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TERAPIA
E PREVENZIONE
DELL'INFEZIONE
DA HIV
E MICRORGANISMI
EMERGENTI

09-10
GIUGNO
2021

VIRTUAL EDITION

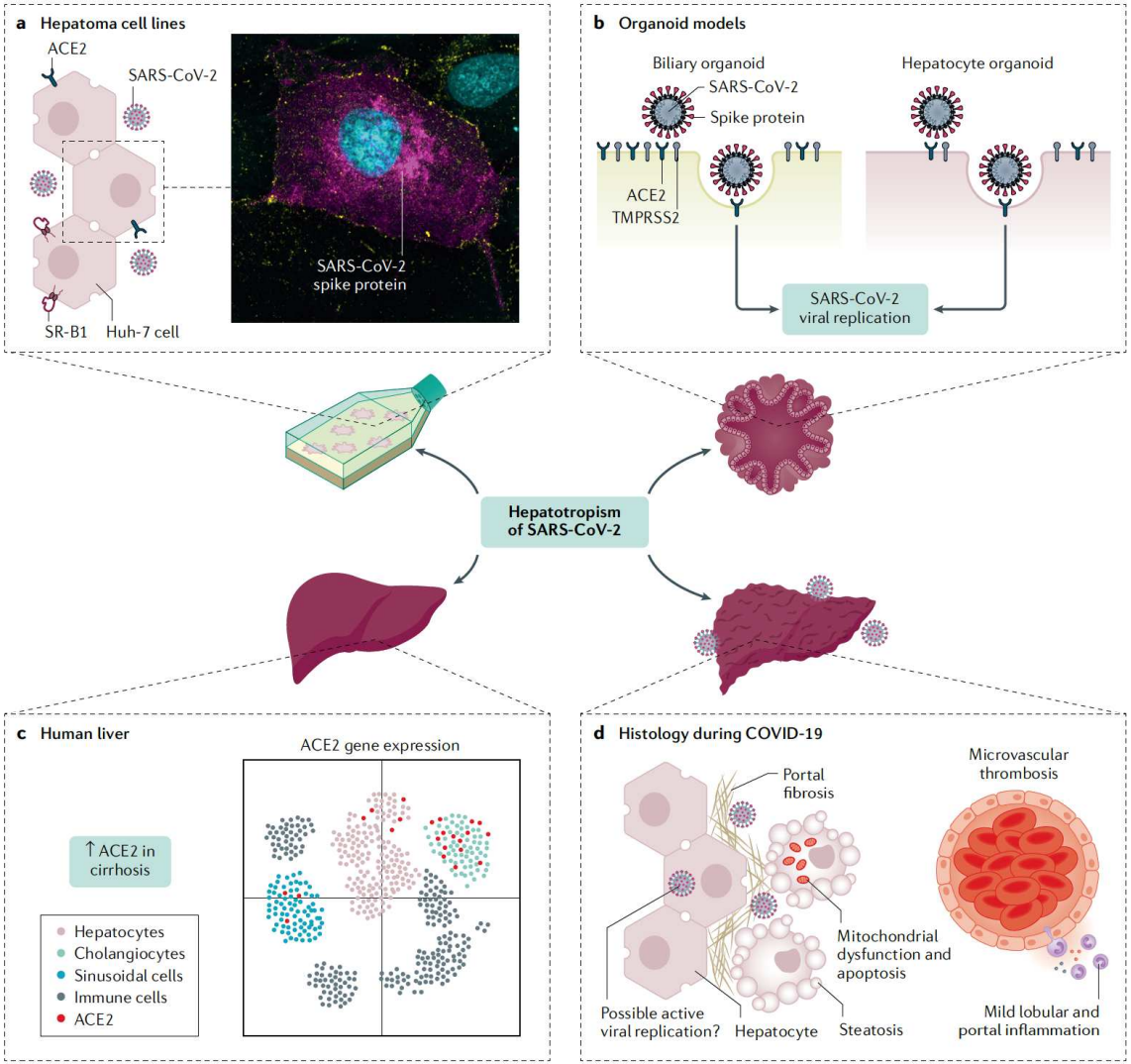
Coinfezioni SARS-CoV2 ed HIV/HCV

Coinfezioni SARS-CoV2 ed HIV/HCV

- SARS-CoV-2 e danno epatico
- Eziologia della malattia epatica e gravità di COVID-19
- Cirrosi e gravità di COVID-19
- COVID-19 nei riceventi di trapianto di fegato
- COVID-19 e screening per HCV

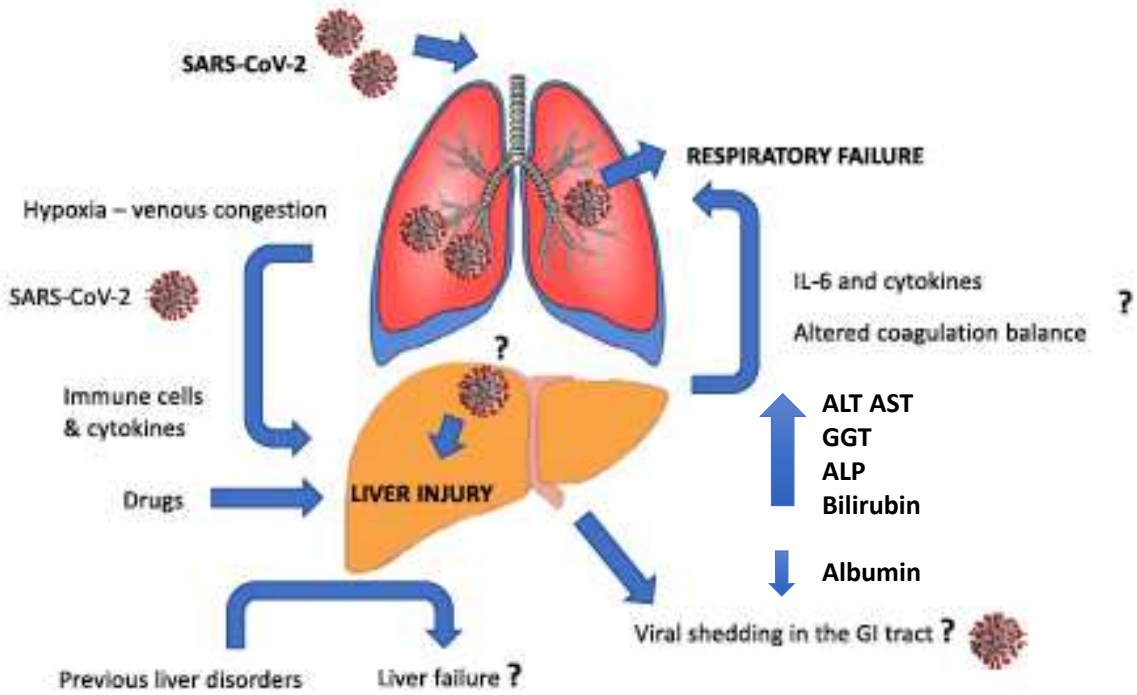
Hepatotropism of SARS- CoV-2: still remains to be determined

- Gene expression levels for ACE2:
  - cholangiocytes → sinusoidal endothelial cells-> hepatocytes
  - Increased by HCV, NASH & obesity but not by steatosis (interpreted with caution truncated form of ACE2?)
- Viral life cycle supported by HCC derived cells, liver ductal organoids but not by primary hepatocyte cultures
- Histological assessment
  - Vascular microabnormalities 100%
  - Micro & macrovescicular steatosis 50%
  - Mild portal inflammation 66%
  - Portal fibrosis 60%
  - No cholagiopathy (reservoir of long term viral replication)
- EM assessment
  - Possible coronavirus like particles in hepatocytes with mithocondrial swelling and apoptosis
- Proteomic landscape little evidence of active viral replication but multi-organ dysfunction, hepatic steatosis and coagulative hepatocyte necrosis



Marjot T et al Nat Rev Gastro and Hepatol https://doi.org/10.1038/s41575-021-00426-4

Mechanisms of liver injury in COVID-19



1. Immune mediated damage
   - ✓ Inflammatory response
   - ✓ Coagulation disorder 👉 Microthromboses
2. Direct cytotoxicity
3. Anoxia
4. Drug-induced liver injury (DILI)
5. Reactivation of pre-existing liver disease
6. Multi Organ Failure

Sun J et al Liver International. 2020;40:1278–1281.

LFT abnormalities
Data at presentation and during hospitalization may differ

	Data at presentation	Data during hospitalization
Direct cytotoxicity	☞	☞
Immune mediated damage Inflammation Coagulation	☞ (only in pts with severe or critical disease at presentation)	☞
Anoxia	☞ (only in pts with severe or critical disease at presentation)	☞
DILI	NO	☞
Reactivation of pre-existing liver disease	NO	☞
Multi Organ Failure	NO	☞

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Liver diseases aetiology and COVID-19 severity

Author	Design	Country Region / Number included	Major findings
Alcohol related liver disease			
Marjot et al. (Oct 2020)	Large international registry study	29 countries; SARS- CoV-2 plus CLD (n = 745); SARS = CoV-2 plus ALD (n = 179)	ALD independent risk factor for death (OR 1.79, 95% CI 1.03–3.13)
Kim et al. (Sep 2020)	Multicentre retrospective cohort study	North America; SARS- CoV-2 plus CLD (n = 867); SARS- CoV-2 plus ALD (n = 94)	ALD independent risk factor for death (HR 2.42, 95% CI 1.29–4.55)
Viral hepatitis			
Marjot et al. (Oct 2020)	Large international registry study	29 countries; SARS- CoV-2 plus CLD (n = 745); SARS- CoV-2 plus HBV (n = 96); SARS- CoV-2 plus HCV (n = 92)	No independent association with death
Kim et al. (Sep 2020)	Multicentre retrospective cohort study	North America; SARS- CoV-2 plus CLD (n = 867); SARS- CoV-2 plus HBV (n = 62); SARS- CoV-2 plus HCV (n = 190)	No independent association with death
Butt et al.182 (Feb 2021)	Population-based study using electronic health record data	USA; SARS-CoV-2 plus HCV (n = 975), SARS-CoV-2 no HCV (n = 975)	SARS-CoV-2 plus HCV more likely to be hospitalised but not at increased risk of death.

Marjot T et al. J. Hepatol. 74, 567–577 (2020) Kim J U Lancet Gastroenterol. Hepatol. 5, 886–887 (2020).Butt A.A Liver Int. https://doi.org/10.1111/liv.14804 (2021).

Liver diseases aetiology and COVID-19 severity

Author	Design	Country Region / Number included	Major findings
Hepatocellular carcinoma			
Marjot et al. (Oct 2020)	Large international registry study	29 countries; SARS- CoV-2 plus CLD (n = 745); SARS- CoV-2 plus HCC (n = 48)	No independent association with death
Kim et al. (Sep 2020)	Multicentre retrospective cohort study	North America;SARS- CoV-2 plus CLD (n = 867); SARS- CoV-2 plus HCC (n = 22); locoregional therapy (n = 8), immunotherapy (n = 2)	Independent risk factor for death (HR 3.96, 95% CI 1.74–8.98)
Autoimmune hepatitis			
Marjot et al. (Jan 2021)	Large international registry study	35 countries; SARS- CoV-2 plus AIH (n = 70); 86% immunosuppression; SARS- CoV-2 plus non- AIH CLD (n = 862); SARS- CoV-2 plus non- CLD (n = 769)	• Immunosuppression not an independent risk factor fo death in patients with AIH; • Equivalent rates of mortality for patients with AIH vs non- AIH CLD; • Higher rates of hospitalization but equivalent rates of mortality for patients with AIH compared to non-CLD

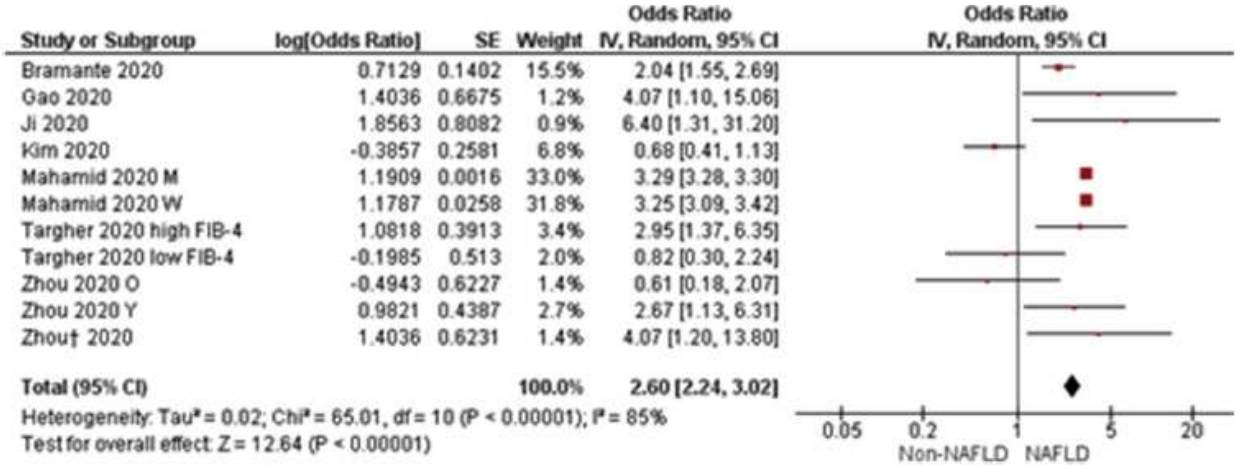
Marjot T et al. J. Hepatol. 74, 567–577 (2020) Kim J U Lancet Gastroenterol. Hepatol. 5, 886–887 (2020). Marjot T et al https://doi.org/10.1016/j.jhep.2021.01.021

Liver diseases aetiology and COVID-19 severity

Author	Design	Country Region / Number included	Major findings
Non Alcoholic Fatty Liver Disease			
Marjot et al. (Oct 2020)	**Large international registry study**	**29 countries; SARS- CoV-2 plus CLD (n = 745); SARS- CoV-2 plus NAFLD (n = 322)**	**No independent association with death controlling for age, sex, ethnicity, liver disease stage, BMI, CVD, T2DM, hypertension, COPD, smoking status**
Kim et al. (Sep 2020)	**Multicentre retrospective cohort study**	**North America; SARS- CoV-2 plus CLD (n = 867); SARS- CoV-2 plus NAFLD (n = 465)**	**No independent association with death controlling for age, sex, ethnicity, cirrhosis, T2DM, hypertension, CVD, COPD, smoking status**

Marjot T et al. J. Hepatol. 74, 567–577 (2020) Kim J U Lancet Gastroenterol. Hepatol. 5, 886–887 (2020

NAFLD/MAFLD and COVID-19 severity



Pooled adjusted risk of COVID severity in NAFLD.

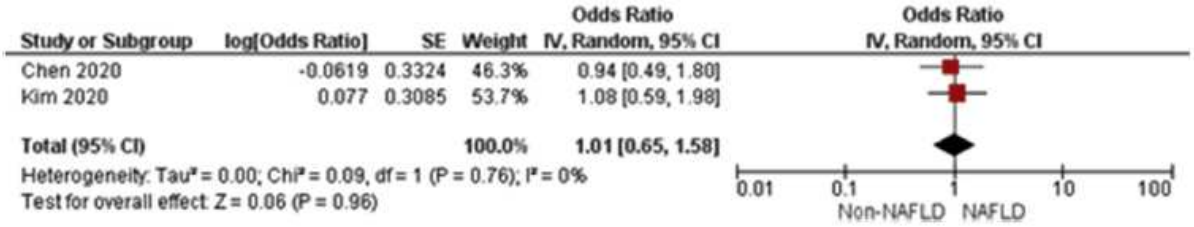


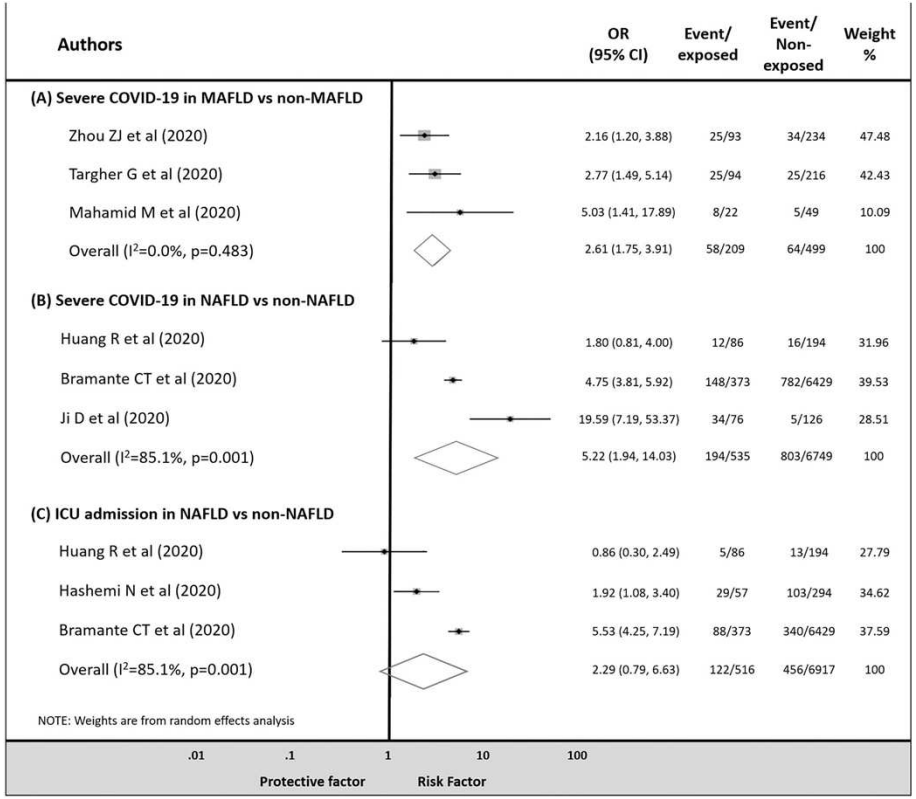
Fig. 4. Pooled adjusted risk of mortality in NAFLD.

Singh A et al Diabetes & Metabolic Syndrome: Clinical Research & Reviews 15 (2021) 813e822

NAFLD/MAFLD and COVID-19 disease severity

Author	Country	Total N⁰ of patients	Female%	Age (year)†	N⁰ of patients with MAFLD or NAFLD (% of total)	Outcome(s)	
						Definition	Event N⁰ (% of total)
NAFLD vs. no-NAFLD comparison							
(9)	USA	6,802	44	46	373 (5.5)	Severe COVID-19/ ICU admission	930 (13.67)
							428 (6.3)
(23)	USA	351	45	63.4	57 (16)	ICU admission/ In-hospital mortality	132 (37.6)
							55 (15.67)
(22)	China	280	48	43	86 (31)	Severe COVID-19/ ICU admission	28 (10)
							18 (6.43)
(24)	China	202	44	44.5	76 (38)	Severe COVID-19	39 (19.31)
MAFLD vs. no-MAFLD comparison							
(27)	China	130	37	46	65 (50)	ICU admission	3 (2.31)
(25)	Israel	71	73	51	22 (31)	Severe COVID-19	13 (18.31)
(26)	China	310	52	47	94 (30)	Severe COVID-19	50 (16.13)
(21)‡	China	327	ND	ND	93 (28)	Severe COVID-19	59 (18)
(10)‡	China	110	26	42	55 (50)	ICU admission	3 (2.73)

†mean or median, ‡prospective study.



Hagy PJ et al Front. Med. 8:626425. doi: 10.3389/fmed.2021.626425

NAFLD/MAFLD and COVID-19 severity : the debate is still open

- Pathogenetic mechanism → altered inflammatory response:
  - Higher IL-6 levels in NAFLD/MAFLD (Gao F Front Endocinol; 2021; 12: Article 604100.
- Diagnostic definition of NAFLD/ MAFLD is heterogeneous across studies (HIS, CT scan NAFLD score)
- Role of confounders: Racial and socioeconomic disparities (AdenjiN et al Gastroenterology 2021;160:1406–1409) , obesity and diabetes are risk factor for COVID-19 severity and mortality
- NAFLD is a predictor of liver injury in COVID-19 hospitalized patients but not of mortality, disease severity on the presentation or progression (Mushtaq K et al Journal of Hepatology 2021 vol. 74 : 469–490)
- The risk factor could be fibrosis rather than steatosis (Campos-Murguja A Digestive and Liver Disease 2021 in press https://doi.org/10.1016/j.dld.2021.01.019)

Coinfezioni SARS-CoV2 ed HIV/HCV

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-

Cirrhosis and COVID-19 severity

Author	Design	Country Region / Number included	Major findings
Cirrhosis			
Iavarone (Jun 2020)	Multicentre retrospective cohort study	Italy; SARS- CoV-2 plus cirrhosis (n = 50); SARS- CoV-2 plus no cirrhosis (n = 399); cirrhosis plus bacterial infection (n = 47)	30- day mortality: SARS- CoV-2 plus cirrhosis vs SARS- CoV-2 plus no cirrhosis (34% vs 18%; P = 0.030); SARS- CoV-2 plus cirrhosis vs cirrhosis plus bacterial infection (34% vs 17%; P = 0.03)
Bajaj (Jun 2020)	Multicentre retrospective cohort study	North America and Canada; SARS- CoV-2 plus no cirrhosis (n = 108); SARS- CoV-2 plus cirrhosis (n = 37); cirrhosis alone (n = 127)	cirrhosis plus SARS- CoV-2 higher mortality compared with patients with SARS- CoV-2 alone (30% vs 13%; P = 0.03) but not between patients with cirrhosis plus SARS- CoV-2 and patients with cirrhosis alone (30% vs 20%; P = 0.16)
Clift et al. (Sep 2020)	Population- based cohort study using electronic health record data	United Kingdom; 6 million adults: 11,865 with cirrhosis, 37 deaths from COVID-19 in patients with cirrhosis and 106 hospitalizations with COVID-19 in patients with cirrhosis	Hazard ratio for COVID-19- related mortality in patients with cirrhosis: women in derivation cohort, 1.8 (95% CI 1.15–2.99); men in derivation cohort, 1.29 (95% CI 0.83–2.02)
Ioannou et al. (Nov 2020)	Population- based study using electronic health record data	North America; SARS- CoV-2 plus cirrhosis (n = 305); SARS- CoV-2 plus no cirrhosis (n = 9,826); cirrhosis alone (n = 3,301)	Patients with SARS- CoV-2 plus cirrhosis 3.5 times more likely to die than those with SARS- CoV-2 without cirrhosis
Sarin et al.179 (Jun 2020)	Multicentre retrospective cohort study	13 countries in Asia; SARS- CoV-2 plus CLD without cirrhosis (n = 185); SARS- CoV-2 plus cirrhosis (n = 43)	Overall mortality: SARS- CoV-2 plus CLD without cirrhosis vs SARS- CoV-2 plus cirrhosis (16% vs 3%; P = 0.002)

Iavarone M et al. J. Hepatol. 73, 1063–1071 (2020).Bjaij M et al Gut 70, 531–536 (2021). Clift AK et al BMJ 371, m3731 (2020) Ioannou GN et al Hepatology https://doi.org/ 10.1002/hep.31649 (2020).Sarin J et al. Hepatol. Int. 14, 690–700(2020).

Cirhosis stage and COVID-19 severity

Author	Design	Country Region / Number included	Major findings
Non Alcoholic Fatty Liver Disease			
Marjot et al. (Oct 2020)	Large international registry study	29 countries; SARS- CoV-2 infection plus cirrhosis (n = 386); SARS- CoV-2 plus CLD without cirrhosis (n = 359); SARS- CoV-2 plus non- CLD (n = 620)	• Overall mortality: CP- A (19%), CP- B (35%), CP- C (51%), CLD without cirrhosis (8%); • increased risk of death cirrhosis vs CLD without cirrhosis: CP- A (OR 1.9, 95% CI 1.03–3.5), CP- B (OR 4.1, 95% CI 2.4–7.77), CP- C (OR 9.32, 95% CI 4.80–18); • increased risk of death compared with propensity score- matched patients without CLD: CP- B (+20%, 8.8–31.3%) and CP- C (+38%, 27.1–49.2%)
Kim et al. (Sep 2020)	Multicentre retrospective cohort study	North America; SARS- CoV-2 plus CLD without cirrhosis (n = 620); SARS- CoV-2 plus cirrhosis (n = 227)	• Increased risk of death with decompensated cirrhosis(OR 2.91, 95% CI 1.70–5.00); • no increased risk with compensated cirrhosis (OR 0.83, 95% CI 0.46–1.49)

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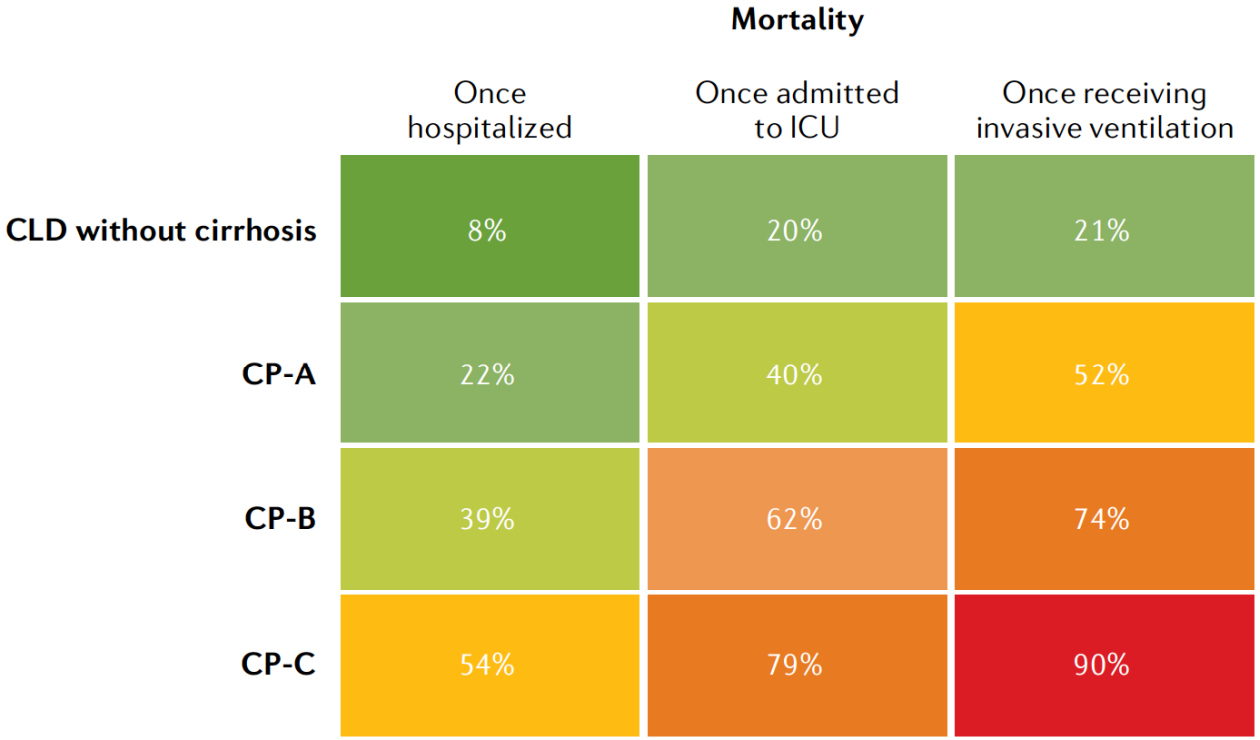
Mortality following SARS-CoV-2 infection according to baseline liver disease stage and level of medical support and according to CCI and CLIF OF



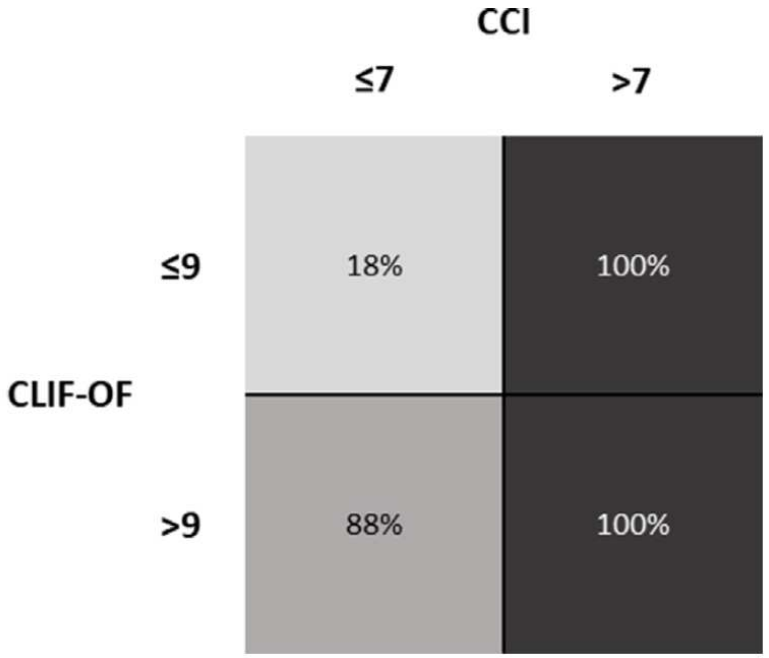


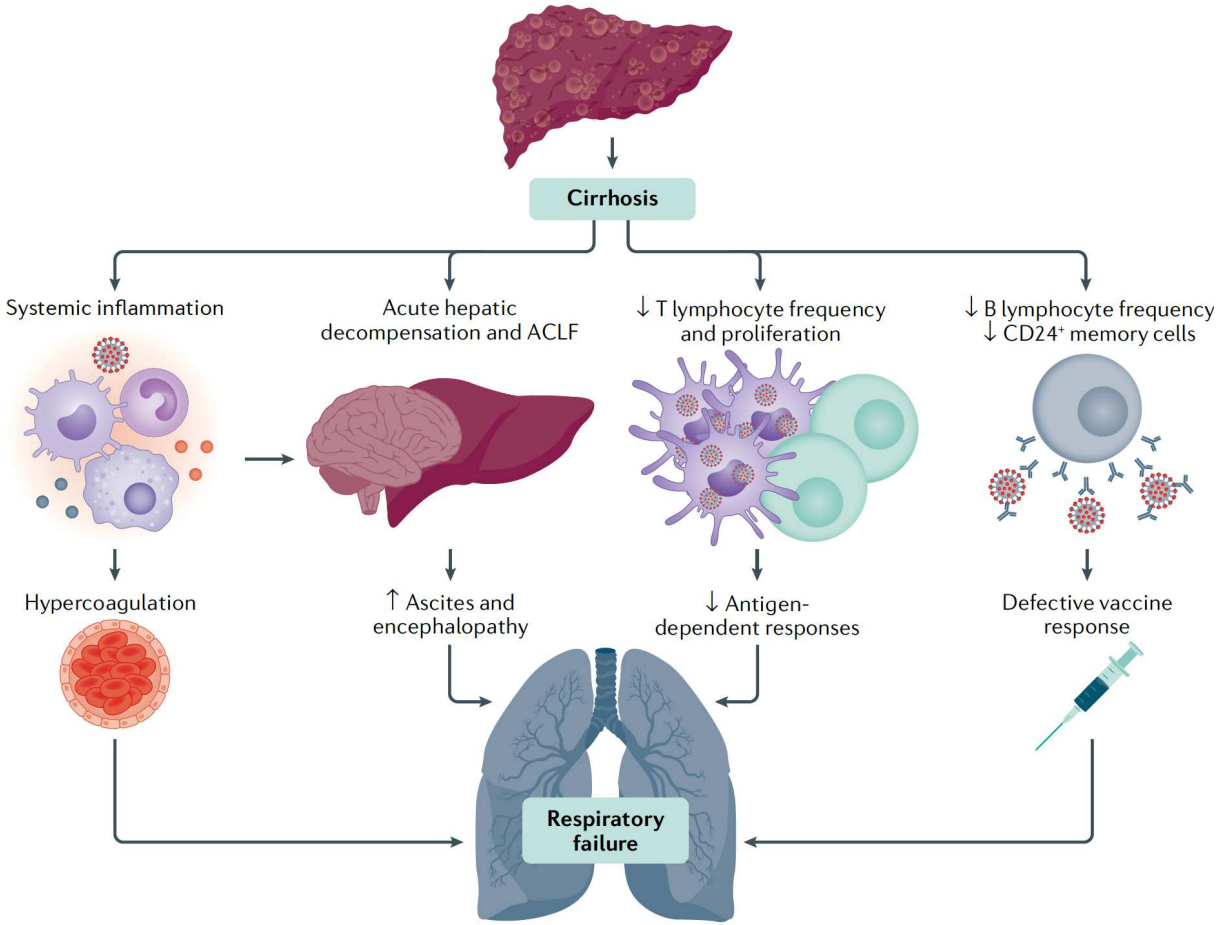
Figure 1 Rates of 30-day mortality in the 50 cirrhotics with SARS-CoV-2 infection, according to CLIF-OF and CCI combination.

Marjot T et al. J. Hepatol. 74, 567–577 (2020)
Iavarone M et al Gut 2020;0:1–2. doi:10.1136/gutjnl-2020-322929

COVID-19 as a cause of liver decompensation

- Cause of death in cirrhotics with COVID-19
  - 1st respiratory insufficiency and MOF
  - 2nd liver decompensation
- COVID-19 can cause acute- on- chronic liver failure (ACLF).
  - In the SECURE- Cirrhosis and COVID- Hep registries, hepatic decompensation events were more frequent with increasing severity of liver disease
  - mortality increased with worsening ACLF as measured by the CLIF- C score (Horwitz LI et al J. Hosp. Med. 16, 90–92 (2021).
- Rates of death and re- admission at 90- days are comparable to those with cirrhosis alone (Bajaj JS et al. Liver Transpl. https://doi.org/10.1002/lt.25981 (2021))

Possible mechanisms for adverse CoVID-19 outcomes in patients with cirrhosis.



Marjot T et al Nat Rev Gastro and Hepatol https://doi.org/10.1038/s41575-021-00426-4

COVID-19 management in pts with liver disease

- **Patients with cirrhosis are a vulnerable population: behavioural prevention and proactive testing (even in outpatients with decompensation)**
- **NO EUA for Monoclonal antibodies in pts with cirrhosis ->**
  - **RCT of new monoclonal antibodies → when cirrhosis is not an exclusion criteria**
  - **Request for Hyperimmune plasma compassionate use in pts with mild-moderate disease in the first 72 h after diagnosis may be considered**
- **Remdesivir**
  - **Should be used in patients with hepatic impairment when benefits outweigh risks**
  - **Not started or stopped when ALT > 5 x UNL**

MAb

Quali pazienti

Criteri di selezione dei pazienti

Tabella 1. Criteri di selezione dei pazienti candidabili alla terapia con anticorpi monoclonali per COVD-19 inclusi nel DM del 6 febbraio 2021 (GU n. 32 del 8-2-2021).
• BMI≥35
• Soggetti cronicamente sottoposti a dialisi peritoneale o emodialisi
• Diabete mellito non controllato (HbA1c≥9.0% 75 mmol/mol) o con complicanze croniche
• Immunodeficienze primitive
• Immunodeficienze secondarie con particolare riguardo ai pazienti onco-ematologici in trattamento con farmaci mielo/immunosoppressivi, mielosoppressivi o a meno di 6 mesi dalla sospensione delle cure.
• ≥65 anni (in questo caso deve essere presente almeno un ulteriore fattore di rischio)
• ≥ 55 anni con o malattia cardio-cerebrovascolare (inclusa ipertensione con concomitante danno d'organo) o BPCO e/o altre malattie respiratorie croniche (soggetti affetti da fibrosi polmonare o che necessitano di O2-terapia per ragioni differenti da SARS-CoV-2)
12-17 anni con: • BMI ≥ 85esimo percentile per età e genere; • anemia falciforme; • malattie cardiache congenite o acquisite; • malattia del neurosviluppo, • dipendenza da dispositivo tecnologico (p.es. soggetti con tracheotomia, gastrostomia, etc); • asma, o altre malattie respiratorie che richiedono medicazioni giornaliere per il loro controllo.
Sono esclusi soggetti ricoverati per COVID-19, o che ricevono ossigenoterapia per COVID-19

Quali prescrittori

a) la selezione del paziente e' affidata ai medici di medicina generale, ai pediatri di libera scelta, ai medici delle USCA(R) e, in generale, **ai medici che abbiano l'opportunita' di entrare in contatto con pazienti affetti da COVID di recente insorgenza** e con sintomi lievi-moderati e di indirizzarli rapidamente alla struttura presso la quale effettuare il trattamento e deve avvenire nel rispetto dei criteri fissati dalla CTS, di cui all'allegato 1;

b) la **prescrivibilita'** del prodotto e' limitata ai **medici operanti nell'ambito delle strutture identificate a livello locale per la somministrazione**;

c) e' raccomandato il trattamento nell'ambito di una struttura ospedaliera o comunque in setting che consentano una pronta ed appropriata gestione di eventuali reazioni avverse gravi;

d) la prescrizione ed il trattamento devono garantire la somministrazione del prodotto il piu' precocemente possibile rispetto all'insorgenza dei sintomi, e comunque non oltre i dieci giorni dall'inizio degli stessi.

2. La definizione del percorso attraverso il quale vengono identificati i pazienti eleggibili al trattamento e' rimessa ai provvedimenti delle regioni e delle province autonome.

COVID-19 management in pts with liver disease

- **Steroids can be used in pts with Oxygen supplementation**
  - **HBV reactivation in HBsAg+ have been described**
  - **SBP higher risk in pts with ascites**
  - **Higher risk of fungal infection should be considered**
- **No contraindications to Thromboprophylaxis; debate is open on enhanced thromboprophylaxis (cirrhotics patients excluded from ongoing trials)**
- **Tocilizumab**
  - **LT elevations are frequent but clinically apparent liver injury with jaundice seem to be rare**
  - **Patients with decompensated cirrhosis should not be treated**
  - **Consider risk of HBV reactivation**
- **Baricitinib**
  - **Might induce liver enzymes elevation**
  - **Not indicated in Child C cirrhosis**

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Liver Transplant Recipients and COVID-19 severity

Author	Design	Country Region /Number Included	Major findings
Webb et al. (Aug 2020)	Large international registry study	18 countries; SARS-CoV-2 plus LT recipient (*n* = 151); SARS-CoV-2 plus non-LT recipients from Oxford University Hospitals (*n* = 627)	Overall mortality (19%); LT did not significantly increase the risk of death (absolute risk difference 1.4%, 95% (CI –7.7 to 10.4);
Colmenero et al. (Aug 2020)	Prospective multicentre cohort study	Spain; SARS-CoV-2 plus LT recipient (*n* = 111); SARS-CoV-2 plus general population during study period (*n* = 150,000); LT recipients without SARS-CoV-2 (*n* = 13,000)	Mortality in LT recipients (18%) lower than the matched general population; SMR 95.5 (95% CI 94.2–96.8); SIR 191.2 (95% CI 190.3–192.2)
Rablee et al (Sep 2020)	Multicentre retrospective cohort study	SARS-CoV-2 plus LT recipient (*n* = 112)	Overall mortality (22%);
Ravanan et al (Aug 2020)	National cohort study: National Health Service Blood and Transplant registry data	England; SARS-CoV-2 plus LT recipient (*n* = 64); rates of infection and mortality compared with all SARS-CoV-2-positive general English population	Overall mortality (23%); reduced risk of SARS-CoV-2 infection (OR 0.53, 95% CI 0.40–0.70)
Kates et al. (Aug 2020)	Multicentre prospective cohort study	USA; SARS-CoV-2 plus LT recipients (*n* = 73)	28-day mortality (21%); within whole solid organ transplant cohort (*n* = 482), LT not independently associated with death
Belli et al (Dec 2020)	European registry study	9 European countries; SARS-CoV-2 plus LT recipient (*n* = 243)	Overall mortality (20%)

COVID-19 Predictors of outcome in Liver Transplant Recipients

Author	Design	Country Region /Number Included	Major findings
Webb et al. (Aug 2020)	Large international registry study	18 countries; SARS-CoV-2 plus LT recipient (*n* = 151); SARS-CoV-2 plus non-LT recipients from Oxford University Hospitals (*n* = 627)	risk factors for mortality within LT recipients: age, renal function and non-HCC cancer
Colmenero et al. (Aug 2020)	Prospective multicentre cohort study	Spain; SARS-CoV-2 plus LT recipient (*n* = 111); SARS-CoV-2 plus general population during study period (*n* = 150,000); LT recipients without SARS-CoV-2 (*n* = 13,000)	Baseline mycophenolate independent risk factor for severe COVID-19 (ICU, IPPV or death) (RR 3.94, 95% CI 1.59–9.74; *P* = 0.003).
Webb et al (Feb 2021)	Combined analysis of Webb et al and Colmenero et al.	18 countries including 108 cases from Spain; SARS-CoV-2 plus LT recipient (*n* = 258)	Age and Charlson Comorbidity Index independently associated with death; no association with type of immunosuppression regime
Rablee (Sep 2020)	Multicentre retrospective cohort study	SARS-CoV-2 plus LT recipient (*n* = 112)	no independent risk factors for death identified
Belli (Dec 2020)	European registry study	9 European countries; SARS-CoV-2 plus LT recipient (*n* = 243)	Risk factors for mortality: age, diabetes, chronic kidney disease; Tacrolimus had positive independent effect of survival (0.55; 95% CI 0.31–0.99)

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COVID-19 Has Had a Significant Impact on HCV Management and Delayed Elimination Efforts

Disruption in access to HCV services[1–4]

- Containment policies and other restrictions have made it harder to reach patients[5]

Disruption in access to drug services and harm reduction[1,4]

- Many everyday services have been closed or are operating reduced hours[5]

Deprioritization of HCV screening and treatment[3–4]

- Deprioritization of services will impact on the incidence of viral hepatitis[5]

Diversion of resources to support COVID-19-related activities[4]

- Illness from COVID-19 negatively impacted staff availability[4]

COVID-19, coronavirus disease.

1. ASHM. COVID-19 taskforce interim recommendations. 2020. Available at: https://ashm.org.au/covid-19/clinical-care/hcv/ (Accessed May 10, 2021); 2. HCV Action. Hepatitis C services during and beyond the COVID-19 outbreak, June 2020. Available at: http://www.hcvaction.org.uk/sites/default/files/resources/HCV%20Action%20Hepatitis%20C%20Covid-19%20webinar%20summary%20report.pdf (Accessed May 10, 2021); 3. Kondili LA, et al. *Dig Liver Dis* 2020;52:947–949; 4. Dunlop A, et al. *Harm Reduct J* 2020;17:26; 5. Picchio C, et al. *Harm Reduc J* 2020;17:87.

Initiatives Employed in Italy During the COVID-19 Pandemic

4,082,198 COVID-19 cases and 122,263 deaths on May 7, 2021[1]

February 21, 2020
COVID-19 pandemic reaches Italy[2]

March 15, 2020
Italy enters a nationwide lockdown; there is no access to hospitals for "non-urgent" needs[2]

May 4, 2020
Lockdown measures begin to be eased[2]

HCV elimination scenario post-lockdown[2]:

- Utilization of shorter treatment regimens
- Simplified follow-up procedures and utilization of telemedicine
  - Only pretreatment & 12-week posttreatment appointments required
- Increased support from nurses for treatment monitoring
- Combined SARS-CoV-2 and HCV screening

HCV elimination scenario during lockdown[2]:

- Telemedicine consultations for patients on treatment and posttreatment follow-up
- Anti-HCV drugs moved to local pharmacies (previously only in hospital pharmacies)
- Delay in treatment initiation for F0–F2 patients
- Liver ultrasound surveillance and elastography delayed

May–June 2020
Joint SARS-CoV-2/HCV testing program[3]

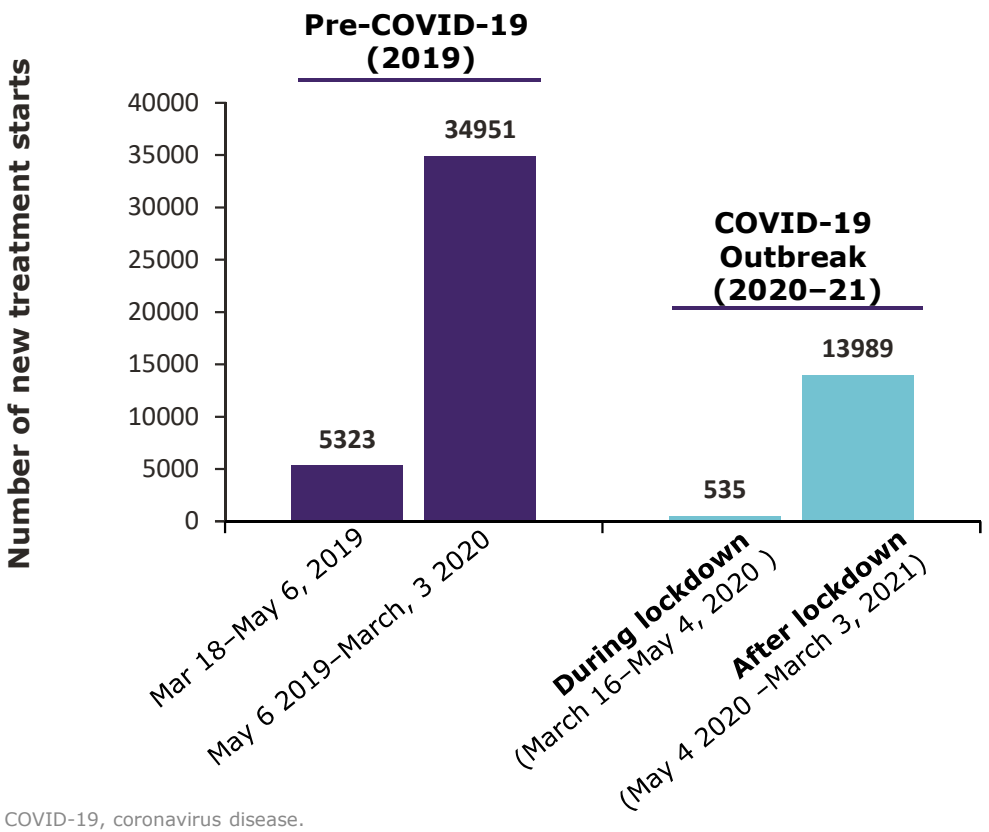
June 22, 2020
ACE position paper proposing SARS-CoV-2/HCV screening[4]

August–November 2020
Joint SARS-CoV-2/HCV testing programs in Northern Italy[5]

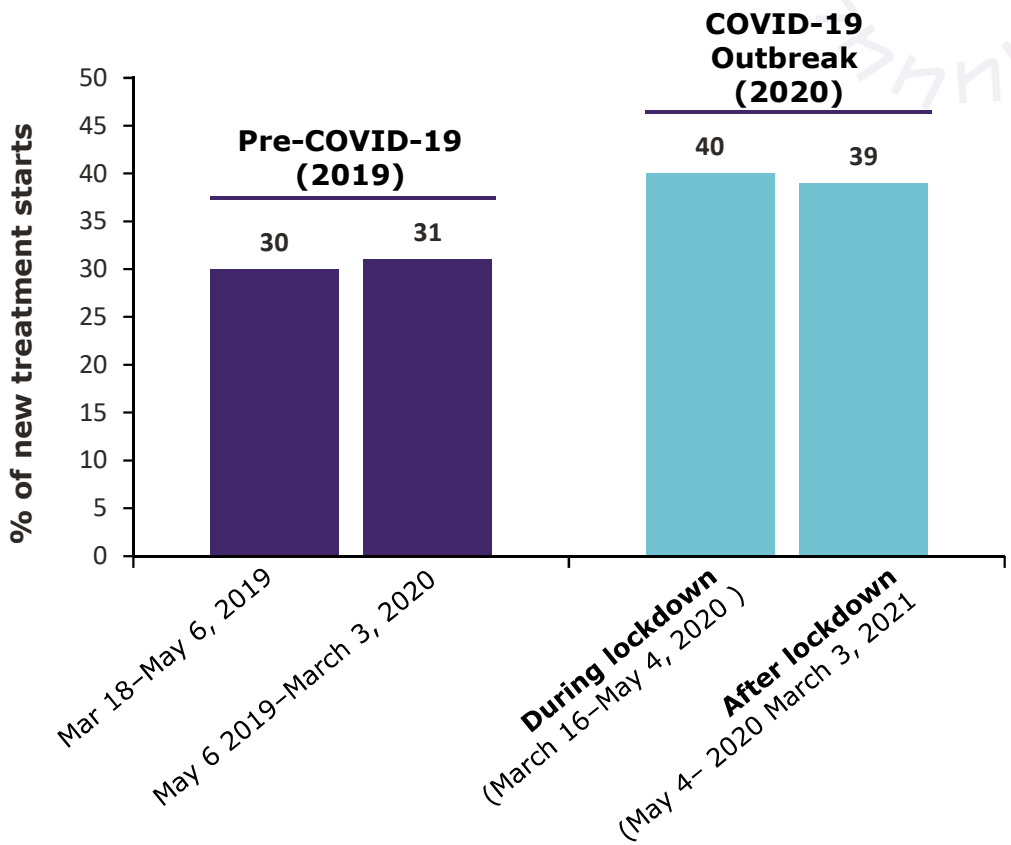
ACE, Allenza contro l'Epatite; COVID-19, coronavirus disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. 1. Johns Hopkins University of Medicine, Coronavirus Resource Center, Italy. https://coronavirus.jhu.edu/region/italy (Accessed May 7, 2021) 2. Massimo Puoti, personal communication; 3. Pagani G, et al. *J Infect* 2020;81:e10-e12; 4. ACE position paper: HCV/COVID-19 Joint Screening. Available at: https://www.epac.it/cm-files/2020/07/14/position-paper-ace-2020-en.pdf (Accessed May 5, 2021) 5. Giacomelli A, et al. *J Hepatol* 2021;S0168-8278(21)00009-X.

The COVID-19 Outbreak Has Led to a Reduction in HCV Treatment Rates in Italy

Number of new treatment starts

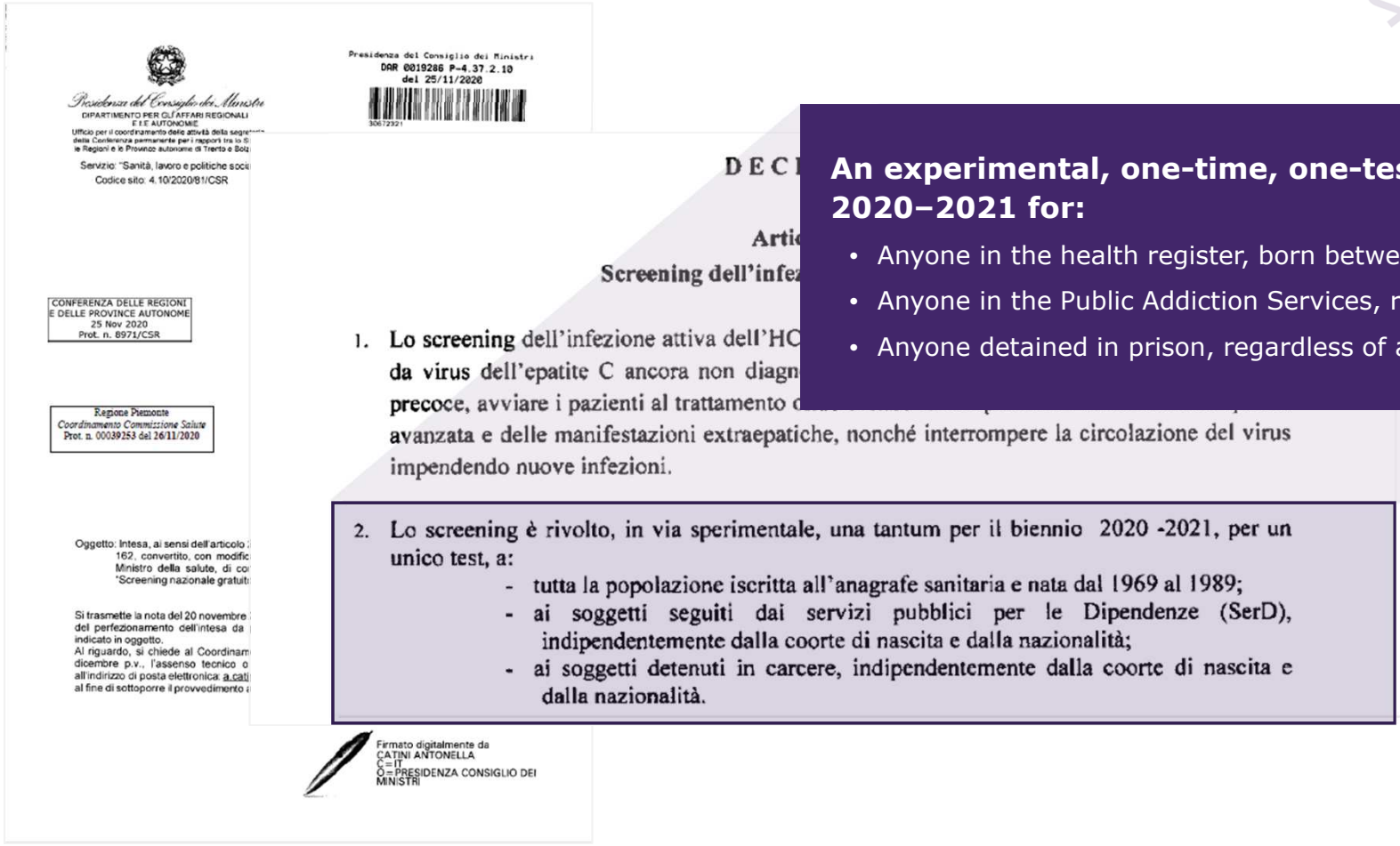


Percentage of new treatment starts in F3/F4



COVID-19, coronavirus disease.
Italian Medicine Agency. 2020. Available at: www.aifa.gov (Accessed May 10, 2021).

Decree of HCV National Screening Fund



Presidenza del Consiglio dei Ministri
DIPARTIMENTO PER GLI AFFARI REGIONALI E LE AUTONOMIE

Presidenza del Consiglio dei Ministri
DAR 0019286 P-4.37.2.10
del 25/11/2020

Servizio: "Sanità, lavoro e politiche soci
Codice sito: 4.10/2020/81/CSR

CONFERENZA DELLE REGIONI E DELLE PROVINCE AUTONOME
25 Nov 2020
Prot. n. 8971/CSR

Regione Piemonte
Coordinamento Commissione Salute
Prot. n. 00039253 del 26/11/2020

Oggetto: Intesa, ai sensi dell'articolo
162, convertito, con modific
Ministro della salute, di co
"Screening nazionale gratuit

Si trasmette la nota del 20 novembre
del perfezionamento dell'intesa da
indicato in oggetto.
Al riguardo, si chiede al Coordinam
dicembre p.v., l'assenso tecnico o
all'indirizzo di posta elettronica: a.cati
al fine di sottoporre il provvedimento

DEC

Arti

Screening dell'infez

1. Lo screening dell'infezione attiva dell'HC
da virus dell'epatite C ancora non diagn
precoce, avviare i pazienti al trattamento
avanzata e delle manifestazioni extraepatiche, nonché interrompere la circolazione del virus
impendendo nuove infezioni.

2. Lo screening è rivolto, in via sperimentale, una tantum per il biennio 2020 -2021, per un unico test, a:
   - tutta la popolazione iscritta all'anagrafe sanitaria e nata dal 1969 al 1989;
   - ai soggetti seguiti dai servizi pubblici per le Dipendenze (SerD), indipendentemente dalla coorte di nascita e dalla nazionalità;
   - ai soggetti detenuti in carcere, indipendentemente dalla coorte di nascita e dalla nazionalità.

Firmato digitalmente da
CATINI ANTONELLA
C=IT
O=PRESIDENZA CONSIGLIO DEI MINISTRI

An experimental, one-time, one-test screening, running 2020–2021 for:

- Anyone in the health register, born between 1969–1989
- Anyone in the Public Addiction Services, regardless of age and nationality
- Anyone detained in prison, regardless of age and nationality

Italian Ministry of Health and Ministry of Economy. Decree of free national screening aimed at HCV elimination. November 2020. Available at: http://www.quotidianosanita.it/allegati/allegato5926494.pdf (Accessed May 10, 2021).

Planned Screening Program by Lombardy Regional Health Service

Populations at risk	Screening recommendations
Anyone in the public addiction services*	Voluntary screening for HCV by POC/blood test for all attendees of the drug rehabilitation centers and communities and street facilities
Anyone detained in prison*	Voluntary screening for HCV by POC/blood test in all prisons
People born from 1969 to 1989	• Opportunistic screening after counselling and exclusion of people who underwent pharmacological eradication of HCV with DAA o POC testing offered at SARS-CoV-2 vaccination o POC testing offered at cervical cancer screening o Blood test offered before planned hospitalization, or at emergency hospitalization, or at any blood sampling for other purposes • Recall of people untested

*Regardless of age and nationality.
POC, point of care; SARS-CoV-2, severe respiratory coronavirus 2.
Massimo Puoti, personal communication.

Epatite C semplificazione percorso terapeutico dopo lo screening

Ospedale Niguarda — Sistema Socio Sanitario Regione Lombardia

Hepatitis Center

- HCVAb+ allo screening→ trasmissione elenco positivi con recapiti ad Hepatitis Center
- Contatto telefonico per anamnesi terapeutica (già trattato?) e prescrizione HCVRNA su ricetta dematerializzata
- Se HCVRNA + prescrizione esami ecografia e fibroscan su ricetta dematerializzata
- **1 ° Visita** + Fibroscan e prescrizione terapia ed esami
- Ritiro terapia e consegna esami on treatment se necessari
- **2° Visita** a 16 settimane e prescrizione follow up

Attività infermieristica **Attività medica**

Coinfezioni SARS-CoV-2 ed HIV/HCV: Messaggi chiave

- Durante la COVID-19 è presente un danno epatico multifattoriale
- Devono ancora essere definiti
  - il ruolo patogenetico di un possible epatotropismo del virus
  - Ruolo prognostico della presenza di danno epatico alla diagnosi
- Alcuni studi hanno messo in relazione la malattia epatica da alcol con un più grave decorso di COVID-19 (ruolo dei confondenti)
- Non è chiaro se NAFLD/MAFLD siano associate in maniera indipendente ad un decorso più grave della malattia
  - Ruolo dei confondenti
  - Ruolo della fibrosi
  - Impatto della malattia e dei suoi meccanismi patogenetici sulla risposta infiammatoria
- Il decorso della malattia e la mortalità è più rilevante nei soggetti con cirrosi ed aumenta con il grado di scompenso → Pazienti cirrotici popolazione altamente vulnerabile
- La popolazione dei pazienti trapiantati di fegato non sembra avere un decorso peggiore
- Potrebbe essere utile un'azione di SIMIT per aggiungere la cirrosi scompensata tra i criteri di selezione per la terapia precoce con Monoclonali (o di inserire I pazienti con cirrose tra I pazienti con immunodeficienze secondarie)