

# COVID-19

Updates & Key Messages

1 April 2020





## **Christopher B. Hurt, MD**

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Site PI, Ryan White HIV/AIDS Program Part D, UNC ID Clinic  
Co-Leader, UNC CFAR Collaborative HIV Epidemiology &  
Prevention Scientific Working Group

Institute for Global Health & Infectious Diseases  
University of North Carolina at Chapel Hill  
School of Medicine

As of 1 Oct 2018, Dr. Hurt receives salary support for supervising UNC site activities in a Gilead-funded study of PrEP (DISCOVER).

Dr. Hurt is supported by the Centers for Disease Control and Prevention (ELC-2017-J3), Health Resources and Services Administration (HRSA-17-039, U1OHA30535), the National Institute on Drug Abuse (UH3DA044823), and the National Institute of Allergy and Infectious Diseases (P30AI50410, UM1AI069423, UM1AI068619).

**The views expressed are not necessarily those of CDC, HRSA, or the NIH.**

# Definitions

## Coronavirus

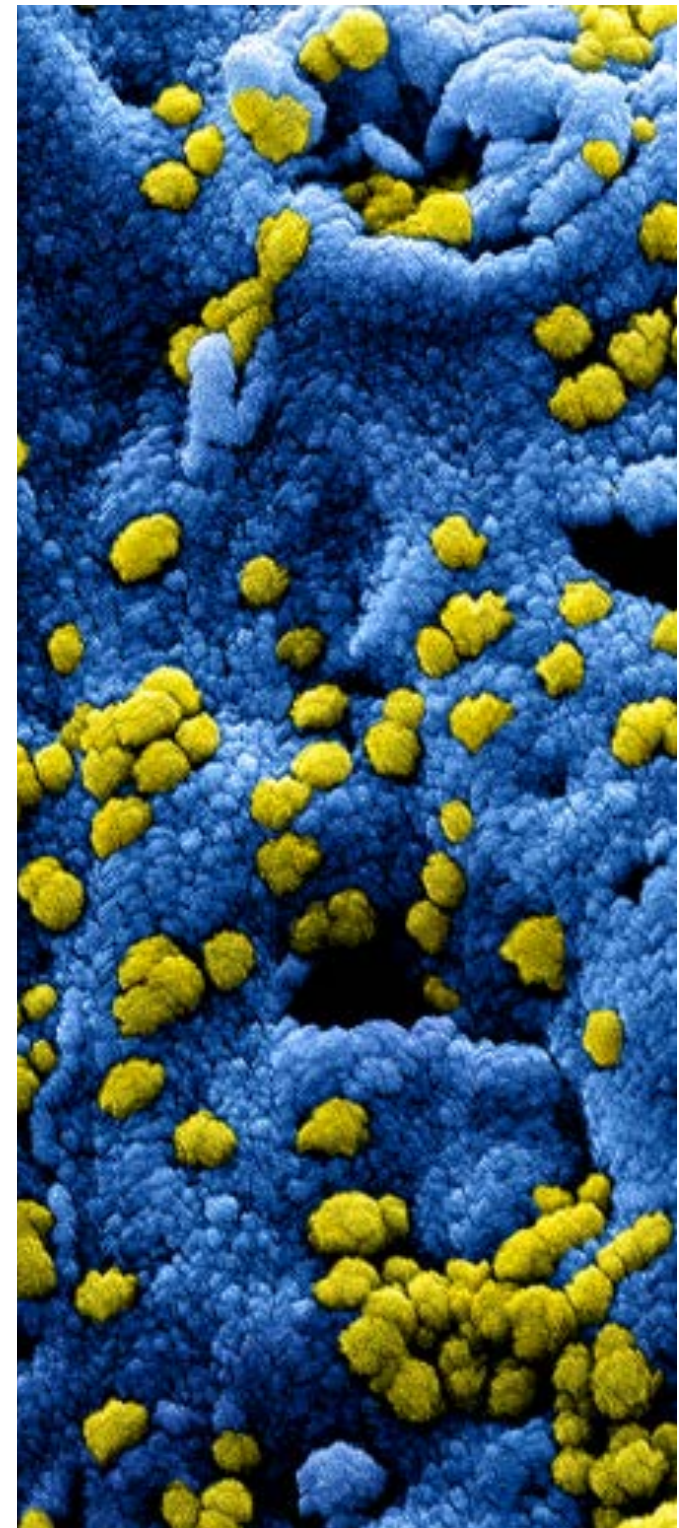
Any of a group of RNA viruses that can infect animals and humans

## SARS-CoV-2

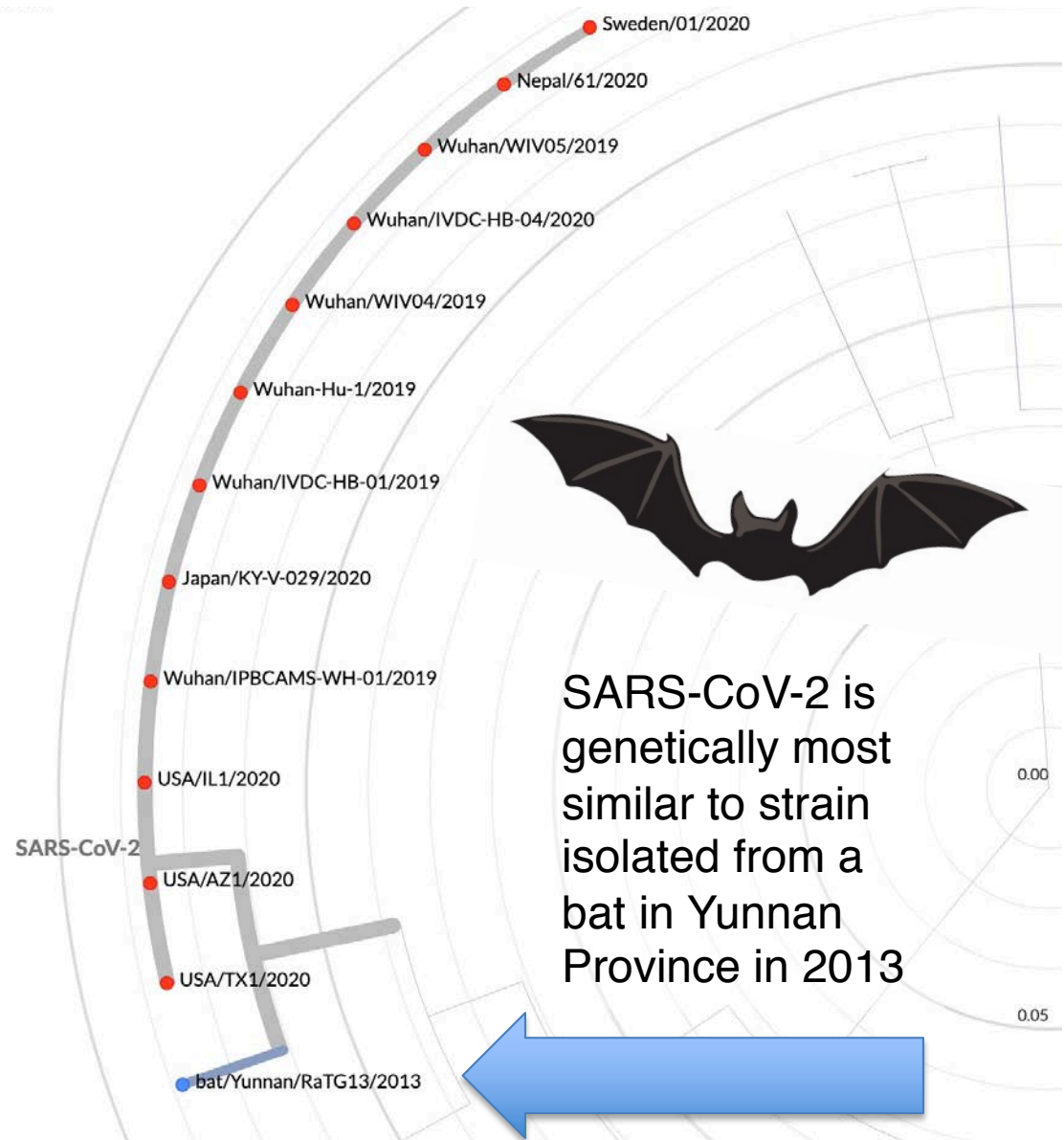
Official name of novel coronavirus causing current epidemic

## COVID-19

Official name of the disease resulting from infection with the SARS-CoV-2 coronavirus



# Where did SARS-CoV-2 come from?



# How did SARS-CoV-2 jump into people?

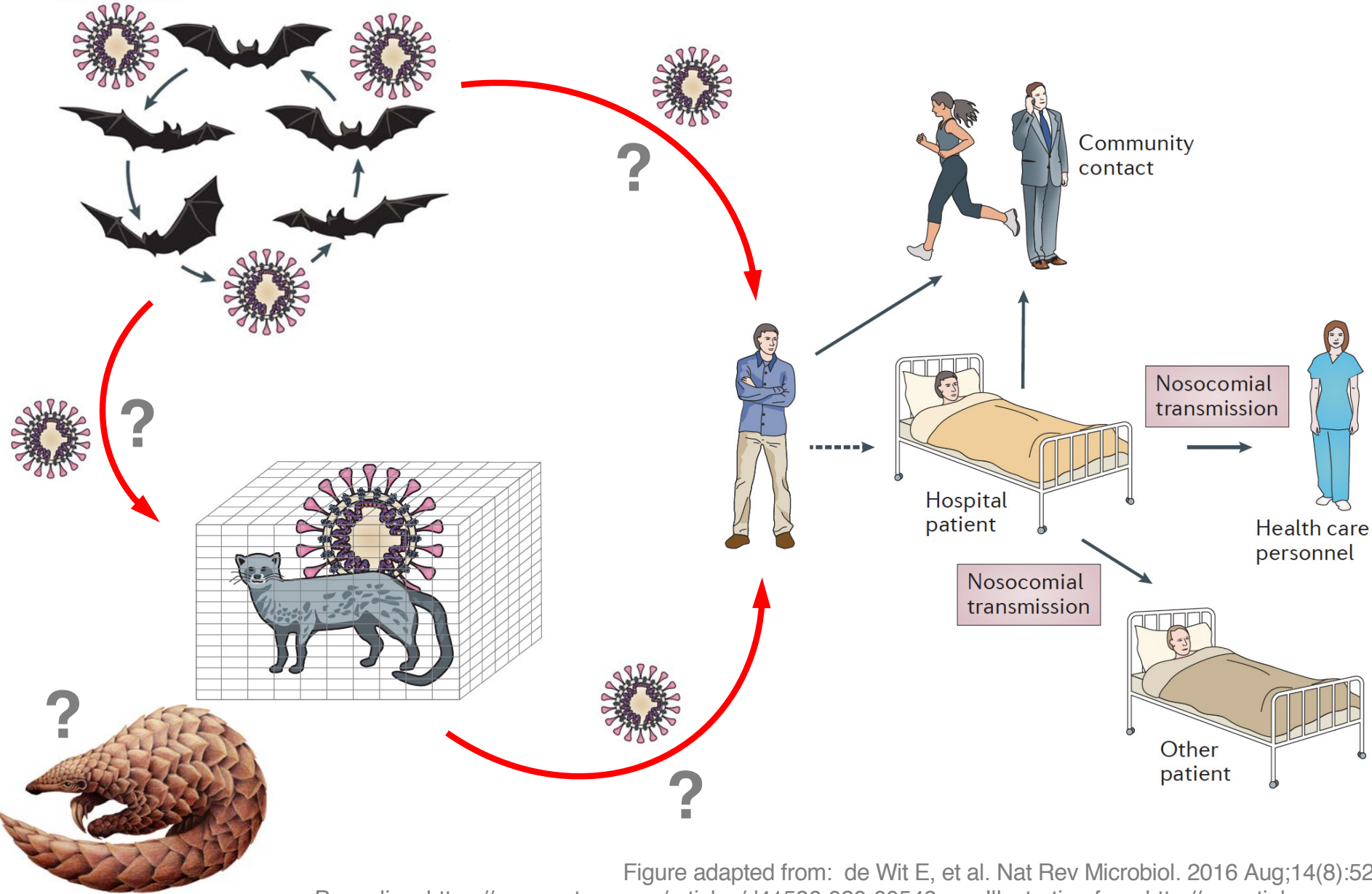
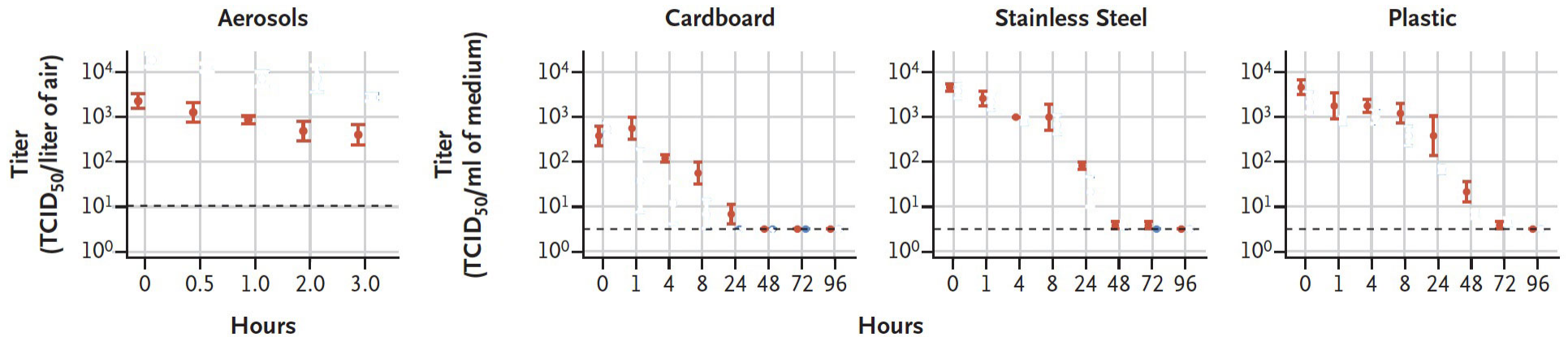


Figure adapted from: de Wit E, et al. Nat Rev Microbiol. 2016 Aug;14(8):523-34  
Pangolins: <https://www.nature.com/articles/d41586-020-00548-w> Illustration from <http://www.tinkerpaws.com/>

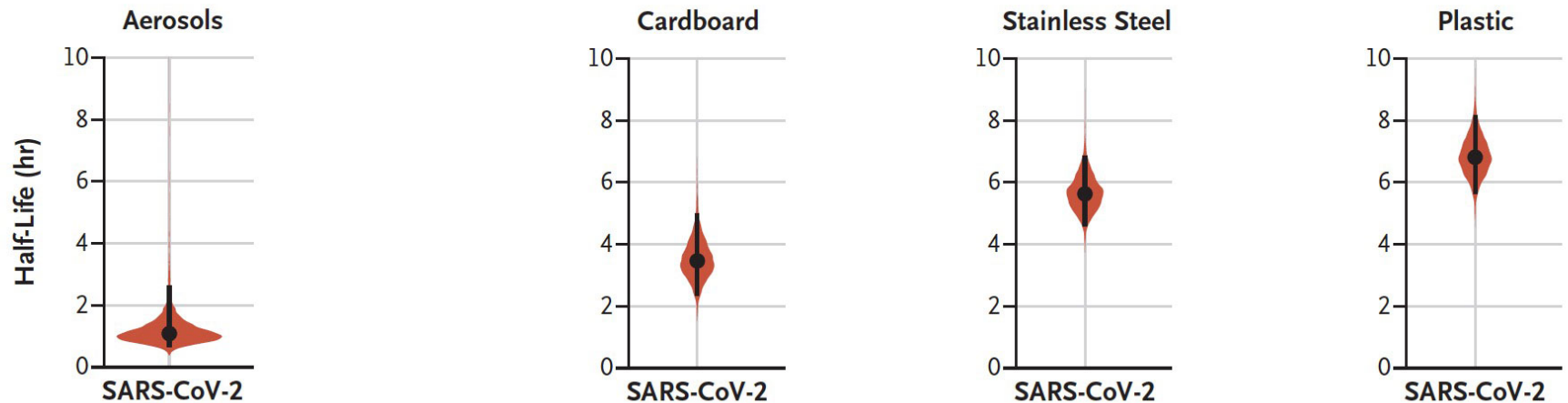
# How is SARS-CoV-2 transmitted?

Dashed horizontal lines are lower limit of detection – CONTROLLED conditions (7d at 21-23°C, 40% humidity)

## A Titers of Viable Virus



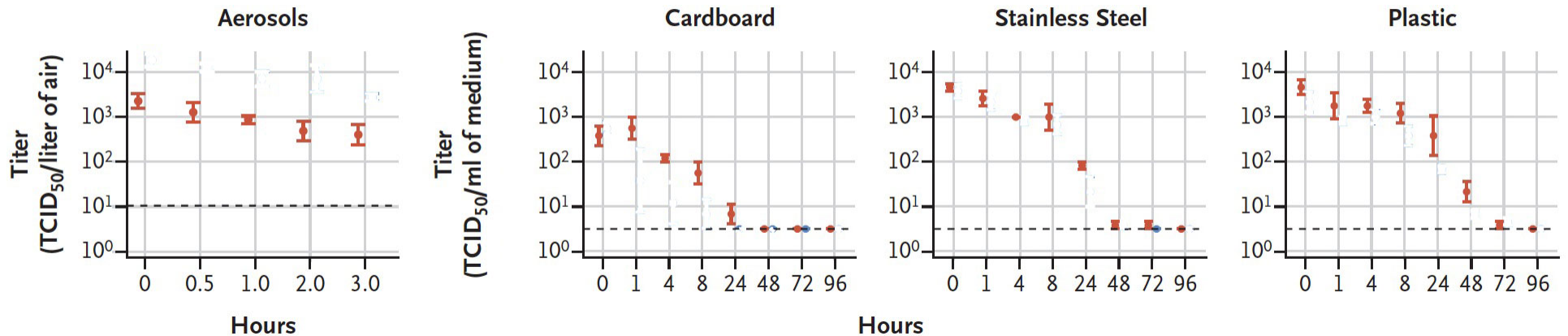
## C Half-Life of Viable Virus



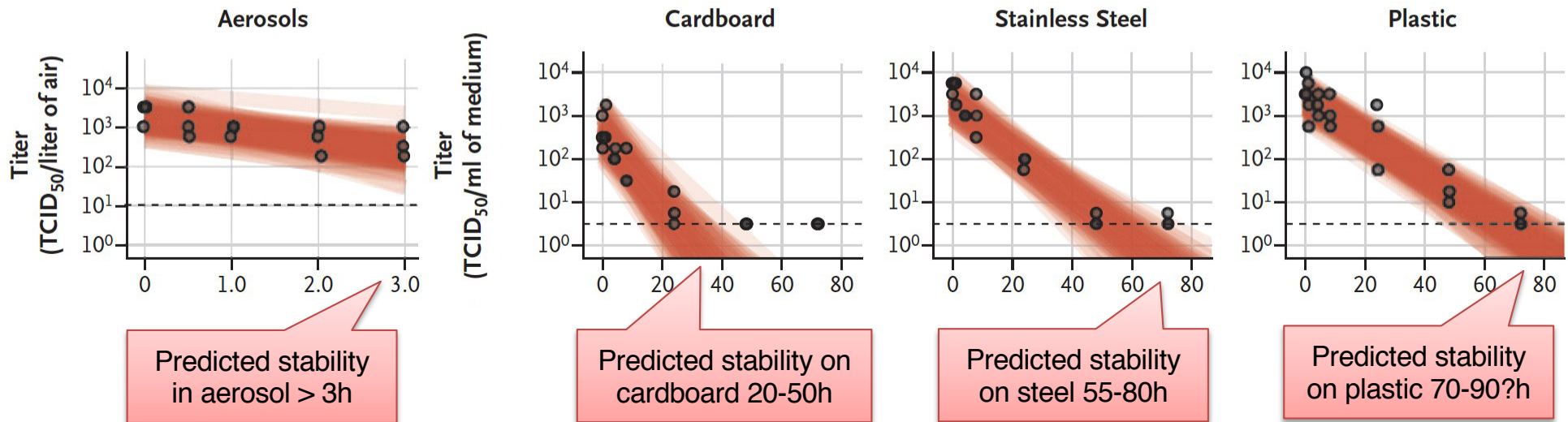
# How is SARS-CoV-2 transmitted?

Dashed horizontal lines are lower limit of detection – CONTROLLED conditions (7d at 21-23°C, 40% humidity)

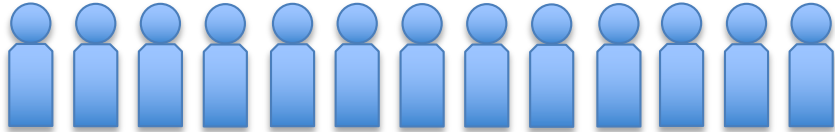
## A Titers of Viable Virus



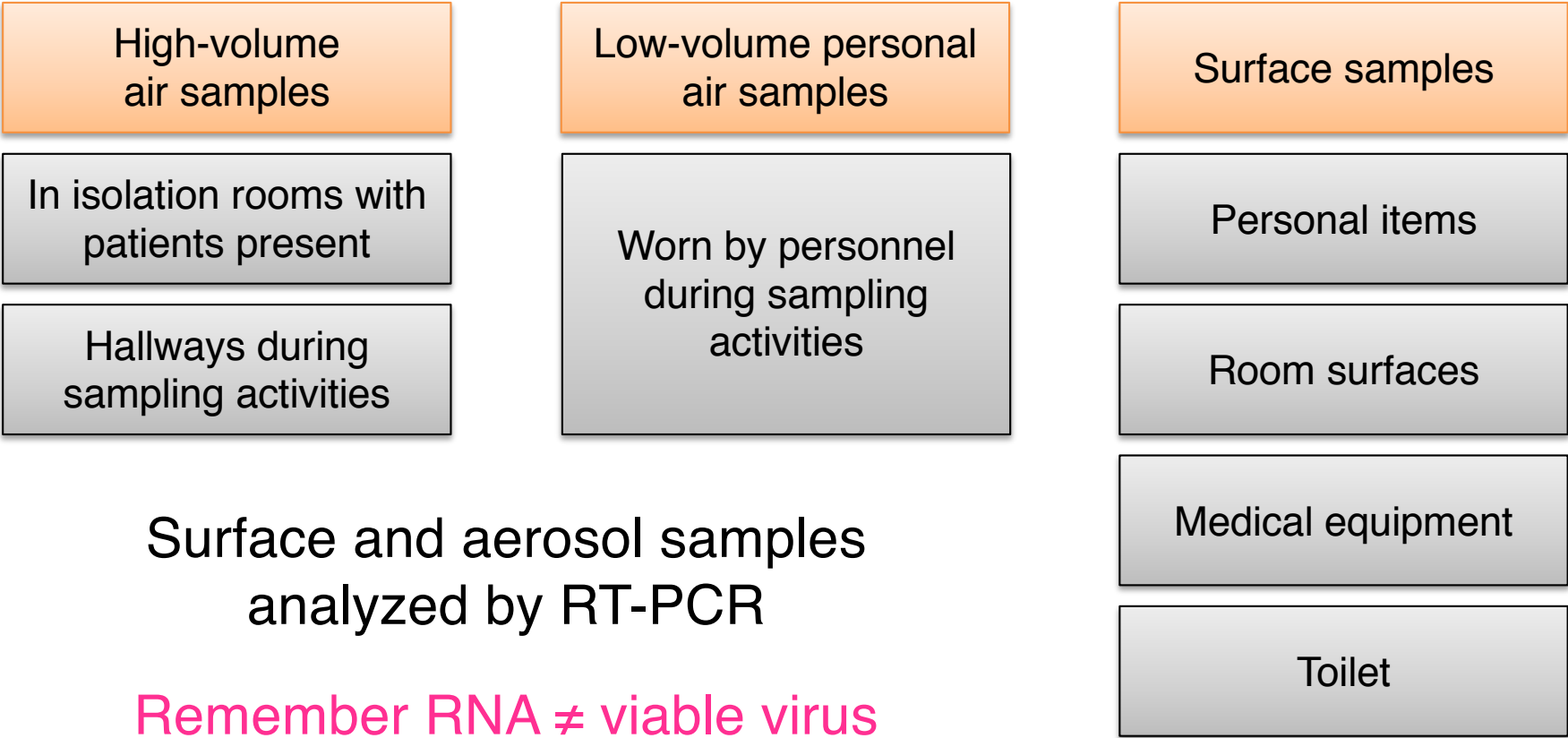
## B Predicted Decay of Virus Titer



# How is SARS-CoV-2 transmitted?



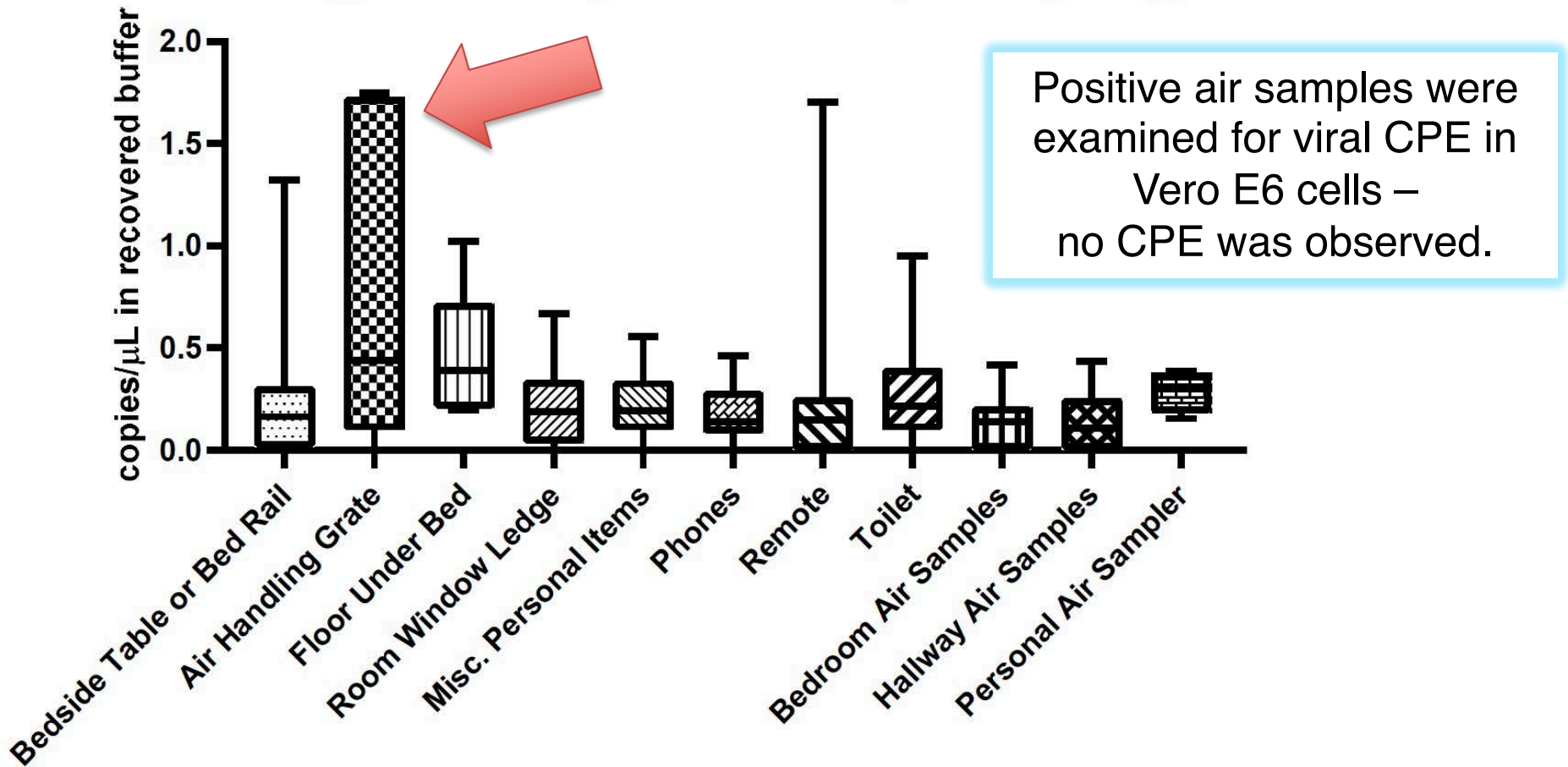
13 patients with **mild-to-moderate** COVID-19 at UNMC





# How is SARS-CoV-2 transmitted?

Range of Gene Copies Recovered per Sample Type



“...the data is [sic] suggestive that viral aerosol particles are produced by individuals that have COVID-19 disease, even in the absence of cough.”

# How is SARS-CoV-2 transmitted?

“SARS-CoV-2 RNA was identified on a variety of surfaces\* in cabins of both symptomatic and asymptomatic infected passengers up to 17 days after cabins were vacated on the Diamond Princess but before disinfection procedures had been conducted (Takuya Yamagishi, National Institute of Infectious Diseases, personal communication, 2020).”

\* remember detectable RNA ≠ viable virus

Centers for Disease Control and Prevention  
**MMWR**

Morbidity and

Early Release / Vol. 69

## Public Health Responses to COVID-19 Outbreaks on Worldwide, February–March 2020

Leah F. Moriarty, MPH<sup>1</sup>; Mateusz M. Plucinski, PhD<sup>1</sup>; Barbara J. Marston, MD<sup>1</sup>; Ekaterina V. Kurbatova, PhD<sup>1</sup>; Murray, PhD<sup>2</sup>; Nicki Pesik, MD<sup>1</sup>; Dale Rose, PhD<sup>1</sup>; David Fitter, MD<sup>1</sup>; Miwako Kobayashi, MD, PhD<sup>1</sup>; Mitchell Scheuer, MPH<sup>3</sup>; Eric S. Halsey, MD<sup>1</sup>; Nicole J. Cohen, MD<sup>1</sup>; Lauren Stockman, MPH<sup>2</sup>; Debra A. Wadford, Green, MD<sup>3</sup>; Joanna J. Regan, MD<sup>1</sup>; Kara Tardivel, MD<sup>1</sup>; Stefanie White, MPH<sup>1</sup>; Clive Brown, MD<sup>1</sup>; Chloé Beth Wittry, MPH<sup>1</sup>; Amy Freeland, PhD<sup>1</sup>; Sara Naramore, MPH<sup>3</sup>; Ryan T. Novak, PhD<sup>1</sup>; David Daigle, MPH<sup>1</sup>; Carolyn Herzig, PhD<sup>1</sup>; Bryan K Kapella, MD<sup>1</sup>; Kathleen R. Jacobson, MD<sup>2</sup>; Katherine Lambda, MPH<sup>2</sup>; Atsuyoshi Erik Svendsen, PhD<sup>1</sup>; Tricia Blocher, MS<sup>2</sup>; Christine Wu, MD<sup>3</sup>; Julia Charles, JD<sup>1</sup>; Riley Wagner, MPH<sup>1</sup>; Elizabeth Kurylo, MCM<sup>1</sup>; Stefanie Campbell, DVM<sup>1</sup>; Rachel Murray, MPH<sup>1</sup>; Paul Weidle, PharmD<sup>1</sup>; Mar CDC Cruise Ship Response Team; California Department of Public Health COVID-19 Team;

An estimated 30 million passengers are transported on 272 cruise ships worldwide each year\* (1). Cruise ships bring diverse populations into proximity for many days, facilitating transmission of respiratory illness (2). SARS-CoV-2, the virus that causes coronavirus disease (COVID-19) was first identified in Wuhan, China, in December 2019 and has since spread worldwide to at least 187 countries and territories. Widespread COVID-19 transmission on cruise ships has been reported as well (3). Passengers on certain cruise ship voyages might be aged ≥65 years, which places them at greater risk for severe consequences of SARS-CoV-2 infection (4). During February–March 2020, COVID-19 outbreaks associated with three cruise ship voyages have caused more than 800 laboratory-confirmed cases among passengers and crew, including 10 deaths. Transmission occurred across multiple voyages of several ships. This report describes public health responses to COVID-19 outbreaks on these ships. COVID-19 on cruise

cruise ship off the coast of Japan subsequently quarantined. COVID-19 had been reported on cruise ship voyages. Avoiding travel on cruise ships during this recommendation for cruise ship travel worldwide conditions and for passengers on Cruise Lines International Association's voluntary suspension of cruise ship operations (5). CDC issued a level 3 travel warning on March 17, recommending that all cruise travel be deferred worldwide.†

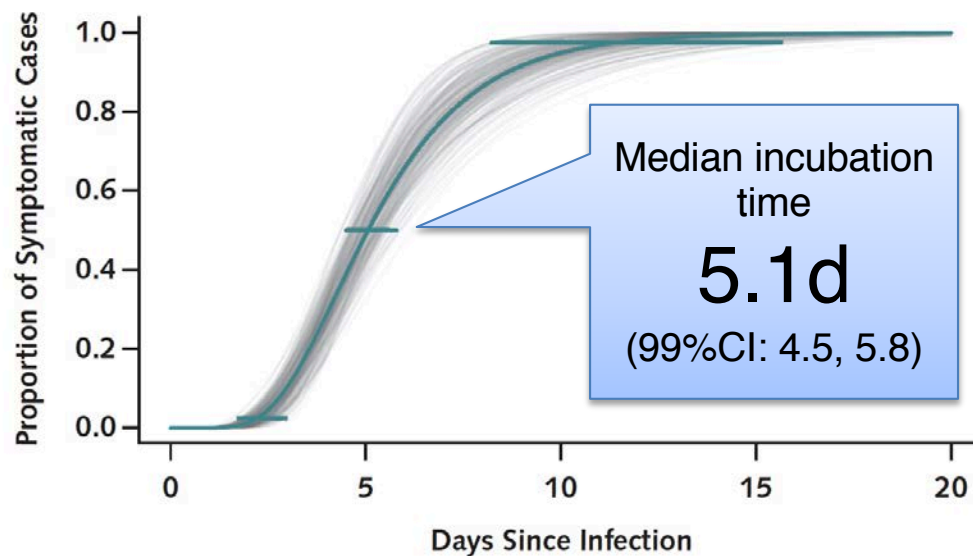
### Diamond Princess

On January 20, 2020, the Diamond Princess cruise ship departed Yokohama, Japan, carrying approximately 3,700 passengers and crew (Table). On January 25, a symptomatic passenger departed the ship in Hong Kong, where he was evaluated and confirmed SARS-CoV-2 infection. On February 3,

Moriarty LF, et al. MMWR.  
ePub: 23 March 2020.  
<http://dx.doi.org/10.15585/mmwr.mm6912e3>

# What's the incubation period for COVID-19?

**Figure 2.** Cumulative distribution function of the COVID-19 incubation period estimate from the log-normal model.

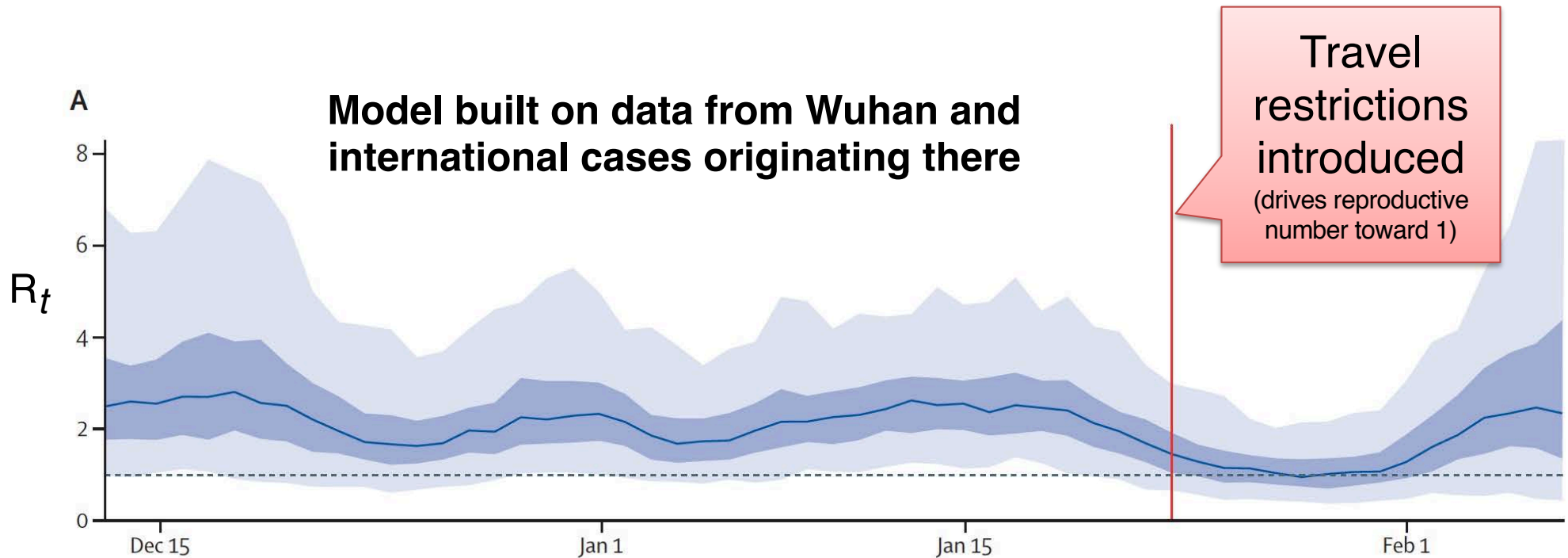


The estimated median incubation period of COVID-19 was 5.1 days (CI, 4.5 to 5.8 days). We estimated that fewer than 2.5% of infected persons will display symptoms within 2.2 days (CI, 1.8 to 2.9 days) of exposure, whereas symptom onset will occur within 11.5 days (CI, 8.2 to 15.6 days) for 97.5% of infected persons. Horizontal bars represent the 95% CIs of the 2.5th, 50th, and 97.5th percentiles of the incubation period distribution. The estimate of the dispersion parameter is 1.52 (CI, 1.32 to 1.72). COVID-19 = coronavirus disease 2019.

Using data from 181 patients, 97.5% developed **any symptom** by day 11.5 (99% CI: 8.2, 15.6) (2.5% will develop sx after 11.5d)

Using data from 99 patients with time to fever onset, 97.5% developed **fever** by day 12.5 (99% CI: 8.2, 17.7) (2.5% will develop fever after 12.5d)

# What's COVID-19's reproductive number?

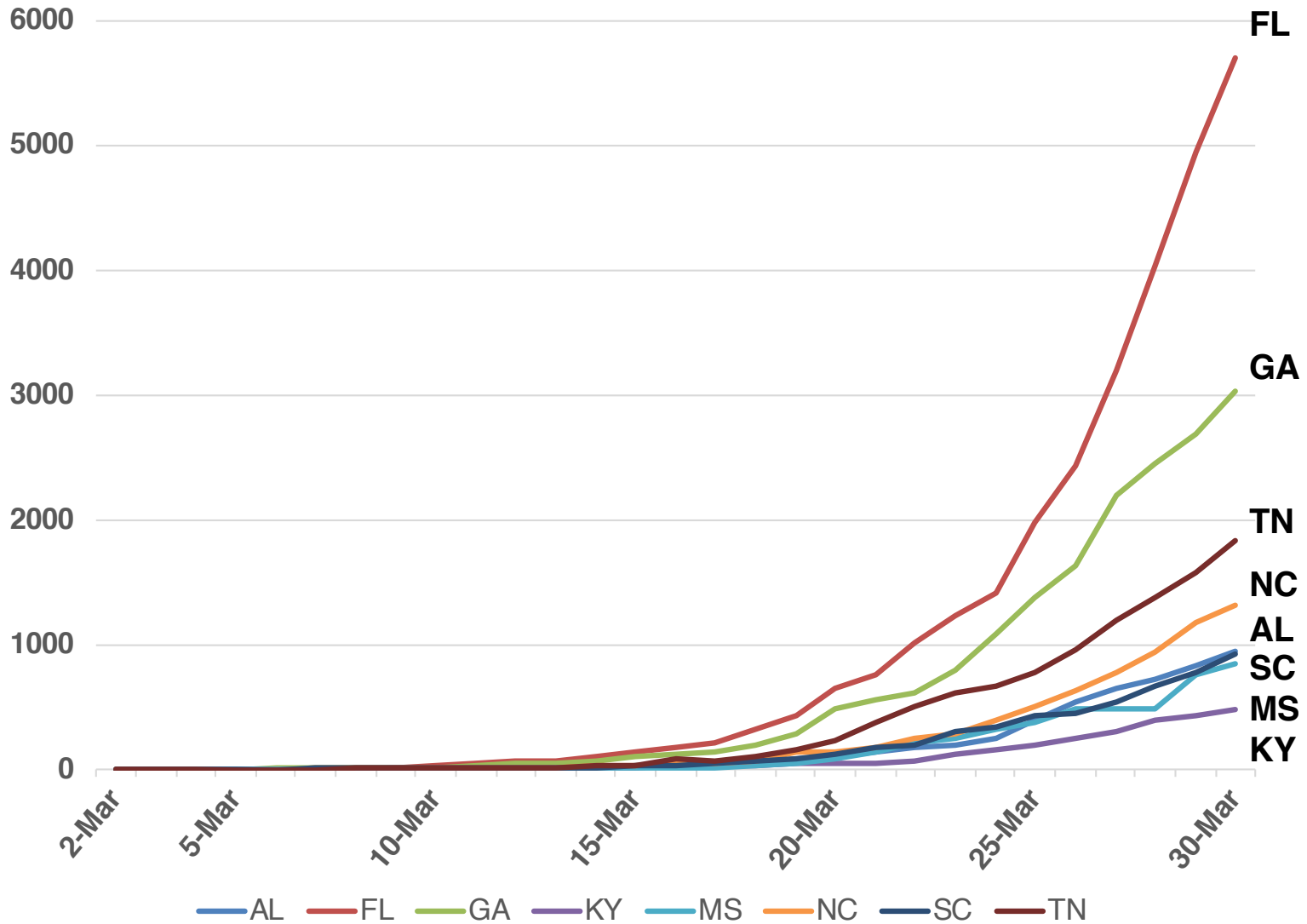


Based on early estimates, each case can be expected to produce **around 2 additional cases**

Secondary attack rate from close contacts may be as high as **35%** (95% CI: 27, 44)

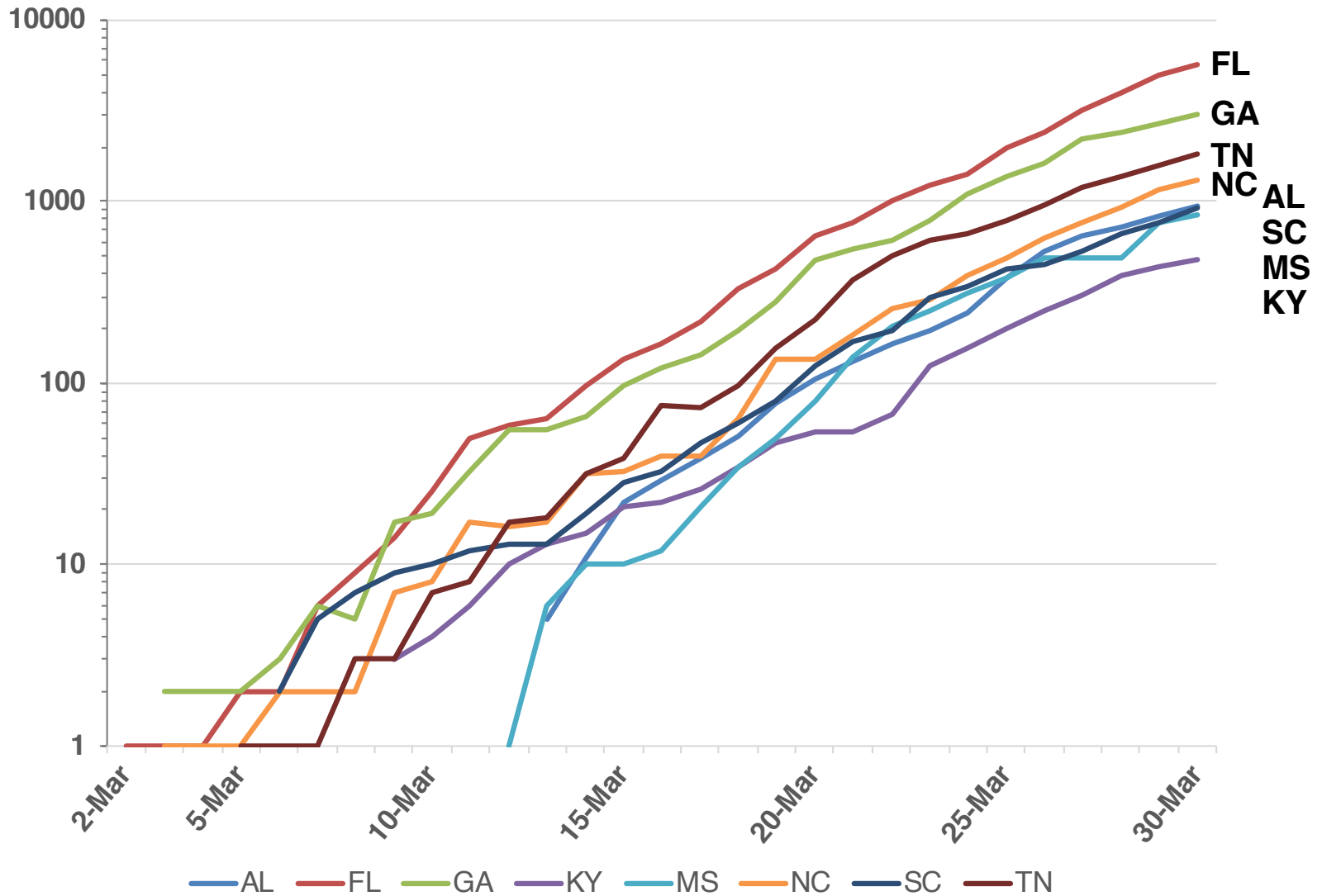
# What's the current status in SE AETC states?

Confirmed Cases through 30 March



# What's the current status in SE AETC states?

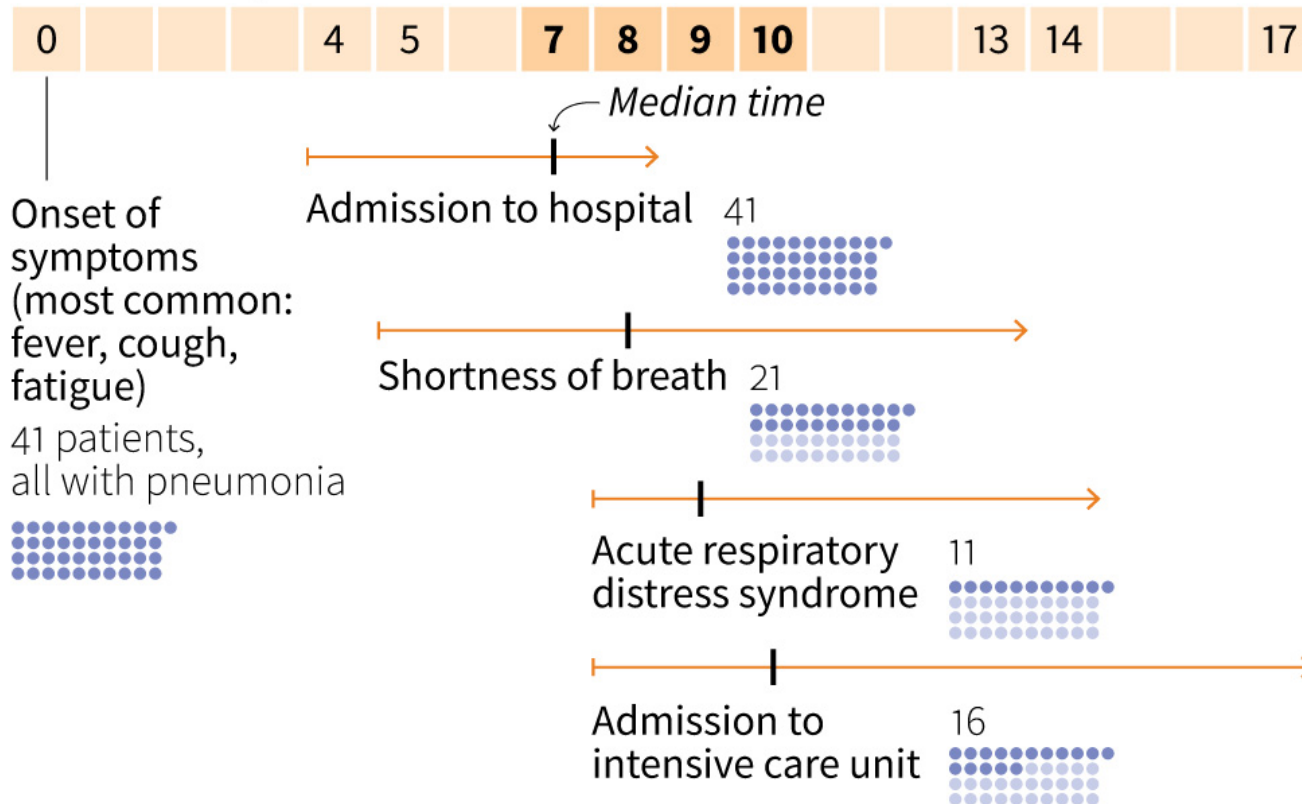
Confirmed Cases through 30 March



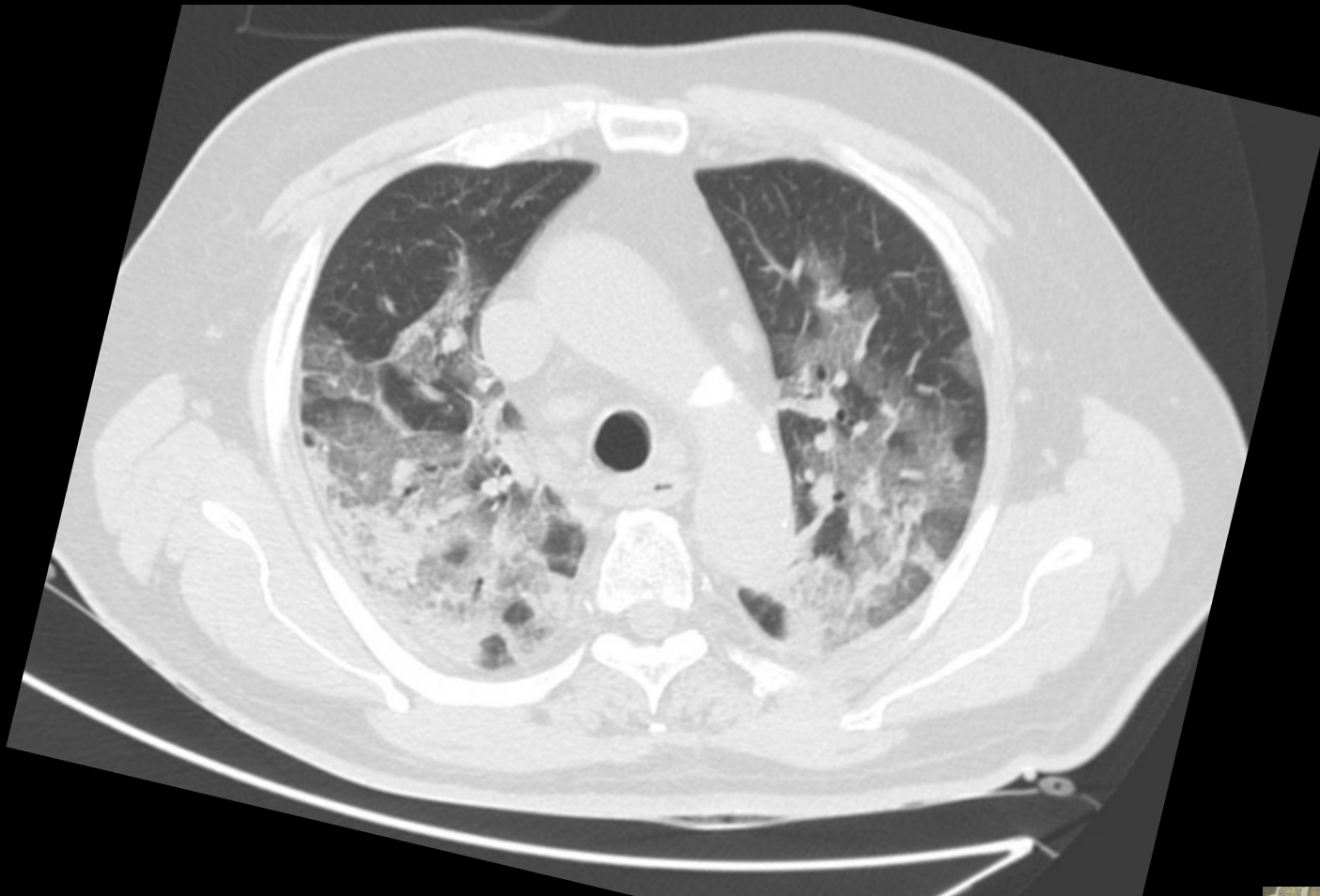
# How does COVID-19 progress?

Based on analysis of 41 patients infected with 2019-nCoV in Wuhan, China

Number of days



**Admit / ED**  
**HD#1**



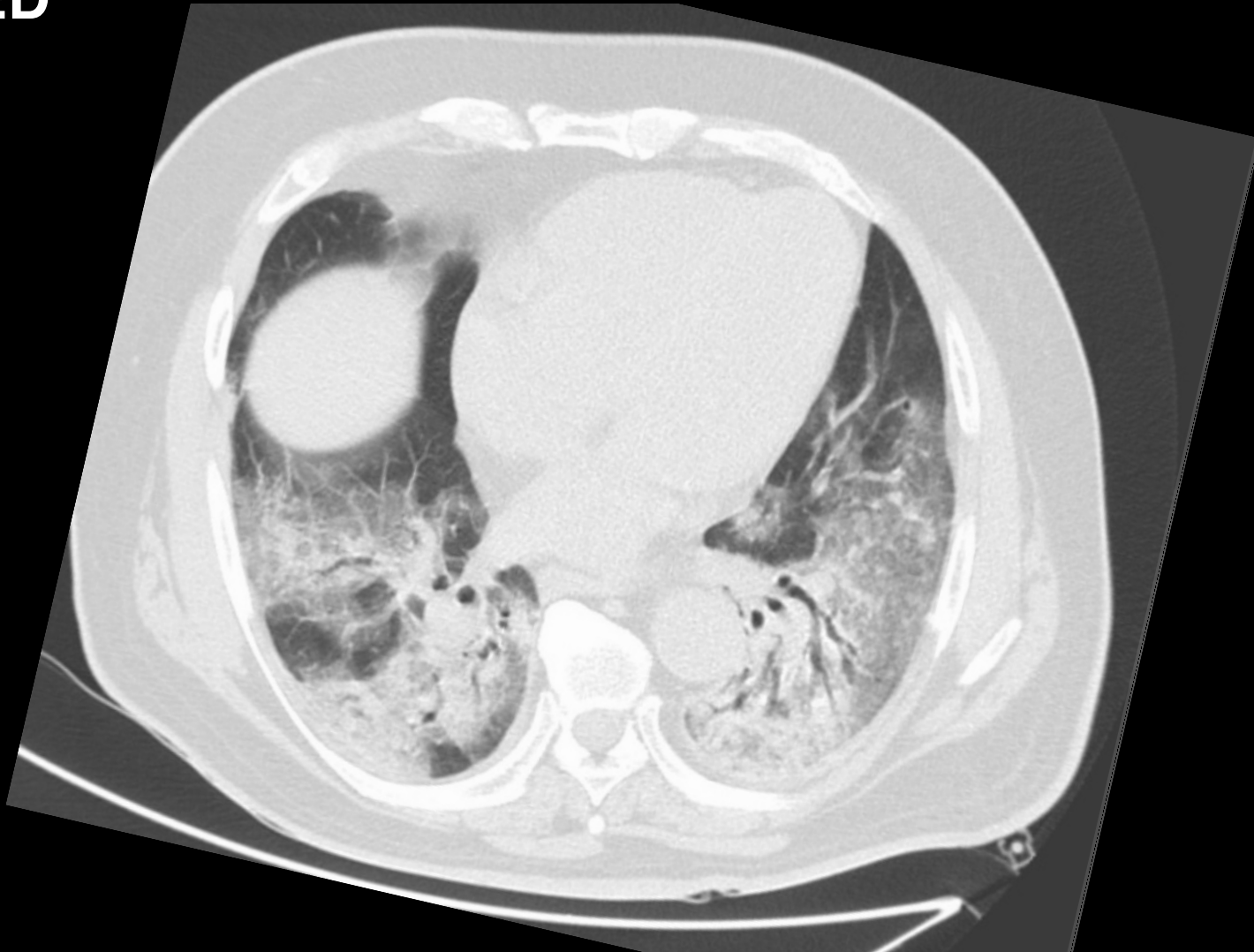
**75yo Italian man with confirmed COVID-19**

“There are bilateral large areas of ground-glass opacities with **crazy paving** → and, more evident at both bases, areas of consolidation.”





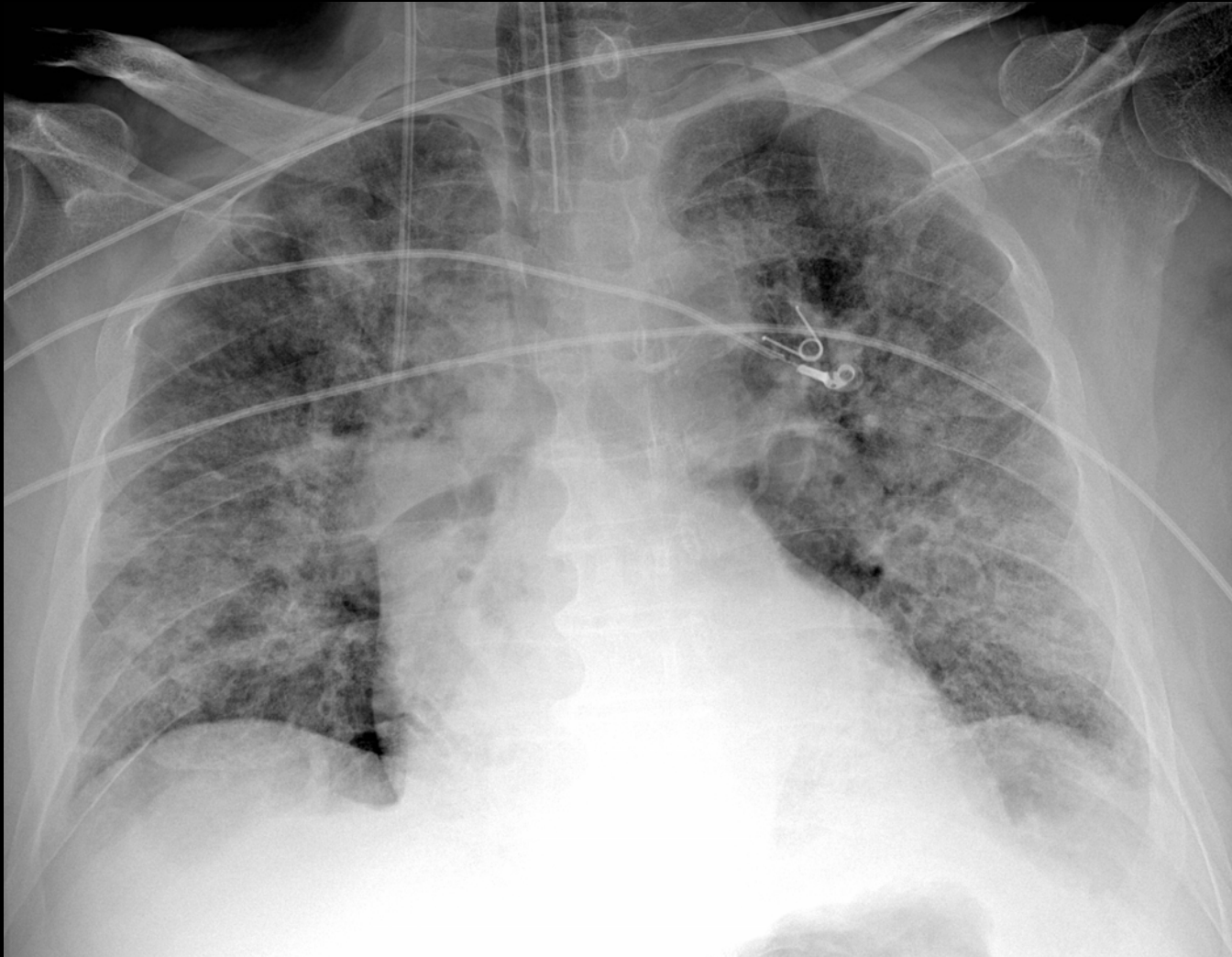
**Admit / ED**  
**HD#1**



**75yo Italian man with confirmed COVID-19**

“There are bilateral large areas of ground-glass opacities with **crazy paving** and, more evident at both bases, areas of consolidation.”

**HD#2**



**75yo Italian man with confirmed COVID-19**

“AP chest radiograph for CVC position shows the presence of extensive bilateral ground-glass opacities as demonstrated on the recent CT. Also right IJV catheter and ETT noted.”

# Who is at risk of dying from COVID-19?

## Case Fatality Rate (%) by Age Group

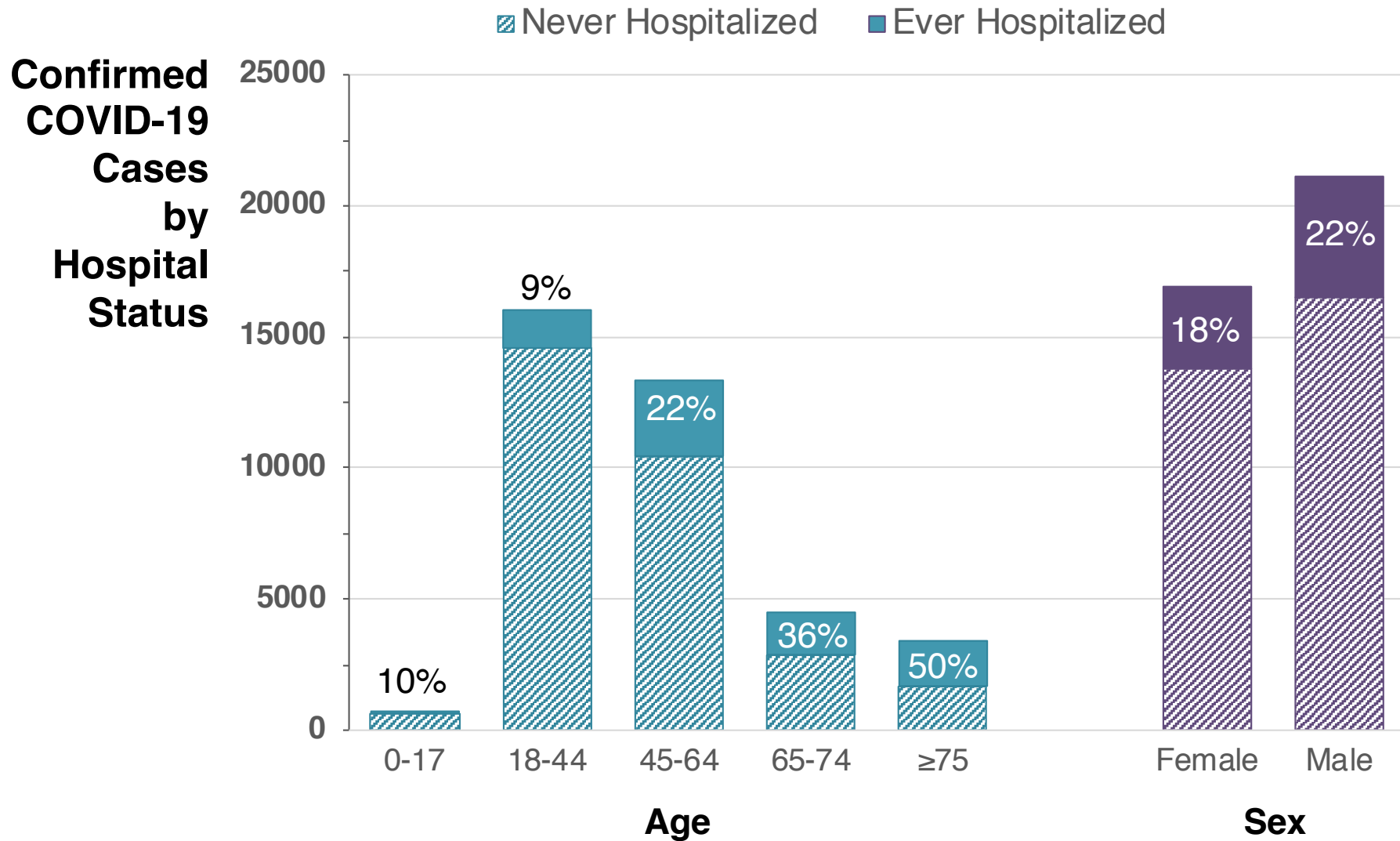
Age group	Italy through 17 March	China through 11 Feb	United States through 16 March
0-9	0	0	0 <sup>0-19</sup>
10-19	0	0.2	
20-29	0	0.2	0.1-0.2 <sup>20-44</sup>
30-39	0.3	0.2	
40-49	0.4	0.4	0.5-0.8 <sup>45-54</sup>
50-59	1.0	1.3	1.4-2.6 <sup>55-64</sup>
60-69	3.5	3.6	2.7-4.9 <sup>65-74</sup>
70-79	12.8	8.0	4.3-10.5 <sup>75-84</sup>
≥80	20.2	14.8	10.4-27.3 <sup>≥85</sup>
≥85			

US data: Lower bound = # deaths ÷ # in age group. Upper bound = # deaths ÷ # in age group w/confirmed death.

US: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6912e2.htm>

Italy & China: Onder G, et al. JAMA. 2020 Mar 23. <https://doi.org/10.1001/jama.2020.4683>

# What can NYC's experience tell us?

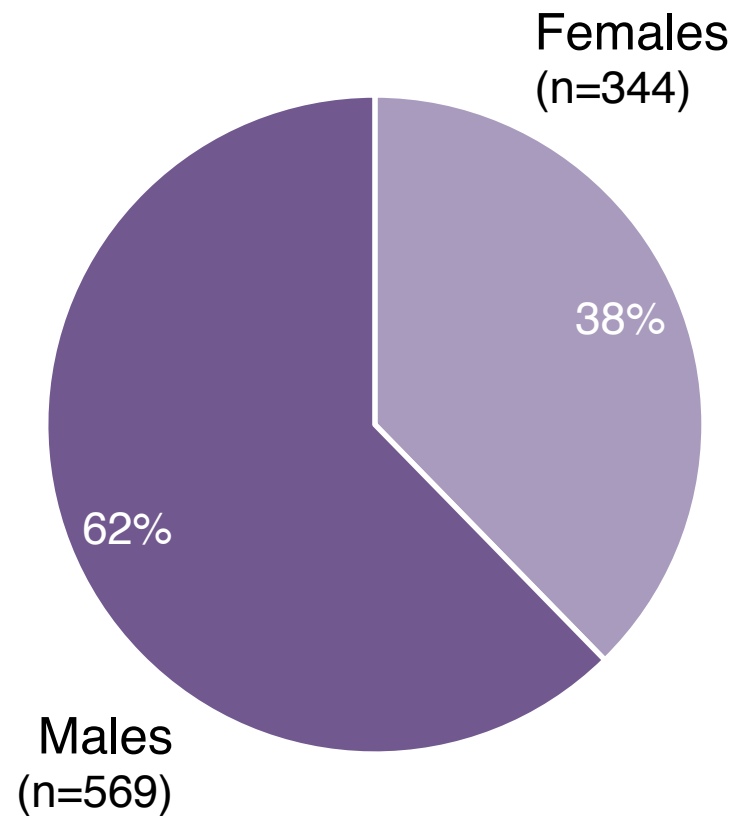
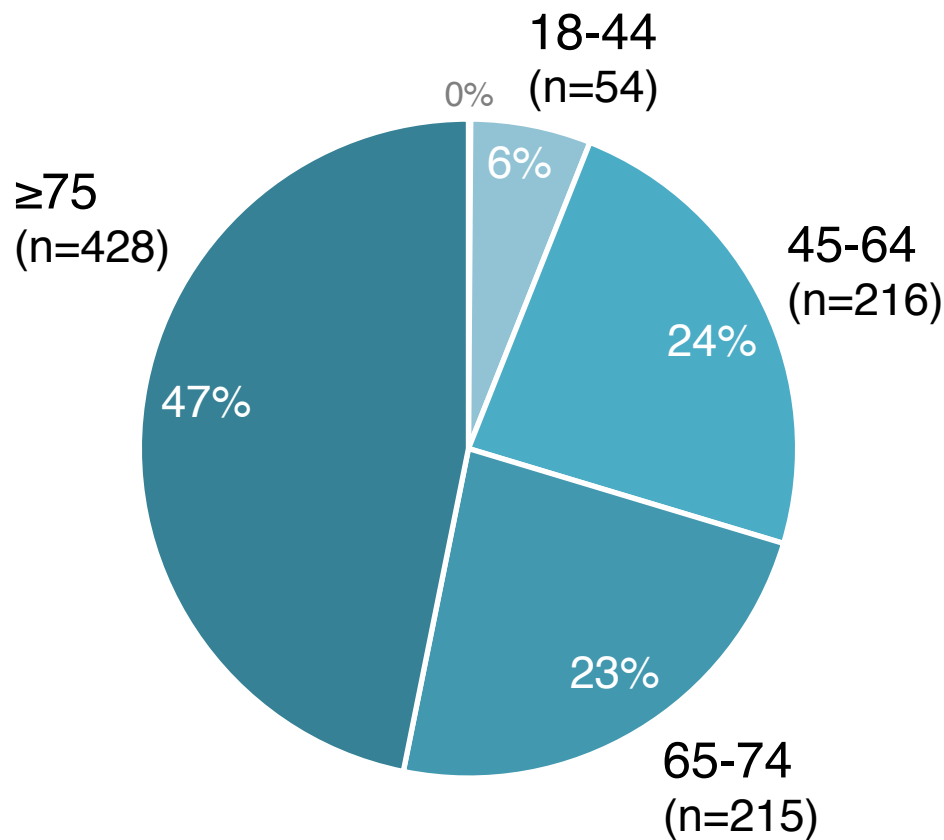


As of 1630 on 30 March

Data from: <https://www1.nyc.gov/site/doh/covid/covid-19-main.page>

# What can NYC's experience tell us?

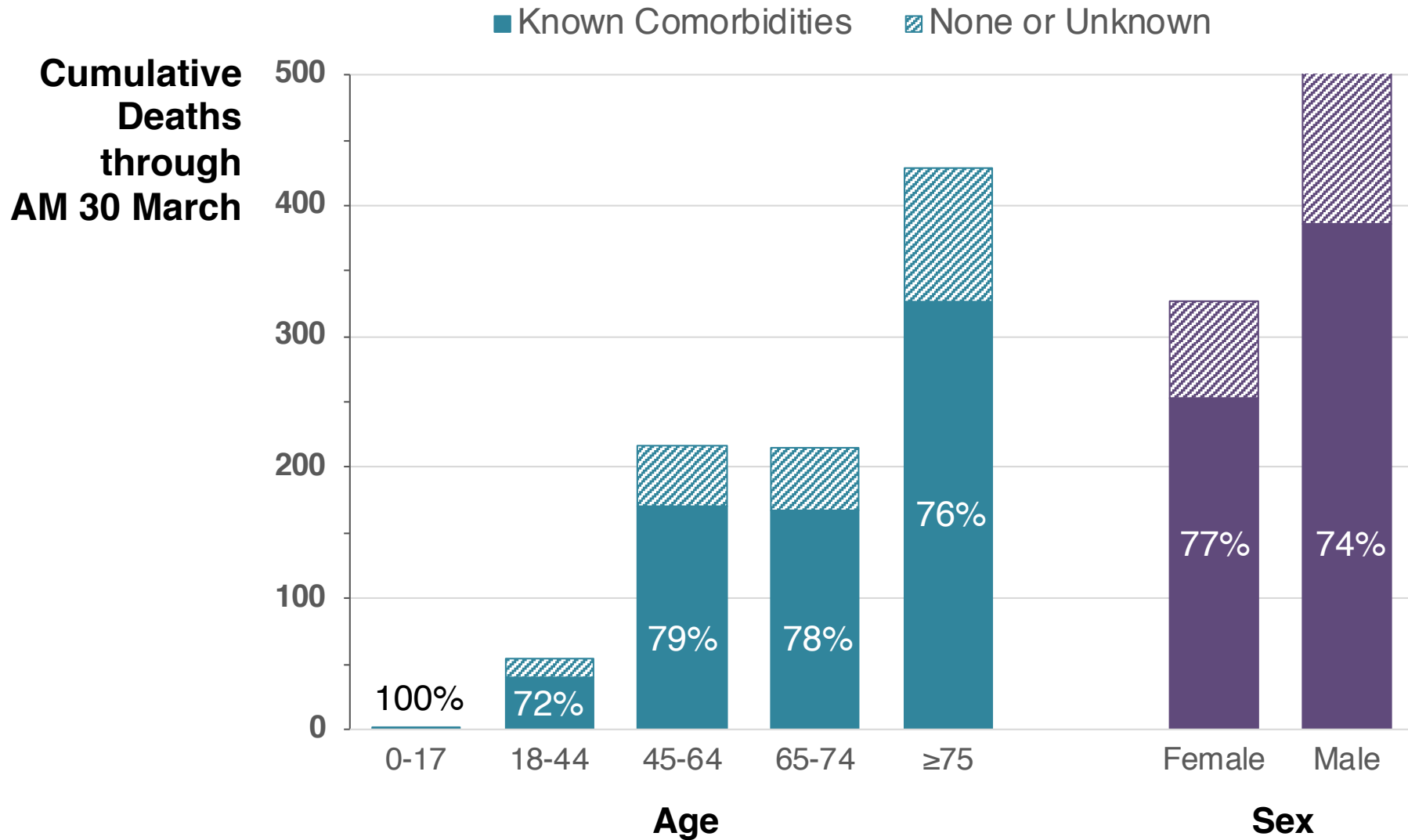
## Cumulative COVID-19-Associated Deaths in New York City



As of 1630 on 30 March

Data from: <https://www1.nyc.gov/site/doh/covid/covid-19-main.page>

# What can NYC's experience tell us?

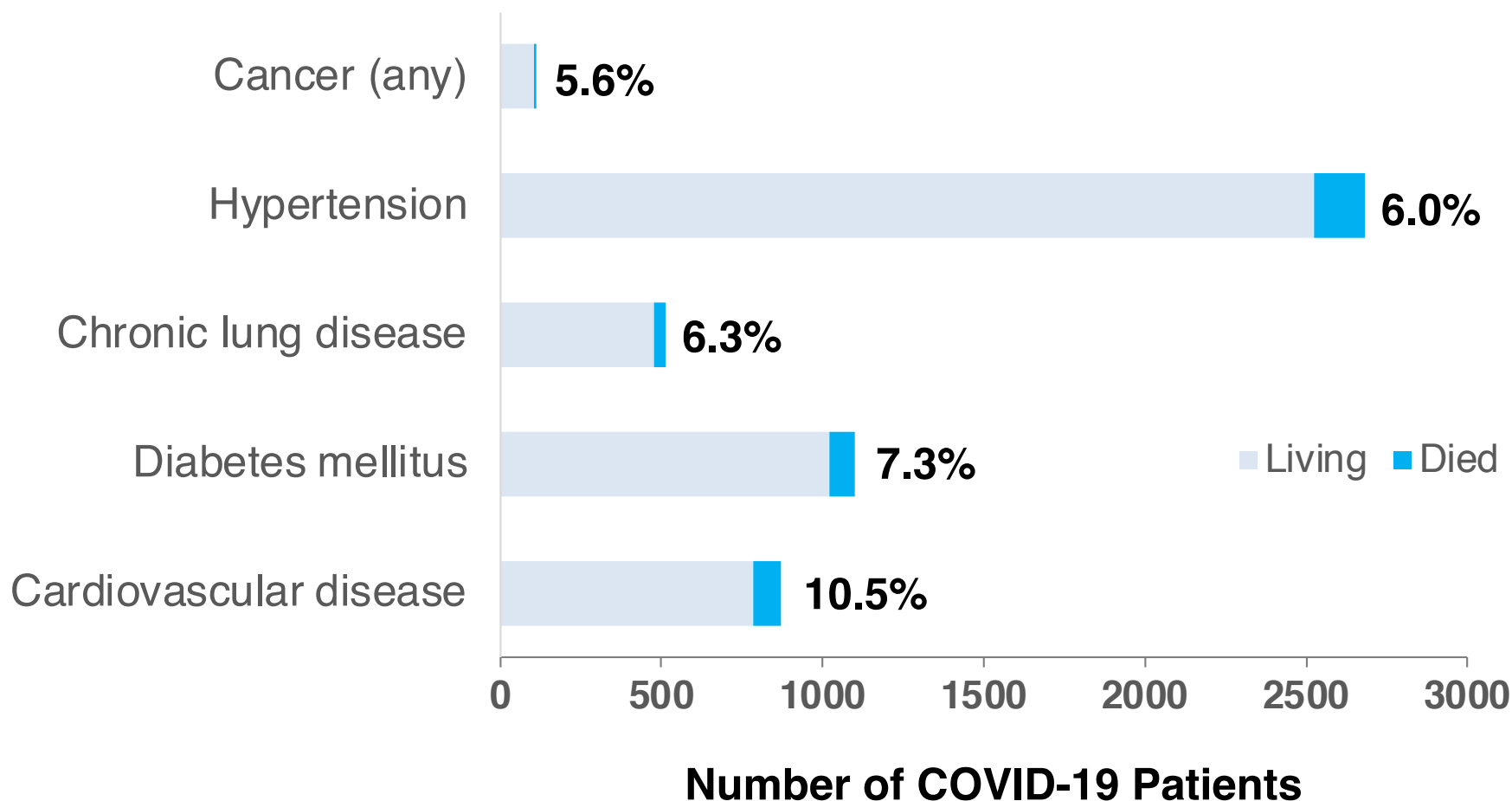


As of 1630 on 30 March

Data from: <https://www1.nyc.gov/site/doh/covid/covid-19-main.page>

# Who is at risk of dying from COVID-19?

## Comorbidities and Case Fatality Rates (%), China



The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) — China, 2020[J]. China CDC Weekly, 2020, 2(8): 113-122.

# What about people with HIV?

<https://aidsinfo.nih.gov/>  
20 March 2020

The screenshot shows the AIDSinfo website header with the U.S. Department of Health and Human Services logo and the text "OFFERING INFORMATION ON HIV/AIDS TREATMENT, PREVENTION, AND RESEARCH". The navigation menu includes "Home", "Guidelines", and "Understanding HIV/AIDS". The main heading is "Interim Guidance for COVID-19 and Persons with HIV". Below the heading, there is a search bar and a blue arrow button labeled "Interim Guidance for COVID-19 and Persons with HIV". A "Related Content" section lists links to CDC COVID-19 information for healthcare professionals, CDC COVID-19 information for people with HIV, AIDSinfo HIV Medical Practice Guidelines, and Coronavirus.gov. The main content area shows the beginning of the "Interim Guidance for Persons with HIV" document, dated March 20, 2020, and includes a search bar and a "Brief Version (N/A)" link.

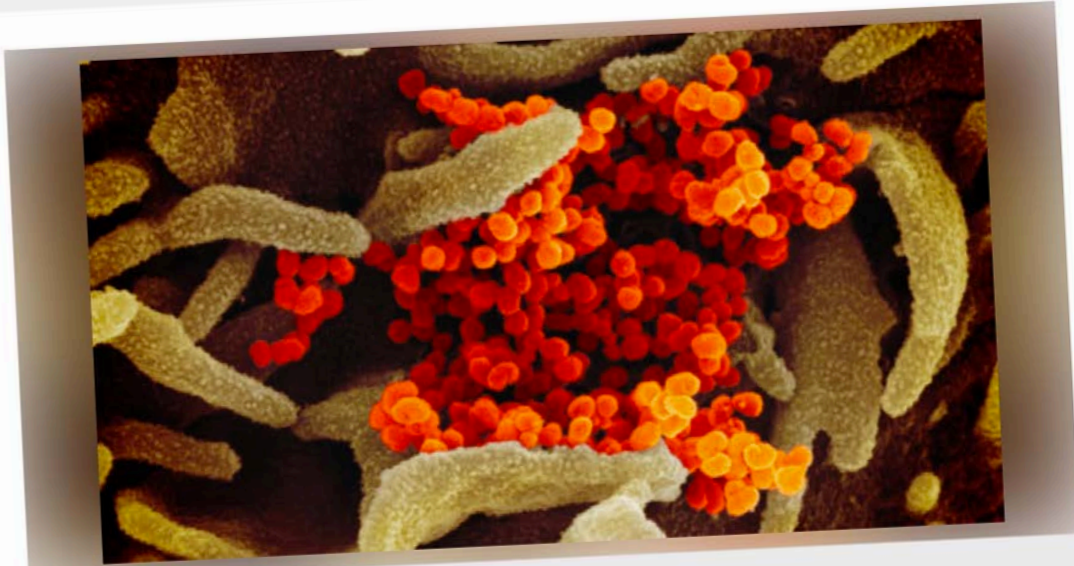
- Greatest concern is for PwH >60yo with DM, HTN, CVD, and/or pulmonary disease
- VERY limited data suggest course of COVID-19 in PwH is similar to HIV-uninfected
- In pre-ART era, CD4 <200 was a risk for respiratory infections (unknown yet if true for COVID-19)
- Be mindful of supply of ART & essential meds and avoid gaps



# What about people with HIV?

<http://bit.ly/covid19hiv>

P25Z



Novel coronavirus SARS-CoV-2  
Courtesy of NIAID

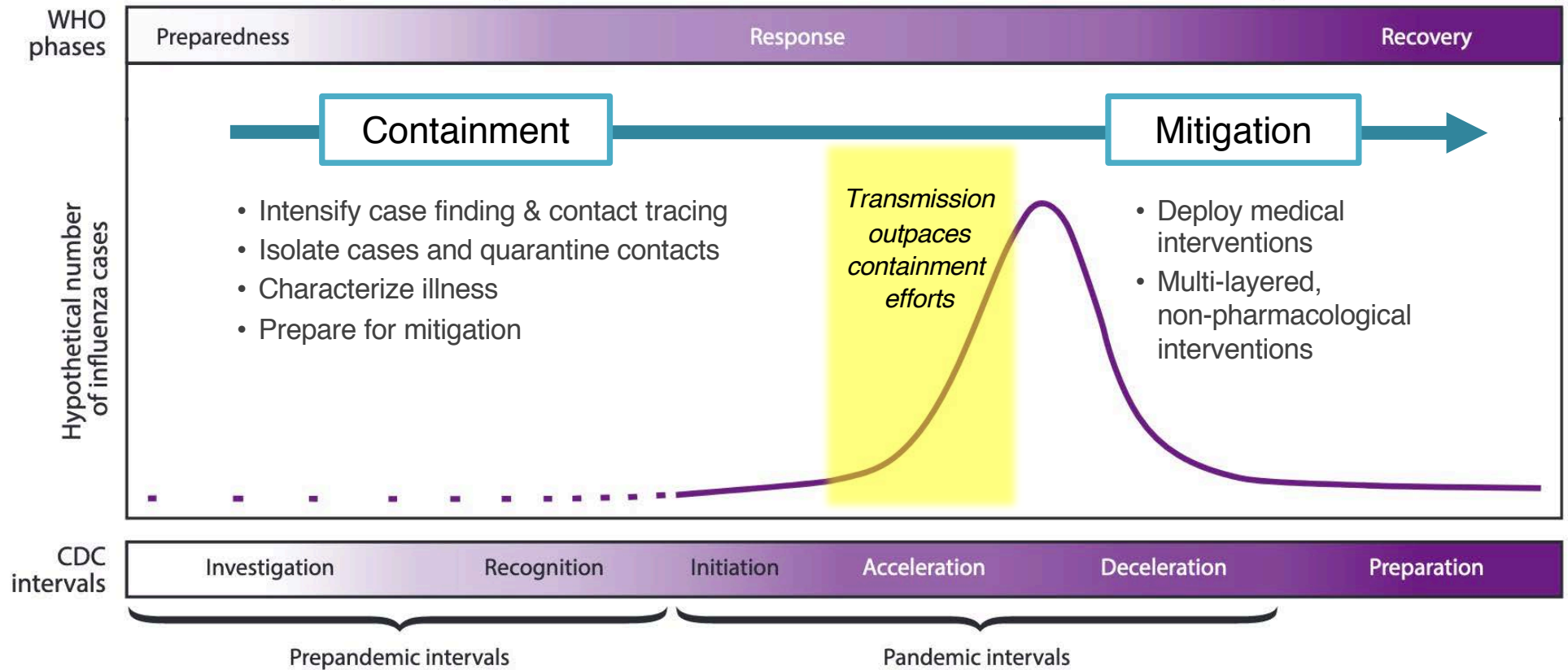
TREATMENT NEWS

## UPDATED: What People With HIV Need to Know About the New Coronavirus

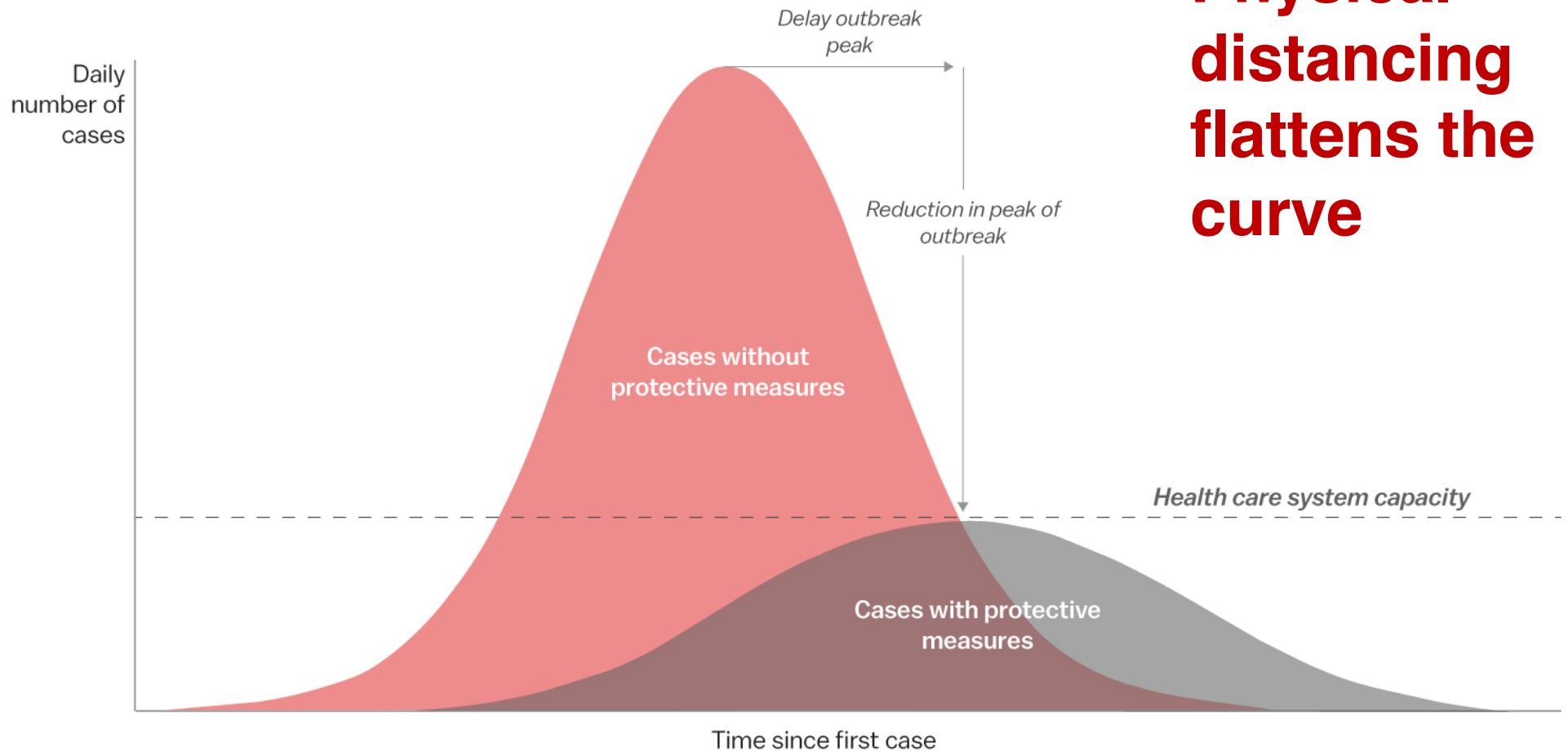
New research is emerging about how the respiratory virus spreads and how people can protect themselves and others.

- **Emphasize common sense approaches!**
- The lower your CD4 count, the more cautious you ought to be
- Negotiate between providers & patients about spacing out visits, doing phone or video, etc. until we're through the worst of things

# What's happening now?



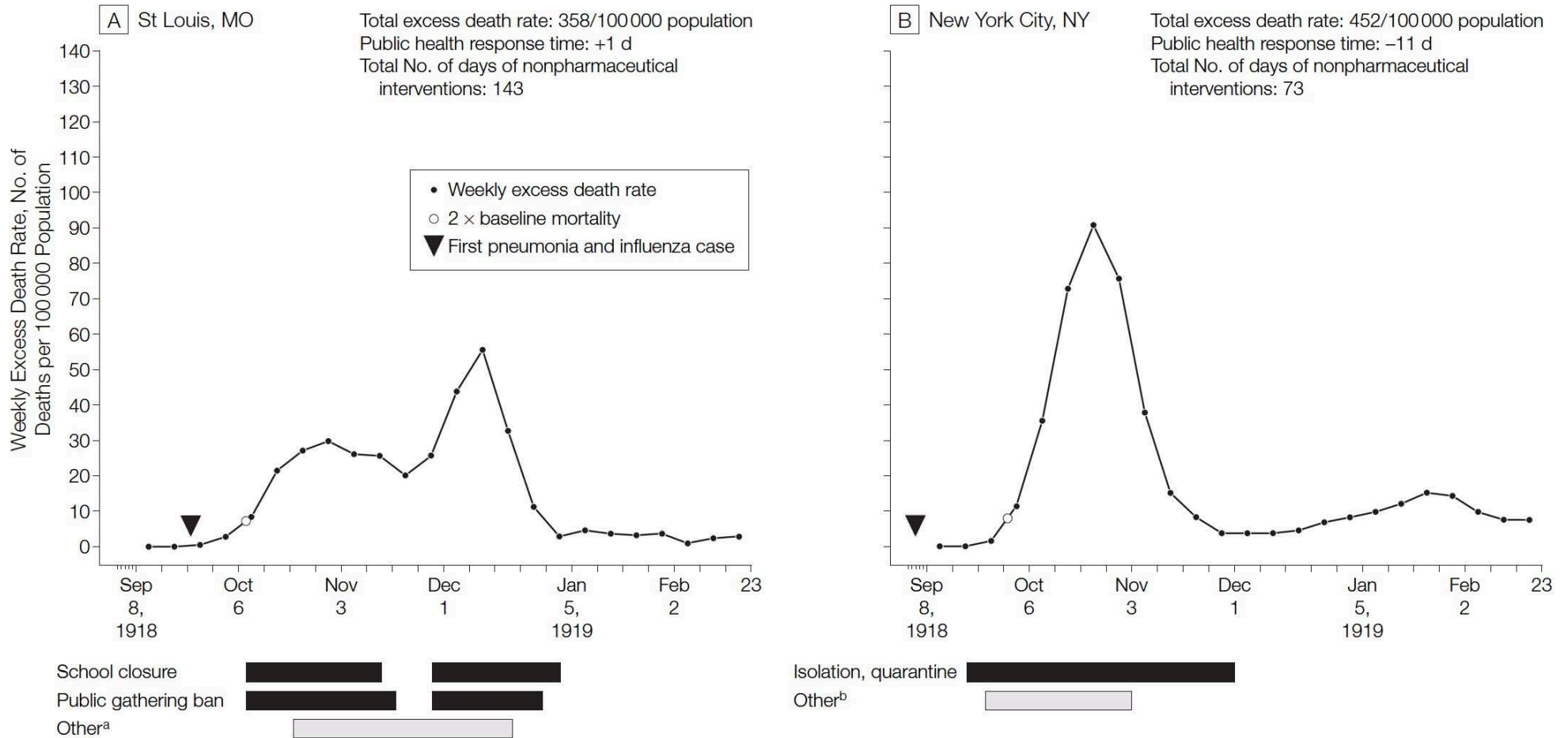
# What's happening now?

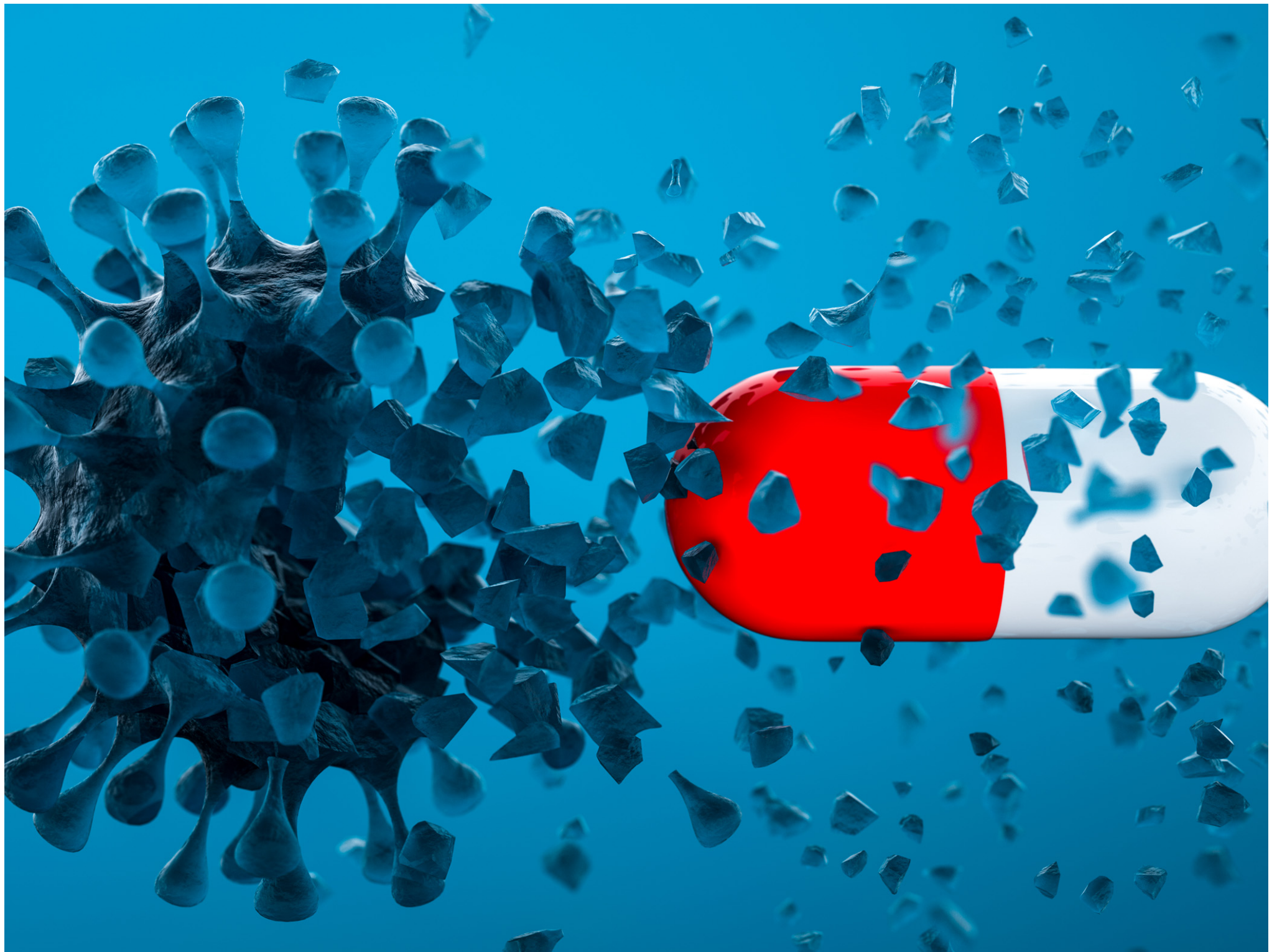


**Physical distancing flattens the curve**

# Physical distancing works

**Figure 3.** Weekly Excess Death Rates From September 8, 1918, Through February 22, 1919





# Resources from Society of ID Pharmacists

<https://www.sidp.org/COVID19>

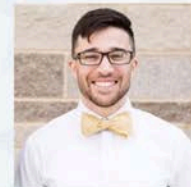
**Chloroquine & Hydroxychloroquine**

**Lopinavir/ritonavir (Kaletra®)**

**Remdesivir (GS-5734)**

A Review of Pertinent Drug Information for SARS-CoV-2

Matt Davis, PharmD  
UCLA Ronald Reagan Medical Center  
Mrdavis@mednet.ucla.edu  
@Mattdavis138



**SIDP** | SOCIETY OF INFECTIOUS  
DISEASES PHARMACISTS

# McCreary & Pogue SIDP reviews

Open Forum Infectious Diseases

IDSIA  
Infectious Diseases Society of America

hivma  
hiv medicine association

Issues ▾ More Content ▾ Publish ▾ Alerts About ▾

<https://doi.org/10.1093/ofid/ofaa105>

Article Navigation

ACCEPTED MANUSCRIPT

## COVID-19 Treatment: A Review

Erin K McCreary, PharmD, BCPS, BCIDP ✉,  
Jason M Pogue, PharmD, BCPS, BCIDP on behalf of the  
*Open Forum Infectious Diseases*, ofaa105, <https://doi.org/10.1093/ofid/ofaa105>  
Published: 23 March 2020 Article history ▾

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- GASTROINTESTINAL INFECTIONS
- HEALTHCARE-ASSOCIATED INFECTIONS (HAI)
- PREVENTION

ARTICLE

### COVID-19 Treatment: Updates March 19-24, 2020

MAR 26, 2020 | ERIN K. MCCREARY, PHARM.D, BCPS, BCIDP\* AND JASON M. POGUE, PHARM.D, BCPS, BCIDP\*\*

Clinicians and researchers across the globe are working with fervor to mitigate the world pandemic caused by SARS-CoV-2, the virus responsible for coronavirus disease 2019 (COVID-19). New data emerge daily, and it is imperative we embrace a deliberate calm to scrutinize the evidence and report it intentionally, despite our overwhelming desire to find an effective treatment. We previously reviewed published literature on experimental treatments for COVID-19 from December 31, 2019 through March 19, 2020. Here, we provide updates from the past 6 days (!!) as we strive to continually analyze data and optimize patient care. We also encourage readers to check out resources from the Society of Infectious Diseases Pharmacists (SIDP) regarding previously reviewed agents with therapeutic potential for COVID-19.

Working Toward a Cure for HIV: Where Are We?  
Is there a cure? How long until we find it? And will it work for the majority of people living with HIV?

<https://www.contagionlive.com/news/covid19-treatment-updates-march-19-24-2020>

# University of Liverpool interaction refs

<https://www.covid19-druginteractions.org/>

<https://hiv-druginteractions.org/checker>

The screenshot shows the 'HIV Drug Interactions' checker interface. The header includes the University of Liverpool logo and navigation links for 'Interaction Checker' and 'Apps'. A green banner below the header states: 'www.covid19-druginteractions.org - a new website for drug interactions with experimental agents used to treat COVID-19.' Below this, a link offers 'Interaction Checker Lite' for users having trouble viewing interactions. The main interface is divided into three columns: 'HIV Drugs', 'Co-medications', and 'Drug Interactions'. Each column has a search bar and filter options (A-Z, Class, Trade). The 'HIV Drugs' and 'Co-medications' columns show a list of drugs with checkboxes and information icons. The 'Drug Interactions' column has a checkbox to 'Check HIV/ HIV drug interactions' and a message: 'Drug Interactions will be displayed here'.

HIV Drugs	Co-medications	Drug Interactions
<input type="text" value="Search HIV drugs"/>	<input type="text" value="Search co-medications..."/>	<input type="checkbox"/> Check HIV/ HIV drug interactions
<input checked="" type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	<input checked="" type="radio"/> A-Z <input type="radio"/> Class <input type="radio"/> Trade	Drug Interactions will be displayed here
Selected HIV Drugs will be displayed here.	Selected Co-medications will be displayed here.	
<input type="checkbox"/> Abacavir (ABC) ⓘ	<input type="checkbox"/> Abacavir (ABC) ⓘ	
<input type="checkbox"/> Albuvirtide ⓘ	<input type="checkbox"/> Acamprosate ⓘ	



# Chloroquine & Hydroxychloroquine

72

BioScience Trends. 2020; 14(1):72-73.

Letter

DOI: 10.5582/bst.2020.01047

**Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies**

Jianjun Gao<sup>1,\*</sup>, Zhenxue Tian<sup>2</sup>, Xu Yang<sup>2</sup>

<sup>1</sup> Department of Pharmacology, School of Pharmacy, Qingdao University, Qingdao, China;

<sup>2</sup> Department of Pharmacy, Qingdao Municipal Hospital, Qingdao, China.

*Who were the patients?*

*What was the control treatment?*

*How long were they treated?*

*At what point in their disease course was therapy introduced?*

## Author Conclusions:

*“Results from more than 100 patients have demonstrated that chloroquine phosphate is superior to the control treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course....”*



SOCIETY OF INFECTIOUS  
DISEASES PHARMACISTS

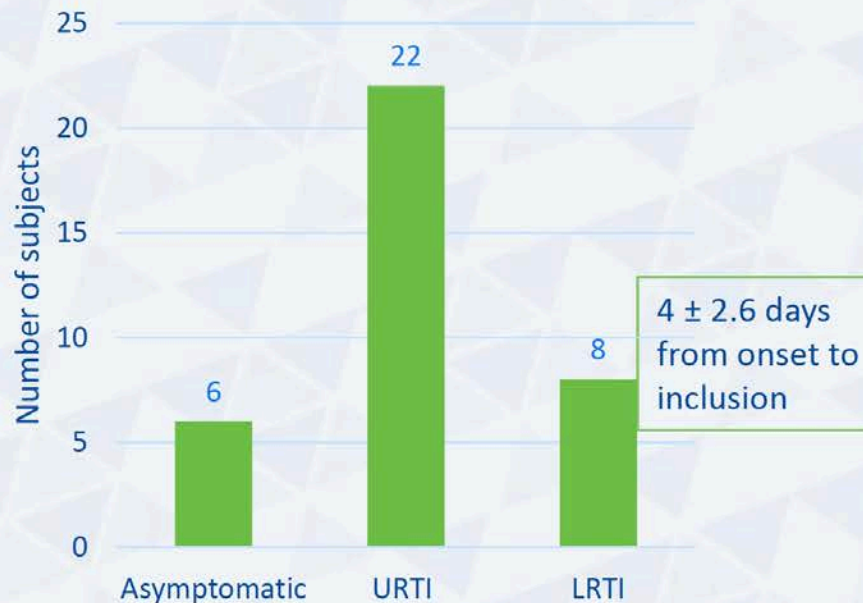
Gao J, Tian Z, Yang X. Biosci Trends Feb 19 [Epub ahead of print] Available at:  
[https://www.jstage.jst.go.jp/article/bst/14/1/14\\_2020.01047/article](https://www.jstage.jst.go.jp/article/bst/14/1/14_2020.01047/article)

<https://sidp.org/covid19>

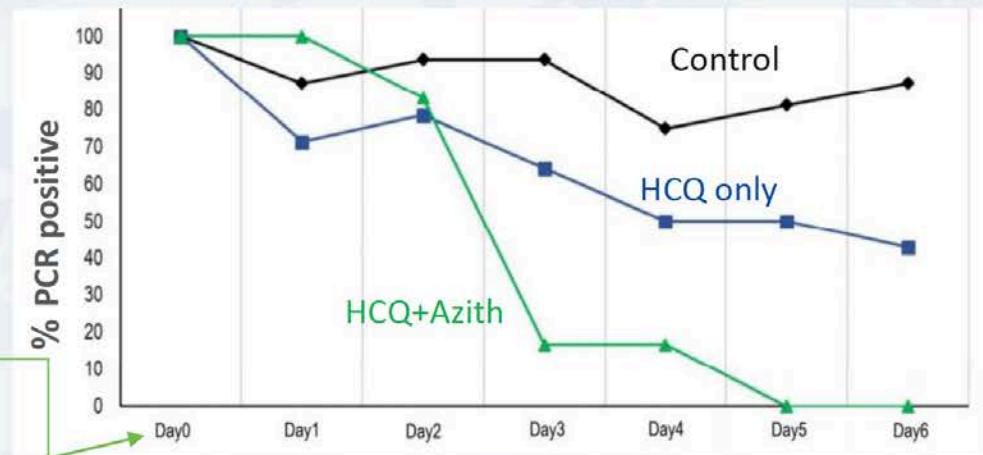
# Chloroquine & Hydroxychloroquine

## What about Hydroxychloroquine + Azithromycin

36 Hospitalized patients  $45 \pm 22$  years old with COVID19



Primary outcome: Viral suppression 6 days after inclusion



N = 16: Controls

N = 14: HCQ 200 mg PO TID x10 days

N = 6: HCQ + Azithromycin 500 day 1 then 250mg x 4 days

\*Exclusion criteria: Allergy, G6PD deficient, prolonged QTc, retinopathy

International Journal of Antimicrobial Agents – In Press 17 March 2020

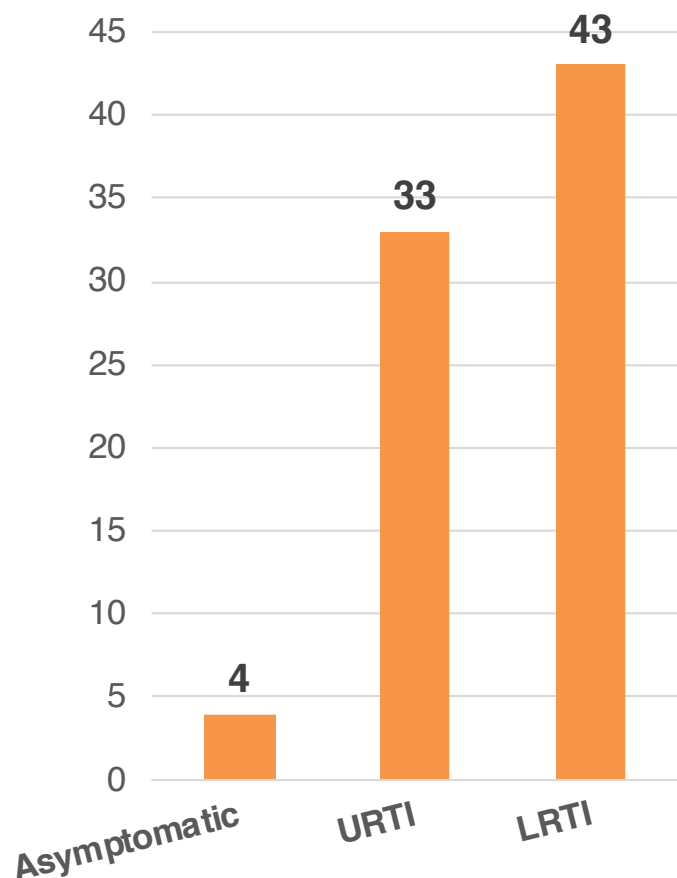
DOI : 10.1016/j.ijantimicag.2020.105949

SLIDE IMAGE FROM SIDP

Gautret et al. Int J Antimicrob Agents 2020. <https://doi.org/10.1016/j.ijantimicag.2020.105949>

# Hydroxychloroquine

**80 Hospitalized Patients**  
**Median Age 52 (range 18-88)**  
**with NP swab PCR+ for SARS-CoV-2**



## Intervention:

- HCQ 200mg PO TID x10d **AND**
- Azithromycin 500mg PO x1 on day 1, then 250mg PO x4d

Mean duration of symptoms at admit:  $4.9 \pm 3.6$  days

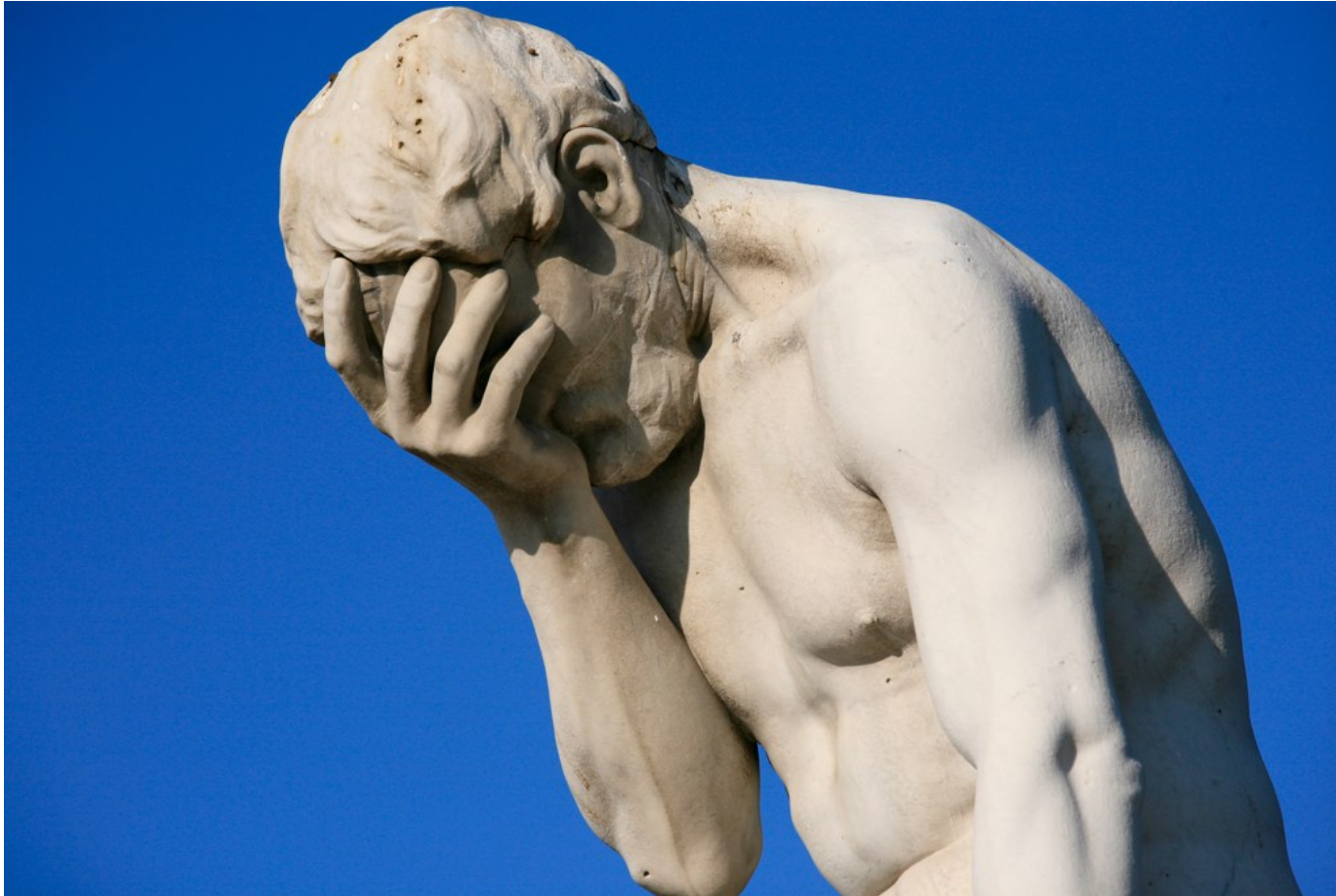
43 / 80 (53.8%) had CT consistent with pneumonia

69 / 75 (92%) had NEWS score 0-4 (low) at baseline – 5 of the 80 had missing data (!?!)

## 79 / 80 (98.8%) alive

- 12 / 80 (15%) needed oxygen
- 14 / 79 (17.7%) still admitted at writing
- 3 / 79 (3.8%) went to ICU → 2 went back to floor
- 65 / 79 (82.3%) were discharged home
  - 61 / 65 (93.8%) had NEWS score 0-4 (low) at time of discharge home

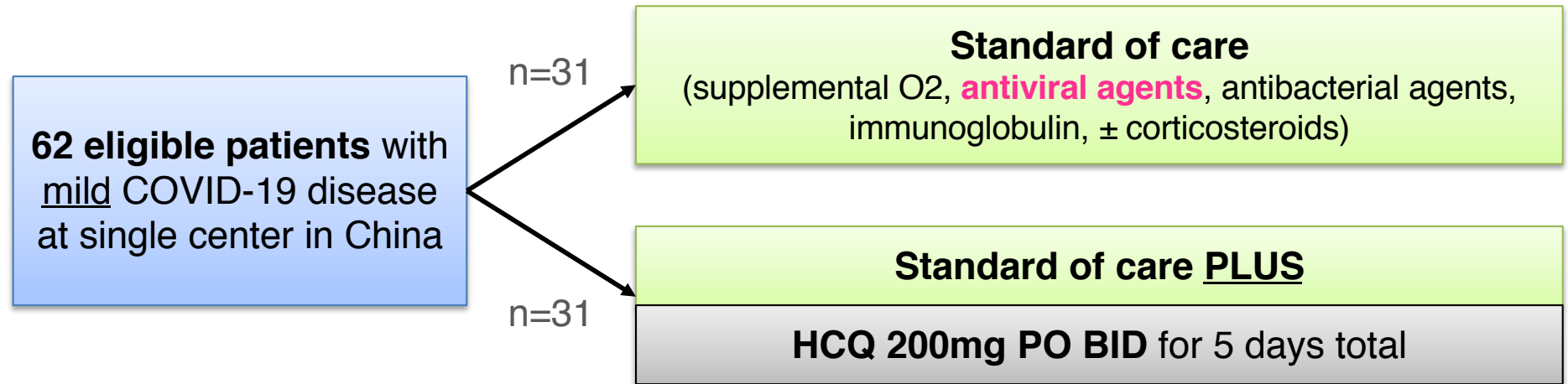
# Hydroxychloroquine



<https://blogs.sciencemag.org/pipeline/archives/2020/03/29/more-on-cloroquine-azithromycin-and-on-dr-raoult>

*Cain* by Henri Vidal, Jardin des Tuileries, Paris (1896)

# Hydroxychloroquine



## Baseline Characteristics

	Control (n=31)	HCQ (n=31)	P
Age, mean (SD)	45.2 (14.7)	44.1 (16.1)	0.88
Male, n (%)	16 (52)	17 (55)	0.80
Febrile day before randomized, n (%)	17 (55)	22 (71)	
Cough day before randomized, n (%)	15 (48)	22 (71)	

## Outcomes

	Control (n=31)	HCQ (n=31)	P
Days to becoming afebrile, mean (SD)	3.2 (1.3)	2.2 (0.4)	0.0008
Days to cough remission, mean (SD)	3.1 (1.5)	2.0 (0.2)	0.0016
Progression to severe, n (%)	4 (12.9)	0 (0%)	–
CT improved, n (%)	17 (55)	25 (81)	0.048

# Lopinavir/ritonavir

## Available Data – Human Data in SARS-CoV-1

Retrospective,  
matched cohort

Probable SARS

Ribavirin 2.4g PO LD, 1.2g PO  
q8h or 8mg/kg IV q8h X 14d  
+ reducing regimen of steroids  
X 21d

PLUS Lopinavir/ritonavir 400mg/100mg PO q12h X 14d as  
*INITIAL THERAPY* (n=44)

PLUS Lopinavir/ritonavir 400mg/100mg PO q12h X 14d  
as *RESCUE THERAPY* (n=31)

Sex

Age (years)

Co-morbidity

Lactate  
dehydrogenase

# Lopinavir/ritonavir

NOTE: Only 576 (90.9%) of these 634 had microbiologically confirmed SARS infection – but to get LPV/r, pts had to have confirmed SARS-CoV

**Table 3. Comparison of outcomes for the group given LPV/r as initial treatment and a matched cohort\***

	LPV/r as initial treatment, n=44 Crude rate or mean (95% CI)	Matched cohort, n=634 Standardised rate or mean <sup>†</sup> (95% CI)	P value
Death rate (%)	2.3 (0-6.8)	15.6 (9.8-22.8)	<0.05
Intubation rate (%)	0	11.0 (7.7-15.3)	<0.05
Desaturation rate (SaO <sub>2</sub> ≤95%) [%]	68.2 (52.3-81.8)	84.5 (74.4-95.2)	NS <sup>‡</sup>
Proportion requiring pulse methylprednisolone rescue (%)	27.3 (11.4-40.9)	55.4 (47.6-63.9)	<0.05
Mean pulse methylprednisolone dose (g)	1.6 (1.1-2.0)	3.0 (2.8-3.2)	<0.05

\* Matched on age, sex, presence/absence of co-morbidity, and initial lactate dehydrogenase level

<sup>†</sup> Standardised based on the percentage distribution of subjects of the treated group across the prognostic strata in Table 1

<sup>‡</sup> NS not significant

NOTE: Only 329 (95.6%) of these 634 had microbiologically confirmed SARS infection – but to get LPV/r, pts had to have confirmed SARS-CoV

**Table 4. Comparison of outcomes of the group given LPV/r as rescue treatment and a matched cohort\***

	LPV/r as rescue, n=31 Crude rate or mean (95% CI)	Matched cohort, n=343 Standardised rate or mean <sup>†</sup> (95% CI)	P value
Death rate (%)	12.9 (0-25.8)	14.0 (5.2-26.3)	NS <sup>‡</sup>
Intubation rate (%)	9.7 (0-22.6)	18.1 (9.0-29.7)	NS
Desaturation rate (SaO <sub>2</sub> ≤95%) [%]	93.5 (80.6-100)	92.1 (75.9-100)	NS
Mean pulse methylprednisolone dose (g)	3.8 (3.5-4.2)	3.0 (2.9-3.2)	<0.05

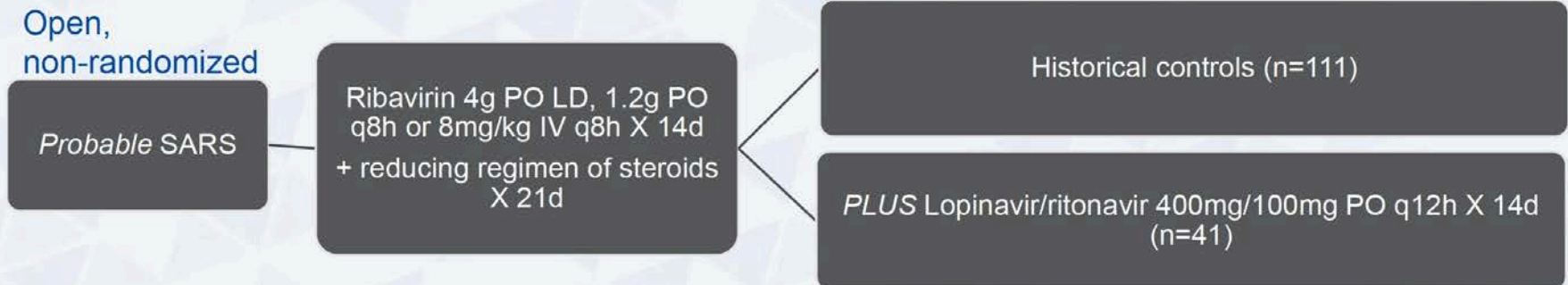
\* Matched on age, sex, presence/absence of co-morbidity, lactate dehydrogenase level before pulse methylprednisolone, and use of pulse methylprednisolone

<sup>†</sup> Standardised based on the percentage distribution of subjects of the treated group across the prognostic strata in Table 1

<sup>‡</sup> NS not significant

# Lopinavir/ritonavir

## Available Data – Human Data in SARS



1° Outcome	Historical Controls (n=111)	Treatment group (n=41)	P-value
Development of ARDS or death w/i 21d	32 (28.8%)	1 (2.4%)	<0.001
Death at day 21	7 (6.3%)	0 (0%)	
ARDS at day 21	25 (22.5%)	1 (2.4%)	



# Lopinavir/ritonavir

## Available Data – COVID-19 in China

Open-label, individually randomized

SARS-CoV-2 PCR(+)  
(n=199)

Standard care PLUS  
LPV/r (400mg/100mg) PO q12h (n=99) X14d

Standard Care (n=100)

**Standard Care:** Supplemental O<sub>2</sub>, noninvasive and invasive ventilation, abx, vasopressor support, renal-replacement therapy, and extracorporeal membrane oxygenation (ECMO)

1° Outcome	LPV/r (n=99)	Standard Care (n=100)	Difference
Time from illness onset to randomization, median days (IQR)	13 (11–17)	13 (10–16)	-
Time to clinical improvement, median days (IQR)	16.0 (13.0 to 17.0)	16.0 (15.0 to 18.0)	1.31 (0.95 to 1.80)
ITT 28d mortality, n (%)	19 (19.2)	25 (25.0)	-5.8 (-17.3 to 5.7)
mITT 28d mortality, n (%)	16 (16.7)	25 (25.0)	-8.3 (-19.6 to 3.0)
Time from randomization to d/c, median days (IQR)	12 (10 to 16)	14 (11 to 16)	1 (0 to 3)
Pts w/ clinical improvement at 14d, n (%)	45 (45.5)	30 (30.0)	15.5 (2.2 to 28.8)

Cao B, et al. NEJM, 2020. <https://doi.org/10.1056/NEJMoa2001282>

# Lopinavir/ritonavir

## Available Data – COVID-19 in China

### Author Conclusions:

LPV/r treatment added to standard txt was **not associated w/ clinical improvements or mortality in seriously ill patients** with COVID-19 vs. standard care alone. Decrease in viral loads over time **did not differ** between the two groups

\*high overall mortality, numerical benefits in early txt group and post-hoc groups

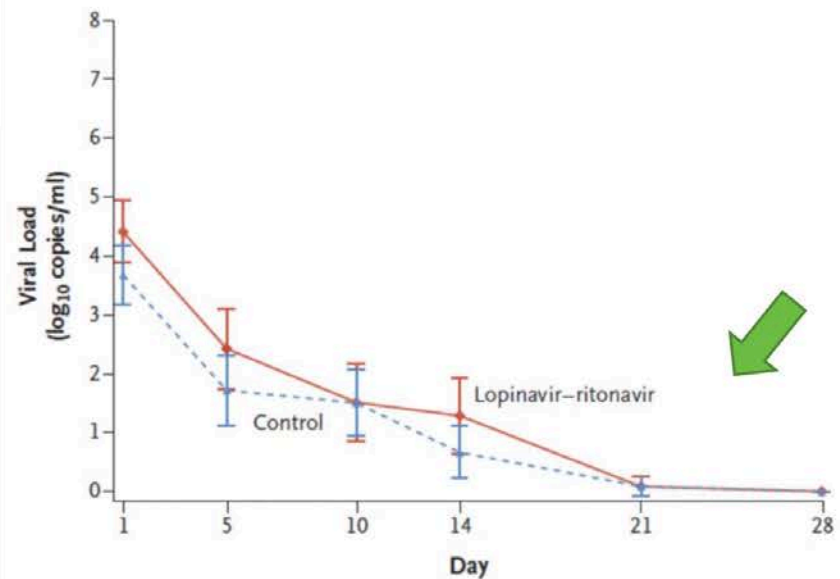


Figure 3. Mean Change from Baseline in SARS-CoV-2 Viral RNA Load by qPCR on Throat Swabs.

# Remdesivir

## Remdesivir (GS-5734)

Mechanism of Action: Interference with viral RNA-dependent RNA polymerase; premature termination of viral RNA transcription

Status: Investigational, COVID-19 Phase III trials ongoing

Formulation: Intravenous only

Dosing: 200 mg IV loading dose, then 100 mg IV daily for 5-10 days

Pediatric Dosing: 5 mg/kg IV loading dose (max 200 mg), then 2.5 mg/kg IV daily (max 100 mg)

Manufacturer: Gilead Sciences



\*Optimal duration currently under investigation

Tchesnokov; Viruses 2019.

# Remdesivir

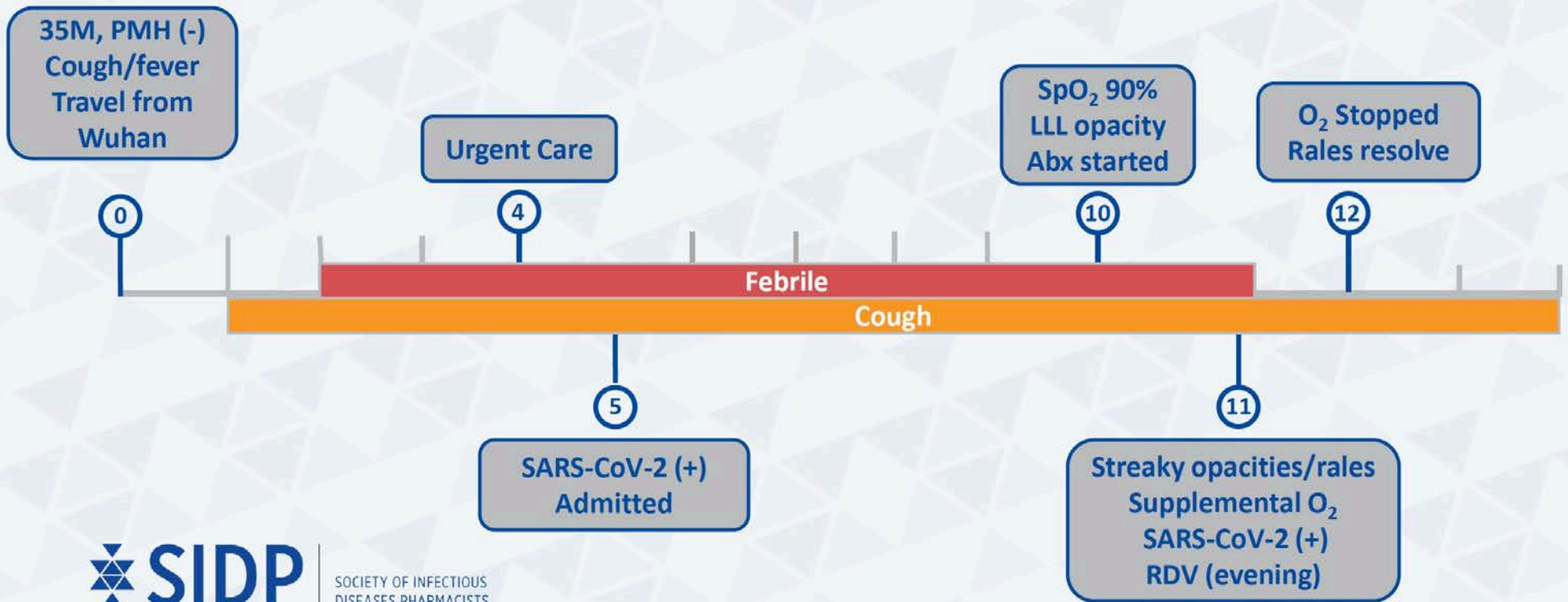
## *In vitro* Activity

Virus	EC50 (cells)	CC50 (cells)	Selectivity Index
SARS-CoV-2	<b>0.77 <math>\mu</math>M (Vero E6)</b>	>100 $\mu$ M (Vero E6)	>130
SARS-CoV-1	0.069 $\mu$ M (HAE)	> 10 $\mu$ M (HAE)	>144
MERS	0.074 $\mu$ M (HAE)	> 10 $\mu$ M (HAE)	>135
Ebola	0.086 $\mu$ M (MCR)	6.1 (Hep-2)	N/A

EC50 = 50% effective concentration; CC50 = 50% cytotoxic concentration; Selectivity Index = CC50/EC50; Vero E6 = African monkey kidney cells; HAE = human airway epithelial cells; MCR = macrophages; Hep-2 = human epithelial type 2 cells

# Remdesivir

## First U.S. COVID-19 Case Report



# Remdesivir



Thank you for your interest in emergency treatment with remdesivir. Remdesivir is an investigational agent and is not approved for use in any country. It has not been demonstrated to be safe or effective for any use. Enrollment in clinical trials remains the primary way to access remdesivir to generate critical data that inform the appropriate use of this investigational medicine.

Please note that we cannot guarantee access to remdesivir. Our ability to provide access to remdesivir, and the timeframe for processing requests and providing investigational medicine, varies from country to country for many reasons, including national and local laws as well as health authority requirements.

Emergency treatment requests will only be considered when enrollment in a clinical trial is not a feasible option.

To report an adverse event associated with the compassionate use of remdesivir, please contact +1(800) 445-3235, option 3 (Hours: 24 hrs/day, 7 days/week).

I'm a healthcare professional

I'm a patient or patient's caregiver

By clicking "I'm a healthcare professional," you are acknowledging that you are a healthcare professional and that you have read and understood the information above.

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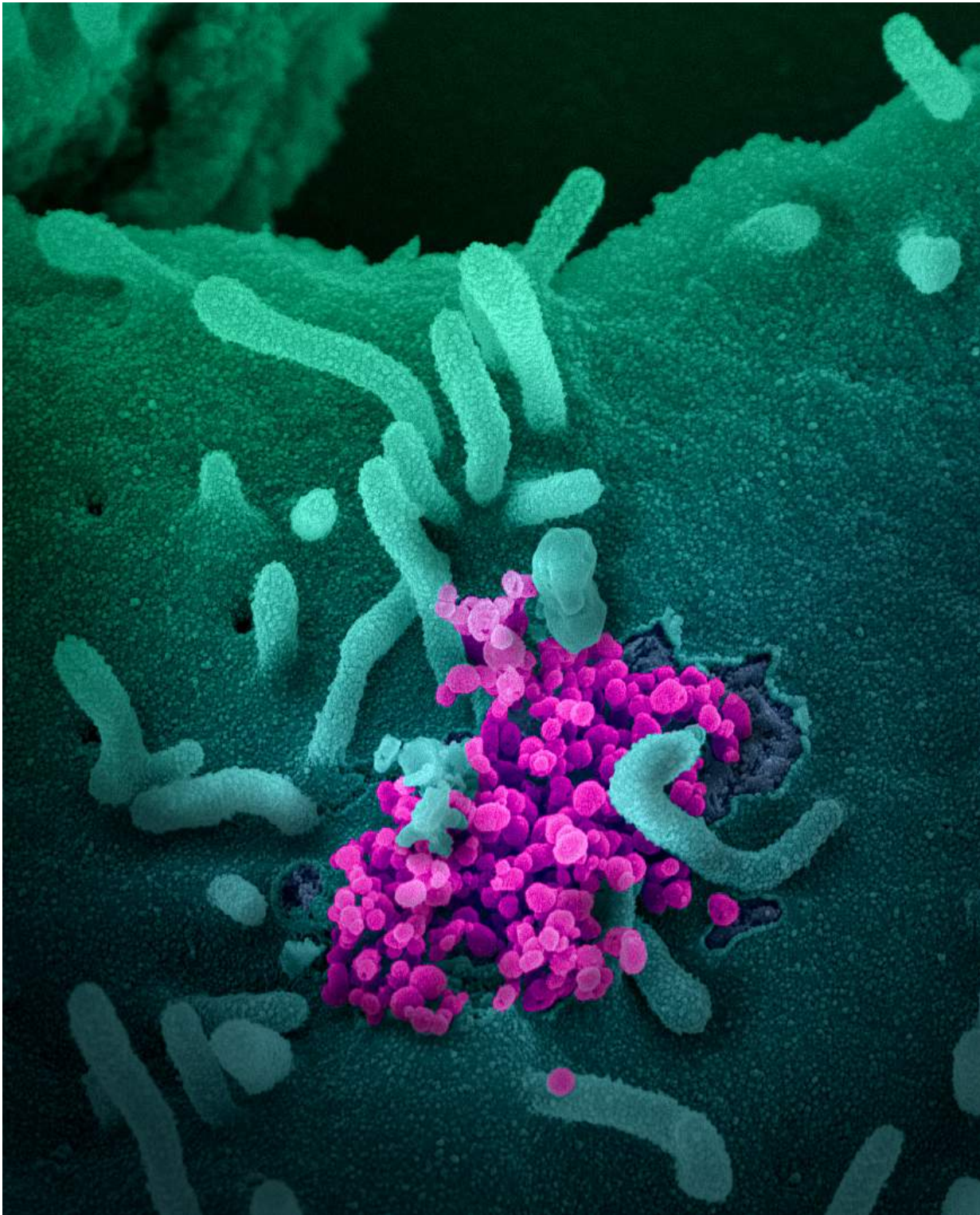
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<https://rdvcu.gilead.com>

# Remdesivir





**What are  
your  
centers  
using?**





I'm just  
trying to hold  
it together.

<https://davidolenick.com/>

**Questions?**

Please email me!

Christopher Hurt, MD  
**churt@med.unc.edu**