

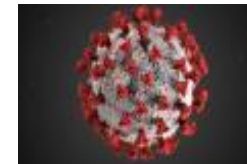
COVID-19 UPDATES

April 13, 2020

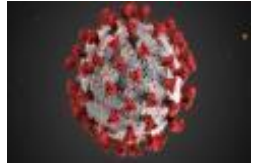
Jorge Mera, MD, FACP

Whitney Essex, MSN, FNP-BC

Cherokee Nation Health Services

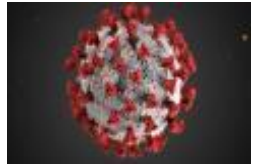


Outline



- Virology
- Epidemiology
- Clinical Manifestations
- Infection Control
- Treatment

Virology



- **Virus**

- RNA viruses with spike-like surface proteins
- SARS-CoV: **Severe Acute Respiratory Syndrome CoronaVirus** (2003 outbreak)
- SARS-CoV2: **Cause of present coronavirus Pandemic**

- **Disease**

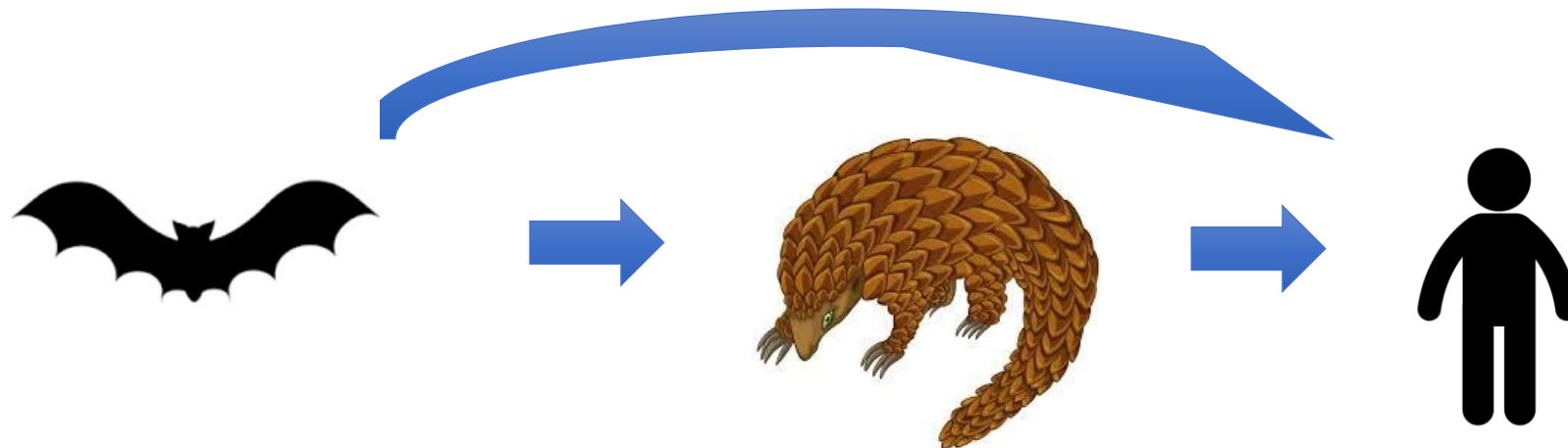
- CoVID-19: **Coronavirus disease** from SARS-CoV2 discovered in **2019**

- **Human origin** cause human URIs

- HKU1/NL63/229E/OC43

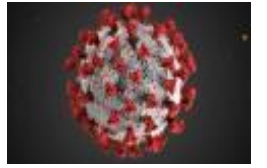
- **Animal Origin**

- SARS-CoV: 2003, China
- MERS-CoV: 2012, Arabian peninsula
- SARS-CoV2: 2019, China



Epidemiology

(Lauer et al, Ann Intern Med, 2020)



Transmission

- Droplet is predominant mode of spread
- Contact is secondary
- Airborne ?

Risk of transmission

- One individual transmits it to 0.45% of close contacts^{1,2}

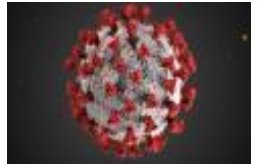
Incubation Period

- 5.1 days from infection to symptoms [2-14 day range]
- 97.5% acquire their symptoms within 11.5 days
- 1% will develop symptoms after 14 days of exposure

1. Burke RM et al. MMWR Morb Mortal Wkly Rep. 2020:69

2. Close contact: a) being within approximately 6 feet (2 meters) of a COVID-19 case for a prolonged period of time; close contact can occur while caring for, living with, visiting, or sharing a healthcare waiting area or room with a COVID-19 case OR b) having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on)

Epidemiology



Transmission of SARS-CoV2 (R_0)

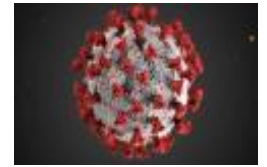
- R_0 = basic reproduction number
 - The number of cases generated by a single infectious case in a population without immunity
 - $R_0 \geq 2$ = exponential growth
- R_0 of SARS-CoV2 = 2.24-3.58
- R_0

• Measles:	15.0
• Smallpox:	4.8
• SARS:	3.0
• COVID-19:	2.8
• Ebola:	1.9
• Seasonal Influenza:	1.3
• MERS:	0.8

Why is it spreading faster than SARS

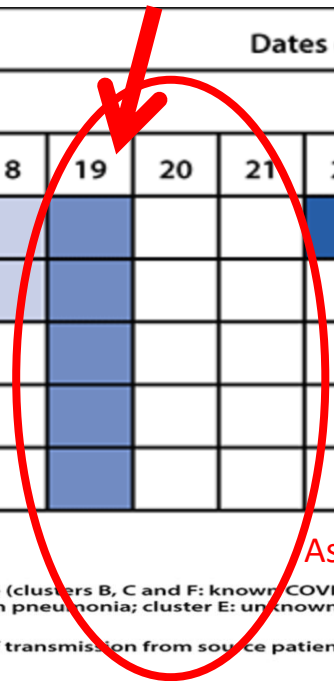
- Survival in surfaces is similar
- Retention in aerosols is similar
- High level early viral shedding from upper respiratory tract
- Asymptomatic transmission has been documented

Epidemiology: Asymptomatic Transmission



- Asymptomatic Transmission has been reported in 6.4% of the Cases in Singapore and 12.6% of the cases in China

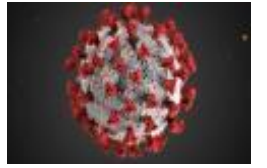
Cluster A	Dates of likely transmission, symptom onset, and other exposure																	Symptoms
	Jan														Feb			
	18	19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	
Patient A1 ★																		Fever
Patient A2 ★																		Fever
Patient A3																		Fever
Patient A4																		Fever, cough
Patient A5																		Fever, sore throat



Asymptomatic

- ★ Source patient
- Other exposure (clusters B, C and F: known COVID-19 case; cluster A: unknown exposure in Wuhan, China; cluster D: patient in Philippines with pneumonia; cluster E: unknown exposure in Japan; cluster G: unknown exposure in Indonesia)
- Likely period of transmission from source patient to secondary patients
- Symptom onset date

Epidemiology: Asymptomatic Transmission



Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020

Weekly / April 3, 2020 / 69(13);377-381

On March 27, 2020, this report was posted online as an MMWR Early Release.

- ❑ Once SARS-CoV-2 is introduced in a long-term care skilled nursing facility (SNF), rapid transmission can occur.
- ❑ Following identification of a case of coronavirus disease 2019 (COVID-19) in a health care worker, 76 of 82 residents of an SNF were tested for SARS-CoV-2; 23 (30.3%) had positive test results, **approximately half of whom were asymptomatic or pre-symptomatic on the day of testing.**
- ❑ Symptom-based screening of SNF residents might fail to identify all SARS-CoV-2 infections.

Age Distribution and Case Fatality Rates Among more than 44,000 confirmed cases of COVID-19 in China

Most patients aged 30–69 years (77.8%), and approximately 19% were severely or critically ill.

Overall case fatality rate among patients who reported no underlying medical conditions was 0.9%,

Case-fatality proportion among cases aged ≥ 60 years was:

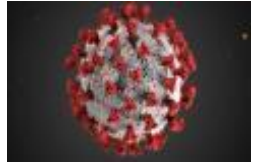
- 60-69 years: 3.6%
- 70-79 years: 8%
- ≥ 80 years: 14.8%.

Case fatality among patients with comorbidities:

- Cardiovascular disease 10.5%
- Diabetes 7%
- Chronic respiratory disease, hypertension, and cancer 6%

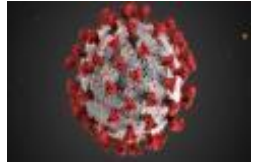
Case fatality for patients who developed respiratory failure, septic shock, or multiple organ dysfunction was 49%.

Clinical Manifestations



- Common Symptoms
 - Fever in > 75% at some point (~50% on admission)
 - Cough 45-80% (dry > productive)
 - SOB 20-40%
 - Myalgia 10-50%
 - Triad of fever/Cough/SOB in only 15%
- Less Common Symptoms
 - URI symptoms (HA, sore throat, rhinorrhea) < 15%
 - GI symptoms (N/V < 10%, diarrhea < 25%)

Clinical Manifestations



Lab findings

Frequency

- Leukopenia 17%
- Leukocytosis 21%
- Lymphopenia 40%
- Thrombocytopenia 7%
- ALT > 40 31%

Radiology

- Ground glass opacity on CT 71%
- Consolidation 59%
- Bilateral Infiltrates 75%

Clinical Manifestations: Risk of Hospitalization

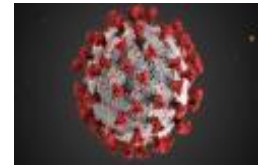


TABLE 2. Hospitalization with and without intensive care unit (ICU) admission, by age group among COVID-19 patients aged ≥19 years with and without reported underlying health conditions — United States, February 12–March 28, 2020*



Age group (yrs)	Hospitalized without ICU admission, No. (% range [†])		ICU admission, No. (% range [†])	
	Underlying condition present/reported [§]		Underlying condition present/reported [§]	
	Yes	No	Yes	No
19–64	285 (18.1–19.9)	197 (6.2–6.7)	134 (8.5–9.4)	58 (1.8–2.0)
≥65	425 (41.7–44.5)	58 (16.8–18.3)	212 (20.8–22.2)	20 (5.8–6.3)
Total ≥19	710 (27.3–29.8)	255 (7.2–7.8)	346 (13.3–14.5)	78 (2.2–2.4)

◆ Key Points

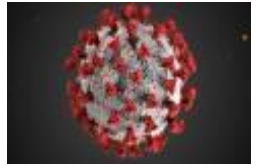
- ✧ Adults > 65 years are:
 - ✧ 31% of cases
 - ✧ 45% of hospitalizations
 - ✧ 53% of ICU admissions
 - ✧ 80 % of deaths

* Includes COVID-19 patients aged ≥19 years with known status on underlying conditions.

[†] Lower bound of range = number of persons hospitalized or admitted to an ICU among total in row stratum; upper bound of range = number of persons hospitalized or admitted to an ICU among total in row stratum with known outcome status: hospitalization or ICU admission status.

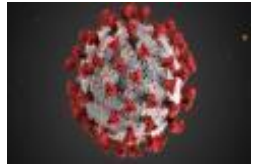
[§] Includes any of following underlying health conditions or risk factors: chronic lung disease (including asthma, chronic obstructive pulmonary disease, and emphysema); diabetes mellitus; cardiovascular disease; chronic renal disease; chronic liver disease; immunocompromised condition; neurologic disorder, neurodevelopmental, or intellectual disability; pregnancy; current smoker; former smoker; or other chronic disease.

Clinical Manifestation: Coinfection



- Coinfection with bacteria has been reported between 0-6% but unclear since systematic testing not performed
- Coinfection with other viruses including influenza
- Detection of an alternative viral or bacterial infection does not rule out COVID-19

Chen et al, Lancet; Tav et al, CID. Young et al, JAMA; Wu et al, CID. Han et al, J Med Virol. Zhao et al, CID. Lin et al, Sci China Life Sci. Want et al, CID Mo et al CID, Wu et al CID



Infection Control: Who to Test for COVID-19

1

Hospitalized patients
who have fever or
respiratory symptoms

Health Care Workers
with symptoms

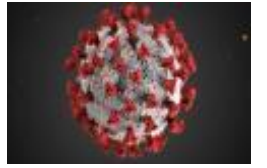
2

Symptomatic older
adults and individuals
with chronic medical
conditions: DM, CHF,
COPD, CKD, Cirrhosis,
Obese
Immunosuppressed

3

Patients with fever
(subjective or objective)
OR cough **OR** shortness
of breath

Infection Control: Testing for COVID-19



- **PCR**

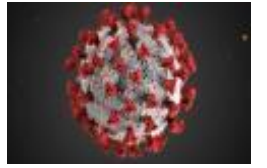
- Use only synthetic fiber swabs with plastic shafts. DO NOT use calcium alginate swabs or swabs with wooden shafts¹.
- Nasopharyngeal swab preferred but may also test oropharynx, nasal mid-turbinate.
- Leave swab in place for 2-3 seconds then rotate completely around for 10-15 seconds. If the patient has a productive cough a PCR test should be done on the sputum sample
- Sensitivity 75-80%

- **Serology**

- FDA approved emergency use of first commercial serology test for qualitative detection of IgM and/or IgG (Cellex)
- Finger stick with results in 15 min.
- Nearly 94% positive % agreement with RT-PCR and a 96% negative % agreement with RT-PCR
- Not to be used as the sole basis to diagnose or exclude SARS-CoV-2 infection

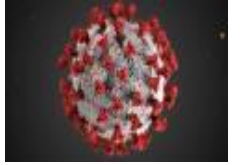
1. CDC.gov Accessed 3/18/2020
2. UW Medicine, COVID-19 Website

Infection Control: Personal Protective Equipment



PPE must include

- Gown
- Nonsterile gloves
- N95 (Mandatory when aerosols are generated)
 - Intubation (Box NEJM 2020)
 - Nebulization
 - Inducing sputum
- Eye protection (Face shield or goggles)

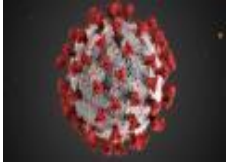


Infection Control: UV light germicidal irradiation

- Researchers from Nebraska Medicine have developed a procedure for decontaminating N95 respirators using ultraviolet germicidal irradiation
- <https://www.nebraskamed.com/sites/default/files/documents/covid-19/n-95-decon-process.pdf>

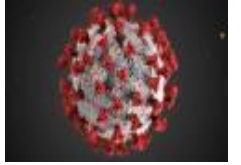


Infection Control: Vaporized Hydrogen Peroxide Gas Plasma Sterilization



- The FDA granted the EUA to Advanced Sterilization Products (ASP) for the STERRAD Sterilization Cycles (STERRAD 100S Cycle, STERRAD NX Standard Cycle, or STERRAD 100NX Express Cycle), which uses vaporized hydrogen peroxide gas plasma sterilization. There are approximately 9,930 STERRAD Sterilization systems in approximately 6,300 hospitals across the U.S. STERRAD 100S Cycle, STERRAD NX Standard Cycle and STERRAD 100NX Express Cycle vary in reprocessing times from 55 minutes, to 28 minutes, and 24 minutes. Each can reprocess approximately 480 respirators per day.

Infection Control: Barrier Enclosure during Endotracheal Intubation



Aerosol Box

Protection without access to standard personal protective equipment during endotracheal intubation

Without the box, contamination as far as 2 meters from the patient

Video

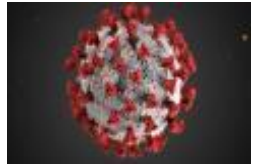


Barrier Enclosure during Endotracheal Intubation (04:18)

NEJM April 3, 2020

DOI: 10.1056/NEJMc2007589

Infection Control: CDC Community Recommendations



Masks for the community

- Virus can spread between people interacting in close proximity
- CDC recommends wearing cloth face coverings in public settings where other social distancing measures are difficult to maintain
- Maintaining 6-foot social distancing remains important to slowing the spread of the virus

Infection Control: Recommendations for Discontinuing Home Isolation of Symptomatic COVID-19 Positive Patients

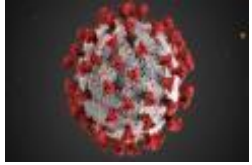
Individuals with laboratory-confirmed COVID-19 who have symptoms

- **Non-test-based strategy (time-since-illness-onset and time-since-recovery strategy):**
 - 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*.
- **Test-based strategy**
 - 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).
- **Should be used for patients discharged from the hospital, patients returning to nursing homes or immunocompromised patients**

Individuals with laboratory-confirmed COVID-19 who have not had any symptoms may discontinue home isolation when at least 7 days have passed since the date of their first positive COVID-19 diagnostic test and have had no subsequent illness

Infection Control:

Return to Work Practices and Work Restrictions



- After returning to work, HCP should:
 - Wear a facemask at all times while in the healthcare facility until all symptoms are completely resolved or until 14 days after illness onset, whichever is longer
 - Be restricted from contact with severely immunocompromised patients (e.g., transplant, hematology-oncology) until 14 days after illness onset
 - Adhere to hand hygiene, respiratory hygiene, and cough etiquette in CDC's interim infection control guidance (e.g., cover nose and mouth when coughing or sneezing, dispose of tissues in waste receptacles)
 - Self-monitor for symptoms, and seek re-evaluation from occupational health if respiratory symptoms recur or worsen

Planning at the Clinic Level

Limit the number of entrances

- Screen for fever/cough at entrance
- Have a protocol ready

Triage patients with respiratory symptoms to a designated area

- Have a dedicated team

Process to track patients and results

- Employee Health Nurse/Public Health Nurse/Case manage

Keep your healthcare workforce healthy

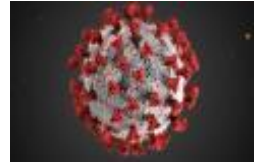
- Send home those who can work from home or who have risk factors

Patients should be managed at home if possible

- Prepare for working from home, telemedicine/phone
- Plan for medication refills and delivery



Treatment



Day 1-9 disease is probably viral mediated

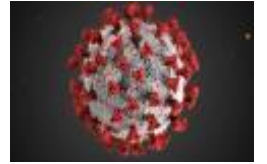
- ACE/ARB: RCT ongoing
- Remdesivir: RCT results pending
- Favipriavir:
 - 1 open label control study in patients without hypoxemia revealed faster viral clearance and radiologic improvement vs Lopinavir/ritonavir (Cai et al Engineering 2020)
- Lopinavir/Ritonavir
 - 1 published RCT did not reveal benefits
- Hydroxychloroquine (HC)
 - 1 open label study of 36 patients showed higher rates of undetectable viral RNA at day 6 that improved with the addition of azithromycin (Gautret et al International Journal of Antimicrobial Agents)
 - 1 randomized trial of 30 adults in Shanghai reported did not show higher rates of viral clearance (Chen et al. Journal of Zhejiang University 2020)
 - 1 unpublished randomized clinical trial reported symptom and radiological improvement as well as lower likelihood of progression in patients without hypoxemia (Chen)

Day 10 onwards disease is probably immune mediated

- IL-6 receptor blockers
 - Tocilizumab, Sarilumab and siltuximab
- Glucocorticoids
 - Not to be used in non critically ill patients unless there is a separate evidence-based indication (CDC)
 - ARDS: Conflicting evidence
- Plasma from convalescent donors (JAMA March 2020)
 - March 24, FDA announced that convalescent plasma may be collected from recovered COVID-19 patients and considered for emergency administration under a single patient emergency Investigational New Drug application for individual patients with life threateningly severe disease but may be used in individual patients outside of clinical trial.*
 - Hyperimmune globulin from convalescent donors

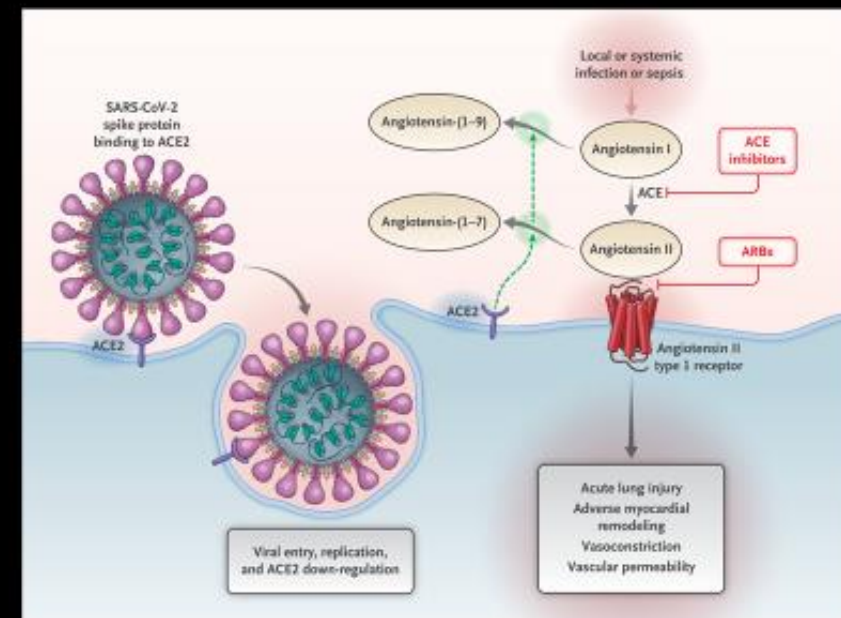
*Complete FDA form 3926) or if urgent call FDA office of Emergency Operations at 1-866-300-4374)

Key Points Related to the Interplay between Covid-19 and the Renin–Angiotensin–Aldosterone System

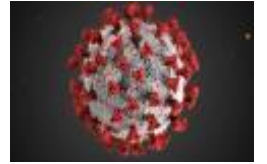


- ACE2, an enzyme that physiologically counters RAAS activation, is the functional receptor to SARS-CoV-2, the virus responsible for the Covid-19 pandemic
- Select preclinical studies have suggested that RAAS inhibitors may increase ACE2 expression, raising concerns regarding their safety in patients with Covid-19
- Insufficient data are available to determine whether these observations readily translate to humans, and no studies have evaluated the effects of RAAS inhibitors in Covid-19
- Clinical trials are under way to test the safety and efficacy of RAAS modulators, including recombinant human ACE2 and the ARB losartan in Covid-19
- Abrupt withdrawal of RAAS inhibitors in high-risk patients, including those who have heart failure or have had myocardial infarction, may result in clinical instability and adverse health outcomes
- Until further data are available, we think that RAAS inhibitors should be continued in patients in otherwise stable condition who are at risk for, being evaluated for, or with Covid-19

Interaction between SARS-CoV-2 and the Renin–Angiotensin–Aldosterone System.

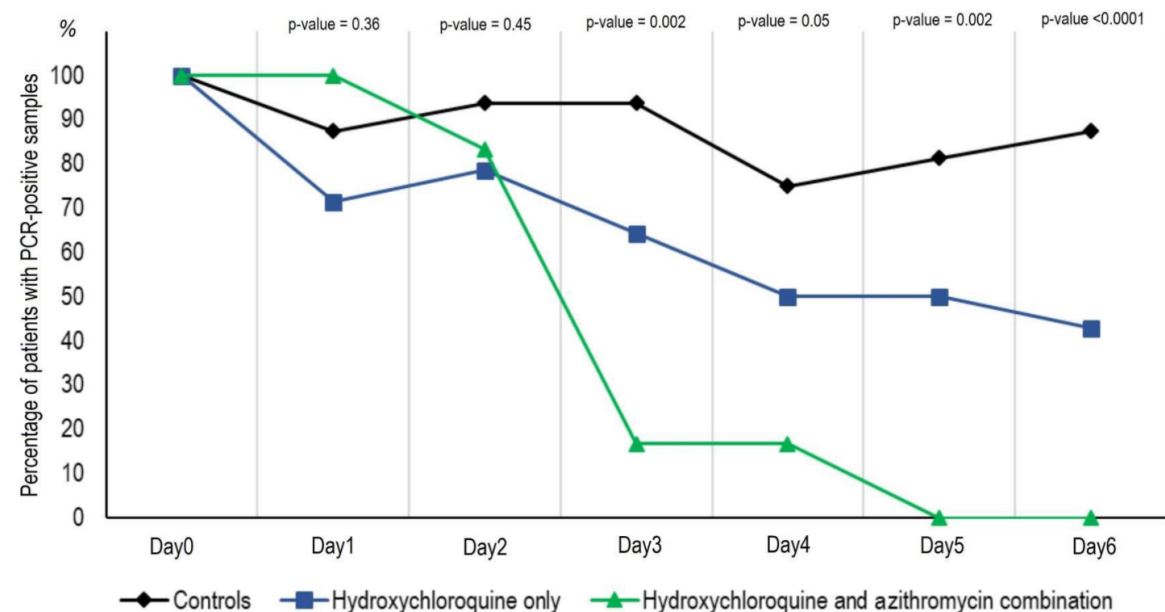


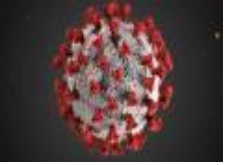
Hydroxychloroquine (HC) / Azithromycin (AZ)



- 26 Patients received HC 200mg by mouth 3 times a day x 10 days +/- azithromycin and 16 were control patients
- At day 6 post-inclusion, 100% of patients treated with HC and AZ combination were virologically cured comparing with 57.1% in patients treated with HC alone, and 12.5% in the control group

Figure 2. Percentage of patients with PCR-positive nasopharyngeal samples from inclusion to day6 post-inclusion in COVID-19 patients treated with hydroxychloroquine only, in COVID-19 patients treated with hydroxychloroquine and azithromycin combination, and in COVID-19 control patients.

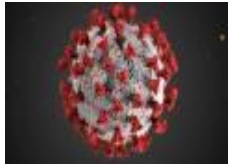




Treatment: Hydroxychloroquine side effects

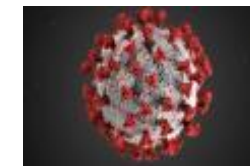
- We report the change in the QT interval in 84 adult patients with SARS-CoV-2 infection treated with Hydroxychloroquine/Azithromycin combination.
- QTc prolonged maximally from baseline between days 3 and 4. in 30% of patients QTc
- Increased by greater than 40ms. In 11% of patients QTc increased to >500 ms, representing high risk group for arrhythmia.
- The development of acute renal failure but not baseline QTc was a strong predictor of extreme QTc prolongation

Effectiveness of convalescent plasma therapy in severe COVID-19 patients (Profile Kai Duan, PNAS 2020)

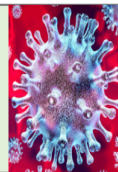


- Ten COVID + patients with severe disease
- One dose of 200 mL of convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640 was transfused to the patients as an addition to maximal supportive care and antiviral agents.
- The primary endpoint was the safety of CP transfusion. The second endpoints were the improvement of clinical symptoms and laboratory parameters within 3 d after CP transfusion.
- Results:
 - The median time from onset of illness to CP transfusion was 16.5 d. After CP transfusion,
 - The clinical symptoms significantly improved along with increase of oxyhemoglobin saturation within 3 d.
 - Several parameters tended to improve as compared to pretransfusion
 - Increased lymphocyte counts ($0.65 \times 10^9/L$ vs. $0.76 \times 10^9/L$) and decreased C-reactive protein (55.98 mg/L vs. 18.13 mg/L).
 - Radiological improvement within 7 d.
 - The viral load was undetectable after transfusion in seven patients who had previous viremia.
 - No severe adverse effects were observed.
- This study showed CP therapy was well tolerated and could potentially improve the clinical outcomes through neutralizing viremia in severe COVID-19 cases.
- **The optimal dose and time point, as well as the clinical benefit of CP therapy, needs further investigation in larger well-controlled trials.**

Compassionate Use of Remdesivir for Patients with Severe Covid-19



- **In vitro activity against an array of RNA virus families including:**
 - *Filoviridae*, *Paramyxoviridae*, *Pneumoviridae*, and *Coronaviridae*



Intravenous administration once daily via 30 min infusion

- Loading dose is Remdesivir 200mg
- Maintenance dose is Remdesivir 100mg
- Available in solution and lyophilized formulation



- Remdesivir is not suitable for oral administration due to almost complete first pass metabolism
- The $T_{1/2}$ of GS-443902 observed in vitro in human macrophages (11 hours) and in vivo in rhesus monkey PBMCs following IV administration (22 hours) supports once-daily dosing
- Metabolism is to be predominantly mediated by hydrolase activity
- Major routes of elimination include renal (74%) and biliary (18%)

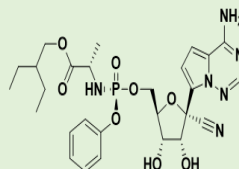
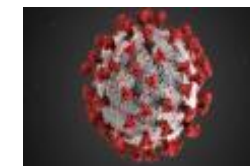


Table 1. Baseline Demographic and Clinical Characteristics of the Patients.*

Characteristic	Invasive Ventilation (N=34)	Noninvasive Oxygen Support (N=19)	Total (N=53)
Median age (IQR) — yr	67 (56–72)	53 (41–68)	64 (48–71)
Age category — no. (%)			
<50 yr	6 (18)	8 (42)	14 (26)
50 to <70 yr	14 (41)	7 (37)	21 (40)
≥70 yr	14 (41)	4 (21)	18 (34)
Male sex — no. (%)	27 (79)	13 (68)	40 (75)
Region — no. (%)			
United States	14 (41)	8 (42)	22 (42)
Japan	8 (24)	1 (5)	9 (17)
Europe or Canada	12 (35)	10 (53)	22 (42)
Oxygen-support category — no. (%)			
Invasive ventilation	34 (100)	—	34 (64)
Invasive mechanical ventilation	30 (88)	—	30 (57)
Extracorporeal membrane oxygenation	4 (12)	—	4 (8)
Noninvasive oxygen support	—	19 (100)	19 (36)
Noninvasive positive-pressure ventilation	—	2 (11)	2 (4)
High-flow oxygen	—	5 (26)	5 (9)
Low-flow oxygen	—	10 (53)	10 (19)
Ambient air	—	2 (11)	2 (4)
Median duration of symptoms before remdesivir therapy (IQR) — days	11 (8–15)	13 (10–14)	12 (9–15)
Coexisting conditions — no. (%)			
Any condition	25 (74)	11 (58)	36 (68)
Hypertension	9 (26)	4 (21)	13 (25)
Diabetes	8 (24)	1 (5)	9 (17)
Hyperlipidemia	6 (18)	0	6 (11)
Asthma	5 (15)	1 (5)	6 (11)
Median laboratory values (IQR)			
ALT — IU per liter	48 (31–79)	27 (20–45)	37 (25–61)
AST — IU per liter	39 (30–76)	35 (28–46)	36 (29–67)
Creatinine — mg per deciliter	0.90 (0.66–1.17)	0.79 (0.63–1.00)	0.89 (0.64–1.08)

* ALT denotes alanine aminotransferase, AST aspartate aminotransferase, and IQR interquartile range. To convert the values for creatinine to micromoles per liter, multiply by 88.4.

Compassionate Use of Remdesivir for Patients with Severe Covid-19



Oxygen-Support Status at Baseline and after Treatment.

		No. of Patients in Oxygen-Support Group at Baseline (%)			
		Invasive (N=34)	Noninvasive (N=7)	Low-flow oxygen (N=10)	Ambient air (N=2)
Category on ordinal scale →		5	4	3	2
No. of Patients in Oxygen-Support Group after Treatment (%)	Death	6 (18)	1 (14)	0	0
	Invasive	9 (26)	1 (14)	0	0
	Noninvasive	3 (9)	0	0	0
	Low-flow oxygen	0	0	0	0
	Ambient air	8 (24)	0	0	0
	Discharged	8 (24)	5 (71)	10 (100)	2 (100)
	Improvement	19 (56)	5 (71)	10 (100)	2 (100)
	Category on ordinal scale ↑				

Figure 1. Oxygen-Support Status at Baseline and after Treatment. For each oxygen-support category, percentages were calculated with the number of patients at baseline as the denominator. Improvement (blue cells), no change (beige) and worsening (gray) in oxygen-support status are shown. Invasive ventilation includes invasive mechanical ventilation, extracorporeal membrane oxygenation (ECMO), or both. Noninvasive ventilation includes nasal high-flow oxygen therapy, noninvasive positive pressure ventilation (NIPPV), or both.

Compassionate Use of Remdesivir for Patients with Severe Covid-19

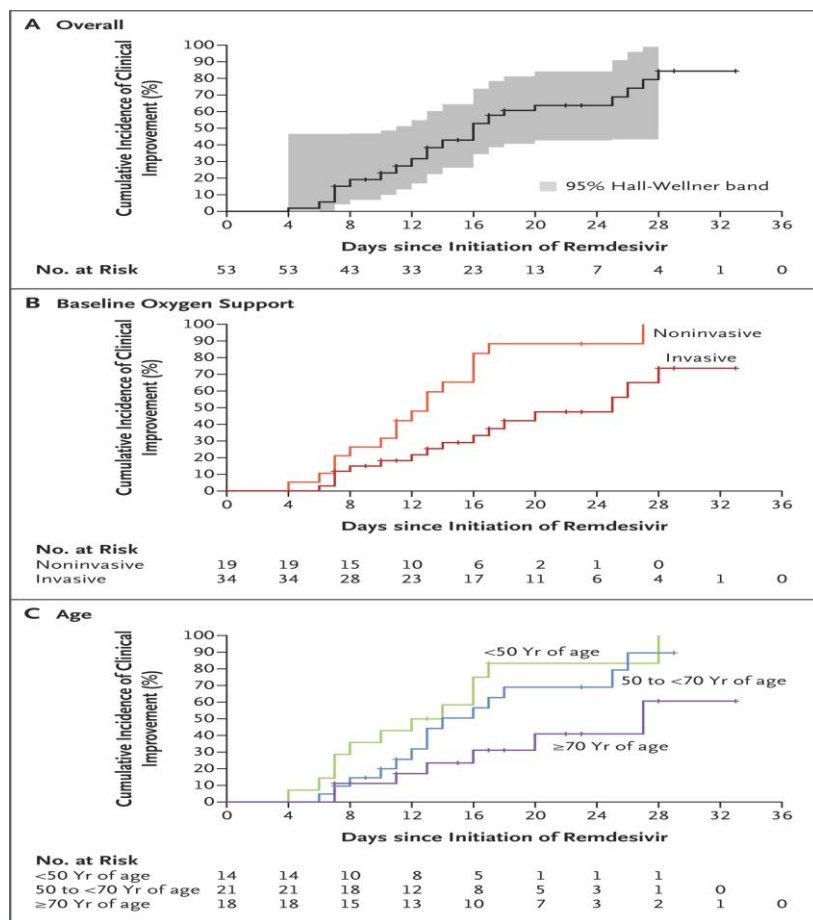
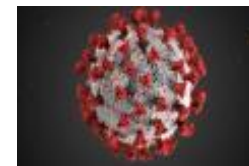


Figure 3. Cumulative Incidence of Clinical Improvement from Baseline to Day 36. Clinical improvement is shown in the full cohort, in the cohort stratified according to ventilation status at baseline, and in the cohort stratified by age.

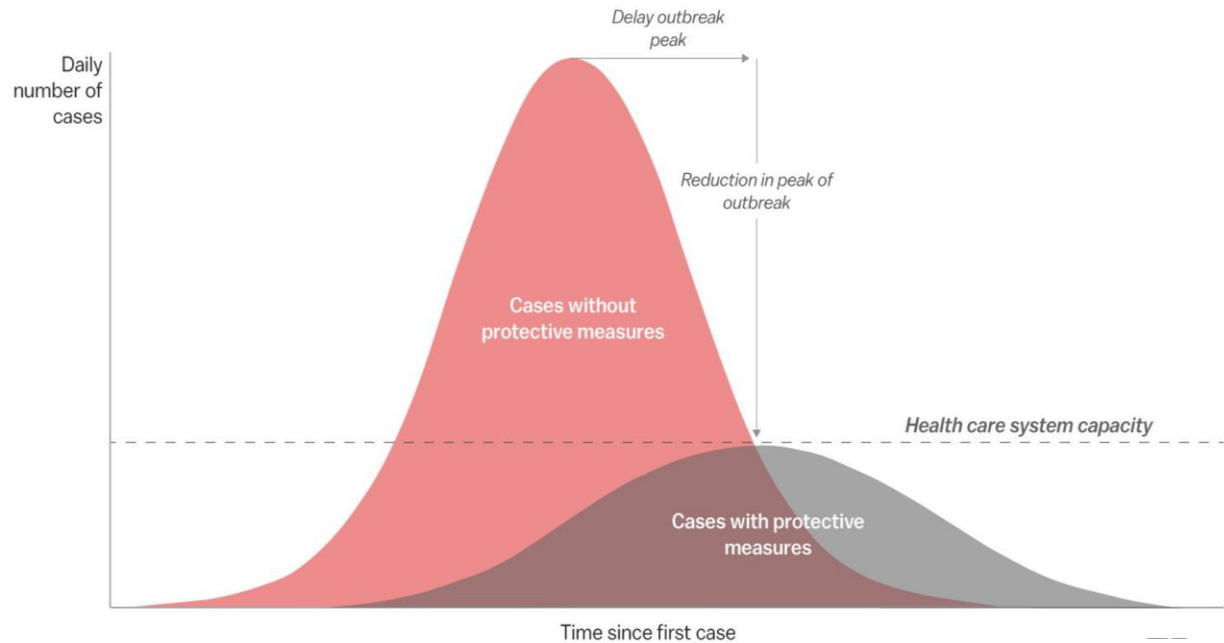
Table 2. Summary of Adverse Events.

Event	Invasive Ventilation (N=34)	Noninvasive Oxygen Support (N=19)	Total (N=53)
<i>number of patients (percent)</i>			
Any adverse event	22 (65)	10 (53)	32 (60)
Adverse events occurring in 2 or more patients			
Hepatic enzyme increased*	8 (24)	4 (21)	12 (23)
Diarrhea	1 (3)	4 (21)	5 (9)
Rash	3 (9)	1 (5)	4 (8)
Renal impairment	4 (12)	0	4 (8)
Hypotension	3 (9)	1 (5)	4 (8)
Acute kidney injury	2 (6)	1 (5)	3 (6)
Atrial fibrillation	2 (6)	1 (5)	3 (6)
Multiple-organ-dysfunction syndrome	3 (9)	0	3 (6)
Hypernatremia	3 (9)	0	3 (6)
Deep-vein thrombosis	3 (9)	0	3 (6)
Acute respiratory distress syndrome	1 (3)	1 (5)	2 (4)
Pneumothorax	2 (6)	0	2 (4)
Hematuria	2 (6)	0	2 (4)
Delirium	1 (3)	1 (5)	2 (4)
Septic shock	2 (6)	0	2 (4)
Pyrexia	1 (3)	1 (5)	2 (4)
Any serious adverse event	9 (26)	3 (16)	12 (23)
Serious events occurring in 2 or more patients			
Multiple-organ-dysfunction syndrome	2 (6)	0	2 (4)
Septic shock	2 (6)	0	2 (4)
Acute kidney injury	2 (6)	0	2 (4)
Hypotension	2 (6)	0	2 (4)

* Adverse-event terms are based on the *Medical Dictionary for Regulatory Activities*, version 22.1. Hepatic enzyme increased includes the following terms: hepatic enzyme increased, alanine aminotransferase increased, aspartate aminotransferase increased, and transaminases increased. Elevated hepatic enzymes resulted in discontinuation of remdesivir therapy in 2 patients.

Conclusions

Flattening the curve



- **How to curb the pandemic:**
 - Early detection and isolation
 - Consider everyone with a fever, cough or Shortness of Air as a “Potential COVID Case” and TEST (if available)
 - Isolate cases and quarantine close contacts
 - Isolation at work and at **home**
- **No proven treatment available**
- **This is a new virus: We are learning every day and need to readily ADAPT and ADOPT**