



# SARS-CoV-2 and COVID-19 Challenges in Containment and Management



**iHART**

INNOVATIONS IN HEALTHCARE ADVOCACY,  
RESEARCH AND TRAINING

PROVIDING INNOVATIVE HEALTHCARE SOLUTIONS  
FOR SAFER, BETTER CARE OF ALL PATIENTS.

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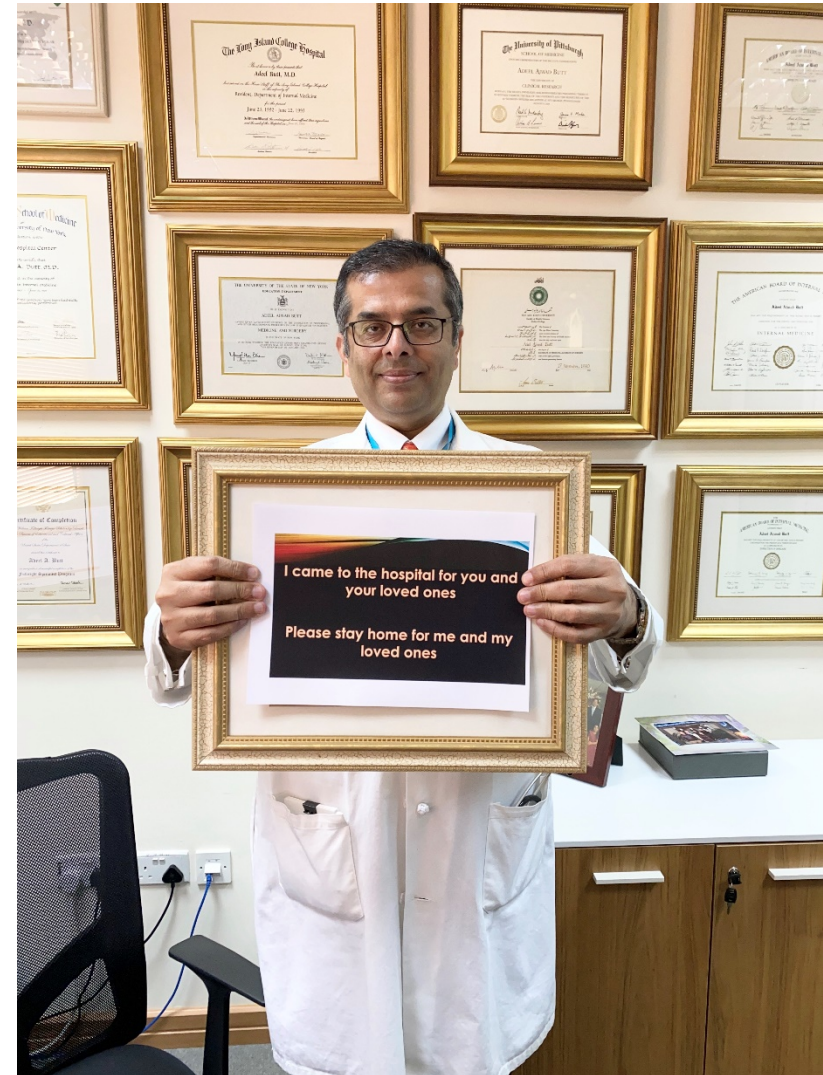
Member WHO Advisory Group on MERS-CoV and COVID-19

For APPNA membership and all healthcare workers

April 2020

# Disclosures

- I have no disclosures related to this talk



# Objectives

- Brief history of coronaviruses
- Epidemiology of the current outbreak
- Myths vs. Facts
- Treatment
- Diagnosis
- Prevention

# Brief history

- Betacoronaviruses frequently infect animals
- Seven species known to infect humans
  - SARS-CoV, MERS-CoV and SARS-CoV-2 can cause severe disease
  - HKU1, NL63, OC43 and 229E are associated with mild symptoms
- SARS
  - November 2002 through July 2003
  - 8,098 people worldwide became sick with severe acute respiratory syndrome
  - 774 died
  - By late July 2003, no new cases were being reported, and WHO declared the global outbreak to be over.
- MERS CoV
  - By November 2019, 8,494 cases reported
  - 858 deaths
  - Sporadic cases still occurring

# SARS-CoV2

- SARS-CoV-2 is the seventh coronavirus known to infect humans
- Has a receptor binding domain (RBD) with high affinity for ACE2 receptors from humans, ferrets, cats and other species
- Genetic data irrefutably show that SARS-CoV-2 is not derived from any previously used virus backbone

**SARS-CoV-2: causative organism**

**COVID-19: disease name caused by SARS-CoV-2**

# How did SARS-CoV-2 enter human population?

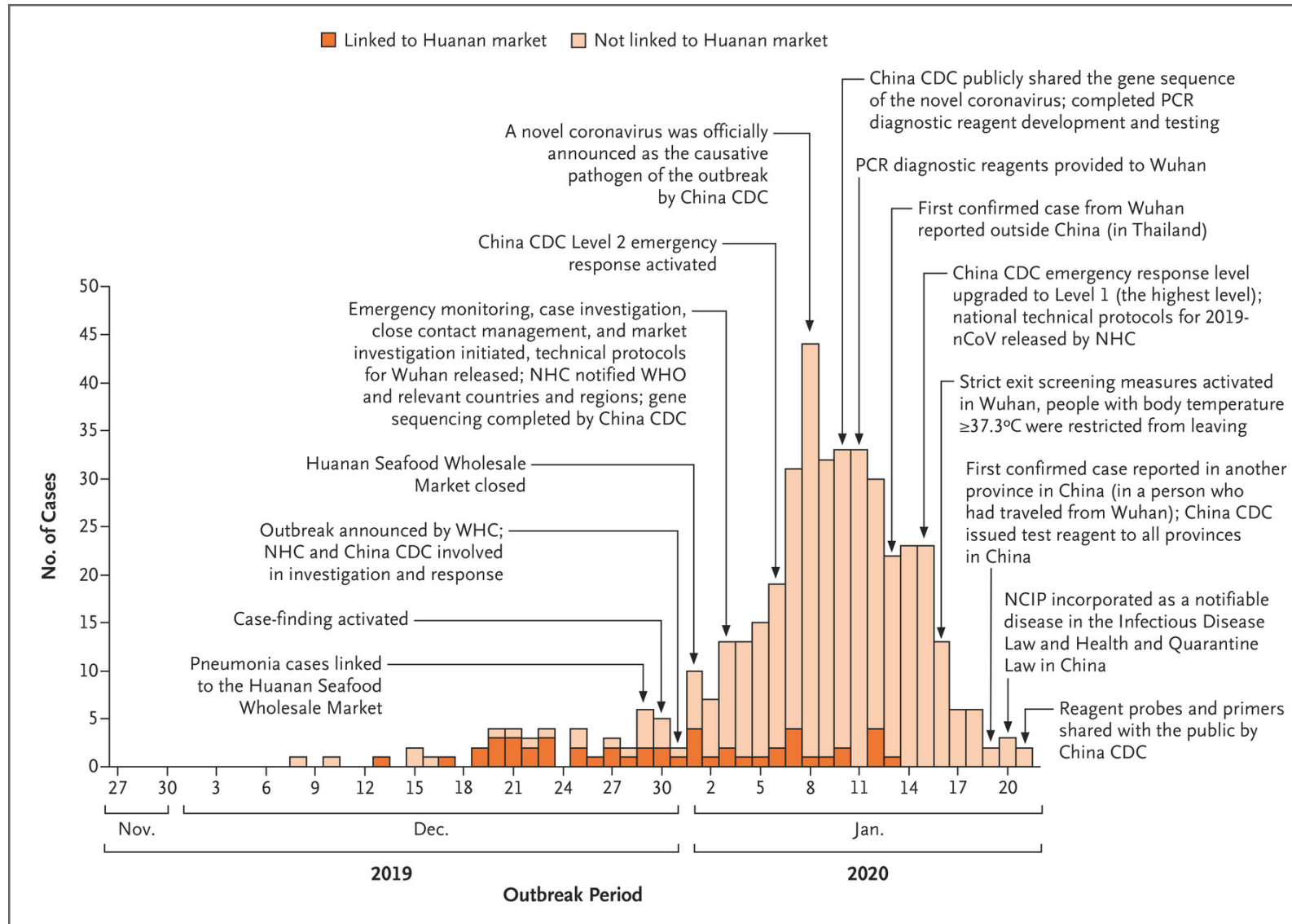
## STEP 1: Natural selection in an animal host before zoonotic transfer

- Many early cases linked to an animal market
- Similarity with bat SARS-CoV, but spike in RBD is divergent suggesting it may not bind efficiently to human ACE2
- Similarity with coronaviruses in illegally imported Malayan pangolins, with very similar RBD
- However, neither the bat betacoronaviruses nor the pangolin betacoronaviruses have polybasic cleavage sites, which suggests natural selection and not a man-made virus

## STEP 2: Natural selection in humans following zoonotic transfer

- Possible that a progenitor of SARS-CoV-2 jumped into humans acquiring adaptations during early undetected human-to-human transmission
- At some point, the cluster became large enough to trigger surveillance and alarm
- Gene sequencing data suggests species jump occurred in late Nov/early Dec 2019

# December 2019 – January 2020



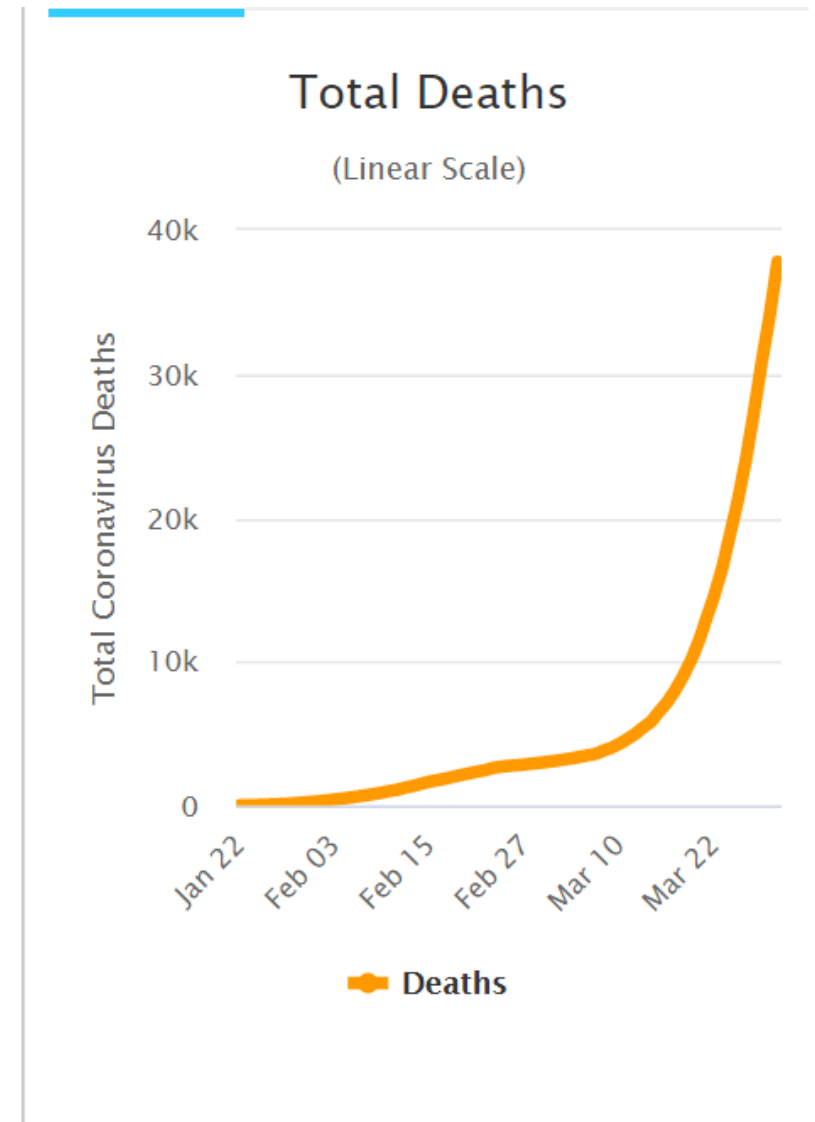
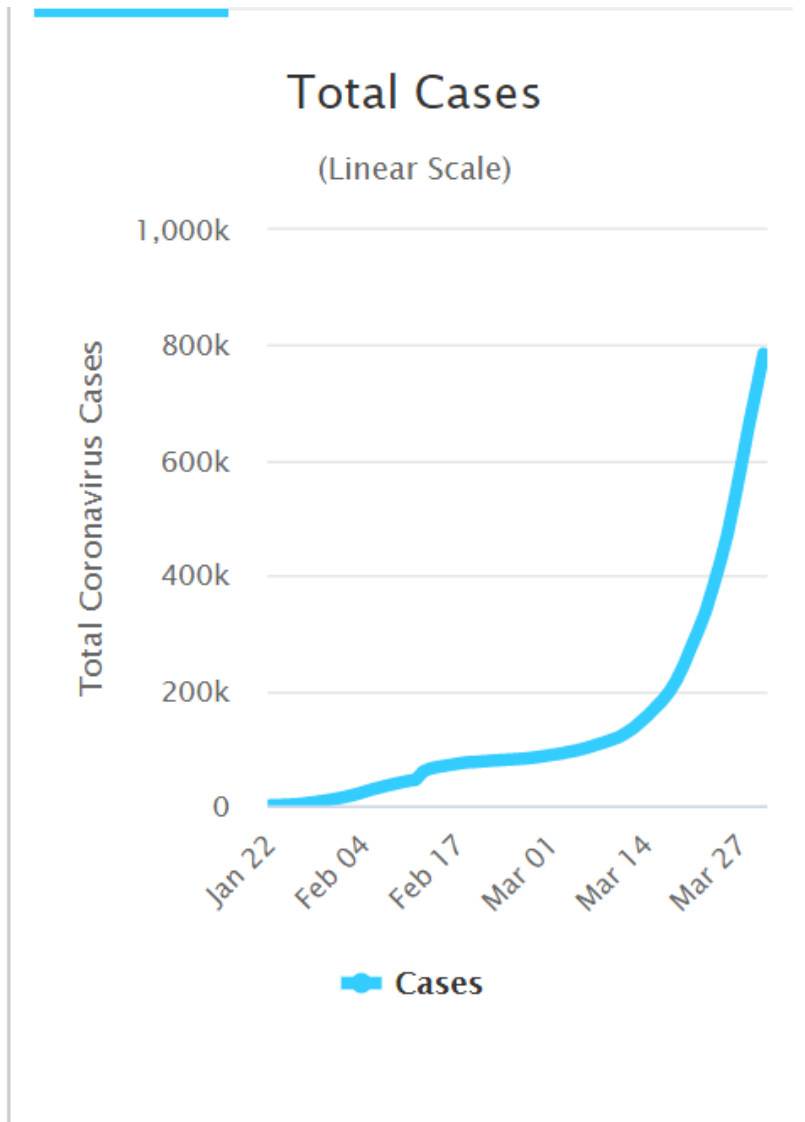
# Situation report

As of 31 March 2020, 7:30 AM EST

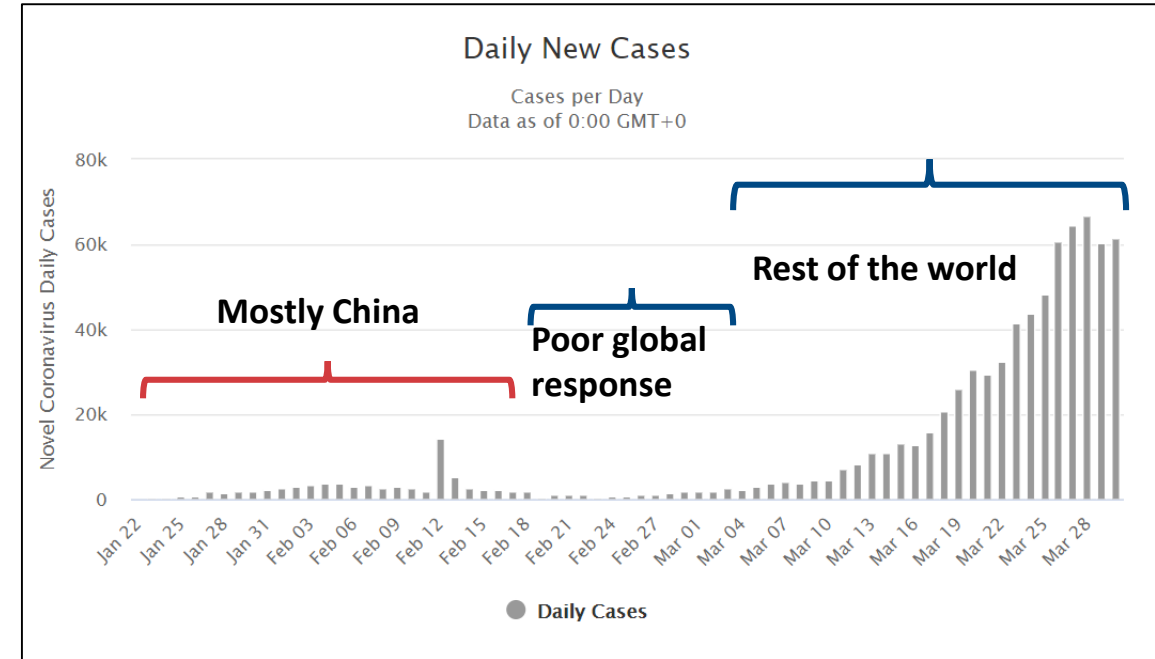
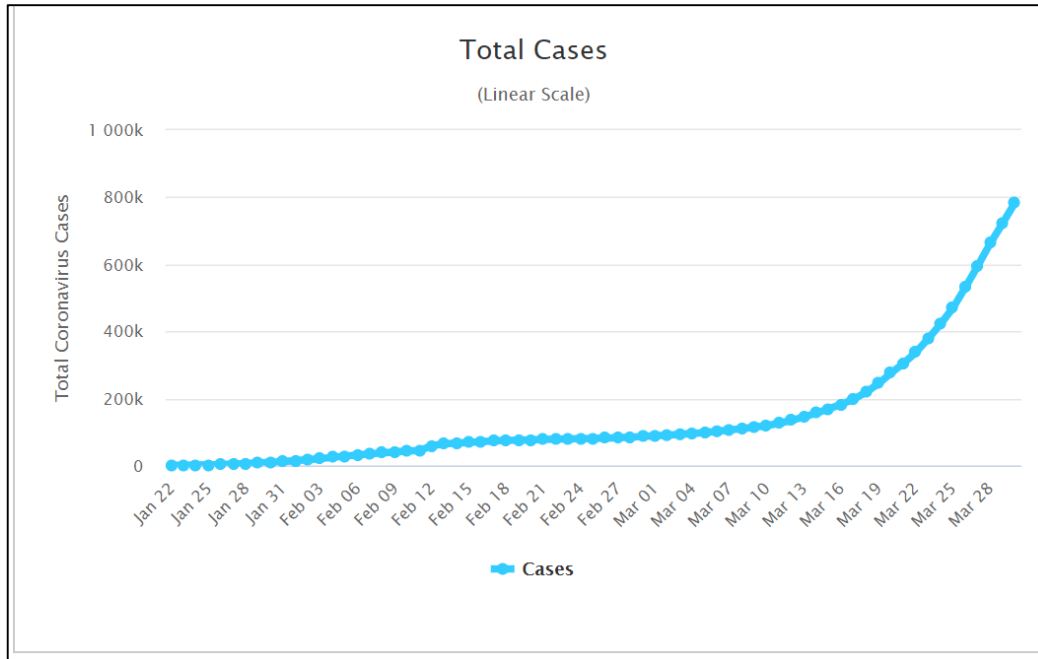
**802,369 cases**  
**38,990 deaths**



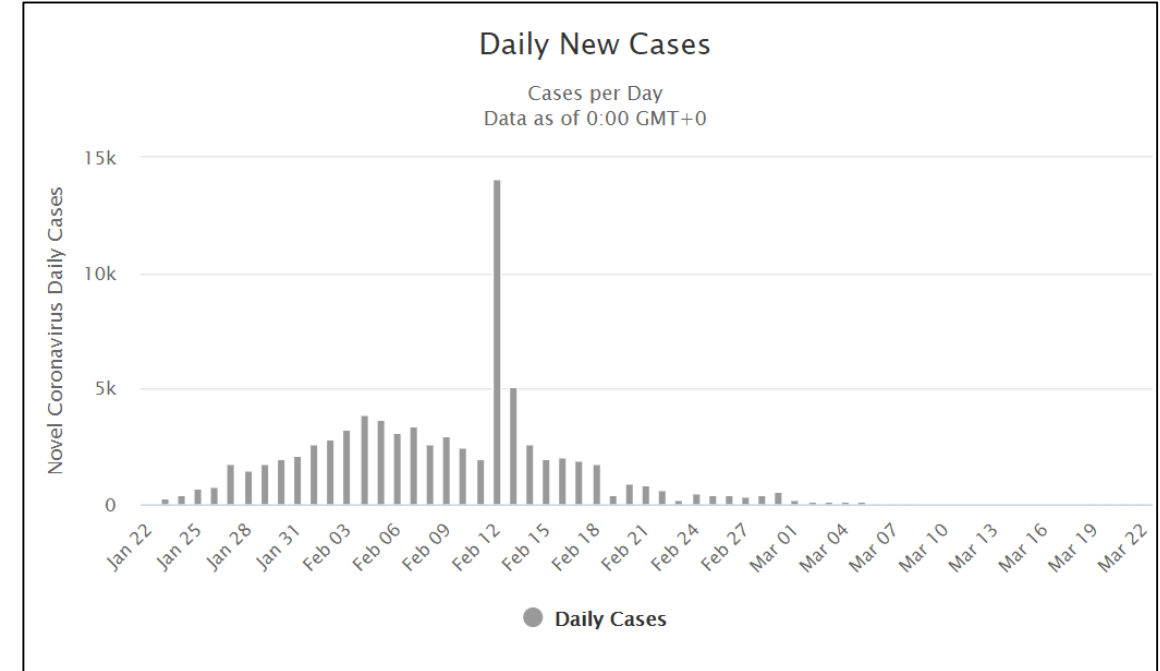
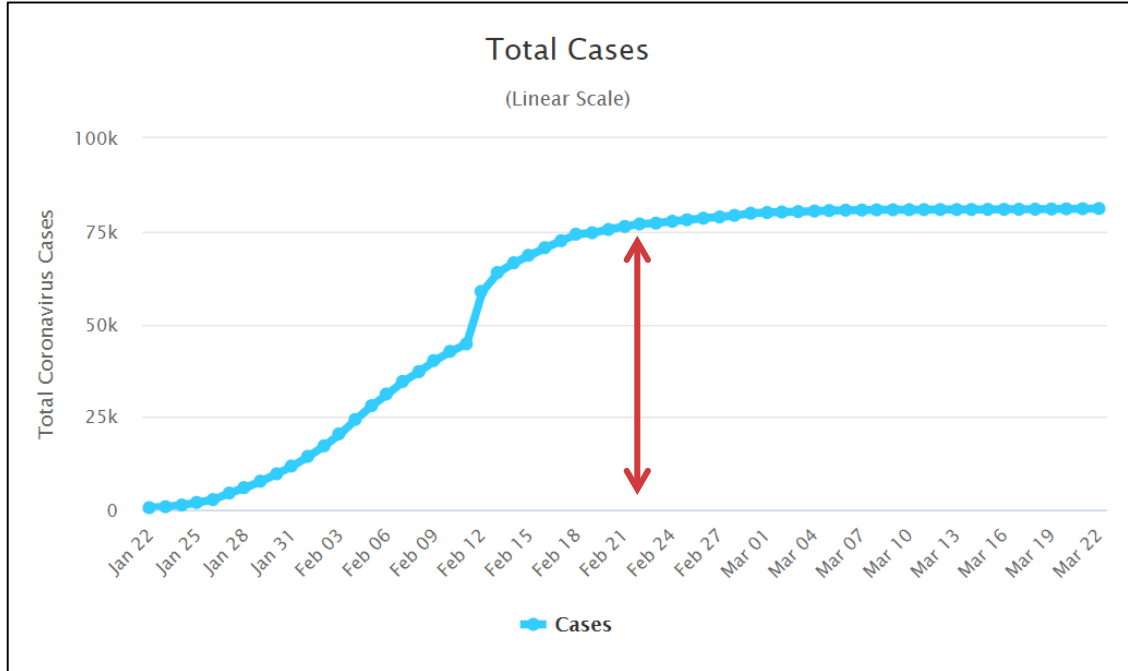
# Global situation – March 31, 2020



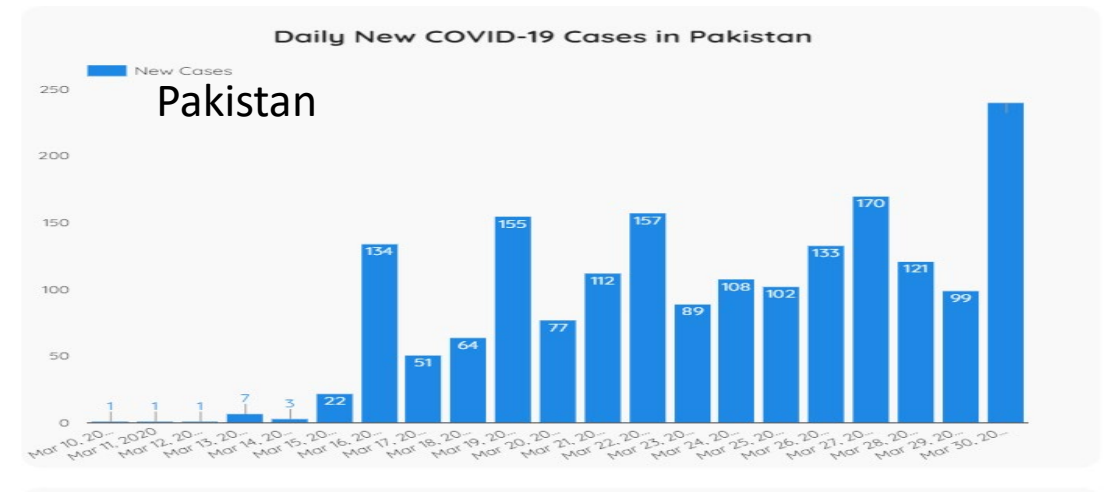
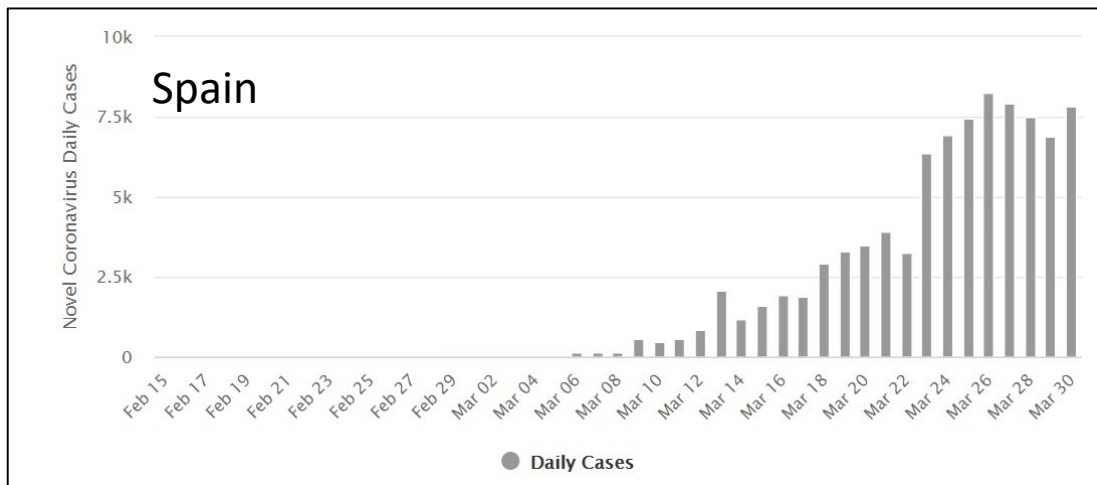
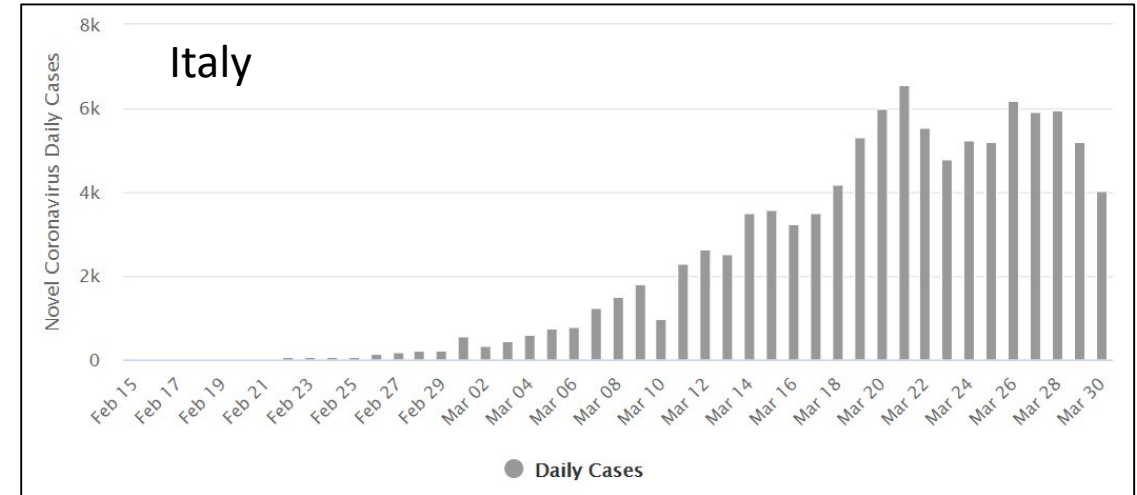
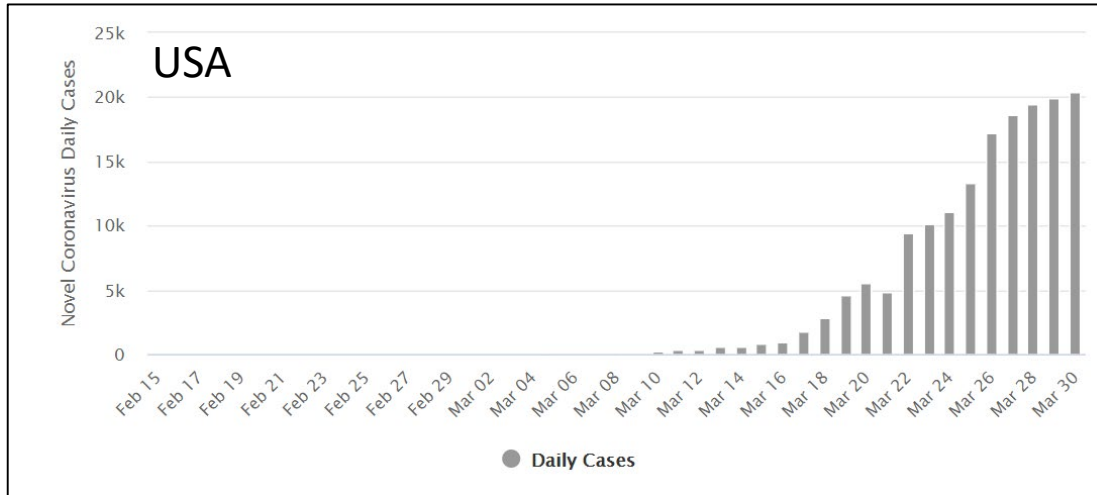
# Global situation – March 31, 2020



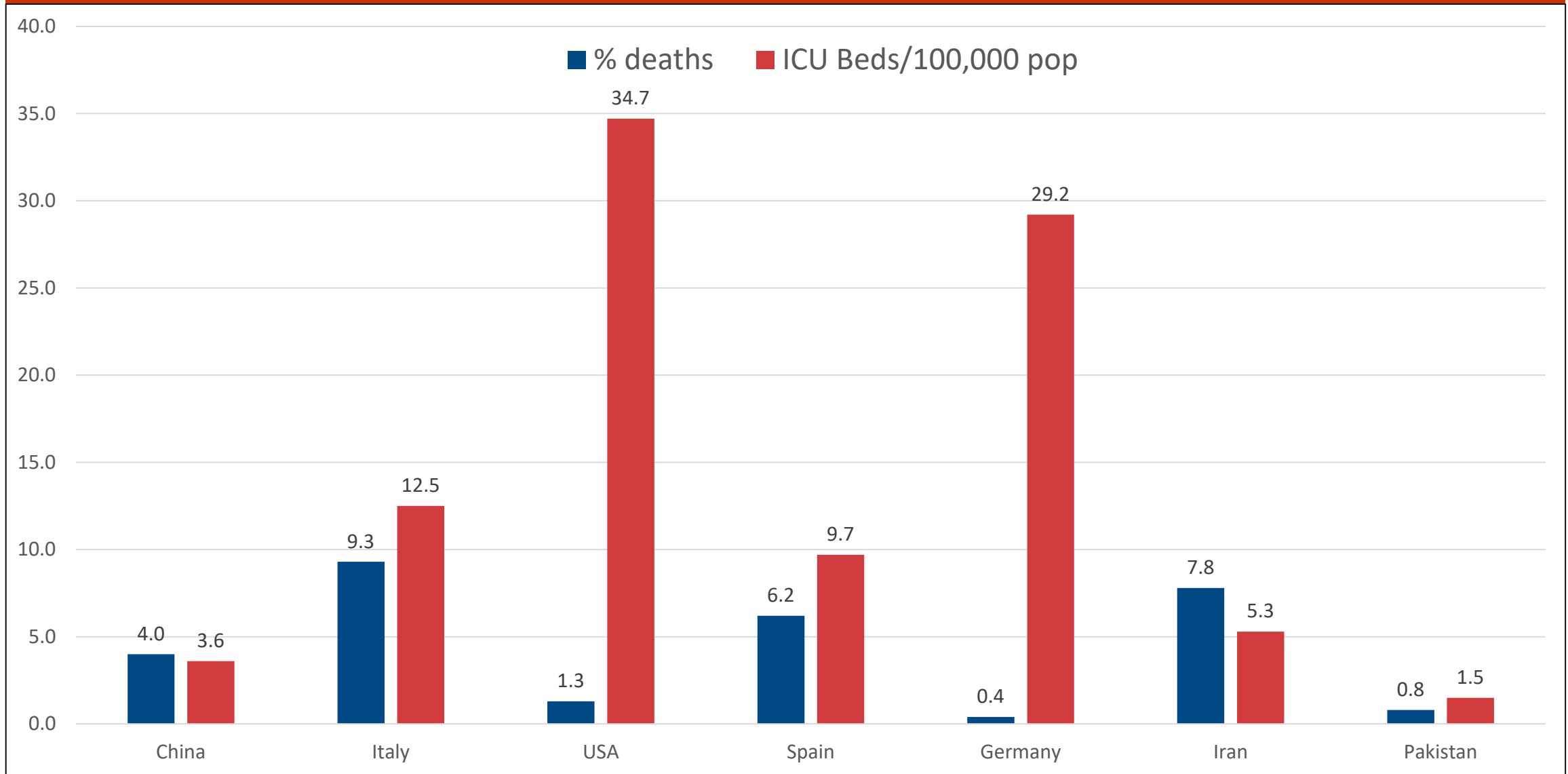
# China



# Daily new cases – 30 March 2020



# Proportion died and ICU beds/100,000 population



**Let's bust some myths first**

# Myth vs. Fact

- **TRUE or FALSE?**

**COVID-19 is like the regular flu**

**FALSE**

- COVID-19 is more infectious than the regular influenza virus and more lethal. However, while more infectious than other recent novel corona viruses (SARS and MERS CoV), it is less lethal than both.

# Myth vs. Fact

- **TRUE or FALSE?**

**I am young and otherwise healthy. I have nothing to fear**

**FALSE**

- While COVID-19 is more likely to cause serious illness and death in the elderly and those with chronic medical conditions, there have been plenty of severe cases and even deaths in the younger population. Also, young persons play a role in transmission of infection.



# Myth vs. Fact

- **TRUE or FALSE?**

**A vaccine to cure COVID-19 is available**

**FALSE**

- Vaccine trials have started and first group of patients have been enrolled. However, a safe, effective and viable vaccine is probably at least 12-18 months away.

# Myth vs. Fact

- **TRUE or FALSE?**

**You can protect yourself by swallowing or gargling with bleach, taking acetic acid or steroids, or using essential oils, salt water, ethanol or other substances**

**FALSE**

- There is no truth to such remedies being touted on social media. While some of these remedies may help with general wellness, others may be quite harmful. Do not forward or share such posts on social media. Always verify your sources and rely on highly reliable sources such as CDC and WHO.

# Myth vs. Fact

- **TRUE or FALSE?**

**The new coronavirus was deliberately created  
or released by people**

**FALSE**

- There is no truth to this. In fact recent a recent paper in a major medical journal has debunked that myth.

# Myth vs. Fact

- **TRUE or FALSE?**

**Ordering or buying products shipped from  
China will make a person sick**

**FALSE**

- There is no evidence of any transmission through trade or trade goods. In fact, with the infection rates dramatically reduced in China with exponential increase in cases in many other developed countries, this does not make sense.

# Myth vs. Fact

- **TRUE or FALSE?**

**A face mask will protect you from COVID-19.**

**FALSE**

- For proper protection, a professional fitted N-95 mask is required. CDC and WHO do not recommend regular face masks for all persons. However, those with symptoms of a respiratory infection should wear a surgical mask to prevent spreading the infection.

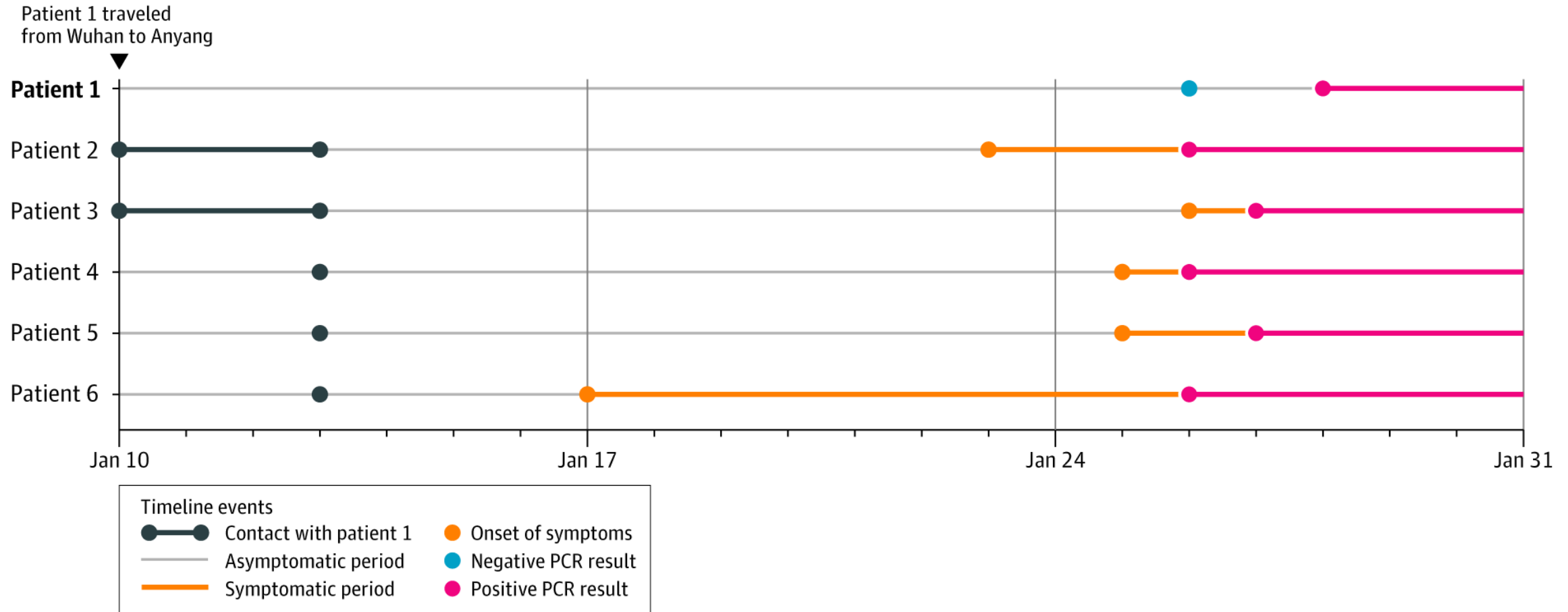
**How does the virus spread?**

# Viability of SARS-CoV-1 and SARS-CoV-2 in aerosols and on various surfaces

## Viability of SARS-CoV-2 on various surfaces

<b>Copper:</b>	<b>Upto 4 hours</b>
<b>Cardboard:</b>	<b>Upto 24 hours</b>
<b>Plastic:</b>	<b>2 to 3 days</b>
<b>Stainless steel:</b>	<b>2 to 3 days</b>
<b>Aerosols:</b>	<b>Upto 3 hours</b>

# Presumed asymptomatic carrier transmission





# Risk factors for healthcare workers

Factor	Relative risk (95% CI)
Diagnosed family member	2.76 (2.02 – 3.77)
Suspected family member	1.30 (0.31 – 5.35)
Diagnosed patient	0.36 (0.22 – 0.59)
Suspected patient	0.49 (0.27 – 0.89)
Suboptimal hand hygiene before patient contact	3.10 (1.43 – 6.73)
Improper PPE	2.82 (1.11 – 7.18)

**How does it present?**

# Clinical characteristics

<b>Fever at admission</b>	<b>44%</b>
<b>Fever during hospitalization</b>	<b>89%</b>
<b>Cough</b>	<b>68%</b>
<b>Fatigue</b>	<b>38%</b>
<b>Sputum production</b>	<b>34%</b>
<b>Shortness of breath</b>	<b>19%</b>
<b>Myalgias/arthralgias</b>	<b>15%</b>
<b>Sore throat</b>	<b>14%</b>
<b>Headache</b>	<b>14%</b>
<b>Chills</b>	<b>12%</b>
<b>Nausea/vomiting</b>	<b>5%</b>
<b>Nasal congestion</b>	<b>5%</b>
<b>Diarrhea</b>	<b>4%</b>

# Clinical features of patients with pneumonia

Initial common symptoms	
Fever	188 (93.5)
Cough	163 (81.1)
Productive cough	83 (41.3)
Dyspnea	80 (39.8)
Fatigue or myalgia	65 (32.3)
Chest imaging, infiltrate <sup>a</sup>	
Unilateral	10 (5.0)
Bilateral	191 (95.0)
Comorbidities	
Hypertension	39 (19.4)
Diabetes	22 (10.9)
Cardiovascular disease	8 (4.0)
Liver disease	7 (3.5)
Nervous system disease	7 (3.5)
Chronic lung disease	5 (2.5)
Chronic kidney disease	2 (1.0)
Clinical outcomes	
ARDS	84 (41.8)
ICU admission	53 (26.4)
Death	44 (21.9)

# Risk of ARDS and death

Patient characteristics and findings	ARDS		Death	
	HR (95% CI)	P value	HR (95% CI)	P value
<b>Clinical characteristics</b>				
Age ( $\geq 65$ vs $< 65$ ), y	3.26 (2.08-5.11)	$<.001$	6.17 (3.26-11.67)	$<.001$
Gender (male vs female)	1.47 (0.92-2.36)	.11	0.56 (0.30-1.05)	.07
Highest patient temperature ( $\geq 39$ °C vs $< 39$ °C)	1.77 (1.11-2.84)	.02	0.41 (0.21-0.82)	.01
<b>Comorbidities</b>				
Hypertension (yes vs no)	1.82 (1.13-2.95)	.01	1.70 (0.92-3.14)	.09
Diabetes (yes vs no)	2.34 (1.35-4.05)	.002	1.58 (0.80-3.13)	.19

Infection-related indices				
hs-CRP, mg/L ( $> 5$ vs $\leq 5$ )	4.81 (1.52-15.27)	.008	NA	NA
IL-6, pg/L	1.02 (1.00-1.05)	.09	1.03 (1.01-1.05)	.01
ESR, mm/h	1.01 (1.00-1.02)	.19	1.01 (0.99-1.02)	.32
Serum ferritin, ng/mL ( $> 300$ vs $\leq 300$ )	3.53 (1.52-8.16)	.003	5.28 (0.72-38.48)	.10
Coagulation function				
PT, s	1.56 (1.32-1.83)	$<.001$	1.08 (0.84-1.38)	.54
APTT, s	0.97 (0.94-1.01)	.13	0.96 (0.91-1.00)	.06
D-dimer, $\mu\text{g/mL}$	1.03 (1.01-1.04)	$<.001$	1.02 (1.01-1.04)	.002

# Risk factors for more severe disease

- Older age
- Comorbidities
  - Diabetes
  - Hypertension
  - Chronic kidney disease
  - Chronic lung disease
  - Chronic liver disease
- Reduced immunity

# Case fatality rate

- China: 2.3%
- Korea: 1.0%
- Italy: 7.2%
  - Older demographic (23% > 65) and 37.6% of cases in Italy were in people > 70
  - Italian CFR uses death from any cause, not limited to “COVID-19-related deaths”
  - Stringent testing policy (only hospitalized, high risk patients), may have decreased denominator and therefore increased CFR

Age, y	Deaths, No. (% of total)	Case-fatality rate, %
0-9	0	0
10-19	0	0
20-29	0	0
30-39	4 (0.25)	0.3
40-49	10 (0.62)	0.4
50-59	43 (2.65)	1.0
60-69	139 (8.55)	3.5
70-79	578 (35.57)	12.5
80-89	694 (42.71)	19.7
≥90	156 (9.6)	22.7
Not reported	1 (0.06)	0.6
<b>Total</b>	<b>1625 (100)</b>	<b>7.2</b>

Cases by region/province of diagnosis



**Authors:** Edward Livingston, MD;  
Karen Bucher, MA, CMI

**Sources:** Adapted from the COVID-19 Task Force of the Department of Infectious Diseases and the IT Service Istituto Superiore di Sanità. <https://www.iss.it/infografiche>  
**Please cite as:** JAMA. Published online March 17, 2020. doi:10.1001/jama.2020.4344



JAMA Network

**How to diagnose?**



# Diagnosis

- Nasopharyngeal swab
- Lower respiratory secretions
- Bronchoalveolar lavage fluid
- Also found in sputum and stool
- Serology (IgG, IgM)
- Radiographic (CXR or CT scan)
- New assays being developed
- Antigen detection

Not recommended unless  
no other option due to  
high risk of infection

Rapid, point-of-care

To confirm presence and extent of  
pneumonia rather than etiologic diagnosis

Real time RT-PCR

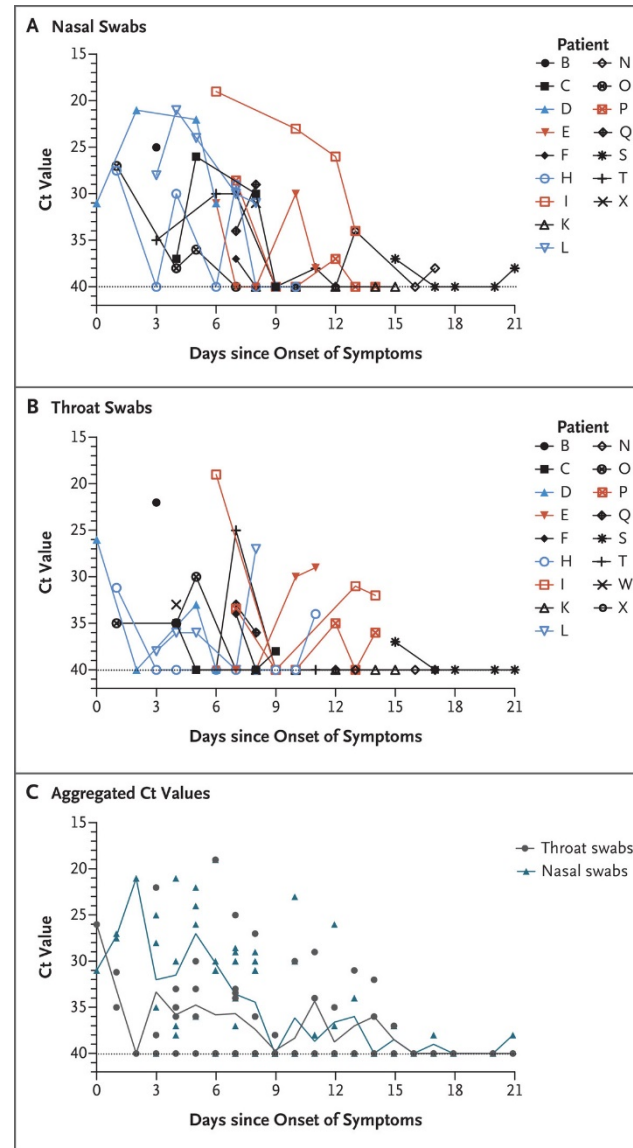
# Detection in different types of clinical specimens

Table. Detection Results of Clinical Specimens by Real-Time Reverse Transcriptase–Polymerase Chain Reaction

Specimens and values	Bronchoalveolar lavage fluid (n = 15)	Fibrobronchoscope brush biopsy (n = 13)	Sputum (n = 104)	Nasal swabs (n = 8)	Pharyngeal swabs (n = 398)	Feces (n = 153)	Blood (n = 307)	Urine (n = 72)
Positive test result, No. (%)	14 (93)	6 (46)	75 (72)	5 (63)	126 (32)	44 (29)	3 (1)	0
Cycle threshold, mean (SD)	31.1 (3.0)	33.8 (3.9)	31.1 (5.2)	24.3 (8.6)	32.1 (4.2)	31.4 (5.1)	34.6 (0.7)	ND
Range	26.4-36.2	26.9-36.8	18.4-38.8	16.9-38.4	20.8-38.6	22.3-38.4	34.1-35.4	
95% CI	28.9-33.2	29.8-37.9	29.3-33.0	13.7-35.0	31.2-33.1	29.4-33.5	0.0-36.4	

Abbreviation: ND, no data.

# Viral load in upper and lower respiratory specimen



**How to treat?**

# Treatment principles

- On 30 March 2020, FDA issued an EUA (Emergency Use Authorization) to allow chloroquine and hydroxychloroquine for treatment of certain patients with COVID-19 infection. This does not include prophylaxis.
- Treatment is otherwise largely supportive

Caring for critically ill patients with COVID-19 is based on the usual management of viral pneumonia with respiratory failure with additional precautions to reduce risk of transmission.

## Usual critical care

Many patients with severe COVID-19 develop acute respiratory distress syndrome (ARDS). Evidence-based guidelines for ARDS in the context of COVID-19 include treatments such as

- Conservative intravenous fluid strategies
- Lung-protective ventilation strategies
- Empirical early antibiotics for possible bacterial pneumonia
- Periodic prone positioning during mechanical ventilation
- Consideration for early invasive ventilation
- Consideration of extracorporeal membrane oxygenation

## Modifications to usual critical care

- Admission of patients with suspected disease to private rooms when possible
- Use of medical face masks for symptomatic patients during assessment and transfer
- Maintain distancing of at least 2 m between patients
- Caution when using high-flow nasal oxygen or noninvasive ventilation due to risk of dispersion of aerosolized virus in the health care environment with poorly fitting masks
- Clinicians involved with aerosol-generating procedures should use additional airborne precautions including N95 respirators and eye protection

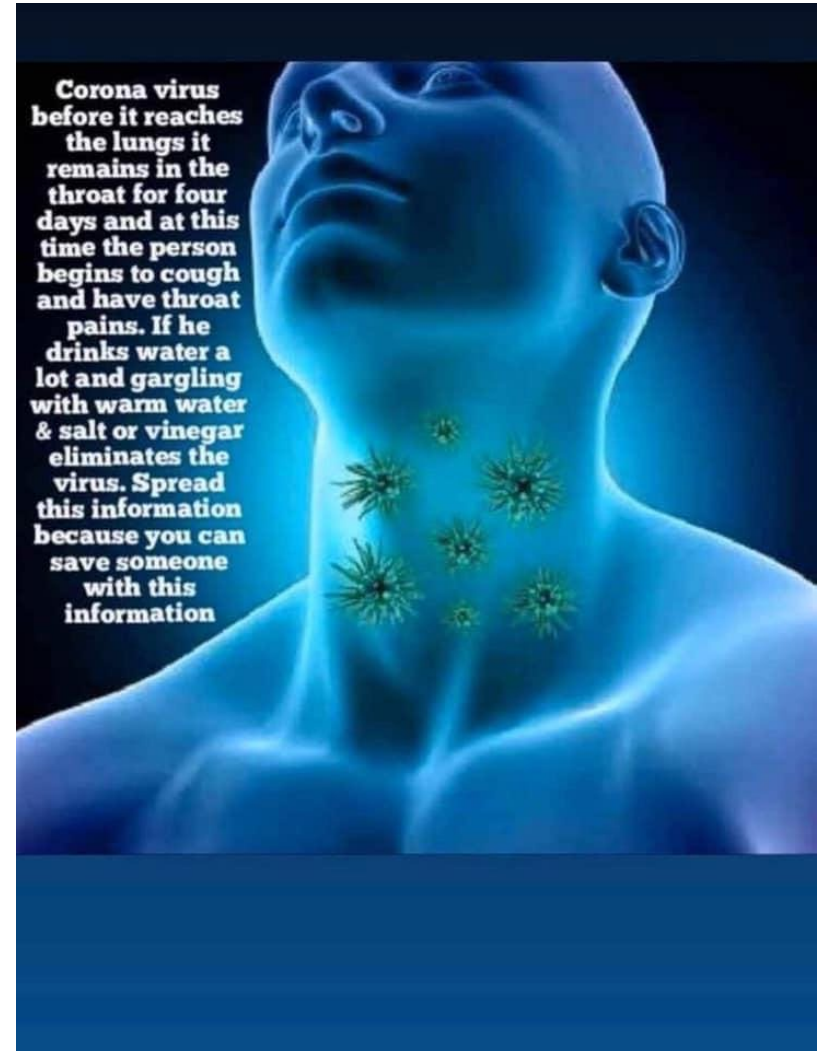
## Facility planning

- Ensure staff have updated training in infection prevention and control including personal protective equipment
- Planning at local and regional levels for a potential surge in the need for critical care resources

## COVID-19-specific considerations

Antiviral or immunomodulatory therapies are not yet proven effective for treatment of COVID-19. Patients should be asked to participate in clinical trials of supportive or targeted therapies.

# First do no harm: what DOES NOT work



# Potential treatment regimens

## Possible role

- Chloroquine/azithromycin
- Convalescent plasma/serum
- Remdesivir
- IL-6 receptor blockers (e.g. tocilizumab)

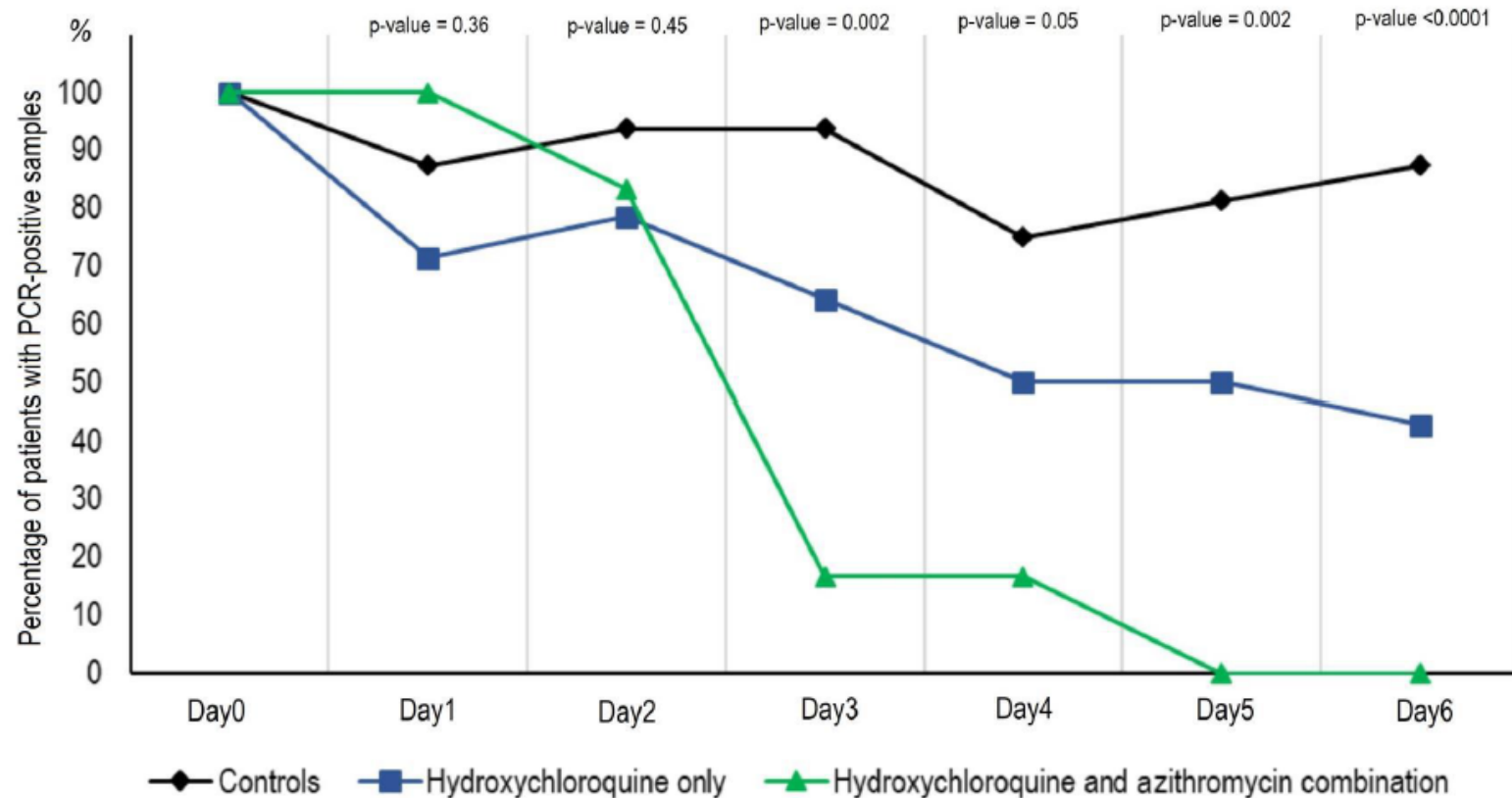
## No role (except specific other need)

- Steroids
- ACE-inhibitors
- Oseltamivir

## Unsure

- Lopinavir/ritonavir
- Interferon/ribavirin
- NSAIDS
- Vitamin C

# Hydroxychloroquine + azithromycin



- Only 20 subjects in the active treatment arm
- No control group
- Varying disease severity



# Hydroxychloroquine + azithromycin

## Study Design

COVID-19

URTI

LRTI

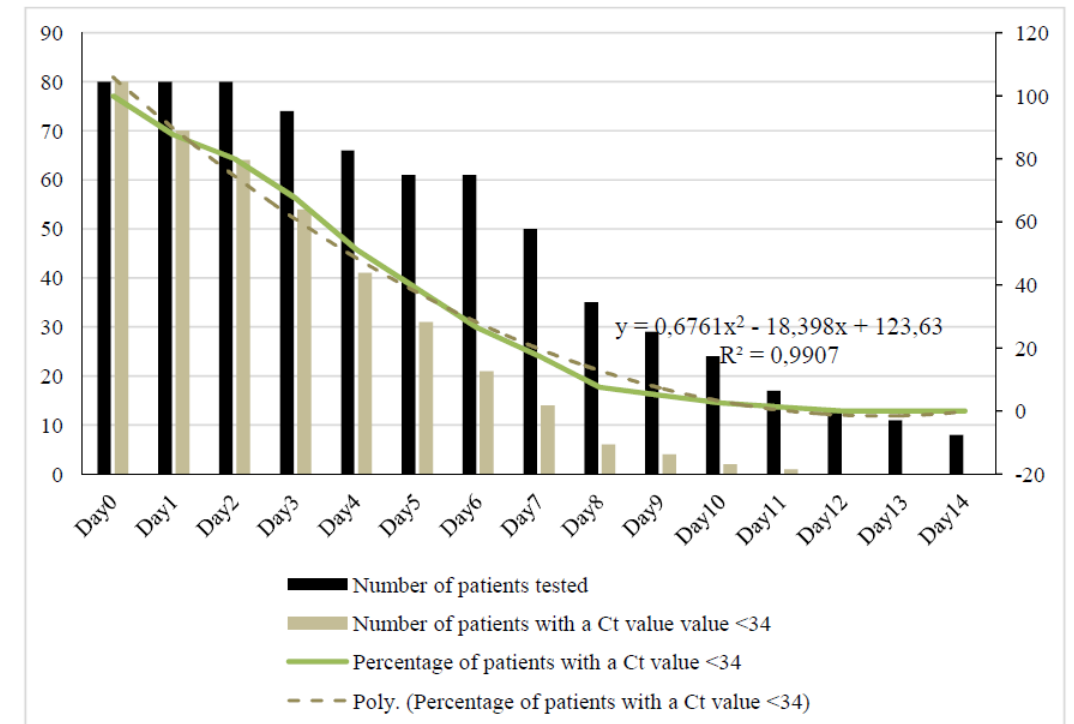
HCQ 200 mg TID x 10 d  
Azithro 500mg x 1; then 250 QD x 4 d

Aggressive course (O2 requirement; ICU admission)  
Contagiousness (PCR<34; culture negative)  
LOS in ID ward

Clinical Classification		
Asymptomatic	5.0%	
URTI	41.2%	
LRTI	53.8%	
Severity (based on NEWS score)	At admission	At discharge
Low	92.0%	93.8%
Medium	5.3%	6.2%
High	2.7%	-
Pneumonia on CT		
Not done	20.0%	
No pneumonia	26.2%	
Pneumonia present	53.8%	

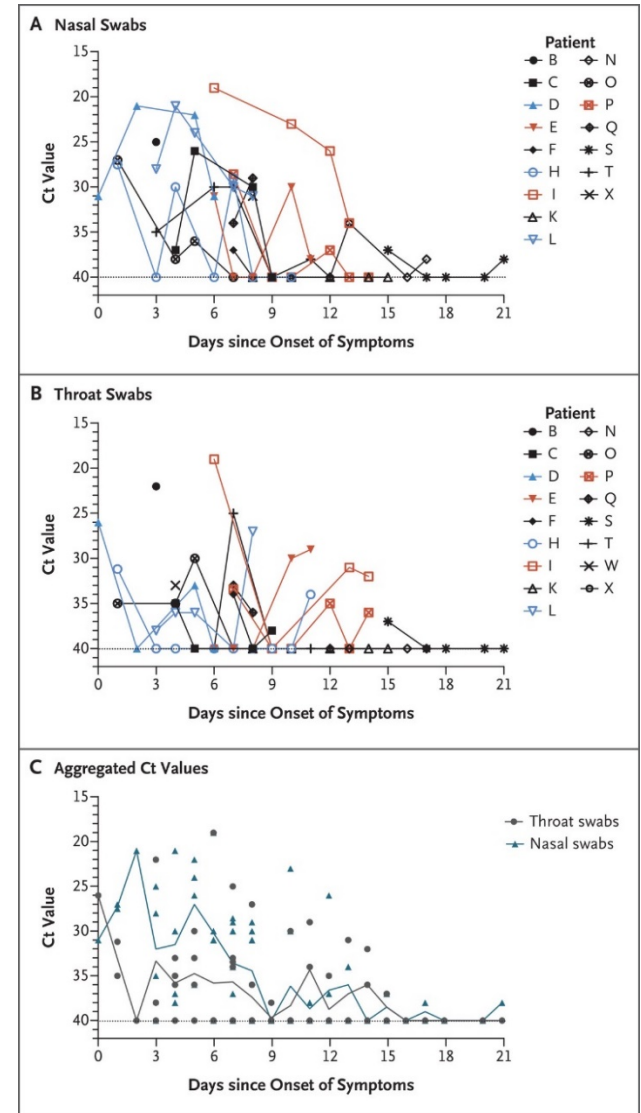
Number of patients

Percentage

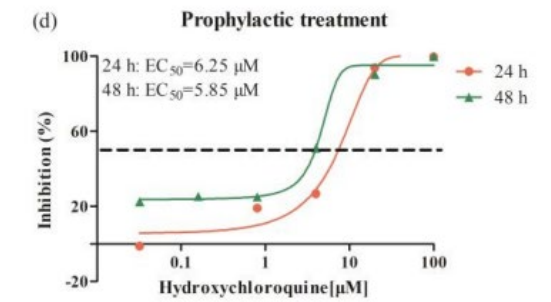
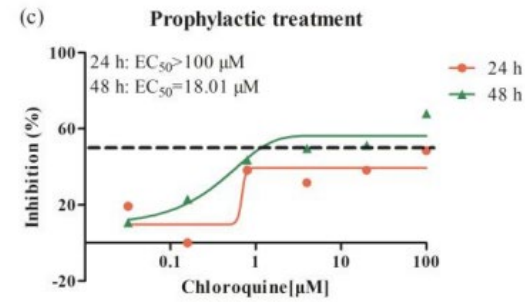
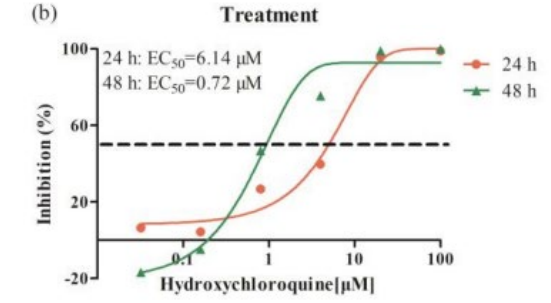
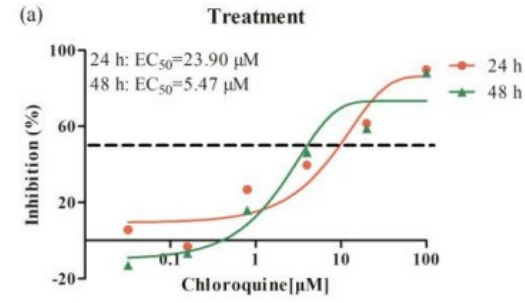
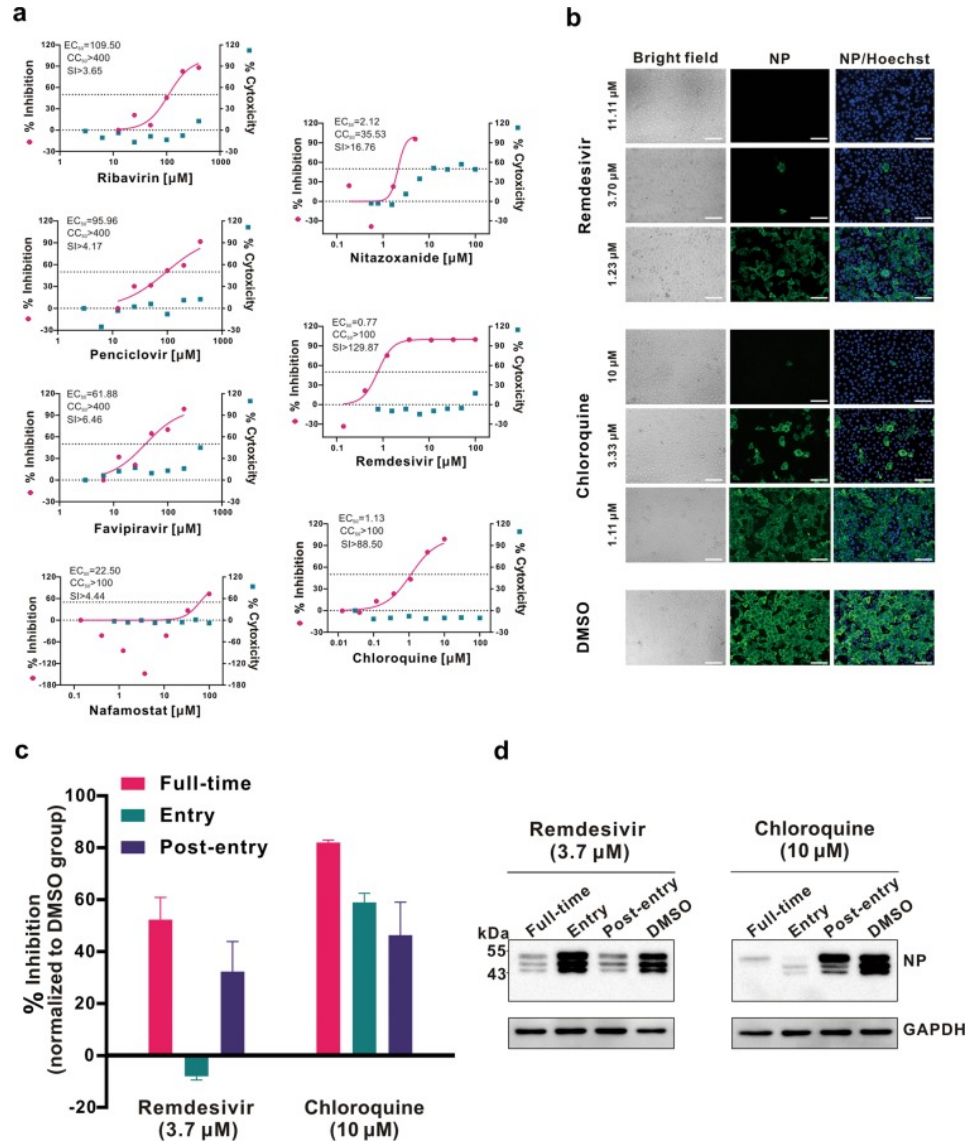


## Concerns

- No control group
- Varying severity of disease
- Other treatments unclear
- No change in disease severity
- Even patients with pneumonia may have had mild disease
- Decreasing numbers tested from day 3 onwards



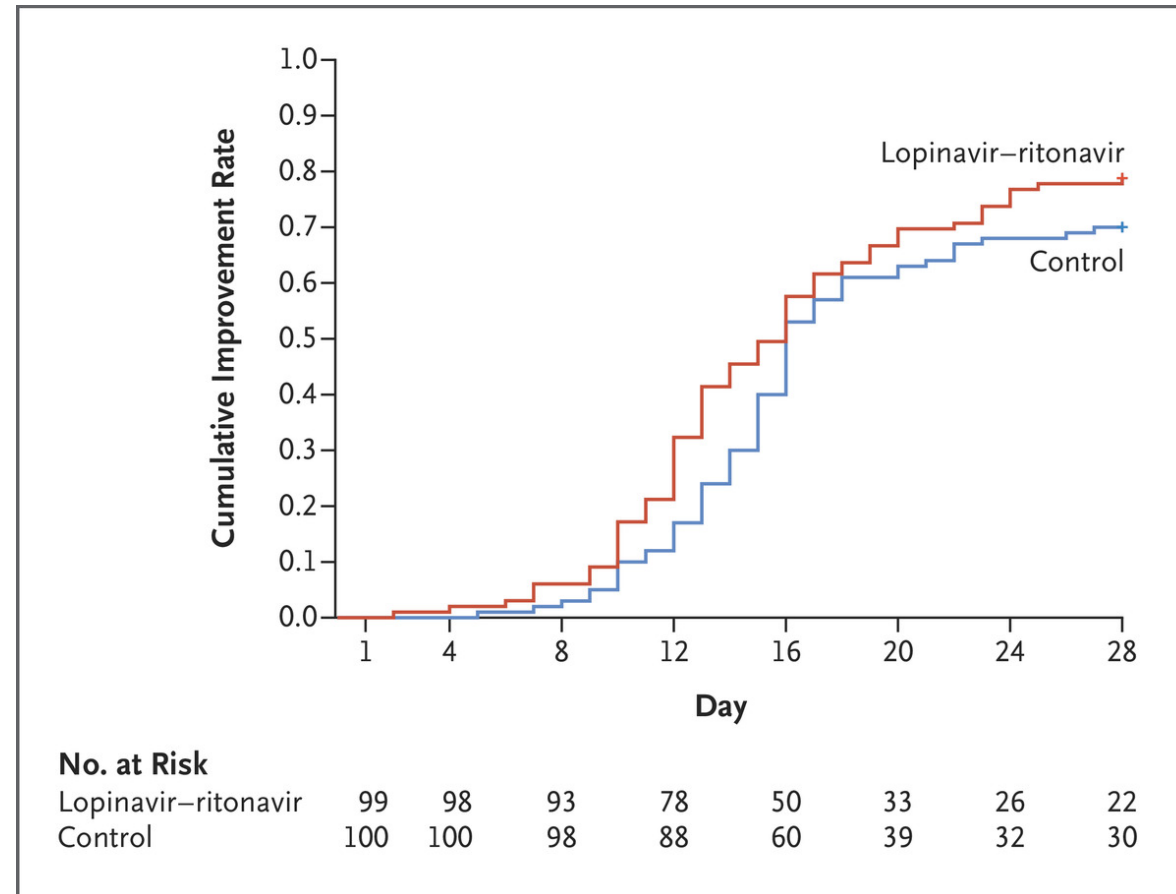
# Remdesivir, chloroquine, hydroxychloroquine



- Benefit observed *in vitro*
- Increased inhibition of virus

# Lopinavir/ritonavir

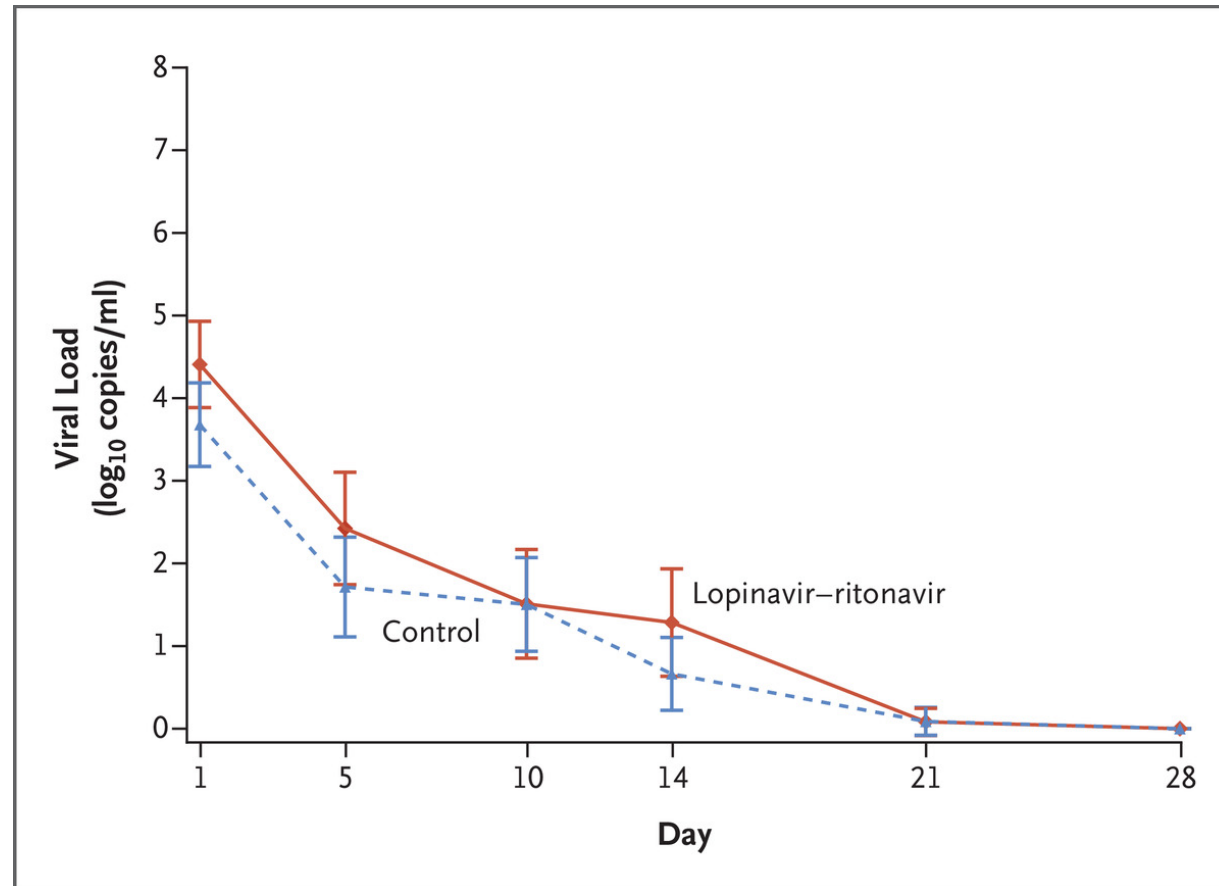
## Time to Clinical Improvement in the Intention-to-Treat Population



- Large enough study
- No benefit of Lopinavir/ritonavir observed

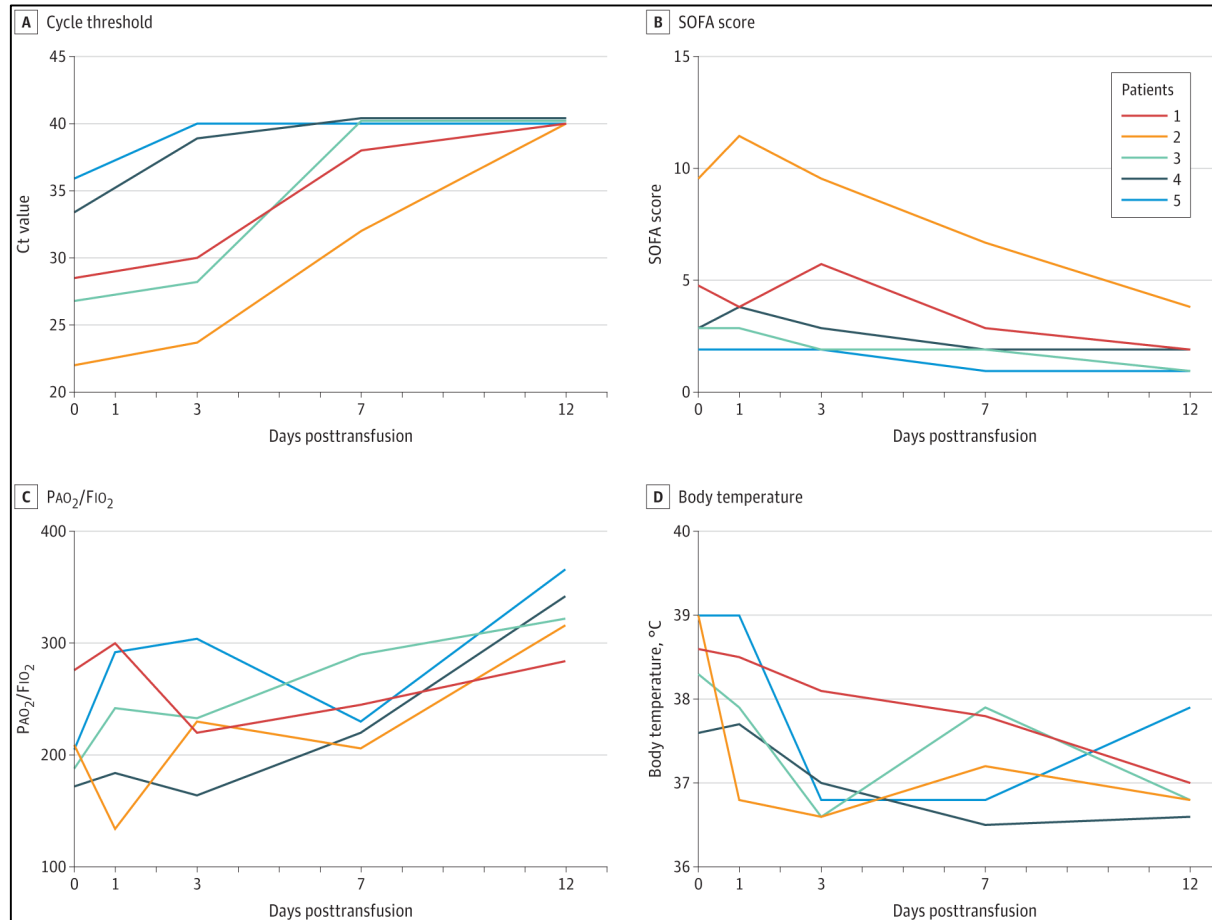
# Lopinavir/ritonavir

Mean Change from Baseline in Viral RNA Load by qPCR on Throat Swabs.



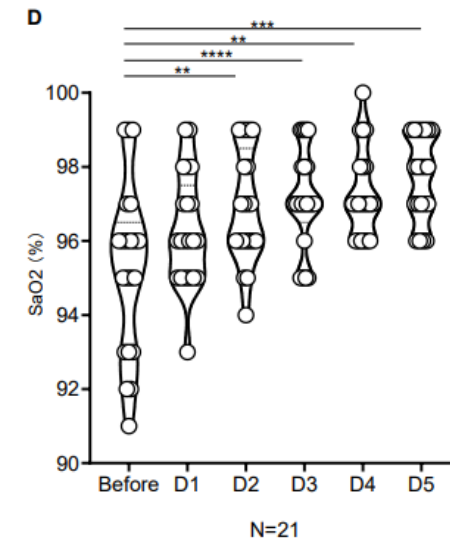
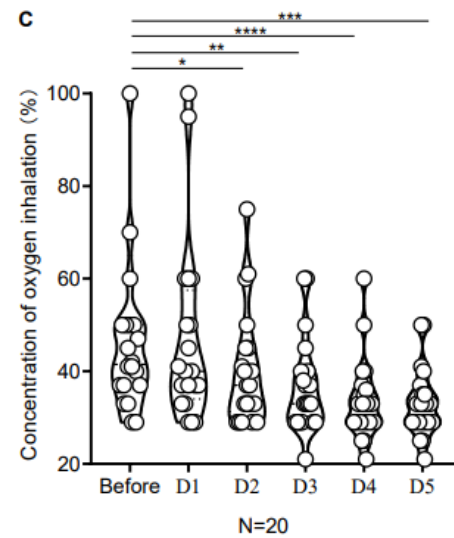
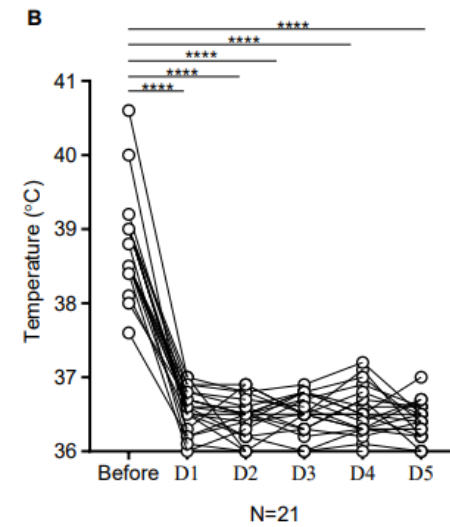
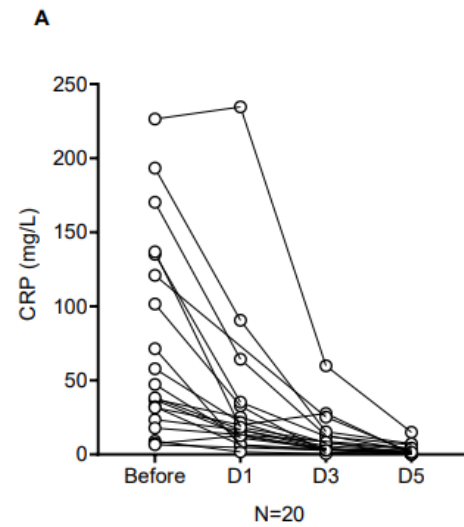
- Large enough study
- No benefit of Lopinavir/ritonavir observed

# Convalescent serum



- Only 5 subjects; No control group
- Also received other treatments (antivirals)
- Plasma transfusion done 10-22 after admission

# Tocilizumab

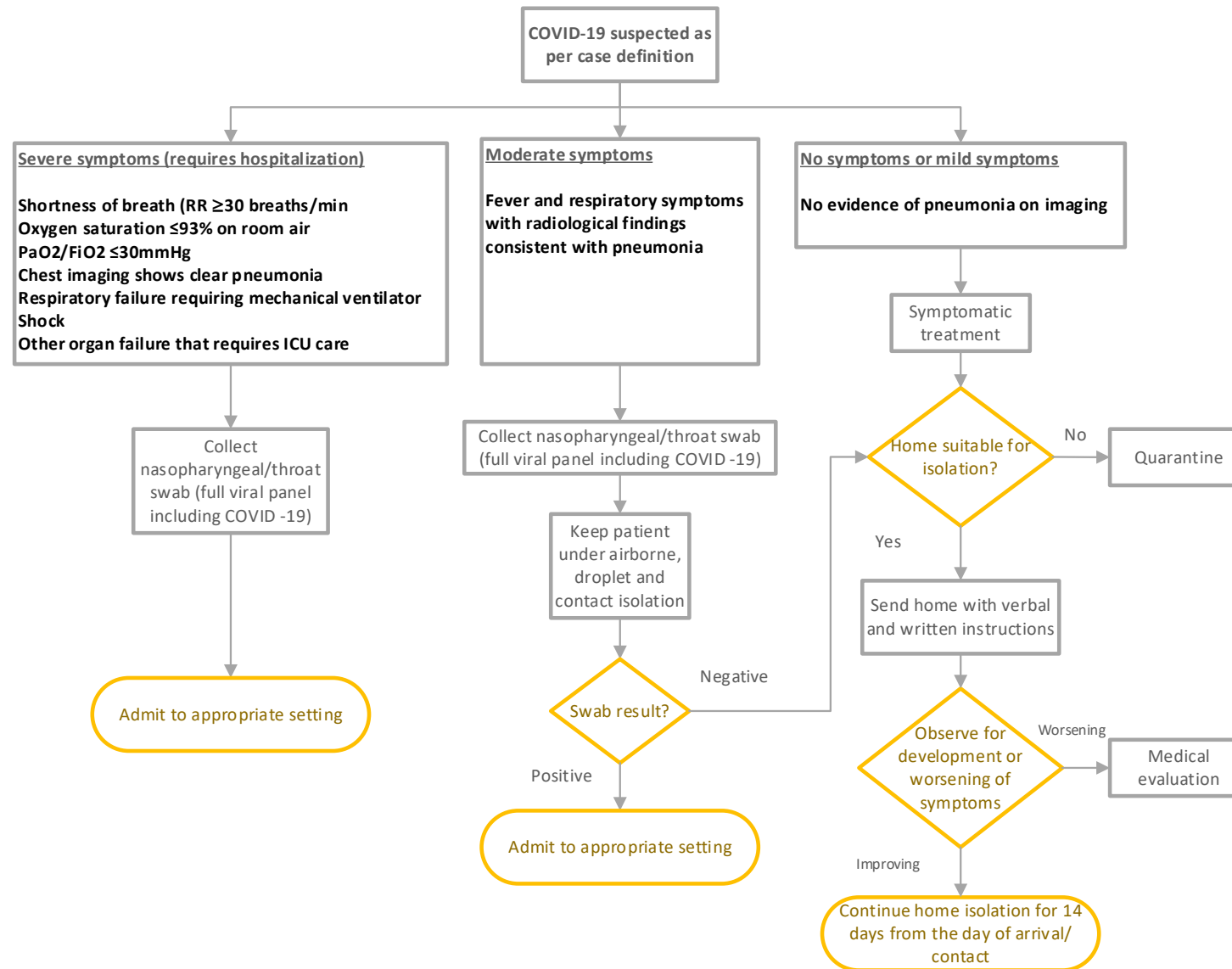


# Treatment for severe ARDS

Therapy	Implementation
High-flow nasal oxygen	Might prevent or delay the need for intubation
Tidal volume	Use 6 mL/kg per predicted bodyweight (can reduce to 4 mL/kg per predicted bodyweight)
Plateau airway pressure	Maintain at <30 cm H <sub>2</sub> O if possible
Positive end-expiratory pressure	Consider moderate to high levels if needed
Recruitment manoeuvres	Little value
Neuromuscular blockade	For ventilator dyssynchrony, increased airway pressure, hypoxaemia
Prone positioning	For worsening hypoxaemia, PaO <sub>2</sub> :FiO <sub>2</sub> <100–150 mm Hg
Inhaled NO	Use 5–20 ppm
Fluid management	Aim for negative fluid balance of 0.5–1.0 L per day
Renal replacement therapy	For oliguric renal failure, acid-base management, negative fluid balance
Antibiotics	For secondary bacterial infections
Glucocorticoids	Not recommended
Extracorporeal membrane oxygenation	Use EOLIA trial criteria <sup>3</sup>

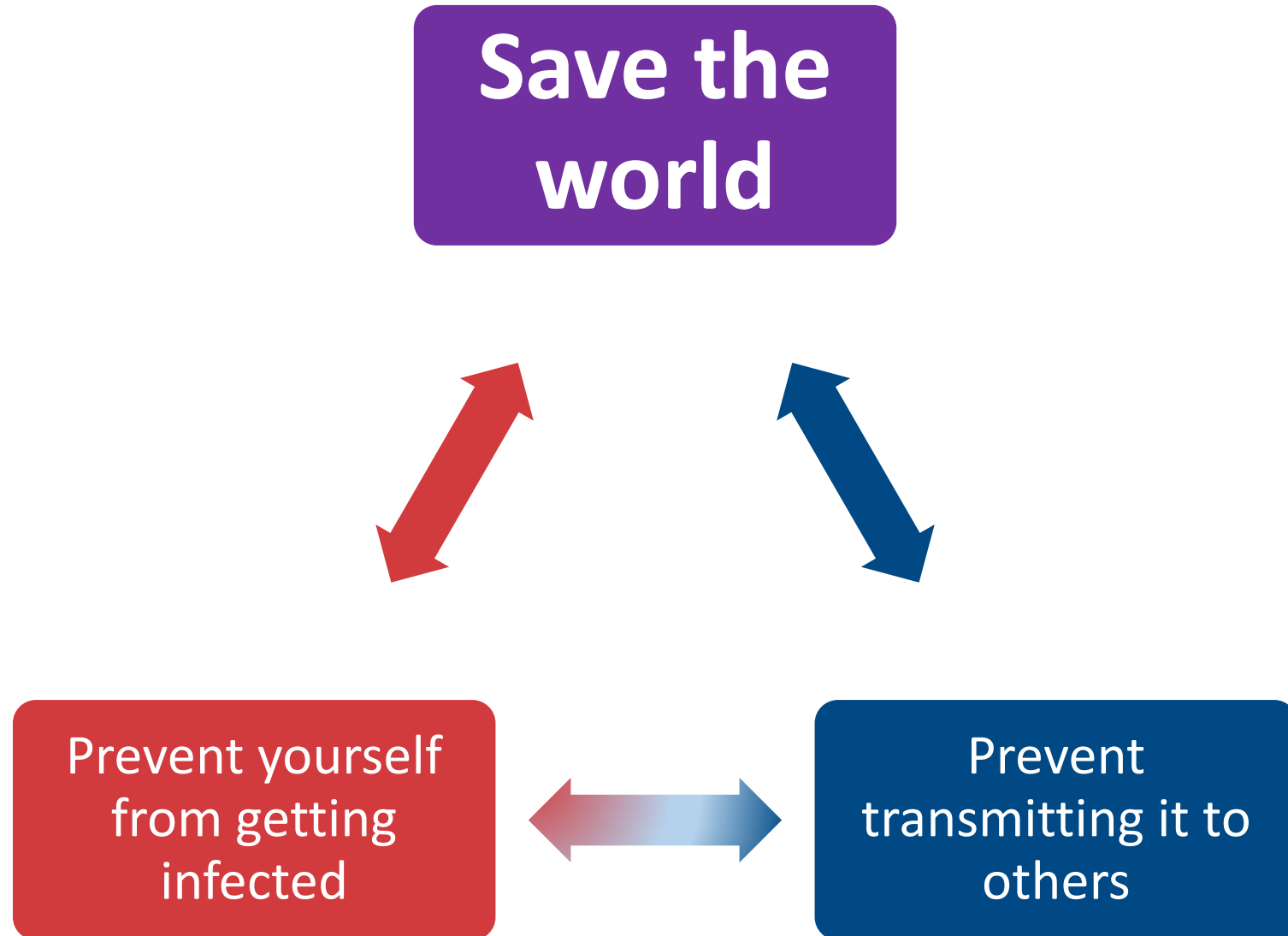


# Triage algorithm (one of many such available)



**How to prevent?**

# Prevention



# Break the cycle of transmission

## Social distancing

No handshakes, hugs  
Work from home

## Hygiene

Frequent handwashing or sanitization  
Proper cough etiquette

**BREAK THE CYCLE**

## Stay at home

Work from home  
Restrict travel to critical travel

## No mass gathering

Avoid malls, restaurants, weddings,  
funerals, mosques

# Management of contacts

- Medical evaluation
- If contact with a confirmed case, then test and isolate
  - Distance <6 feet (some say 4 feet) for >15 minutes (some say 30 minutes)
- Further management based on meeting case definition and symptoms
  
- Contact of an asymptomatic contact
  - General preventive measures only
  - Strict quarantine not indicated
  - Stay at home, social distancing, hygienic principles

# At the workplace (other than healthcare facilities)

- Work from home wherever and whenever possible
- Audio or videoconferencing for meetings
- Do not gather in large numbers
- No handshakes
- Close or avoid common areas (water cooler, cafeteria, etc.)
- Frequent hand hygiene
- Frequent and meticulous cleaning of common areas and surfaces

# Summary

- Pandemic is on the upswing in most areas of the world
- However, good news is that China managed to stem it relatively quickly
- Public health measures do work
  
- Public has to take responsibility
- Governments must provide unified and clear advice and enforce public health measures



INNOVATIONS IN HEALTHCARE ADVOCACY,  
RESEARCH AND TRAINING

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# Reimagining Healthcare

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