

## Coronavirus 2020 What Do You Need To Know?

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### Disclosures

- Henry Masur MD has no financial relationships with commercial interests to disclose
- Any unlabeled/unapproved uses of drugs or products referenced will be disclosed

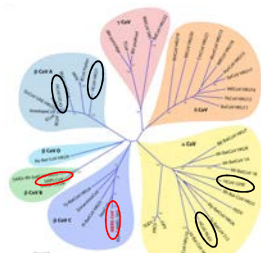
### Objectives

- Outline the current U.S COVID-19 pandemic
- Provide overview of clinical manifestations
- Explain the most recent treatment and prevention guidelines

### Coronavirus Biology

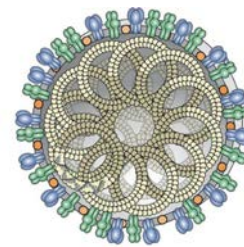
### Human Coronaviruses

- **Endemic human CoVs**
  - 229E, NL63, OC43, HKU1
  - 15-30% of common colds
- **SARS-CoV**
  - Global epidemic, 2002-2003
  - 8096 cases, 774 deaths (9.6%)
- **MERS-CoV**
  - Recognized in 2012 and ongoing
  - 2494 cases, 858 deaths (34.4%)



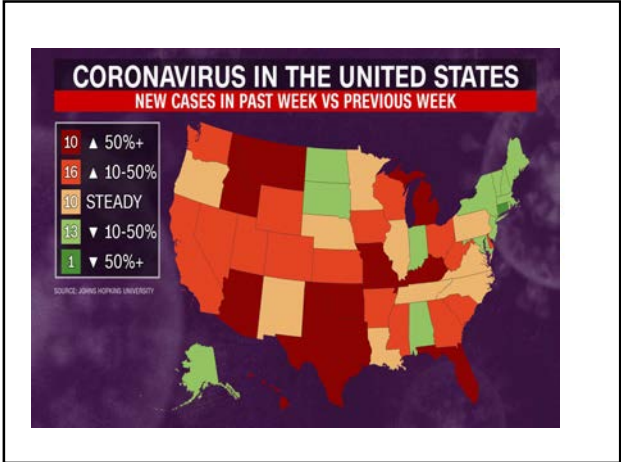
Chan JF. Clin Microbiol Rev. 2015; 28: 465-522.

### COVID-19



Structural proteins: Spike, Envelope, Membrane, Nuclear

## COVID-19 Epidemiology



- ### Transmission
- Droplets
  - Aerosols
  - Mucous Membranes
  - Fomites
  - Indoors/Outdoors
  - Temperature
  - Humidity

- ### Prevention
- Social Distancing
  - Masks
  - Hand Hygiene



- ### Diagnosis
- Viral Detection
    - Culture of live virus is definitive
      - Only available in research setting
    - PCR detection of RNA is standard
      - Sensitivity depends on specimen collection
      - Test performance depends on platform
  - Antibody
    - Large variability in sensitivity and specificity
    - If accurate, indicates past infection
    - No role in detecting acute infection
    - No clear relationship to immunity

### How Much Testing is Appropriate

- Screening of Asymptomatic

### One Approach

- According to health protocols agreed upon by Major League Baseball and the MLB Players' Association
  - Players are to be tested every other day and receive results within 24 to 48 hours

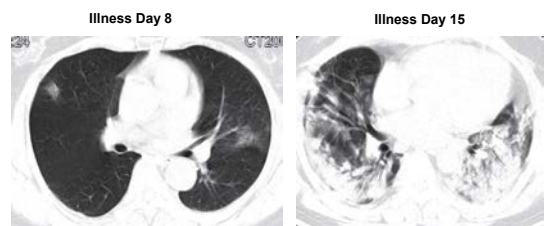


### How Much Testing is Appropriate

- Screening of Asymptomatic
- Diagnosis of Symptomatic

### COVID-19 Clinical Findings

### Rapidly Progressive Respiratory Failure



Huang C. *Lancet*. 2020 Jan 24.

### Clinical Findings, 1099 Hospitalized Patients

Characteristic	All patients	ICU care	No ICU care
Median age, year	47	52	45
Female	42%	42%	42%
Any comorbidity	24%	39%	21%
Fever	89%	92%	88%
Cough	68%	71%	67%
Fatigue	38%	40%	38%
Dyspnea	18.7%	38%	15%

Guan W et al. *N Engl J Med*. 2020 Feb 28.

### Common Laboratory Findings Among Hospitalized Patients

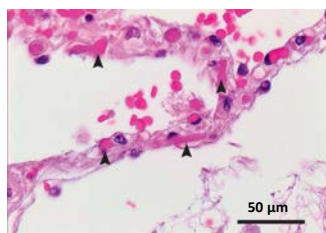
- Leukopenia, lymphopenia, leukocytosis
- Among severe illness
  - Elevated serum creatinine
  - Elevated transaminases
  - Elevated inflammatory markers (ESR, CRP, Ferritin) and d-dimer

Guan W et al. *N Engl J Med.* 2020 Feb 28.

### Clinical Complications

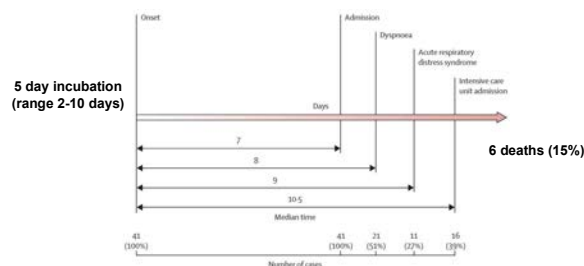
- ARDS/bacterial co-infection
- Acute kidney injury
- Hepatic injury
- Small and large vessel thrombosis
- Vasodilatory and cardiogenic shock

### Microthrombi in Interstitial Septa



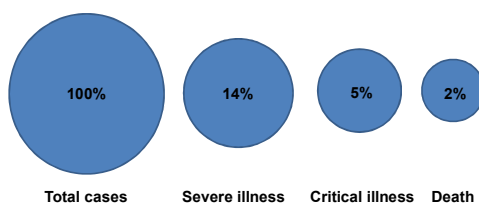
*N Engl J Med.* 2020 May 23.

### Illness Timeline During Severe COVID-19



*Lancet.* 2020 Jan 24.

### Estimated Distribution of Case Severity

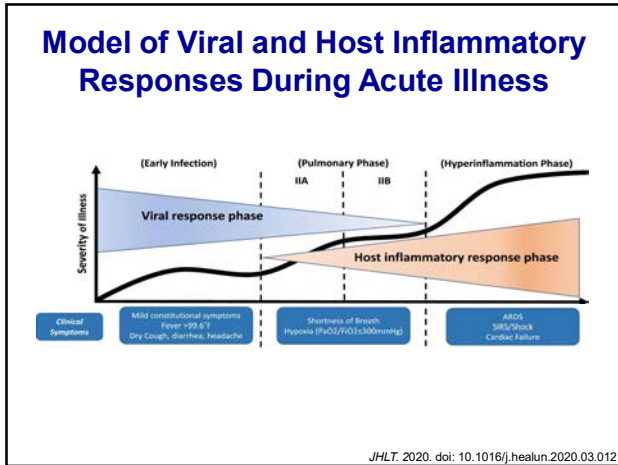


Wu Z. et al. *JAMA.* 2020 Feb 24.

### Age-specific Case Fatality Rates

	Confirmed cases, N (%)	Deaths, N (%)	Case fatality rate, %
Age, years			
0-9	416 (0.9)	0	0
10-39	11,768 (26.3)	26 (2.5)	0.2
40-49	8,571 (19.2)	38 (3.7)	0.4
50-59	10,008 (22.4)	130 (12.7)	1.3
60-69	8,583 (19.2)	309 (30.2)	3.6
70-79	3,918 (8.8)	312 (30.5)	8.0
≥ 80	1408 (3.2)	208 (20.3)	14.8

China CDC Weekly. 2020, Vol 2, No. 8.



### Cytokine Storm Is This Really An Entity?

	Total population		Severe disease		Measurement platform	
	No.	IL-6 levels, pg/mL	No.	IL-6 levels, pg/mL		
COVID-19						
Zhou et al <sup>3</sup>	191	7 (5-11)	54 <sup>b</sup>	11 (8-14)	CL	
Wu et al <sup>1</sup>	123	7 (6-9)	84 <sup>c</sup>	7 (6-11)	CL	
Mo et al <sup>5</sup>	155	45 (17-96)	85 <sup>d</sup>	64 (31-165)	CL	
Qin et al <sup>2</sup>	452	21 (6-47)	286 <sup>e</sup>	25 (10-55)	CL	
Cummings et al <sup>6</sup>	NR	NR	237 <sup>f</sup>	26 (11-69)	CL	
	Total population		Hypoinflammatory		Hyperinflammatory	
ARDS	No.	IL-6 levels, pg/mL	No.	IL-6 levels, pg/mL	No.	IL-6 levels, pg/mL
ALVEOLI <sup>7</sup>	521	238 (94-741) <sup>g</sup>	386	154 (67-344)	135	1525 (584-3802)
FACTT <sup>8</sup>	884	130 (46-411) <sup>g</sup>	638	86 (34-216)	246	578 (181-2621)
SAILS <sup>9</sup>	720	443 (173-1513) <sup>g</sup>	451	282 (115-600)	269	1618 (517-3205)

Sinha P et al. JAMA Intern Med. Published online June 30, 2020.

NIH COVID-19 Treatment Guidelines

## Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

VIEW GUIDELINES

<http://covid19treatmentguidelines.nih.gov>  
Live 4.21.2020

### Why Do We Need These Guidelines?

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- Medical Professionals and Public
  - Bombarded with press releases and news stories
- Literature is evolving quickly
  - Multiple different journals
- Need for Trusted, Unbiased, Science Based Guidance

### Summary of Recommendations

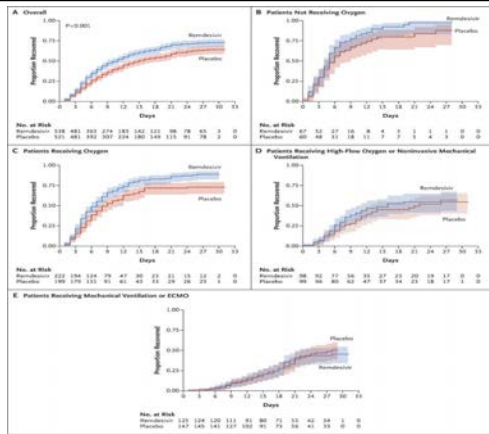
	Preexposure prophylaxis	Postexposure prophylaxis	Presymptomatic/symptomatic	mild	moderate	severe	Critical
<b>Antivirals</b>							
HCQ							
HCQ + Azithromycin							
Remdesivir							
Immunomodulators							
Convalescent plasma							
IL1 antagonists							
IL6 antagonists							
Interferons							
JAK inhibitors							
Corticosteroids							

  Recommend against the use  
  Not recommended outside of a clinical trial  
  Insufficient data to recommend for or against the use  
  Recommended

## Antiviral Therapy

## Remdesivir

- What is the Evidence, Is It Effective
  - ACT I-NIH Randomized, Placebo Controlled Study



JH Beigel et al. N Engl J Med 2020

## Anti-inflammatory Therapy

## History of Acute Respiratory Distress Syndrome

- The term “ARDS” first appeared in 1967 authored by Ashbaugh
- Military physicians described “Da Nang” lung around the same time
- Military physicians described this syndrome even earlier during World War I

“Edema of the lungs, with general asphyxia. Livid cyanosis with great dyspnea is the outstanding clinical feature. . . . A yellow serous fluid fills the air passages

- 1915, *Canadian Military Medical Textbook*

Ashbaugh Lancet 1967 “Acute Respiratory Distress in Adults”  
Morris Military Medicine 2006 “ARDS in Combat Casualties: Military Medicine”

## Meta-Analyses and Clinical Practice

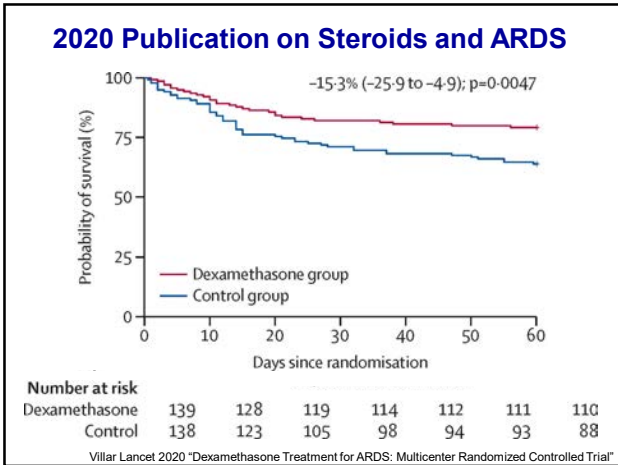
	RCTs	Other	Conclusion
Agarwal 2007	3	3	Does not support steroids
Meduri 2008	3	2	Support steroids
Peter 2008	8	1	Does not support steroids
Tang 2009	3	6	Support steroids
Lamontagne 2010	4	1	Inconclusive
Ruan 2014	8	10	Does not support steroids
Meduri 2018	9	0	Supports steroids

Survey of 103 Practitioners in USA/Canada ICUs (2013):

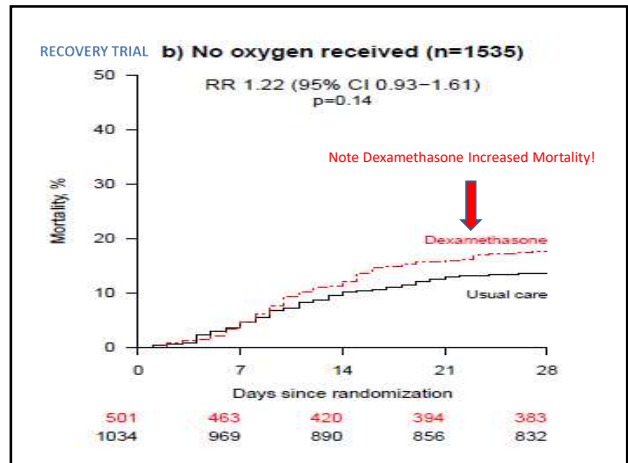
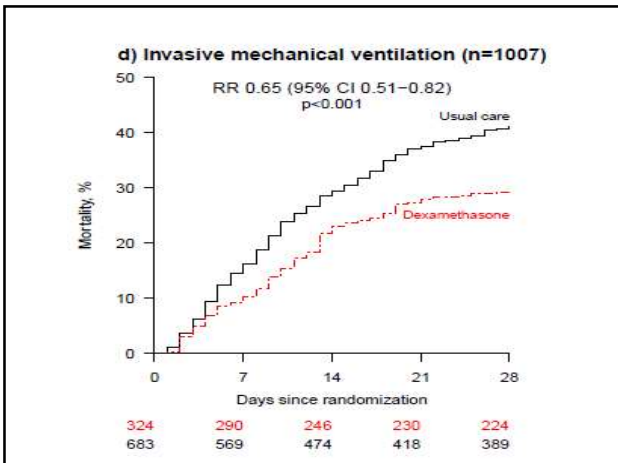
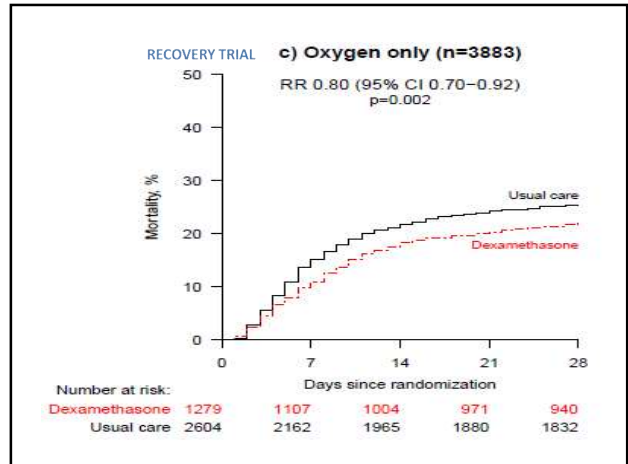
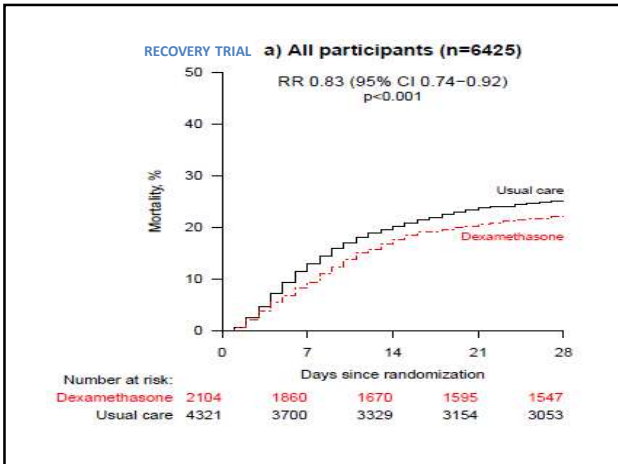
Would you give steroids in ARDS?

- 67% Almost never or 24% Usually not
- 12% Sometimes

Lamontagne J Can Anesth 2013 “Corticosteroids Use in the ICU: A Survey of Intensivists”

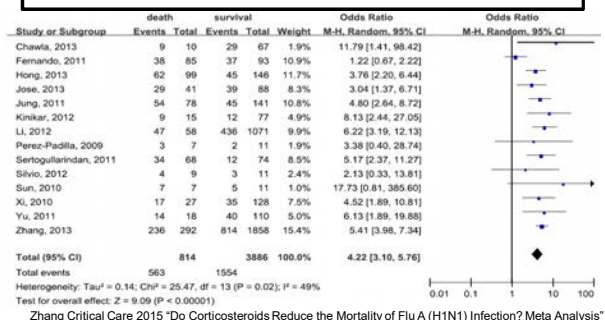


- ### RECOVERY Trial Randomization
- Lopinavir-ritonavir 400/100 PO/NGT q12 x10d
  - Low dose corticosteroids 6mg PO/IV qDay x10days
    - In pregnant or breastfeeding women: prednisolone 40mg PO or IV hydrocort 80mg BID
  - Hydroxychloroquine 800mg load, 800mg 6hr later, 400mg 6h later, 400 12hr later, then q12 x9d. (10d course)
  - Azithromycin 500 PO/NGT/IV x10d
  - No additional treatment



### Can We Extrapolate from Influenza?

#### Meta Analysis of Corticosteroids in Influenza 23 Studies (9 Cohort, 14 Case Control)



### Summary of Recommendations

	Preexposure prophylaxis	Postexposure prophylaxis	Presymptomatic/symptomatic	mild	moderate	severe	Critical
<b>Antivirals</b>							
H2O							
H2O + Azithromycin							
Lopinavir or HIV protease							
Remdesivir							
<b>Immunomodulators</b>							
Convalescent plasma							
IL1 antagonists							
IL6 antagonists							
Interferons							
JAK inhibitors							
Corticosteroids							

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### Recommendations Evolve!

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