronica Nguyen & Geoffrey Block, Banner University Medical Center/University of Arizona, Tucson, USA Vincent Cheung & James Maggs, Stoke Mandeville Hospital, UK Wim Laleman, University Hospital Leuven, Belgium Wong Yu Jun, Changi General Hospital, Singapore Xavier Verhelst, Ghent University Hospital, Belgium Xiaolong Qi & CHESS, CHESS, China Xiaolong Qi & CHESS, Guangdong, China Xiaolong Qi & CHESS, Guangxi, China Xiaolong Qi & CHESS, Hubei, China Xiaolong Qi & CHESS, Jiangsu, China Xiaolong Qi & CHESS, Tianjin, China

Supplementary annex – COVID-Hep and SECURE-Cirrhosis case report form

Inclusion Criteria:

1) Chronic liver disease or post-liver transplantation AND

2) Laboratory confirmed COVID 19 infection

Ideally this form should be completed after the patient has had COVID 19 for a long enough duration to experience complete recovery, discharge, or death.

If you have any questions, please reach out to info@covid-hep.net

Reporter Information		
Name of reporter		
Email address of reporter		
Name of lead physician providing care for liver		
disease/post-liver transplant		
Name of center providing care for liver		
disease/post-liver transplant		
Name of hospital where patient received care for		
COVID 19 (enter 'NA' if patient not hospitalized)		
Patient Information		
Patient information		
Is the patient >90 years of age?	○ Yes ○ No	
	\bigcirc	

Age Country of residence Drop down options Drop down options

State of residence	 ALABAMA ALASKA AMERICAN SAMOA ARIZONA ARKANSAS CALIFORNIA COLORADO CONNECTICUT DELAWARE DISTRICT OF COLUMBIA FLORIDA GEORGIA GUAM HAWAII IDAHO ILLINOIS INDIANA IOWA KANSAS KENTUCKY LOUISIANA MAINE MARYLAND MASSACHUSETTS MICHIGAN MINNESOTA MISSISSIPPI MISSOURI MONTANA NEBRASKA NEVADA NEW HAMPSHIRE NEW JERSEY NEW MEXICO NEW YORK NORTH CAROLINA NORTH DAKOTA OHIO OKLAHOMA OREGON PENNSYLVANIA PUERTO RICO RHODE ISLAND SOUTH CAROLINA SOUTH DAKOTA TENNESSE TEXAS UTAH VERMONT VIRGIN ISLANDS VIRGINIA WASHINGTON WEST VIRGINIA
Gender	 Female Male Other
Race/Ethnicity (may check more than one)	 White Black or African American American Indian / Native Alaskan East Asian (incl. Chinese, Japanese, Korean) South / South-East Asian (incl. Bangladeshi, Indian, Pakistani, Sri Lankan) Native Hawaiian / Pacific Islander Arabic Other Unknown
Other race/ethnicity	
Hispanic ethnicity	 Hispanic/Latino Not Hispanic/Latino Unknown
Patient BMI category (in kg/m2)	 < 18.5 (Underweight) 18.5-24.9 (Normal weight) 25.0-29.9 (Pre-obesity) 30.0-34.9 (Obesity class I) 35.0-39.9 (Obesity class II) >39.9 (Obesity class III) Unknown



Liver transplantation questions

Has the patient had a liver transplantation?

⊖ Yes ⊖ No What year was the liver transplantation performed?

Indication for liver transplant (select all that apply)

Decompensated cirrhosis Hepatocellular carcinoma Acute liver failure Other

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Other indication for liver transplantation	
Underlying aetiology of liver disease (select all that apply)	 Non-alcoholic fatty liver disease (NAFLD) Alcohol-related liver disease (ALD) Hepatitis C virus (HCV) Hepatitis B virus (HBV) Autoimmune hepatitis (AIH) IgG4-related disease Primary biliary cholangitis (PBC) Primary sclerosing cholangitis (PSC) Hemochromatosis Wilson's disease Other
Other aetiology	
Immunosuppression regimen at time of COVID 19 infection (select allthat apply)	 Prednisone Tacrolimus Sirolimus Everolimus Cyclosporine Mycophenolate mofetil (MMF) Azathioprine Cyclophosphamide Other Unknown
What other immunosuppression medication was used at the time of COVID 19infection?	
Current prophylactic antimicrobial regimen (select all that apply)	 Trimethoprim/sulfamethoxazole or Co-trimoxazole Dapsone Pentamidine Acyclovir/valacyclovir Fluconazole Ganciclovir/valganciclovir Foscarnet Other Unknown None

Other prophylactic antimicrobial regimen

Does the patient have any of the following comorbidities (check all that apply)?	 Cardiovascular disease (coronary artery disease, heart failure, arrhythmia, etc.) Diabetes Asthma COPD Other Chronic Lung Disease (NOT asthma/COPD) Hypertension Non-HCC cancer History of stroke Chronic renal disease (CKD, etc.) Human immunodeficiency virus (HIV) infection Current cigarette smoker Current user of tobacco products other than cigarettes (vaping, etc) Current heavy alcohol use (>2 drinks/day for men, >1 drink/day for women) History of illicit drug use including injectable drugs or inhaled crack/cocaine but excluding marijuana
Chronic liver disease questions	
Aetiology of liver disease (select all that apply)	 Non-alcoholic fatty liver disease (NAFLD) Alcohol-related liver disease (ALD) Hepatitis C virus (HCV) Hepatitis B virus (HBV) Autoimmune hepatitis (AIH) IgG4-related disease Primary biliary cholangitis (PBC) Primary sclerosing cholangitis (PSC) Hemochromatosis Wilson's disease Other
Other aetiology	
Does the patient have cirrhosis?	 Yes No Unknown
Child Pugh grade prior to COVID 19 diagnosis?	 A B C Unknown
Did the patient have ascites prior to COVID 19 diagnosis?	 None Mild/moderate (diuretic responsive) Severe (diuretic refractory) Unknown

What was the worst grade of hepatic encephalopathy patient developed prior to COVID 19 diagnosis?	 None Grade 1 (trivial lack of awareness, shortened attention span) Grade 2 (lethargy, minimal disorientation, subtle personality change) Grade 3 (somnolence to semi-stupor but responsive to verbal stimuli, gross disorientation) Grade 4 (coma - unresponsive to verbal or noxious stimuli) Unknown
Has the patient ever had hepatocellular carcinoma?	 Yes No Unknown
What immunosuppression was the patient taking for IgG4-related disease at time of COVID 19 diagnosis (may check more than one)?	 None Corticosteroids Azathioprine Rituximab Other Unknown
Other immunosuppression for IgG4-related disease	
Has the patient received steroids for alcoholic hepatitis recently (within 4 weeks of COVID 19 diagnosis)?	 Yes No Unknown
Treatment for primary biliary cholangitis (PBC) at time of COVID 19 diagnosis	 Ursodeoxycholic acid Obeticholic acid Fibrate Other No treatment Unknown
Other PBC treatments	
Does the patient have inflammatory bowel disease (IBD)?	 ○ Yes ○ No ○ Unknown
Immunosuppression medication(s) patient was taking for IBD at time of COVID 19 diagnosis	 Prednisone/prednisolone Budesonide Azathioprine Methotrexate Mycophenolate Infliximab Adalimumab Ustekinumab Vedolizumab Other None Unknown

Other immunosuppression for IBD

Treatment for autoimmune hepatitis (AIH) at time of COVID 19 diagnosis	 Prednisone/prednisolone Budesonide Azathioprine Mycophenolate Tacrolimus Other None Unknown
Other treatment for AIH	
Hepatitis B surface antigen (HBsAg) positive	 ○ Yes ○ No ○ Unknown
Treatment for HBV at the time of COVID 19 diagnosis	 Tenofovir Entecavir Interferon None Unknown
Did the patient have detectable hepatitis C virus (HCV) RNA at the time of or prior to COVID 19 diagnosis?	 Yes No Unknown
HCV genotype	 1 2 3 4 5 6 7 Unknown
Active treatment for HCV at the time of COVID 19 diagnosis	 Yes No O Unknown
Does the patient have any of the following comorbidities (check all that apply)?	 Cardiovascular disease (coronary artery disease, heart failure, arrhythmia, etc.) Diabetes Asthma COPD Other Chronic Lung Disease (NOT asthma/COPD) Hypertension Non-HCC cancer History of stroke Chronic renal disease (CKD, etc.) Human immunodeficiency virus (HIV) infection Current cigarette smoker Current user of tobacco products other than cigarettes (vaping, etc) Current heavy alcohol use (>2 drinks/day for men, >1 drink/day for women) History of illicit drug use including injectable drugs or inhaled crack/cocaine but excluding marijuana

Laboratory data (leave fields blank if unknown) If COVID-19 suspected at presentation/admission then use recent pre-admission 	
If hospital acquired COVID-19 suspected then	please use first laboratory values obtained
during hospitalisation as baseline.	
Baseline serum sodium (mmol/L)	
	(Before COVID 19 infection)
Nadir serum sodium (mmol/L)	
	(During COVID 19 infection)
Creatinine units	○µmol/L ○ mg/dl
Baseline serum creatinine	
	(Before COVID 19 infection)
Peak serum creatinine	
	(During COVID 19 infection)
Baseline prothrombin time (sec)	
	(Before COVID 19 infection)
Peak prothrombin time (sec)	
	(During COVID 19 infection)
Albumin units	⊖g/dl ⊖g/liter
Baseline albumin	
	(Before COVID 19 infection)
Nadir albumin	
	(During COVID 19 infection)
Total bilirubin units	○µmol/L ○ mg/dl
Baseline total bilirubin	
	(Before COVID 19 infection)
Peak total bilirubin	
	(During COVID 19 infection)
Baseline alanine aminotransferase (ALT) (IU/L)	

(Before COVID 19 infection)

Peak alanine aminotransferase (ALT) (IU/L)	
	(During COVID 19 infection)
Baseline alkaline phosphatase (IU/L)	
	(Before COVID 19 infection)
Peak alkaline phosphatase (IU/L)	
	(During COVID 19 infection)
COVID 19 questions	
Was this lab confirmed COVID 19 infection?	 Yes No Unknown
What symptoms did the patient have at the time of COVID 19 diagnosis?	 GI symptoms (abdominal pain, diarrhea, nausea, vomiting) Respiratory symptoms (shortness of breath, cough) Both GI and respiratory symptoms Neither GI or respiratory symptoms Unknown
Did patient test positive for influenza at time of COVID 19 infection?	 Yes No Unknown
What complications did the patient develop during COVID 19 infection?	 New or worsening ascites Spontaneous bacterial peritonitis Hepatic encephalopathy Non-variceal upper GI bleeding Variceal upper GI bleeding New requirement for renal replacement therapy (e.g. hemodialysis) Other
Other complications of COVID 19 infection	
What was the grade of ascites during COVID 19 infection?	 Mild/moderate Severe Unknown
What was the worst grade of hepatic encephalopathy during COVID 19 infection (based on West Haven Criteria)?	 Grade 1 (trivial lack of awareness, shortened attention span) Grade 2 (lethargy, minimal disorientation, subtle personality change) Grade 3 (somnolence to semi-stupor but responsive to verbal stimuli, gross disorientation) Grade 4 (coma - unresponsive to verbal or noxious stimuli) Unknown
Did the patient receive specificantiviral treatment for COVID 19 infection?	 ○ Yes ○ No ○ Unknown

Which of the following treatment(s) did patient receive for COVID 19 (select all that apply)?	 Remdesivir Tocilizumab Lopinovir/ritonavir Chloroquine/hydroxychloroquine Ribavirin Interferon-alpha Other Unknown
Other type of antiviral treatment(s) received for COVID-19	
What was the reason the patient did not receive COVID 19 antiviral treatment (select all that apply)?	 Elevated liver enzymes Underlying liver fibrosis/cirrhosis Other contraindication (eg AKI) Treatment not available Other Unknown
What was the reason the patient did not receive COVID 19 antiviral treatment?	
Did the patient die?	 Yes No Unknown
What was the primary cause of death?	 Liver-related complications COVID 19-related lung disease Cardiogenic shock Other
Other cause of death	
Has the patient been hospitalized?	 ○ Yes ○ No ○ Unknown
Has the patient been discharged from the hospital?	 ○ Yes ○ No ○ Unknown
Length of hospital stay (days)	
Did patient receive invasive ventilation?	 ○ Yes ○ No ○ Unknown
Did the patient receive non-invasive ventilation?	 ○ Yes ○ No ○ Unknown
Was the patient admitted to an intensive care unit?	 ○ Yes ○ No ○ Unknown

Why was the patient not admitted to an intensive care unit?

- $\stackrel{\text{O}}{\circ}$
- Disease not severe enough Disease was severe enough but limited availability of intensive care unit
 - Disease was severe enough but escalation to intensive care unit not felt to be appropriate.
 - ◯ Unknown