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SARS-CoV-2 and COVID-19 Update

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Disclaimer

No conflicts of interest to declare.

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Zoonotic Spillover and
Virus Overview

Dr. Foster-Moumoutijis Clinical Perspective

Dr. Fatteh

Broward County –
Are we ready?

Dr. Fredericks

Potential COVID-19
Treatment Options

Global numbers

- 203,612 cases in 169 nations and territories, including the international conveyance (Diamond Princess cruise ship)
 - **Closed cases:** 91,095 (44.7% of total cases)
 - **8,229 deaths** (9% closed cases; 4% total cases)
- **82,866 recovered** (91% of closed cases)
- Currently infected: 112,517 (55.3% total cases)
 - **106,089 (94%) in mild condition**
 - **6,428 serious or critical cases (6%)**

Numbers in the U.S.

- 6,534 cases
- NY: 1,653
- WA: 1,012
- CA: 596
- NJ: 267
- MA: 218
- 116 deaths
 - 1.8% mortality



Numbers in Florida:

- 216 cases
- 7 deaths
- Broward county: 55
- Miami-Dade: 43
- Palm Bch: 13

How does SARS-CoV-2 spread?

- mainly from person-to-person
- close contact (within ~6 feet)
- via respiratory droplets ← coughs or sneezes



Pic credit: James Gathany; CDC



References:

<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

<https://www.medrxiv.org/content/10.1101/2020.03.09.20033217v2.full.pdf>

How does SARS-CoV-2 spread?

- symptomatic and asymptomatic spread
- from contaminated surfaces or objects
 - virus can remain viable and infectious in aerosols for multiple hours and on surfaces up to days

References:

<https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>

<https://www.medrxiv.org/content/10.1101/2020.03.09.20033217v2.full.pdf>

Protect yourself



What are coronaviruses?

- large, enveloped, +RNA viruses
 - accumulate mutations
- 4 human coronavirus (HCoVs) are endemic globally
 - HCoV 229E, NL63, OC43, and HKU1
 - cause 10 – 30% of URT infections in adults
 - bats and rodents are reservoirs
 - camelids are intermediate hosts

Ancestry?

- phylogeny indicates → beta-coronavirus genus
 - same as SARS-CoV and MERS-CoV
 - greater similarity to SARS-CoV →
 - hence name suggested is SARS-CoV-2
- SARS-CoV-2 shows >96% identity to a known bat coronavirus



Pangolins = potential source of SARS-CoV-2

- based on 99% genetic similarity b/w CoVs from pangolins & infected humans
- Research paper under review

SARS-CoV

- Natural reservoir →
 - bats

atypical pneumonia

- 8,098 individuals infected and 774 died, across 37 countries
 - 9% mortality
 - > 50% mortality in $\geq 65y$
- Intermediate host →
 - masked palm civet



Differences between SARS and COVID-19

SARS-CoV-2 **may be less pathogenic** than SARS-CoV.



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COVID-19 Clinical Perspective

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What are the symptoms of COVID-19 in adults?

Common Symptoms:

Fever (77-98%)

Cough (46-82%)

Muscle aches or fatigue
(11-52%)

Shortness of breath (3-31%)

Less common symptoms:

Sore throat

Headache

Cough with sputum

Nausea

Diarrhea

What are the symptoms of COVID-19 in children?

Reported Symptoms:

Fever

Cough

Runny nose

Congestion

Possibly

Vomiting

Diarrhea

Clinical Course of COVID-19

Severity



Clinical Progression



Severe COVID-19

- **Acute respiratory distress syndrome (ARDS)**

Requiring high flow oxygen or mechanical ventilation

- **Other complications**

Secondary infections

Cardiac injury

Arrhythmias

Septic shock

Liver dysfunction

Acute kidney injury

Multiorgan failure

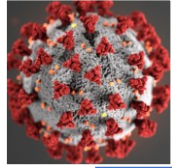
Who is at risk for COVID-19?

Persons who have had prolonged, unprotected close contact with a patient with symptomatic, confirmed COVID-19 and those who live in or have recently been to areas with sustained transmission

Who is at risk for **severe** COVID-19?

From the limited data, it is possible that older adults, and persons with underlying chronic medical conditions and immunocompromising conditions, may be at risk for more severe outcomes.

Differentiating COVID-19 from other conditions



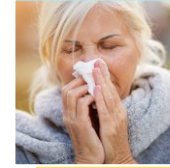
COVID-19

- Gradual progression of symptoms
- Dry cough
- Fever
- Shortness of breath



Influenza

- Abrupt onset of symptoms
- Fever
- Body aches
- Headache
- Fatigue



Seasonal allergies

- Sneezing
- Stuffy nose
- Runny nose
- Itchy eyes
- Cough

Getting Tested for SARS-CoV-2

Currently, the CDC states:

“Clinicians should use their judgment to determine if a patient has signs and symptoms compatible with COVID-19 and whether the patient should be tested”



Clinical Screening Tool for Identifying Persons Under Investigation for Coronavirus Disease 2019 (COVID-19) per Centers for Disease Control and Prevention (CDC)

Symptomatic individuals should be asked to wear a surgical mask upon arrival. Initiate contact and airborne precautions, using appropriate personal protective equipment (PPE).

Version 4.2 | March 15, 2020

SCREENING CRITERIA

If your patient is exhibiting **symptoms** of acute lower respiratory illness (e.g., fever, cough, and shortness of breath) **and** meets one or more of the following criteria:

1. Persons who have had a close contact with a laboratory-confirmed COVID-19 case
2. Persons hospitalized with acute lower respiratory illness of unknown origin
3. History of travel to or from an affected geographic area with widespread community transmission
4. History of international travel or a cruise
5. ≥65 with chronic health conditions
6. Immunocompromised persons



TESTING

If individual meets criteria for testing, wear appropriate PPE and initiate contact and airborne precautions.

1. The health care provider is responsible for specimen collection, handling and shipping. Please follow [CDC guidance](#).
2. Collected specimens should be processed within your health care facility, if available; a commercial laboratory (e.g., [LabCorp](#) and [Quest](#)); or a [Florida Bureau of Public Health Laboratory \(BPHL\)](#)
3. Before sending specimens to BPHL, notify your local county health department [CHD Epidemiology Contacts](#).
4. Health care providers may consult local county health departments for additional guidance as needed.



EXPANDED CRITERIA

If your patient does not meet the above criteria, testing may occur based on clinician's judgement.

1. The health care provider is responsible for specimen collection, handling and shipping. Please follow [CDC guidance](#) and use proper PPE.
2. Collected specimens should be processed within your health care facility or a commercial laboratory (e.g., [LabCorp](#) and [Quest](#)).
3. Follow [CDC guidance](#) for specimen collection, handling and shipping.

FOR ADDITIONAL GUIDANCE

Providers are encouraged to frequently monitor Florida Department of Health and CDC websites for updated guidance on COVID-19.

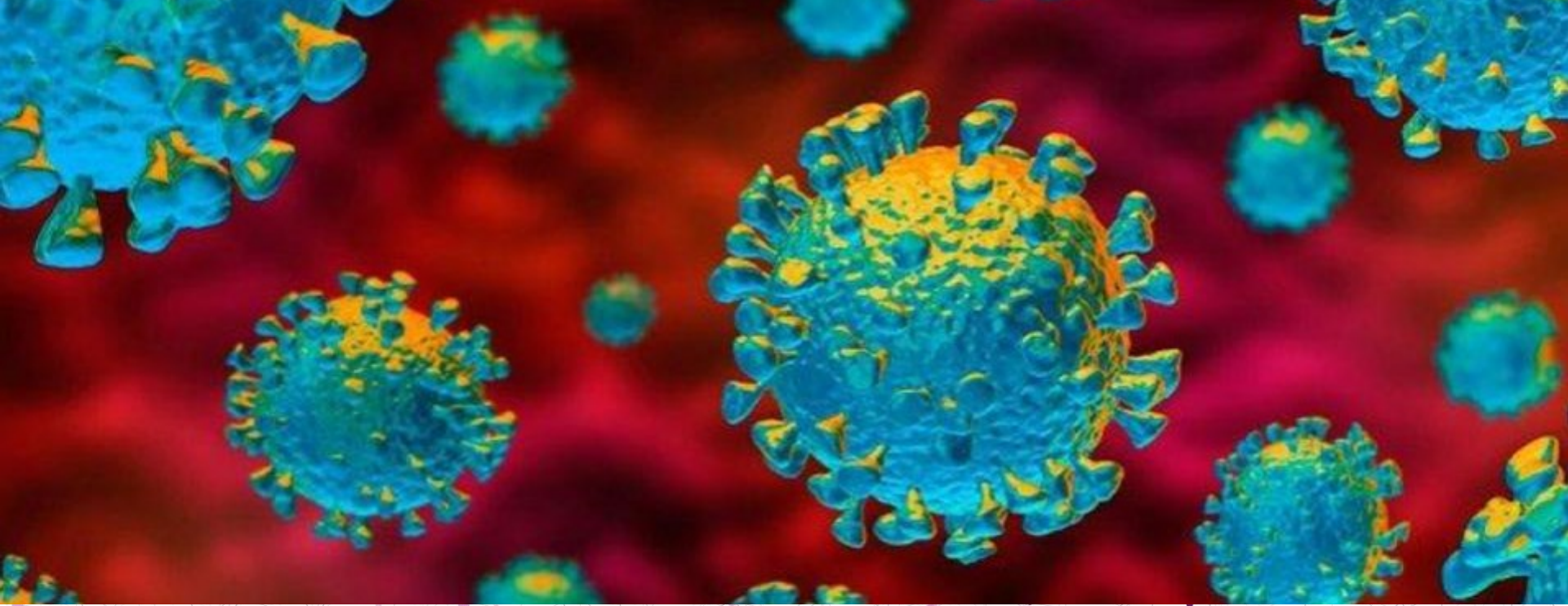
- www.flhealth.gov
- <https://www.cdc.gov/coronavirus/2019-nCoV/index.html>

Please see the CDC's: [Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 \(COVID-19\) in Healthcare Settings](#)

Getting Tested for SARS-CoV-2 in FL

Florida Department of Health Screening Criteria:

- Persons who have had close contact with a laboratory confirmed COVID-19 case
- Persons hospitalized with acute lower respiratory illness of unknown origin
- History of travel to or from an affected geographic area with widespread community transmission
- ≥ 65 with chronic health condition
- Immunocompromised persons



COVID-19: BROWARD COUNTY – ARE WE READY?

SHAHNAZ FATTEH, MD
FAMWA
BCMA PRESIDENT



Disclaimer

No conflicts of interest to declare.

BROWARD LEADS THE CASES OF COVID-19 IN FL



Total Cases by County

Broward Cases: 55
Florida residents: 48
Non-Florida residents: 7

Miami-Dade Cases: 43
Florida residents: 40
Non-Florida residents: 3

Palm Beach Cases: 13
Florida residents: 13
Non-Florida residents: 0

Duval Cases: 10
Florida residents: 10
Non-Florida residents: 0

Volusia Cases: 9
Florida residents: 9
Non-Florida residents: 0

Hillsborough Cases: 9
Florida residents: 7
Non-Florida residents: 2

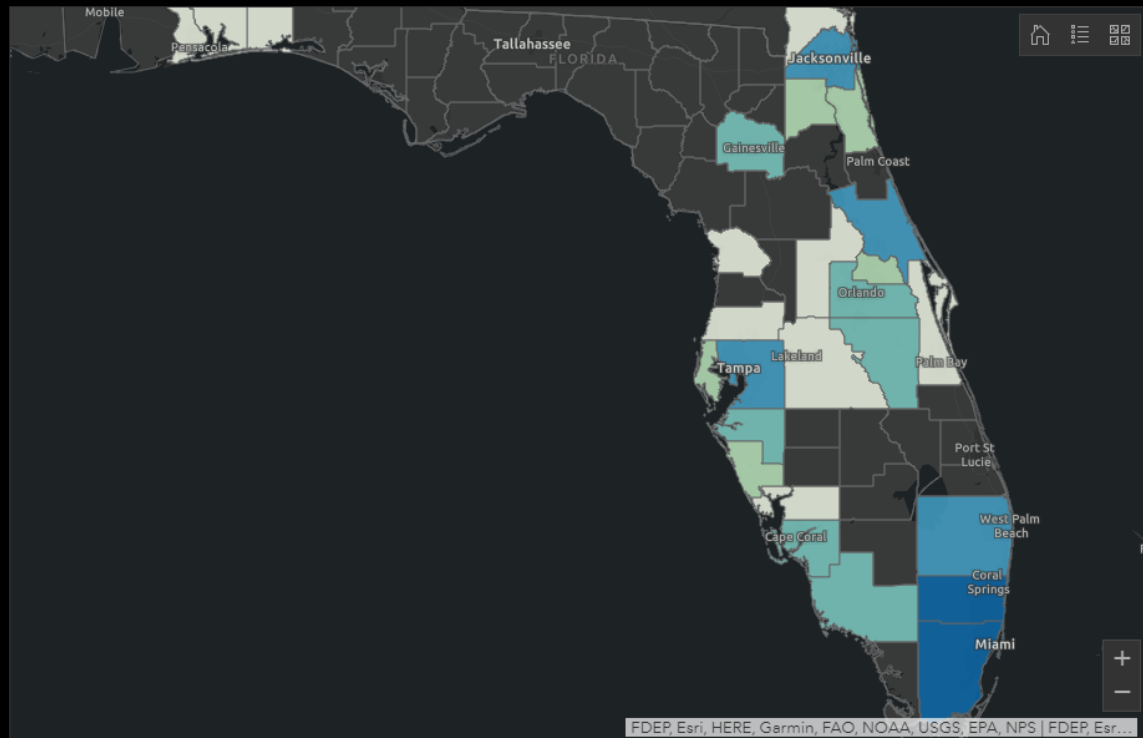
Manatee Cases: 7
Florida residents: 7
Non-Florida residents: 0

Collier Cases: 7
Florida residents: 6
Non-Florida residents: 1

Orange Cases: 6
Florida residents: 6
Non-Florida residents: 0

Osceola Cases: 7
Florida residents: 6
Non-Florida residents: 1

Lee Cases: 7
Counties (by total cases)



USA Cases
6,496

Last update: a few seconds ago

USA World

Total Cases
216

Last update: a few seconds ago

Total Cases

Florida World

Number of People Tested: 2294

Negative: 1,017
Positive: 216
Results Pending: 1,061

Total Positive Persons: 216

Positive Florida Residents: 195
(Includes 6 Florida Residents Tested Elsewhere)
Positive Non-Florida Residents in Florida: 21

Currently Monitored

832

Florida case data last updated:
March 17, 2020 at 18:00 EDT

Broward Hospitals Prepare for COVID-19

How are hospitals responding to increased patients arriving for evaluation and treatment?

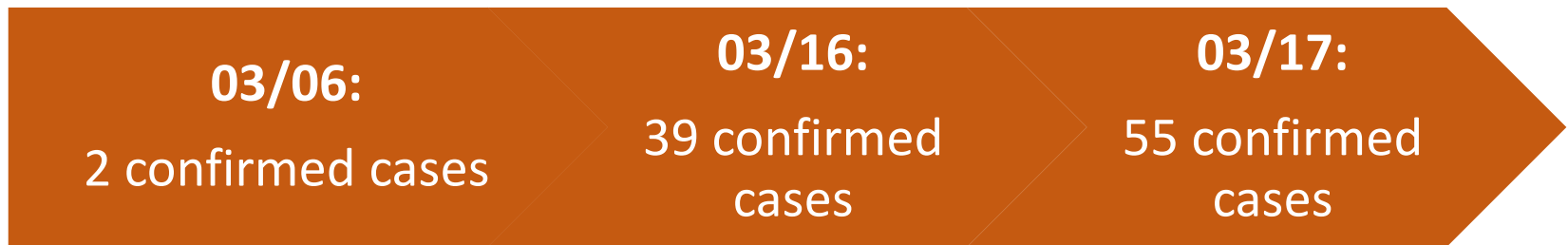
What plans and measures have been implemented?

Do we have enough ventilators and isolation rooms for patients in our county?

What are the unidentified needs and gaps that still need to be addressed?

Coronavirus Cases in Broward County

Broward had the biggest one day jump in new Covid-19 confirmed cases. More than half affected are over 60 years old.



As COVID-19 cases are expected to continue to surge in the next few weeks, are our hospital systems ready?

Are hospitals able to meet patient demand?

Dr. Jha, Chan School of Public Health, Harvard, did the math (NPR) calculated our readiness for COVID-19:

There are approximately **750,000 hospital beds** in the US.



If 20% of the 250 million adults in the US are infected with Covid-19, that would affect **50 million adults**.



If 20% of those infected, develop more acute infection, then we have **10 million persons** with more moderate to severe infection.

Learning from Italy: COVID-19 Preparedness

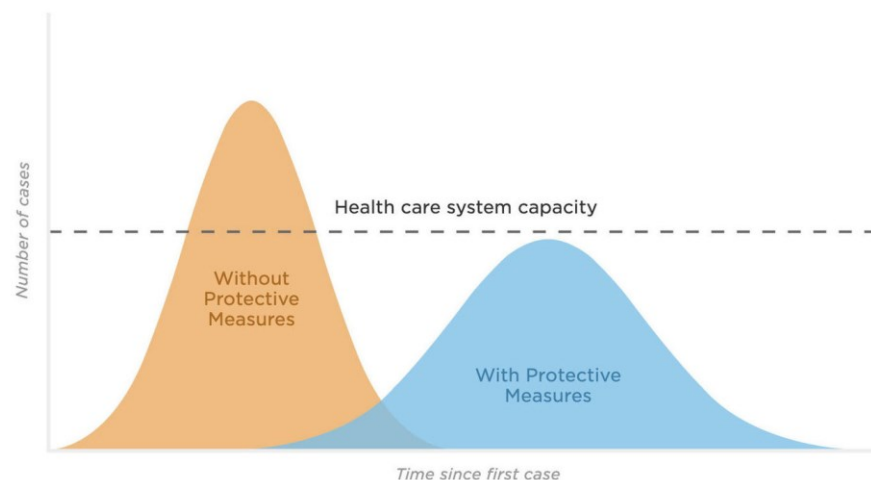
Without taking necessary precautions, hospital systems can become overwhelmed.

Eg: Italy hospital systems were rapidly overwhelmed.

Social distancing and travel restrictions were late by 2 weeks per public health officials.

Delayed implementation of restrictions and social distancing in the US can lead to:

- Shortage of providers
- Shortage of specialized equipment including ventilators, IV pumps, and monitors
- Shortage PPE (personal protective equipment) – N95 masks and gloves



Hospital Readiness: Getting Prepared

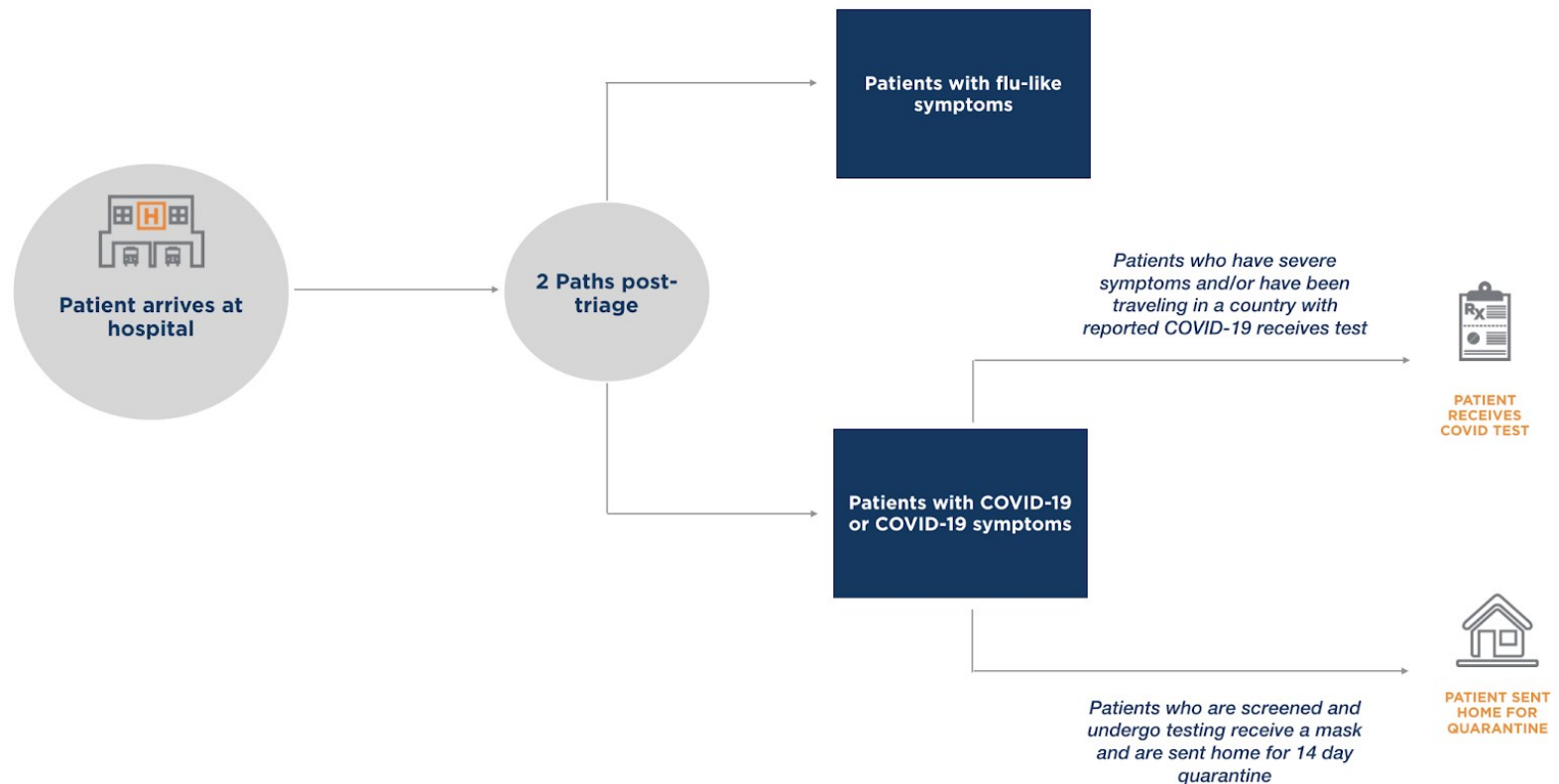
The major hospital systems in Broward County have all implemented protocols to respond to the COVID-19 pandemic.

Hospitals implement new measures, including:

- Protocols set by the CDC
- Workplans collaboratively constructed with CDC, Broward DOH, Florida DOH, community leaders, and key health care stakeholders
- Lab testing and triage capabilities

Hospital triage and clinical workflow

Patients arriving at BGH, WSR, Memorial, are directed into “two lanes” at points of entry for screening questions and temperature testing. Outside tents for screening are present at some places: Memorial Hospital West, Memorial Regional Hospital.



Testing Status

Support from Governor DeSantis will enable more rapid testing in the near future

Current Status

Most people arriving at the hospital are NOT currently being tested. There are limited test kits available. Florida has received 1,000 kits which are being distributed to hospitals and DOH labs.

Future Status

On 3/13 Governor DeSantis ordered 2,500 Covid-19 test kits, which will test 625,000 people.

When do test results come back?

Test results vary amongst facilities:

DOH

Has 3 public testing facilities and results are back in 2-3 days

Memorial Healthcare

Has in-house testing and currently is able to test 100/day and 2 machines capable of ramping up to testing to 1,000 to 4,000 cases/ day. Results are back in hours.

Baptist Health & Broward Health

Sending the tests to outside labs; results may be back in 3-4 days. Both hope to receive reagents which will allow for in-house testing and more rapid results.

Mobile Testing Sites

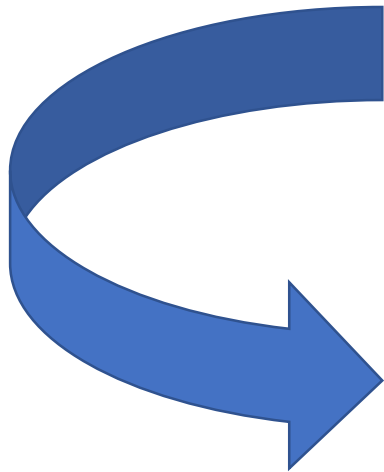
Mobile sites will allow for increased testing and keep patients away from hospitals.

Where does mobile testing exist today?

1. 170 National Guard personnel have been deployed to Broward County to help with mobile testing
2. Memorial Health has started mobile testing in Miramar and looking to add more sites.
3. 300 National Guard members will also be in Broward County to help with “Drive Thru” testing.
4. Broward Health, Cleveland Clinic, Coral Springs Medical Center and also in Palm Beach mobile/ drive thru testing centers are planned to start soon.

BCMA Recommendations

Social distancing involves widespread closure of schools, restrictions on bars, restaurants, and other businesses with covid-19 remaking daily life for all of us.



Social distancing measures have been key to the decrease in spread and new cases of Coronavirus in several regions. Lessons from other countries such as travel restriction, limiting large gatherings, hand hygiene, have led to decreased exposure and spread of Covid -19 infection.

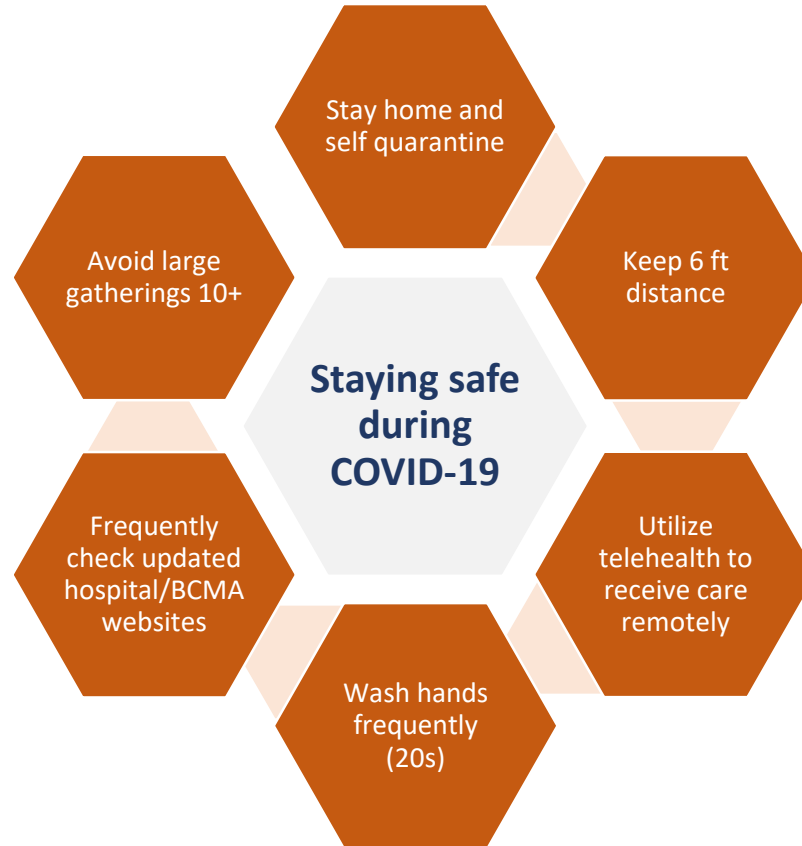
Every day brings new measures

- Social distancing measures need to be implemented in physicians' offices as well as hospitals.
- Elective surgeries are being delayed at local hospitals.
- Visitation hours are being limited as well as number of persons visiting an inpatient (2).
- Nursing homes and assisted living facilities, long-term care facilities and adult group homes have barred individuals from visiting these facilities to limit the potential exposure of residents to Covid-19.
- Screening questions include: recent travel within 14 days, cruise travel within 14 days, close contact with Covid-19 infected person, symptomatic persons with cough, fever, shortness of breath or sore throat.

BCMA Recommendations

- Local hospitals should share data – how many open beds are available and availability of resources like ventilators.
- Staff scheduling and rotations to make sure there are enough workers available.
- As in Hurricane season, additional staff by physicians for coverage should be arranged now.
- There is a risk of shortages of physicians, particularly as physicians also develop Covid-19 infections or are exposed and need to quarantine for 14 days.
- Curfew hours through Broward County as in hurricane emergency should be implemented.

Final Reminders



stay well



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Potential COVID-19 Treatment Options

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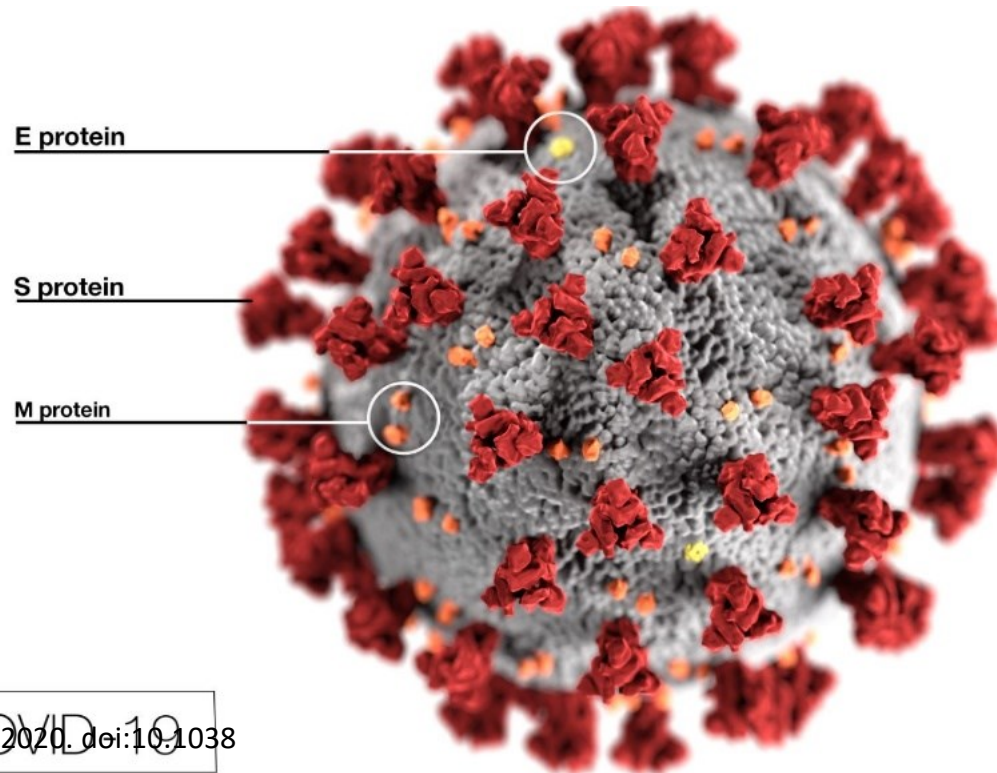
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Disclaimer

- No conflicts of interest to declare
- As of 3/17/20, no compound that specifically targets SARS-CoV-2 has moved beyond phase I studies
- Due to the lack of evidence for treatment options for COVID-19, the following recommendations are not advocated by myself or my employer

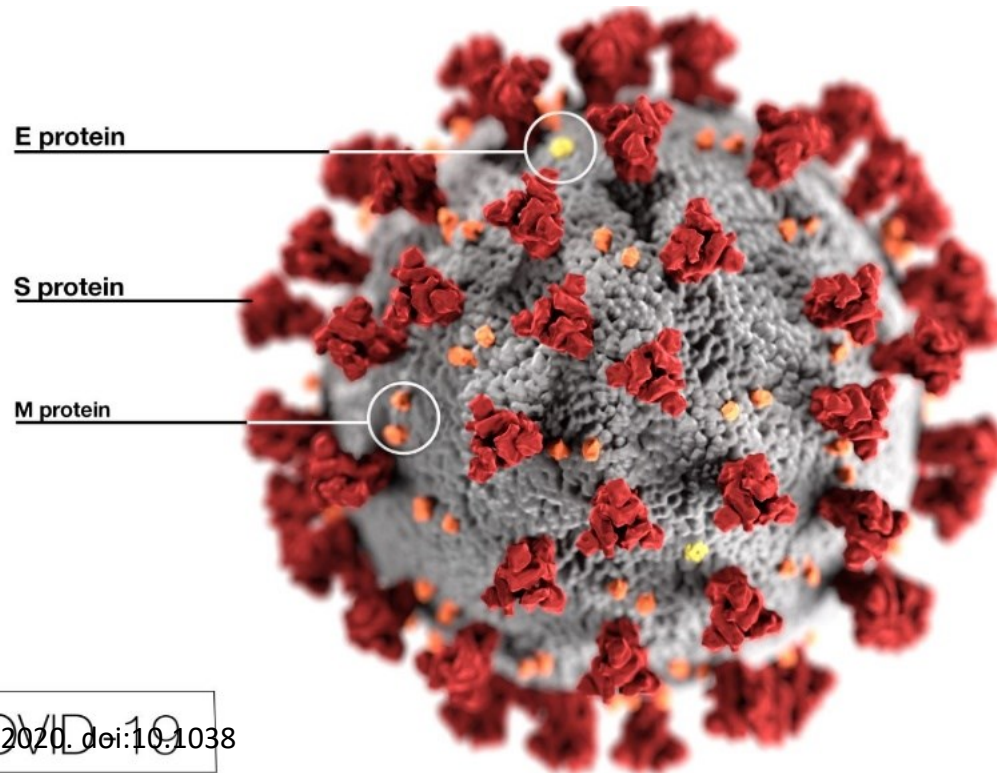
SARS-CoV-2 Pathogen

- Envelope S-protein enables virus to bind to angiotensin converting enzyme II (ACE2) and use as entry into ACE2 expressing cells
 - ACE2 cells common in heart and lungs



SARS-CoV-2 Pathogen

- Shares 80% of sequence identity with SARS-CoV-1
 - Allows us to understand COVID-19 better and apply previous evidence for treatment



Lopinavir/ritonavir (Kaletra)

- **Mechanism of action:** Lopinavir binds to HIV-1 protease activity and inhibits cleavage of polyprotein precursors into functional proteins required to spread infection
- **Dose:** 400/100 mg PO BID
- **Adverse drug reactions:**
 - Possible higher risk of MI
 - Hepatotoxicity
 - Increased cholesterol
 - Pancreatitis
- **Drug-drug interactions:** Lopinavir metabolized by CYP 3A4, ritonavir inhibits CYP3A4
 - Avoid amiodarone, azole antifungals, ticagrelor, rivaroxaban, tacrolimus



Lopinavir/ritonavir (Kaletra)

- **Study design:** Retrospective matched cohort study
- **Intervention:** Lopinavir/ritonavir + standard treatment protocol (STP) compared to matched patients receiving STP for SARS-CoV-1
- **Size of study:** 75 lop/rit + STP vs 977 STP in four acute hospitals in Hong Kong in 2003

- **Results:**

Treatment Groups	Intubation Rate	Overall Death Rate
Lopinavir/ritonavir + STP	0%	2.3%
STP	11%	15.6%

Lopinavir/ritonavir (Kaletra)

- **Study design:** Matched cohort study
- **Intervention:** Lopinavir/ritonavir + ribavirin as post exposure prophylaxis (PEP) for high risk healthcare workers (HCW) vs. no prophylaxis in matched high risk cases for **MERS-CoV**
- **Size of study:** 22 lop/rit + ribavirin vs 21 no PEP throughout 5 hospitals in South Korea
- **Results:**
 - **PEP group:** 0/22 HCWs developed MERS
 - **Non PEP:** 6/21 (28.5%) HCWs developed subsequent MERS
 - **Tolerability:** 21/22 (95%) of PEP group complained of ADRs: diarrhea, nausea, stomatitis, fever

Lopinavir/ritonavir (Kaletra)

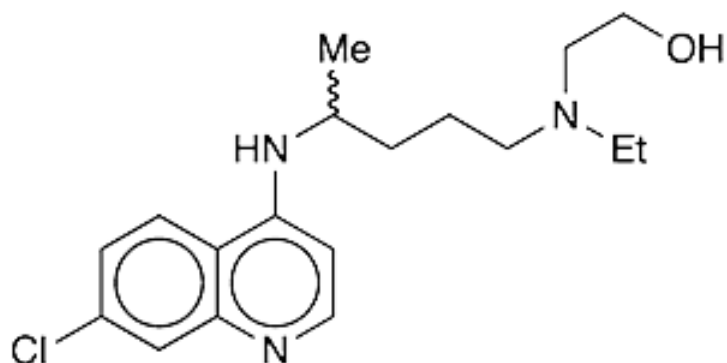
- No current well defined studies published examining lopinavir/ritonavir's role in COVID-19
 - Several case studies published from China
- Currently recommended in China's COVID-19 Treatment Guideline
- May extrapolate evidence of activity against SARS-CoV-1 and MERS-CoV to SARS-CoV-2

Chloroquine (Aralen)

- **Mechanism of action:** binds to DNA & RNA polymerase and interferes with metabolism and hemoglobin utilization by parasites
- **Dose:** 500 mg PO BID
- **Adverse drug reactions:**
 - Cardiomyopathy resulting in cardiac failure
 - EPS effects
 - Agranulocytosis, aplastic anemia, neutropenia, pancytopenia
 - Hypoglycemia
- **Drug-drug interactions:** May increase levels of beta-blockers, dapsone, haloperidol
 - Avoid with other agents that may cause QT prolongation

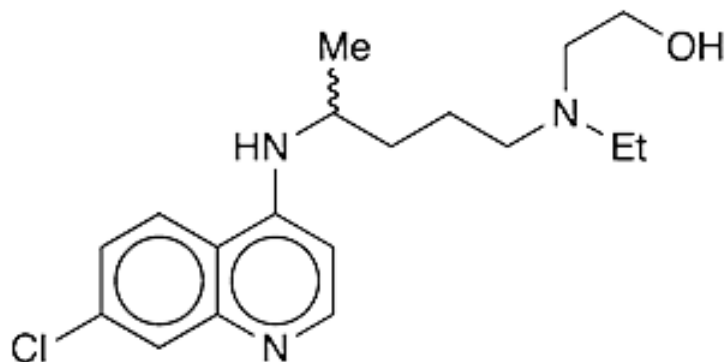
Hydroxychloroquine (Plaquenil)

- **Mechanism of action:** interferes with vacuole function within malaria parasites by increasing pH, also impairs chemotaxis of eosinophils and complement-dependent antigen-antibody reactions
 - Less toxic metabolite of chloroquine
- **Dose:** 400 mg PO BID x 1 day, 200 mg PO BID (administer with food)



Hydroxychloroquine (Plaquenil)

- **Adverse drug reactions:**
 - Cardiomyopathy causing cardiac failure
 - Skin reactions causing dermatitis
 - Bone marrow suppression (prolonged therapy)
 - Hypoglycemia
- **Drug-drug interactions:** May increase levels of beta-blockers, dapson, haloperidol
 - Avoid with other agents that may cause QT prolongation



Hydroxychloroquine (Plaquenil)

- **Study design:** In-vitro study, physiologically-based pharmacokinetic model (PBPK)
- **Intervention:** Activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2 infected vero cells
- **Size of study:** 5 different dosing regimens examined for hydroxychloroquine
- **Results:** Hydroxychloroquine found to be more potent than chloroquine
 - Study found optimal regimen was 400 mg PO BID x 2, 200 mg PO BID x 5 days

Hydroxychloroquine (Plaquenil)

- Chloroquine investigated for use in enteroviruses, coronaviruses, chikungunya, dengue
- Chloroquine interferes with terminal glycosylation of the ACE2 cellular receptor
 - This may disrupt SARS-CoV-1-receptor binding resulting in inhibition of infection and spread of disease
- International community urges China to publish peer reviewed evidence

Oseltamivir (Tamiflu)

- **Mechanism of action:** inhibits influenza viral neuraminidase, responsible for cleaving immature virus from host
- **Dose:** 75 mg PO BID
- **Adverse drug reactions:** Recent South Korean analysis reviewed for neuropsychiatric events in 1,266,780
 - Incidence was lower compared to controls not prescribed oseltamivir, warning appears unwarranted
- **Drug-drug interactions:** probenecid may increase levels
 - Metabolized hepatically but not by CYP enzymes

Oseltamivir (Tamiflu)

- **Study design:** Case series
- **Intervention:** Healthcare workers exposed to patient with COVID-19, quarantined and received oseltamivir
- **Size of study:** 4 healthcare workers
- **Results:** 3/4 had clinical symptoms and CT imaging abnormalities resolve



Remdesivir (GS-5734)

- **Mechanism of action:** Broad spectrum nucleotide analog, obscures viral RNA polymerase
 - Has previously demonstrated activity against MERS-CoV and SARS-CoV-1
- **Dose:** Under investigation
 - Regimens investigated include: 200 mg IV loading dose, 100 mg IV once daily x 9 days
- **Adverse drug reactions:** Unknown
- **Drug-drug interactions:** Unknown
- Investigational agent currently in phase III studies
 - Can acquire if site enrolled in study or application for expanded access (compassionate use)

Remdesivir (GS-5734)

- Was used as compassionate use in first case of COVID-19 in Washington state
 - Patient improved after starting regimen on day 7 of hospitalization
- Efficacy in larger studies remains to be seen
 - While SARS-CoV-2 shares approximately 80% of RNA sequencing with SARS-CoV-1 it's estimated to share 96% of RNA polymerase sequence identity

Summary

- The following summaries are based on currently available data
- Information is quickly evolving with COVID-19
 - May discover new or old agents with activity or synergy
- Who should receive pharmacotherapy?
- Important to remain vigilant and updated with latest peer-reviewed medical literature

More Resources

- Centers for Disease Control and Prevention (CDC) Coronavirus (COVID-19)
 - <https://www.cdc.gov/coronavirus/2019-nCoV/index.html>
- Florida Department of Health
 - <http://www.floridahealth.gov/>
- Infectious Diseases Society of America (IDSA) COVID-19 Resource Center
 - <https://www.idsociety.org/public-health/COVID-19-Resource-Center/>

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