COVID-19: KEEPING UP WITH A MOVING TARGET JUNE 17, 2020 UPDATE

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COVID-19
KEEPING UP WITH A MOVING TARGET

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COVID-19: Keeping Up with a Moving Target

Twice Weekly @ COVID19.DKBmed.com

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CME Information

Jointly provided by Postgraduate Institute for Medicine, DKBmed, and the Institute for Johns Hopkins Nursing.

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The faculty reported the following financial relationships or relationships they or their spouse/life partner have with commercial interests related to the content of this continuing education activity:

Name of Faculty or Presenter	Reported Financial Relationship
Paul G. Auwaerter, MD, MBA, FIDSA	Scientific Advisor: DiaSorin, Shionogi Inc. JNJ: Ownership equity

Dr. Auwaerter has indicated that he will be referencing the unlabeled or unapproved use of agents currently being investigated in on-going studies and trials. These include hydroxychloroquine/chloroquine, hydroxychloroquine/chloroquine in combination with azithromycin, lopinavir plus ritonavir, tocilizumab, corticosteroids, and COVID-19 convalescent plasma. All activity, content, and materials have been developed solely by the activity directors, planning committee members, and faculty presenters, and are free of influence from a commercial entity.

CME Information

To attest for CME/CE credit, please visit

COVID19.DKBmed.com

Learning Objectives

- Identify risk factors for complications of COVID-19 including age, race and ethnicity, and comorbidities
- Discuss risks for severe and critical COVID-19 patients
- Discuss data pertaining to use of convalescent plasma in people with severe COVID-19

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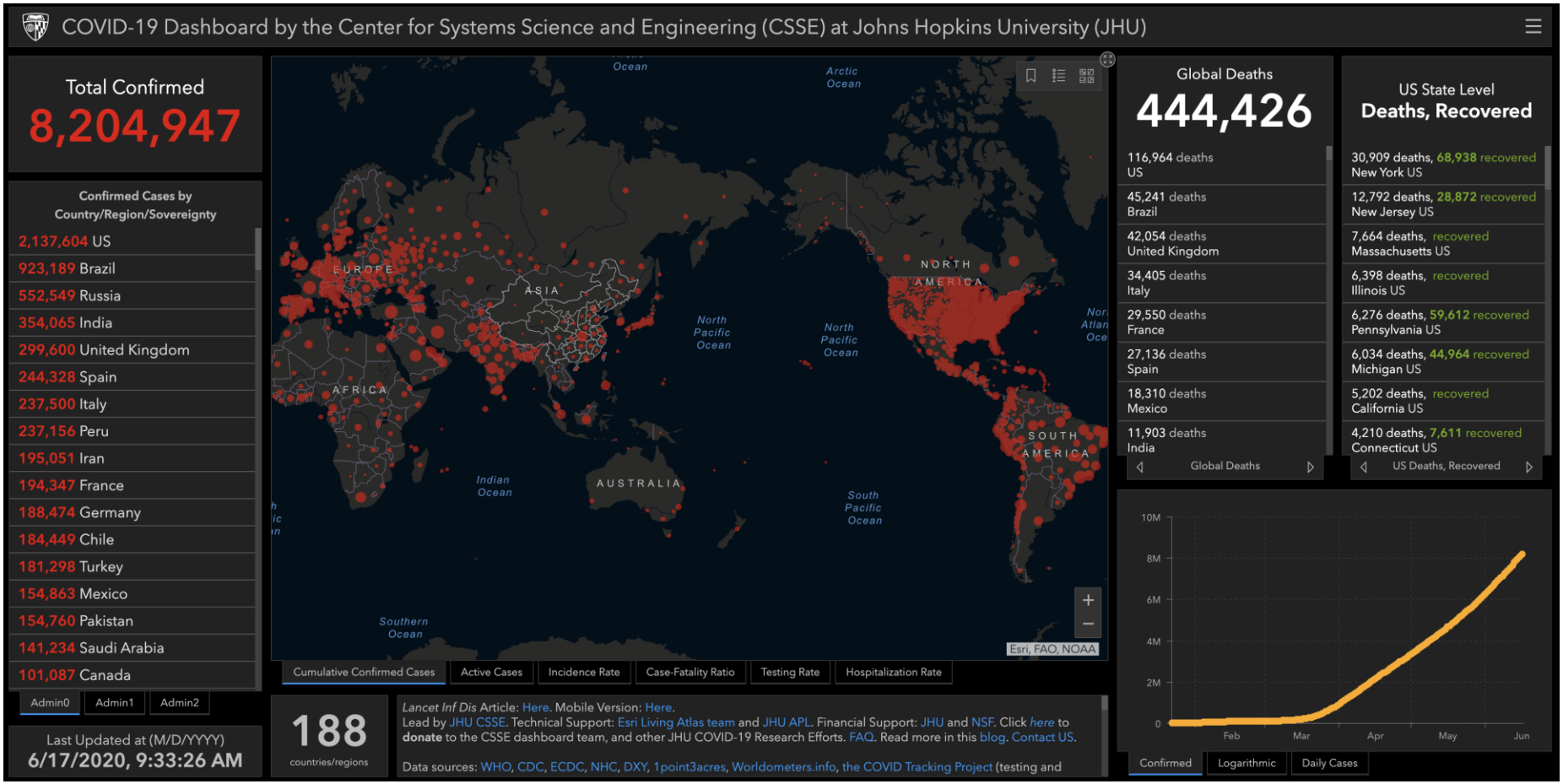
Thank You

This program is brought to you through the generous support of DKBmed, Postgraduate Institute for Medicine, and the Institute for Johns Hopkins Nursing.

Please see **COVID19.DKBmed.com** for additional resources and educational activities

Total Global Cases (6/17/20)



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coronavirus.jhu.edu/map.html

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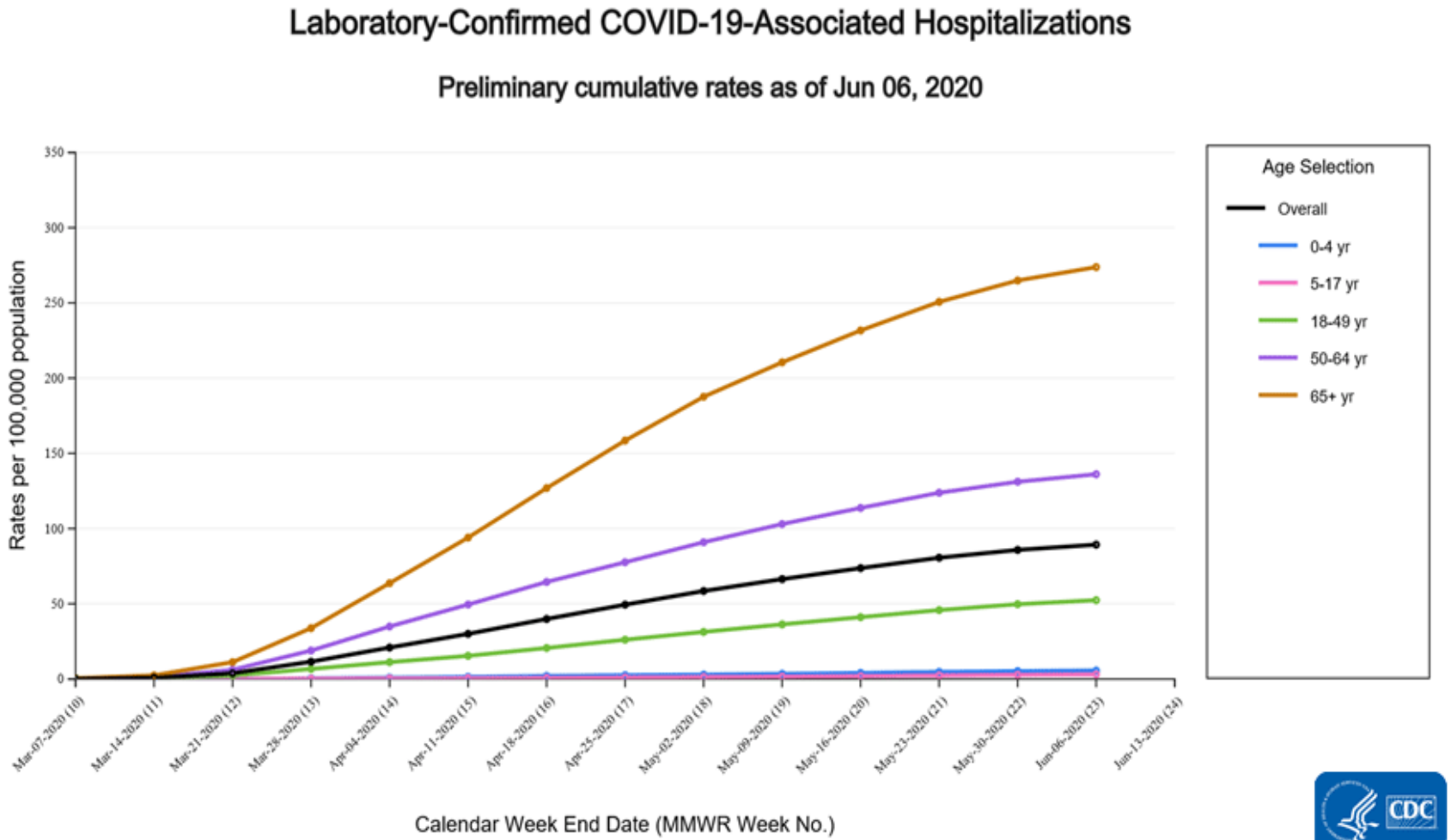
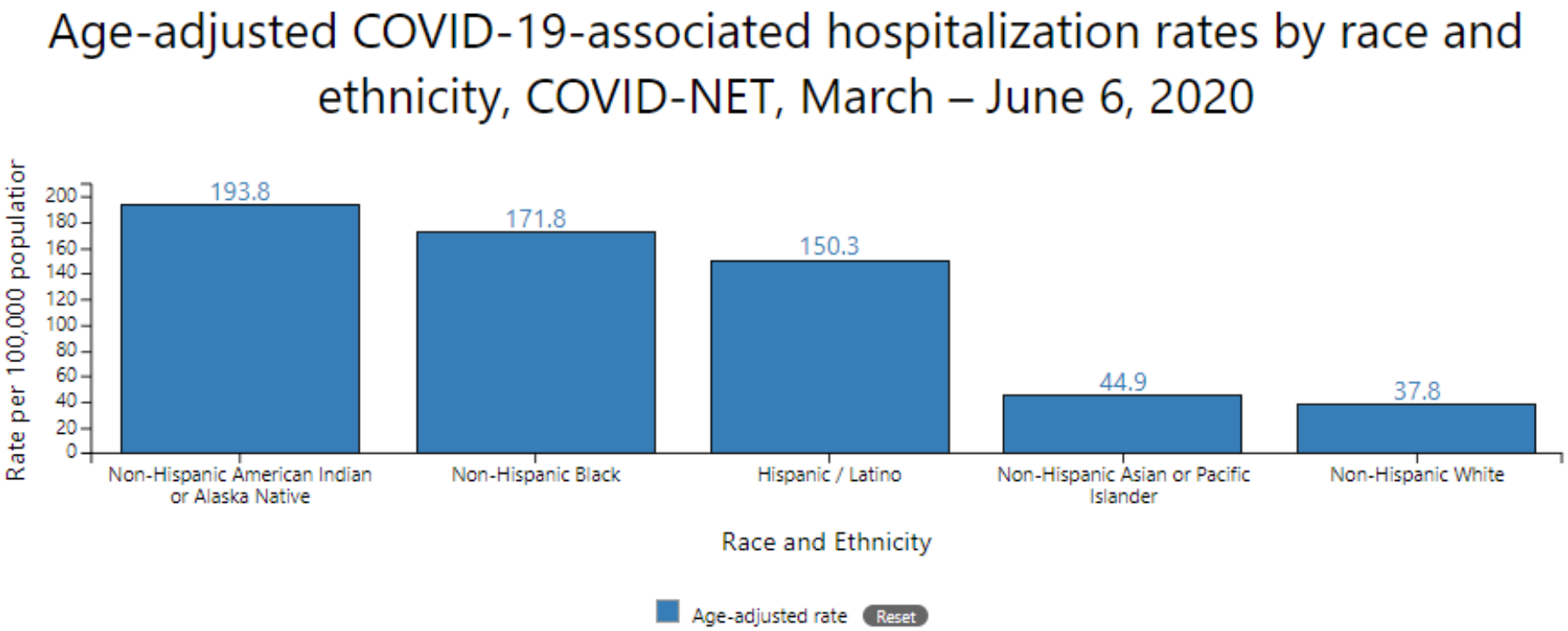
Risks for COVID-19 Hospitalization

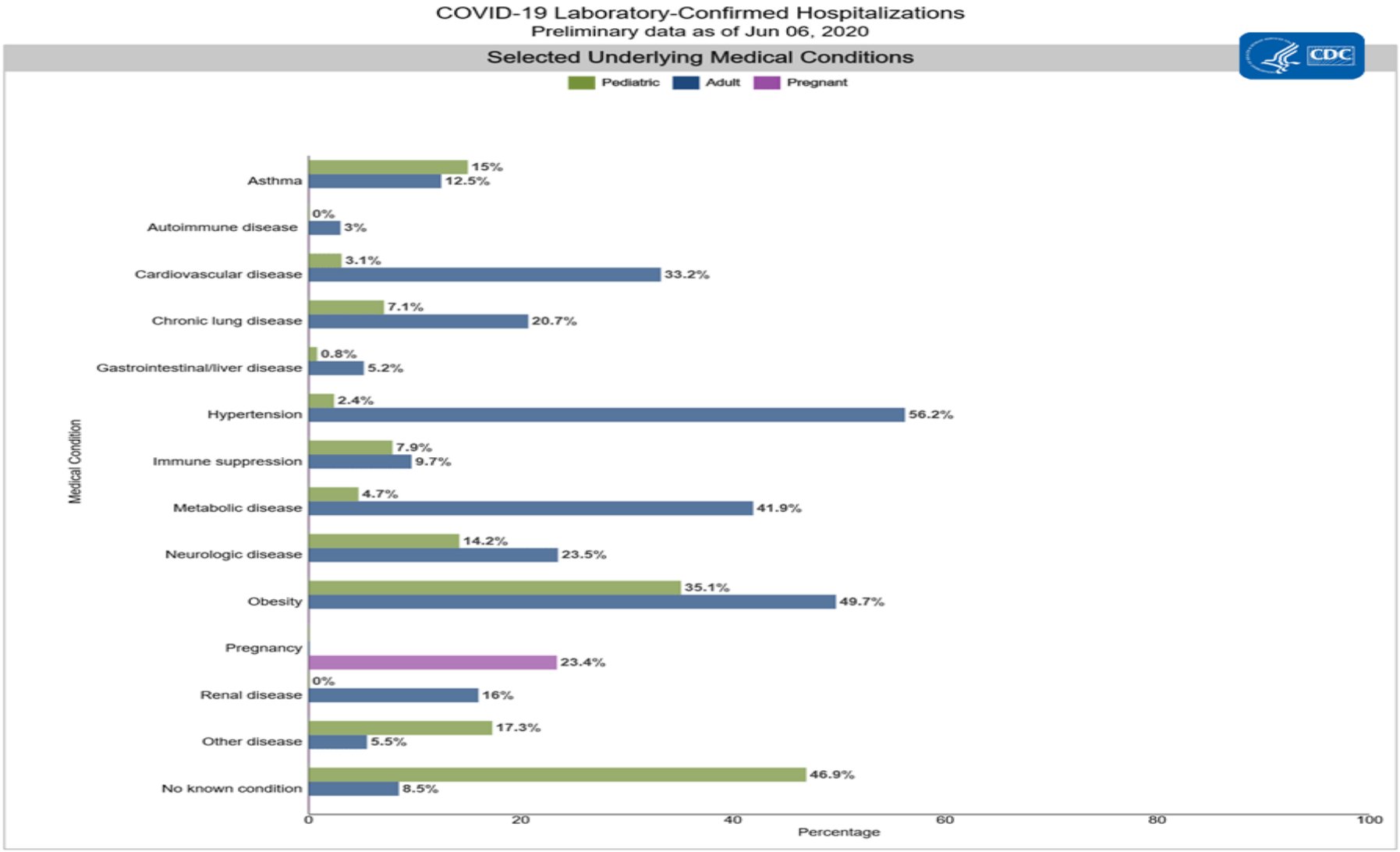


https://www.cdc.gov/coronavirus/2019-ncov/covid-data/pdf/covidview-06-12-2020.pdf

Risks by Race and Ethnicity

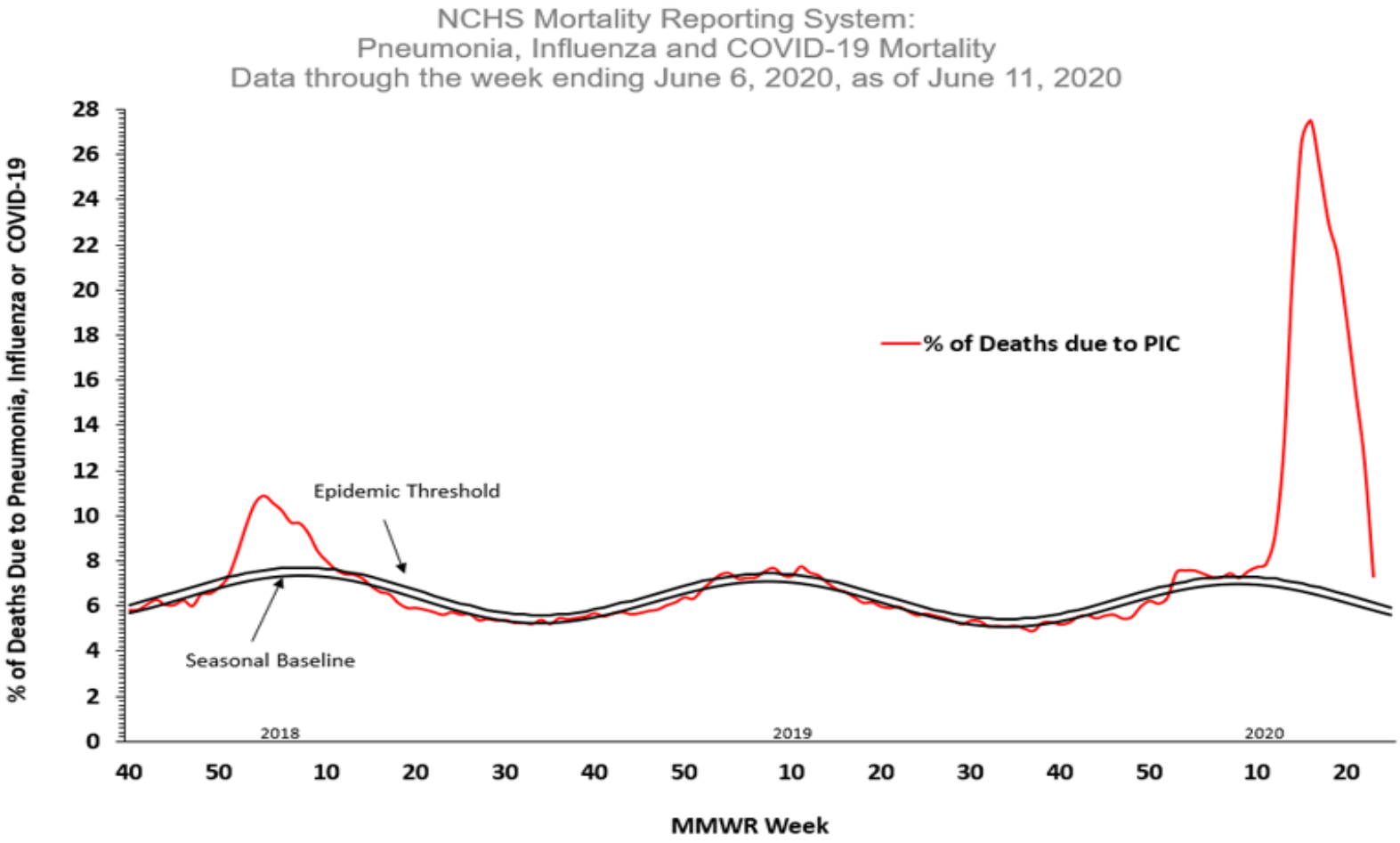


COVID-19 Hospitalizations by Comorbidities



https://www.cdc.gov/coronavirus/2019-ncov/covid-data/pdf/covidview-06-12-2020.pdf

Cumulative Mortality Pneumonia, Influenza and COVID-19



CDC

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https://www.cdc.gov/coronavirus/2019-ncov/covid-data/pdf/covidview-06-12-2020.pdf

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Risks for Severe/Critical COVID-19

Comments (38)

The ABO blood group locus and a chromosome 3 gene cluster associate with SARS-CoV-2 respiratory failure in an Italian-Spanish genome-wide association analysis

David Ellinghaus, Frauke Degenhardt, Luis Bujanda, Maria Buti, Agustin Albillos, Pietro Invernizzi, Javier Fernandez,

Spain, Italy: 1980 COVID-19 patients with respiratory failure v. population controls
Not entire human sequencing, analyzed 8,582,968 SNPs. Approach increases uncertainty

Associations:

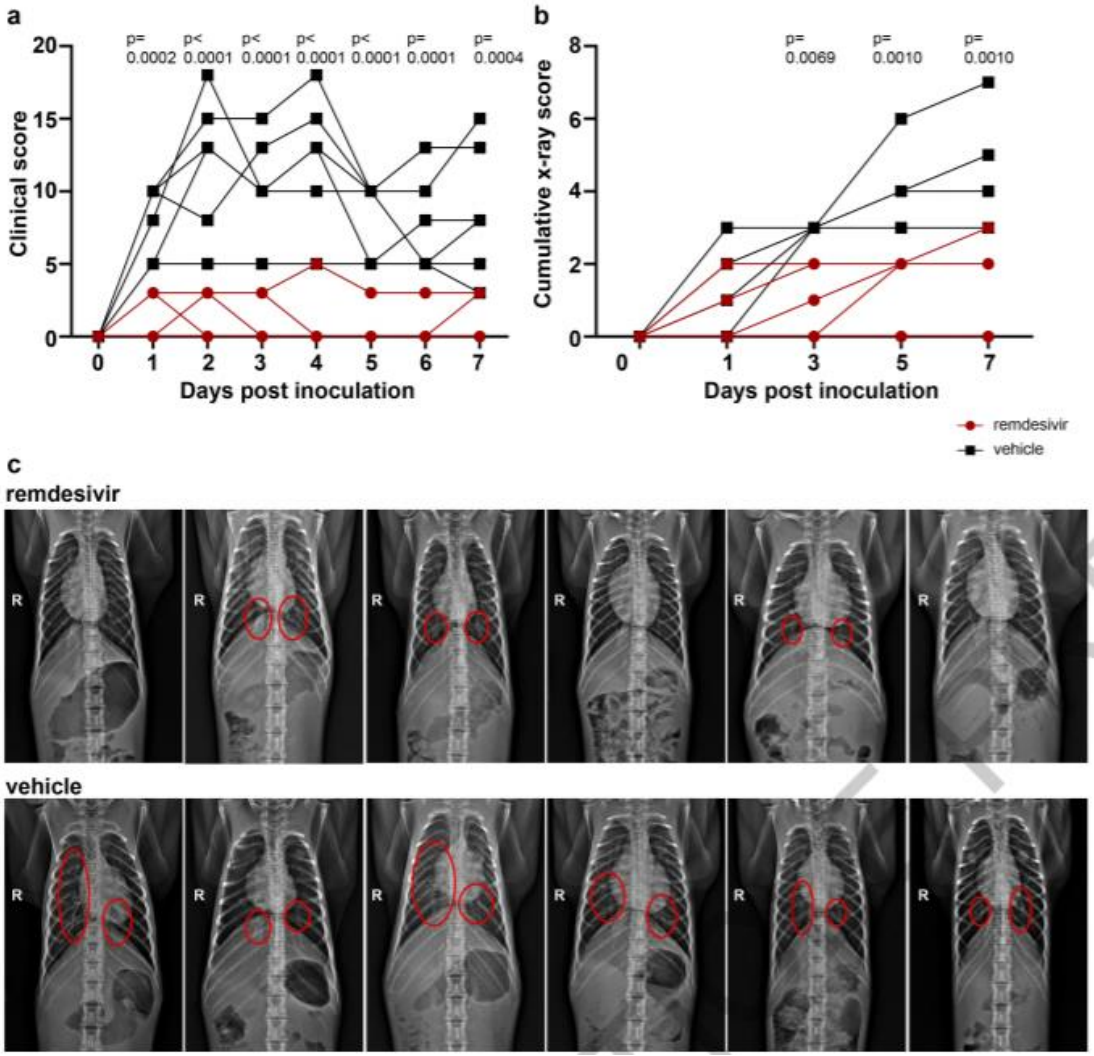
9q34 chromosome → risk A+ blood group [OR 1.45, 95% CI 1.20-1.75]
→ protective O group [OR 0.65, 95% CI 0.53-0.79]

3p21.31 chromosome → six genes, known interaction with ACE2

COVID-19 Therapeutics

Remdesivir

Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2



https://www.nature.com/articles/s41586-020-2423-5

RDV in Rhesus Macaques

- 6 received RDV, 6 vehicle solution
- Administered 12 hours post inoculation

Findings:

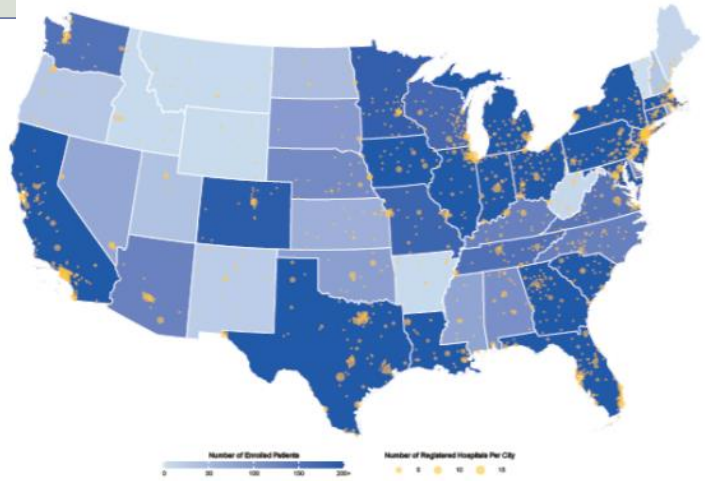
1. Lack of respiratory disease
2. Decreased viral replication in lungs
   → but not viral shedding
   ? RDV better penetration in lung tissues than upper airways
   Especially early in course, patients likely remain infectious
3. Reduced pneumonia

Conclusion: administration RDV ASAP may improve efficacy of RDV

https://www.nature.com/articles/s41586-020-2423-5

Convalescent Plasma

Early safety indicators of COVID-19 convalescent plasma in 5,000 patients



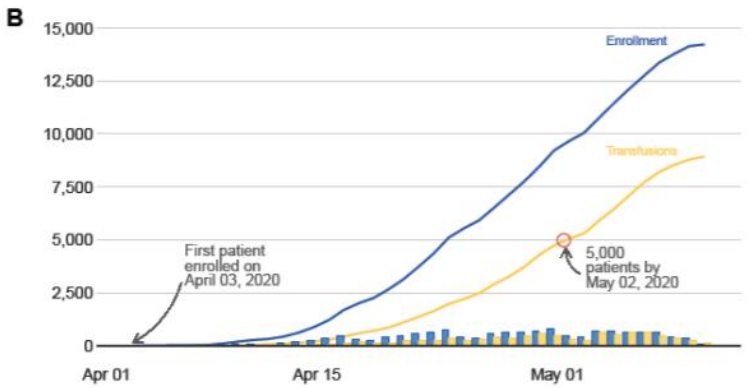


Figure 1. Participation in the US COVID-19 Convalescent Plasma Expanded Access Program (EAP) including data extracted on May 11, 2020. A. Choropleth

https://www.medrxiv.org/content/10.1101/2020.05.12.20099879v1

Early Safety Data, Convalescent Plasma

Table 2. Serious Adverse Event (SAE) Characteristics. (n=5,000)

Four Hour Reports	Reported *(n = 36)*	Related[a] *(n = 25)*	Estimate (95% CI)
Mortality	15	4	0.08% (0.03%, 0.21%)
Transfusion-Associated Circulatory Overload (TACO)	7	7	0.14% (0.07%, 0.29%)
Transfusion-Related Acute Lung Injury (TRALI)	11	11	0.22% (0.12%, 0.39%)
Severe allergic transfusion reaction	3	3	0.06% (0.02%, 0.18%)
Seven Day Reports	**Reported**		**Estimate (95% CI)[b]**
Mortality	602		14.9% (13.8%, 16.0%)

Footnotes

[a]This category of serious adverse events (SAE) reports the aggregate total of possibly-, probably- and definitely-related SAEs, as attributed based on the site investigator's determination. The estimate is based on the number of related SAEs relative to the denominator of 5,000.

[b]The estimated seven-day mortality rate is based on a Kaplan-Meier estimate using all reported deaths. See methods for further estimation details including handling of censoring due to ongoing data collection.

Severe or life-threatening COVID-19

All incidences of TACO and TRALI were judged as related
(possibly, n=9; probably, n=7; definitely, n=2)

15 deaths (4h, 0.3% of all transfusions)
4 deaths related (possibly, n=3; probably, n=1; definitely, n=0)

Conclusion: Serious AE < 1 %, mortality not deemed excessive

https://www.medrxiv.org/content/10.1101/2020.05.12.20099879v1

Dexamethasone Trial Arm (RECOVERY Trial: Prelim Statements)

RECOVERY
Randomised Evaluation of COVID-19 Therapy

UNIVERSITY OF OXFORD

Oxford University News Release
EMBARGOED UNTIL 16 June 2020, 13:00 (UK Time)

Low-cost dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of COVID-19

In March 2020, the RECOVERY (Randomised Evaluation of COVid-19 thERapY) trial was established as a randomised clinical trial to test a range of potential treatments for COVID-19, including low-dose dexamethasone (a steroid treatment). Over 11,500 patients have been enrolled from over 175 NHS hospitals in the UK.

On 8 June, recruitment to the dexamethasone arm was halted since, in the view of the trial Steering Committee, sufficient patients had been enrolled to establish whether or not the drug had a meaningful benefit.

A total of 2104 patients were randomised to receive dexamethasone 6 mg once per day (either by mouth or by intravenous injection) for ten days and were compared with 4321 patients randomised to usual care alone. Among the patients who received usual care alone, 28-day mortality was highest in those who required ventilation (41%), intermediate in those patients who required oxygen only (25%), and lowest among those who did not require any respiratory intervention (13%).

Dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88]; p=0.0003) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; p=0.0021). There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75]; p=0.14).

Based on these results, 1 death would be prevented by treatment of around 8 ventilated patients or around 25 patients requiring oxygen alone.

Given the public health importance of these results, we are now working to publish the full details as soon as possible.

https://www.recoverytrial.net/files/recovery_dexamethasone_statement_160620_v2final.pdf

Dexamethasone Trial Arm (RECOVERY Trial: Prelim Statements)

- Target: hyperinflammatory state, trial halted
- UK trial
  - 2104 v. 4321 controls
- NNT avoid 1 death
  - Ventilated patients: 8
    - Mortality rate 40% → 28%
  - On oxygen: 25
    - Mortality rate 25% → 20%
  - No benefit if not on oxygen

Conclusion: first to show decreased mortality in RCT
inexpensive (IV or PO)

Caveats: Press release data

Hydroxychloroquine Trial Arm (RECOVERY Trial: Prelim Statements)

Conclusion: no benefit in hospitalized patients

FDA pulled Emergency Use authorization for both hydroxychloroquine and chloroquine

Caveats: Press release data

https://www.statnews.com/2020/06/16/major-study-finds-common-steroid-reduces-deaths-among-patients-with-severe-covid-19/

June 26, 2020

To submit your own question, please email QA@dkbmed.com

I've heard children don't have a large enough viral load to spread the virus. Is this the case?

Will children need to wear face masks at school?

I am an employer in a large city that was the epicenter of new cases. Our governor will soon approve reopening of our business, but when can we truly safely ask employees to return?

To receive CME/CE credit:

- Complete the evaluation on at COVID19.DKBmed.com
- Upon registering and successfully completing the activity evaluation, you will have immediate access to your certificate.

To access more resources related to COVID-19:

- Access our resource hub at COVID19.DKBmed.com

To ask your own question to Dr. Auwaerter:

- Email QA@dkbmed.com