Covid-19 Update for Hospitalized Patients

Chris Tymchuk, MD, PhD

Infectious Diseases and Hospital Medicine

Tara Vijayan, MD, MPH

Infectious Diseases and Antimicrobial Stewardship

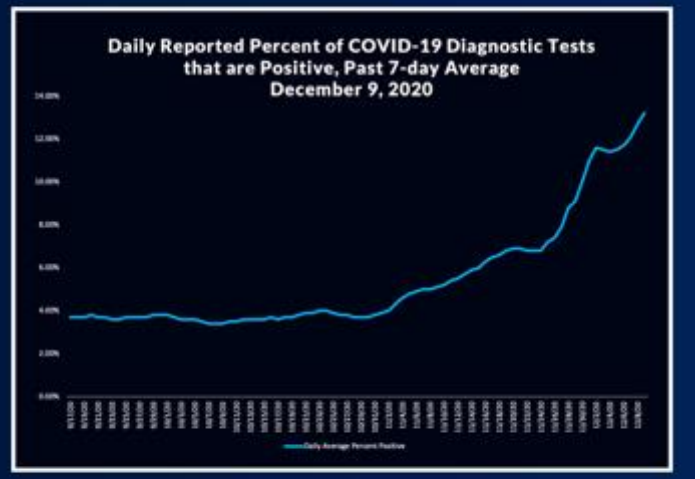
Adrian Mayo, MD

Hospital Medicine

Overview

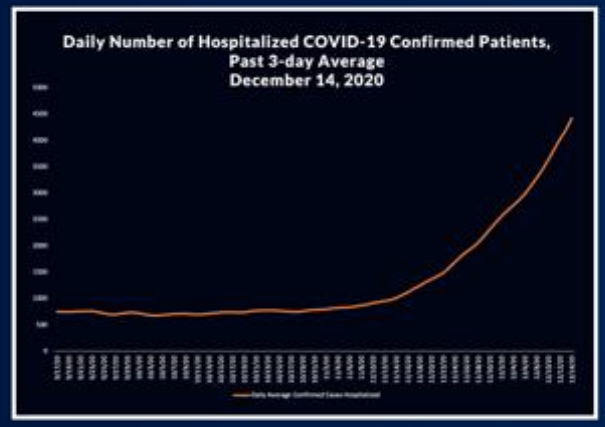
- Clinical Presentation
- Diagnosis
- Management
- Clinical Trials
- Discharge and outpatient follow up
- Vaccines

Testing Positivity Rate



7-Day Daily Average: 13.2%

Hospitalizations



Current Hospitalizations (12/16): 4,656

Cases

22,422

New Cases Reported (12/16)*

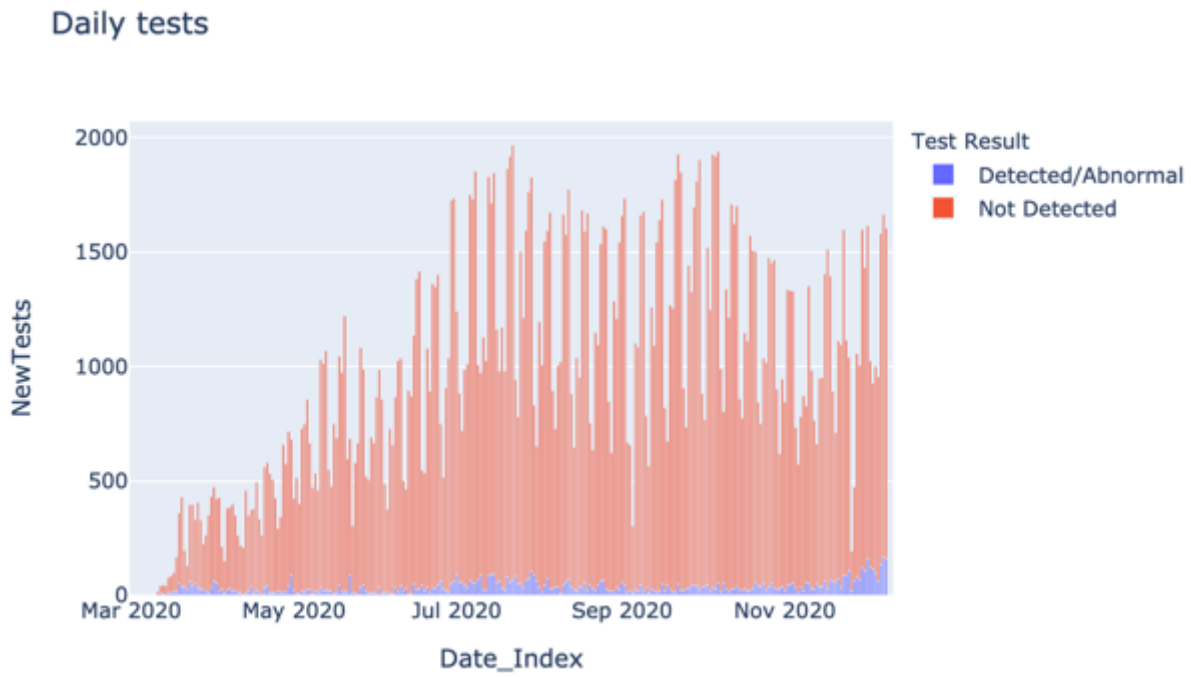
566,005

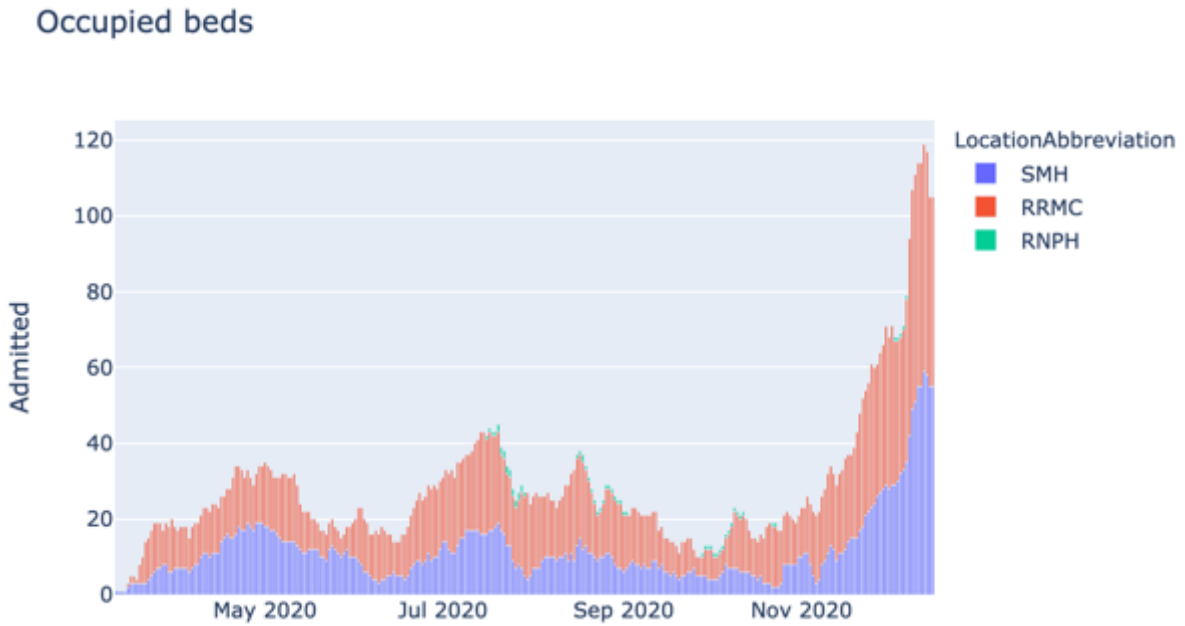
Total Cases Reported*

**including cases reported by Long Beach and Pasadena Health Departments*

Covid-19 cases continue to rise

Covid-19 cases at UCLA





Covid-19 Clinical Presentation

- Fever (77-98%, 44% on admission)
- Cough (46-82%, non-productive in 66%)
- Myalgia or fatigue (11-52%)
- Shortness of breath (3-31%)
- Headache (13.6%)
- Nasal congestion <5%
- Nausea/vomiting/diarrhea <5%
- Ageusia- Anosmia or ageusia (23-68%)

Only 44% of patients presented with fever

Guan W et al. NEJM 2020

Characteristic	All Patients (N=1099)
Age	
Median (IQR) — yr	47.0 (35.0–58.0)
Distribution — no./total no. (%)	
0–14 yr	9/1011 (0.9)
15–49 yr	557/1011 (55.1)
50–64 yr	292/1011 (28.9)
≥65 yr	153/1011 (15.1)
Female sex — no./total no. (%)	459/1096 (41.9)
Smoking history — no./total no. (%)	
Never smoked	927/1085 (85.4)
Former smoker	21/1085 (1.9)
Current smoker	137/1085 (12.6)
Exposure to source of transmission within past 14 days — no./total no.	
Living in Wuhan	483/1099 (43.9)
Contact with wildlife	13/687 (1.9)
Recently visited Wuhan‡	193/616 (31.3)
Had contact with Wuhan residents‡	442/611 (72.3)
Median incubation period (IQR) — days§	4.0 (2.0–7.0)
Fever on admission	
Patients — no./total no. (%)	473/1081 (43.8)
Median temperature (IQR) — °C	37.3 (36.7–38.0)
Distribution of temperature — no./total no. (%)	
<37.5°C	608/1081 (56.2)
37.5–38.0°C	238/1081 (22.0)
38.1–39.0°C	197/1081 (18.2)
>39.0°C	38/1081 (3.5)
Fever during hospitalization	
Patients — no./total no. (%)	975/1099 (88.7)
Median highest temperature (IQR) — °C	38.3 (37.8–38.9)
<37.5°C	92/926 (9.9)
37.5–38.0°C	286/926 (30.9)
38.1–39.0°C	434/926 (46.9)
>39.0°C	114/926 (12.3)

Symptoms — no. (%)	
Conjunctival congestion	9 (0.8)
Nasal congestion	53 (4.8)
Headache	150 (13.6)
Cough	745 (67.8)
Sore throat	153 (13.9)
Sputum production	370 (33.7)
Fatigue	419 (38.1)
Hemoptysis	10 (0.9)
Shortness of breath	205 (18.7)
Nausea or vomiting	55 (5.0)
Diarrhea	42 (3.8)
Myalgia or arthralgia	164 (14.9)
Chills	126 (11.5)
Signs of infection — no. (%)	
Throat congestion	19 (1.7)
Tonsil swelling	23 (2.1)
Enlargement of lymph nodes	2 (0.2)
Rash	2 (0.2)
Coexisting disorder — no. (%)	
Any	261 (23.7)
Chronic obstructive pulmonary disease	12 (1.1)
Diabetes	81 (7.4)
Hypertension	165 (15.0)
Coronary heart disease	27 (2.5)
Cerebrovascular disease	15 (1.4)
Hepatitis B infection¶	23 (2.1)
Cancer‖	10 (0.9)
Chronic renal disease	8 (0.7)
Immunodeficiency	2 (0.2)

Labs at Presentation

- Lymphocytopenia (83-90%)
- Thrombocytopenia (27-36%)
- Elevated AST/ALT (22%)
- Leukocytosis (6%)

Risk Factors for Progression

- Age >60 years*
- Persistent leukopenia
- LDH >500
- D-dimer >1000ng/mL may be seen more commonly in ICU patients**
- D-dimer >2000ng/mL may suggest thromboembolic disease

* Guan, W et al. NEJM 2020

** Zhou, F et al. Lancet 2020

Covid-19 Testing

- Rapid (“Expedited”) RT-PCR: 99.4% sensitivity and 96.8% specificity compared to in-lab RT-PCR
- 30-45min turn around time (TAT)
- STEMI, trauma, stroke, transplant screening, overnight testing, ED transfers to Resnick Neuropsychiatric, same day surgery, patients being admitted with ILI
- Ambulatory: COVID 19, Flu A, Flu B PCR (12-24hr TAT)
- In-patient: COVID 19, Flu A, Flu B, RSV PCR (4-6hr TAT)
- Repeat NP PCR once if high suspicion and concern for inadequate specimen collection

Respiratory Co-Infection testing

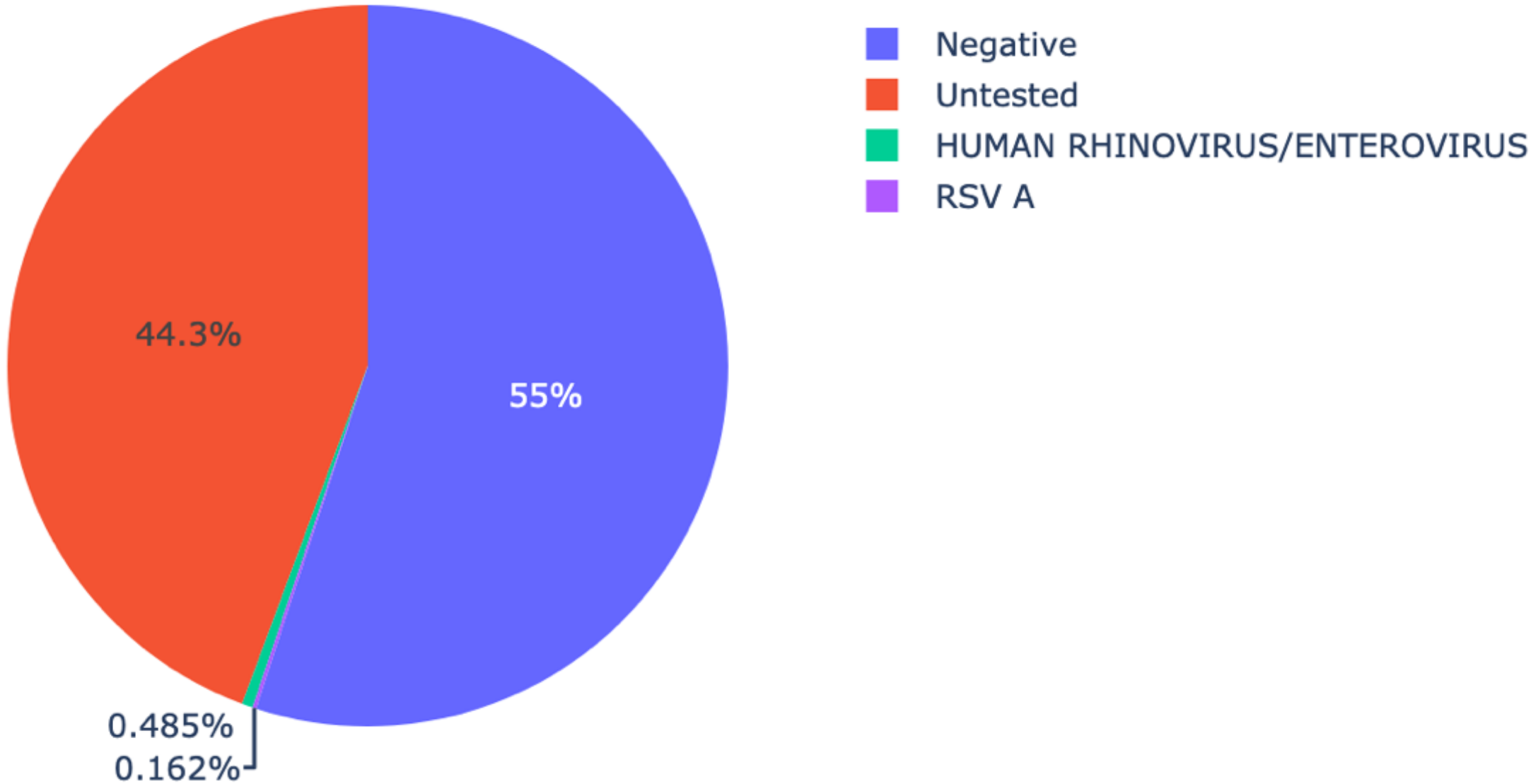
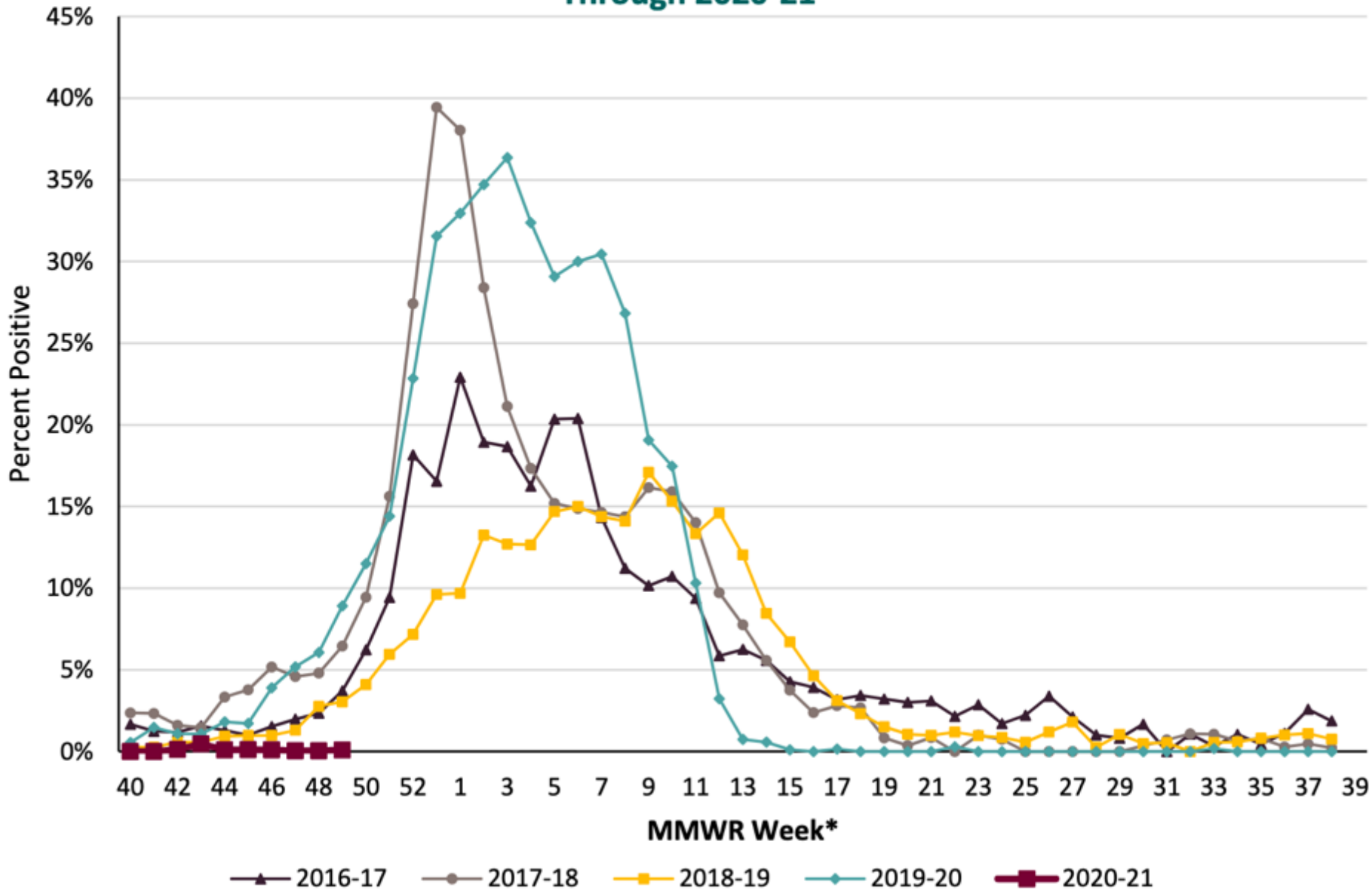


Figure 2. Percentage of Respiratory Specimens Testing Positive for Influenza at LAC Sentinel Surveillance Laboratories by Season, 2016-17 Through 2020-21



Lab Testing

Baseline bloodwork

- CBC with diff, CMP

In anticipation of dexamethasone use

- MTB quant, cocci EIA, Hepatitis BsAg, sAb, cAb, HCV Ab, strongyloides Ab, HIV Ab

Daily bloodwork

- CBC with diff, CMP

If worsening hypoxemia or respiratory distress

- D-dimer, CRP, LDH, Ferritin
- Sputum bacterial and fungal cultures
- Blood cultures if other signs of sepsis
- BNP

Lab Testing

Labs for immunocompromised patients if clinical worsening

- Beta-d-glucan
- Aspergillus EIA
- Cryptococcal Ag
- Cocci EIA

For cardiac disease/CMY

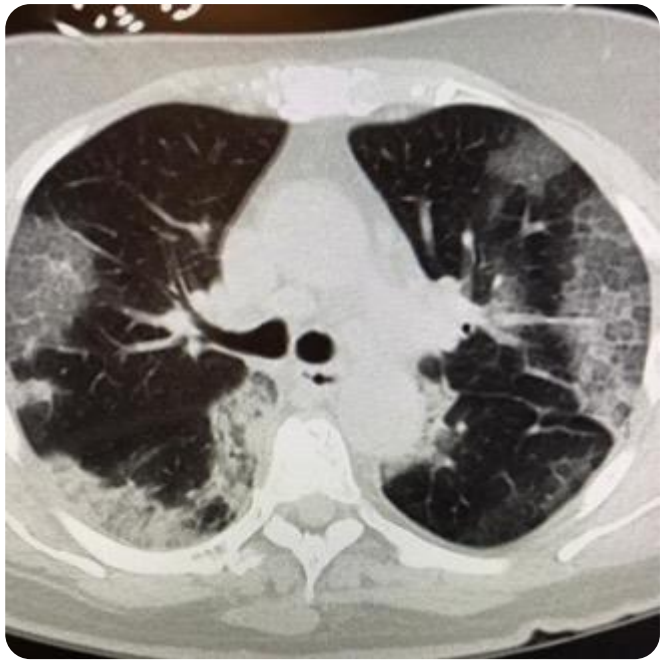
- CK
- Troponin
- BNP
- TTE if BNP elevated
- EKG
- Continuous telemetry

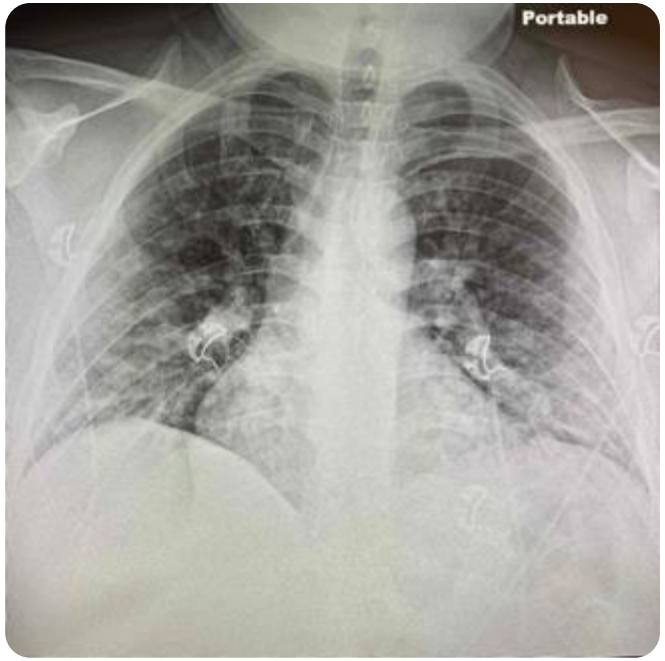
Imaging

Portable CXR on admission

CT Chest not routinely recommended

Consider CTA PE protocol if concern for PE

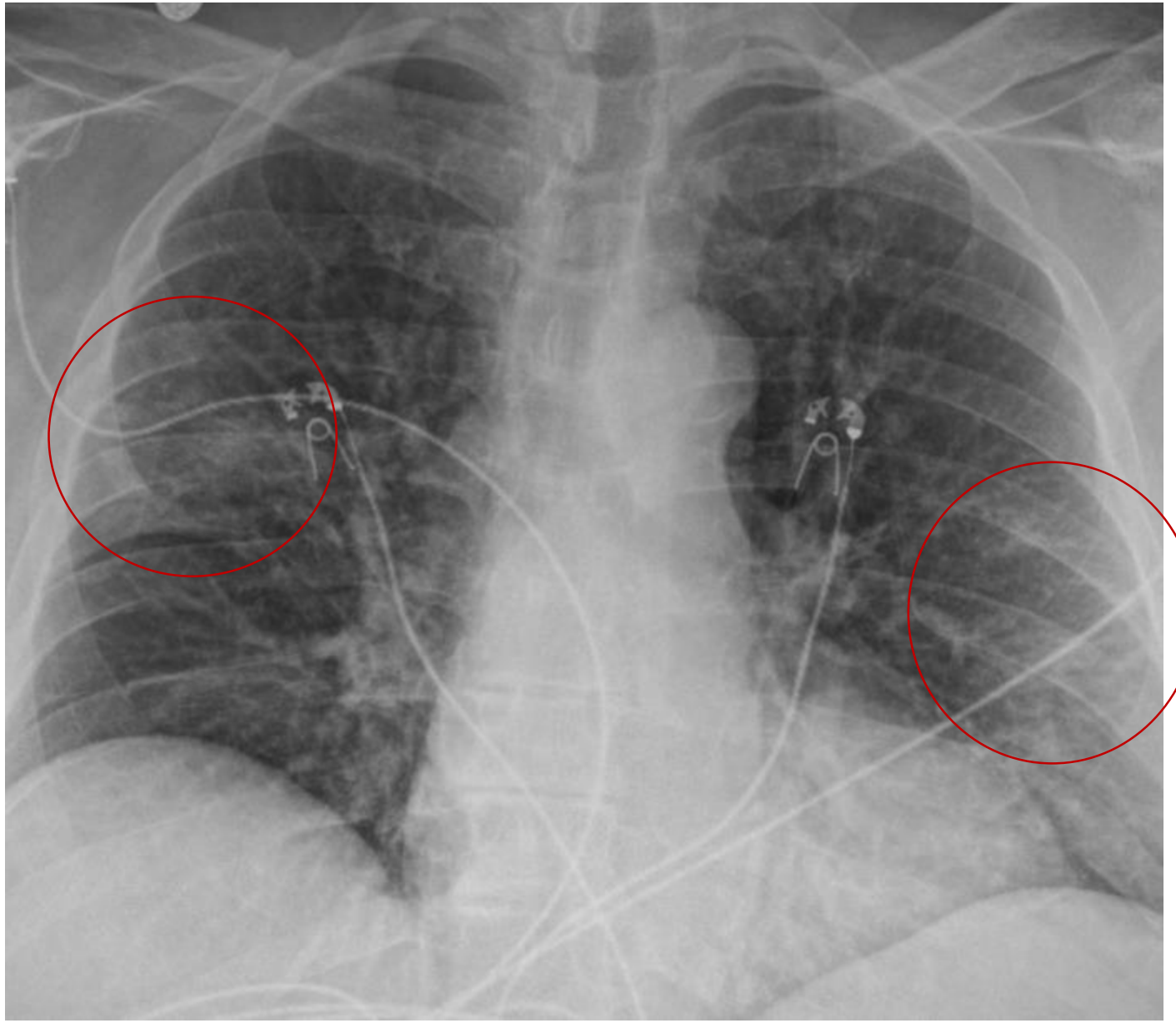




Imaging Findings

- Chest xray
  - Bilateral, patchy opacities
- Chest CT abnormalities in Covid patients
- Study of 81 patients hospitalized with Covid
  - Bilateral (79%)
  - Peripheral (54%)
  - Ground glass opacities (65%)
  - RLL predominant (27%)
- Difficult to differentiate from other viral or atypical causes of pneumonia

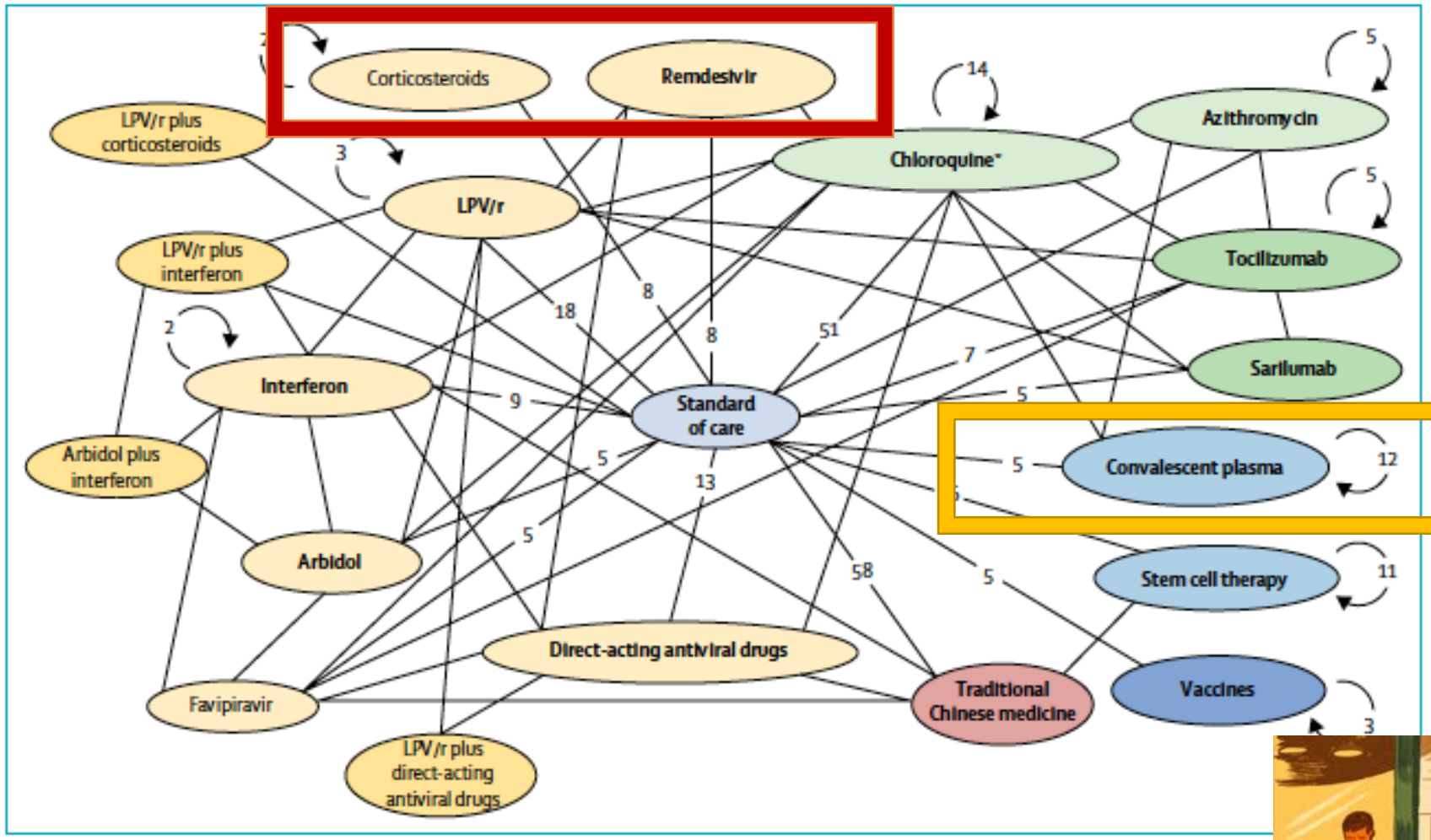
Shi H et al. Lancet 2020



Clinical Decision-Making: Goals of Therapy

- Primary goal: First do no harm
- Primary goal: prevent death (unless death is inevitable)
  - Mortality from COVID-19 ranges from 0.1-15%
  - Depends on how many tested, age of population, resources
  - Mortality among hospitalized patients: 18-21%
  - Who is at risk of dying?
- Secondary goal: Preventing mechanical ventilation
- Secondary goal: Facilitating recovery
- Emphasize enrollment in trials

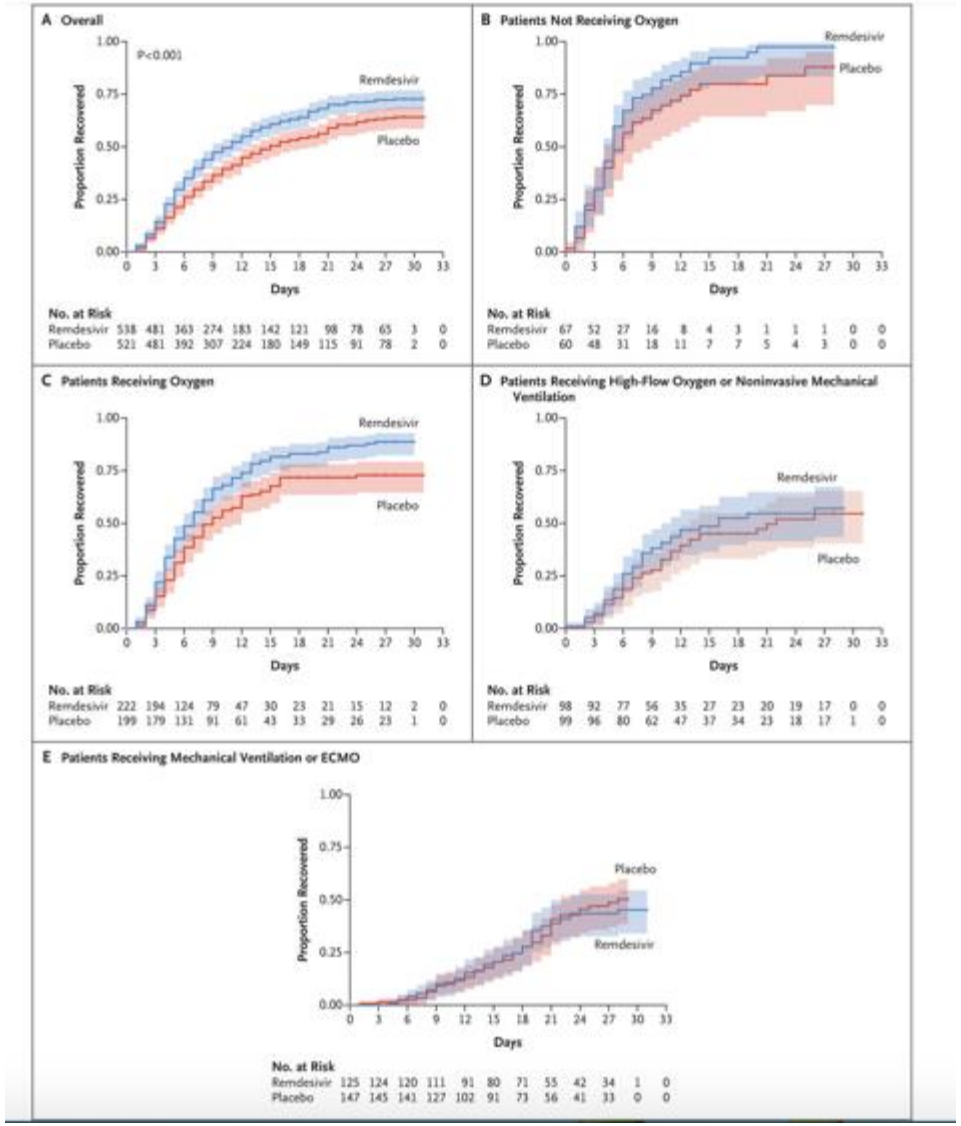
https://coronavirus.jhu.edu/data/mortality
Richardson, R, JAMA, April 22, 2020



Lancet Digital Health, April 2020

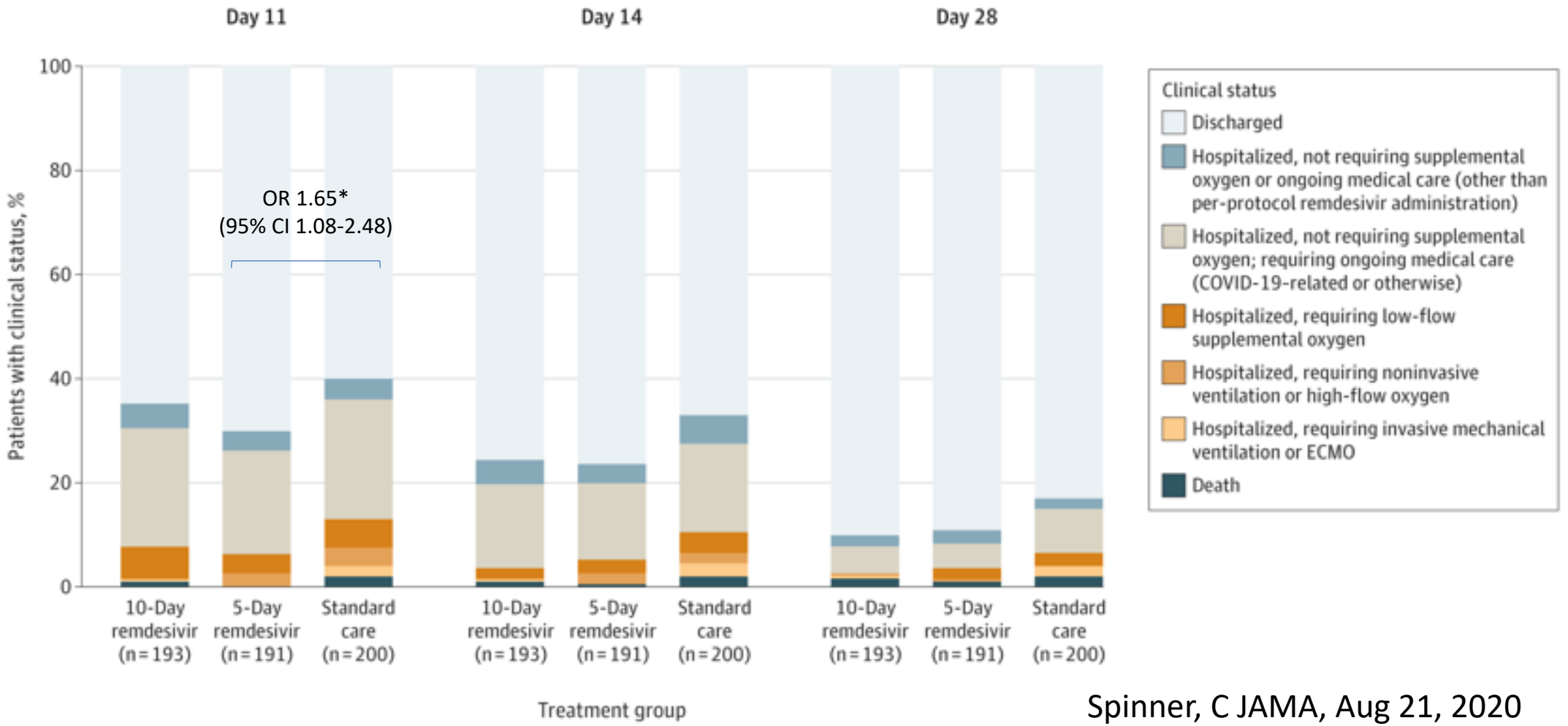
Mike Reddy, StatNews

The data to date: remdesivir



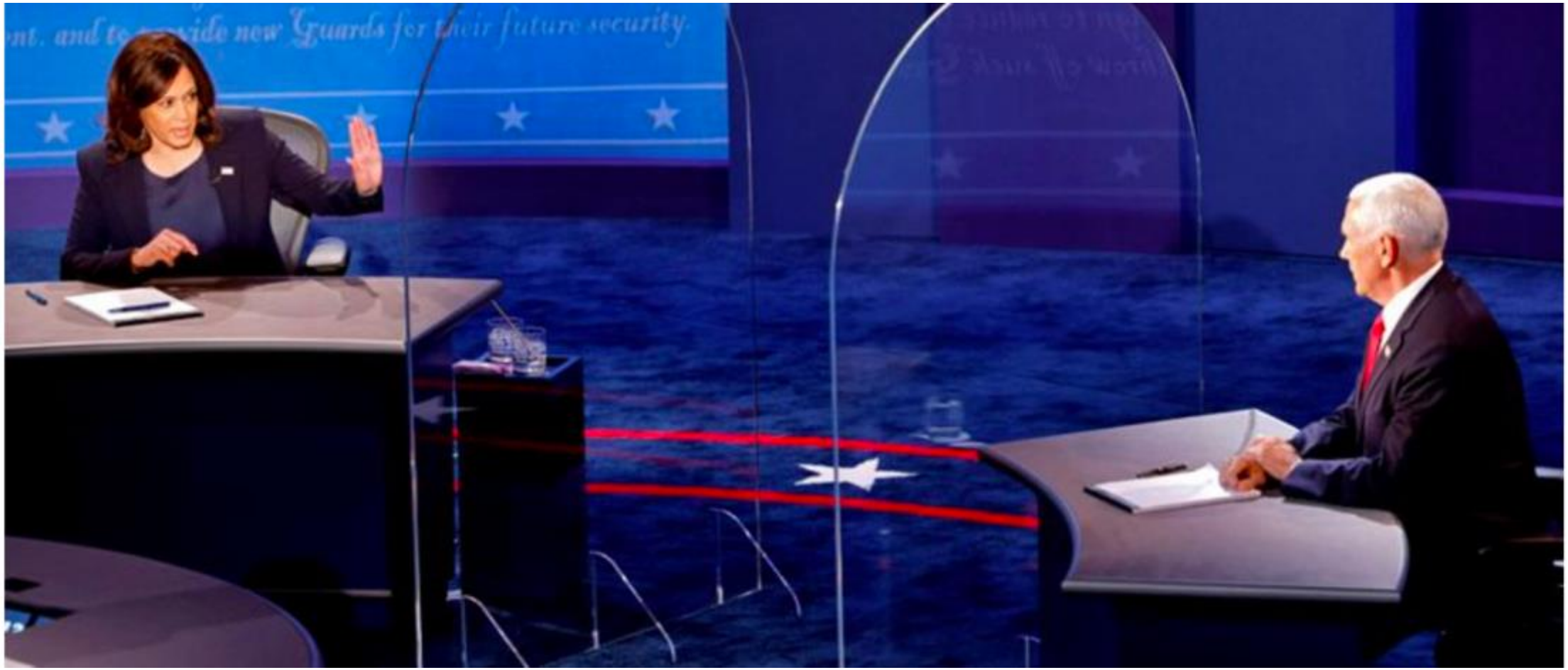
Beigel, NEJM, May 22, 2020

The data to date: remdesivir



Spinner, C JAMA, Aug 21, 2020

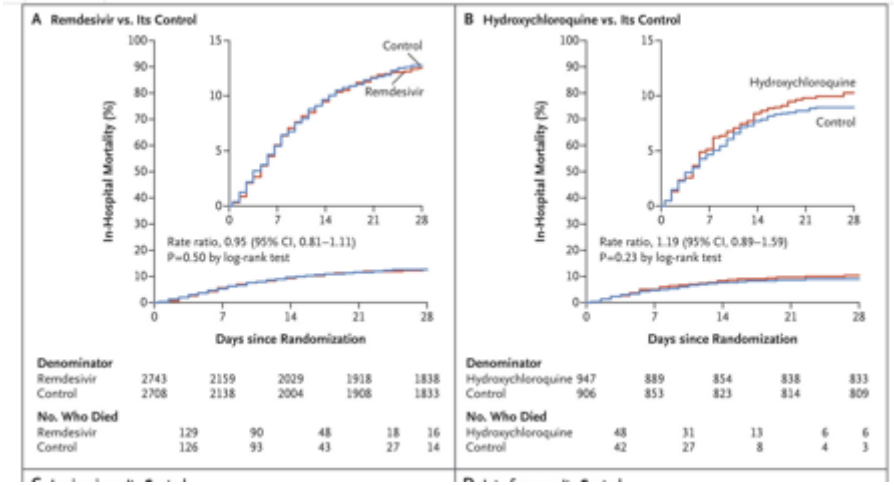
Solidarity Trial: controversies



Reuters, October 2020

Solidarity Trial, WHO
Preprint Oct 15
NEJM Dec 2, 2020

- A pragmatic trial design: Lop/r, RDV, IFN-b, HCQ, local standard
- SARS CoV2 PCR positivity not required



Subgroup	Active Treatment	Control	Log-Rank Statistics for No. of Deaths in Active-Treatment Group O−E	Variance	Rate Ratio for Death (99% CI; 95% CI for total)
	no. of deaths reported/no. of patients (%)				
Remdesivir					
Age at entry					
<50 yr	61/961 (6.9)	59/952 (6.8)	2.3	29.8	1.08 (0.67–1.73)
50–69 yr	154/1282 (13.8)	161/1287 (14.2)	−7.6	77.5	0.91 (0.68–1.21)
≥70 yr	86/500 (20.5)	83/469 (21.6)	−2.9	41.5	0.93 (0.63–1.39)
Respiratory support at entry					
No mechanical ventilation	203/2489 (9.4)	232/2475 (10.6)	−15.8	108.0	0.86 (0.67–1.11)
Mechanical ventilation	98/254 (43.0)	71/233 (37.8)	7.6	40.8	1.20 (0.80–1.80)
Total	**301/2743 (12.5)**	**303/2708 (12.7)**	**−8.3**	**148.8**	**0.95 (0.81–1.11)**
Heterogeneity around total: χ^2_3=3.9					P=0.50
Hydroxychloroquine					
Age at entry					
<50 yr	19/335 (5.7)	19/317 (5.8)	0.9	9.2	1.10 (0.47–2.57)
50–69 yr	55/410 (12.1)	31/396 (7.1)	10.8	21.2	1.66 (0.95–2.91)
≥70 yr	30/202 (14.0)	34/193 (17.8)	−3.5	15.8	0.80 (0.42–1.53)
Respiratory support at entry					
No mechanical ventilation	69/862 (7.4)	57/824 (6.6)	4.7	31.4	1.16 (0.73–1.84)
Mechanical ventilation	35/85 (39.2)	27/82 (32.3)	3.4	14.8	1.26 (0.65–2.46)
Total	**104/947 (10.2)**	**84/906 (8.9)**	**8.1**	**46.2**	**1.19 (0.89–1.59)**
Heterogeneity around total: χ^2_3=5.0					P=0.23

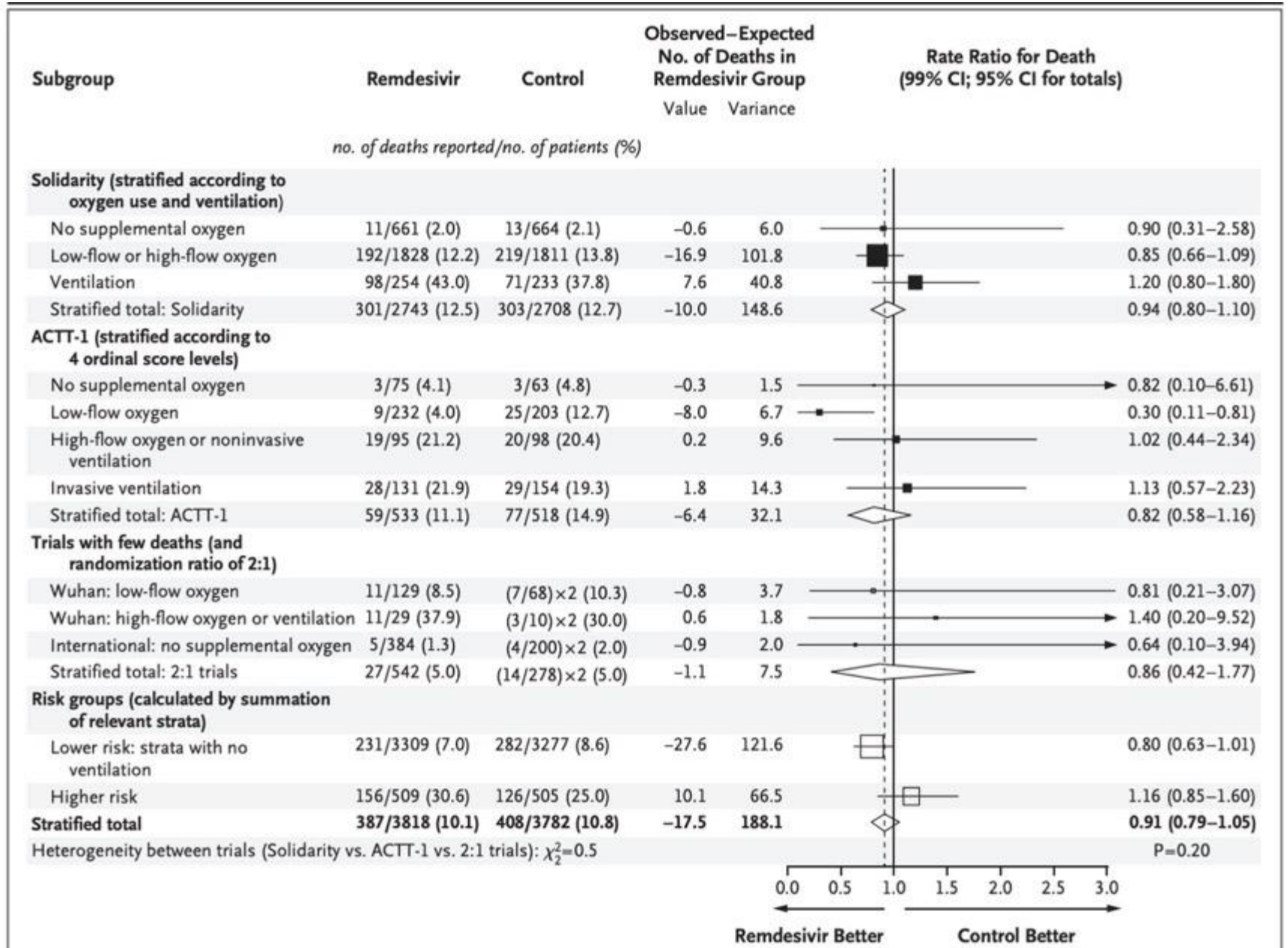
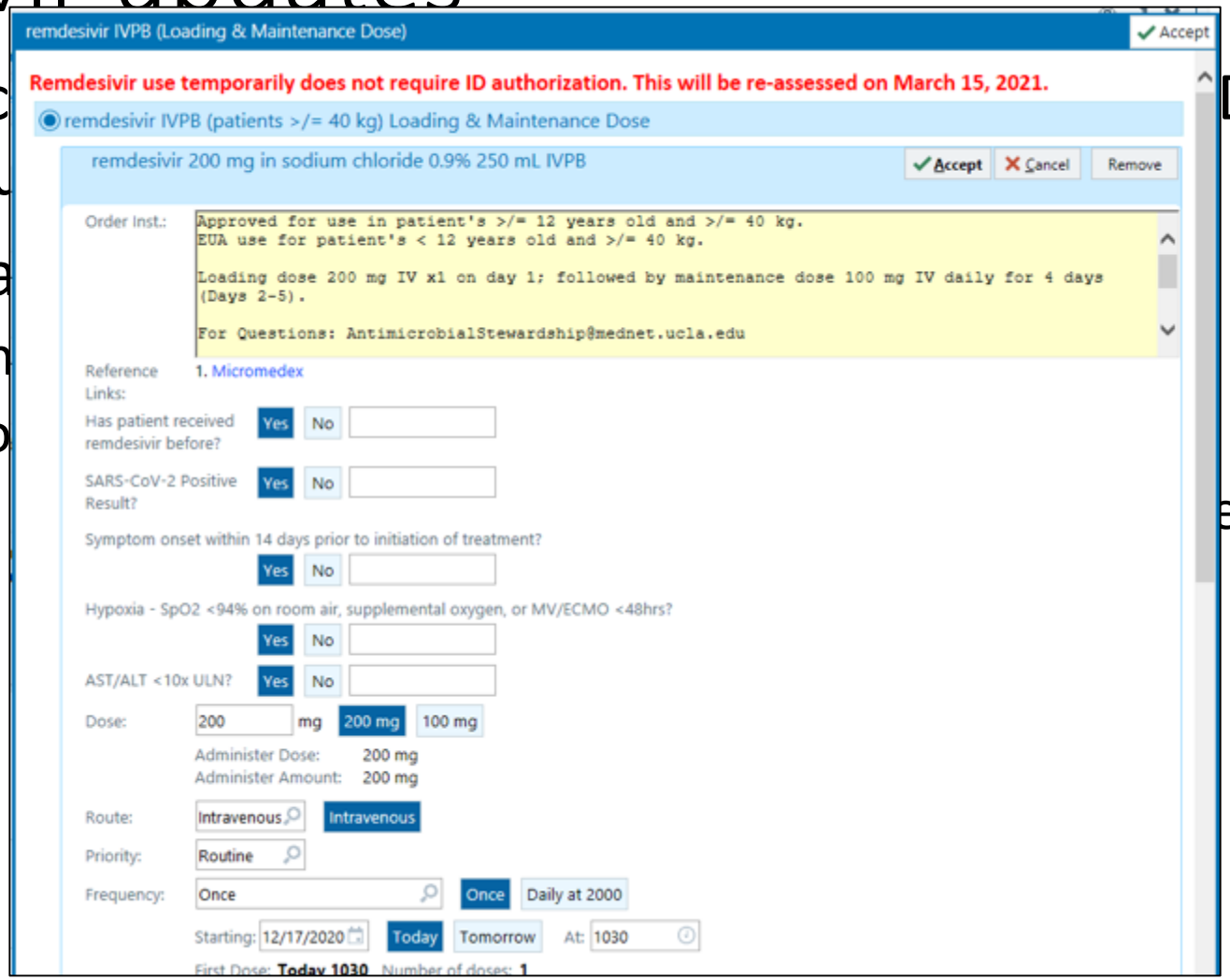


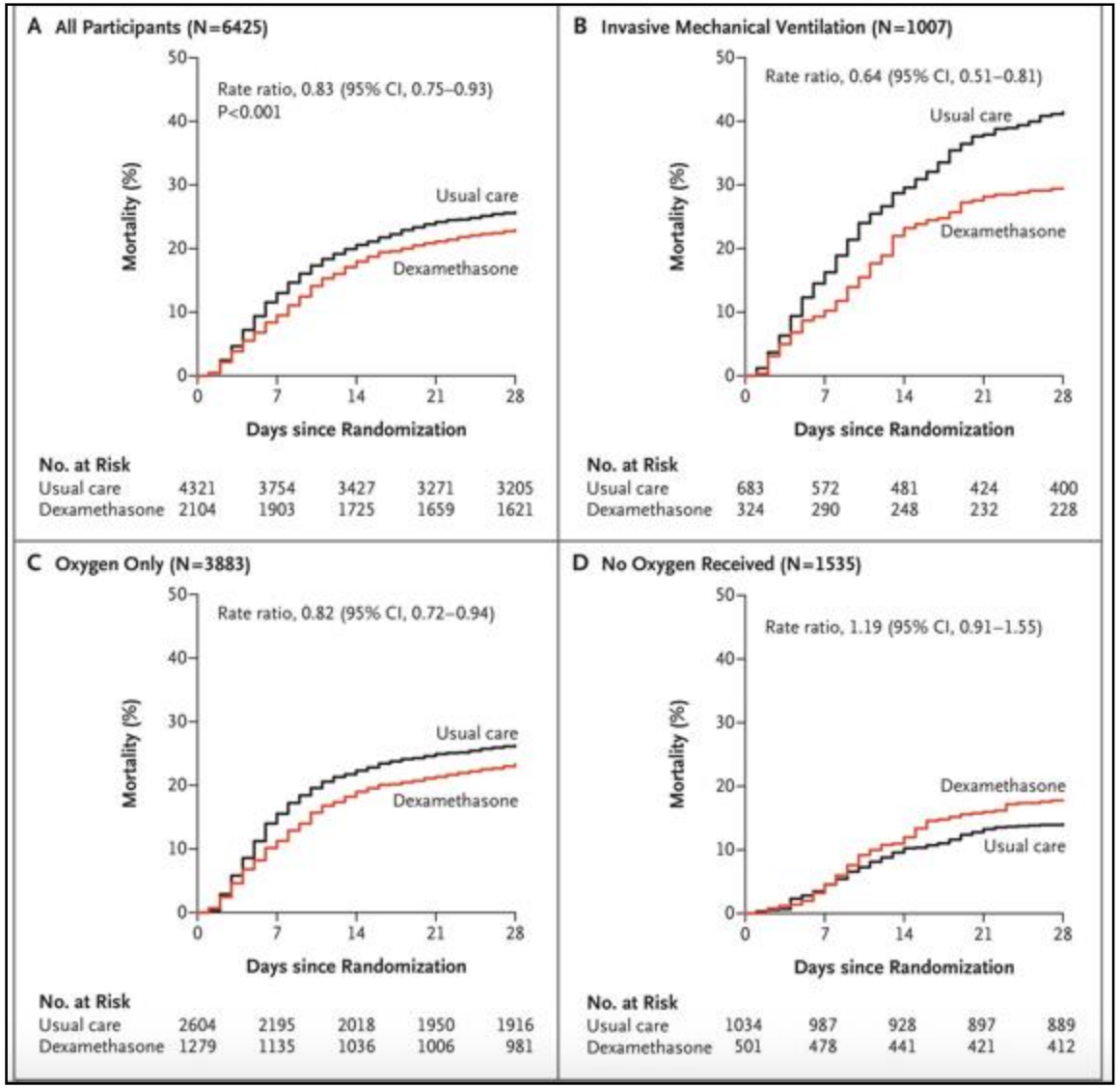
Figure 4. Meta-Analysis of Mortality in Trials of Random Assignment of Remdesivir or Its Control to Hospitalized Patients with Covid-19.

Remdesivir updates

- Tuesday, Dec … D approval not needed u…
- Criteria rema…
  - O2<94% on…
  - Symptom o…
  - Exceptions … ecommended



The data to date: steroids



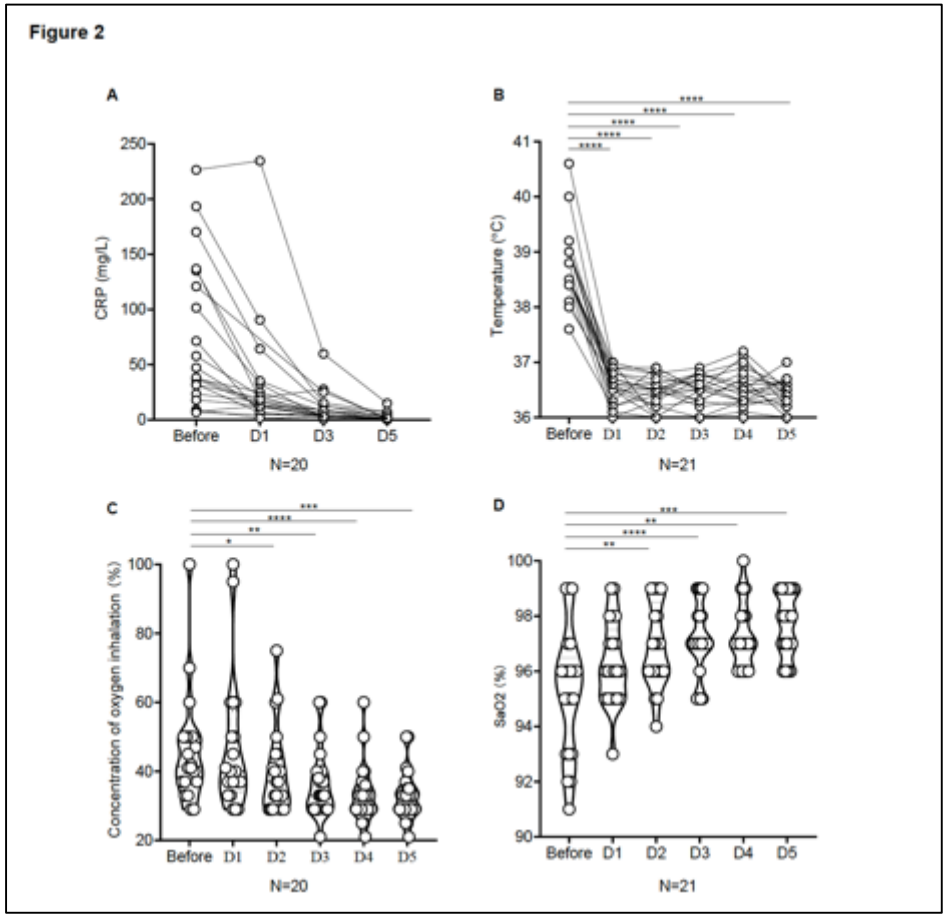
Dexamethasone
Tocilizumab
Colchicine
Convalescent Plasma
REGN-Cov2
Aspirin

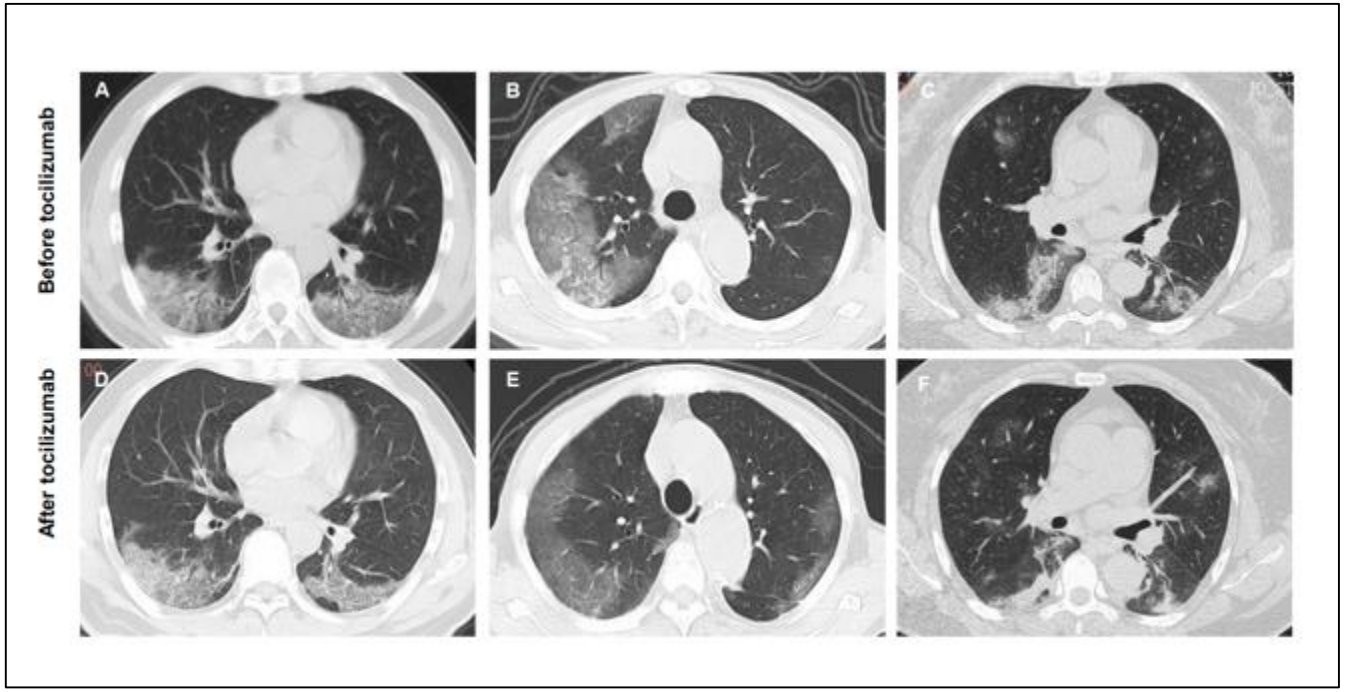
Recovery, NEJM, July 17, 2020

The data to date: Convalescent Plasma

- Ling, L and colleagues published RCT showing improvement in clinical recovery in those with severe disease: 91.3% (21/23) of the convalescent plasma group vs 68.2% (15/22) of the control group (JAMA, June 3, 2020)
- Pre-print Mayo Clinic observational study published Aug 12, 2020
  - Mortality benefit in patients who were given plasma within 3 days of diagnosis (8.7% v 11.9%)
  - High titers associated with greater benefit
- No benefit in severe disease, median time to dose was 8d (NEJM, 11/24)
- At this time, UCLA is using at least FDA minimum titer standard, prioritizing higher titer plasma if possible

Tocilizumab: theory

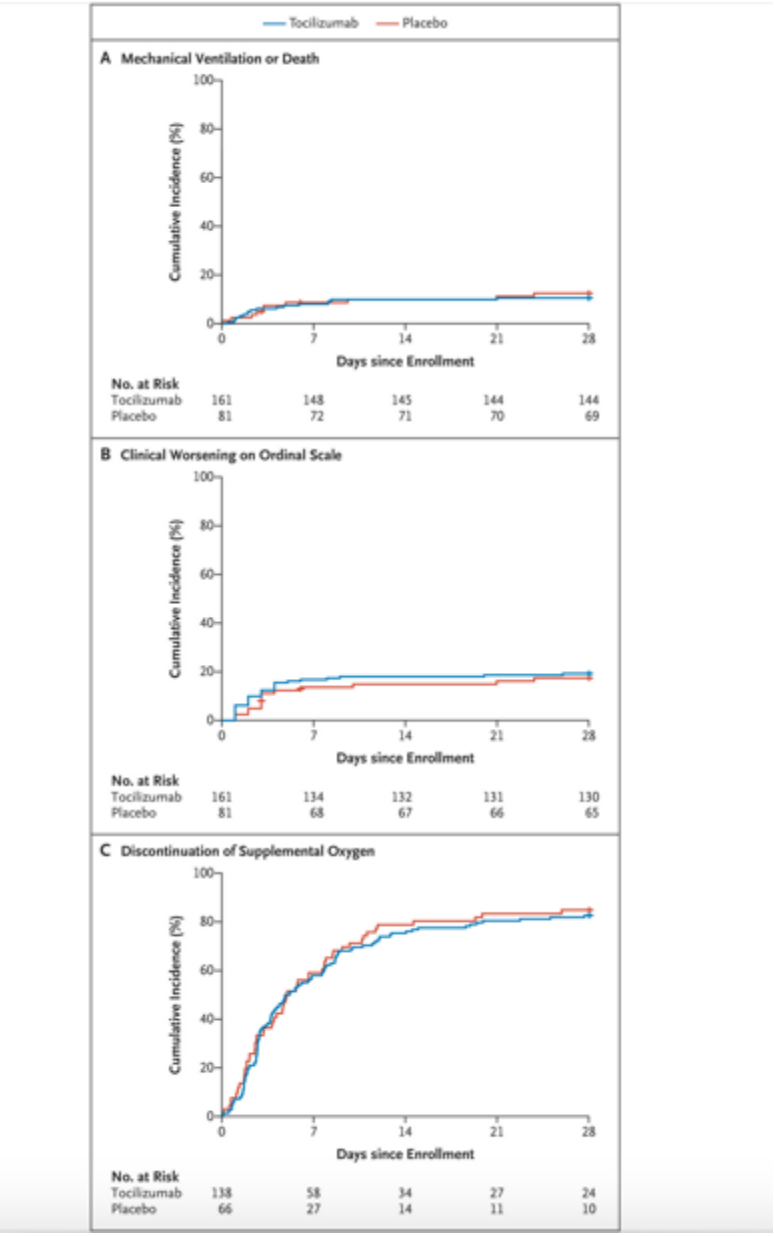




Xu X, Han M, Li T, Sun W, Wang D, Fu B, Zhou Y, Zheng X, Yang Y, Li X, Zhang X, Pan A, Wei H. Effective treatment of severe COVID-19 patients with tocilizumab. Proc Natl Acad Sci U S A. 2020 May 19;117(20):10970-10975. doi: 10.1073/pnas.2005615117. Epub 2020 Apr 29. PMID: 32350134;

Tocilizumab: data

- Double blind RCT
- 243 patients, 45% Hispanic/Latinx
- HR death/MV: 0.83 (95% CI 0.38, 1.81)
- HR disease progression 1.11 (95% CI 0.59, 2.11)



Stone, JH and colleagues, NEJM, Oct 21, 2020

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Peter Horby
@PeterHorby

RECOVERY Update
- colchicine added today
- still studying aspirin, convalescent plasma, REGN-CoV2, and tocilizumab
- just passed 19,000 patients enrolled.

Thank you everyone who has made this possible. Incredible effort that will soon give us more robust results.

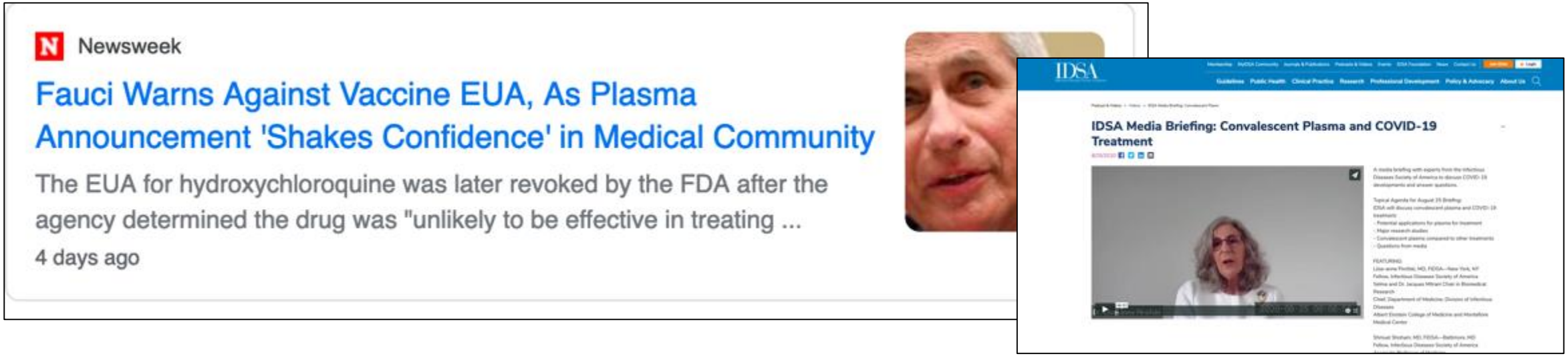
RECOVERY
Randomised Evaluation of COVID-19 Therapy

5:33 AM · Nov 27, 2020 · Twitter Web App

129 Retweets **22** Quote Tweets **577** Likes

A history of Emergency Use Authorization

- March 28, 2020 FDA issued EUA for hydroxychloroquine
- May 3, 2020 FDA issued EUA for remdesivir
- June 15, 2020 FDA retracts EUA for hydroxychloroquine
- August 23, 2020 FDA issues EUA for convalescent plasma



Side effects:

- Antivirals
  - Remdesivir: elevated liver enzymes (allowing 10x ULN)
  - Convalescent plasma: transfusion reaction, need to type and screen first
- Immunomodulators
  - Dexamethasone: hyperglycemia, immunosuppression (low dose less likely)
  - ~~IL-6r blockade: bacterial infections, fungal and TB reactivation~~

Available trials

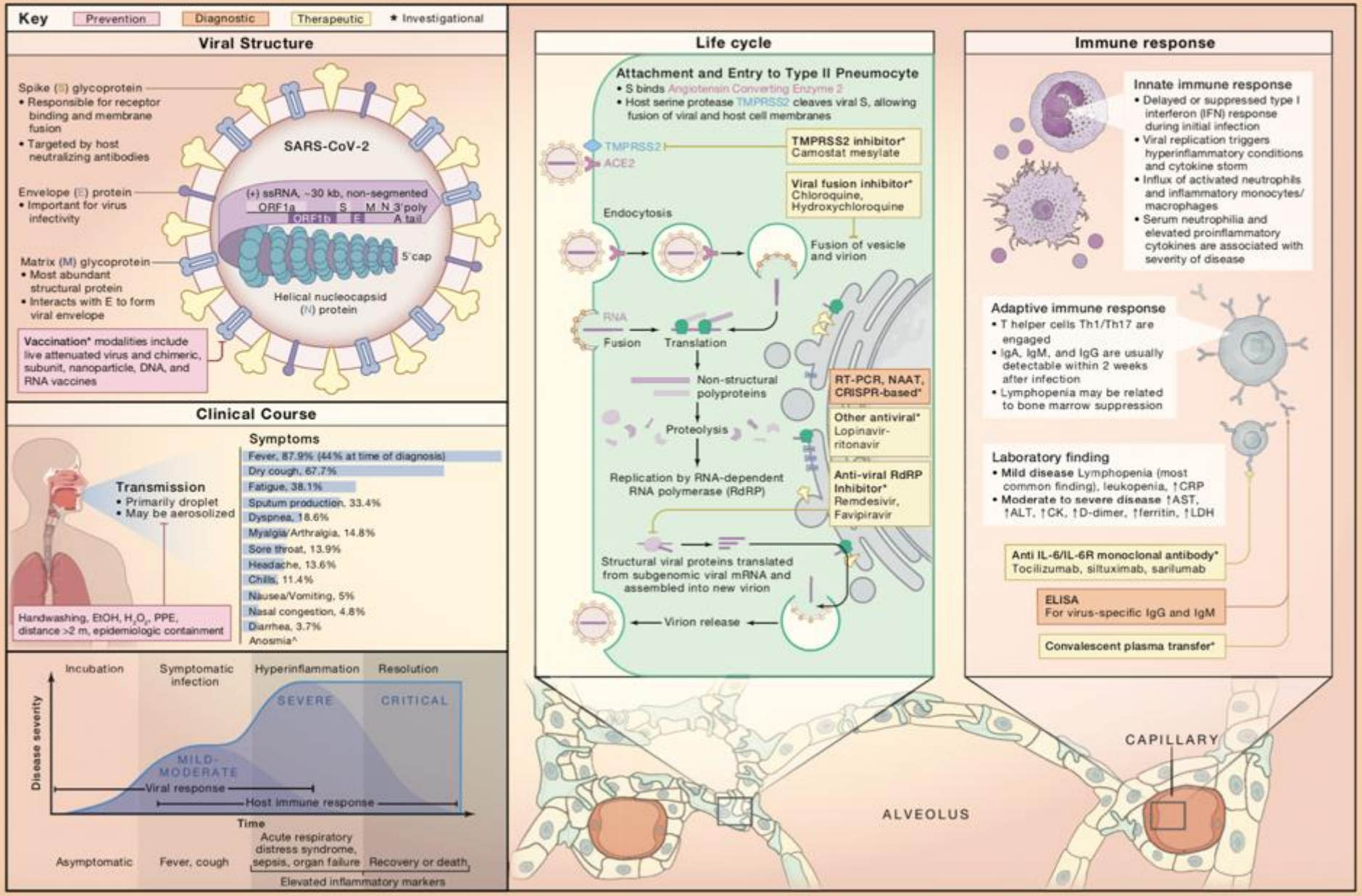
- Leronlimab: CCR5 receptor blocker ended enrollment 12/16/2020
- Mavrilimumab: GM-CSF blockade
- EIDD-2801
- ACTT-4: baricitnib + RDV vs dexamethasone + RDV

954 Cell 181, May 14, 2020 © 2020 Elsevier Inc. DOI https://doi.org/10.1016/j.cell.2020.04.013

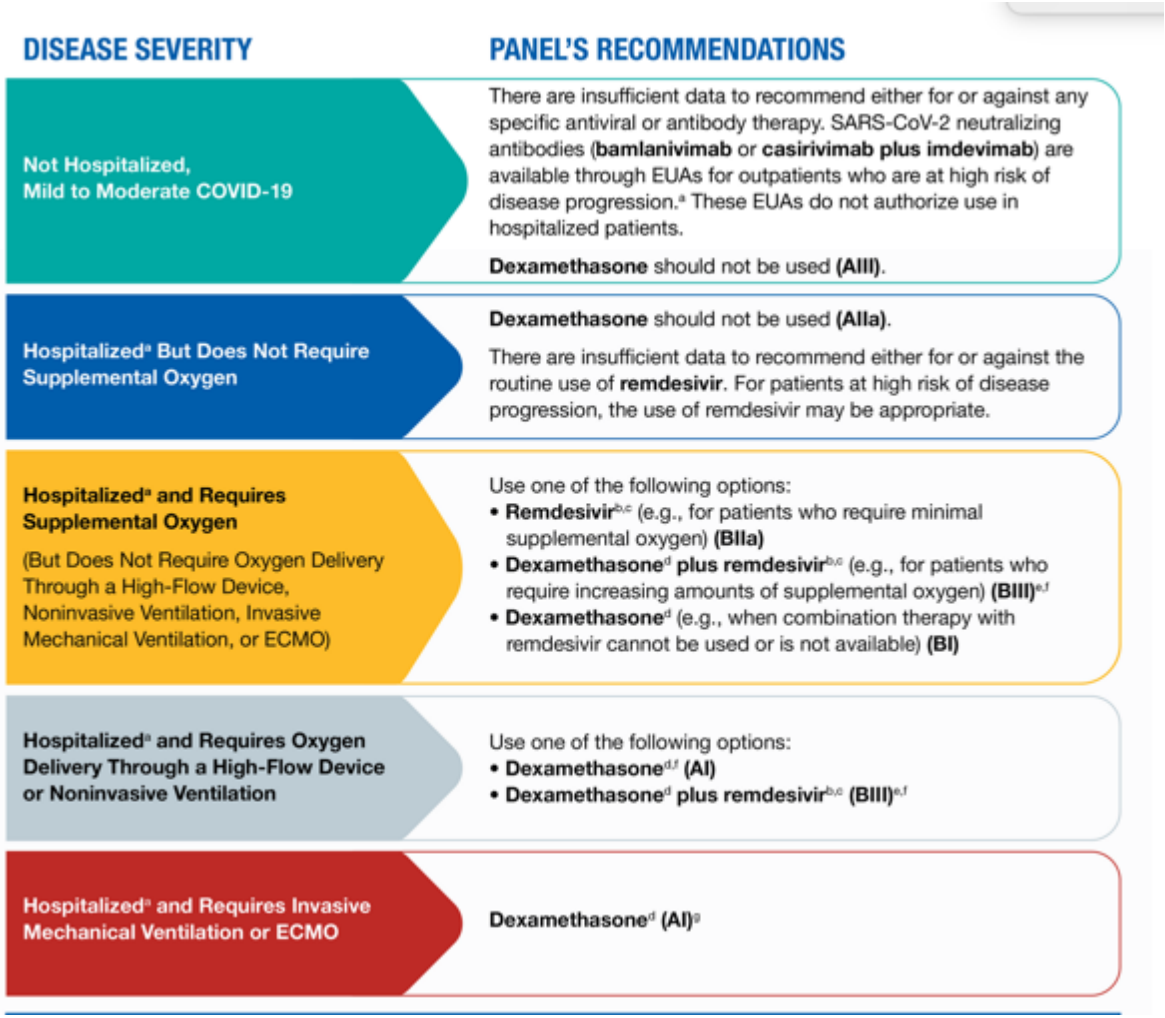
SnapShot: COVID-19

Blake Oberfeld,[1] Aditya Achanta,[1] Kendall Carpenter,[1] Pamela Chen,[1] Nicole M. Gilette,[1] Pinky Langat,[1] Jordan T. Said,[1] Abigail E. Schiff,[1,2,*] Allen S. Zhou,[1] Amy K. Barczak,[1,2] and Shiv Pillai[1,2]; [1]Harvard Medical School, Boston, MA 02115, USA; [2]Ragon Institute of MGH, MIT, and Harvard, Cambridge, MA 02139, USA; *Correspondence: abigail_schiff@hms.harvard.edu

Cell



Summary

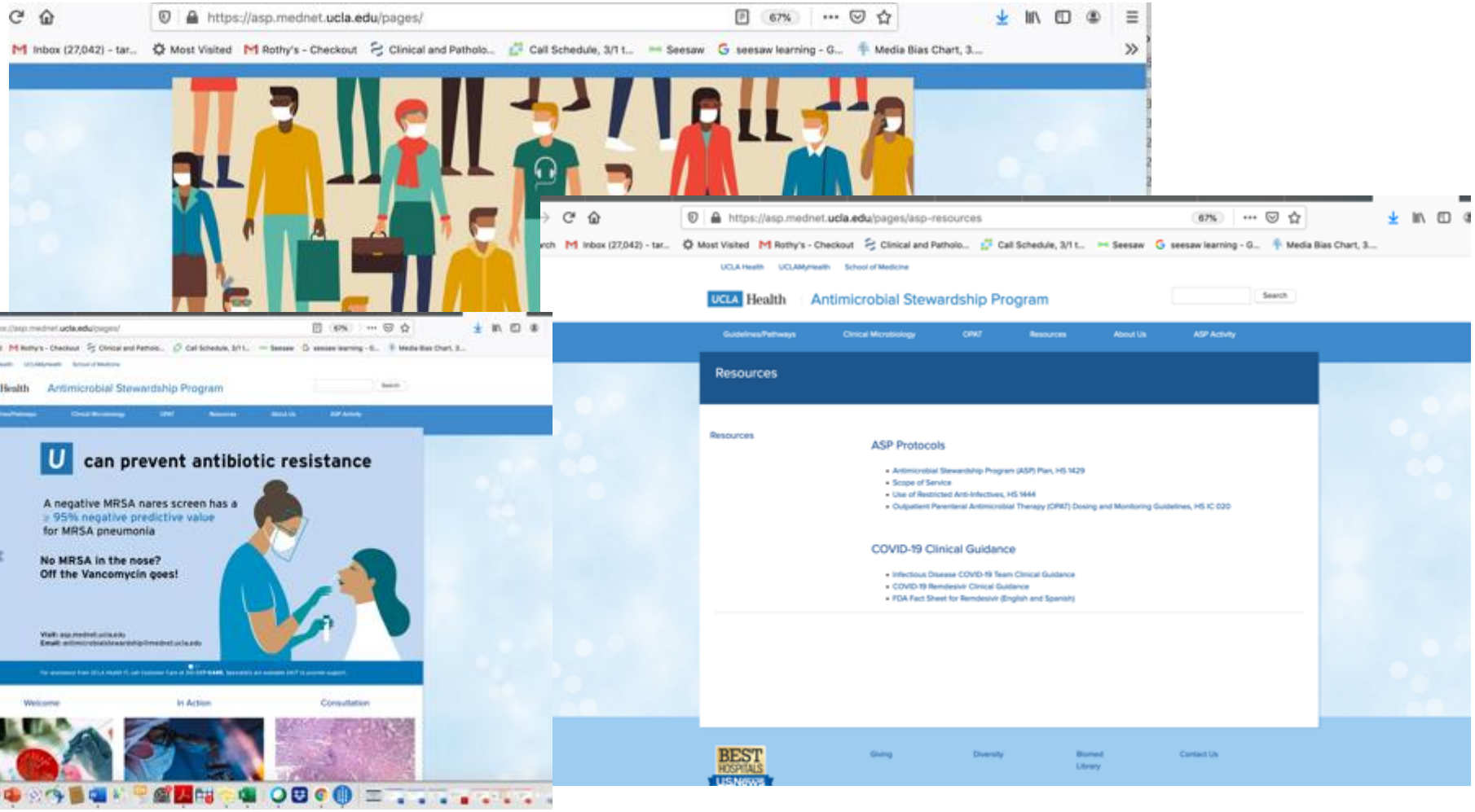


DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Not Hospitalized, Mild to Moderate COVID-19	There are insufficient data to recommend either for or against any specific antiviral or antibody therapy. SARS-CoV-2 neutralizing antibodies (**bamlanivimab** or **casirivimab plus imdevimab**) are available through EUAs for outpatients who are at high risk of disease progression.[a] These EUAs do not authorize use in hospitalized patients. **Dexamethasone** should not be used **(AIII)**.
Hospitalized[a] But Does Not Require Supplemental Oxygen	**Dexamethasone** should not be used **(AIIa)**. There are insufficient data to recommend either for or against the routine use of **remdesivir**. For patients at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized[a] and Requires Supplemental Oxygen (But Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO)	Use one of the following options: • **Remdesivir**[b,c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[d] **plus remdesivir**[b,c] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)**[e,f] • **Dexamethasone**[d] (e.g., when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized[a] and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[d,f] **(AI)** • **Dexamethasone**[d] **plus remdesivir**[b,c] **(BIII)**[e,f]
Hospitalized[a] and Requires Invasive Mechanical Ventilation or ECMO	**Dexamethasone**[d] **(AI)**[g]

https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

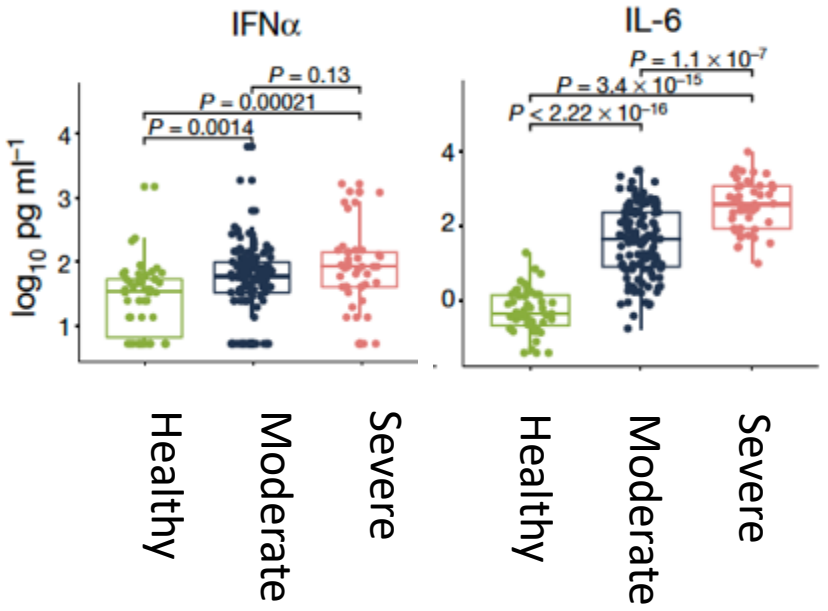
Resources

- ASP website
- Box folder
- Other



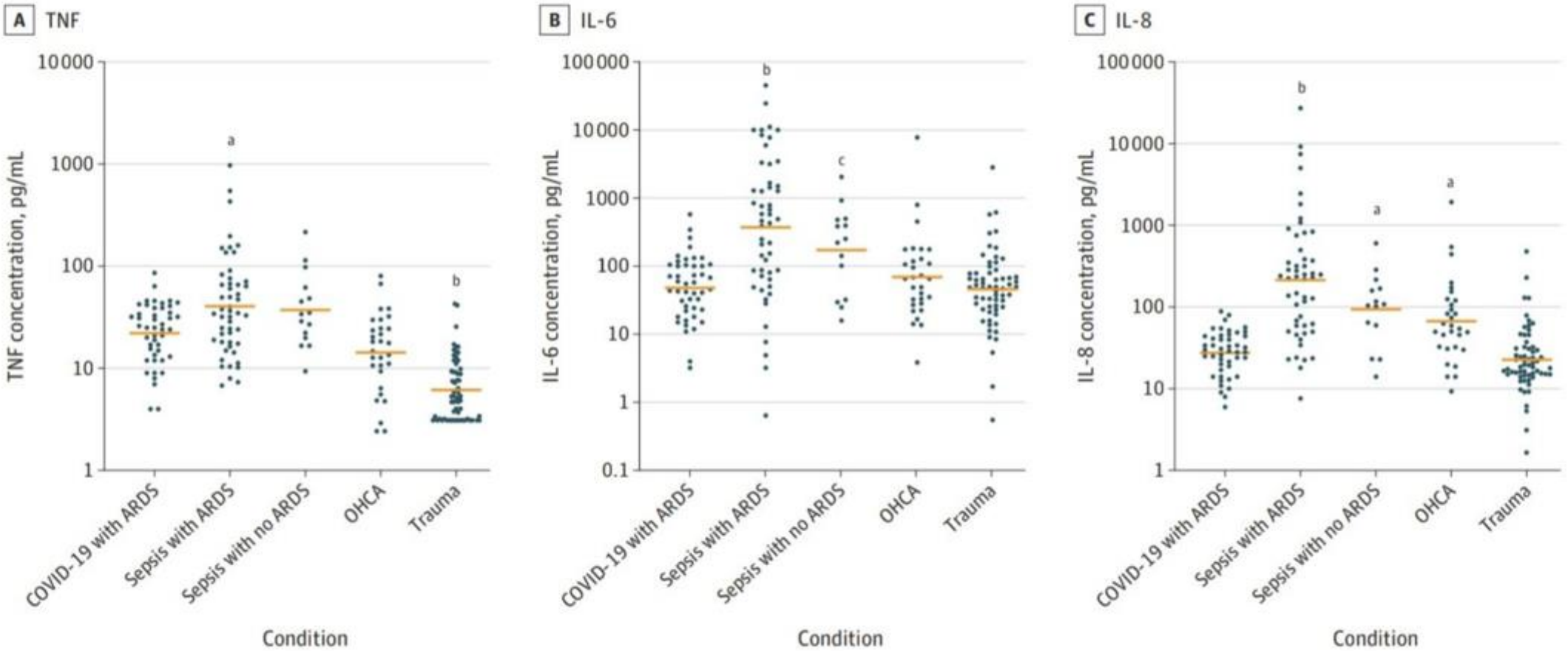
Complications we are still trying to understand

- Pulmonary Embolisms (25% in some studies)
- Central (strokes, encephalopathy (1/3)), peripheral nervous system
- Cardiomyopathy, MI
- Kidney failure
- Derm manifestations (chilblains)
- Liver enzyme elevations
- “Cytokine storm”
- Psychiatric: PTSD



Lucas et al., Nature 2020
Cui, S. J Thromb Haemost April 9 2020
Grillet, F. Radiology, April 23, 2020

Figure. Cytokine Levels in Critically Ill Patients With Coronavirus Disease 2019 (COVID-19) and Other Conditions



Plasma concentrations of tumor necrosis factor (TNF) (A), IL-6 (B), and IL-8 (C) in patients with COVID-19 and acute respiratory distress syndrome (ARDS) (n = 46), septic shock with ARDS (n = 51), septic shock without ARDS (n = 15), out-of-hospital cardiac arrest (OHCA; n = 30), and multiple traumas (n = 62). Data are

Kox, M, JAMA, Sept 3, 2020

Cardiac Involvement:

- Troponin elevation in up to 20-40%, with increased mortality
- 68% of TTEs are abnormal in hospitalized patients
- Half of discharged patients without known etiology of troponin show myocardial scarring on MRI
- When to consult cardiology?
  - Elevated troponin or concern for ACS or myocarditis
  - Hx of congenital heart disease
  - Unstable arrythmia
  - EF <50% or concern for cardiogenic shock
  - New/decompensated CHF
  - Infiltrative CM
  - Prior transplant or LVAD

Other Systems:

- **DO NOT ANCHOR ON COVID – rule out common causes**

- Renal or Hepatic involvement
- Neuro – delirium may be severe and prolonged
- GI– have seen some with severe PO intolerance, one requiring d/c with G-tube

Hypoxia

- Can be severe and largely asymptomatic (“silent hypoxia”)
- Only mildly improved with bronchodilators
- Avoid nebs
- Conservative fluid strategy
- Incentive spirometer may help, encourage ambulation in room
- Standing cough medications may help some
- Awake Proning can greatly improve O2
  - Among patients who sustained PP for 3 hours or more, PaO2 increased from a mean of 73.6 (SD, 15.9) mm Hg before PP to 94.9 (SD, 28.3) mm Hg during PP (difference, 21.3 [95% CI, 6.3-36.3] mm Hg; P = .006) (Elharrar – JAMA)
  - Do as tolerated, laying on side may be beneficial

Oxygen Goals:

- NIH: recommends 92-96%
  - However often go as low as 90%
  - Absence of data for COVID, some theoretical concern given thrombi, increased ACE2 receptor with hypoxia

  - 88-92% for COPD as normal
  - Consider ≥95% in pregnant patients

Hypoxia continued..

- 6L O2 no longer used as cutoff for MICU
  - No longer favoring early intubation
- HFNC is “accepted” on floor HOWEVER usually MICU downgrades
  - Possibly ok at SM – 5MN / step down?
  - Usually more for patients downgraded but not quite off HFNC
  - Should consider ICU eval if considering HFNC
- Many with lingering O2 requirements
  - Sending MANY patients home with persistent 1-2 L O2 requirement
  - **SHORTAGE – order early!**

Thrombosis Risk – Unanswered Question

- Known hypercoagulability in COVID
  - Thought to have increased strokes, MI, DVT/PE
  - Autopsy data suggesting microthrombi in pulmonary vasculature in patients
  - All-cause mortality possibly twice as high In those with thrombotic events
  - Among non-ICU patients, may be 11.5% (3.6% venous, 8.4% arterial) per one study
  - Vey high D-dimers in patients, associated with mortality and VTE

Research Letter – JAMA

~3000 patients with COVID

Variable	No.	Thrombosis: Any — Hazard ratio (95% CI)	Any — P value	Venous — Hazard ratio (95% CI)	Venous — P value	Arterial — Hazard ratio (95% CI)	Arterial — P value
Age, y							
18-44	529	1 [Reference]		1 [Reference]		1 [Reference]	
45-54	469	1.36 (0.94-1.96)	.10	0.95 (0.57-1.59)	.84	1.97 (1.19-3.25)	.01
55-64	714	1.61 (1.14-2.26)	.01	1.41 (0.89-2.24)	.15	1.65 (1.01-2.71)	.05
65-74	756	1.37 (0.96-1.97)	.08	0.83 (0.49-1.41)	.50	1.91 (1.16-3.15)	.01
≥75	866	1.62 (1.13-2.33)	.01	0.49 (0.27-0.87)	.02	2.71 (1.65-4.43)	<.001
BMI							
<18.5	43	1.52 (0.83-2.78)	.17	0.43 (0.05-3.32)	.42	1.78 (0.94-3.40)	.08
18.5-25	613	1 [Reference]		1 [Reference]		1 [Reference]	
26-30	1019	0.99 (0.78-1.25)	.91	1.16 (0.78-1.73)	.47	0.89 (0.67-1.20)	.45
31-40	936	0.90 (0.69-1.16)	.41	1.14 (0.74-1.75)	.56	0.81 (0.59-1.12)	.21
>40	207	1.18 (0.79-1.78)	.42	0.99 (0.50-1.99)	.99	1.01 (0.59-1.73)	.98
Male sex	2014	1.51 (1.25-1.83)	<.001	1.71 (1.21-2.42)	<.001	1.40 (1.11-1.77)	.004
Current smoker	799	0.97 (0.79-1.19)	.74	1.27 (0.88-1.84)	.20	0.86 (0.67-1.10)	.22
Non-Hispanic White	1444	1 [Reference]		1 [Reference]		1 [Reference]	
Asian	238	1.08 (0.77-1.50)	.66	0.82 (0.46-1.45)	.50	1.24 (0.83-1.85)	.29
Hispanic	49	1.91 (1.15-3.18)	.01	2.01 (0.81-5.00)	.13	1.84 (0.98-3.44)	.06
Non-Hispanic African American	509	0.93 (0.71-1.23)	.62	0.97 (0.60-1.55)	.89	0.99 (0.70-1.38)	.93
Other/multiracial	905	1.10 (0.88-1.36)	.40	0.89 (0.61-1.28)	.52	1.20 (0.92-1.57)	.17
Unknown	189	1.37 (0.97-1.95)	.07	1.37 (0.8-2.33)	.25	1.57 (1.03-2.39)	.04
Comorbidities[b]							
History of myocardial infarction	195	1.43 (1.01-2.03)	.05	0.86 (0.32-2.30)	.76	1.32 (0.90-1.93)	.16
Congestive heart failure	279	1.27 (0.93-1.74)	.13	1.02 (0.43-2.43)	.96	1.30 (0.92-1.85)	.14
Hypertension	1676	0.94 (0.78-1.14)	.52	0.83 (0.58-1.17)	.28	0.99 (0.78-1.25)	.92
Diabetes	1246	0.90 (0.74-1.10)	.31	0.79 (0.55-1.15)	.22	0.97 (0.77-1.23)	.81
Hyperlipidemia	1285	0.88 (0.72-1.08)	.23	0.69 (0.47-1.02)	.06	0.88 (0.69-1.13)	.32
Coronary artery disease	617	1.52 (1.22-1.90)	<.001	0.93 (0.59-1.46)	.75	2.00 (1.54-2.60)	<.001
Initial D-dimer, ng/mL[c]							
<230	619	1 [Reference]		1 [Reference]		1 [Reference]	
230-499	1028	1.17 (0.85-1.60)	.35	1.25 (0.7-2.21)	.45	1.01 (0.7-1.46)	.95
500-1999	690	1.92 (1.4-2.64)	<.001	2.63 (1.49-4.64)	.001	1.52 (1.05-2.19)	.03
2000-4999	157	2.82 (1.87-4.27)	<.001	4.71 (2.26-9.82)	<.001	1.98 (1.23-3.2)	.01
5000-9999	64	5.55 (3.57-8.62)	<.001	14.25 (7.21-28.19)	<.001	2.95 (1.63-5.32)	<.001
≥10 000	79	7.09 (4.69-10.71)	<.001	32.63 (17.2-61.89)	<.001	2.33 (1.32-4.11)	.004
No D-dimer measured	697	1.85 (1.34-2.55)	<.001	2.51 (1.44-4.39)	.001	1.47 (1.00-2.16)	.05

VTE Recommendations:

- No clear consensus, clinical trial underway
- Some institutions doing increased dosing such as daily dose as BID
- Some consider 60mg lovenox for obese >30-35kg
- American Society of Hematology:
  - No clear evidence, recommend participation in trials
- NIH:
  - “there are currently insufficient data to recommend for or against the use of thrombolytics or increasing anticoagulant doses for VTE prophylaxis” (BIII)
- Lovenox preferred due to daily dosing / reduced exposure

Other Meds:

- NSAIDS
  - Some initial concern due to some cases of critically ill young patients with NSAID
  - Some small study (Infx Dz Therapies, Nov)(~500pts) suggest no association with severe disease with acute use during or chronic use prior to COVID
- ACEI/ARB:
  - NEJM Article – Italy -- 6200 patients case-control study
    - Although more ACE/ARB in COVID pts, also more anti-hypertensives
    - ACEi/ARB no association with COVD or in those with severe or fatal COVID (OR 0.83 [CI 0.63-1.10])
- Statins:
  - Some evidence of decreased illness severity and quicker time to recovery in pre-hospital use with continuation (Daniels, Am j Cardiol)
  - LFT abnormalities are very rare

- Cough PRN's
- Can consider diuresis

Rounding:

- Can call room prior to entry (I usually don't)
- Looking at lymphocytes, inflammatory markers if worsening
  - LFT's if on remdesivir
- Follow sugars for most (dex), emphasize mealtime coverage
- **Use EPIC Chat!** -- Helps you and nursing
- Lung auscultation of limited benefit (but I usually do)
- Wean down O2 – let nurse know if changed, watch for ≥3mins
- At RR 7E: can keep face shield and mask between rooms (Stay within red line)
- Wash hands, sanitize prn
- Calling most families

Discontinuing Isolation Precautions

- "COVID Recovered" must be:
  - ≥ 20 days since initial test
  - Improved symptoms (ideally off O2)
  - Afebrile x3 days without anti-pyretics

- OK To transfer to non-COVID teams
- COVID Recovered DO NOT need to be admitted to COVID team

Asymptomatic COVID

- Up to 30-40% by some reports
- At RR-UCLA, can go to: (many with IMCS consult)
  - Neuro/stroke
  - Liver transplant
  - OB
  - Possibly other surgical subspecialties
  - CCU/COU

Asymptomatic COVID

- Consider checking inflammatory markers worsening hypoxia
  - CXR if cough or SOB
- For most: if symptoms attributable develop, can transfer to COVID team
- Likely does not require ID consult as should be asymptomatic, however can discuss if concerns

Discharging – Isolation

Home isolation (CDC Guidelines)

- **Mild-Moderate:**
  - 10 days, afebrile x24hrs without anti-pyretics, improving clinically

- **Severe disease/Immunosuppressed:**
  - 95% have non-infectious viruses / not considered infectious at 15 days, some up to 20 days, especially transplant patients
  - Thus: 20 days with afebrile x24 hours (previously 72h) without anti-pyretics, improving clinically

- DO NOT RETEST – NP PCR can be positive for multiple months

Discharging

- If good enough to d/c, can d/c remdesivir & dexamethasone
- Make sure patient has enough home meds for quarantine period
- Supply with some gloves and masks on d/c (nurses usually)
- Pulse oximeter for all needing O2 or if concerned
- Make sure has social support, able to isolate within home

Discharging -- Destination

- Unable to isolate:
  - UCLA has guest house / hotel that can send patients to
- SNF/ARU
  - Different requirements –speak with CM
  - Previously SNF requiring 1 negative, ARU 2 negatives 24hr apart
- COVID SNF available but limited

Discharging– Home Health

- Transplant patients:
  - Usually require Home health Nursing for tacro level in 1 week
  - ORDER EARLY! – can adjust date later
  - Mention 6am-8am OR 6pm-8pm
  - Consider adding other services

- Otherwise, few issues with HH compared to normal

Discharging – Follow up:

- “We will schedule” follow up with -- (Unless SNF/ARU)
  - PCP
  - Hospitalist x2 days
    - mention that will call when able
  - Extensivists on day 3
    - Also place order for “COVID companion program”
      - Select “NO patient does not have smart phone” in order to proceed with order
    - Add to shared COVID discharge list

- <u>UCANBreathe Follow-up</u>:
  - Post ICU clinic follow up for previously mechanically ventilated patients

Discharging

- On discharge paperwork:
  - Make sure last day of isolation noted and bolded
  - Make sure **specific** O2 goal listed for pulse oximetry
    - Ex/ seek medical attention if O2 <93% for more than 10 minutes

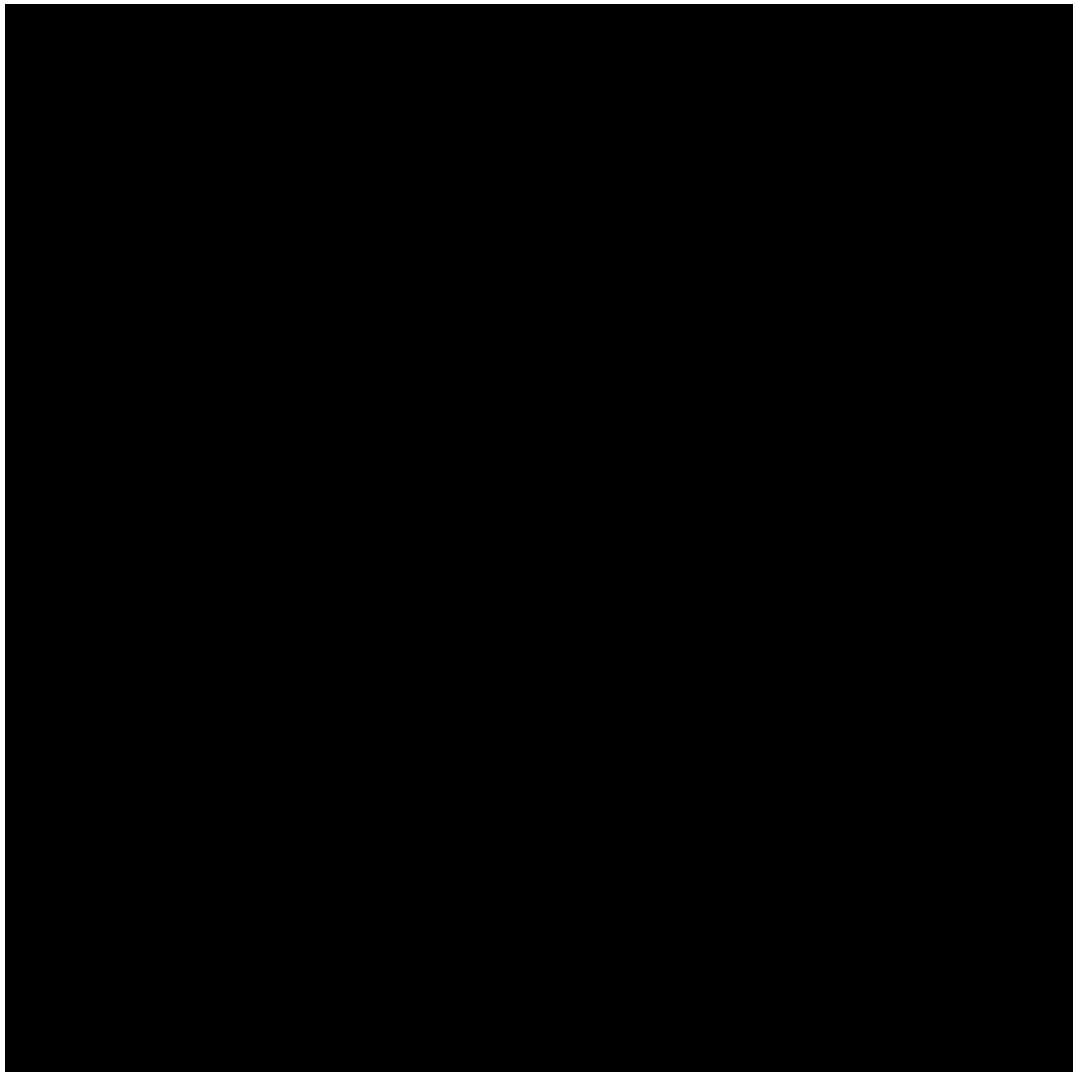
- Discharge Summaries:
  - Make sure to use specific “COVIDhomeDCSUM” or “COVIDSNFdcsum”
  - (should have box with symptom onset, therapeutics… etc)

Long term complications:

- Large number of symptoms: fatigue, dyspnea lasting long time
- High readmission rate and post-discharge mortality:
  - JAMA – Dec – Research Letter --
    - 2179 index hospitalizations at VA - 31% in ICU; 12% intubated
    - ~20% Readmission rate in 60 days
    - 9% of survivors died
    - 27% readmitted or died at 60 days
    - Readmission Dx:
      - COVID (30%)
      - Sepsis (8.5%)
      - PNA (3.1%)
      - Heart failure (3.1%)

“Long-haulers”

- 2-3 months SOB
  - 56% have lung “damage” at 12 weeks
  - 10% longer term lung damage
- Dysautonomia
- Cardiac complications
- Chronic fatigue/ME

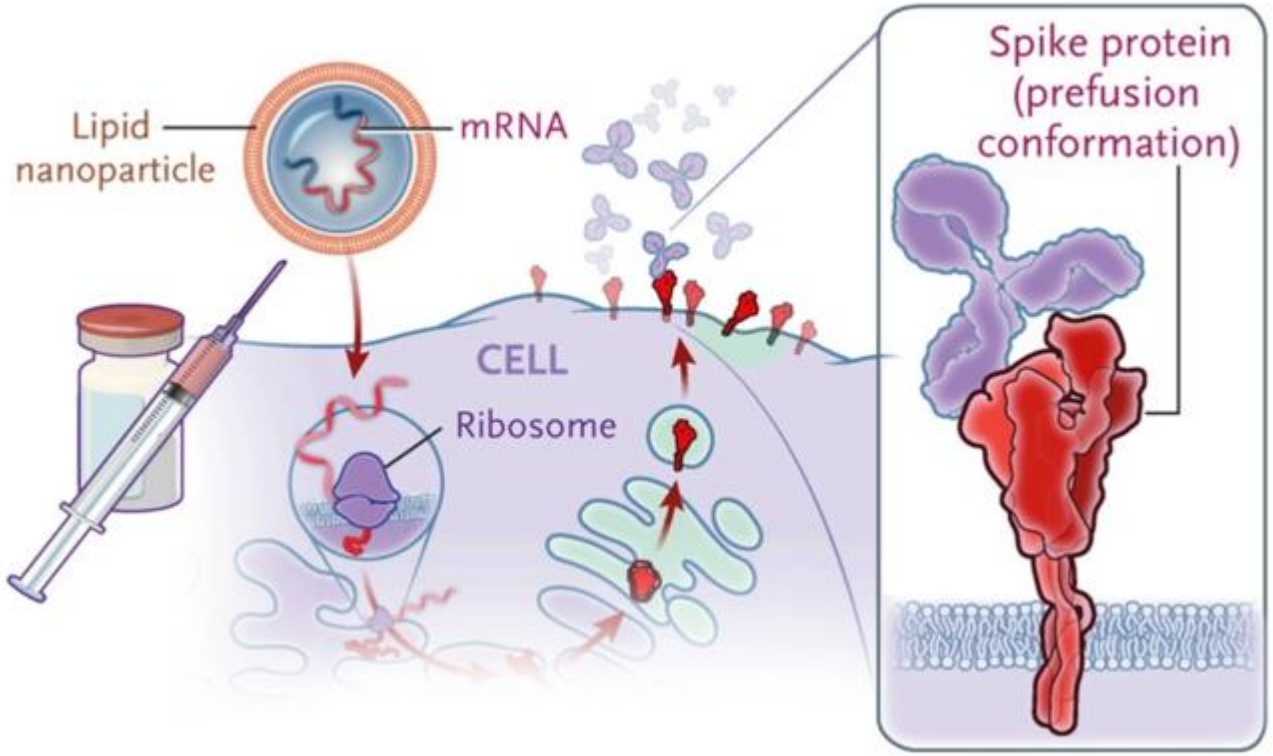


Marshal, Michael, Nature, News feature
Sept 14, 2020

Pregnant Patients

- Likely not increased infection risk but do have increased risk of severe disease
- May have increased preterm birth and c-sections
- Unclear if intrauterine infection occurs, but possibly early infant infection
- Remdesivir seems to be ok – little evidence, animal studies reasuring
- Higher O2 goal (94-96%)
- Lower threshold for ECMO?
- Breastfeeding:
  - No SARS-CoV2 found in breast milk, but have found IgM
  - Wear mask, consider not direct to breast during quarantine period

Covid-19 Vaccines: Pfizer

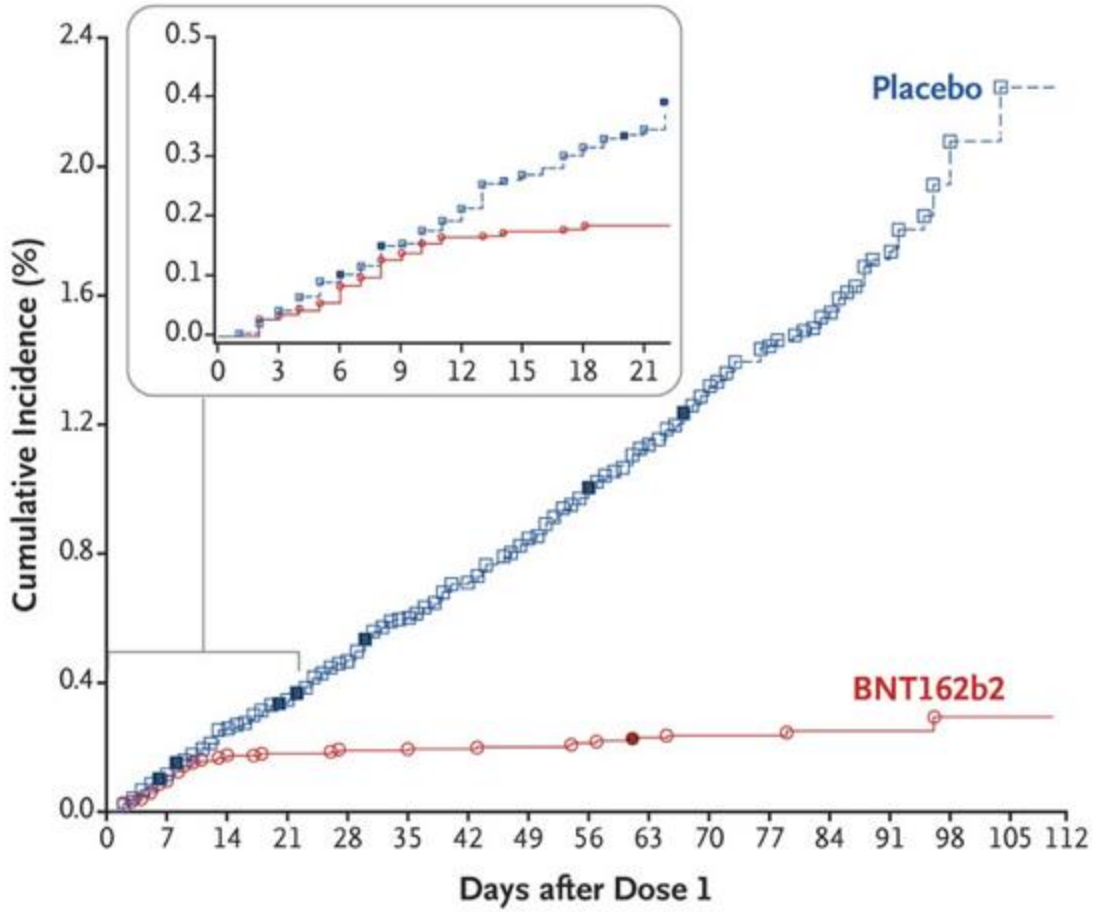


BNT162b2 =

- lipid nanoparticle
- modified RNA vaccine
- encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full length spike protein

Covid-19 Vaccines: Pfizer

- 43,661 participants ages 16 and older were randomized to placebo or mRNA vaccine BNT162b2
- Includes participants from US, Germany, Brazil, South Africa, Turkey and Argentina
- Primary endpoint: laboratory confirmed Covid-19
  - Vaccine: 8 cases
  - Placebo: 162 cases
- 95% vaccine efficacy
- Secondary endpoint: severe Covid-19
- 10 cases of severe Covid-19
  - Vaccine: 1 case
  - Placebo: 9 cases



	BNT162b2 Vaccine	Placebo
Symptomatic Covid-19	8	162
	N=18198	N=18325
Severe Covid-19	1	9
	N=21669	N=21686

Vaccine efficacy of 95% (95% credible interval, 90.3–97.6%)

Table 3. Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr	3	0.980 (7,500)	48	0.983 (7,543)	93.7 (80.6–98.8)
≥65 yr	1	0.508 (3,848)	19	0.511 (3,880)	94.7 (66.7–99.9)
≥75 yr	0	0.102 (774)	5	0.106 (785)	100.0 (–13.1–100.0)
Sex					
Male	3	1.124 (8,875)	81	1.108 (8762)	96.4 (88.9–99.3)
Female	5	1.090 (8,536)	81	1.114 (8,749)	93.7 (84.7–98.0)
Race or ethnic group‡					
White	7	1.889 (14,504)	146	1.903 (14,670)	95.2 (89.8–98.1)
Black or African American	0	0.165 (1,502)	7	0.164 (1,486)	100.0 (31.2–100.0)
All others	1	0.160 (1,405)	9	0.155 (1,355)	89.3 (22.6–99.8)
Hispanic or Latinx	3	0.605 (4,764)	53	0.600 (4,746)	94.4 (82.7–98.9)
Non-Hispanic, non-Latinx	5	1.596 (12,548)	109	1.608 (12,661)	95.4 (88.9–98.5)
Country					
Argentina	1	0.351 (2,545)	35	0.346 (2,521)	97.2 (83.3–99.9)
Brazil	1	0.119 (1,129)	8	0.117 (1,121)	87.7 (8.1–99.7)
United States	6	1.732 (13,359)	119	1.747 (13,506)	94.9 (88.6–98.2)

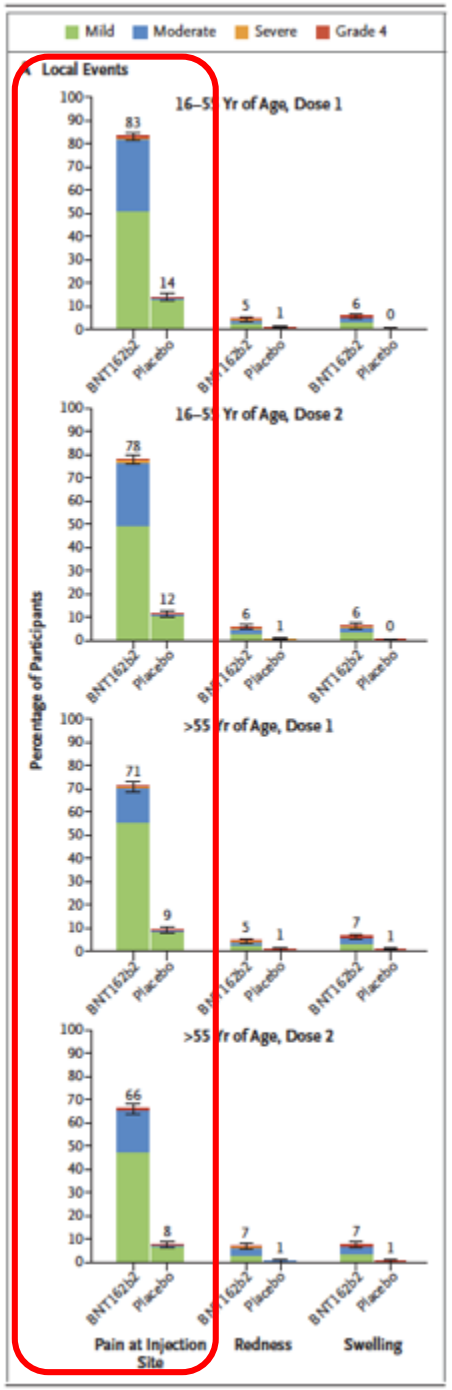
* Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.

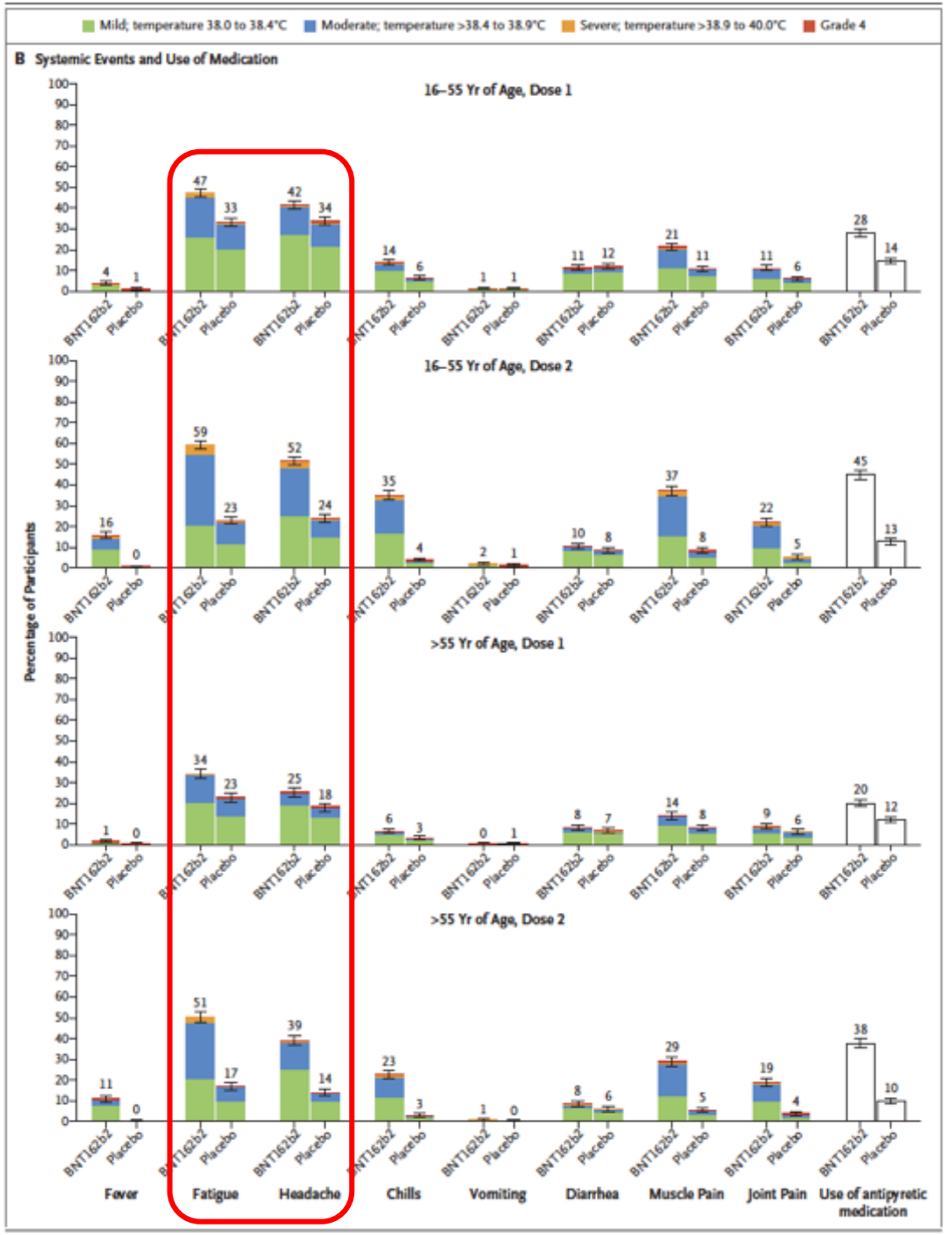
† The confidence interval (CI) for vaccine efficacy is derived according to the Clopper–Pearson method, adjusted for surveillance time.

‡ Race or ethnic group was reported by the participants. "All others" included the following categories: American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported.

Adverse Events

- Pain at injection site: 66-83%
- Redness and swelling at injection site: 5-7%
- Fever: 1-16%
- Fatigue: 34-59%
- Headache: 25-52%
- Chills: 6-35%
- Vomiting: 1-2%
- Diarrhea: 8-11%
- Muscle Pain: 14-37%
- Joint Pain: 9-22%


Mild
Moderate
Severe
Grade 4
A Local Events
16–55 Yr of Age, Dose 1
16–55 Yr of Age, Dose 2
>55 Yr of Age, Dose 1
>55 Yr of Age, Dose 2
Percentage of Participants
BNT162b2
Placebo
Pain at Injection Site
Redness
Swelling


Mild; temperature 38.0 to 38.4°C
Moderate; temperature >38.4 to 38.9°C
Severe; temperature >38.9 to 40.0°C
Grade 4
B Systemic Events and Use of Medication
16–55 Yr of Age, Dose 1
16–55 Yr of Age, Dose 2
>55 Yr of Age, Dose 1
>55 Yr of Age, Dose 2
Percentage of Participants
BNT162b2
Placebo
Fever
Fatigue
Headache
Chills
Vomiting
Diarrhea
Muscle Pain
Joint Pain
Use of antipyretic medication

Serious Adverse Events

- Four serious adverse events among vaccine recipients: shoulder injury related to vaccine administration, axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia)
- Two vaccine recipients died: one from arteriosclerosis, one from cardiac arrest
- Four placebo recipients died: two from unknown causes, one from hemorrhagic CVA, and one from MI
- No deaths were considered to be related to the vaccine or placebo

Further Study

- Safety and efficacy
  - Beyond 2 months
  - In children, pregnant women and immunocompromised people
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons
- How to best manage a missed 2nd dose

Moderna mRNA Vaccine Safety

- Interim analysis of available Phase 3 data by the DSMB did not report any significant safety concerns
- A review of solicited adverse events indicated that the majority of adverse events were mild or moderate in severity
- Grade 3 (severe) events greater than or equal to 2% in frequency
- After the first dose: injection site pain (2.7%)
- After the second dose:
  - Fatigue (9.7%)
  - Myalgia (8.9%)
  - Arthralgia (5.2%)
  - Headache (4.5%)
  - Pain (4.1%)
  - Erythema/redness at the injection site (2.0%)
- FDA to review the emergency use authorization (EUA) request for the vaccine on 12/17

Covid-19 Vaccines: Moderna

- Phase 3 RCT: 30,000 participants ages 18 and older randomized 1:1 to 100ug of mRNA-1273 vaccine
- 7,000 over the age of 65
- 5,000 with diabetes, severe obesity or cardiac disease
- 11,000 from communities of color
- Administered doses at day 1 and day 28
- Primary endpoint: prevention of symptomatic Covid disease
- Secondary endpoints: prevention of severe Covid disease
- Primary endpoint in 196 cases
  - 185 in placebo group
  - 11 in vaccine group
- Vaccine efficacy of 94.1%
- Secondary endpoint in 30 cases
  - 30 in placebo group
  - None in vaccine group

Pfizer vaccine arrives at UCLA!