AASLD-AST COVID-19 and the Liver: Chronic Liver Disease and Transplant

June 25, 2020

5:00pm – 6:00pm EDT

Moderated by:

Elizabeth C. Verna, MD, MS, FAST

Emily Blumberg, MD, FAST

Joint Webinar

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AST | AMERICAN SOCIETY OF TRANSPLANTATION

Presenters:

A. Sidney Barritt IV, MD, MSCR

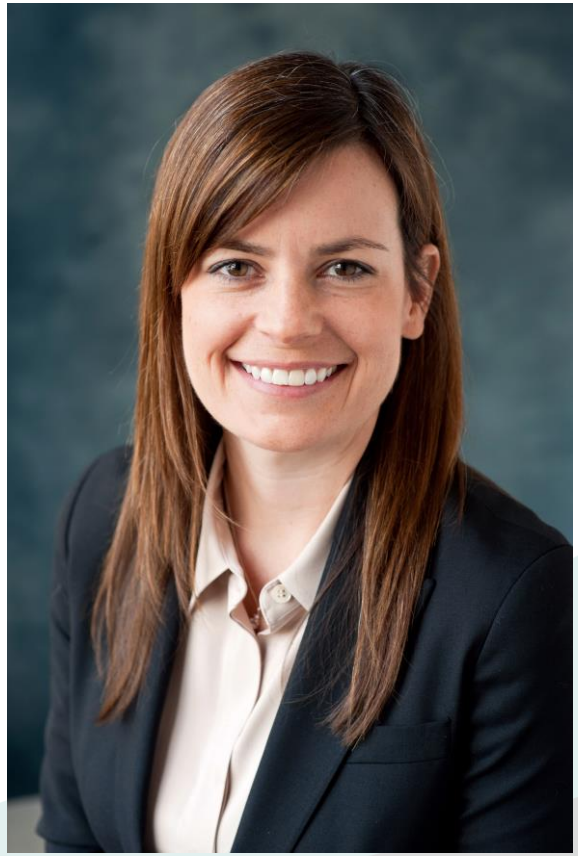
Olivia Kates, MD

Webinar Moderator

Elizabeth C. Verna, MD, MS

Associate Professor of Medicine
Center for Liver Disease and Transplantation and Division of Digestive and Liver Diseases

Columbia University



Webinar Moderator

Emily Blumberg, MD, FAST

Director of the Transplant Infectious Diseases Program and the Infectious Diseases Fellowship

University of Pennsylvania

Webinar Presenter

A. Sidney Barritt IV, MD, MSCR

Associate Professor, Liver Center

Transplant Hepatology Fellowship Program Director

University of North Carolina

Chapel Hill

Webinar Presenter

Olivia Kates, MD

Developer and lead investigator
UW COVID-SOT Registry project

University of Washington

Who is the AST?

Mission Statement:

The American Society of Transplantation is dedicated to advancing the field of transplantation and improving patient care by promoting research, education, advocacy, organ donation, and service to the community.

AST Resources for Patients & Professionals

- The AST continually creates and updates COVID-19 resources for both medical professionals and the transplant community.
- Transplant Community: https://www.myast.org/covid-19
- Professionals: https://www.myast.org/covid-19-information

- General Information About the AST: https://www.myast.org/
- General Information about Power2Save: https://power2save.org/

Connect with AST

twitter.com/AST_infoaasld.org/twitter
@AST_info

facebook.com/AmericanSocietyofTransplantation

www.linkedin.com/american-society-of-transplantation/

The Liver Meeting Digital Experience

#TLMdX

aasld.org/livermeeting

The Liver Meeting Abstracts

Submit abstracts at aasld.org/LMabstracts

AASLD Journals App

Access all four AASLD Journals in a single app

aasld.org/publications

AASLD COVID-19 Resources

For resources and updates on COVID-19 and the liver, visit aasld.org/COVID19

AASLD Member Benefits

- Special Interest Group participation
- Priority housing and registration with discounts to The Liver Meeting® and DDW®
- Free or discounted subscriptions to AASLD journals HEPATOLOGY and *Liver Transplantation*
- Complimentary access to premier hepatology online education in Liver*Learning*®
- Individual and corporate non-physician memberships available

Join or Renew: aasld.org/membership

Connect with AASLD

aasld.org/twitter
@AASLDtweets

aasld.org/linkedin

aasld.org/facebook

aasld.org/instagram

aasld.org/youtube

Join the COVID-19 Discussion Community on Engage

engage.aasld.org/covid19

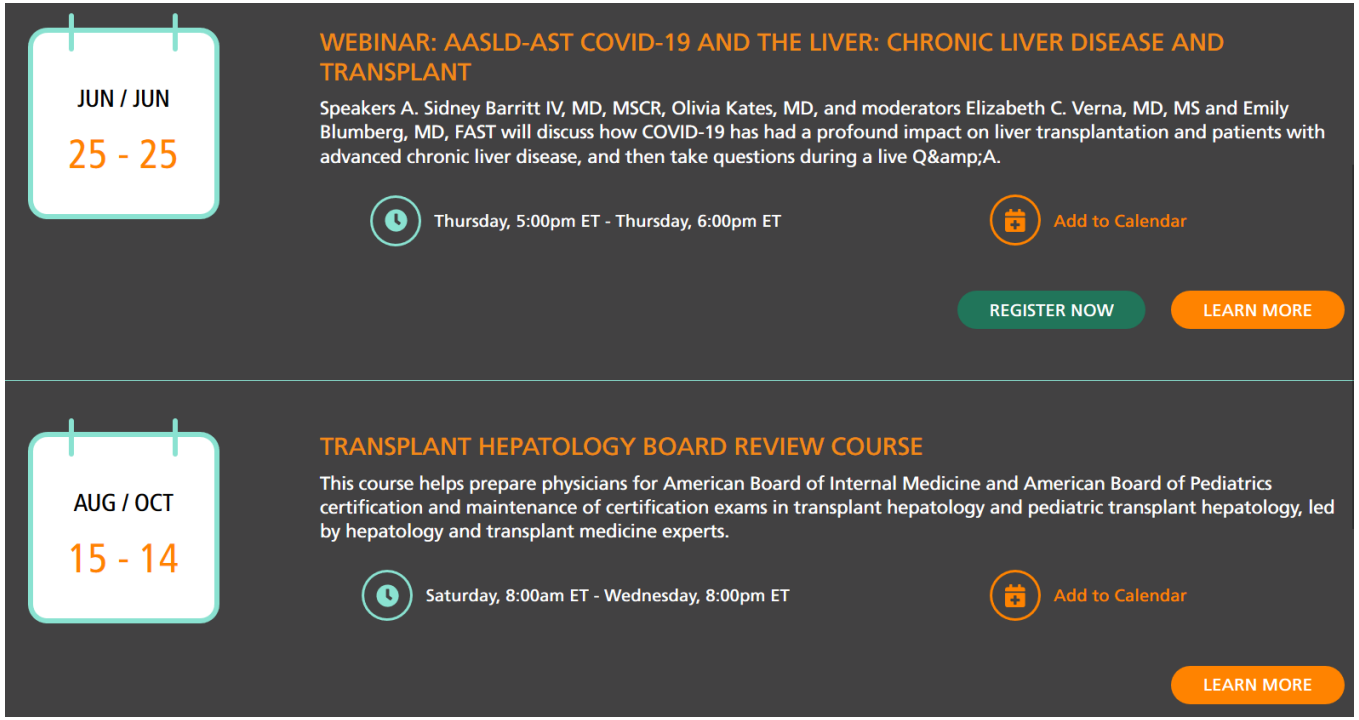
You can help invest in the future of hepatology by supporting more research & advanced career training.

Donate today to AASLD Foundation

aasldfoundation.org/donate

Follow us on Twitter **@AASLDFoundation**

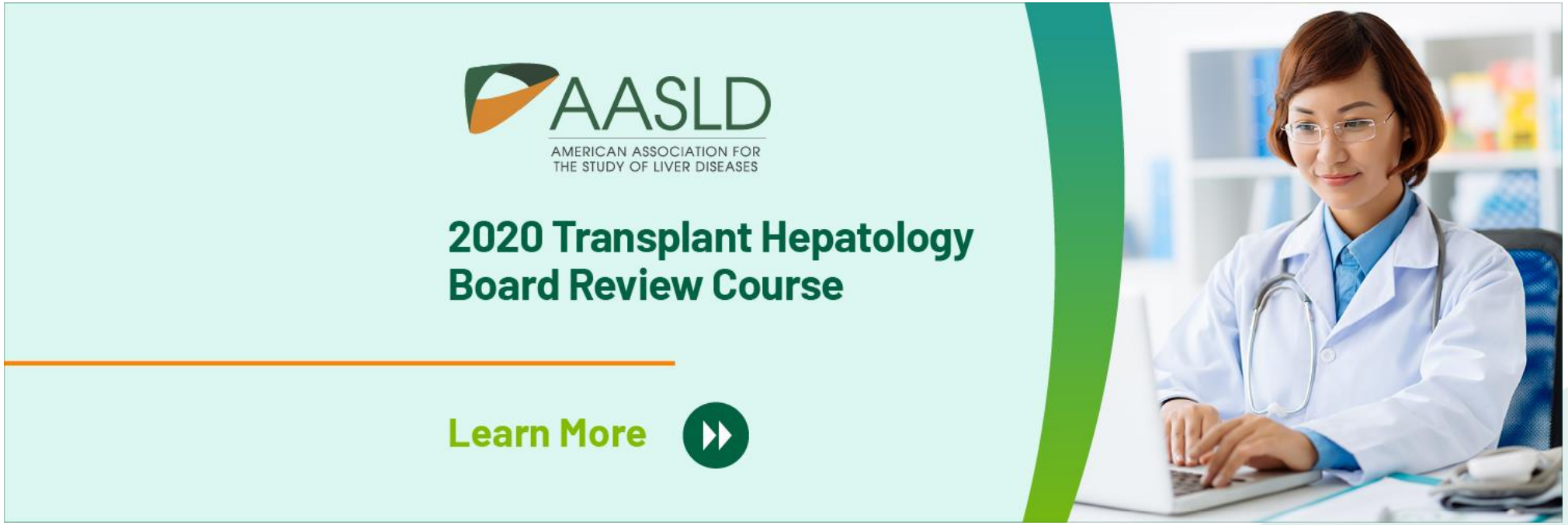
AASLD Calendar of Events



Stay Up-To-Date with the latest AASLD Events & Educational Offerings

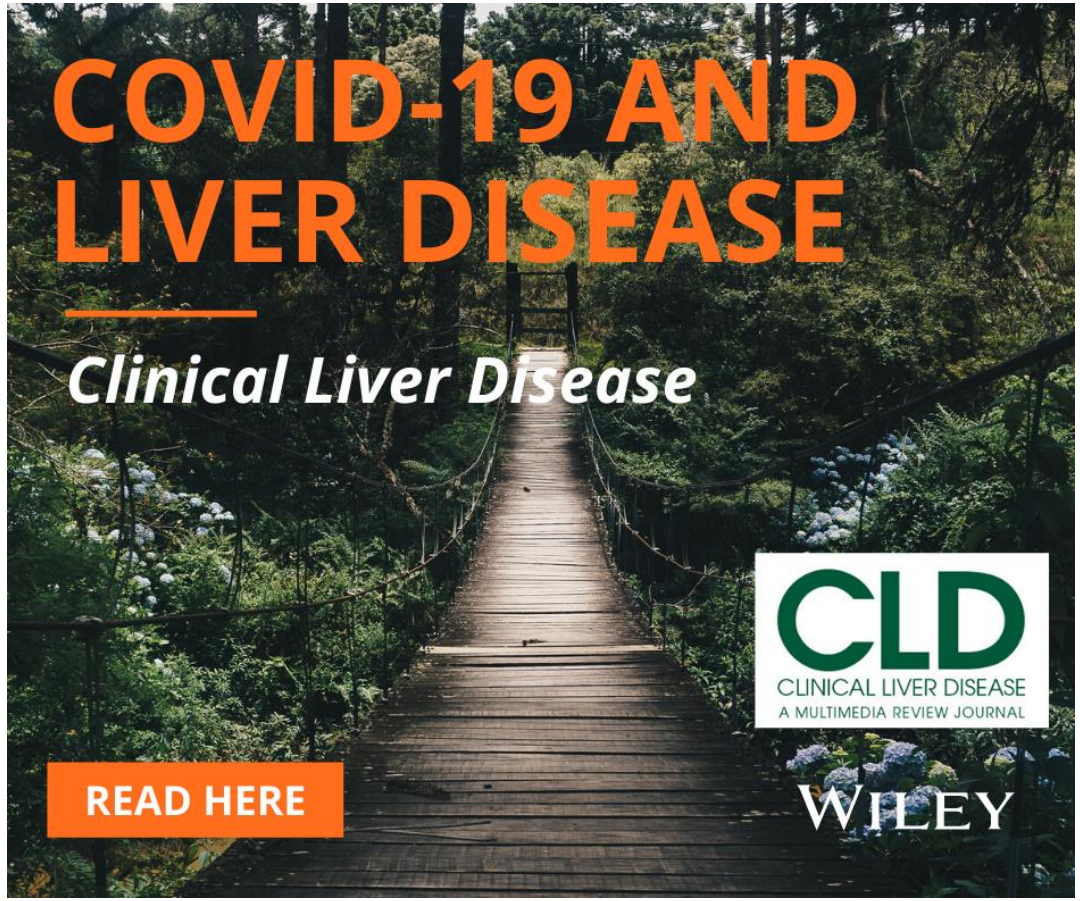
aasld.org/calendar

2020 Transplant Hepatology Board Review Course



aasld.org/TransplantReview

COVID-19 & Liver Disease



View the Latest issue of CLD, AASLD's multimedia journal: COVID-19 & Liver Disease

cldlearning.com

AASLD-AST COVID-19 and the Liver: Chronic Liver Disease and Transplant

June 25, 2020

5:00pm – 6:00pm EDT

Moderated by:

Elizabeth C. Verna, MD, MS, FAST

Emily Blumberg, MD, FAST

Joint Webinar

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AST | AMERICAN SOCIETY OF TRANSPLANTATION

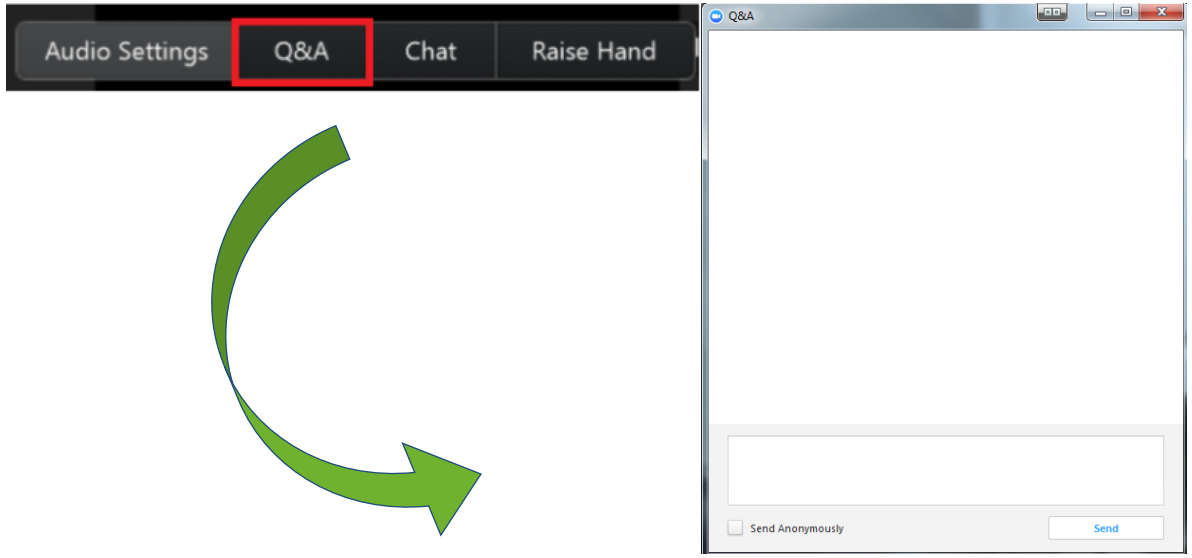
Presenters:

A. Sidney Barritt IV, MD, MSCR

Olivia Kates, MD

Webinar Q&A

Submit your questions in the Q&A box at the top or bottom of your screen.



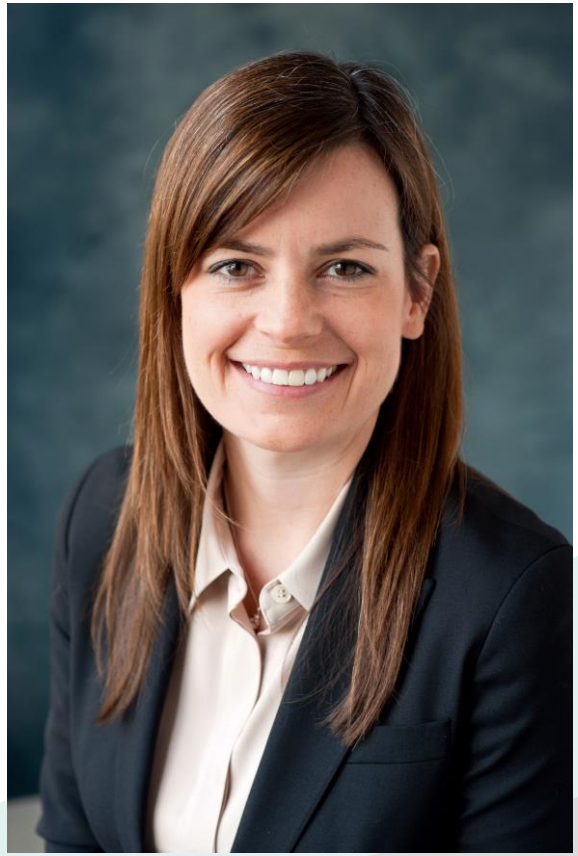
Questions will be answered at the end of the presentation.

Webinar Moderator

Elizabeth C. Verna, MD, MS

Associate Professor of Medicine
Center for Liver Disease and Transplantation and Division of Digestive and Liver Diseases

Columbia University



Webinar Moderator

Emily Blumberg, MD, FAST

Director of the Transplant Infectious Diseases Program and the Infectious Diseases Fellowship

University of Pennsylvania

Webinar Presenter

A. Sidney Barritt IV, MD, MSCR

Associate Professor, Liver Center

Transplant Hepatology Fellowship Program Director

University of North Carolina

Chapel Hill

Webinar Presenter

Olivia Kates, MD

Developer and lead investigator
UW COVID-SOT Registry project

University of Washington

Webinar Panelist

- **Michael L. Schilsky, MD, FAASLD**, Yale New-Haven Hospital
- **Michael Ison, MD, MS**, Northwestern University Feinberg School of Medicine
- **John C. Bucuvalas, MD, FAASLD**, Icahn School of Medicine at Mount Sinai (ISMMS)
- **Jean C. Emond, MD, FAASLD**, Columbia University

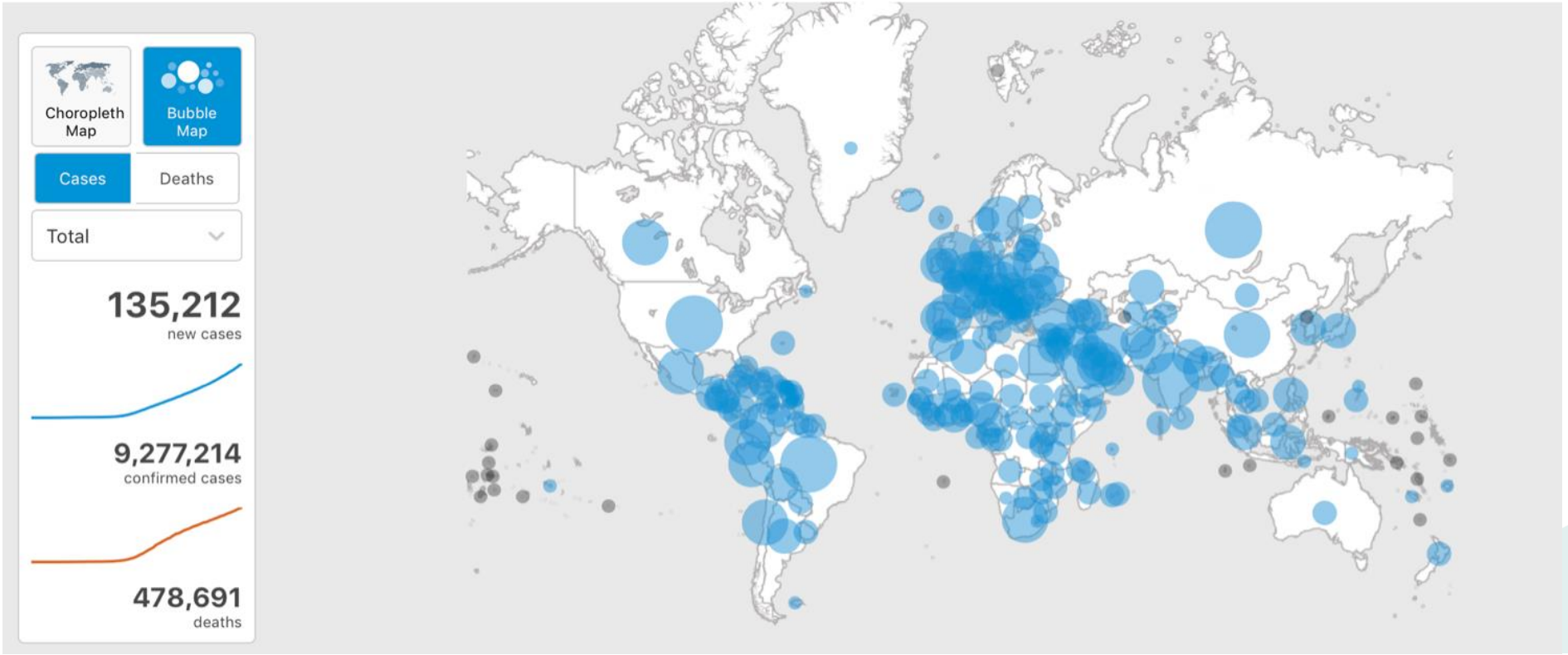
Clinical Oversight Subcommittee

- Co-chair, Oren K. Fix, MD, MSc, FAASLD, Swedish Medical Center (Washington)
- Co-chair, Elizabeth C. Verna, MD, MS, Columbia University (New York)
- Kimberly Brown, MD, Henry Ford Health System (Michigan)
- Jaime Chu, MD, Icahn School of Medicine at Mount Sinai (New York)
- Bilal Hameed, MD, University of California (California)
- Laura M. Kulik, MD, Northwestern Medical Faculty Foundation (Illinois)
- Ryan M. Kwok, MD, Uniformed Services University (Maryland)
- Brendan M. McGuire, MD, University of Alabama (Alabama)
- Jennifer C. Price, MD, PhD, University of California, San Francisco (California)
- Daniel S. Pratt, MD, FAASLD, Massachusetts General Hospital (Massachusetts)
- Nancy S. Reau, MD, Rush University (Illinois)
- Mark W. Russo, MD, MPH, FAASLD, Carolinas Medical Center (North Carolina)
- Michael Schilsky, MD, FAASLD, Yale University (Connecticut)
- Norah Terrault, MD, MPH, FAASLD, Keck Medicine of USC (California)
- Andrew Reynolds, (Patient Advocate)
- Raymond Chung and K. Rajender Reddy (ex-officio)

Webinar Agenda

- Housekeeping Items – Dr. Elizabeth Verna
- Presenter Introductions – Dr. Elizabeth Verna
- Webinar Contributors
- Webinar Introduction – Dr. Elizabeth Verna
- Expert Panel Consensus Document Update – Dr. Oren Fix
- Emerging data on the impact of COVID-19 in advanced liver disease – Dr. A. Sidney Barritt IV
- COVID-19 in Liver Transplant Recipients – Dr. Olivia Kates
- Panel Discussion / Q&A

COVID-19: Persistent Transmission Worldwide



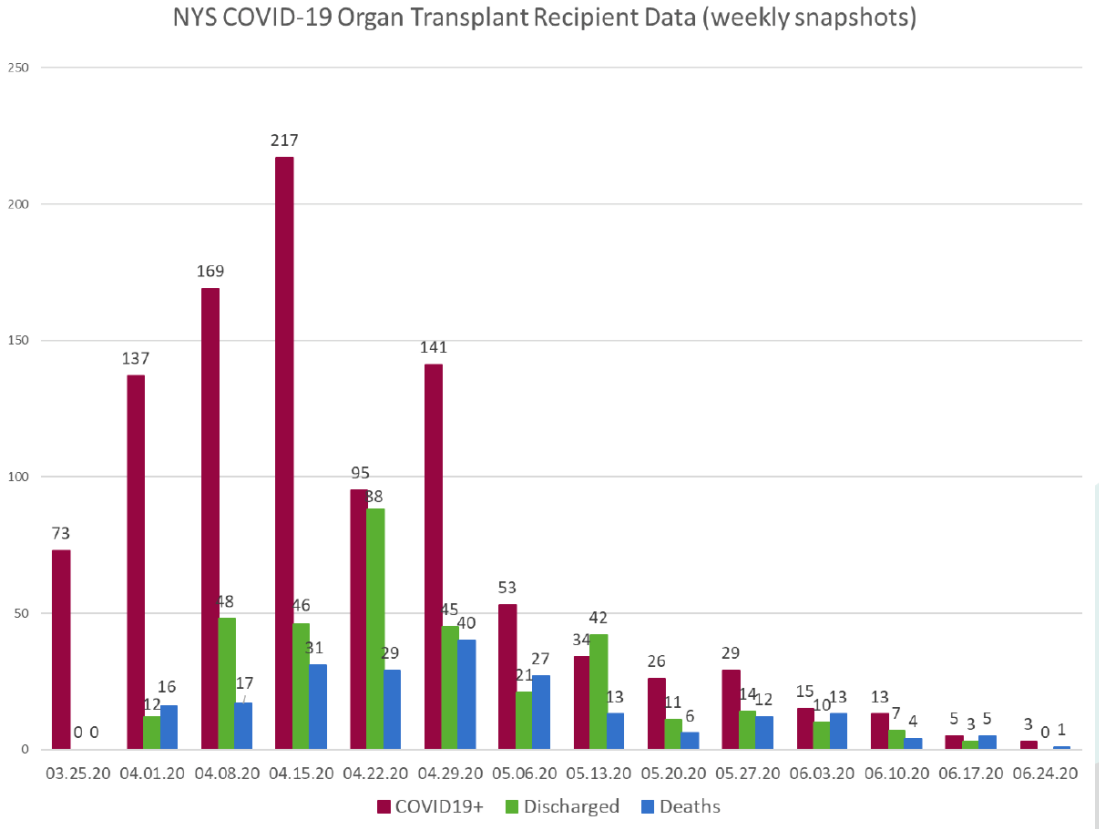
Globally, as of **10:37am CEST, 25 June 2020**, there have been **9,277,214 confirmed cases** of COVID-19, including **478,691 deaths,** reported to WHO.

WHO Coronavirus Disease (COVID-19) Dashboard, accessed June 25, 2020

COVID-19 in Transplant: New York State

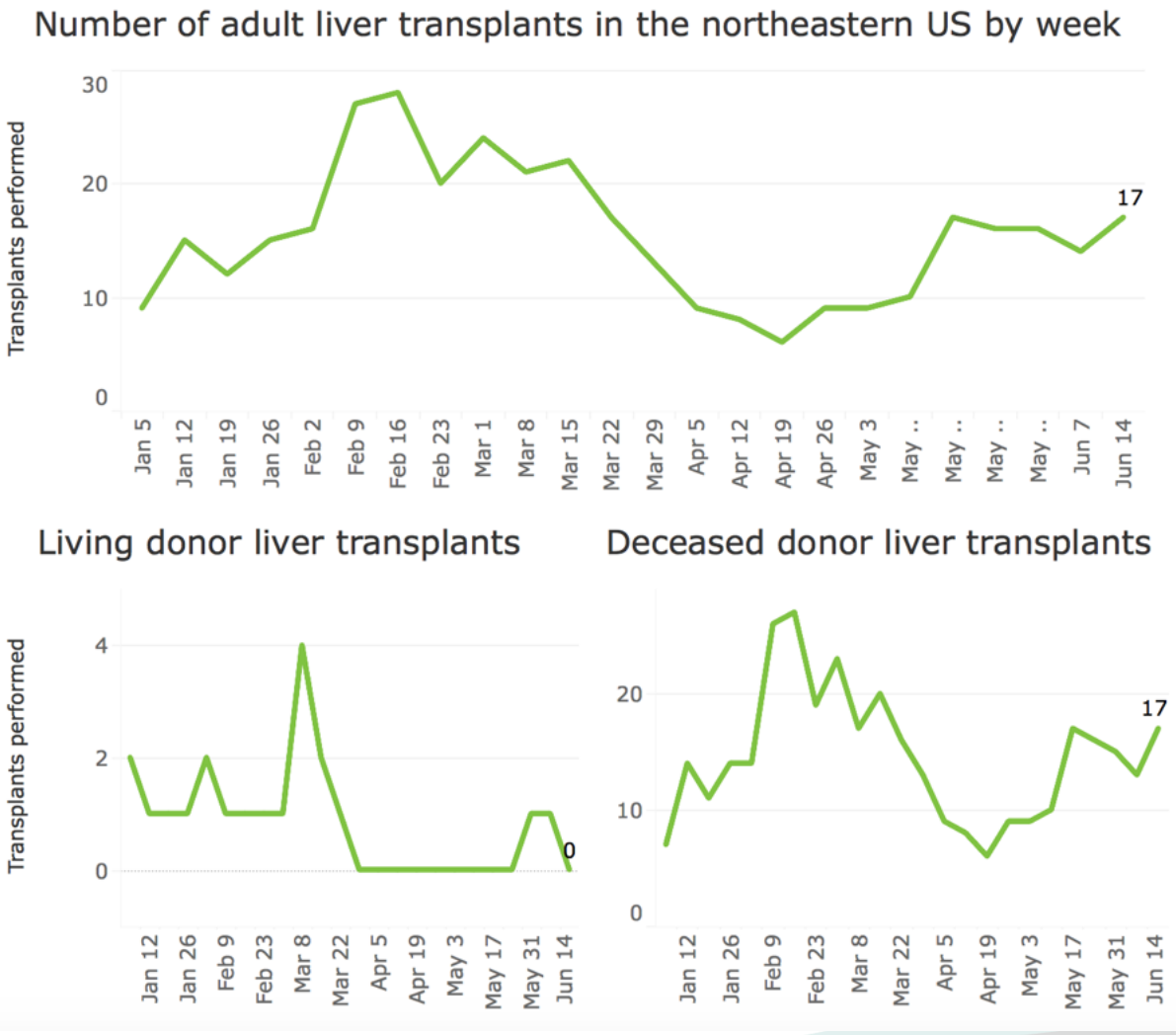
	TOTAL	KI	LI	HT	LU	dual
COVID pos	1010	681	134	129	37	29
Hospitalizations	673	455	74	83	33	28
ICU Admissions	211	145	26	22	9	9
Intubations	161	114	21	14	7	5
Discharged	347	250	39	39	6	13
Deaths	214	160	20	17	10	7

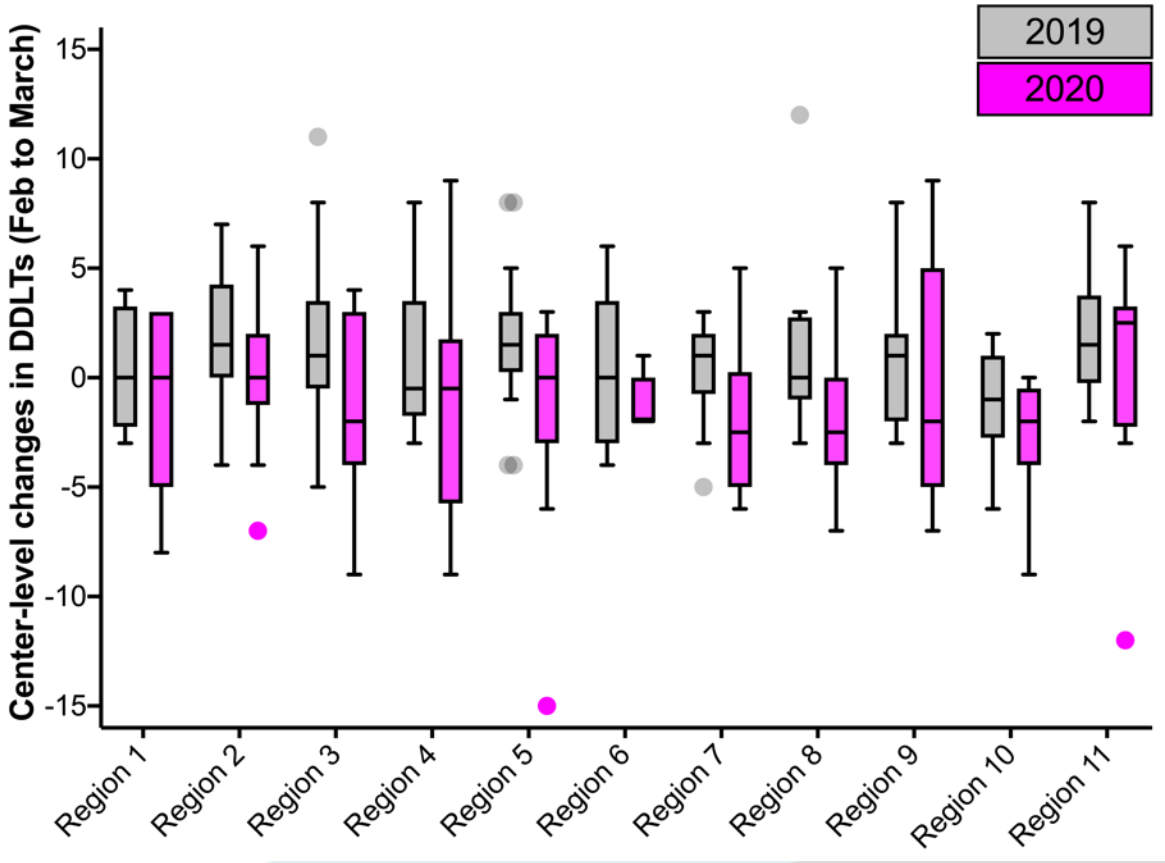
Source: 13/14 Transplant Hospitals reporting
Data is cumulative through June 24, 2020



www.nyclt.org

Impact of COVID-19 on LT Rates

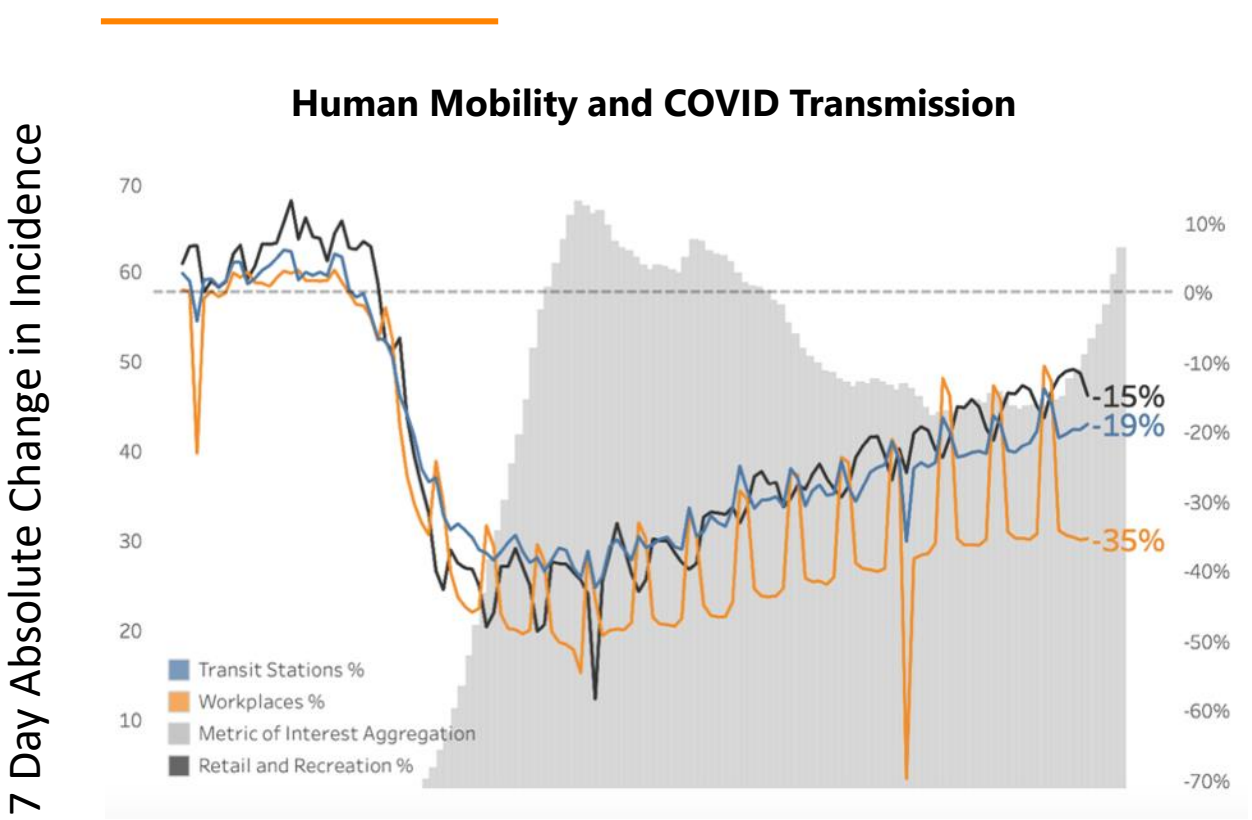


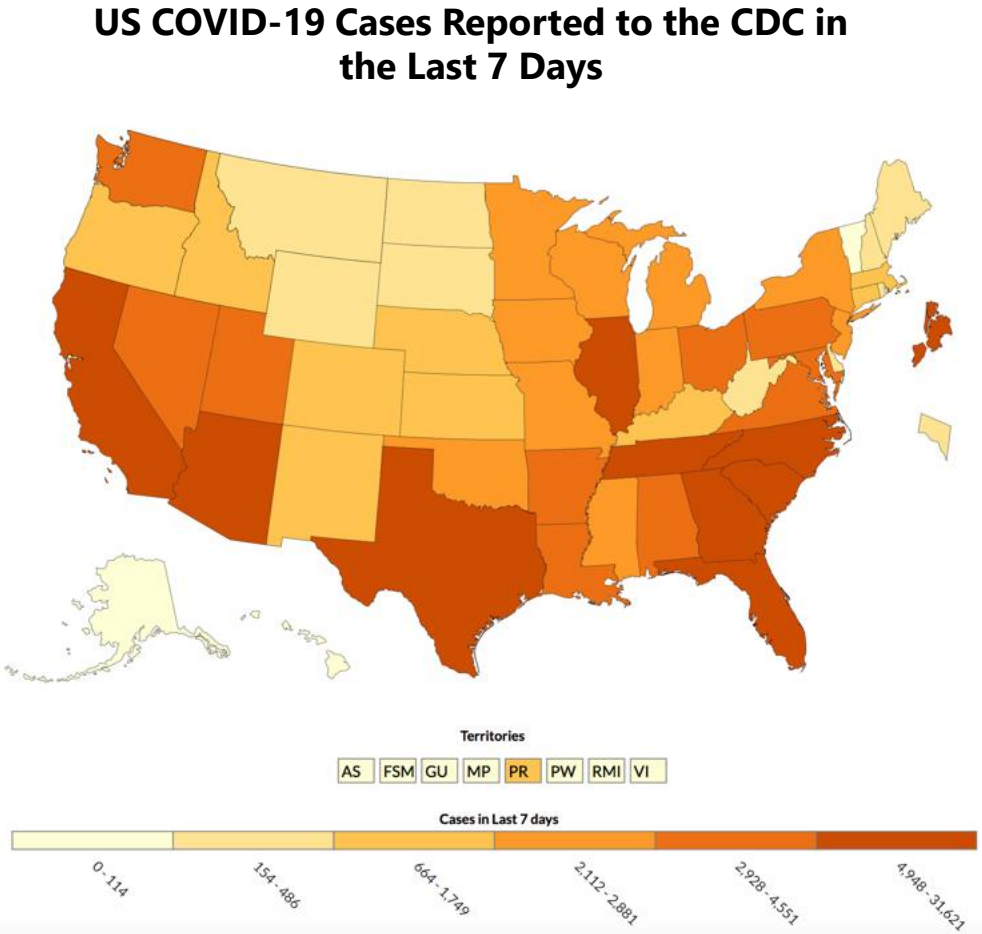


Agopian, Verna and Goldberg, Liver Transpl 2020

https://unos.org/covid/

COVID-19: Increasing Cases in the US





CDC COVID Data Tracker, accessed June 25, 2020

Expert Panel Consensus Updates

Joint Webinar

Oren Fix, MD, MSc, FAASLD

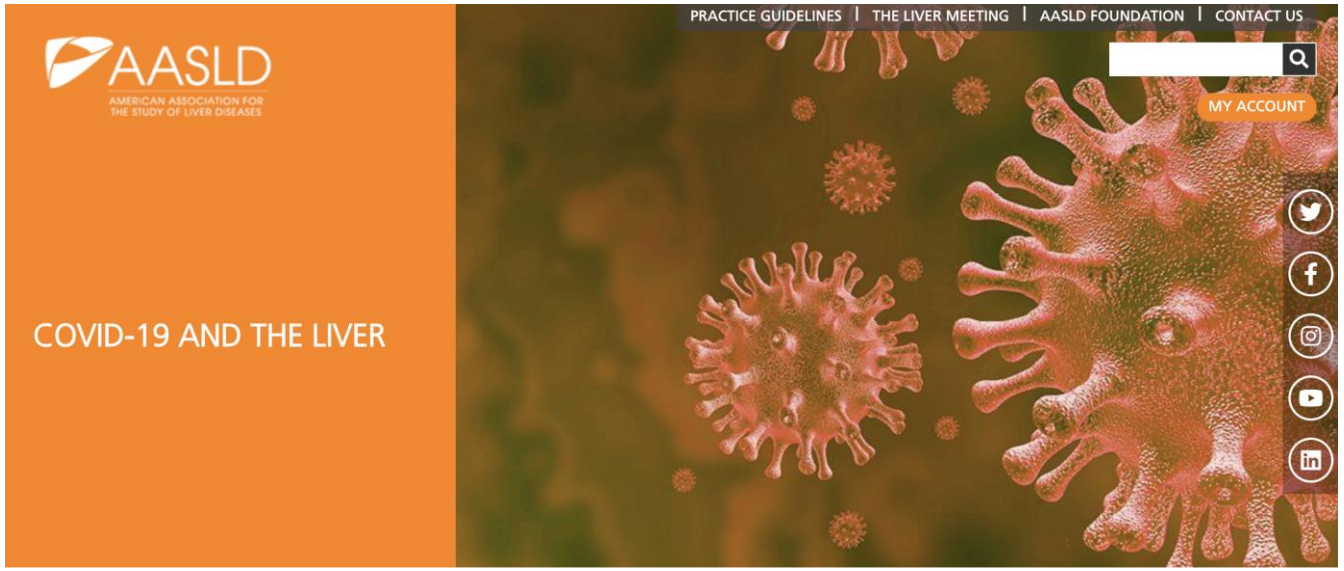
Medical Director, Liver Transplant Program

Swedish Medical Center, Seattle, WA

Clinical Associate Professor

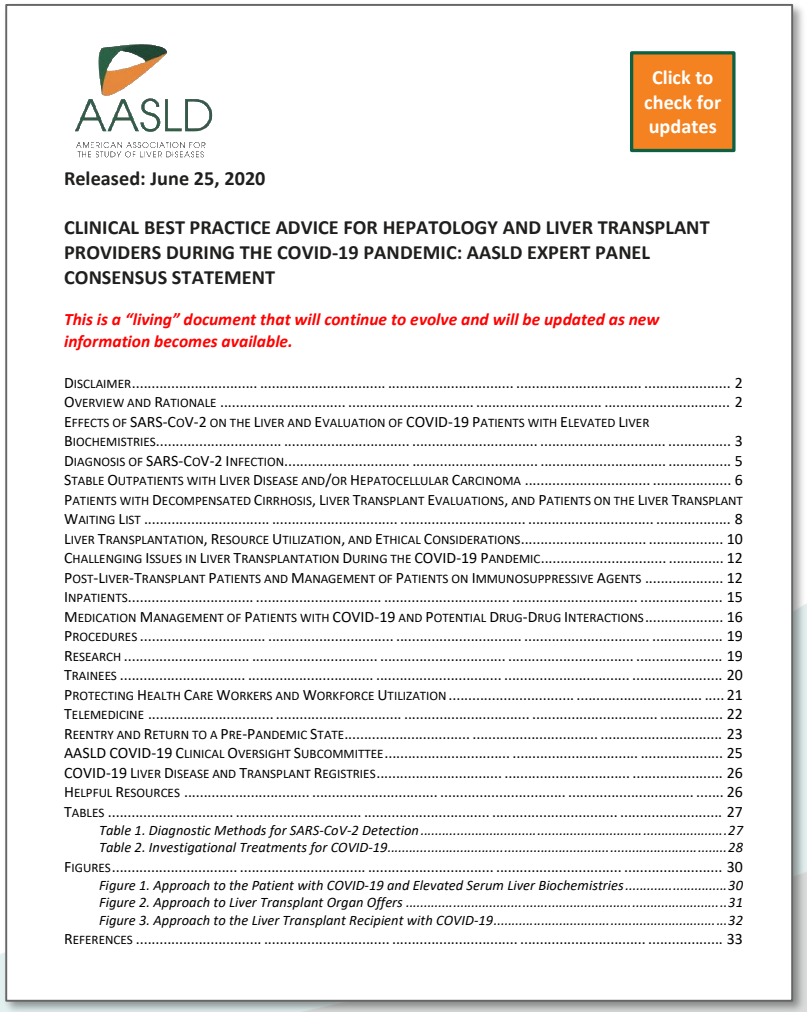
Washington State University Elson S. Floyd College of Medicine

Expert Panel Consensus Statement



- First published online March 23rd
- New update posted today:

  www.aasld.org/covid19



AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Click to check for updates

Released: June 25, 2020

CLINICAL BEST PRACTICE ADVICE FOR HEPATOLOGY AND LIVER TRANSPLANT PROVIDERS DURING THE COVID-19 PANDEMIC: AASLD EXPERT PANEL CONSENSUS STATEMENT

This is a "living" document that will continue to evolve and will be updated as new information becomes available.

Expert Panel Consensus Statement

Major Changes Since June 4, 2020

- Changes reflecting the ramping up of routine and in-person clinical care, procedures, and clinical research
- Clearly identified preprint articles that have not been peer-reviewed

Expert Panel Consensus Statement

Cirrhosis + COVID-19 = Bad

- Retrospective Italian study showing a high mortality rate (35%) in hospitalized patients with cirrhosis and COVID-19

Iavarone M et al. J Hepatol 2020

Expert Panel Consensus Statement

But Cirrhosis – COVID-19 = Also Bad

- Accumulating evidence that patients with cirrhosis and COVID-19 have a higher risk of death compared to patients with COVID-19 alone
- Inpatient mortality in patients with cirrhosis and COVID-19 may be similar to the mortality of patients with cirrhosis alone without COVID-19

Bajaj J et al. Gut 2020. In press

Expert Panel Consensus Statement

Immunosupp + COVID-19 = Not Bad?

- Retrospective Italian report of 10 patients with AIH on immunosuppression and with COVID-19 suggests the course of COVID-19 may be similar to non-immunosuppressed patients
- The authors suggest that pre-emptive reduction in immunosuppression during COVID-19 can be potentially harmful
- Single-center and registry data of liver transplant recipients with COVID-19

Gerussi A et al. Hepatology Communications 2020
Bhoori S et al. Lancet Gastroenterol Hepatol 2020
Webb GJ et al. Lancet Gastroenterol Hepatol 2020
Belli LS et al. Lancet Gastroenterol Hepatol 2020

Expert Panel Consensus Statement

Dexamethasone = Good(?)

- RECOVERY trial demonstrated a significant mortality benefit from dexamethasone in patients receiving invasive mechanical ventilation or oxygen without invasive mechanical ventilation (RR 0.83, 95% CI 0.74-0.92, *P*<.001)
- There was no benefit (and possible harm) from dexamethasone in patients who did not require respiratory support (RR 1.22, 95% CI 0.93-1.61, *P*=.14)

Horby P et al. MedRxiv 2020 (preprint)

Expert Panel Consensus Statement

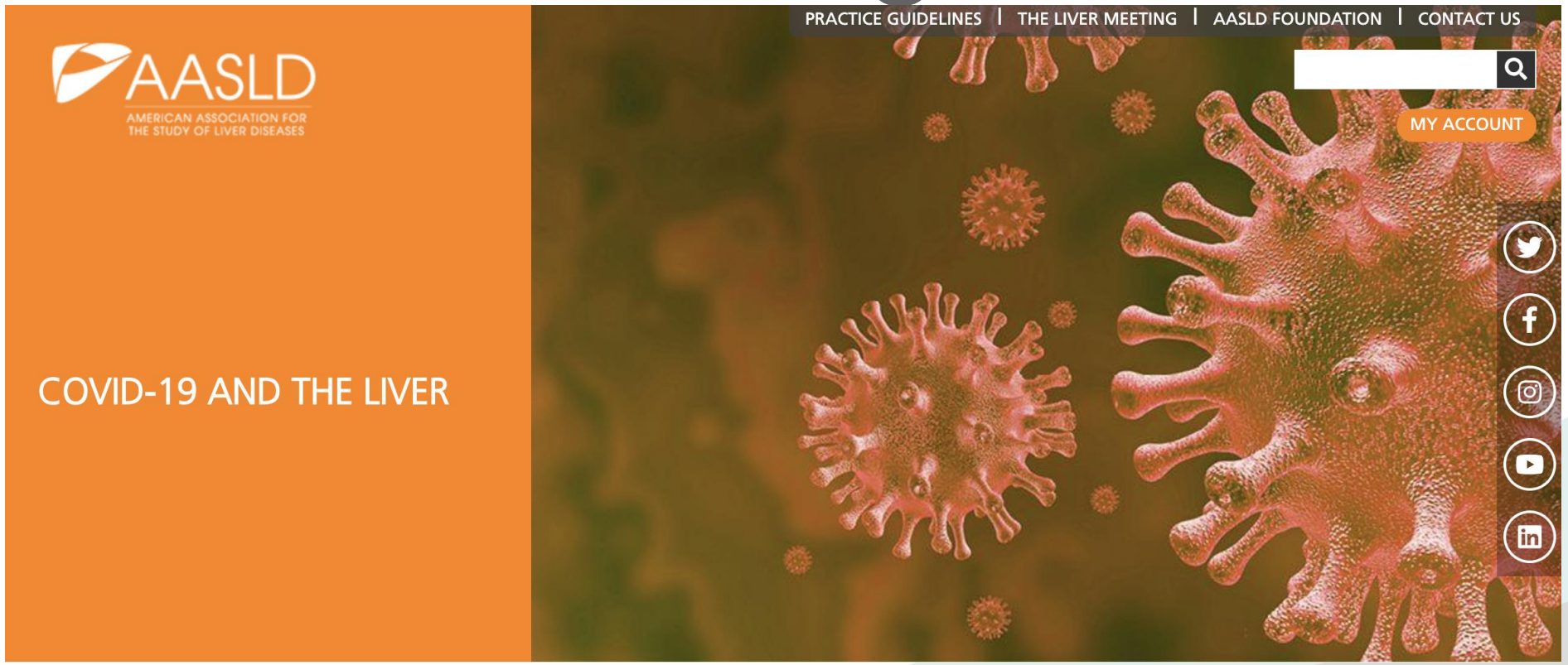
Hydroxychloroquine = Not Good

- The FDA revoked the Emergency Use Authorization for chloroquine and hydroxychloroquine after determining they are unlikely to be effective in treating COVID-19

US Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-chloroquine-and

Expert Panel Consensus Statement

www.aasld.org/covid19



Emerging data on the impact of COVID-19 in advanced liver disease

Joint Webinar

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AST | AMERICAN SOCIETY OF TRANSPLANTATION

A. Sidney Barritt IV, M.D., M.S.C.R.
Medical Director of Liver Transplantation
UNC Liver Center
University of North Carolina
29 April 2020

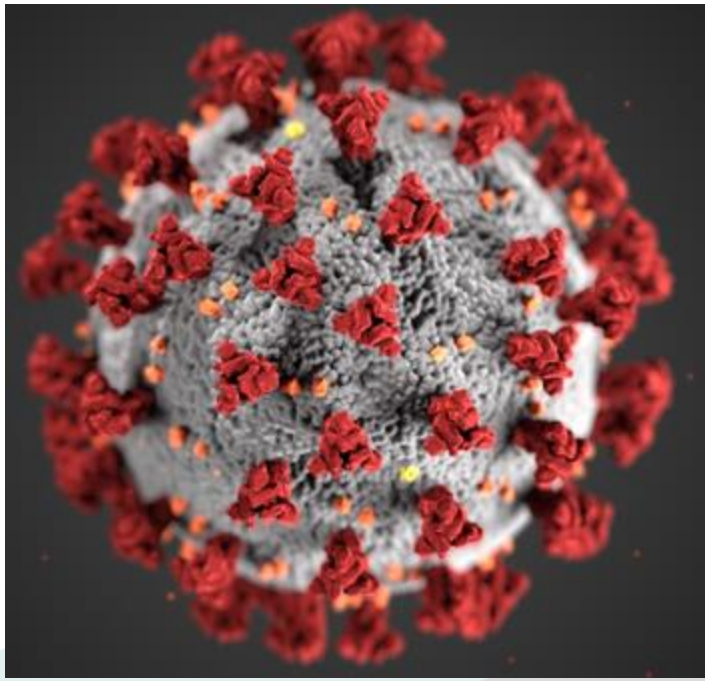
UNC SCHOOL OF MEDICINE

Disclosures

- No relevant conflicts

Roadmap

- Direct and indirect effects of COVID-19 on the liver
- Impact of COVID-19 on patients with chronic liver disease
- Where do we go from here?



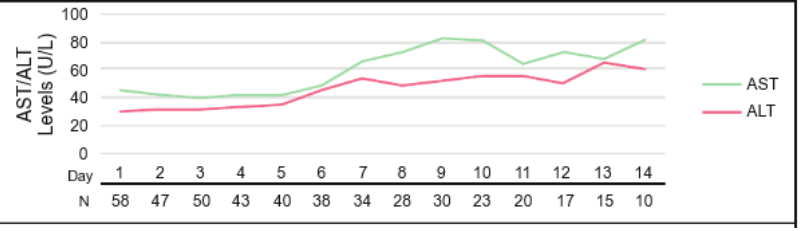
Direct effects of coronavirus on the liver

- Liver damage common with previous coronavirus infections SARS-CoV and MERS-CoV
- SARS-CoV-2 binds to cells through angiotensin-converting enzyme 2 (ACE2)
  - As ACE2 occurs on liver and biliary epithelial cells, the liver is a target for infection
- Data regarding SARS CoV2 (COVID-19) suggest that liver damage might be mediated by a direct cytopathogenic effect or due to an immune-mediated inflammatory response
  - Summary of 12 reports of COVID-19 describe abnormal LFTs in 10-58% with mixed impact on outcomes

Xu L et al. Liver Int 2020; Bhoori et al Lancet Gastrohep 2020; Cai Q et al. Jhep 2020

Direct effects of coronavirus on the liver

- COVID19 infections lead to elevated liver enzymes in up to ½ of patients
- 60 consecutive patients admitted to MGH follow during hospitalization
  - Cholestatic enzyme elevations were rare
  - AST predominance was common
    - Not correlated with CK levels/muscle injury
    - Appears to reflect true hepatic injury
    - No clear demographic or comorbidities associated with injury

Peak Liver Injury Grade	N	Median Liver Biochemistry Over Time
Entire group	59	

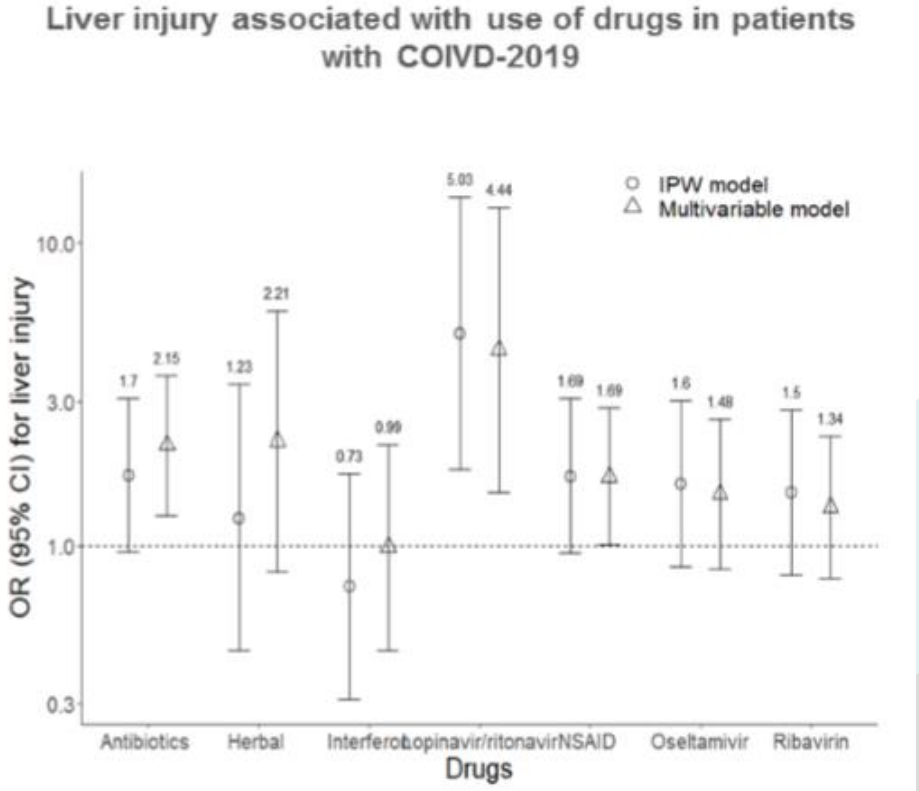
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
r	.74	.56	.33	.32	.44	.10	.09	-.07	-.15	.13	.33	-.07	-.02	.005
P	<.0001	.0003	.06	.06	.02	.59	.67	.74	.50	.60	.21	.79	.95	.99

Bloom et al Hepatology 2020, Xu L et al, Liver Int 2020, Fan et al CGH 2020

Indirect coronavirus impact on the liver

- There may be confounding in regard to abnormal liver enzymes among patients with COVID-19
  - Many critically ill
  - Prevalent chronic liver disease (CLD)?
    - Maybe not – prevalence of CLD lower than expected in most reports of COVID-19 infections
- How does this impact clinical trials for COVID therapies?

- Drug Induced Liver Injury?



Xu L et al, Liver Int 2020

Impact of COVID-19 on patients with liver disease

Patients with chronic liver disease (CLD)

- Limited information available
- Prevalence of CLD in data reported thus far is lower than expected
  - Only 7/12 studies in literature review from China report prevalence of CLD and range is low (2-11%)
  - 5700 COVID-19 patients in NYC, only 19 (0.4%) with cirrhosis
    - Obesity and diabetes common but not designated as NAFLD
  - Patients with CLD/cirrhosis sheltering in place?
  - Misclassification of current data?

Xu L et al, *Liver Int* 2020
Richardson et al, *jamanetwork* 2020

Registry data

- Secure Cirrhosis and COVID-HEP
  - Combined international registry for patients with laboratory confirmed COVID-19 infection and chronic liver disease, cirrhosis and liver transplantation
  - 915 submissions from 34 countries
    - NASH (38%) is the most common etiology

Participating Countries

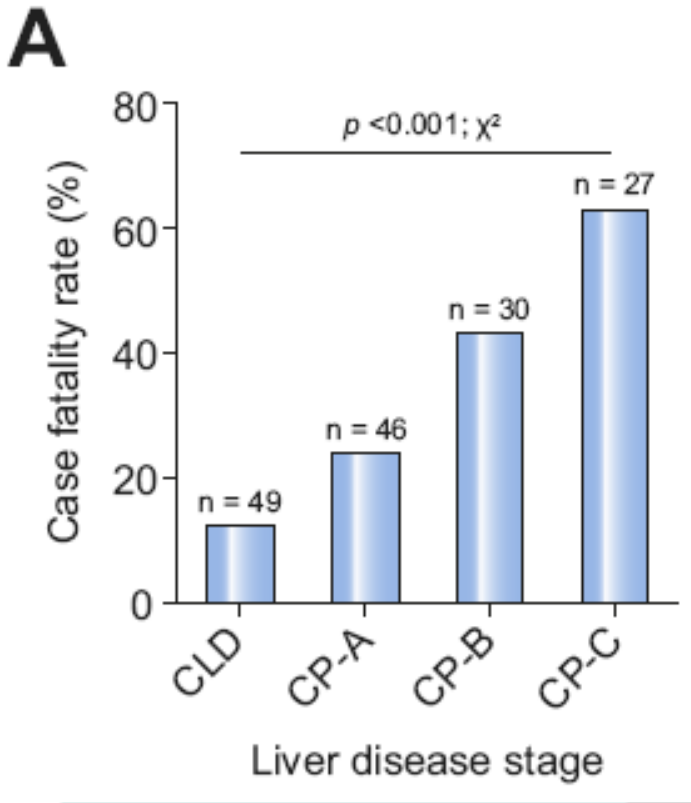
USA (25%), UK (25%), China (18%) submitted greatest number of cases
Ten countries with ≥10 submissions

Unpublished data courtesy of Secure Cirrhosis and COVID-HEP

Impact of COVID-19 on patients with liver disease

Patients with Cirrhosis

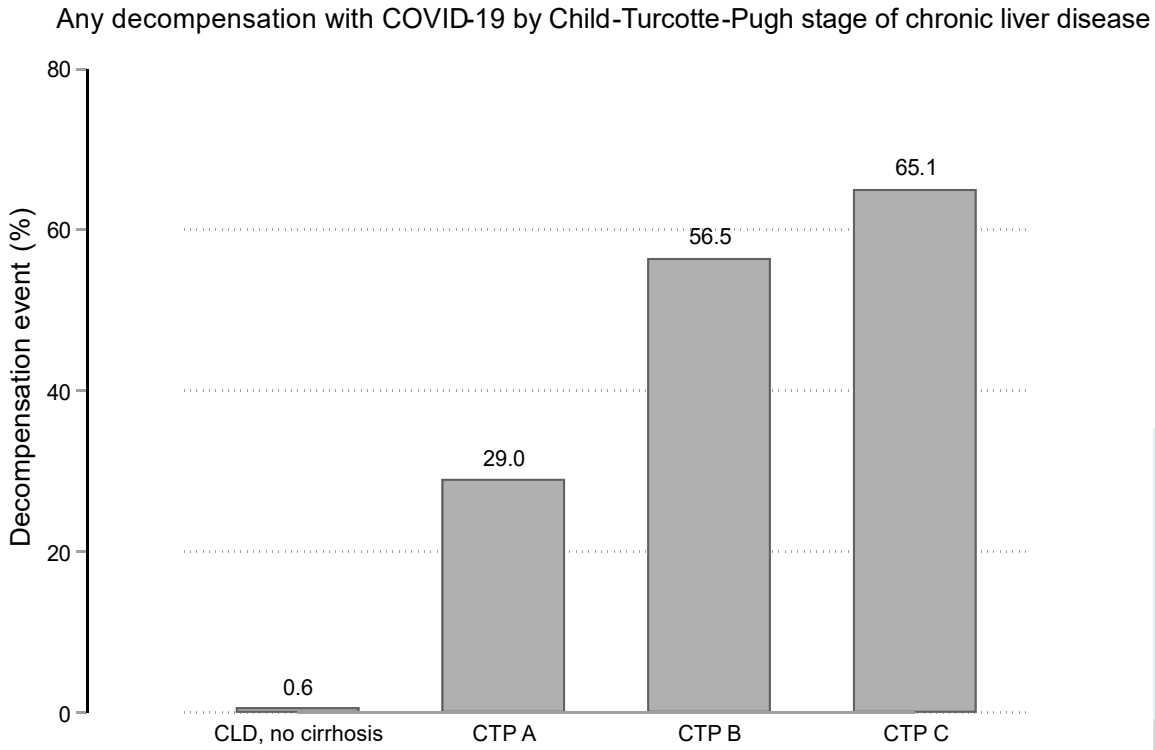
- SECURE-Cirrhosis and COVID-HEP registries' multivariable analysis shows increase in OR of mortality with CTP class
  - CLD w/o cirrhosis [ref]
  - CTP A 1.14, p=0.8
  - CTP B 4.82, p=0.027
  - CTP C 23.6, p<0.001
- Other independent risk factors for mortality include age and obesity
  - Consistent with general population
- Trend consistent with potentially significant risk even for CTP A patients in larger cohort of 750+ patients



Moon, et al, *J Hep* 2020
Unpublished data courtesy of Secure Cirrhosis and COVID-HEP

Hepatic decompensation events

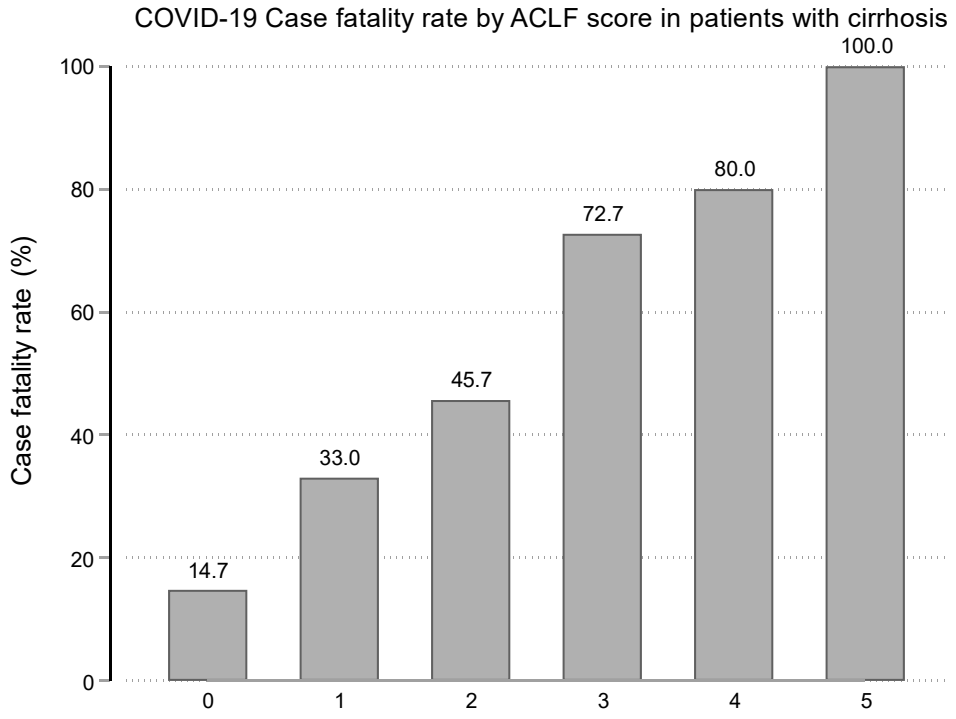
- Decompensation events are common when patients with cirrhosis suffer COVID-19 infections
- Frequency of events increases with severity of cirrhosis as measured by CTP class
- GI symptoms common as a presenting symptom in this population



Unpublished data courtesy of Secure Cirrhosis and COVID-HEP

COVID-19 infection can trigger ACLF

- Acute on chronic liver failure is deadly and frequently triggered by infection
- COVID-19 case fatality associated with rising ACLF score



Unpublished data courtesy of Secure Cirrhosis and COVID-HEP

Care for patients with chronic liver disease

- Abnormal liver enzymes need evaluation
  - HBV or AIH flare? ETOH consumption? COVID-19?
- No need to reduce immunosuppression for asymptomatic/COVID-19 negative patients
- Social distancing, handwashing etc.
- Telephone/video visits
- Do not need to update labs solely for UNOS listing

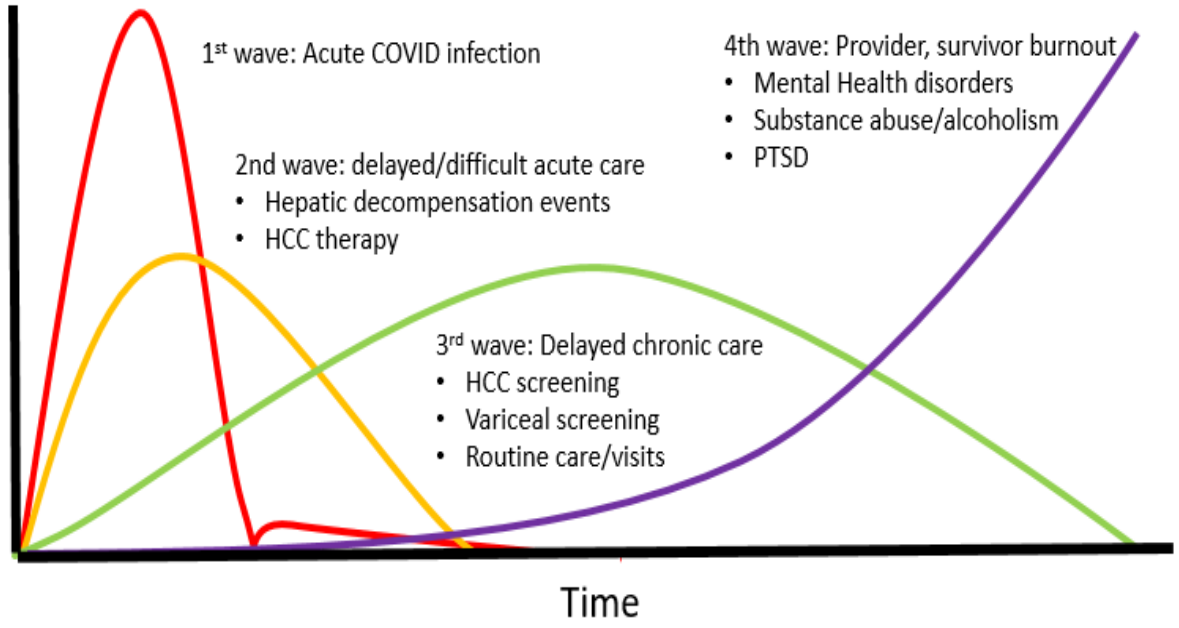
- Need more data, greater numbers and better sense of the denominator of patients with COVID-19 to determine risk factors and role of immunosuppression in disease course

Where do we go from here?

- COVID-19 will have a heterogeneous impact on hepatology practices
  - Geography
  - Population density
  - Second wave?
- Need to acknowledge the limitations of data thus far:
  - Registries subject to selection bias
  - Single center data may not be generalizable
  - Expert opinion
- Practices will evolve over time with more experience and better data

Where do we go from here?

- Cannot forget impact of COVID-19 on patients *without* infection
  - Resource limitations for acute care needs
  - Disruption in chronic care practices
  - Will there be a "4th wave" of post pandemic trauma that has implications for hepatologists?
    - Alcohol/Substance abuse/Mental health
- Economic impact on liver care
  - Impact on liver related public health initiatives
  - Viral hepatitis and alcohol



Pawlotsky Nat Rev Gastro Hep 2020

Acknowledgements

SECURE-Cirrhosis REGISTRY
Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

@SecureCirrhosis

URL: www.covidcirrhosis.org

Andrew Moon (UNC)
Mike Kappelman (UNC)
Erica Brenner (UNC)
Renumathy Dhanasekaran (Stanford)
Nneka Ufere (Mass General)
Ponni Perumalswami (Mount Sinai)
Patricia Jones (University of Miami)
Feng Su (University of Washington)
Xiaolong Qi (Lanzhou University, China)

EASL™ The Home of Hepatology | COVID-HEP REGISTRY
COVID-19 in Patients with Liver Disease or Transplantation

@CovidHep

URL: www.covid-hep.net

Tom Marjot (Oxford, UK)
Gwilym Webb (Oxford, UK)
Ellie Barnes (Oxford, UK)
Tamsin Cargill (Oxford, UK)

Endorsing Organizations

UNITED EUROPEAN GASTROENTEROLOGY ueg
ILCA INTERNATIONAL LIVER CANCER ASSOCIATION
CHESS Chinese Portal Hypertension Diagnosis and Monitoring Study Group
bsg BRITISH SOCIETY OF GASTROENTEROLOGY
BASL British Association for the Study of the Liver
EASL™ The Home of Hepatology

Thank you!

barritt@med.unc.edu

@sidbarritt4

COVID-19 in Liver Transplant Recipients

Outcomes and management

Joint Webinar

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

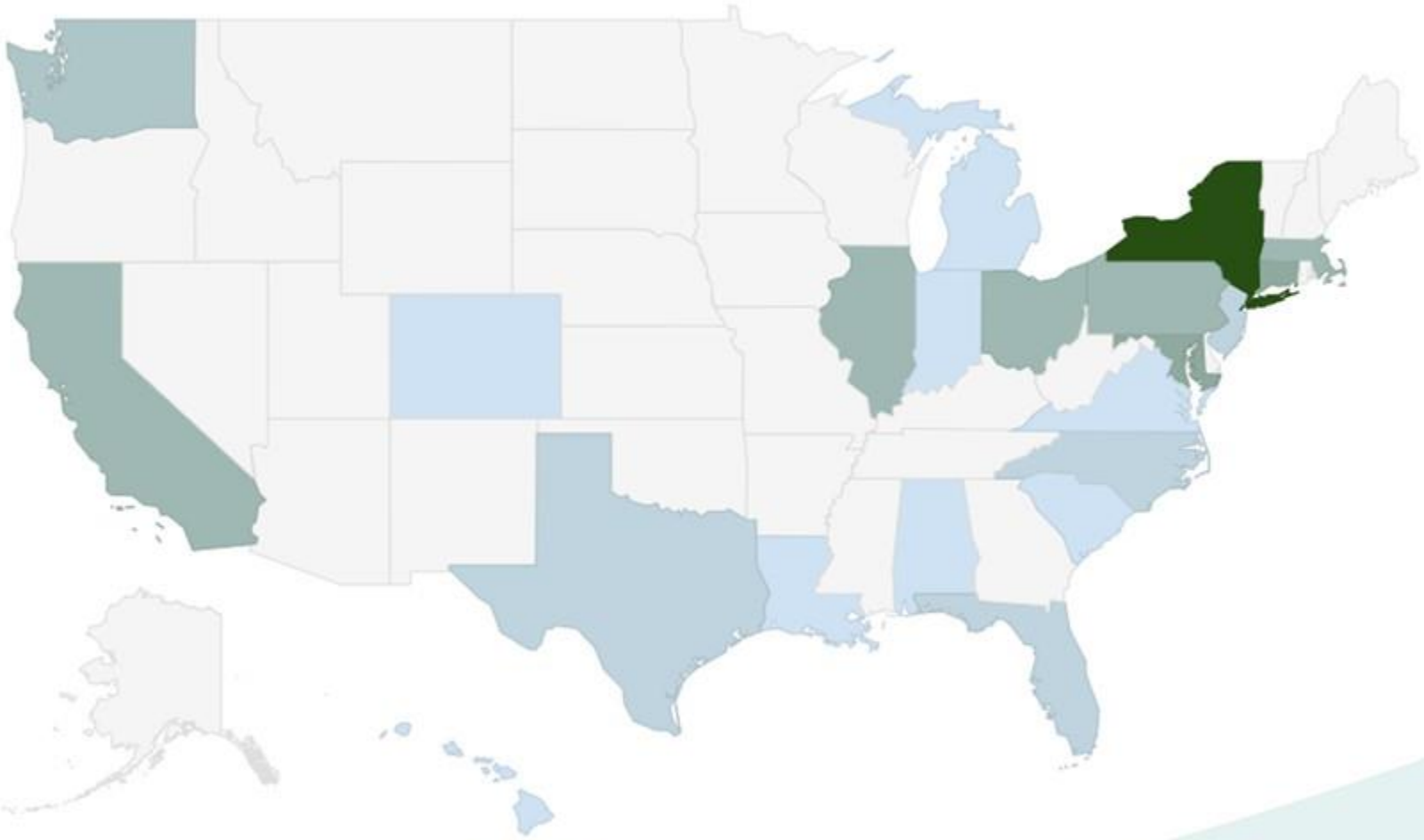
AST | AMERICAN SOCIETY OF TRANSPLANTATION

Olivia Kates, MD
Second-Year Fellow
Division of Allergy and Infectious Diseases
University of Washington

Disclosures

- No financial disclosures
- UW COVID-SOT registry results presented today are preliminary

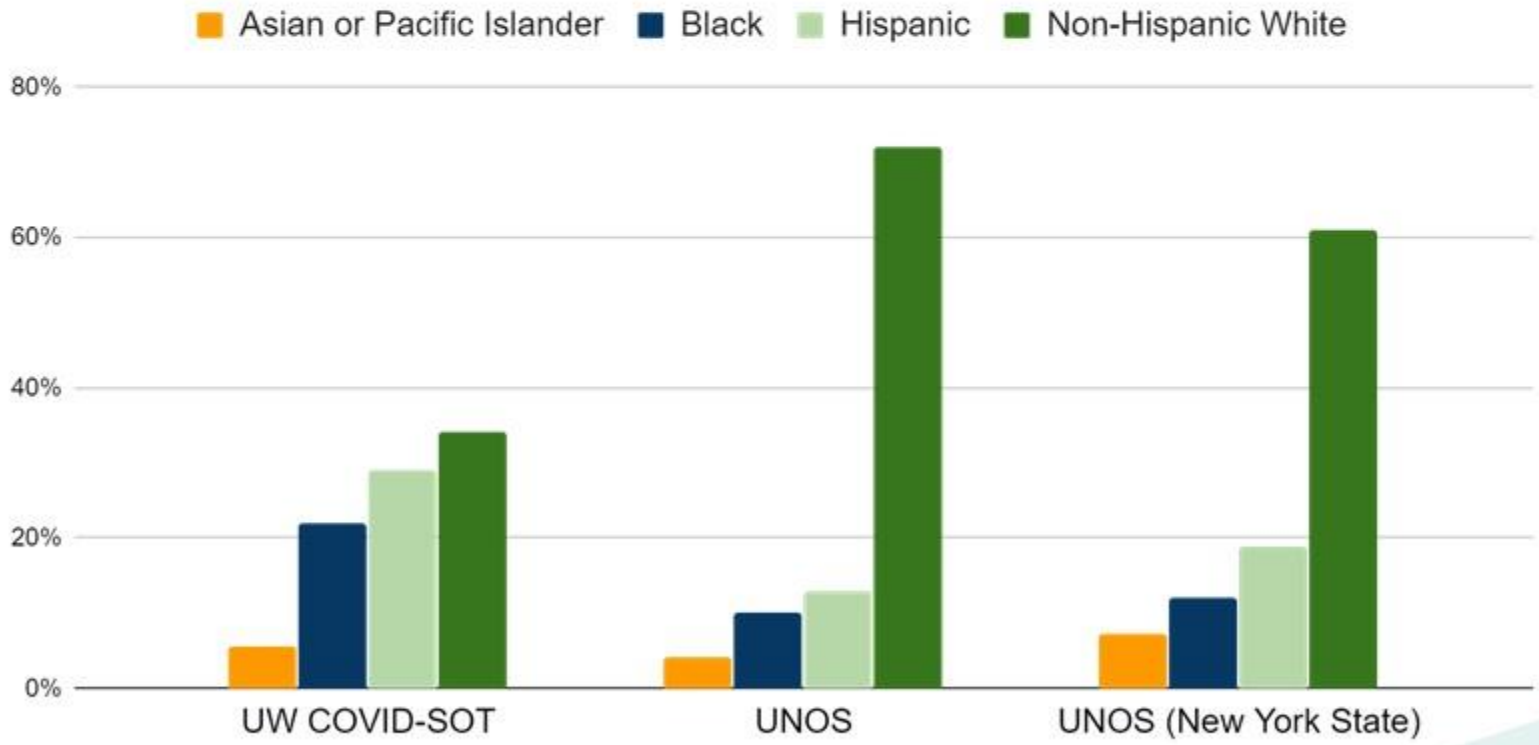
UW COVID-SOT Registry



- 73 Liver transplant recipients
- 16 (22%) liver/kidney

UW COVID-SOT Registry

Race/Ethnicity of cases reported to the UW COVID-SOT Registry compared to liver transplant recipients in U.S. and New York



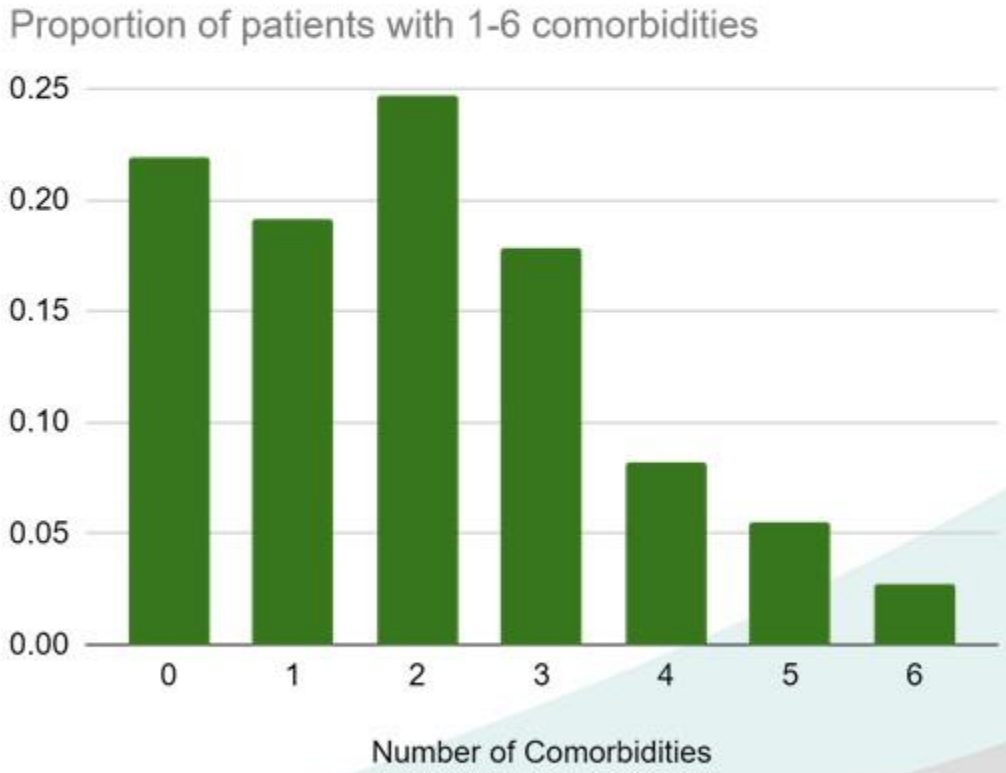
https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/ | 61

UW COVID-SOT Registry

- Median time post-transplant: 5 years (2-11)
  - 8 (11%) transplanted since January 1, 2020
- Maintenance immunosuppression
  - Triple IS (CNI + antimetabolite + steroid): 23 (32%)
  - Two-drug IS (CNI + antimetabolite OR steroid): 21 (28%)
  - mToRi-containing IS: 3 (4.1%)

UW COVID-SOT Registry

- Comorbidities are common
  - Hypertension: 39 (53%)
  - Diabetes: 34 (47%)
  - Obesity: 23 (32%)
  - CKD: 24 (33%)
  - Coronary artery disease: 15 (21%)
  - CHF: 2 (2.7%)
  - Chronic lung disease: 5 (6.8%)



UW COVID-SOT Registry

- Symptoms at presentation are similar to general population
  - Fever: 34 (47%)
  - Cough: 50 (69%)
  - Dyspnea: 40 (55%)
  - URI Symptoms: 24 (33%)
  - GI Symptoms: 29 (40%)

UW COVID-SOT Registry

- Admitted for COVID-19 related illness: 47 (64%)
  - Inpatient for another indication at diagnosis: 8 (11%)
- ICU: 23 (33%)
- Mechanical ventilation: 20 (27%)
- Vasopressors: 15 (21%)

UW COVID-SOT Registry

- **28-day all-cause mortality (all patients): 15 (21%)**
  - Mortality in pts admitted for COVID-19: 12 (26%)
  - Mortality in pts already inpatient for another indication: 2 (25%)
- Still hospitalized as of day 28: 6 (8.2%)

UW COVID-SOT Registry

- Mortality in SOT pts admitted for COVID-19: 12 (26%)

- Inpatient case fatality in the general population?
  - 33% (Buckner, Washington State)
  - 16% (Gold, Georgia)
  - 15% (Imam, Michigan)
  - 21% (Richardson, New York)
  - 23% (Ciceri, Northern Italy)

Buckner FS, McCulloch DJ, Atluri V, et al. Clinical Features and Outcomes of 105 Hospitalized patients with COVID-19 in Seattle, Washington [published online ahead of print, 2020 May 22]. *Clin Infect Dis*. 2020;ciaa632. doi:10.1093/cid/ciaa632

Gold JA, Wong KK, Szablewski CM, et al. Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 — Georgia, March 2020. MMWR Morb Mortal Wkly Rep 2020;69:545–550. DOI: http://dx.doi.org/10.15585/mmwr.mm6918e1

Imam Z, Odish F, Gill I, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States [published online ahead of print, 2020 Jun 4]. J Intern Med. 2020;10.1111/joim.13119. doi:10.1111/joim.13119

Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area [published online ahead of print, 2020 Apr 22] [published correction appears in doi: 10.1001/jama.2020.7681]. JAMA. 2020;323(20):2052-2059. doi:10.1001/jama.2020.6775

Fabio C, Antonella C, Patrizia RQ, et al. Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy [published online ahead of print, 2020 Jun 11]. Clin Immunol. 2020;108509. doi:10.1016/j.clim.2020.108509

UW COVID-SOT Registry

- AKI: 24 (33%)
  - Newly required renal replacement therapy: 5 (6.8%)
- Liver injury: 6 (8.2%)
  - Median peak transaminases: ~200
- Thrombosis: 2 (2.7%)

- AKI in general population with COVID-19: 37%

Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19 [published online ahead of print, 2020 May 16]. Kidney Int. 2020;98(1):209-218. doi:10.1016/j.kint.2020.05.006

UW COVID-SOT Registry

- Bacterial pneumonia
  - Microbiologic diagnosis: 4 (5.5%)
    - *Pseudomonas aeruginosa*, MSSA, *Enterobacter, Klebsiella, H. influenzae*
  - Presumptive: 14 (19%)
- Rhinovirus/enterovirus: 2 (2.7%)
- Invasive fungal infection: 1

- Bacterial PNA among general population with COVID-19: 5-17%

Clancy CJ, Nguyen MH. COVID-19, superinfections and antimicrobial development: What can we expect? [published online ahead of print, 2020 May 1]. Clin Infect Dis. 2020;ciaa524. doi:10.1093/cid/ciaa524

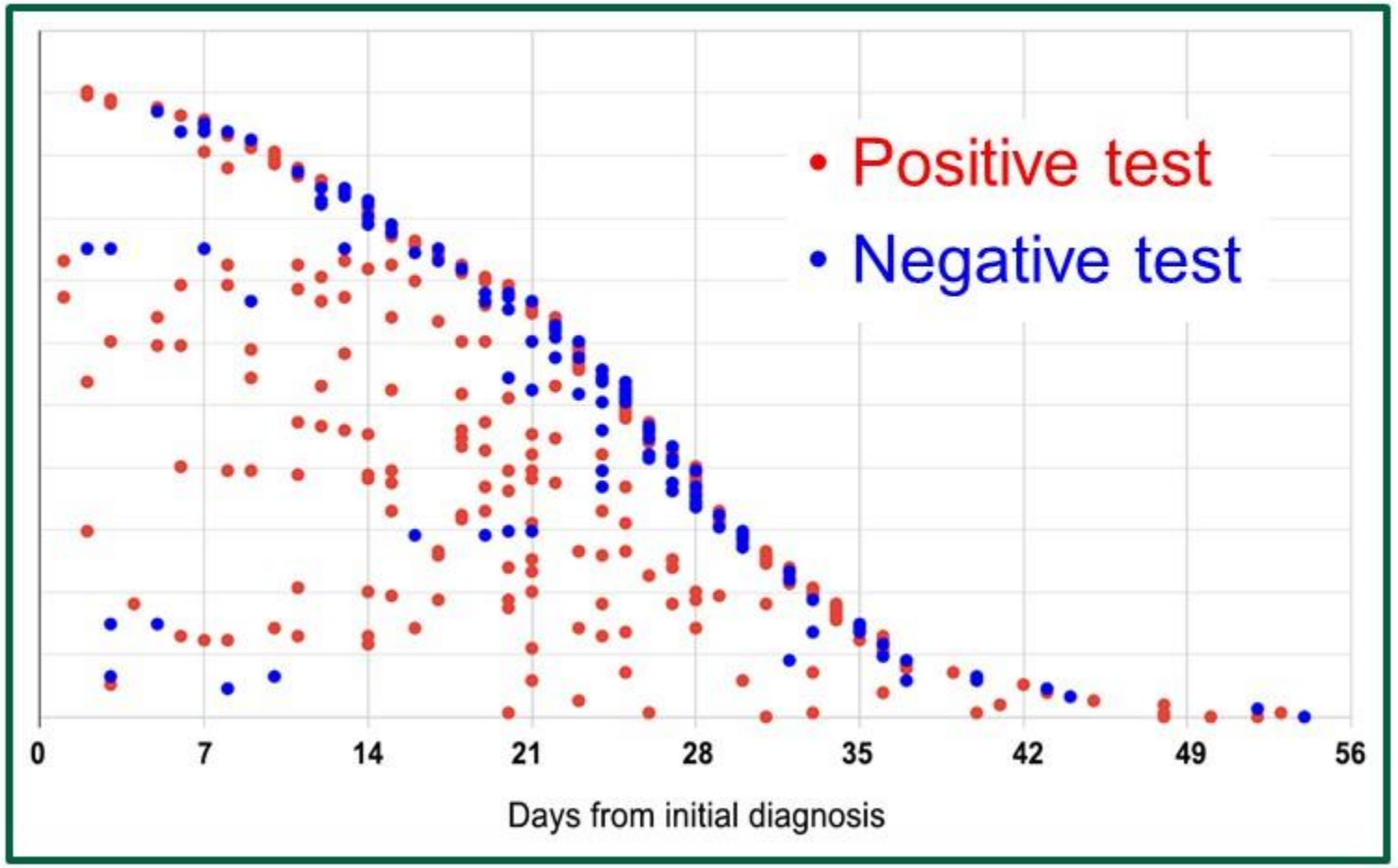
UW COVID-SOT Registry

- Bloodstream infection: 5 (6.8% or 4.1% excluding CoNS)
  - 2 coagulase negative staphylococci (possible contaminant)
  - 1 MRSA
  - 1 polymicrobial with *S. aureus, Citrobacter, Serratia*
  - 1 polymicrobial with *E. coli* (ESBL), *Pseudomonas* (XDR), *VRE*

- BSI among general population with COVID-19: 1.6%

Sepulveda J, Westblade LF, Whittier S, et al. Bacteremia and Blood Culture Utilization During COVID-19 Surge in New York City [published online ahead of print, 2020 May 13]. J Clin Microbiol. 2020;JCM.00875-20. doi:10.1128/JCM.00875-20

UW COVID-SOT Registry



- Day of last positive: **18.5**
- Day of first negative: **24**
- Maximum duration: **52** days

- General population: **~20** days

Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [published correction appears in Lancet. 2020 Mar 28;395(10229):1038] [published correction appears in Lancet. 2020 Mar 28;395(10229):1038]. Lancet. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3

Other Registries

- ELITA Registry (100), reported by Belli et al. in *Lancet GI*
  - Admit rate similar to UW COVID-SOT but less ICU and intubation
  - Mortality 16% of all patients at 18 days, 24% of hospitalized patients
  - Older age predictive of mortality
- SECURE & COVID-Hep (39), reported by Webb et al. in *Lancet GI*
  - Mortality 23%
  - No factors predictive of mortality

Belli LS, Duvoux C, Karam V, et al. COVID-19 in liver transplant recipients: preliminary data from the ELITA/ELTR registry [published online ahead of print, 2020 Jun 4]. Lancet Gastroenterol Hepatol. 2020;S2468-1253(20)30183-7. doi:10.1016/S2468-1253(20)30183-7

Webb GJ, Moon AM, Barnes E, Barritt AS, Marjot T. Determining risk factors for mortality in liver transplant patients with COVID-19. Lancet Gastroenterol Hepatol. 2020;5(7):643-644. doi:10.1016/S2468-1253(20)30125-4

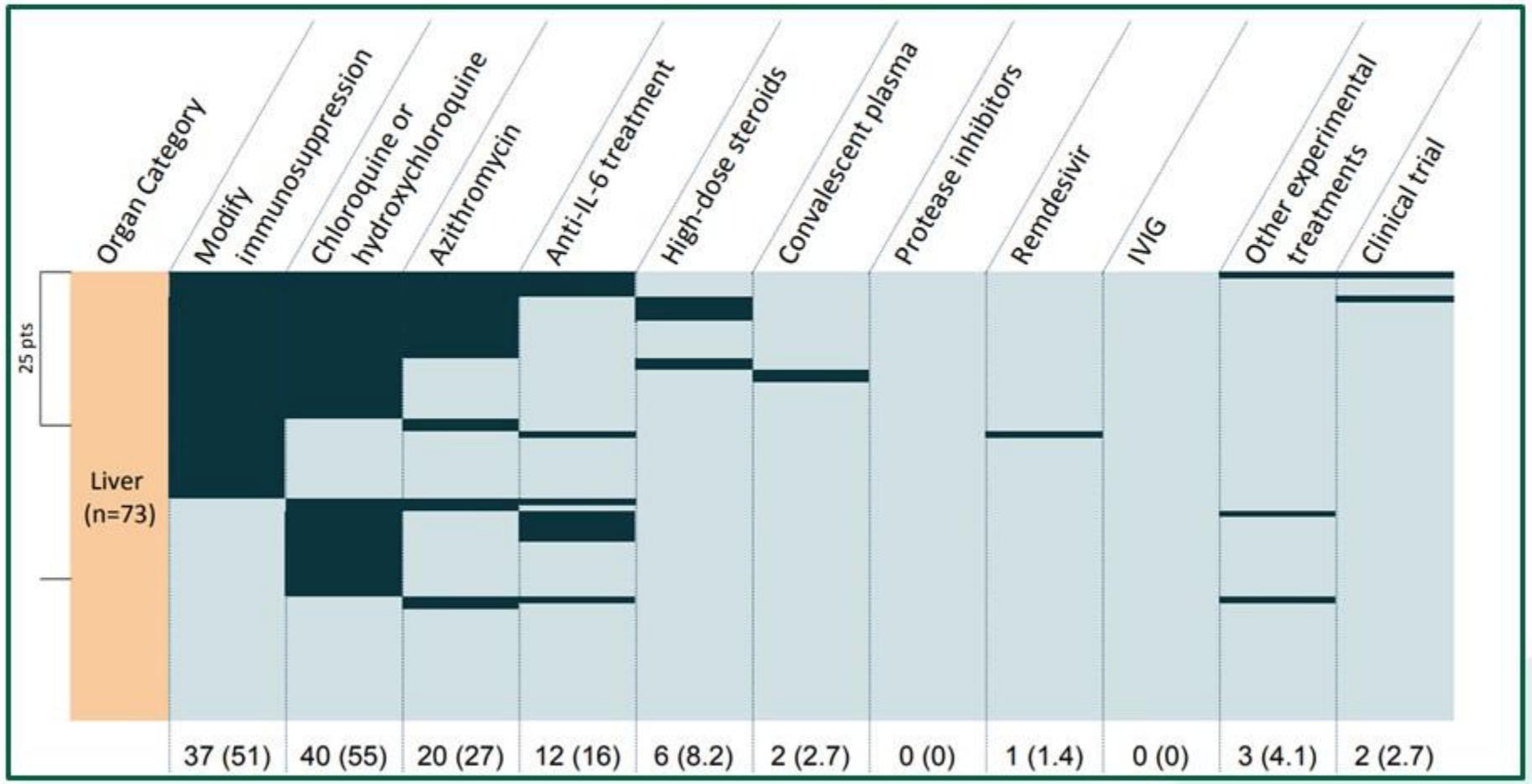
Unanswered questions

- What are **risk factors** for mortality?
  - Evidence to support age & comorbidities
  - To date no evidence to support transplant-related factors
- What are unique **mediators** of mortality?
  - Complications? Renal failure? Secondary infections?

- What is an optimal management strategy?

Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: Initial report from the US epicenter [published online ahead of print, 2020 Apr 24]. Am J Transplant. 2020;10.1111/ajt.15941. doi:10.1111/ajt.15941 | 17

UW COVID-SOT Registry



Immunosuppression management

- Calcineurin inhibitors
  - Inhibits replication of coronaviruses *in vitro*
  - Associated with delayed recurrence of HCV *in vivo*
  - Rodriguez-Cubillo et al. studied change to cyclosporine as a management strategy in 29 kidney transplant patients with COVID-19
    - 23- change tacrolimus to cyclosporine, no reduction in immunosuppression
    - 6- reduce immunosuppression (typically hold MMF, reduce CNI)
    - Lower mortality in the cyclosporine group

Rodriguez-Cubillo B, Moreno de la Higuera MA, Lucena R, et al. Should cyclosporine be useful in renal transplant recipients affected by SARS-CoV-2? [published online ahead of print, 2020 Jun 12]. Am J Transplant. 2020;10.1111/ajt.16141. doi:10.1111/ajt.16141

Immunosuppression management

- Steroids
  - RECOVERY press release: Dexamethasone reduces mortality
  - In patients with inflammatory bowel disease and COVID-19:
    - Baseline steroid use associated with increased risk of infection
    - Baseline steroid use associated with increased mortality (aOR 11.6, CI 2.1 – 64.7)

recoverytrial.net
Lukin DJ, Kumar A, Hajifathalian K, et al. Baseline Disease Activity and Steroid Therapy Stratify Risk of COVID-19 in Patients with Inflammatory Bowel Disease [published online ahead of print, 2020 May 29]. *Gastroenterology*. 2020;S0016-5085(20)34738-7.
Brenner EJ, Ungaro RC, Gearry RB, et al. Corticosteroids, but not TNF Antagonists, are Associated with Adverse COVID-19 Outcomes in Patients With Inflammatory Bowel Diseases: Results from an International Registry [published online ahead of print, 2020 May 18]. *Gastroenterology*. 2020;10.1053/j.gastro.2020.05.032. doi:10.1053/j.gastro.2020.05.032

Treatments in SOT patients

- Remdesivir (ACTT-1)
  - No safety data in CKD, ESRD, or baseline transaminases >5xULN
  - Liver toxicity, although not common
- Dexamethasone (RECOVERY, press release)
  - Drug-drug interactions with CNIs
  - Fluid retention, neuropsychiatric side effects
  - Increased hypokalemia in combination with loop diuretics

Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 - Preliminary Report [published online ahead of print, 2020 May 22]. N Engl J Med. 2020;NEJMoa2007764. doi:10.1056/NEJMoa2007764 recoverytial.net

Treatments in SOT patients

- Tocilizumab (observational data)
  - Safety concerns in patients with hepatic impairment
  - Liver toxicity, infectious complications
- Convalescent plasma (observational data)
  - Theoretical risk of anti-HLA antibodies should be minimized by screening/collection procedures

A way forward?

- SOT patients with COVID-19 are similar to general population patients with regard to known risk factors for infection/mortality, clinical presentation, some complications
- Infectious complications, often with high-concern pathogens, may have more serious implications for SOT patients
- Still unclear what (if anything!) to do about immunosuppression either prior to infection or after diagnosis
- Likely reasonable to extrapolate some treatment data to SOT, but certain toxicities may be more important.

A way forward?

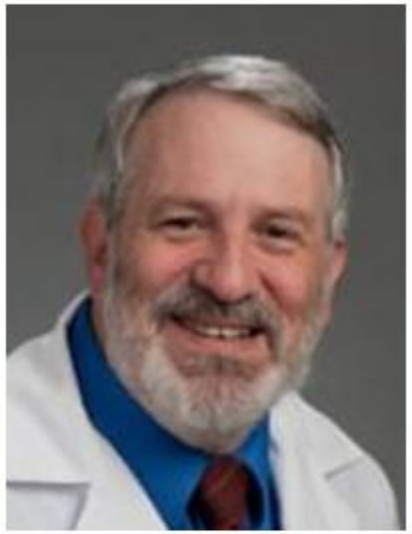
- Continual release of new morbidity and mortality data should motivate continual reassessment of transplantation practices.

Thank you!

Ajit Limaye MD

Cynthia Fisher MD

Erika Lease MD



Robert Rakita MD

Catherine Liu MD
Steve Pergam MD
Gina Campelia PhD
Michael Boeckh MD, PhD

>80 unique contributors to the University of Washington COVID-SOT Case Report Registry

University of Washington Department of Medicine & Department of Surgery Transplant Faculty

University of Washington Institute of Translational Health Science (ITHS)

The American Society of Transplantation (AST)

IDCOP, WHCOP, and Outstanding Questions in Transplantation Community Message Board

American Transplant Society (ATS), International Society for Heart and Lung Transplantation (ISHLT), American Association for the Study of Liver Diseases (AASLD)

Panel Discussion Q&A

Please submit any remaining questions to the Q&A Chat at this time!

Joint Webinar

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

AST | AMERICAN SOCIETY OF TRANSPLANTATION

AASLD COVID-19 Resources

COVID-19 Resources Webpage & Clinical Insights Document: aasld.org/covid19

COVID-19 & the Liver Webinar Page: aasld.org/COVIDwebinars

Join/Engage: COVID-19 Discussion Community: engage.aasld.org/covid19

AST COVID-19 Resources

COVID-19 Resources for Transplant Community: **myast.org/covid-19**

COVID-19 Resources for Transplant Professionals: **myast.org/covid-19-information**

Power2Save: **Power2Save.org**

