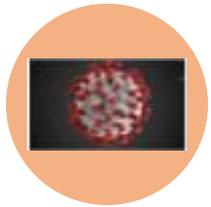
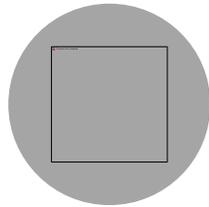


COVID-19 Updates, May 1, 2020

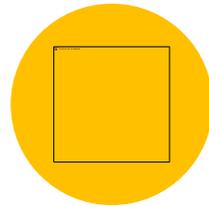
Jorge Mera, MD, FACP
Whitney Essex, MSN, FNP-BC
Cherokee Nation Health Services



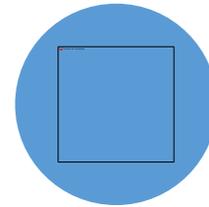
VIROLOGY



EPIDEMIOLOGY

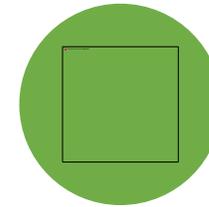


DIAGNOSIS

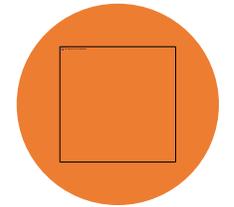


COVID-19 Updates, May 1, 2020
Jorge Mera, MD, FACP
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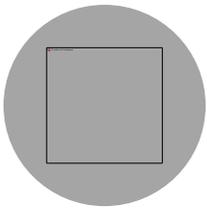
INFECTION
CONTROL



DISEASE



TREATMENT



CDC Update

EPIDEMIOLOGY

Watch for symptoms

People with COVID-19 have had a wide range of symptoms reported – ranging from mild symptoms to severe illness.

These symptoms may appear 2-14 days after exposure to the virus:

- Fever
- Cough
- Shortness of breath or difficulty breathing
- Chills
- Repeated shaking with chills
- Muscle pain
- Headache
- Sore throat
- New loss of taste or smell

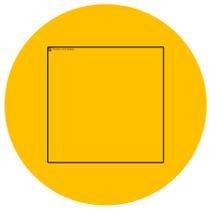
When to Seek Medical Attention

If you have any of these emergency warning signs* for COVID-19 get medical attention immediately:

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion or inability to arouse
- Bluish lips or face

*This list is not all inclusive. Please consult your medical provider for any other symptoms that are severe or concerning to you.

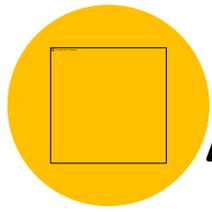
Call 911 if you have a medical emergency: Notify the operator that you have, or think you might have, COVID-19. If possible, put on a cloth face covering before medical help arrives.



DIAGNOSIS

COVID-19 Antibody testing: Information that Antibody Testing Should Provide

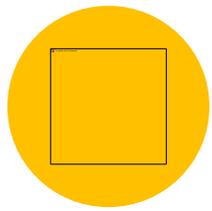
- **The presence of antibodies confirms exposure**
 - Needed epidemiologically
 - Convalescent plasma/hyperimmune serum preparations
- **The presence of antibodies confirms immunity** (neutralizing antibodies)
 - May return to work
- **Antibodies can complement RNA testing to confirm early infection**
 - May confirm the need for isolation or NOT
- **The titer of antibodies predicts severity of disease**
 - May be useful for treatment interventions when available



DIAGNOSIS

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

- Evaluated the dynamics of total antibody (Ab), IgM and IgG against SARS-CoV-2 in serial blood samples in 173 confirmed COVID-19 patients
- COVID -19 Case defined as:
 - Acute respiratory infection syndromes and/or abnormal chest CT images accompanied by detectable respiratory SARSCoV-2 RNA at least one time
- The Ab, IgM and IgG were tested using ELISA.
 - The Ag was the receptor binding domain (RBD) of the spike protein of SARS-CoV-2
- Assay specificity Ab, IgM and IgG was 99.1%, 98.6% and 99.0% by testing of samples collected from healthy individuals prior to the pandemic



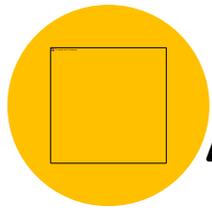
DIAGNOSIS

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

Table 2. Performance of different detections in samples at different time since onset of patients.

Days after onset	n	RNA		Ab		IgM		IgG		RNA+Ab	
		n(+)	Sensitivity (% , 95%CI)	n(+)	Sensitivity (% , 95%CI)	n(+)	Sensitivity (% , 95%CI)	n(+)	Sensitivity (% , 95%CI)	n(+)	Sensitivity (% , 95%CI)
Total	173	112 [§]	67.1 (59.4, 74.1)	161	93.1 (88.2, 96.4)	143	82.7 (76.2, 88)	112	64.7 (57.1, 71.8)	172	99.4 (96.8, 100.0)
1-7	94	58 [§]	66.7 (55.7, 76.4)	36	38.3 (28.5, 48.9)	27	28.7 (19.9, 39.0)	18	19.1 (11.8, 28.6)	74	78.7 (69.1, 86.5)
8-14	135	67 [§]	54.0 (44.8, 63.0)	121	89.6 (83.2, 94.2)	99	73.3 (65.0, 80.6)	73	54.1 (45.3, 62.7)	131	97.0 (92.6, 99.2)
15-39	90	25 [§]	45.5 (32.0, 59.5)	90	100.0 (96.0, 100.0)	83*	94.3 (87.2, 98.1)	71 [#]	79.8 (69.9, 87.6)	90	100.0 (96.0, 100.0)

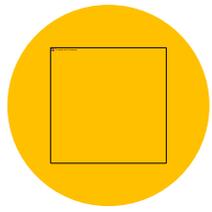
* Two patients missed IgM tests due to inadequate plasma samples. # One patient missed IgG tests due to inadequate plasma samples. § There were 7, 11 and 35 patients had not been performed RNA testing during the 1-7 onset day, 8-14 onset day and 15-39 onset day, respectively.



DIAGNOSIS

Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019

- **The seroconversion rate for Ab, IgM and IgG was 93.1%, 82.7% and 64.7%, respectively.**
- **The median seroconversion time for Ab, IgM and then IgG were day-11, day-12 and day-14, separately.**
- **The presence of antibodies was <40%** among patients within 1-week since onset, and rapidly increased to 100.0% (Ab), 94.3% (IgM) and 79.8% (IgG) since day-15 after onset.
- **RNA detectability decreased from 66.7% (58/87) before day-7 to 45.5% (25/55) day 15-39.**
- **Combining RNA and antibody detections significantly improved the sensitivity of pathogenic diagnosis for COVID-19 ($p < 0.001$), even in early phase of 1-week since onset ($p = 0.007$)**
- **A higher titer of Ab was independently associated with a worse clinical classification ($p = 0.006$)**



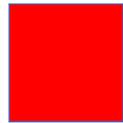
DIAGNOSIS

COVID-19 Antibody testing: Information that Would be Useful

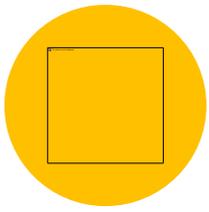
- The presence of antibodies confirms exposure
- The presence of antibodies confirms immunity (neutralizing antibodies)
- Antibodies can complement RNA testing to confirm early infection
- The titer of antibodies predicts severity



Bueno



No Bueno



DIAGNOSIS

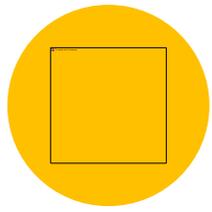
COVID-19 Antibody Test Limitations

- This test has not been reviewed by the FDA.
- Results from antibody testing should not be used as a sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status.
- Negative results do not rule out SARS CoV-2 infection, particularly in those who have been in contact with the virus.
- Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus.
- Not for the screening of donated blood

Sample	Days after symptom onset	Disease severity	EUROIMMUN Anti-SARS-CoV-2 ELISA			
			IgA (ratio)	IgA	IgG (ratio)	IgG
			pos.: ≥ 1.1	Results	pos.: ≥ 1.1	Results
			borderl.: 0.8 – 1.0		borderl.: 0.8 – 1.0	
< 10 days after onset of symptoms						
1	4	mild	0.2	neg.	0.1	neg.
2	7	severe	7.2	pos.	4.4	pos.
3	8	severe	2.0	pos.	0.3	neg.
4	8	severe	0.2	neg.	0.8	borderl.
> 10 days after onset of symptoms						
5	13	mild	2.3	pos.	0.3	neg.
6	13	mild	2.1	pos.	1.3	pos.
7	16	mild	8.5	pos.	6.7	pos.
8	18	mild	2.7	pos.	1.9	pos.
9	32	mild	1.8	pos.	1.1	pos.

Group	EUROIMMUN Anti-SARS-CoV-2 ELISA IgA			
	positive	borderline	negative	Sensitivity
< 10 days after onset of symptoms	2	0	2	50.0%
> 10 days after onset of symptoms	5	0	0	100%

Group	EUROIMMUN Anti-SARS-CoV-2 ELISA IgA & IgG combined			
	positive	borderline	negative	Sensitivity
< 10 days after onset of symptoms	2	1	1	66.7%
> 10 days after onset of symptoms	5	0	0	100%



DIAGNOSIS

Role of Antibody Testing in COVID-19

- No study has assessed whether the presence of antibodies to SARS-CoV-2 confers immunity to subsequent infection by this virus in humans and that tests that detect antibodies to SARS-CoV-2 in people need further study to establish accuracy and reliability¹
- IDSA spokesperson explained “Most patients who develop and recover from COVID-19 infection will develop antibodies or will have detectable antibodies in their blood approximately 10 to 14 days after the onset of their illness,” the hope for antibodies has been that the detection of them in the blood represents protection for reinfection. That's really the million-dollar question and we do not know if patients with these antibodies are still at risk for reinfection.

1. WHO. Immunity passports in the context of COVID-19. <https://www.who.int/news-room/commentaries/detail/immunity-passports-in-the-context-of-covid-19>. Accessed April 27, 2020.1.



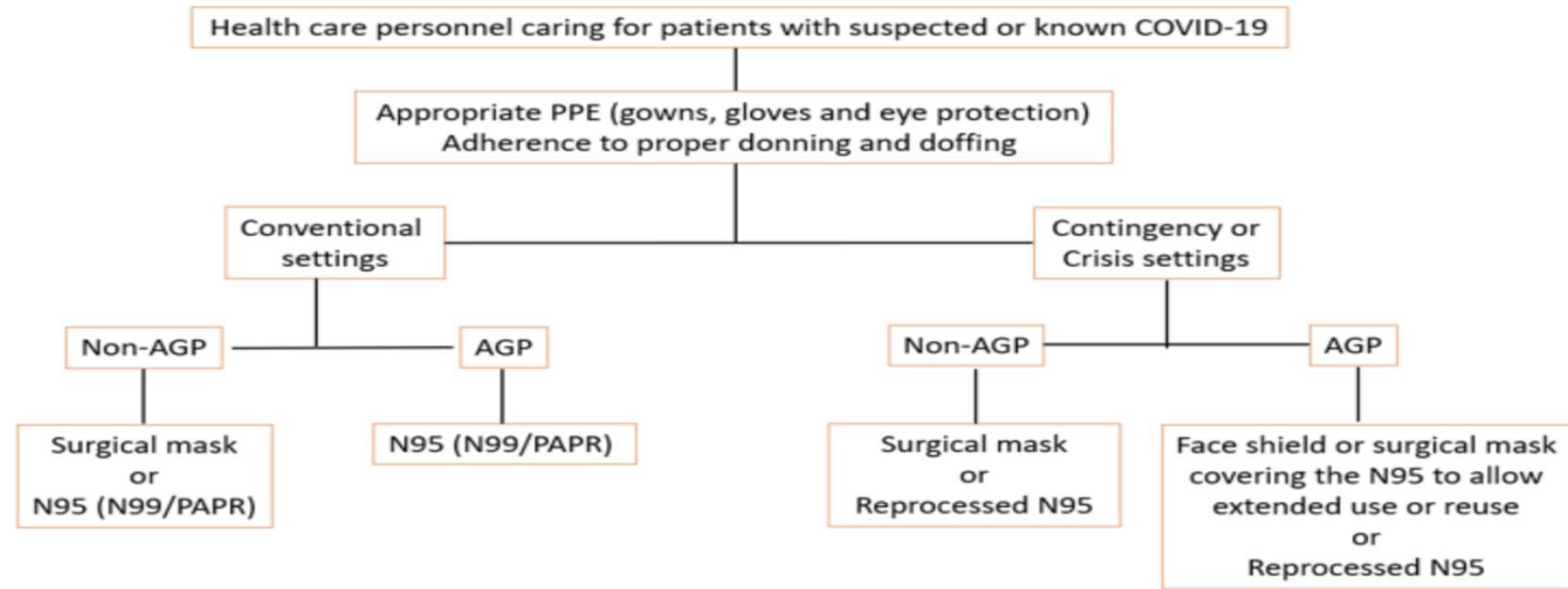
INFECTION
CONTROL

Infectious Diseases Society of America Guidelines on Infection Prevention in Patients with Suspected or Known COVID-19

- Definitions:
 - Conventional capacity: Usual supplies available and used
 - Contingency capacity: Conservation, adaptation and substitution of supplies with occasional reuse of select supplies
 - Crisis capacity: Critical supplies lacking
- All of the recommendations are for health care personnel caring for patients with suspected or known COVID-19

COVID-19: IDSA HCW PROTECTION GUIDELINES

Figure 1. IDSA Algorithm for Appropriate PPE in Conventional and Contingency or Crisis Settings



AGP: aerosol-generating procedures; **PPE:** personal protective equipment



INFECTION
CONTROL

Infectious Diseases Society of America Guidelines on Infection Prevention in Patients with Suspected or Known COVID-19

- **Routine Patient Care in CONVENTIONAL Settings**
 - 1: Use** either a surgical mask or N95 (or N99 or PAPR) respirator as part of appropriate PPE¹. (Strong recommendation, moderate certainty of evidence)
- **Routine Patient Care in CONTINGENCY or CRISIS CAPACITY Settings²**
 - 2: Use** a surgical mask or reprocessed respirator instead of no mask as part of appropriate PPE*. (Strong recommendation, moderate certainty of evidence)
- **Routine Patient Care in CONVENTIONAL, CONTINGENCY, or CRISIS CAPACITY Settings**
 - 3: No recommendation** for the use of double gloves versus single gloves for health care PPE¹. (Knowledge gap)
 - 4: No recommendation** for the use of shoe covers versus no shoe covers for health care personnel caring for patients with suspected or known COVID-19 as part of appropriate PPE¹. (Knowledge gap)

1. Appropriate personal protective equipment includes, in addition to a mask or respirator, eye protection, gown and gloves.

2. Respirator shortages



INFECTION
CONTROL

Infectious Diseases Society of America Guidelines on Infection Prevention in Patients with Suspected or Known COVID-19

- **Aerosol-Generating Procedures in CONVENTIONAL Settings**

5: Recommends that HCP use an N95 (or N99 or PAPR) respirator instead of a surgical mask, as part of appropriate PPE¹. (Strong recommendation, very low certainty of evidence) Comment: Despite the very low quality and indirect evidence supporting this recommendation, the IDSA guideline panel placed a high value on avoiding serious harms to exposed health care personnel.

- **Aerosol-Generating Procedures in CONTINGENCY or CRISIS CAPACITY Settings²**

6: Suggests that HCP use a REPROCESSED N95 respirator for reuse instead of surgical masks as part of appropriate PPE¹. (Conditional recommendation, very low certainty evidence)

7: Recommends that HCP add a face shield or surgical mask as a cover for the N95 respirator to allow for EXTENDED use as part of appropriate PPE¹. (Strong recommendation, very low certainty evidence)³.

8: Suggests that HCP add a face shield or surgical mask as a cover for the N95 respirator to allow for REUSE as part of appropriate PPE¹. (Conditional recommendation, very low certainty evidence)³.

1. Appropriate personal protective equipment includes, in addition to a mask or respirator, eye protection, gown and gloves. 2. Respirator shortages. 3: This recommendation assumes correct doffing sequence and hand hygiene is performed before and after removing the face shield or surgical mask covering the respirator.



INFECTION
CONTROL

Assessment of SARS-CoV-2 Infection Prevalence in Homeless Shelters — Four U.S. Cities, March 27–April 15, 2020

- 1,192 residents and 313 staff members in 19 homeless shelters in four cities.
- Testing followed identification of a cluster:
 - **Boston:** 36% of residents and 30% of staff
 - **San Francisco:** 66% of residents and 16% of Staff
 - **Seattle** 17% of residents and 17% of staff
- Testing that occurred in shelters with one or no reported cases:
 - **Seattle:** 5% of residents and 1% of staff
 - **Atlanta:** 4% of residents and 2% of staff

TABLE. SARS-CoV-2 testing among residents and staff members at 19 homeless shelters in four U.S. cities with community transmission of COVID-19, March 27–April 15, 2020



City	No. of shelters assessed	Date of testing	Residents		Staff members	
			No. tested	No. (%) positive	No. tested	No. (%) positive
Shelters reporting ≥2 cases in 2 weeks preceding testing						
Seattle	3	Mar 30–Apr 8	179	31 (17)	35	6 (17)
Boston	1	Apr 2–3	408	147 (36)	50	15 (30)
San Francisco	1	Apr 4–15	143	95 (66)	63	10 (16)
Subtotal	5	March 30–April 15	730	273 (37)	148	31 (21)
Shelters reporting 1 case in 2 weeks preceding testing						
Seattle	12	Mar 27–Apr 15	213	10 (5)	106	1 (1)
Shelters reporting no cases in 2 weeks preceding testing						
Atlanta	2	Apr 8–9	249	10 (4)	59	1 (2)
Total	19	Mar 27–Apr 15	1,192	293 (25)	313	33 (11)

The CDC recommends that homeless service providers implement infection control practices, apply social distancing measures, and promote use of cloth face coverings.



INFECTION
CONTROL

COVID-19: FEDERAL PRISONS

- Only about 2% of the federal prison population has been tested
- Over 70% of the 2700 federal prison inmates tested for COVID-19 were positive

<https://www.wsj.com/articles/more-than-70-of-inmates-tested-in-federal-prisons-have-coronavirus-11588252023>



INFECTION
CONTROL

Management of Employee Health Travel Cherokee Nation Health Services

- **International or cruise travel:** 14 day quarantine upon return
- **Domestic travel** (50 states or D.C.):
 - *If known exposure* to covid-19 suspected or confirmed positive person, quarantine for 14 days from the date of last contact.
 - *If symptomatic*, arrange for testing and appropriate follow
 - *If asymptomatic* and regardless of state of travel
 - **Pre-Screen:** Employers should measure the employee's temperature and assess symptoms prior to them starting work. Ideally, temperature checks should happen before the individual enters the facility.
 - **Regular Monitoring:** As long as the employee doesn't have a temperature or symptoms, they should self-monitor under the supervision of their employer's occupational health program.
 - **Wear a Mask:** The employee should wear a face mask at all times while in the workplace for 14 days after last exposure.
 - **Social Distance:** The employee should maintain 6 feet and practice social distancing as work duties permit in the workplace.
 - **Disinfect and Clean work spaces:** Clean and disinfect all areas such as offices, bathrooms, common areas, shared electronic equipment routinely.
 - Testing should be considered depending on testing capacity



Older People Act Weird: Really?

- Older adults with COVID-19, the illness caused by the coronavirus, have several “atypical” symptoms, complicating efforts to ensure they get timely and appropriate treatment, *according to physicians*.
- COVID-19 is typically signaled by three symptoms: a fever, an insistent cough and shortness of breath. But older adults — the age group most at risk of severe complications or death from this condition — may have none of these characteristics.
- **Instead, seniors may seem “off” — not acting like themselves** — early on after being infected by the coronavirus. They may sleep more than usual or stop eating. They may seem unusually apathetic or confused, losing orientation to their surroundings. They may become dizzy and fall. Sometimes, seniors stop speaking or simply collapse.

Younger patients with MAFLD are at increased risk of severe COVID-19 illness: A multicenter preliminary analysis

Table 1. Association between the presence of MAFLD and COVID-19 severity in younger and older patients.

	Younger patients			Elderly patients		
	OR	95% CI	P	OR	95% CI	P
60 years as the cut-off	n=253	[72(28.5%) MAFLD, 34(13.4%) severe cases]		n=74	[21(28.4%) MAFLD, 25(33.8%) severe cases]	
Unadjusted	3.97	1.89-8.35	< 0.001	0.72	0.24-2.15	0.55
Adjusted model I	3.25	1.47-7.16	0.003	0.75	0.25-2.28	0.61
Adjusted model II	2.49	1.04-5.96	0.04	0.45	0.13-1.59	0.22
Adjusted model III	2.67	1.13-6.34	0.03	0.61	0.18-2.03	0.42
55 years as the cut-off	n=199	[56(28.1%) MAFLD, 21(10.6%) severe cases]		n=128	[37(28.9%) MAFLD, 38(29.7%) severe cases]	
Unadjusted	6.48	2.45-17.1	< 0.001	1.00	0.44-2.31	0.99
Adjusted model I	5.02	1.81-13.90	0.002	1.02	0.44-2.39	0.96
Adjusted model II	3.10	1.01-9.56	0.05	0.77	0.30-1.99	0.60
Adjusted model III	3.63	1.20-10.95	0.02	0.91	0.37-2.28	0.85
65 years as the cut-off	n=276	[80(29.0%) MAFLD, 41(14.9%) severe cases]		n=51	[13(25.5%) MAFLD, 18(35.3%) severe cases]	
Unadjusted	3.13	1.59-6.18	0.001	0.76	0.20-2.94	0.69
Adjusted model I	2.69	1.31-5.53	0.01	0.75	0.19-2.94	0.68
Adjusted model II	2.22	1.02-4.86	0.04	0.33	0.07-1.69	0.19
Adjusted model III	2.41	1.12-5.22	0.03	0.59	0.13-2.64	0.49

Data are presented as odds ratios (ORs) and 95% confidence intervals (CIs) measured by univariable and multivariable logistic regression analyses.

Model I: adjusted for age and sex.

Model II: adjusted for age, sex, smoking, obesity, diabetes mellitus and hypertension.

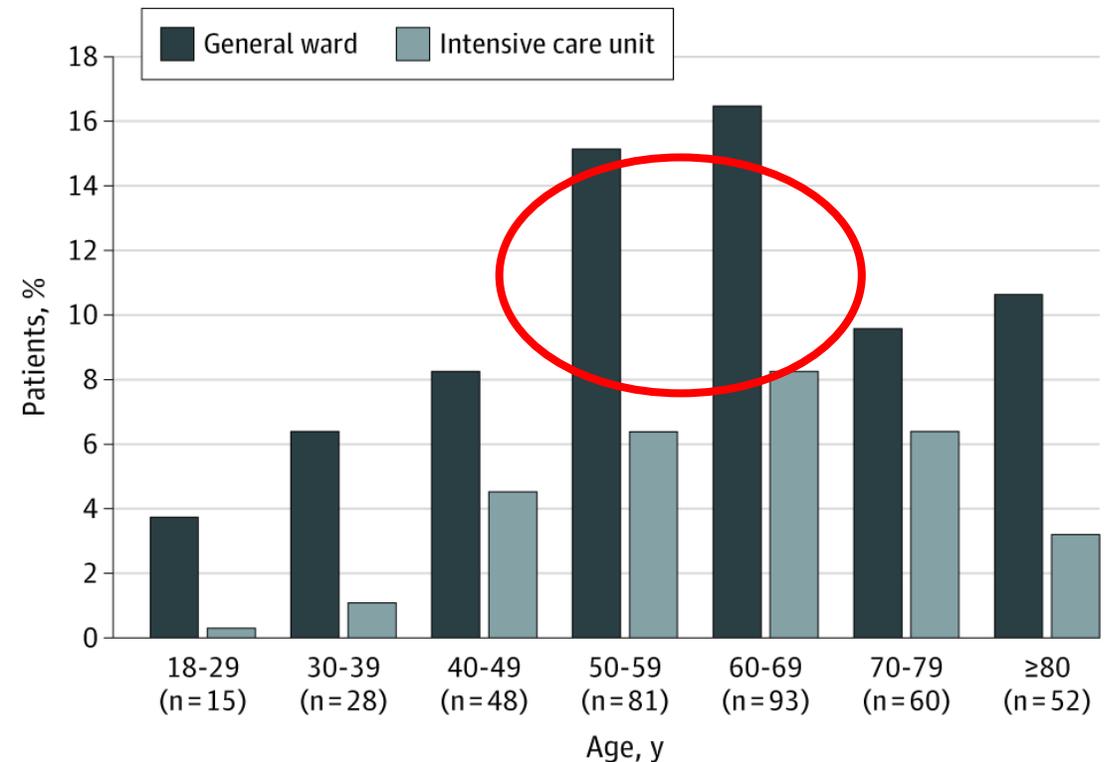
- In patients aged younger than 60 years, a **more than two-fold higher prevalence of severe COVID-19 was observed in MAFLD patients** compared to those without; this association remained significant after adjusting for age, sex, smoking status, overweight, diabetes, and hypertension (adjusted-OR 2.67, 95%CI 1.13-6.34, P=0.03).
- **MAFLD was not associated** with disease severity in multivariable analysis in elderly patients (P >0.05). We performed sensitivity analysis by setting a cut-off point other than 60 years to define younger and elderly patients. Similar results were observed at cut-offs using 55 and 65 years.

Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California

1,299 California patients who tested positive for SARS-CoV-2

- The most common comorbidity was hypertension.
- 377 (29%) were treated as inpatients
- 113 (29.9%) in the ICU.
- Of the 264 not ICU patients, 54.9% received supplemental oxygen.
- Of 321 patients with discharge dispositions
 - 50 (15.6%) died in the hospital (mortality rates were 6.3% on the ward and 50.0% in the ICU).

Distribution by Age



Distribution by Age Group of Adult Patients Admitted to General Ward and Intensive Care Unit With Coronavirus Disease 2019. Patients treated in intermediate care units are grouped under general ward.



Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area

- 5,700 patients with COVID-19 admitted to 12 hospitals in New York City, Long Island, and Westchester County, New York.
 - Their median age **was 63 years**, and 39.7% were women.
 - The most common comorbidities were **hypertension**, obesity, and diabetes.
 - At triage, **30.7% of patients were febrile**, 17.3% had a respiratory rate greater than 24 breaths/min, and 27.8% received supplemental oxygen.
 - Of the 2,634, 14.2% were treated in the ICU, 12.2% were on mechanical ventilation, and **21% died**.
 - **Of the 320 ICU patients** who received mechanical ventilation and weren't still in the hospital at the study's end, **282 had died**.

Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China

- Clinical Characteristic of Pregnant Women with COVID-19 Chen et al, NEJM, April 2017
- 118 pregnant women diagnosed with COVID-19 identified in
- Median age 31 years
- Disease severity: 92% mild, 8% severe
- Symptoms: Fever (75%), Cough (73%)
- Lymphopenia: 44%; Abnormal CT: 79%, No maternal deaths
- 3 spontaneous & 4 induced abortions, 2 ectopic pregnancies
- 68 deliveries ☐ Median APGAR score 9 with no neonatal asphyxia or deaths

The present data do not suggest an increased risk of severe disease among pregnant women, as has been observed with influenza



INFECTION
CONTROL

COVID-19: BREAST-FEEDING GUIDELINES

- CDC has issued guidance on breast-feeding during the COVID-19 pandemic
- Limited data on whether SARS-CoV-2 can be transmitted through breast milk
- Mothers with suspected or confirmed COVID-19 should take precautions when breast-feeding
 - wash hands first
 - wear a cloth face covering
- Breast-fed infants of infected mothers should be considered as having suspected COVID-19 for duration of the mother's recommended period of home isolation and 14 days thereafter



Are ACE/ARB safe in patients with COVID-19?

Study	Center	Number of Patients	% taking ACE and/or ARB	Outcome	Adjustment for cofounders	Adjusted Hazard Ration
1	Single	362	32% ACE or ARB	Mortality: No Difference	no	
2	Multicenter	1128	17% ACE or ARB	Mortality: ACE/ARB: 3.7% No ACE/ARB: 9.8%	yes	0.37
3	Two Centers	205	18% ACE	Mortality and ICU Need: ACE/ARB: 14.7% No ACE/ARB: 29%	Yes	0.29

1. Li J et al China. JAMA Cardiol 2020 Apr 23; [e-pub]. 2, Zhang P et al. Circ Res 2020 Apr 17; [e-pub]. 3. Bean DM et al. MedRxiv 2020 Apr 11; [preprint]



Treatment

REMDESIVIR TRIALS

- Preliminary findings from a randomized, placebo-controlled trial of IV Remdesivir in nearly 1100 patients hospitalized with COVID-19 with lung involvement, including those requiring supplemental oxygen or mechanical ventilation
- Interim analysis shows that the median time to recovery
 - 31% faster with Remdesivir than placebo (11 vs. 15 days)
 - Mortality rate 8.0% with Remdesivir and 11.6% with placebo (p=0.059)
- FDA plans to authorize emergency use of the drug



REMDESIVIR TRIALS

- The Lancet published findings from an underpowered, randomized trial of Remdesivir
 - 240 adults in China with severe COVID-19 who were within 12 days of symptom onset randomized to receive IV remdesivir or placebo for 10 days
 - Study aimed to enroll roughly 450 patients
- Primary outcome: time to clinical improvement within 28 days after randomization
 - did not differ significantly between the remdesivir and placebo groups (median: 21 and 23 days respectively)
 - patients treated within 10 days of symptom onset, time to clinical improvement numerically shorter with Remdesivir than with placebo (18 vs. 23 days)



Treatment

REMDESIVIR TRIALS

- Gilead, Remdesivir's manufacturer reported 5- and 10-day courses of the drug similarly efficacious for severe COVID-19
- Results not yet been published in a peer-reviewed journal

<https://www.gilead.com/news-and-press/press-room/press-releases/2020/4/gilead-announces-results-from-phase-3-trial-of-investigational-antiviral-remdesivir-in-patients-with-severe-covid-19>

COVID-19: MENTAL HEALTH

- Medical staff and affiliated healthcare workers (staff) are under both physical and psychological pressure
- This adds to an existing baseline of psychological pathology and low morale in the healthcare sector
- Supporting the mental health of these individuals is a critical part of the public health response
- Scope of the paper addresses some of the organizational, team and individual considerations for supporting staff (pragmatically) during this pandemic