The impact of COVID-19 on HIV Practice

AMERICAN ACADEMY OF HIV MEDICINE Webinar April 1, 2020

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Objectives

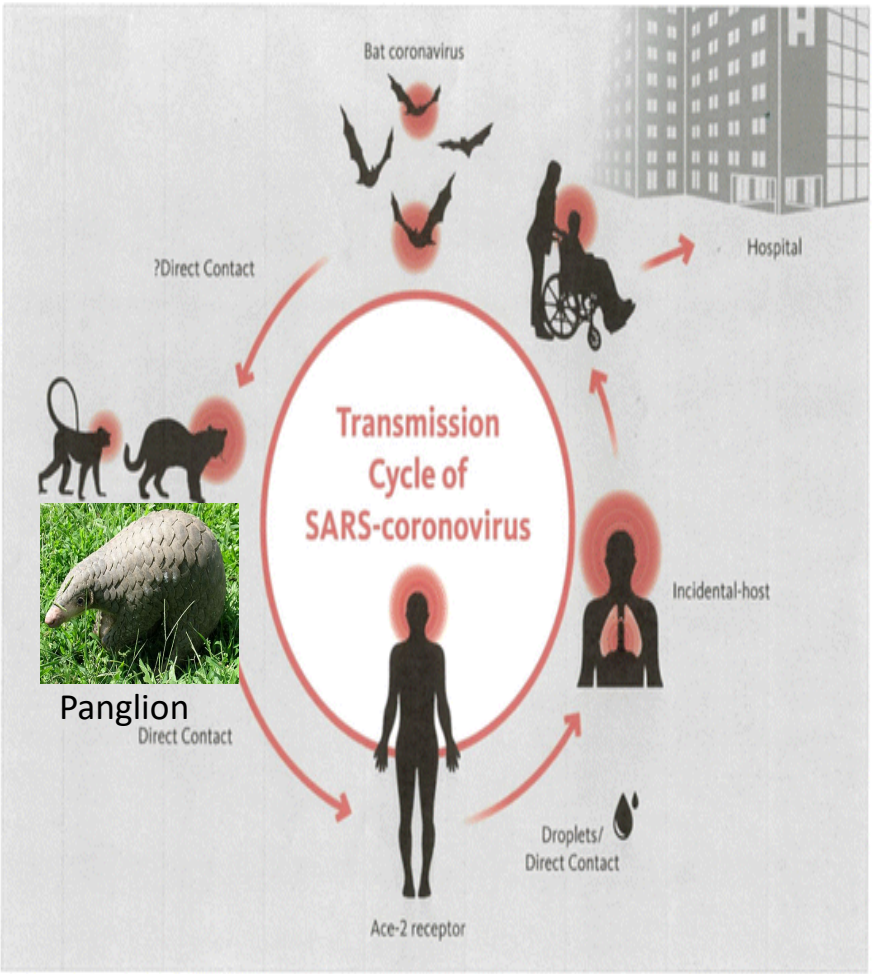
- To understand the latest epidemiological data on COVID-19
- Appreciate the latest clinical evidence on COVID -19
- Review the most recent US guidelines for persons with HIV

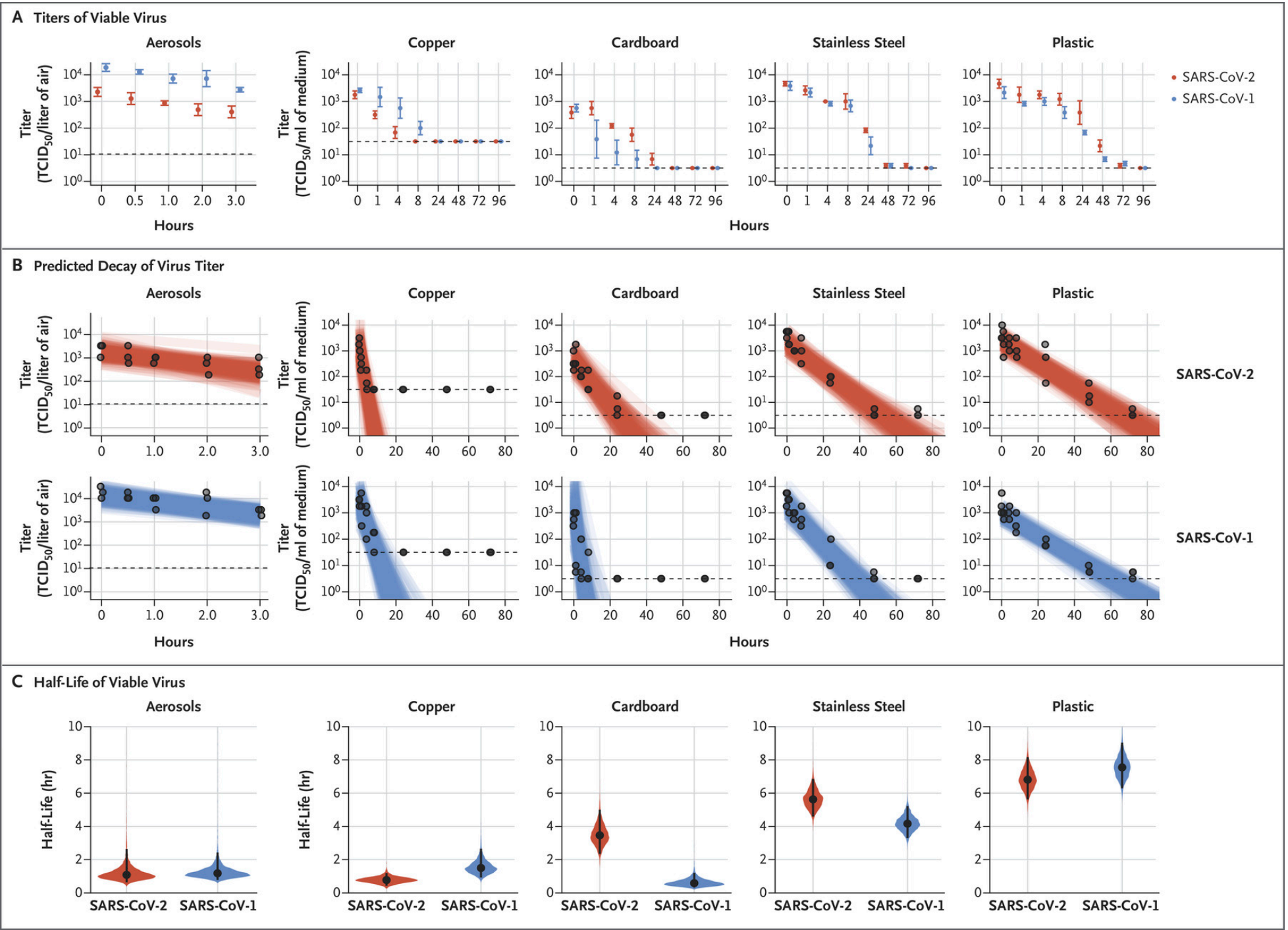
Epidemiology

- COVID-19 caused by Severe Acute Respiratory Syndrome Corona Virus 2- SAR Cov 2, Single Stranded RNA Virus- Corona Virus Family (influenza)
- Transmission may occur from both symptomatic (80%) and asymptomatic (20%) patients, with secondary infection rates ranging 0.5-5%.
- No underlying population immunity
- The median incubation time is 4-5 days and 97.5% will experience symptoms within 11.5 days of exposure.
- The serial interval is between 5-6 days (time between successive cases)
- Ro- 2-3 (Infectivity) 1 person can pass on to 2- 3 persons

Mode of Transmission

- Direct Contact
- Respiratory droplets
- Faeco-oral –detected in stool
- Perinatal limited data
- Zoonotic Transmission – Bats, Mammals



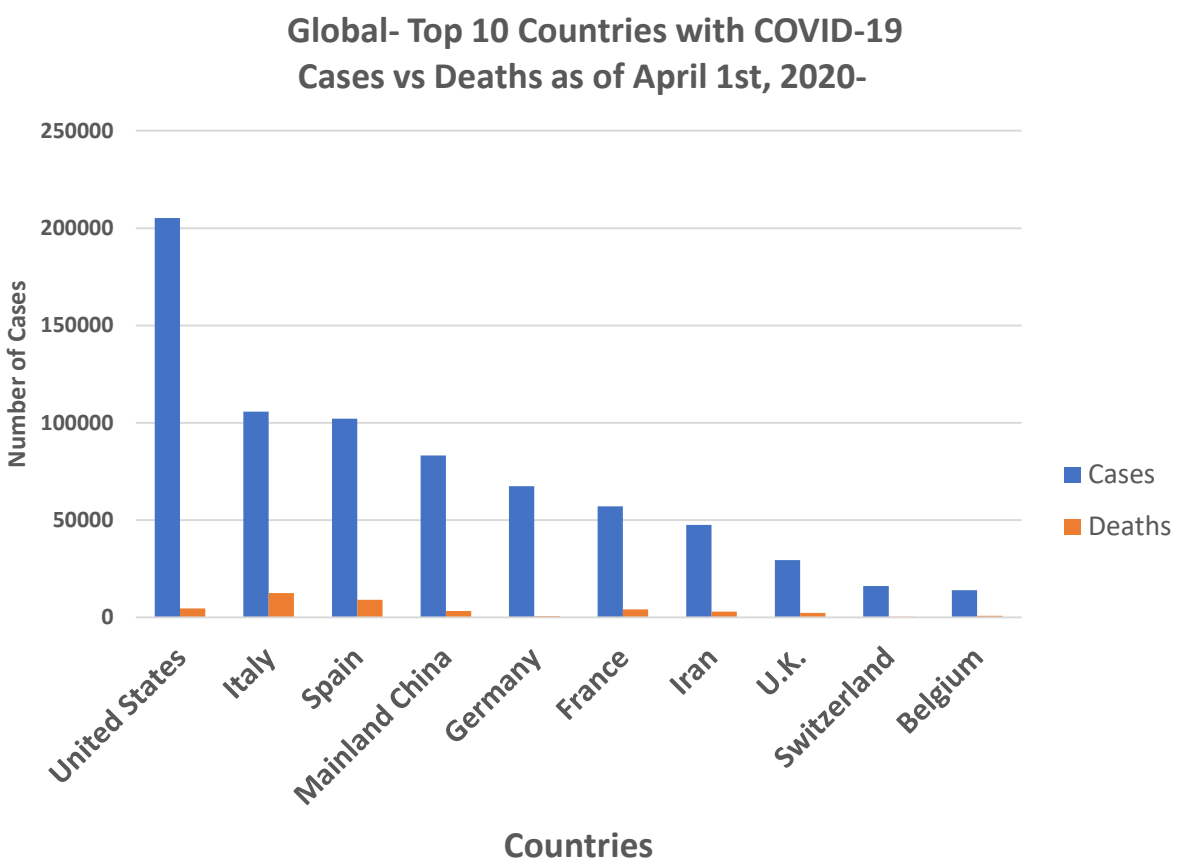


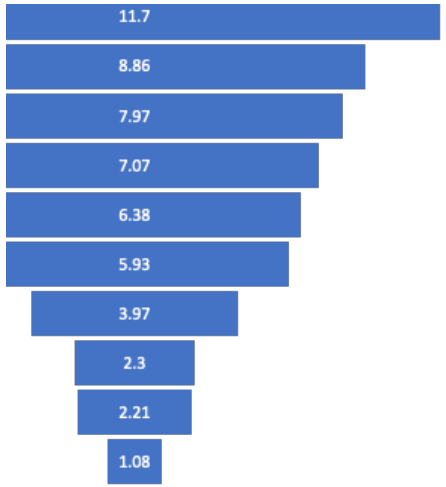
Viability of SAR-CoV-2

- **Plastic** – 72 hours
- **Stainless steel-** 48 hours
- **Cardboard** – 24 hours
- **Copper-** 4 hours
- **Airborne**- 3 hours

Source: Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. New England journal of Medicine. March 17, 2020

Global- Epidemiology





Source: Johns Hopkins Corona Virus Resource Center April 1, 2020

US- Epidemiology

- Washington State has recorded a decrease in their case fatality rate of 10.2 % over the last 5 days after having recorded the first case of COVID-19
- Epicenter of the pandemic is in New York with the most cases , deaths and fastest increase in case fatality rates.
- Louisiana and Washington have the has the highest case fatality rates of above 4.2%
- There has been a 31.6 % increase in the case fatality over the last 5 days for the top 10 States.
- “Hot spots” are developing in different cities

Table1. COVID-19 Analysis of Top 10 US States as of April 1, 2020

State	Cases	Deaths	Case Fatality Rate%	% CFR in 5 days
New York	83,760	1,941	2.32	86.0
New Jersey	22,255	267	1.20	1.81
California	8,582	183	2.13	6.29
Michigan	7,630	264	3.46	36.7
Florida	6,955	87	1.25	9.63
Massachusetts	6,620	89	1.34	23.0
Louisiana	6,424	273	4.25	-1.97
Illinois	5,994	107	1.78	40.4
Pennsylvania	5,805	74	1.27	22.2
Washington	5,292	226	4.27	-10.2
TOP 10 States	159,317	3511	2.20	31.6

Source: Johns Hopkins Corona Virus Resource Center April 1, 2020

High Risk Groups

- Within the next few years more than half of the people living with HIV in the US will be over 50 yrs

(The HIV and Aging Consensus Project.) Abrass, Christine K., et al.)

- Multimorbidity syndrome is increasing in the Aging HIV populations i.e heart disease, diabetes, smoking, alcohol)

(Greene 2013 : Greene 2015; Singh 2017: Greene 2017)

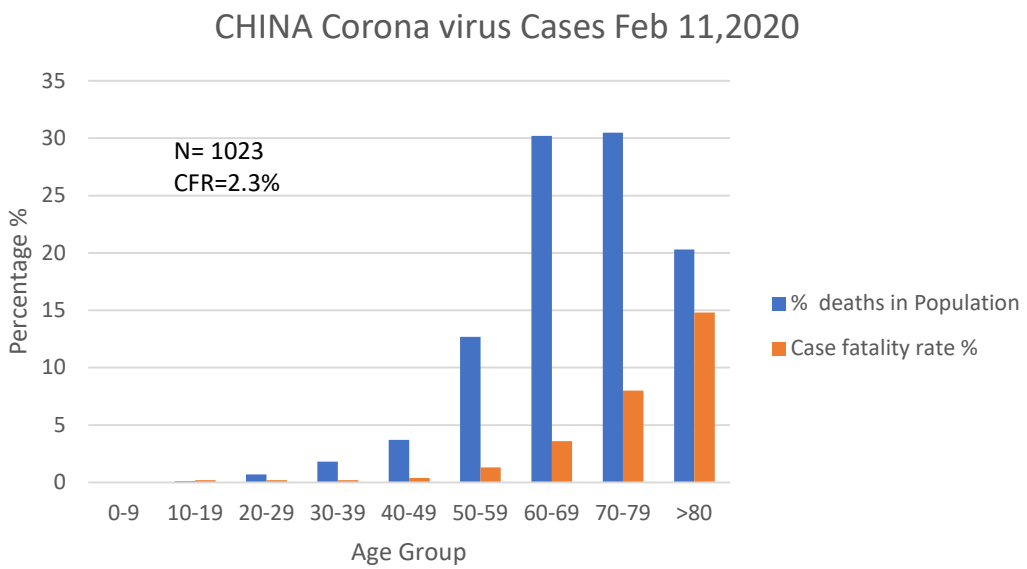
- “HIV disproportionally affects the most vulnerable in society”

(Policy position statement. American Academy of HIV Medicine)

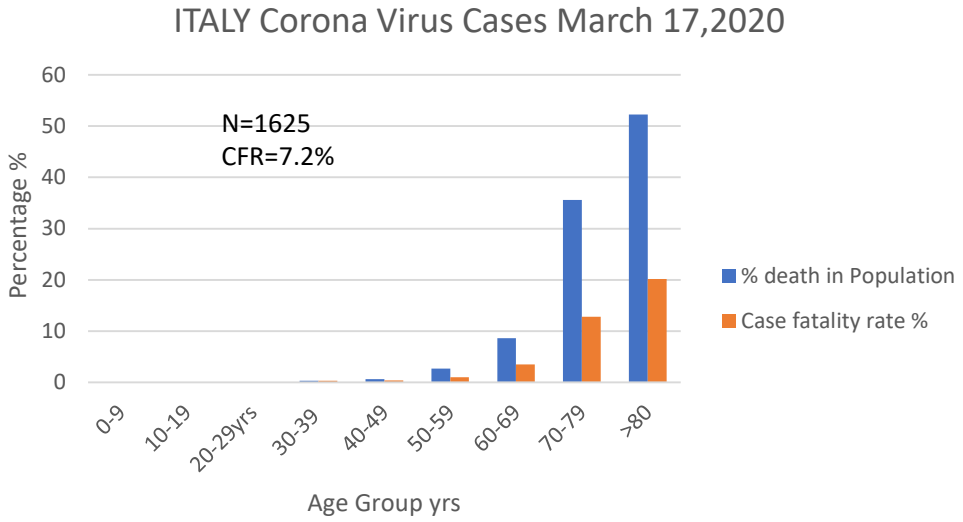
COVID-19-Vulberable Groups

World Health Organization

RISK FACTORS- Age Distribution and Patient Death



Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. *JAMA.* Published online March 23, 2020.



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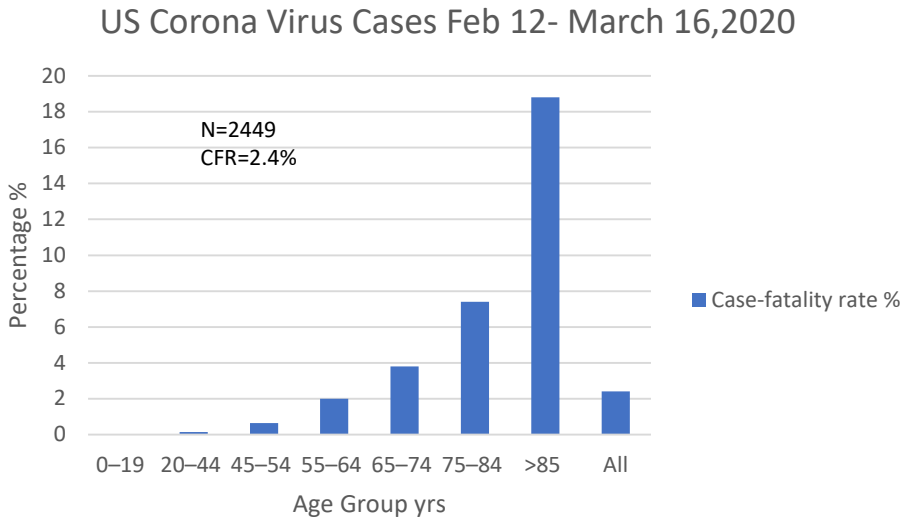
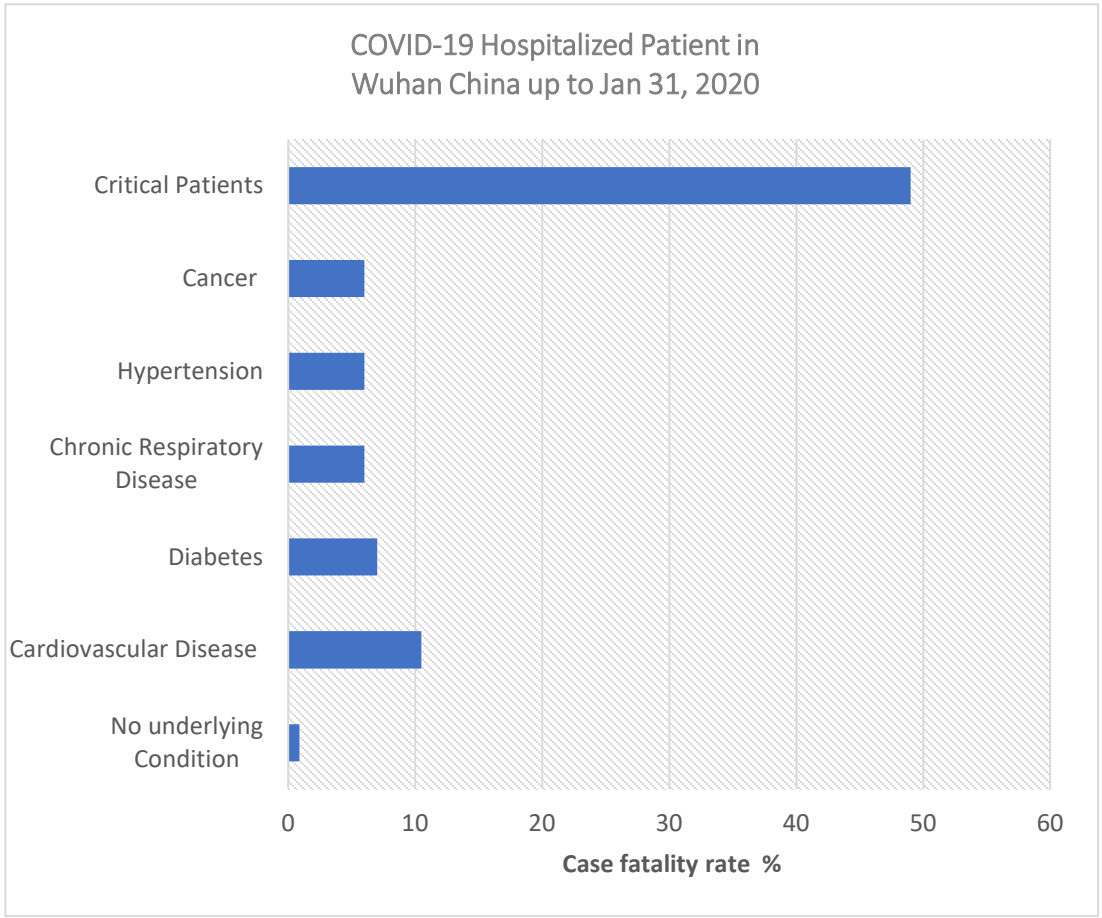


Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020 Morbidity and Mortality Report*Weekly* / March 26, 2020 / 69(12);343-346

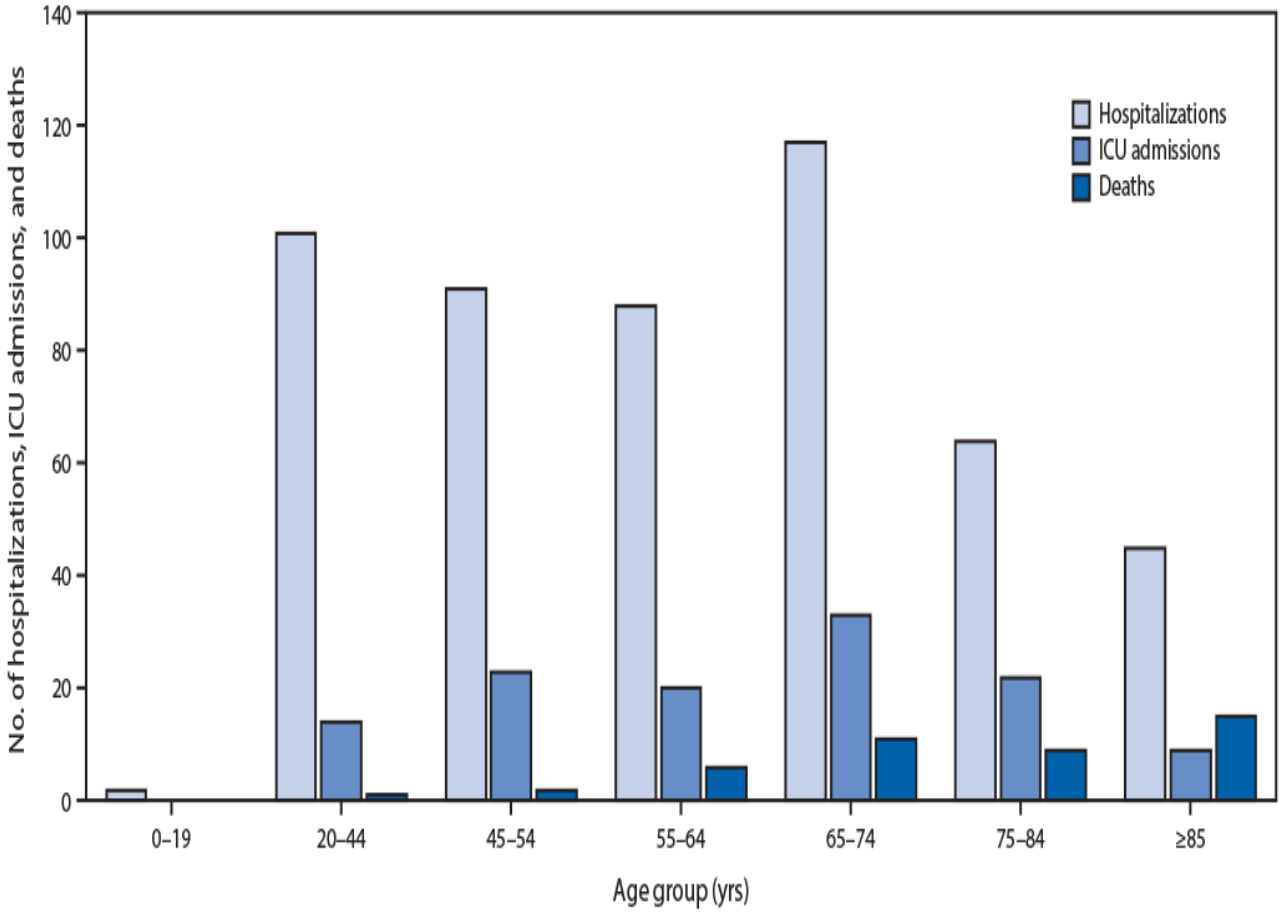
Hospitalizations

China Hospitalizations Wuhan Jan 2020



Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Fei Zhou*,. The Lancet March 12,2020

FIGURE 1. Coronavirus disease 2019 (COVID-19) hospitalizations,* intensive care unit (ICU) admissions,† and deaths,§ by age group — United States, February 12– March 16, 2020



Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020 Morbidity and Mortality Report*Weekly* / March 26, 2020 / 69(12);343-346

PATHOGENESIS

Similar Mechanisms to SARS-CoV and MERS-CoV

Cell Entry

- Mediated by its envelope spike glycoprotein binding to its cellular receptor, Angiotensin Converting Enzyme 2 receptor on host cells myocytes and vascular endothelial cells in lung, hear kidney.

Replication

- Virus genome released in cytoplasm. Translation of MRNA in cytoplasm combined with RNA synthesis. Packing in Golgi complex. Release by fusion with cell membrane.

Antigen Presentation

- Similar presentation with SAR-Cov in terms of MH1-MH2 have been suggested

Coronavirus Evasion

- Avoids host detection of its dsRNA through lack of production of double-membrane vesicles that lack Pattern recognition receptors (PRR).
- Downregulation of IFN 1 which and Gene expression for antigen presentation

Cytokine Storm in COVID-19 –

- Uncontrolled systemic inflammatory response leading to release of proinflammatory cytokines (IL-6, TNF-α, and chemokines ((CCL2,CXCL10, etc.) by immune effector cells in SAR Cov
- .Cytokine storm will trigger a violent attack by the immune system to the Body leading to ARDS , multiple organ failure and death.

- **Humoral and cellular Immunity :**
  - Produces Specific IgM and IgG antibodies. IgM disappears at 12 weeks, IgG can last for a long time.
  - Despite severe decrease of $CD4^+$ T and $CD8^+$ T cells in acute phase , $CD4^+$ and $CD8^+$ memory T cells can persist for four years and can perform T cell proliferation, DTH response and production of IFN-γ

Li. Xiaowei. Journal of pharmaceutical analysis. March 2020Molecular immune pathogenesis and diagnosis of COVID-19

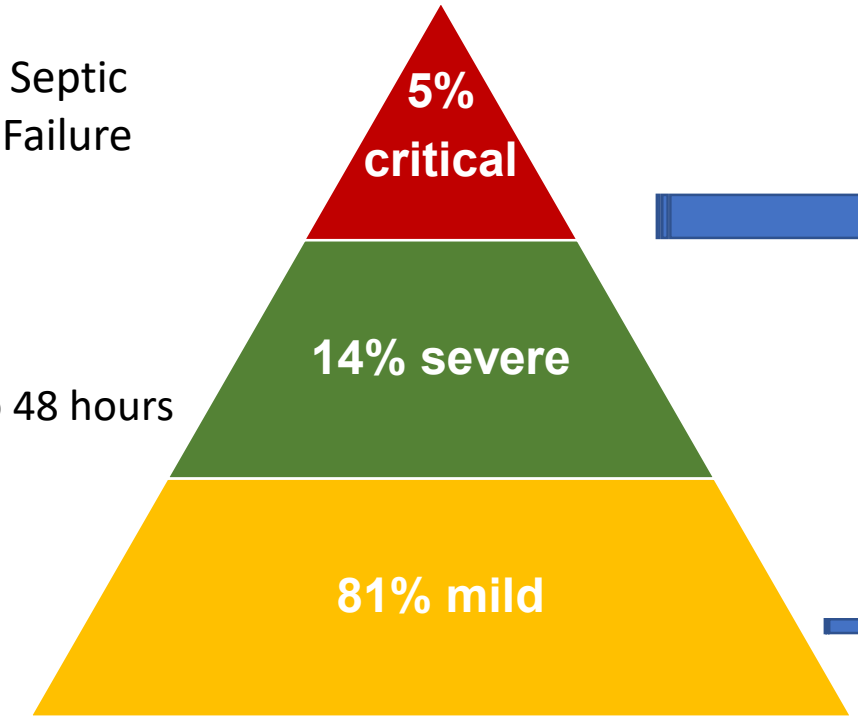
SIGNS and SYMPTOMS

Spectrum of COVID-19 Clinical Manifestations

Respiratory Failure, Septic Shock, Multi-organ Failure

Dyspnea, RR rate ≥30/min,
O2 saturation ≤93%, PaO2 /FIo2 <300
and/or lung infiltrates >50% within 24 to 48 hours

No Pneumonia &
Mild Pneumonia cases



- Most Common symptoms
  - Dry cough with sputum (67.7%)
  - Fever 38.4 C, 100 F (88%)
  - Fatigue (11-52%)
  - Shortness of breath (3-31%)
  - Diarrhea and nausea (4-15%
  - Rhinorrhea (4.8%)

China CDC Weekly 17 Feb 2020

Radiological and Laboratory Findings

Laboratory Findings

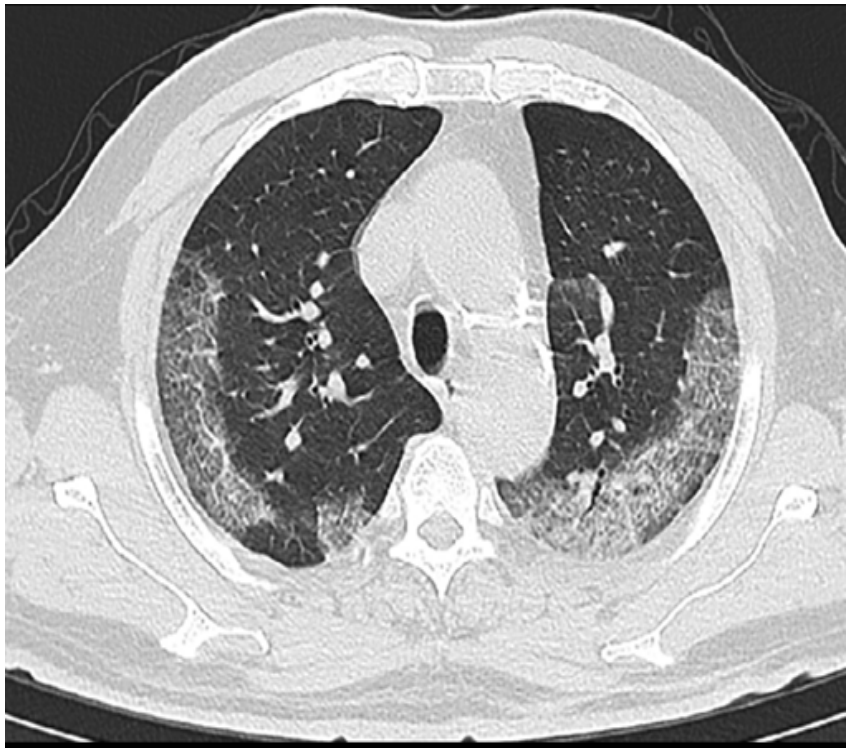
- COVID-19 Lymphocytopenia (83%), Thrombocytopenia (36%), Leukopenia (34%)
- LFT's- Elevated ALT, ALP, GGT

Severe disease risk (14%)

- Increase in Proinflammatory cytokines (IL-6, IFN-α, and CCL5)
- Low sequential organ failure assessment score (SOFA)
- Increase Anticoagulant PT, INR , D-Dimer > 1 µg/mL
- Decreased CD+, CD8+ cells/ul ,
- High sensitivity cardiac troponin 1, Lactate dehydrogenase
- Increase creatinine, procalcitonin

(ARDS, Kidney failure, Septic shock, , Multi-organ failure)

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospectivecohort study. Fei Zhou*,



High Resolution CT Scan- Bilateral pulmonary parenchymal ground-glass and consolidative pulmonary opacities, sometimes with a rounded morphology and a peripheral lung distribution.

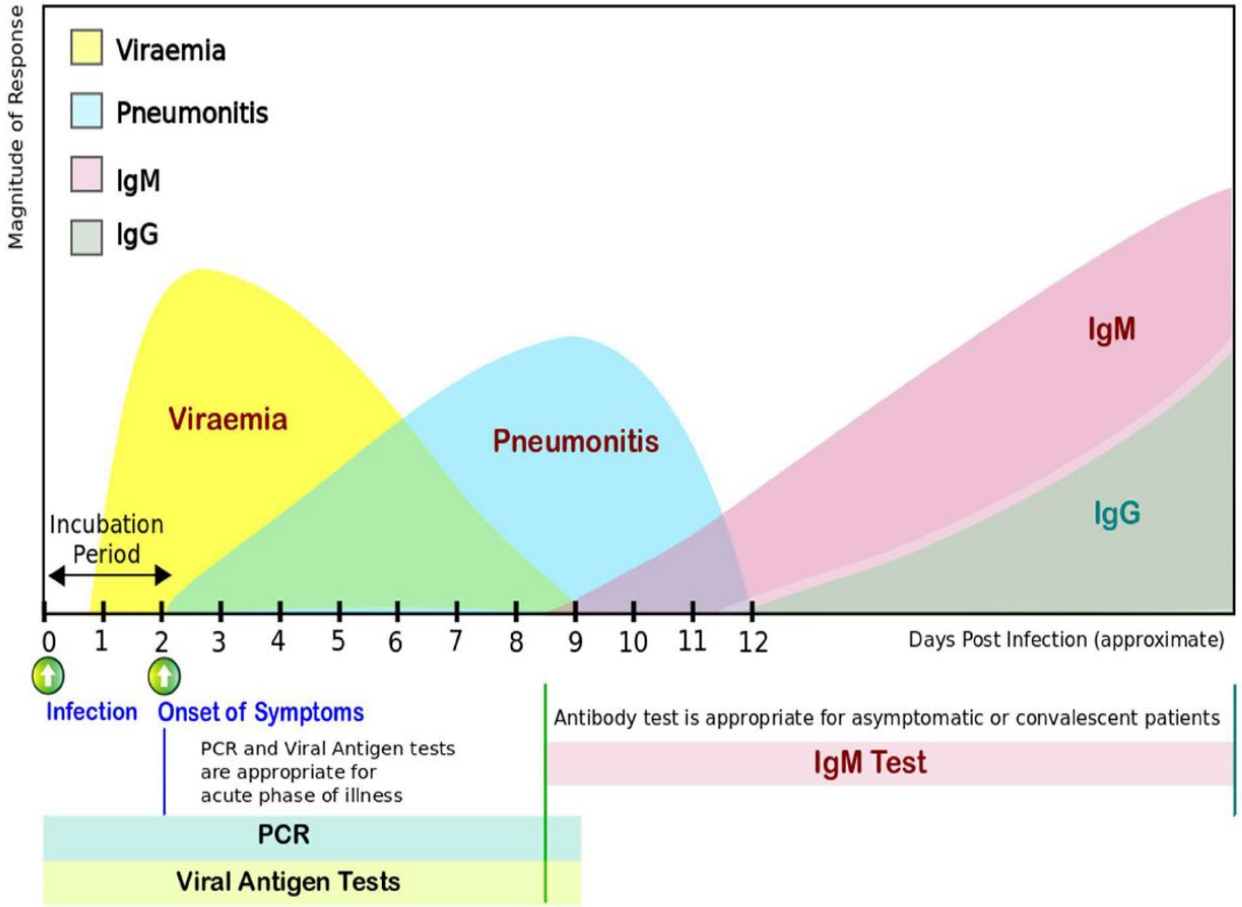
(Risk for Chronic interstitial lung damage)

Journal of Pharmaceutical Analysis, March 2020

Diagnosis

Clinical diagnosis is based on epidemiology history, clinical manifestations and auxiliary examinations such as,

- **Nucleic Acid detection Technology-** (RT-qPCR) (most common straight forward method of detection in respiratory secretions nasal or pharyngeal swab and blood
- Immune identification technology (Point-of-care Testing (POCT) antibody of IgM/IgG , Elisa
- Virus Blood culture and genome sequencing- Authoritative
- High resolution Chest CT- sensitive (HRCT)
- Combination: RT-PCR and HRCT = high yield



Illustrative graphic of Disease Progression and laboratory test for COVID-19: CMLF

Journal of Pharmaceutical Analysis, March 2020

TREATMENT STRATEGIES

There is no FDA approved Drugs to Treat Corona virus

CDC Recommended Treatment: Infection Prevention and Control and Supportive Care: Oxygen Therapy, Ventilation as needed

Class	Drug	Mechanism of Action	Status
Viral Target Inhibitor-broad spectrum	Remdesivir	Adenosine analog blocks RNA synthesis and viral replication	Clinical Trials-NIH Orphan Drug rescinded by Gilead
Viral inhibitor/ Antibiotic	Hydroxychloroquine Azithromycin	PH and antiviral effect invitro	Clinical Trial – WHO Clinical Trial
Immunotherapy	Convalescent Plasma	Neutralizing antibodies from recovered patient	FDA approved Investigational New Drug Application (IND)
Protease Inhibitor	Lopinavir/Ritonavir	Inhibits viral protease synthesis	Not found to be effective in recent Clinical trial in China. WHO Clinical Trail ongoing
Humanized IgG4 monoclonal antibody (mAb)	Leronlimab	Binds to hydrophilic extracellular domains on CCR5 and competitively inhibits CCR5-mediated HIV-1 viral entry.	Clinical Trial – FDA Granted emergency access. CytoDyn Inc.
Vaccine	mRNA-1273	Illicit protective immune response to virus antigen	Clinical Trial NIH Phase 1

Source: CDC, NIH

Infection Prevention and Control-COVID-19

- Universal Safety Precautions
- Disinfect office and clean services often
- Hand washing
- Respiratory Hygiene
- Triage: Patient Identification, isolation, diagnosis, Treatment
- Personal Protective Equipment, based on risk assessment, testing for COVID-19
- Social distancing- Stay Home
- Implementation of Infection Control Plan

PPE Health Care Facilities

Personal Protection	Staff Clothing	Cleaning Supplies
• Protective Goggles • Face Shield, • Fit test Kit • Particulate respirator, grade N95 or FFP2	• Surgical Mask-patient and Provider • Scrubs, tops • Apron -Heavy Duty • Gown • Examination Gloves	• Hand drying tissue • Soap • Gloves-cleaning • Chlorine • Alcohol base Hand rub • Biohazard bag, • Safety box

WHO: Operational Support & Logistics Disease Commodity Packages

Health and Human Services- Interim Guidelines on COVID-19 for all Persons with HIV

- Elderly population 60 >yr and persons with co-morbidities are at greater risk for more severe disease particularly smokers.
- The limited data currently available do not indicate that the disease course of COVID-19 in persons with HIV differs from that in persons without HIV. Before the advent of effective combination antiretroviral therapy (ART), advanced HIV infection (i.e., CD4 cell count <200/mm^3) was a risk factor for complications of other respiratory infections. Whether this is also true for COVID-19 is yet unknown.
- Until more data is available caution is advised for PLHIV with advanced and poorly controlled disease.
- ART and concomitant medication supply for PLHIV should be prioritized and minimum of 30 days and maximum of 90 days supply of ART is advised.
- Influenza and pneumococcal vaccinations should be kept up to date. **(boosted and cross immunity)**
- Persons with HIV should follow all applicable recommendations of the U.S. Centers for Disease Control and Prevention (CDC) to prevent COVID-19, such as social distancing and proper hand hygiene. These recommendations are regularly updated.
- Guidelines for prevention in children, health care providers , general public and pregnant women prevention are available from the CDC.

HHS. March 20,2020

Antiretroviral Therapy

Persons with HIV should:

- Maintain on-hand at least a 30-day supply—and ideally a 90-day supply—of antiretroviral (ARV) drugs and other medications. **(Drug stock out-adherence)**
- Talk to their pharmacists and/or healthcare providers about changing to mail order delivery of medications when possible.(**Limit face to face interaction)**
- Persons for whom a regimen switch is planned should consider delaying the switch until close follow-up and monitoring are possible. **(Cost benefit analysis)**
- Lopinavir/ritonavir (LPV/r) has been used as an off-label treatment for patients with COVID-19 and clinical trials are underway globally. If protease inhibitors (PIs) are not already part of a person's ARV regimen, their regimen **should not be changed** to include a PI to prevent or treat COVID-19, except in the context of a clinical trial and in consultation with an HIV specialist. **(treatment interruption, viral rebound, resistance risk)**

HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020

Children with HIV:

- From the limited available data, children appear less likely to become severely ill with COVID-19 infection than older adults.[10-12] However, there may be subpopulations of children at increased risk of more severe COVID-19 illness; in studies of infection with non-COVID-19 coronaviruses in children, younger age, underlying pulmonary pathology, and immunocompromising conditions were associated with more severe outcomes.[13]

- Infants and children with HIV should be up to date on all immunizations, including influenza and pneumococcal vaccines. Refer to the Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children information on immunizations, including a vaccine schedule for children with HIV.

(No specific changes except caution in younger age children with co-morbidities)

HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020

Pregnant Individuals with HIV:

- Currently, there is limited information about pregnancy and maternal outcomes in individuals who have COVID-19.
- Immunologic and physiologic changes during pregnancy generally increase a pregnant individual's susceptibility to viral respiratory infections, possibly including COVID-19. As observed with other coronavirus infections, the risk for severe illness, morbidity, or mortality with COVID-19 may be greater among pregnant individuals than among the general population.[2]
- Although limited, currently available data do not indicate that pregnant individuals are more susceptible to COVID-19 infection or that pregnant individuals with COVID-19 have more severe illness.[6,7] Adverse pregnancy outcomes, such as fetal distress and preterm delivery, were noted in a small series of pregnant women with COVID-19 infection and have been reported with SARS and MERS infections during pregnancy.[3-5]
- Findings from a small group of pregnant women with COVID-19 did not find evidence for vertical transmission of COVID-19, although at least one case of neonatal COVID-19 has been described.[7-9]
- Information on pregnancy and COVID-19 is available from CDC, the Society for Maternal-Fetal Medicine, and the American College of Obstetricians and Gynecologists.

(Limited data and no specific changes)

HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020

Persons with HIV and in Opioid Treatment Programs:

- Clinicians caring for persons with HIV who are enrolled in opioid treatment programs (OTPs) should refer to the Substance Abuse and Mental Health Service Administration (SAMHSA) website for updated guidance on avoiding treatment interruptions. State methadone agencies are also responsible for regulating OTPs in their jurisdictions and may provide additional guidance.

HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020

Guidance for Persons with HIV who have Fever or Respiratory Symptoms and are Seeking Evaluation and Care

Health Care Workers Should:

- Follow CDC recommendations, as well as state and local health department guidance on infection control, triage, diagnosis, and management. **(Inform patient in advance of infection control policy)**

Persons with HIV Should:

- Follow CDC recommendations regarding symptoms.
- If they develop a fever and symptoms (e.g., cough, difficulty breathing), they should call their health care provider for medical advice.
- Call the clinic in advance before presenting to the care providers.
- Use respiratory and hand hygiene and cough etiquette when presenting to the healthcare facility and request a face mask as soon as they arrive. If they present to a clinic or an emergency facility without calling in advance, they should alert registration staff immediately upon arrival of their symptoms so that measures can be taken to prevent COVID-19 transmission in the health care setting. Specific actions include placing a mask on the patient and rapidly putting the patient in a room or other space separated from other people. **(Quarantine)**

HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020

Guidance for Managing Persons with HIV who develop COVID-19

HIV patients with mild clinical symptoms may not initially require hospitalization and may be managed at home.

- Note clinical signs and symptoms may worsen with progression to lower respiratory tract disease during 2 week of illness: All patients should be monitored closely
- Risk factors for disease progression include pre-existing cardiovascular disease, diabetes, renal disease, liver disease, pregnancy and other immunocompromising condition
- The decision to monitor a patient in the inpatient or outpatient basis should be made on a case by case basis
- Determining factors for such a decision will depend on

  A) Clinical Presentation and

  B) Social consideration:
  - Patient's ability to engage in home monitoring
  - Home isolation
  - Risk of transmission in the patients' home environment
- No specific treatment for COVID-19 is currently available. Treatment is supportive.

CDC Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), March 20,2020

Guidance for Managing Persons with HIV who Develop COVID-19

When the Person with HIV is Hospitalized:

- ART should be continued. If the ARV drugs are not on the hospital's formulary, administer medications from the patients' home supplies.
- ARV drug substitutions **should be avoided**. If necessary, clinicians may refer to recommendations on ARV drugs that can be switched in the U.S. Department of Health and Human Services (HHS) guidelines for caring for persons with HIV in disaster areas. **(Generic brand switch in case of emergency)**
- For patients who receive ibalizumab (IBA) intravenous (IV) infusion every 2 weeks as part of their ARV regimen, clinicians should arrange with the patient's hospital provider to continue administer of this medication without interruption.
- For patients who are taking an investigational ARV medication as part of their regimen, arrangements should be made with the investigational study team to continue the medication if possible.
- For critically ill patients who require tube feeding, some ARV medications are available in liquid formulations and some, but not all, pills may be crushed. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way for a patient with a feeding tube to continue an effective ARV regimen. Information may be available in the drug product label or from this document from the Toronto General Hospital Immunodeficiency Clinic.

HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020

Guidance for Persons with HIV in Self-Isolation or Quarantine Due to SARS-CoV-2 Exposure

Health Care Workers Should:

- Verify that patients have adequate supplies of all medications and expedite additional drug refills as needed.
- Devise a plan to evaluate patients if they develop COVID-19-related symptoms, including for possible transfer to a health care facility for COVID-19-related care.

Persons with HIV Should:

- Contact their health care provider to report that they are self-isolating or in quarantine.
- Specifically, inform their health care provider how much ARV medications and other essential medications they have on hand.

  (Inform health care provider of disease progression)

CDC Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), March 20,2020

CDC Guidelines on discontinuation of In-Home isolation for HIV immunocompromised Persons with COVID-19 (Interim)

Where there is concern that a person living with HIV may continue to shed virus after recovery, jurisdictions may wish to consider the utility of a test-based strategy. However, a test-based strategy is contingent on the availability of ample testing supplies and laboratory capacity as well as convenient access to testing and in the absence of these conditions may not be feasible.

Possible strategy to discontinue Home Isolation For Immunocompromised Persons with COVID-19 When A Test-Based Strategy is Feasible and Desired:

Maintain home isolation until:

- Resolution of fever without the use of fever-reducing medications **and**
- Improvement in respiratory symptoms (e.g., cough, shortness of breath) **and**
- Negative results of an FDA Emergency Use Authorized molecular assay for COVID-19 from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of two negative specimens)

When a test-based strategy is not feasible or desired, healthcare providers and public health officials should follow the **non-test-based strategy** outlined in the guidance for non-immunocompromised persons.

CDC Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), March 20,2020

CDC Guidelines on discontinuation of In-Home isolation for HIV immunocompromised Persons with COVID-19 (Interim)

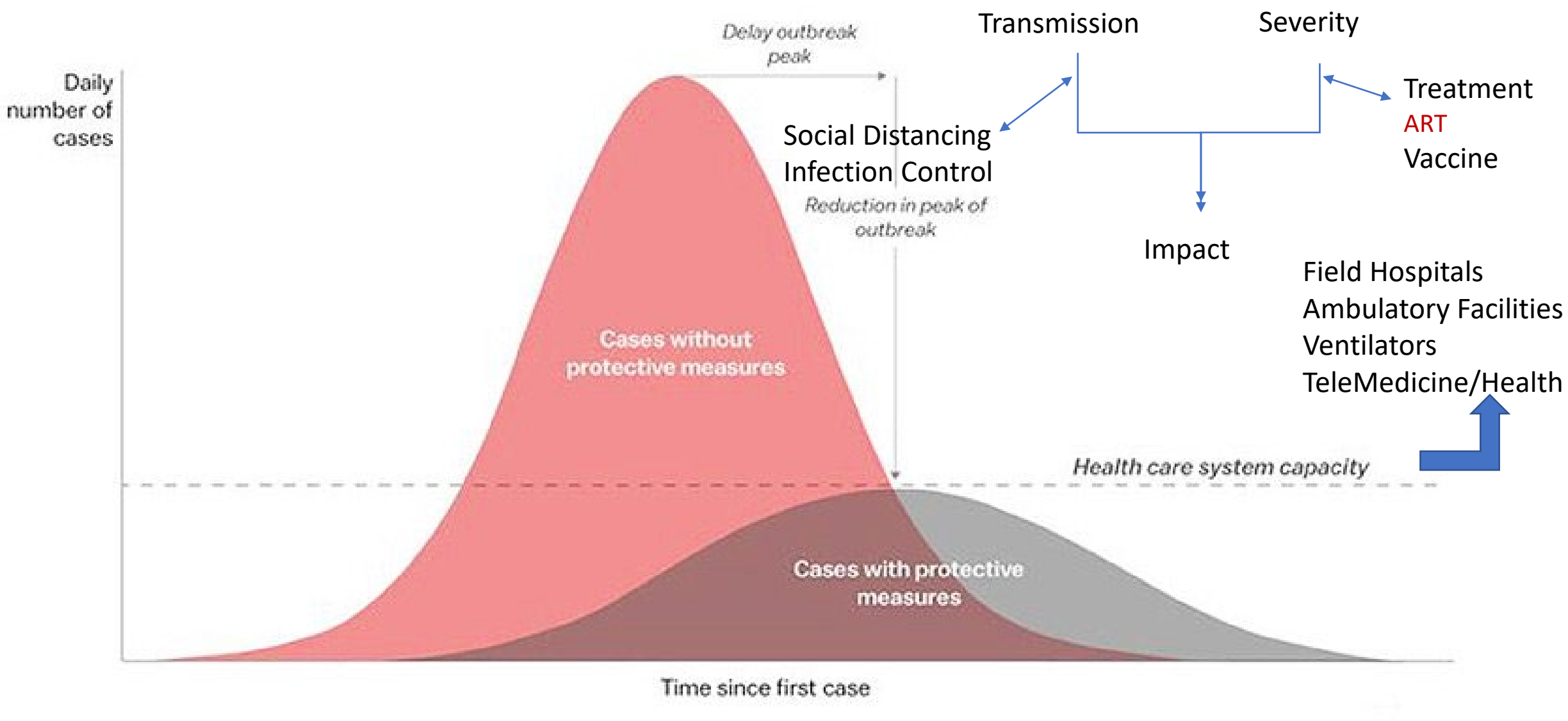
Time-since-illness-onset and time-since-recovery strategy (non-test-based strategy)* **Persons with COVID-19 who have symptoms** and were directed to care for themselves at home may discontinue home isolation under the following conditions:

- At least 3 days (72 hours) have passed *since recovery* defined as resolution of fever without the use of fever-reducing medications **and** improvement in respiratory symptoms (e.g., cough, shortness of breath); **and,**
- At least 7 days have passed *since symptoms first appeared*.

(10 DAYS TOTAL FROM ONSET TO RECOVERY FOR CLEARANCE)

CDC Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), March 20,2020

Flattening the HIV population Curve



Clinical Consideration for HIV patient

- Prioritize older AIDS patients with multiple co-morbidities for care
- Ensure patients have adequate supply of ART and PreP
- Fast tracking and extending prescriptions refills especially for special population harm reduction
- Avoid switching ART Medication
- Devise means to limit face to face interaction: Telemedicine, Phone call, apps
- Encourage patient education home infection control, condom use and social care plans
- Provide options for Mental Health referrals
- Consider joint COVID-19/HIV testing for all COVID-19 suspects cases
- Practice stringent infection control and prevention

Thank you!

References

- Johns Hopkins University Corona Virus Resource Center . Corona virus Data.
- Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020 Morbidity and Mortality ReportWeekly / March 26, 2020 / 69(12);343-346
- Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA. Published online March 23, 2020.
- Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Fei Zhou*,. The Lancet March 12,2020
- The HIV and Aging Consensus Project. Abrass, Christine K., et al.
- Multimorbidity Syndrome: Greene 2013 : Greene 2015; Singh 2017: Greene 2017
- Policy Position statement. American Academy of HIV Medicine
- Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. New England journal of Medicine. March 17, 2020
- CDC: What to Know About HIV and COVID-19.
- https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/hiv.html?
- Li. Xiaowei. Journal of pharmaceutical analysis. March 2020Molecular immune pathogenesis and diagnosis of COVID-19
- Rothan. etal Journal of Autoimmunity Feb 2020
- Journal of Pharmaceutical Analysis, March 2020
- Illustrative graphic of Disease Progression and laboratory test for COVID-19: Caribbean Med Labs Foundation (CMLF)
- National Institute of Health: Corona virus update: https://www.nih.gov/health-information/coronavirus
- CDC: Information for Clinicians on Therapeutic Options for COVID-19 Patients: https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html
- HHS: Interim Guidance for COVID-19 and Persons with HIV, March 20,2020
- CDC Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), March 20,2020
- American Academy of HIV Medicine: https://aahivm.org/hiv-care-covid-19/
- **Coronavirus Disease 2019 (COVID-19) and Cardiovascular Disease. K. Clerkin .Circulation Mar 21 , 2020**