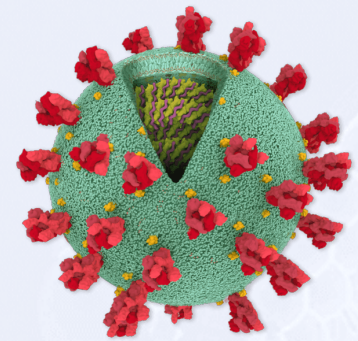


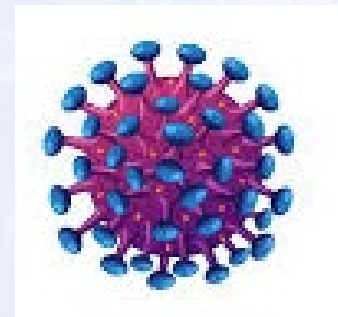


COVID-19 Pathogenesis and HIV



SARS CoV-2

Yue Chen, PhD
Associate Professor
Department of Infectious Diseases
and Microbiology
Graduate School of Public Health
University of Pittsburgh



HIV

MAAETC webinar 09-11-2020



Speaker Disclosure

I don't have any commercial relationships.



The CSSE at Johns Hopkins: Global COVID-19 Dashboard



Confirmed Cases
Global: 27,902,002

- US: 6,363,729
- India: 4,465,863
- Brazil: 4,197,889
- Russia: 1,042,836

Deaths
Global: 904,485

- US: 190,887
- Brazil: 128,539
- India: 75,062
- Mexico: 69,049

Last updated: September 10, 2020, 10:28 AM EDT.



Slide credit: clinicaloptions.com

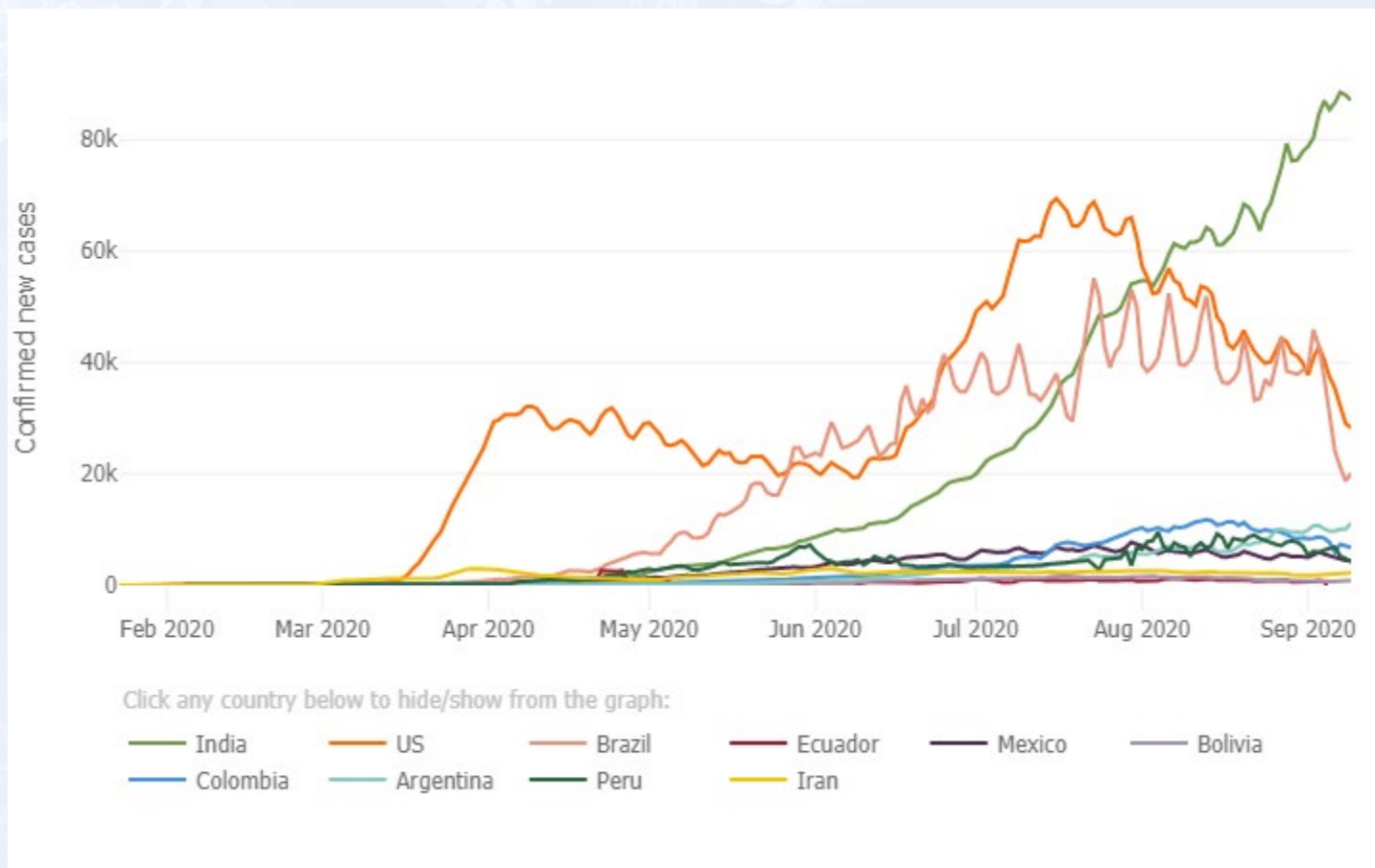
Linda R. Frank, PhD, MSN, ACRN, FAAN

Dong. Lancet Infect Dis. 2020;20:533. <https://coronavirus.jhu.edu/map.html>



The CSSE at Johns Hopkins: Global COVID-19 Dashboard

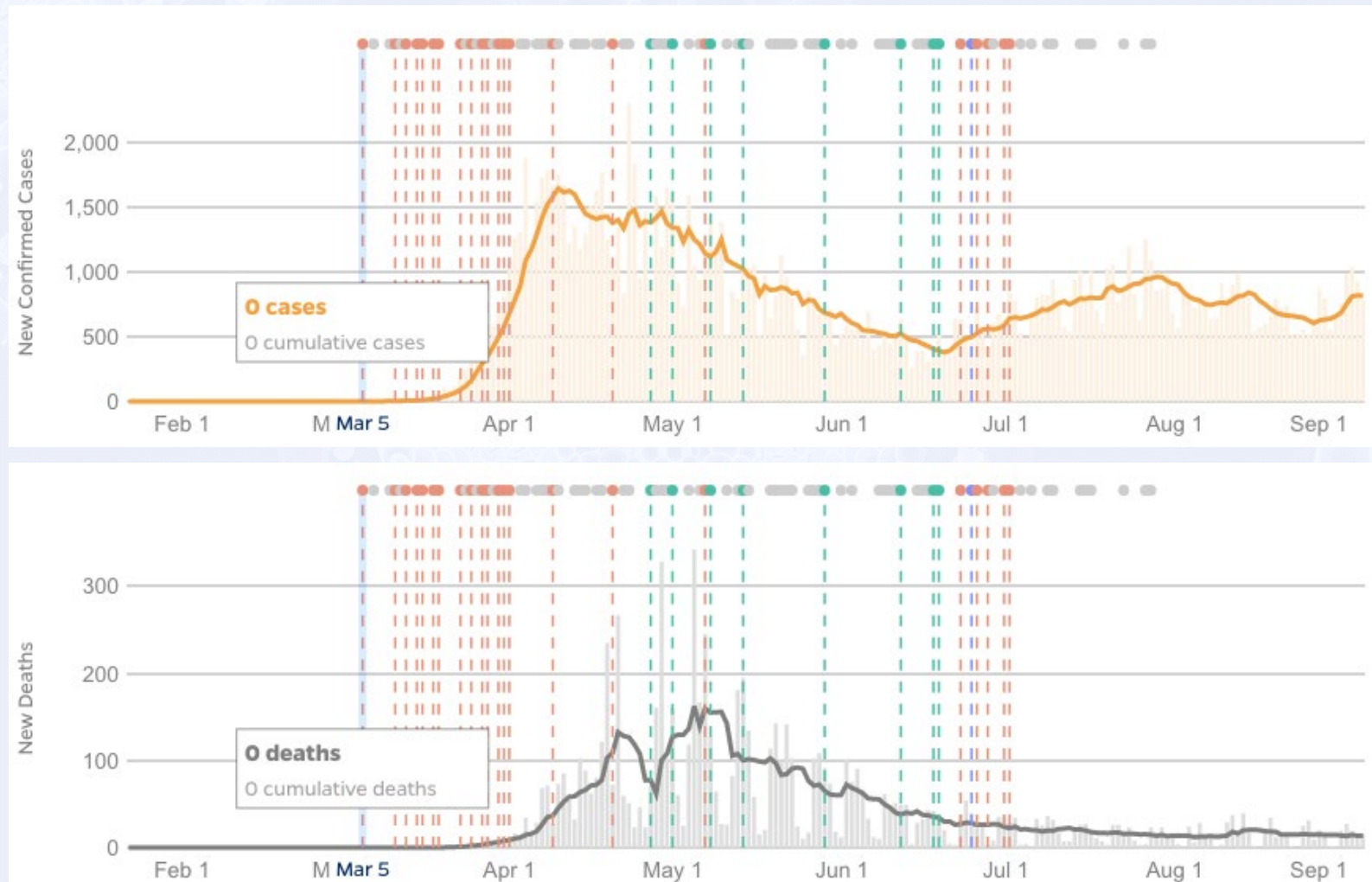
DAILY CONFIRMED NEW CASES (5-DAY MOVING AVERAGE)



Linda R. Frank, PhD, MSN, ACRN, FAAN

The CSSE at Johns Hopkins: Global COVID-19 Dashboard

PENNSYLVANIA



COVID-19 and SARS CoV-2

- COVID-19: CORONAVIRUS DISEASE 2019
- SARS-Coronavirus type 2 (SARS CoV-2) is the virus that causes COVID-19



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COVID-19 and SARS CoV-2

- COVID-19: CORONAVIRUS DISEASE 2019
- SARS-Coronavirus type 2 (SARS CoV-2) is the virus that causes COVID-19

Severe Acute Respiratory Syndrome (SARS)



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COVID-19 Timeline to Pandemic

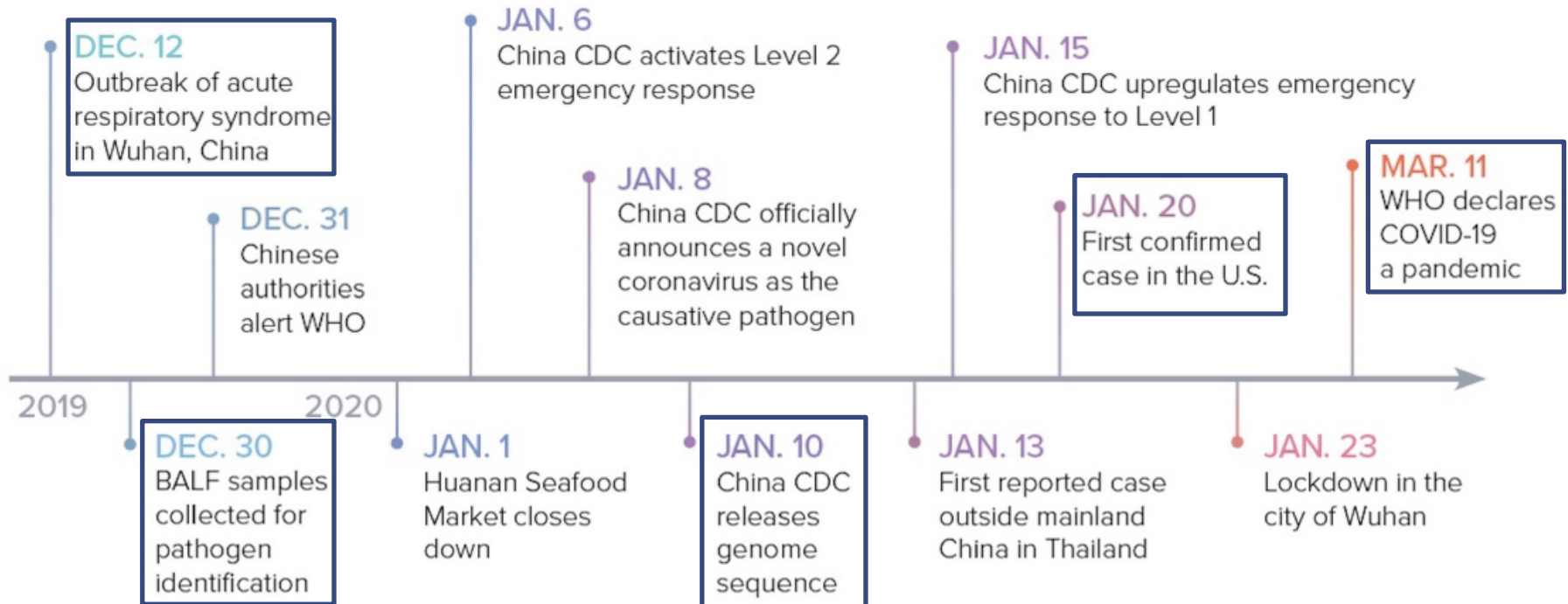
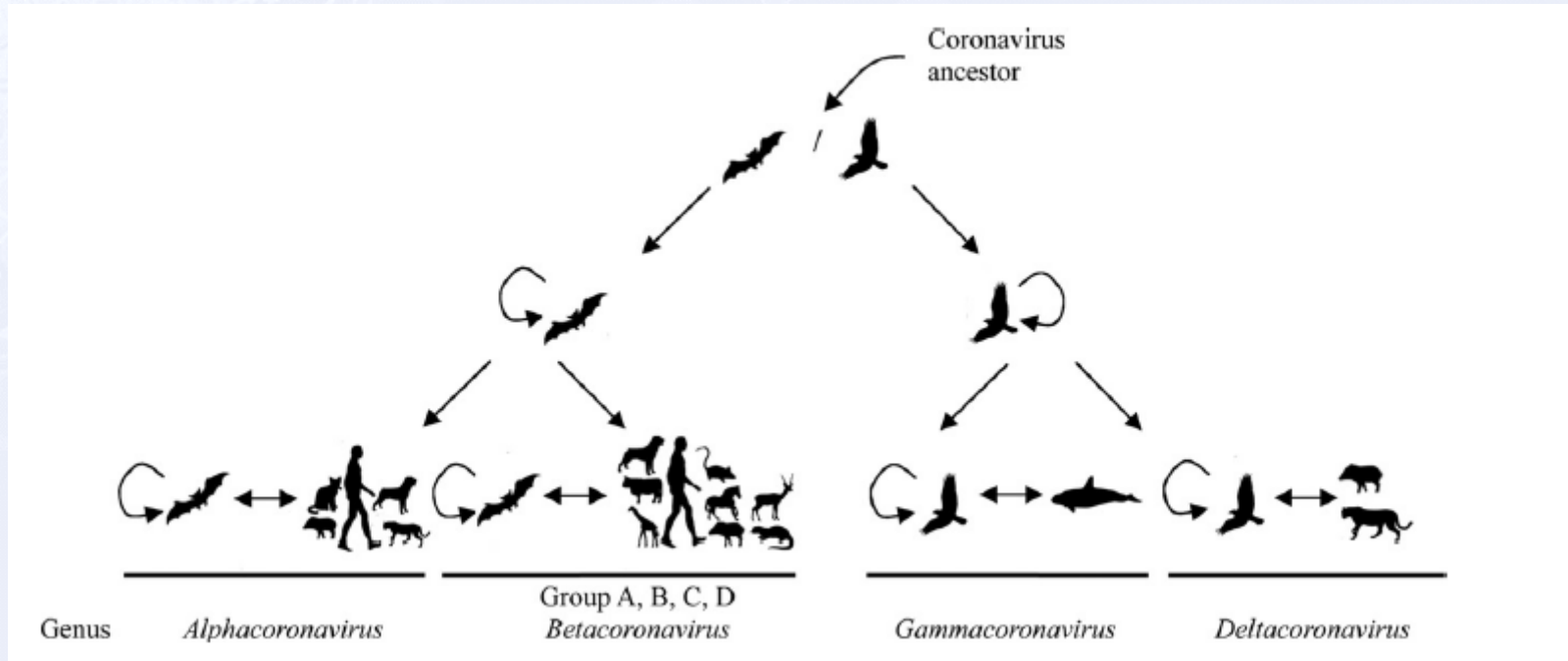


FIGURE 1 | COVID-19: timeline to pandemic. The sequence of events from the outbreak in Wuhan, China to the declaration of the COVID-19 pandemic. BALF, bronchoalveolar lavage fluid.

There are 7 Human Coronaviruses



HCoV-NL63
HCoV-229E

HCoV-OC43
HCoV-HKU1

Causing 10-15% common cold

SARS

MERS– Middle East Respiratory Syndrome

SARS CoV-2

<https://jvi.asm.org/content/86/7/3995.long>

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Comparison between SARS-CoV-2, MERS-CoV, and SARS-CoV

	SARS-CoV-2	MERS-CoV	SARS-CoV
Pandemic/ epidemic year	2019-Present	2012	2002–2003
Coronavirus subfamily	Beta–Coronavirus	Beta–Coronavirus	Beta–Coronavirus
Natural reservoir	Bat	Bat	Bat
Intermediate host	Pangolin	Dromedary camel	Palm civets
Origin	Wuhan, China	Arabian Peninsula	Guangdong, China
Country spread	>180	27	26
Total cases to date	>7,000,000	2,494	8,096
Total deaths to date	>400,000	858	774
Total cases in the U.S. to date	>1,900,000	2	27
Case fatality rate*	1–7.2%	34.4%	9.6%

<https://www.frontiersin.org/articles/10.3389/fpubh.2020.00383/full>

Zoonotic transfer of Corona Viruses

SARS

Bats: the natural reservoir?



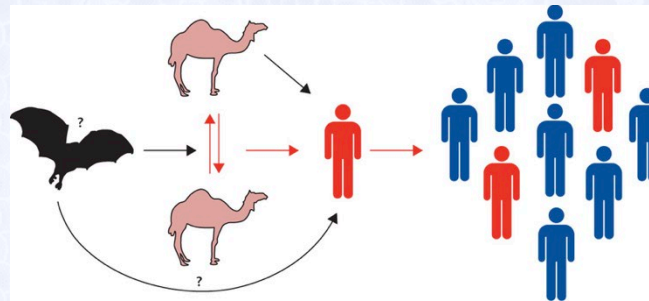
Evolution of RBM (+)

Palm civets: the interim reservoir



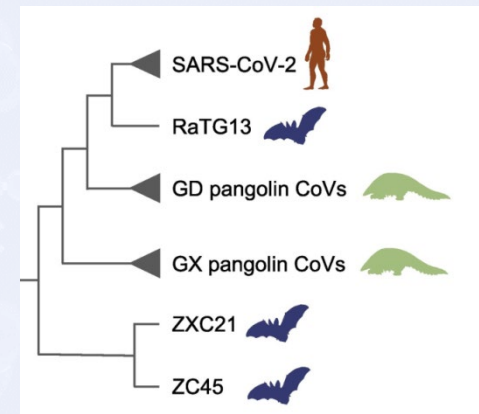
https://www.msi.umn.edu/~lifang/flpapers/fang_li_avr_sars_rbd_2013.pdf

MERS-CoV



Lancet Infectious Diseases
vol 15 pp495-497 (2015)

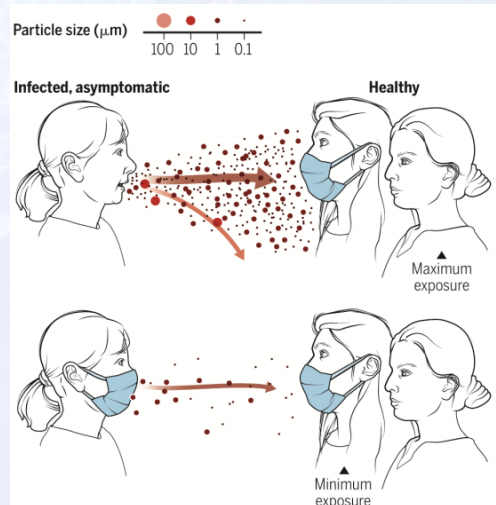
SARS-CoV-2



[https://www.cell.com/trends/microbiology/fulltext/S0966-842X\(20\)30090-1](https://www.cell.com/trends/microbiology/fulltext/S0966-842X(20)30090-1)

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COVID-19 Pathogenesis



Science vol **368** pp1422-1424 (2020)



Symptoms of CORONAVIRUS (COVID-19)



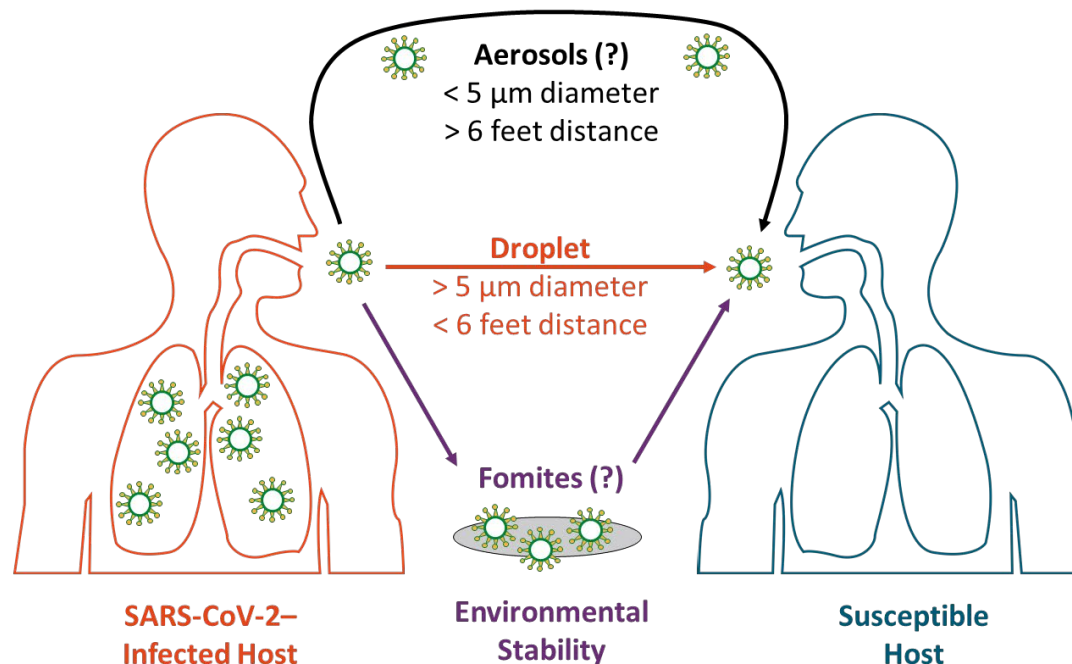
<https://www.theverge.com/2020/7/8/21317128/improved-covid-treatment-hospitals-remdesivir-dexamethasone>

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SARS CoV-2 Transmission

- Spread mainly from person-to-person.
- Spread in other ways.
- Spread between animals and people

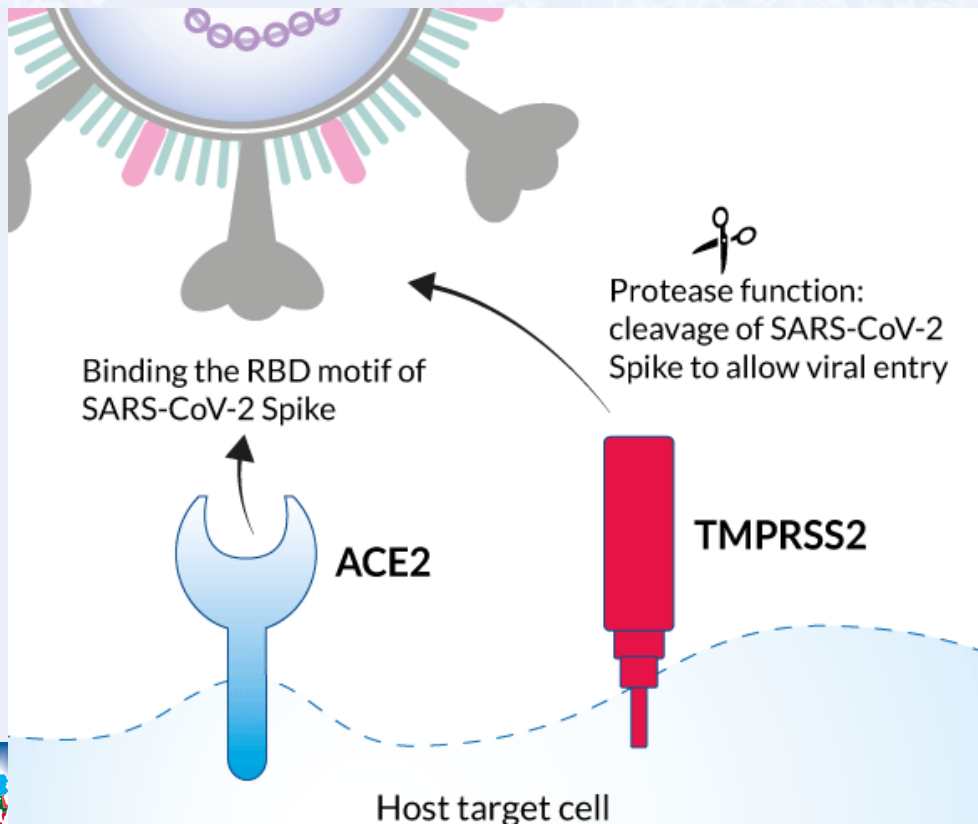
Proposed Routes of SARS-CoV-2 Transmission



SARS CoV-2 Replication Cycle

SARS CoV-2 entry into a host cell

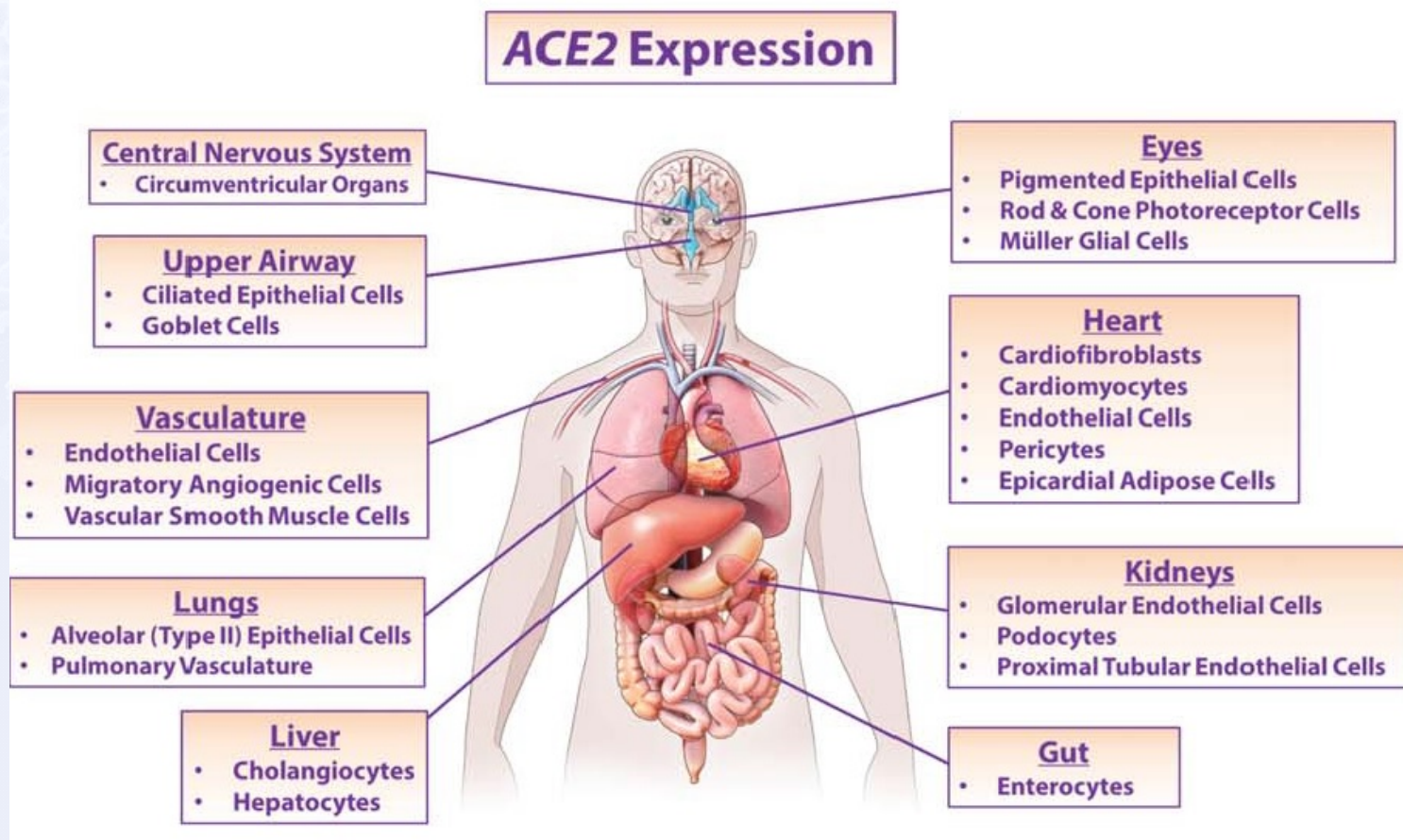
- SARS-CoV-2 use the receptor: ACE2 (angiotensin-converting enzyme 2) to infect cells.



<https://www.invivogen.com/ace2-and-tmprss2-expression-vectors>

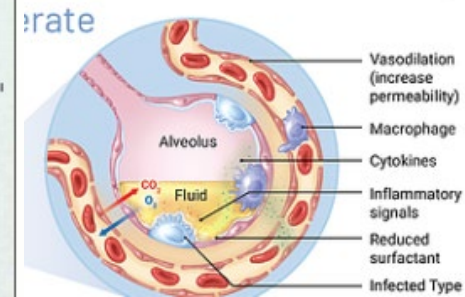
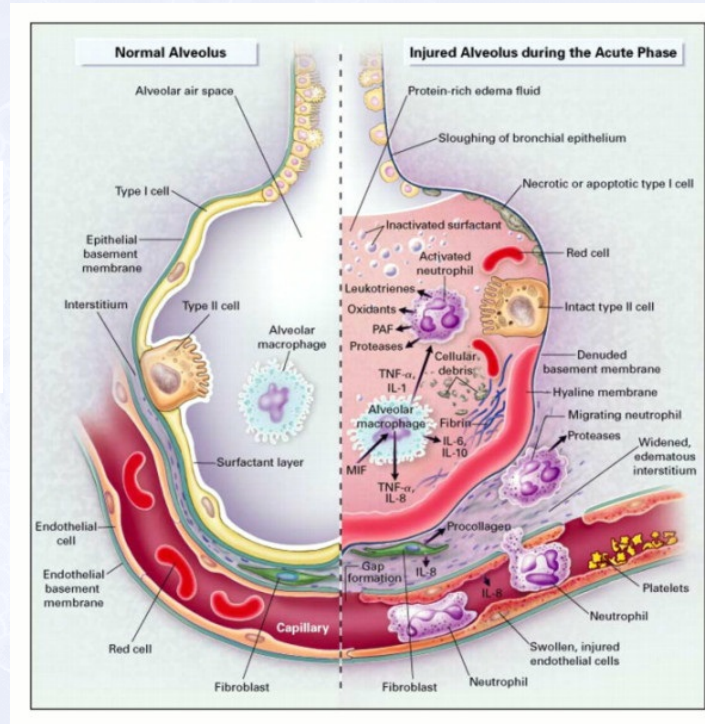
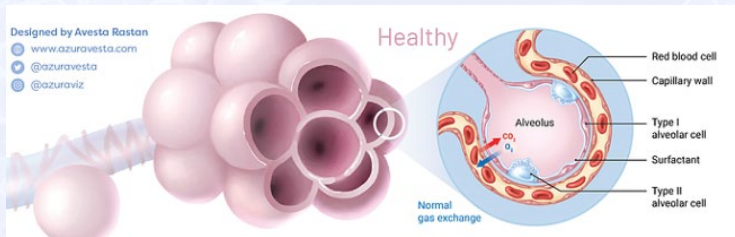
-06-2020

ACE2 Expression in Human Tissues



<https://hcs-pharma.com/biomimesys-hydroscaffold-for-your-coronavirus-related-research-in-3d/>

Immune System Activation and Cytokine Storm Syndrome



Hypoxemia
(low blood oxygen)

<https://asm.org/Articles/2020/June/The-Biology-and-Immunology-of-COVID-19-Susceptibil>

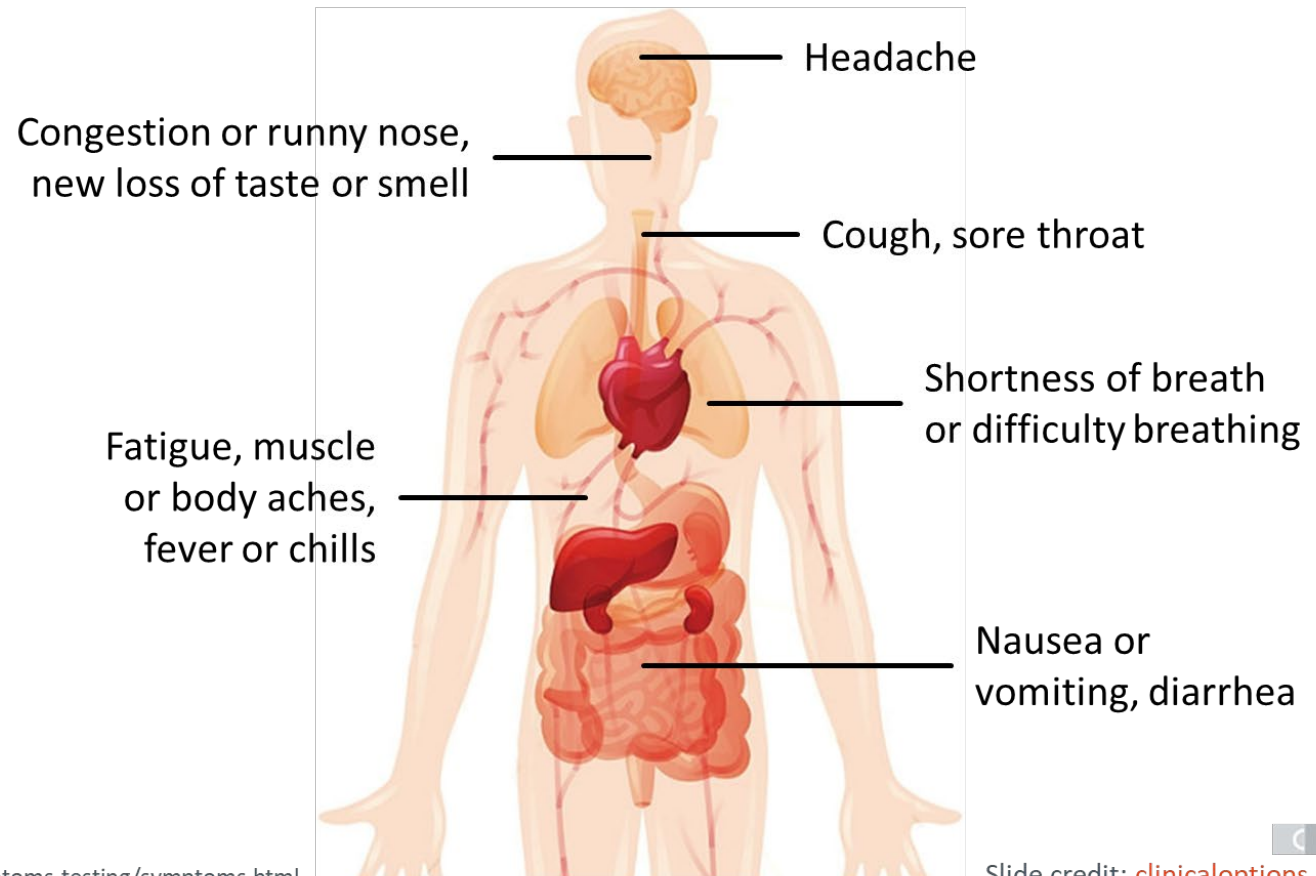
COVID-19 Clinical Symptoms

--Asymptomatic

--Symptoms ranging from mild symptoms to severe illness.

Primary Symptoms of COVID-19

“Symptoms may appear **2-14 days** after exposure to the virus.”



COVID-19 emergency warning signs:

- Trouble breathing
- Persistent pain or pressure in the chest
- New confusion
- Inability to wake or stay awake
- Bluish lips or face

COVID-19 Complications:

ARDS– Acute Respiratory Distress Syndrome

Heart Failure

Septic Shock

Coagulopathy --- Thrombotic Complications

Linda R. Frank, PhD, MSN, ACRN, FAAN

COVID-19 Complications:

ARDS– Acute Respiratory Distress Syndrome

Heart Failure

Septic Shock

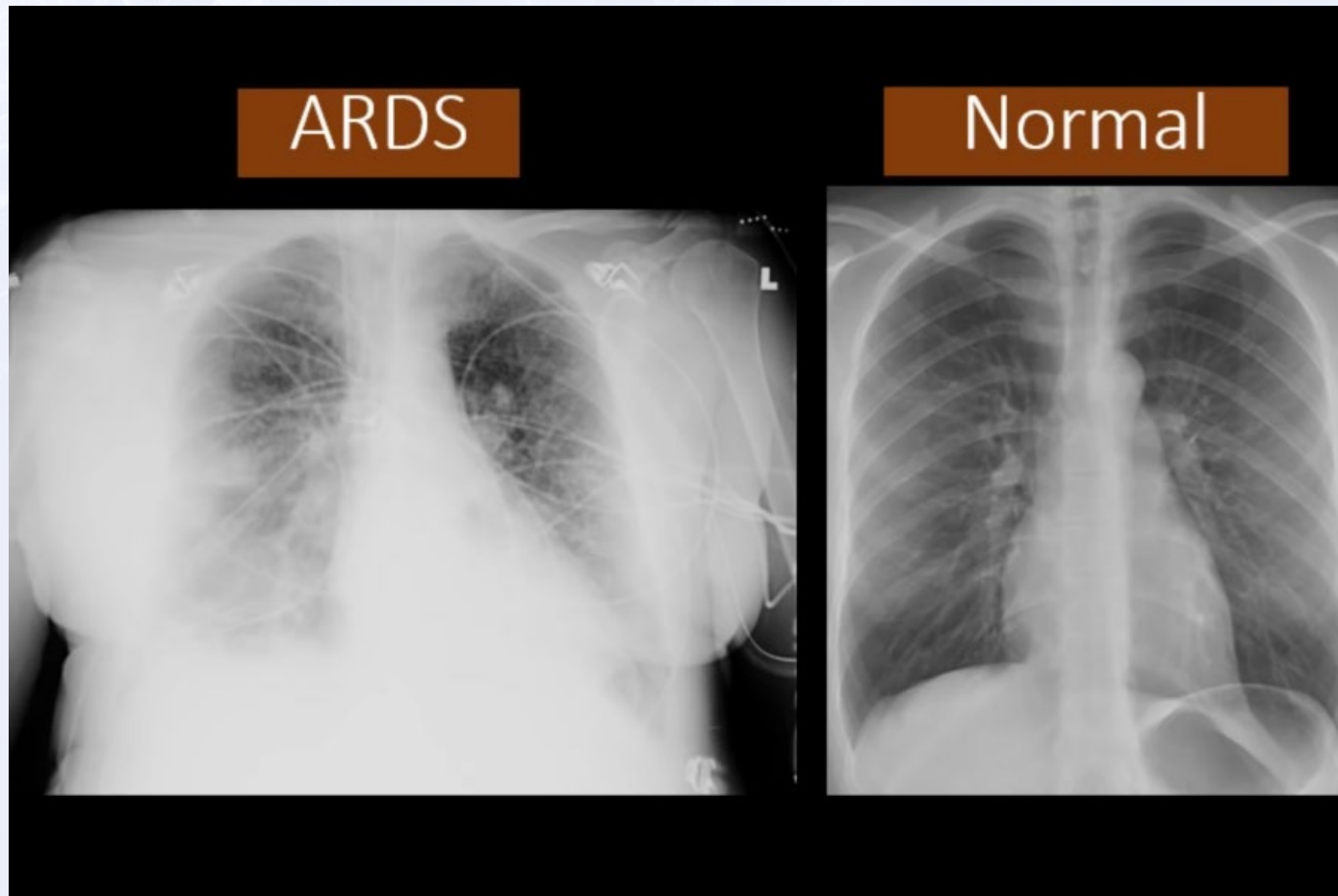
Coagulopathy --- Thrombotic



[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31305-2/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31305-2/fulltext)

Linda R. Frank, PhD, MSN, ACRN, FAAN

COVID-19 Complications:



Linda R. Frank, PhD, MSN, ACRN, FAAN

<https://www.airforcemag.com/for-recruits-covid-19-is-just-another-preexisting-condition/>

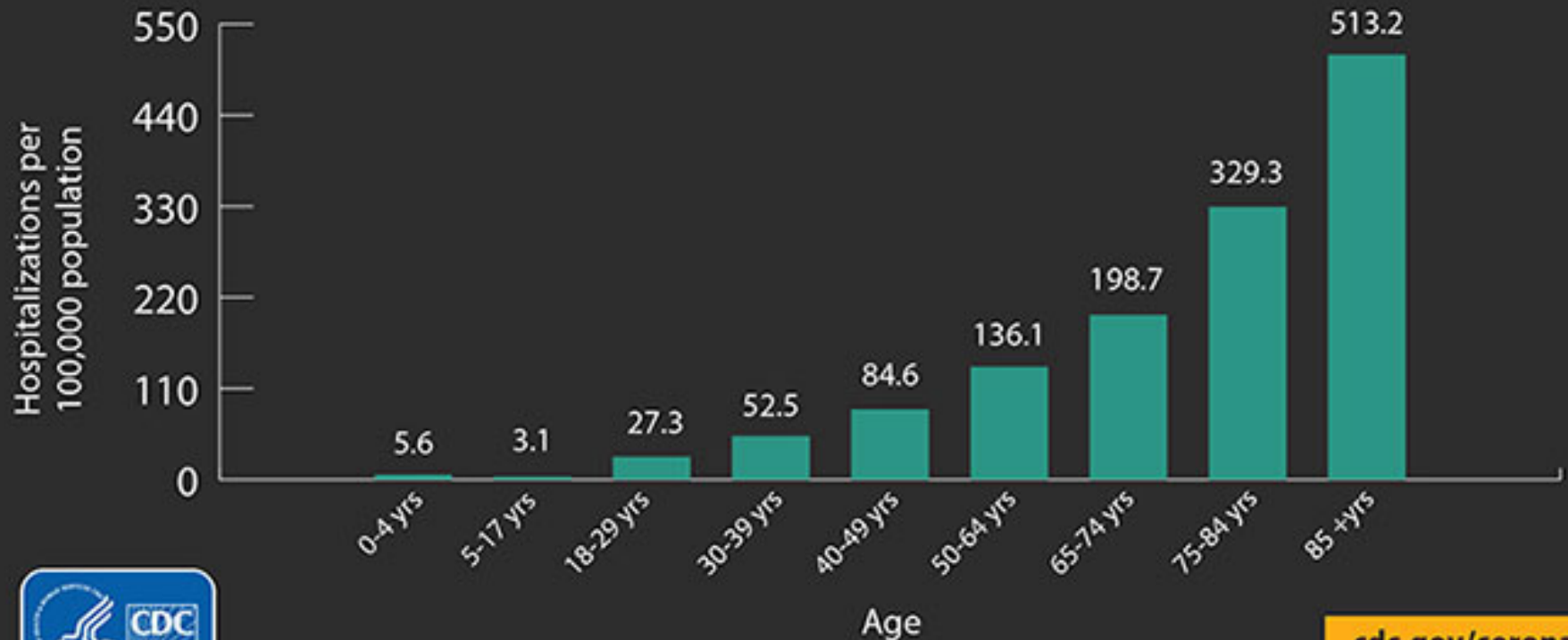
People at higher risk for severe illness

Older adults

NATIONAL CENTER FOR HEALTH STATISTICS (NCHS) MORTALITY REPORTING SYSTEM
 Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization
 Surveillance Network (COVID-NET)
 DATA THROUGH WEEK ENDING JUNE 6, 2020

**LATEST
DATA**

JUNE 6, 2020

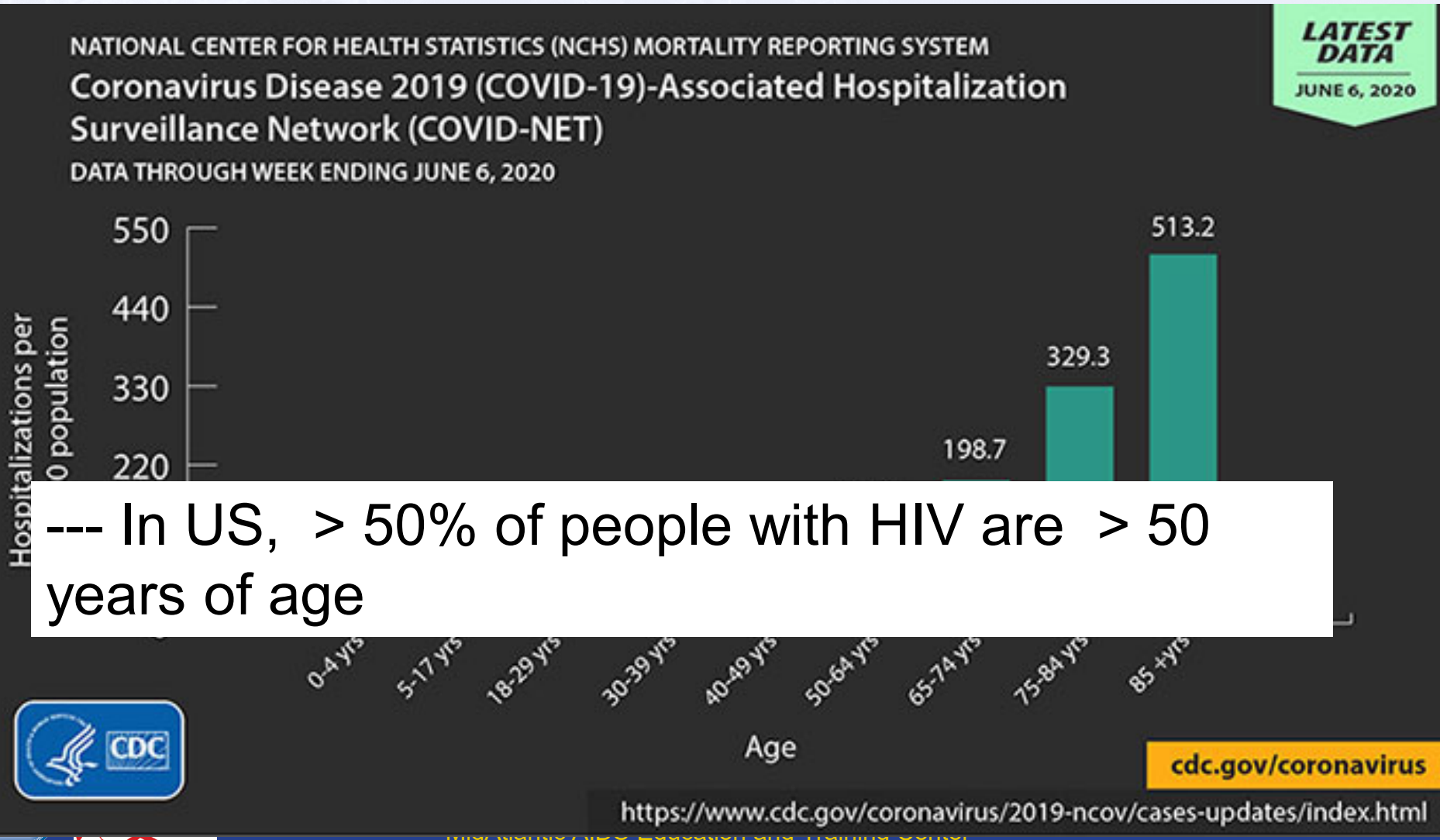


[cdc.gov/coronavirus](https://www.cdc.gov/coronavirus)

<https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/index.html>

People at higher risk for severe illness

Older adults



Risk Factors Associated with severe Illness

Older adults

People with underlying medical comorbidities:

COVID-19 ASSOCIATED HOSPITALIZATION RELATED TO UNDERLYING MEDICAL CONDITIONS

FACTORS THAT INCREASE COMMUNITY SPREAD AND INDIVIDUAL RISK



CROWDED
SITUATIONS



CLOSE / PHYSICAL
CONTACT



ENCLOSED SPACE



DURATION
OF EXPOSURE

RISK FOR HOSPITALIZATION IF YOU HAVE ANY OF THESE CONDITIONS AND
GET COVID-19 COMPARED TO PEOPLE WITHOUT THE CONDITION(S).



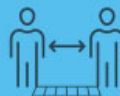
Data has shown that racial and ethnic minority groups with the referenced conditions are at even higher risk for severe COVID-19 illness. Race and ethnicity are risk markers for other underlying conditions that impact health — including socioeconomic status, access to health care, and increased exposure to the virus due to occupation (e.g., frontline, essential, and critical infrastructure workers).

*Conditions include asthma, obesity, diabetes, chronic kidney disease, severe obesity, coronary artery disease, history of stroke and COPD.

ACTIONS TO REDUCE RISK OF COVID-19



WEARING A MASK



SOCIAL DISTANCING
(6 FT GOAL)



HAND HYGIENE



CLEANING AND
DISINFECTION



ALTHOUGH RISK GENERALLY INCREASES WITH AGE, ALL INDIVIDUALS SHOULD ROUTINELY TAKE ACTIONS TO REDUCE RISK OF INFECTION AND AVOID ACTIVITIES THAT INCREASE COMMUNITY SPREAD.

cdc.gov/coronavirus

Source: Ko JY, Danielson ML, Town M et al. 2020.

CS319360-A 08/08/2020

Risk Factors Associated with severe Illness

Older adults

People with underlying medical comorbidities:

COVID-19 ASSOCIATED HOSPITALIZATION RELATED TO UNDERLYING MEDICAL CONDITIONS

FACTORS THAT INCREASE COMMUNITY SPREAD AND INDIVIDUAL RISK



CROWDED
SITUATIONS



CLOSE / PHYSICAL
CONTACT



ENCLOSED SPACE



DURATION
OF EXPOSURE

--- People with HIV have higher risk of comorbidities than HIV negative individuals of similar age.

*Conditions include asthma, obesity, diabetes, chronic kidney disease, severe obesity, coronary artery disease, history of stroke and COPD.

ACTIONS TO REDUCE RISK OF COVID-19



WEARING A MASK



SOCIAL DISTANCING
(6 FT GOAL)



HAND HYGIENE



CLEANING AND
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cdc.gov/coronavirus

Source: Ko JY, Danielson ML, Town M et al. 2020.

CS319360-A 08/08/2020

Risk Factors Associated with severe Illness

COVID-19 CASES, HOSPITALIZATION, AND DEATH BY RACE/ETHNICITY

FACTORS THAT INCREASE COMMUNITY SPREAD AND INDIVIDUAL RISK



CROWDED SITUATIONS



CLOSE / PHYSICAL CONTACT



ENCLOSED SPACE



DURATION OF EXPOSURE

Rate ratios compared to White, Non-Hispanic Persons

American Indian or Alaska Native, Non-Hispanic persons

Asian, Non-Hispanic persons

Black or African American, Non-Hispanic persons

Hispanic or Latino persons

CASES¹

2.8x higher

1.1x higher

2.6x higher

2.8x higher

HOSPITALIZATION²

5.3x higher

1.3x higher

4.7x higher

4.6x higher

DEATH³

1.4x higher

No Increase

2.1x higher

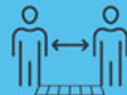
1.1x higher

Race and ethnicity are risk markers for other underlying conditions that impact health — including socioeconomic status, access to health care, and increased exposure to the virus due to occupation (e.g., frontline, essential, and critical infrastructure workers).

ACTIONS TO REDUCE RISK OF COVID-19



WEARING A MASK



SOCIAL DISTANCING (6 FT GOAL)



HAND HYGIENE



CLEANING AND DISINFECTION



¹ Data source: COVID-19 case-level data reported by state and territorial jurisdictions. Case-level data include about 80% of total reported cases. Numbers are unadjusted rate ratios.

² Data source: COVID-NET (<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html>, accessed 08/06/20). Numbers are ratios of age-adjusted rates.

³ Data source: NCHS Provisional Death Counts (<https://www.cdc.gov/nchs/nvss/vsrr/COVID19/index.htm>, accessed 08/06/20). Numbers are unadjusted rate ratios.

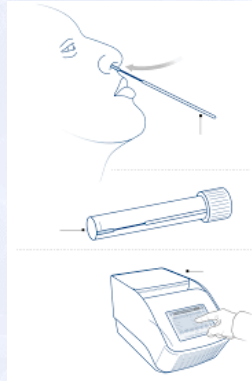
cdc.gov/coronavirus

CS319360-A 08/08/2020

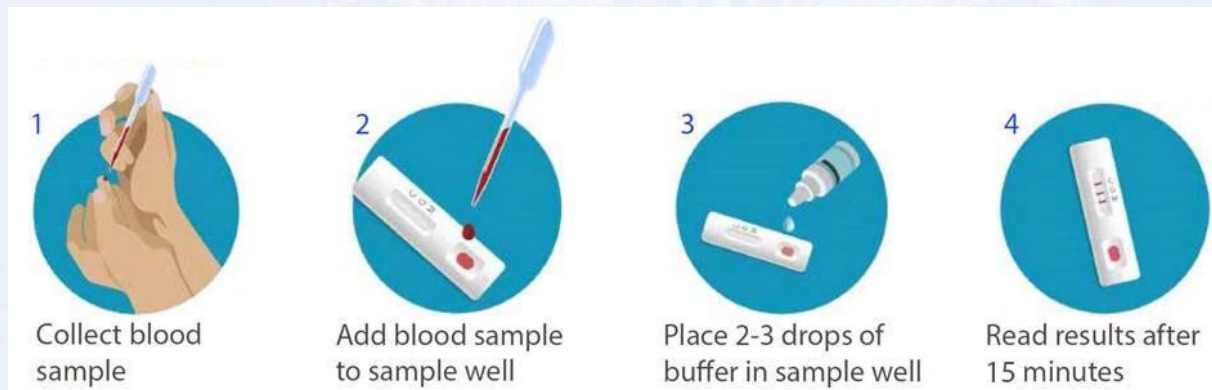
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COVID-19 Tests – FDA Emergency Use Authorizations (EUAs)

- Tests for current infection:



- Tests for past infection: An antibody test



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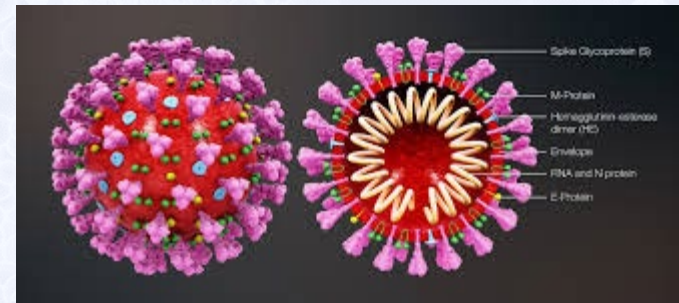
COVID-19 Tests – FDA Emergency Use Authorizations (EUAs)

- Diagnostic Tests:

Tests that detect parts of the SARS-CoV-2 virus and can be used to diagnose infection with the SARS-CoV-2 virus. These include molecular tests and antigen tests.

PCR

SARS CoV-2 Antigen Test



<https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas#individual-antigen>

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COVID-19 Tests – FDA Emergency Use Authorizations (EUAs)

Serology/Antibody Tests:

- -Tests that detect antibodies (e.g., IgM, IgG) to the SARS-CoV-2 virus. Serology/antibody tests cannot be used to diagnose a current infection.

COVID-19 Tests – FDA Emergency Use Authorizations (EUAs)

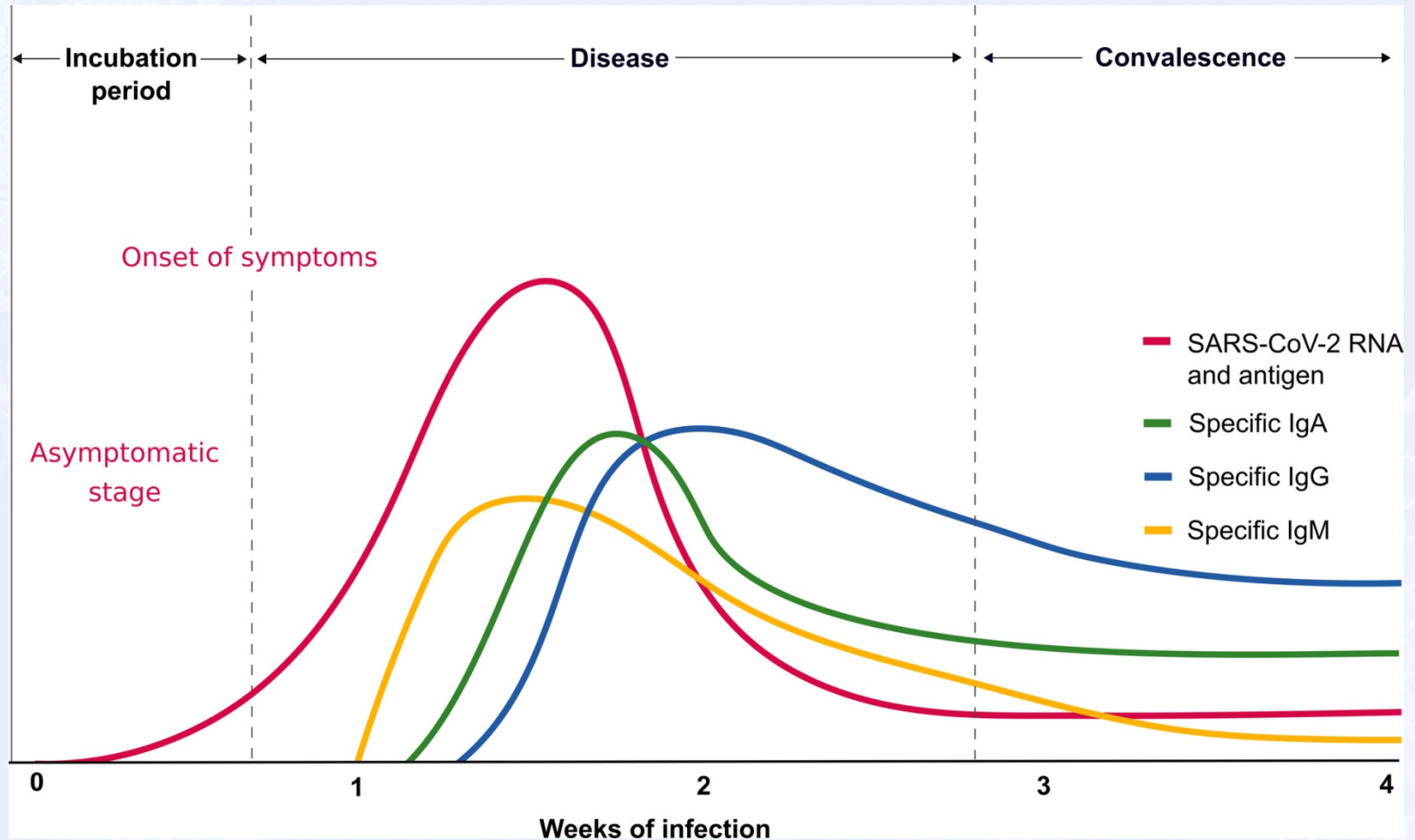
Tests for Management of COVID-19 Patients

- Tests that detect biomarkers related to inflammation. Once patients receive a COVID-19 diagnosis, these additional tests can be used to inform patient management decisions.



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Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19



Allergy, Volume: 75, Issue: 7, Pages: 1564-1581, First published: 12 May 2020, DOI: (10.1111/all.14364)

Linda R. Frank, PhD, MSN, ACRN, FAAN

How long can someone spread the virus after infection?

- It is still under investigation.
- It's possible for people to spread the virus for about 2 days before experiencing signs or symptoms and remain contagious for at least 10 days after signs or symptoms first appeared.
- If someone is asymptomatic, it's possible to remain contagious for at least 10 days after testing positive for COVID-19.

COVID-19 Treatment

-- Antiviral Therapy

Remdesivir

-- Immune-Based Therapy

COVID-19 convalescent plasma

SARS-CoV-2 immunoglobulins

-- Immunomodulators

Dexamethasone



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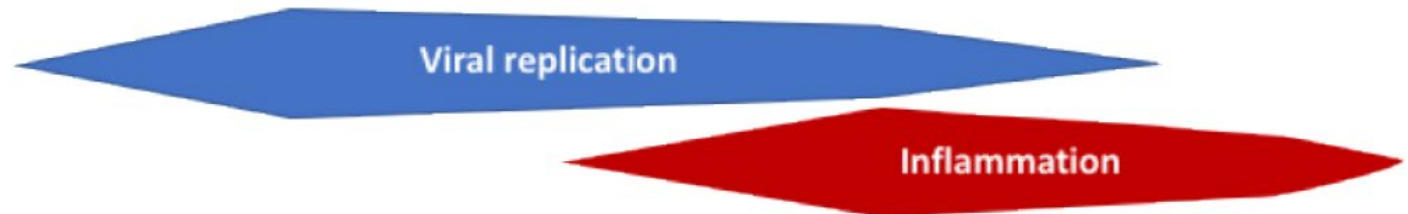
MidAtlantic AIDS Education and Training Center

Multidimensional Challenge of Treating COVID-19

Stage/
Severity:

Asymptomatic/ Presymptomatic	Mild Illness	Moderate Illness	Severe Illness	Critical illness
+ SARS-CoV-2 test but no symptoms	Mild symptoms (eg fever, cough, taste/smell changes); no dyspnea	O ₂ saturation $\geq 94\%$, lower respiratory tract disease	O ₂ saturation $< 94\%$, respiratory rate >30/min; lung infiltrates >50%	Respiratory failure, shock, multi-organ dysfunction/failure

Disease
Pathogenesis:



Potential
treatment:

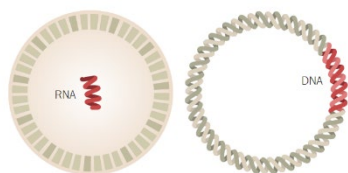


<https://pubmed.ncbi.nlm.nih.gov/32735655/>

COVID-19 Vaccine Development

Genetic Vaccines

Vaccines that use one or more of the coronavirus's own genes to provoke an immune response.

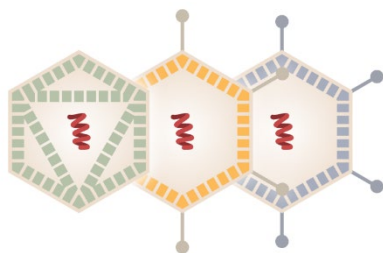


PHASE III

moderna **NIH** National Institutes of Health
Turning Discovery Into Health

Viral Vector Vaccines

Vaccines that use a virus to deliver coronavirus genes into cells and provoke an immune response.



PHASE II PHASE III COMBINED PHASES

AstraZeneca **UNIVERSITY OF OXFORD**

Protein-Based Vaccines

Vaccines that use a coronavirus protein or a protein fragment to provoke an immune response.

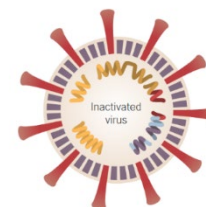


PHASE II

ZFSW **INSTITUTE OF MEDICAL BIOLOGY**
The Beijing Company CHINESE ACADEMY OF MEDICAL SCIENCES

Whole-Virus Vaccines

Vaccines that use a weakened or inactivated version of the coronavirus to provoke an immune response.



PHASE III

武汉生物制品研究所有限责任公司
WUHAN INSTITUTE OF BIOLOGICAL PRODUCTS CO.,LTD.

The New York Times, July 27th 2020

FDA sets rules for the three phases of clinical trials of a vaccine candidate

Phase 1: 20-100 health volunteers

Phase 2: several hundred volunteers

Phase 3: hundreds or thousands of volunteers

FDA licenses the vaccine only if:

- it's safe and effective
- benefits outweigh risks

Linda R. Frank, PhD, MSN, ACRN, FAAN

Covid-19 Drugs & Vaccines Tracker

Company	University of Oxford and AstraZeneca
Stage	Phase 3
Updates	<p>Aug. 31: AstraZeneca begins enrollment in a U.S. Phase 3 trial that will involved 30,000 volunteers.</p> <p>Sept. 8: AstraZeneca says a hold has been put on the trial following a suspected adverse reaction in a participant.</p>

<https://www.statnews.com/feature/coronavirus/drugs-vaccines-tracker/>

Linda R. Frank, PhD, MSN, ACRN, FAAN

Covid-19 Drugs & Vaccines Tracker

Company	Moderna Therapeutics
Stage	Phase 3
Updates	July 27: Moderna begins enrollment in a 30,000-subject Phase 3 trial.

<https://www.statnews.com/feature/coronavirus/drugs-vaccines-tracker/>

Linda R. Frank, PhD, MSN, ACRN, FAAN

Covid-19 Drugs & Vaccines Tracker

Company	BioNTech and Pfizer
Stage	Phase 3
Updates	July 27: Pfizer and BioNTech begin enrollment on a 30,000-volunteer study, expecting data as early as October.

<https://www.statnews.com/feature/coronavirus/drugs-vaccines-tracker/>

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COVID-19 and HIV Infection

Is HIV a risk factor for COVID-19?

- People with HIV and on effective antiretroviral treatment (ART) are not at greater risk of getting coronavirus.
- People with HIV not on treatment or virally suppressed may be at a greater risk.

<https://www.avert.org/coronavirus/covid19-HIV>

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Is HIV a risk factor for severe COVID-19?

- There are no data indicating that people with HIV will get sicker than people without HIV or will have worse outcomes.
- Heightened awareness for severe disease should be considered for persons with HIV, particularly those who have other comorbidities associated with worse COVID-19 outcomes or CD4+ T cells $<200/\text{mm}^3$ and viral loads $>1000/\text{ml}$.
- Antiretroviral therapy should be continued during hospitalization for COVID-19 without interruption and changes in therapy are generally not recommended.
- Medications used for treatment of COVID-19 may interact with some HIV medications.

<https://www.idsociety.org/globalassets/idsa/public-health/covid-19/covid-19-special-considerations.pdf>

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Do HIV medications have activity against SARS CoV-2?

None of our HIV medicines has been proved to have an effect against Covid-19

Lopinavir/ritonavir

- Lopinavir/ritonavir inhibit SARS-CoV protease in vitro
- Results from large randomized clinical trials show: No effect in vivo.

Cao B, NEJM, 2020 <https://www.nejm.org/doi/full/10.1056/NEJMoa2001282>

Ann Int Med, 2020 <https://www.acpjournals.org/doi/10.7326/M20-1550>

Linda R. Frank, PhD, MSN, ACRN, FAAN

What is the impact of COVID-19 on HIV Care?

- WHO survey: there are significant disruptions in access to HIV treatment because of COVID-19.
- Survey of >13500 LGBTI+ people in 138 countries: 26% of people with HIV reported difficulty with access to ART refills
- Disruption in PrEP care in the US: especially among vulnerable subpopulations

Linda R. Frank, PhD, MSN, ACRN, FAAN

People with HIV

- All patients should be educated on the importance of following the CDC guidelines to promote physical distancing and to wear face coverings in public to reduce spread of the virus.
- Changes in antiretroviral therapy to prevent or treat COVID-19 are generally not recommended.
- Laboratory monitoring for HIV remains important and should follow current guidelines.
- Patients should maintain at least a supplemental 30-day supply of their medications to prevent the possibility of treatment interruptions.

<https://www.idsociety.org/globalassets/idsa/public-health/covid-19/covid-19-special-considerations.pdf>

Linda R. Frank, PhD, MSN, ACRN, FAAN



MidAtlantic AIDS Education and Training Center - Contact Information

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Principal Investigator and Program Director
Professor of Public Health, Medicine & Nursing
University of Pittsburgh

