Clinical Management of Critically Ill Adults with COVID-19

Clinician Outreach and Communication Activity (COCA) Webinar

Thursday, April 2, 2020

Continuing Education

Continuing Education is not offered for this COCA Call.

To Ask a Question

- Using the Webinar System
  - Click the Q&A button.
  - Type your question in the Q&A box.
  - Submit your question.
- If we are unable to get to your question during the call, you may also email your question to coca@cdc.gov.
- For media questions, please contact CDC Media Relations at 404-639-3286, or send an email to media@cdc.gov.

For More **Clinical Care** Information on COVID-19

- **Call** COVID-19 Clinical Call Center at 770-488-7100 (24 hours/day).
- **Refer** patients to state and local health departments for COVID-19 testing and test results.
  - Clinicians should NOT refer patients to CDC to find out where or how to get tested for COVID-19, OR to get COVID-19 test results.
- **Visit** CDC's Coronavirus (COVID-19) website: https://www.cdc.gov/coronavirus
- **Visit** emergency.cdc.gov/coca over the next several days to learn about future COCA Calls.
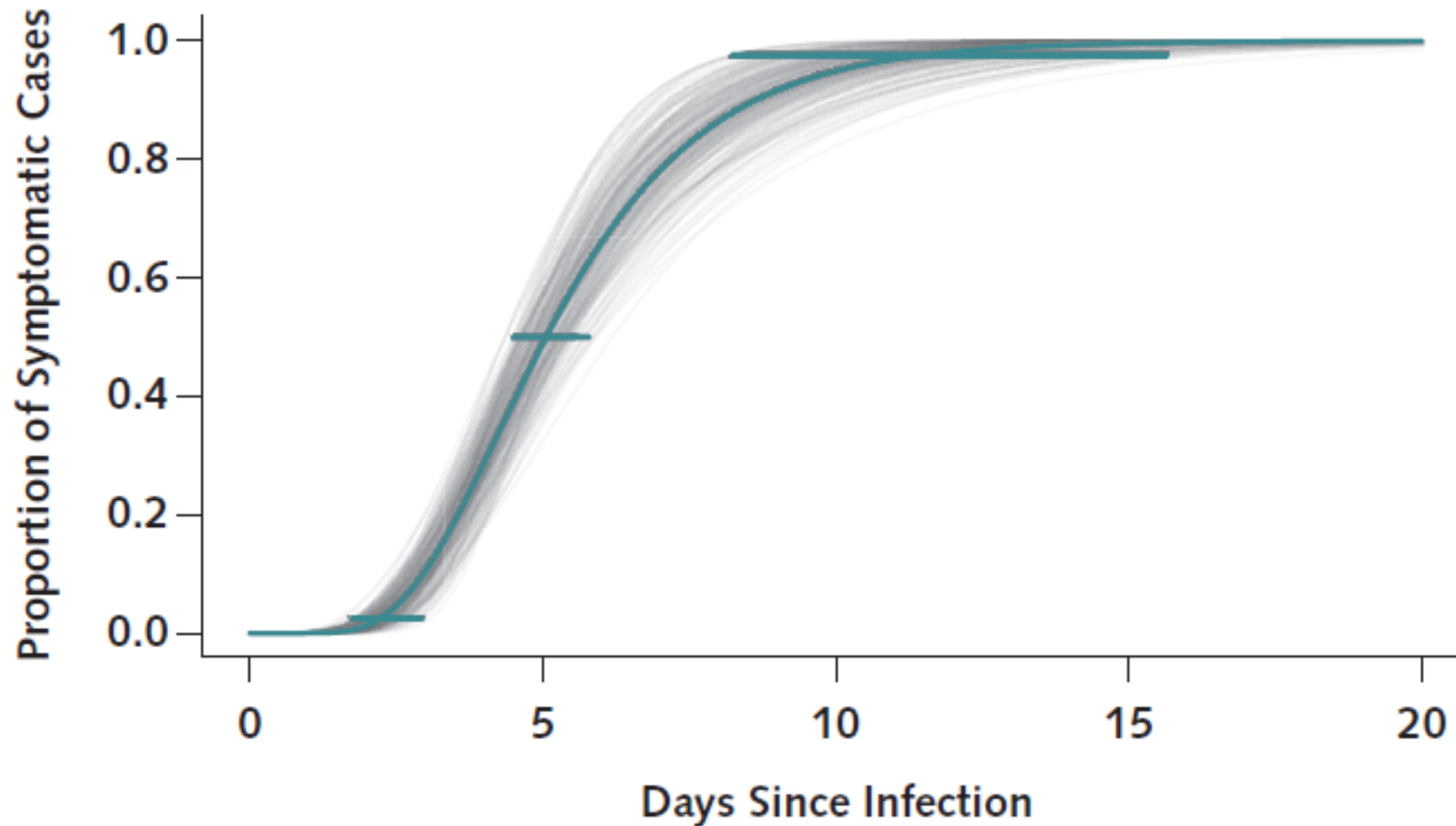
Today's Presenters

- **CAPT Tim Uyeki, MD**
  Clinical Team Lead
  COVID-19 Response
  Centers for Disease Control and Prevention

- **Michael Bundesmann, MD, FCCP**
  Medical Director of Respiratory Therapy
  Pulmonary and Critical Care Medicine
  EvergreenHealth
  Kirkland, WA

- **Waleed Alhazzani, MD, MSc, FRCPC**
  Associate Professor Department of Medicine,
  McMaster University
  Hamilton, Ontario, Canada

COVID-19 Overview for Clinicians

Tim Uyeki MD, MPH

Clinical Team

CDC COVID-19 Response

April 2, 2020

For more information: **www.cdc.gov/COVID19**
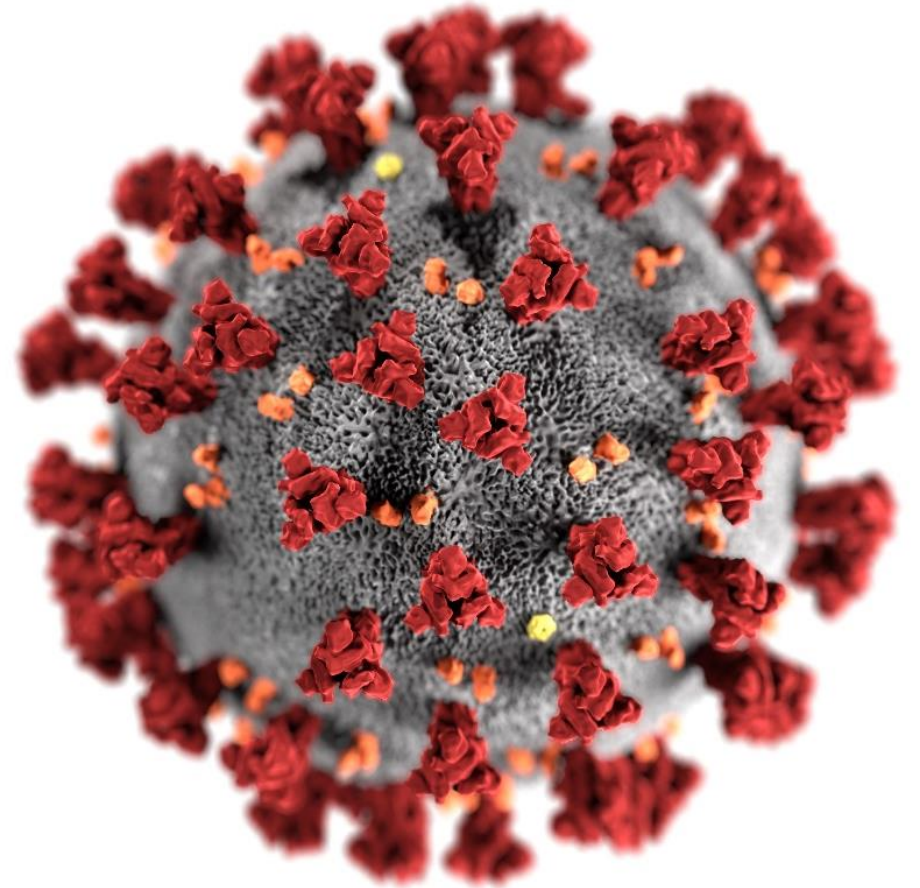
Median incubation period is 4-5 days (range: 2-14 days)

Links: *Lauer Ann Intern Med 2020*, *Xu BMJ 2020*, *Guan NEJM 2020*

COVID-19: Wide spectrum of disease
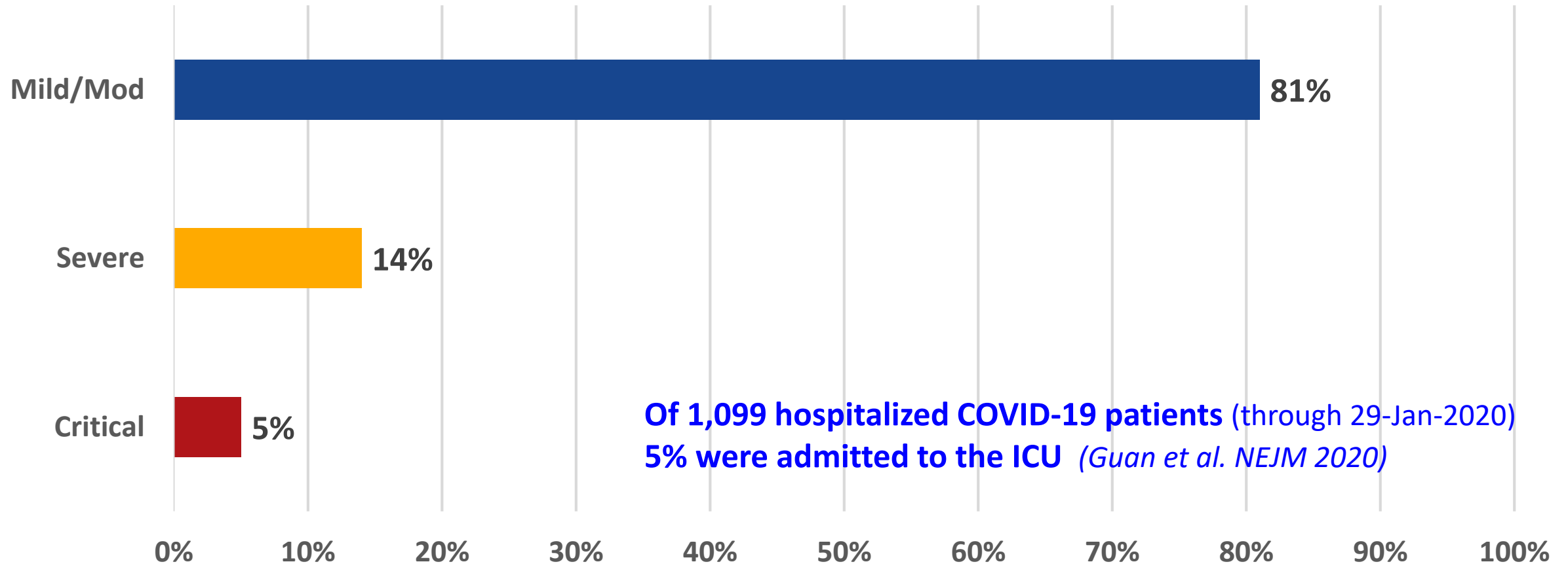
Mild Illness	Uncomplicated upper respiratory tract viral infection
Moderate Pneumonia	Pneumonia without the need for supplemental oxygen
Severe Pneumonia	Pneumonia with dyspnea, respiratory distress, SpO2≤93% on RA, P/F ratio <300
Critical Illness	Respiratory failure, septic shock, multiple organ dysfunction/failure

Link: WHO Guidelines 2020

Most patients had mild to moderate disease, but nearly 20% had severe or critical illness

COVID-19 - China through 11-Feb-2020 (N=44,415)

Mild/Mod — 81%
Severe — 14%
Critical — 5%

Of 1,099 hospitalized COVID-19 patients (through 29-Jan-2020)
5% were admitted to the ICU *(Guan et al. NEJM 2020)*

Links: *Wu JAMA 2020*

Potential for patients to have acute deterioration in the second week of illness
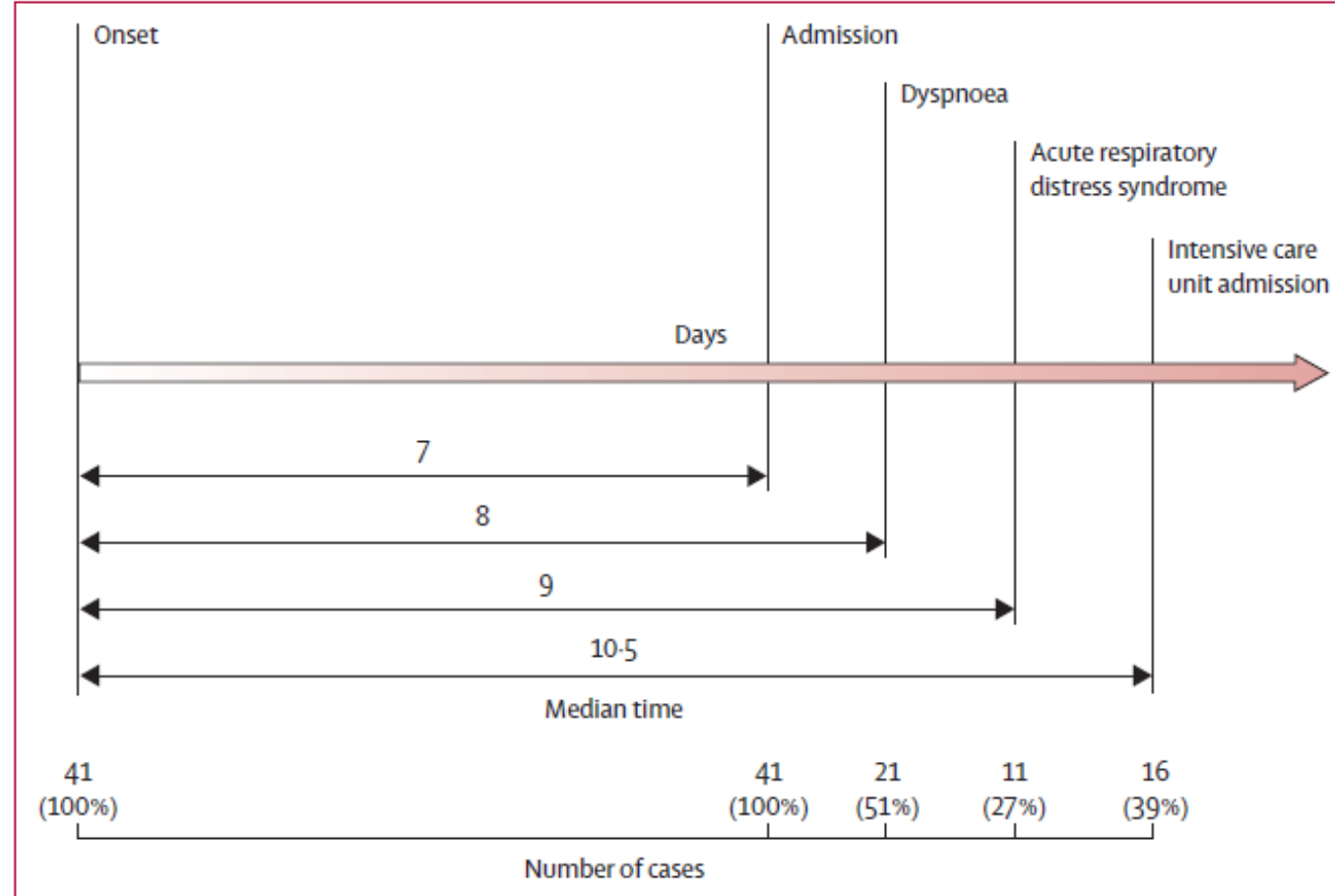
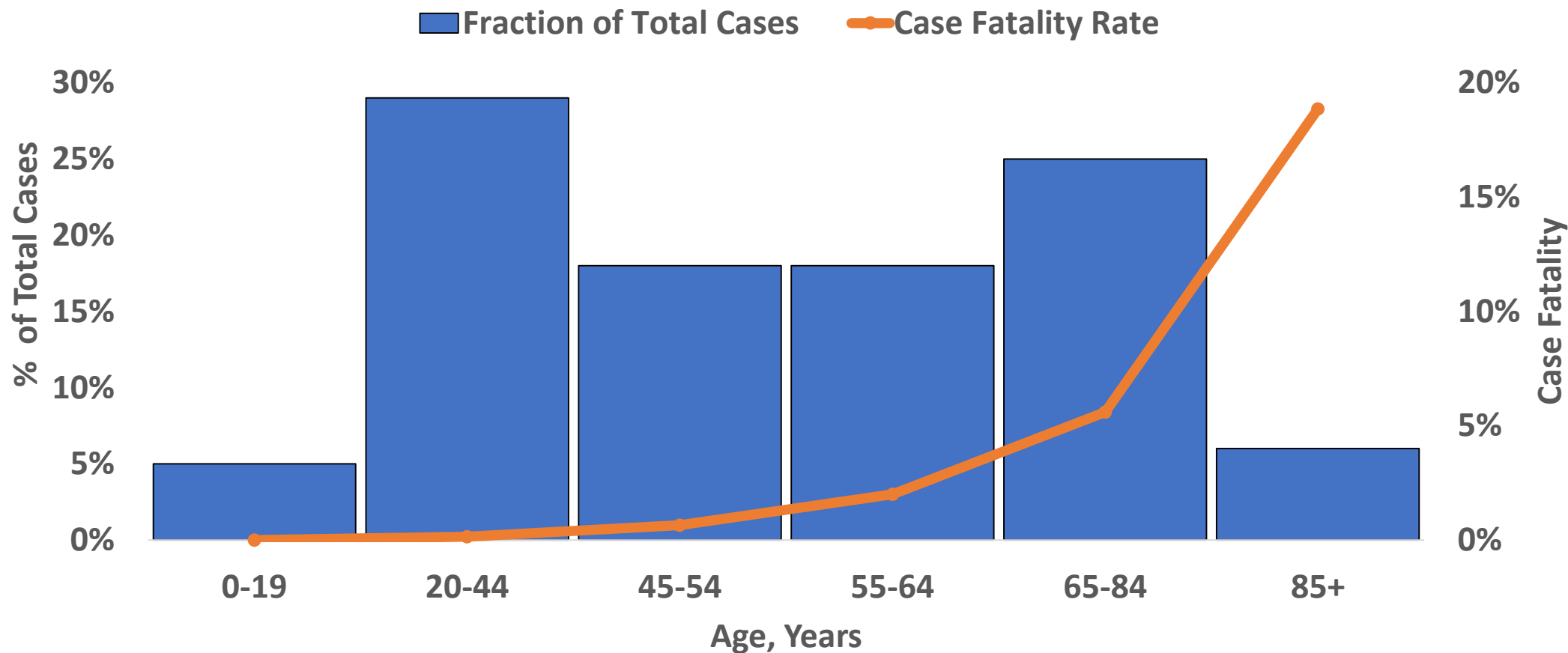## COVID-19 - China through 2-Jan-2020 (N = 41)

**Figure 2:** Timeline of 2019-nCoV cases after onset of illness

But the case-fatality is disproportionately higher among older adults

COVID-19 - United States, February 12–March 16, 2020 (N = 4,226)

Links: *MMWR 2020*

Older adults: More likely to require ICU care and die, but hospitalizations and ICU admissions also occur among non-elderly adults

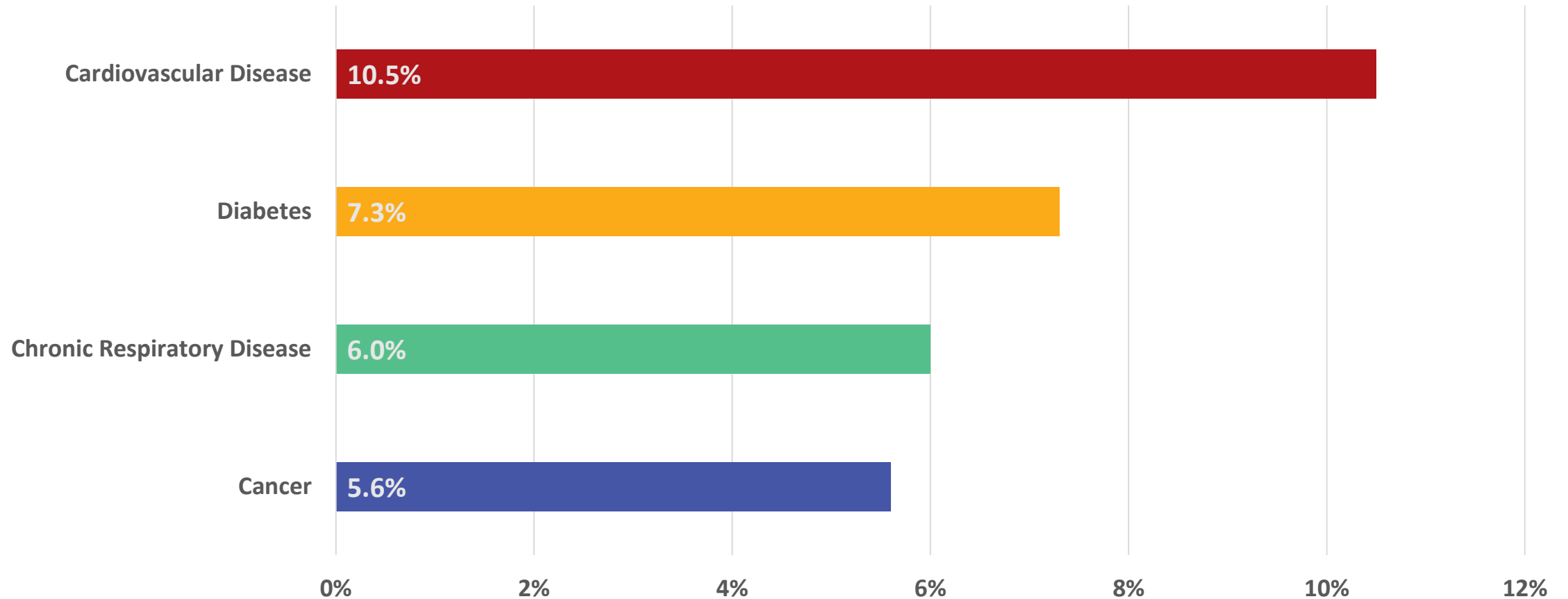## COVID-19 United States, February 12–March 16, 2020 (N = 4,226)
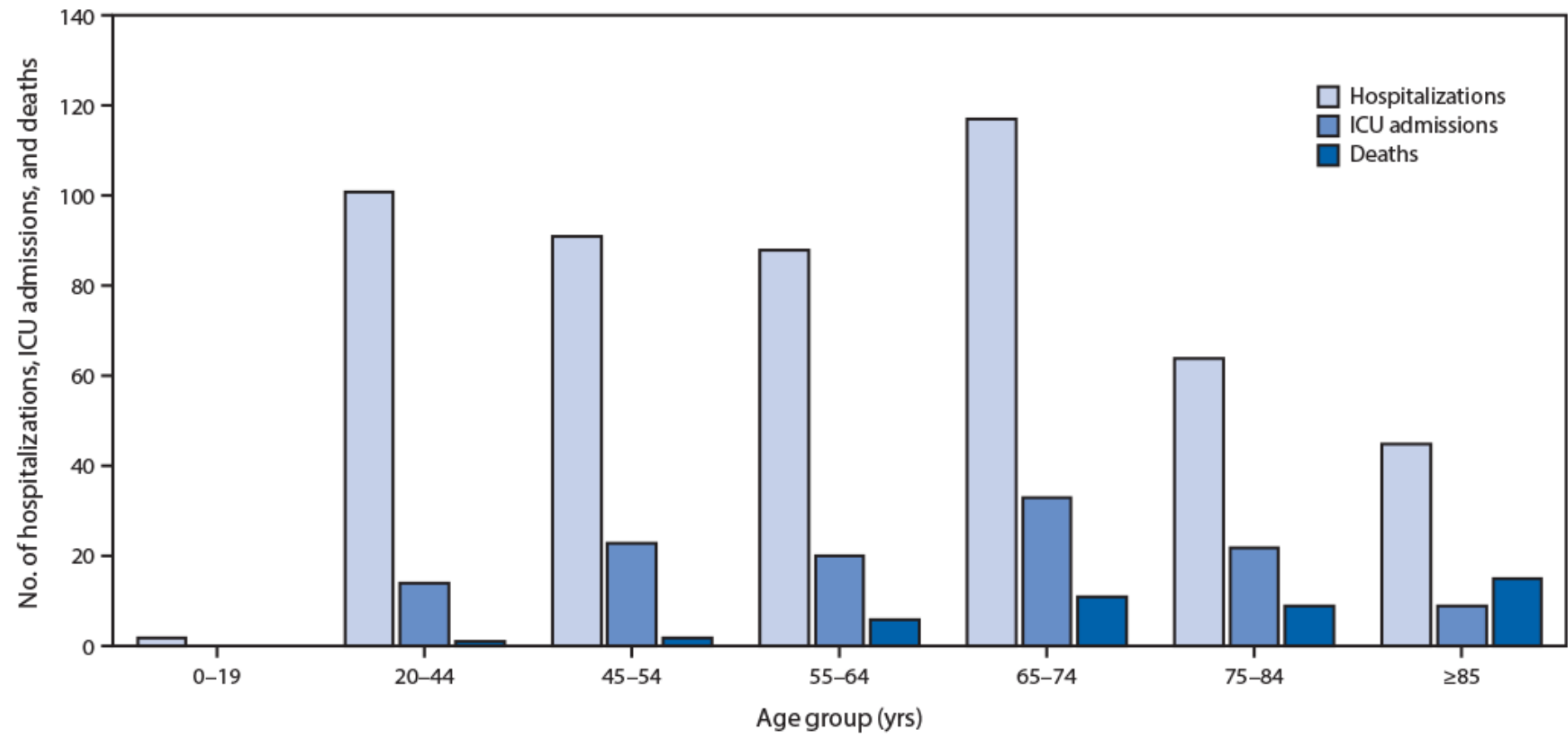
Mortality from COVID-19 is highest among persons with underlying medical conditions

COVID-19 - China through 11-Feb-2020

Link: China COVID-19 Epi Team 2020

Most, but not all patients have fever, cough, or shortness of breath on hospital admission (China, Singapore, U.S.)

> **2 US ICU cohorts: 50-52% had fever at admission**

Percent with Symptoms on Hospital Admission
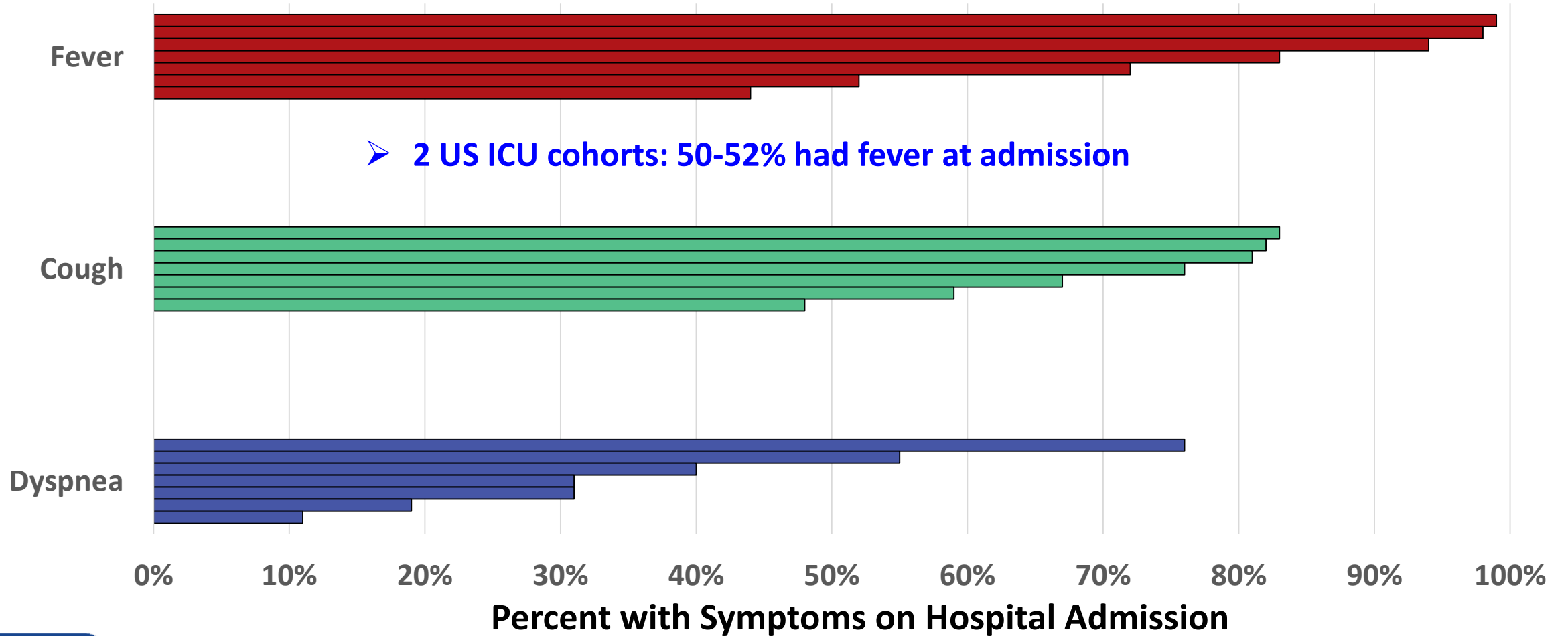
Links: *Arentz JAMA 2020*, *Chen Lancet 2020*, *Guan NEJM 2020*, *Huang Lancet 2020*, *Wang JAMA 2020*, *Wu JAMA IM 2020*, *Young JAMA 2020*; *Bhatraju NEJM 2020*

Lower respiratory specimens may have higher virus yield than upper respiratory specimens, China (N = 205) Jan 1-Feb 17 2020

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.

Link: *Wang JAMA 2020*

Laboratory findings at hospital admission

➢ **Lymphopenia** (83%)

▪ Thrombocytopenia (36%)

▪ Leukopenia (34%)

▪ C-reactive protein ≥10 mg/L: (61%)

▪ Elevated AST, ALT: (20-39%) - higher with severe disease

▪ Procalcitonin - typically normal on admission

➢ Co-infections:

  ➢ Sporadic viral co-infections reported (e.g., influenza, parainfluenza)

  ➢ Community-acquired secondary bacterial infection not reported in published case series (blood cultures: negative)

Link: CDC Clinical Guidance 2020

Laboratory abnormalities in severe disease

- **Associated with severe or critical illness:**

  ↓lymphocytes, ↑neutrophils

  ↑alanine aminotransferase and ↑aspartate aminotransferase levels

  ↑lactate dehydrogenase, ↑PCT, ↑CRP, ↑ferritin levels

  ↑serum levels of pro-inflammatory cytokines and chemokines

  ➢ Evidence of immune dysregulation: Higher plasma levels of pro-inflammatory cytokines (TNFα, IL-1, IL-6) and chemokines (IL-8) in severe/critically ill patients vs less severely ill patients
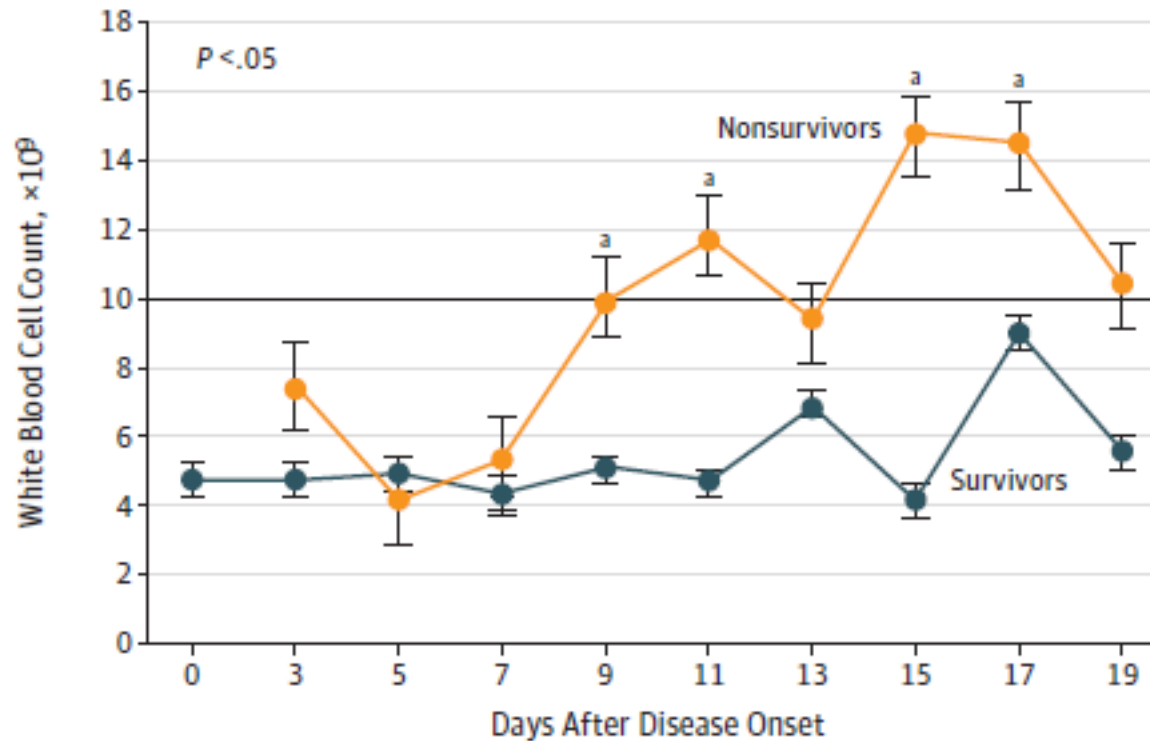
- **Associated with mortality:** ↑D-dimers and lymphopenia

Link: *Qin CID 2020*; *Huang Lancet 2020*; *Wang JAMA 2020*; *Yang Lancet 2020*; *Arentz JAMA 2020*

Leukocytosis, specifically neutrophilia, during hospitalization is associated with death (N = 138, China, Jan 1-28, 2020)

Link: *Wang JAMA 2020*
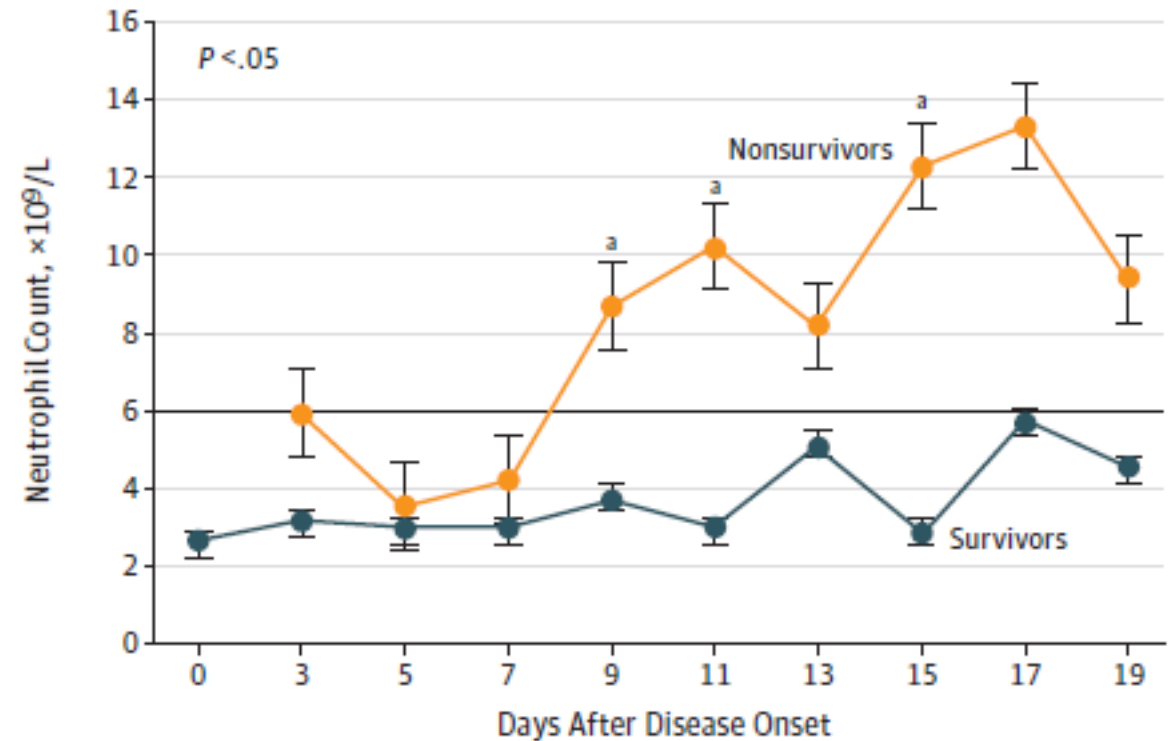
Lymphopenia is common in all patients, but may be lower in non survivors than survivors (N = 138, China, Jan 1-28, 2020)

C Lymphocyte count

Survivors

Nonsurvivors

P < .05

Lymphocyte Count, ×10⁹/L

Days After Disease Onset

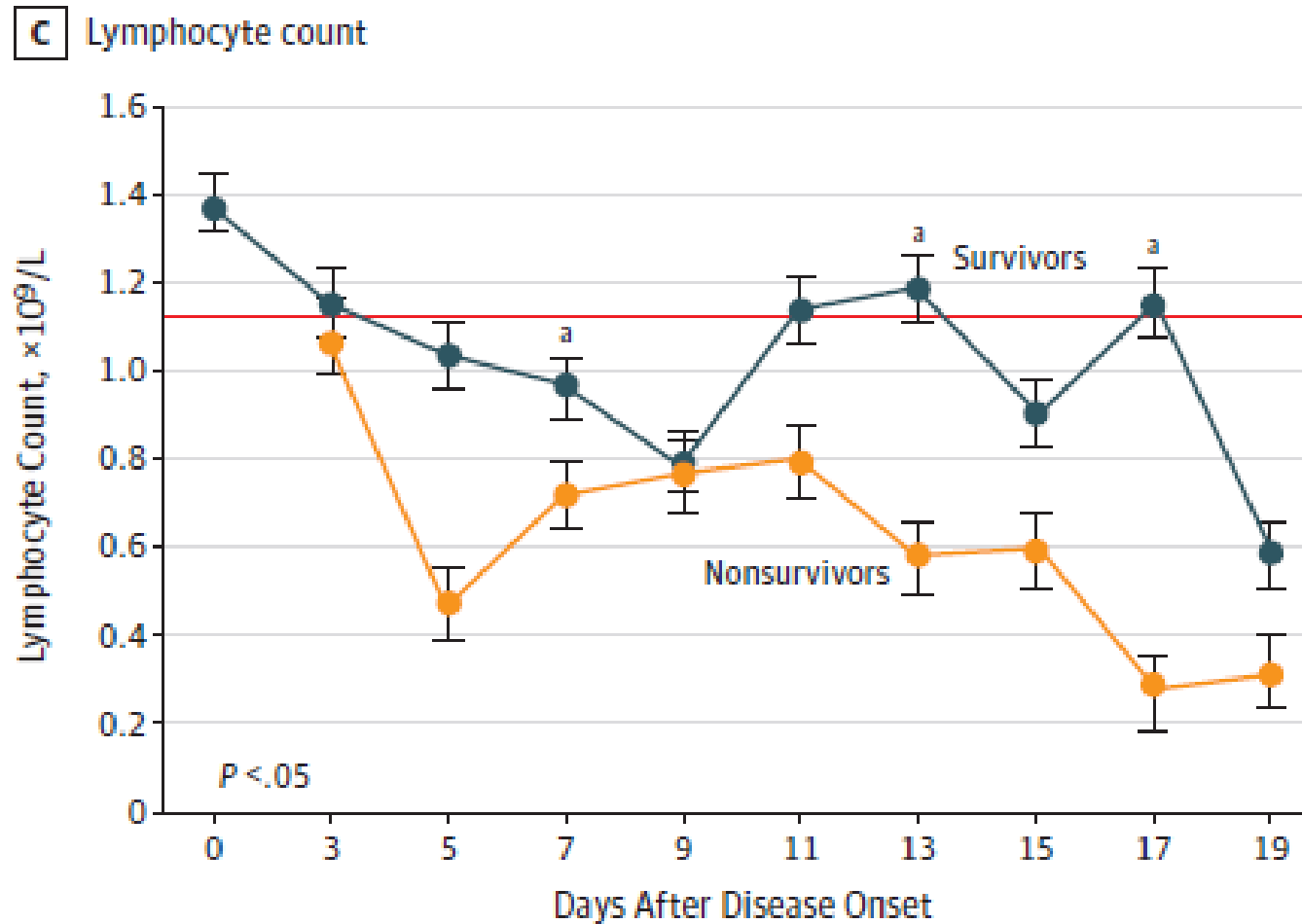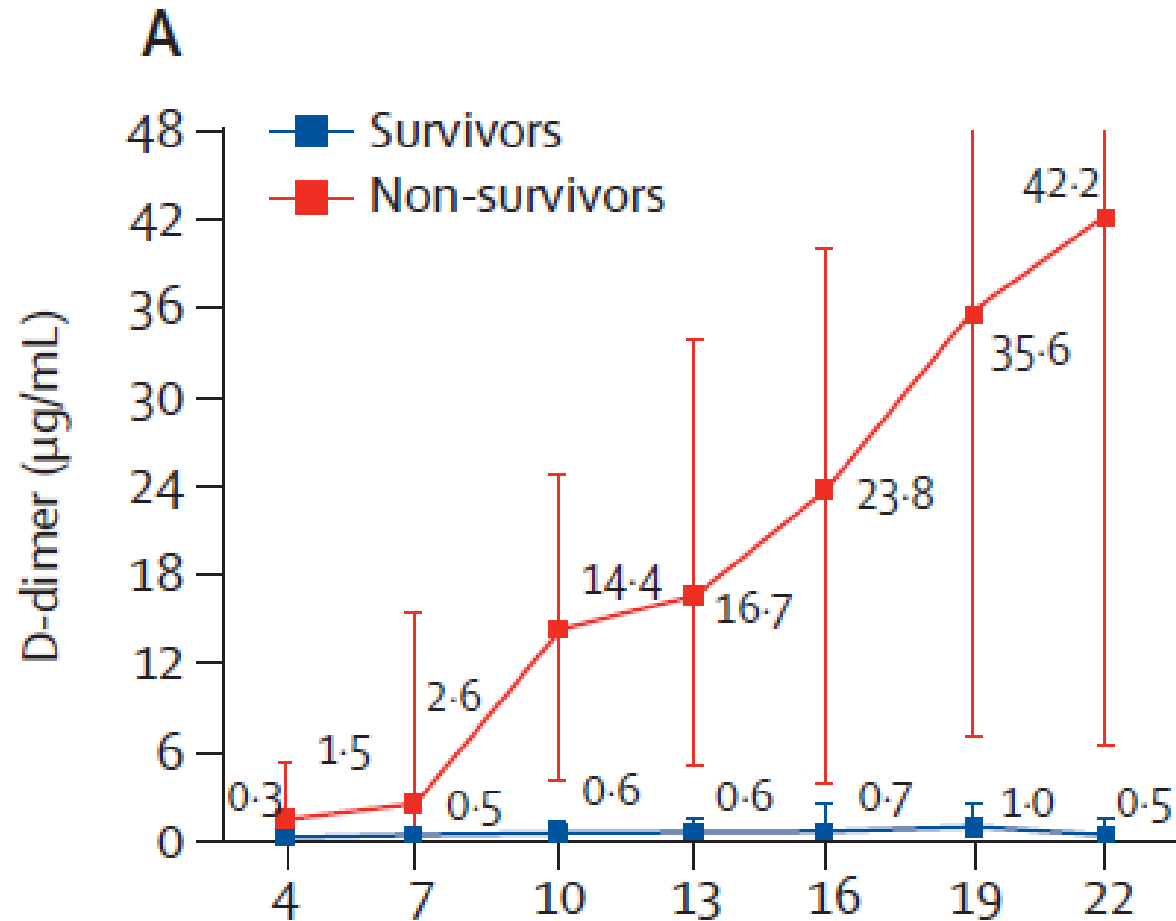# D-dimer is a strong predictor of death when compared with other markers of COVID-19 severity (N = 191), China, Dec 28, 2019 - Jan 28, 2020

A

	Univariable OR (95% CI)	p value	Multivariable OR (95% CI)	p value
Demographics and clinical characteristics				
Age, years*	1·14 (1·09–1·18)	<0·0001	1·10 (1·03–1·17)	0·0043
SOFA score	6·14 (3·48–10·85)	<0·0001	5·65 (2·61–12·23)	<0·0001
D-dimer, µg/mL				
≤0·5	1 (ref)	..	1 (ref)	..
> 0·5	1·96 (0·52–7·43)	0·32	2·14 (0·21–21·39)	0·52
> 1	20·04 (6·52–61·56)	<0·0001	18·42 (2·64–128·55)	0·0033

Table 3: Risk factors associated with in-hospital death

Link: *Zhou Lancet 2020*

Adult ICU Case Series, U.S.
(N = 21) Feb 20-March 5, 2020; (N=24) Feb 24-March 9, 2020

- Common co-morbidities
  - Heart failure (0-43%)
  - COPD (4-33%)
  - Diabetes (33-58%)
  - Kidney disease (21-48%)
  - Obstructive sleep apnea (21-29%)
- Onset to ICU admission: @4.5-7 days
- Mean age: 70 years (43-92); 63 years (23-97)
- Complications
  - Respiratory failure requiring mechanical ventilation: (71-75%)
  - Shock requiring vasopressors: (67-71%)
  - Acute kidney failure: (0-19%)
  - Cardiomyopathy: (0-33%)
  - Bacterial co-infection (1/21; 0/20)
- Mortality: (50-52%)

COVID-19: Inpatient clinical management

- **No proven FDA-approved treatment for COVID-19**

- **Management is supportive**
  - Hypoxemic respiratory failure/ARDS
  - Septic shock
  - Cardiomyopathy/arrhythmia
  - Common critical care complications

Link: CDC Clinical Guidance 2020

COVID-19: Therapeutics

- **No FDA-approved specific treatment for COVID-19 patients**

  ➤ Corticosteroids **should be avoided** unless indicated for other reasons
    - May prolong viral replication
    - Data supporting use is uncontrolled and not high quality

  ➤ Several drugs under investigation:
    - Remdesivir
    - Hydroxychloroquine or chloroquine
    - Lopinavir/ritonavir
    - IL-6 blockers (e.g., tocilizumab, sarilumab)

Link: CDC Clinical Guidance 2020

Resources for Inpatient COVID-19 Management

Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19)

Waleed Alhazzani[1,2], Morten Hylander Møller[3,4], Yaseen M. Arabi[5], Mark Loeb[1,2], Michelle Ng Gong[6], Eddy Fan[7], Simon Oczkowski[1,2], Mitchell M. Levy[8,9], Lennie Derde[10,11], Amy Dzierba[12], Bin Du[13], Michael Aboodi[6], Hannah Wunsch[14,15], Maurizio Cecconi[16,17], Younsuck Koh[18], Daniel S. Chertow[19], Kathryn Maitland[20], Fayez Alshamsi[21], Emilie Belley-Cote[1,22], Massimiliano Greco[16,17], Matthew Laundy[23], Jill S. Morgan[24], Jozef Kesecioglu[10], Allison McGeer[25], Leonard Mermel[8], Manoj J. Mammen[26], Paul E. Alexander[2,27], Amy Arrington[28], John Centofanti[29], Giuseppe Citerio[30,31], Bandar Baw[1,32], Ziad A. Memish[33], Naomi Hammond[34,35], Frederick G. Hayden[36], Laura Evans[37], Andrew Rhodes[38]

Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected

Interim guidance
13 March 2020

World Health Organization

This is the second edition (version 1.2) of this document, which was originally adapted from Clinical management of severe acute respiratory infection when MERS-CoV infection is suspected (WHO, 2019).

It is intended for clinicians involved in the care of adult, pregnant, and paediatric patients with or at risk for severe acute respiratory infection (SARI) when infection with the COVID-19 virus is suspected. Considerations for paediatric patients and pregnant women are highlighted throughout the text. It is not meant to replace clinical judgment or specialist consultation but rather to strengthen clinical management of these patients and to provide up-to-date guidance. Best practices for infection prevention and control (IPC), triage and optimized supportive care are included.

Strong	Must do or must avoid
Best Practice	Must do or must avoid
Weak	Consider doing or consider avoiding

✅	Strong recommendation or best practice
⚠️	Consider in select patients
❌	Intervention is harmful

Link: WHO Guidelines 2020, Surviving Sepsis Campaign 2020

COVID-19 Case Examples

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EVERGREEN HEALTH, KIRKLAND, WA

CDC COCA CALL, APRIL 2, 2020

Disclaimer

The views expressed in this presentation are those of the author and do not necessarily represent the opinion of the Centers for Disease Control and Prevention.
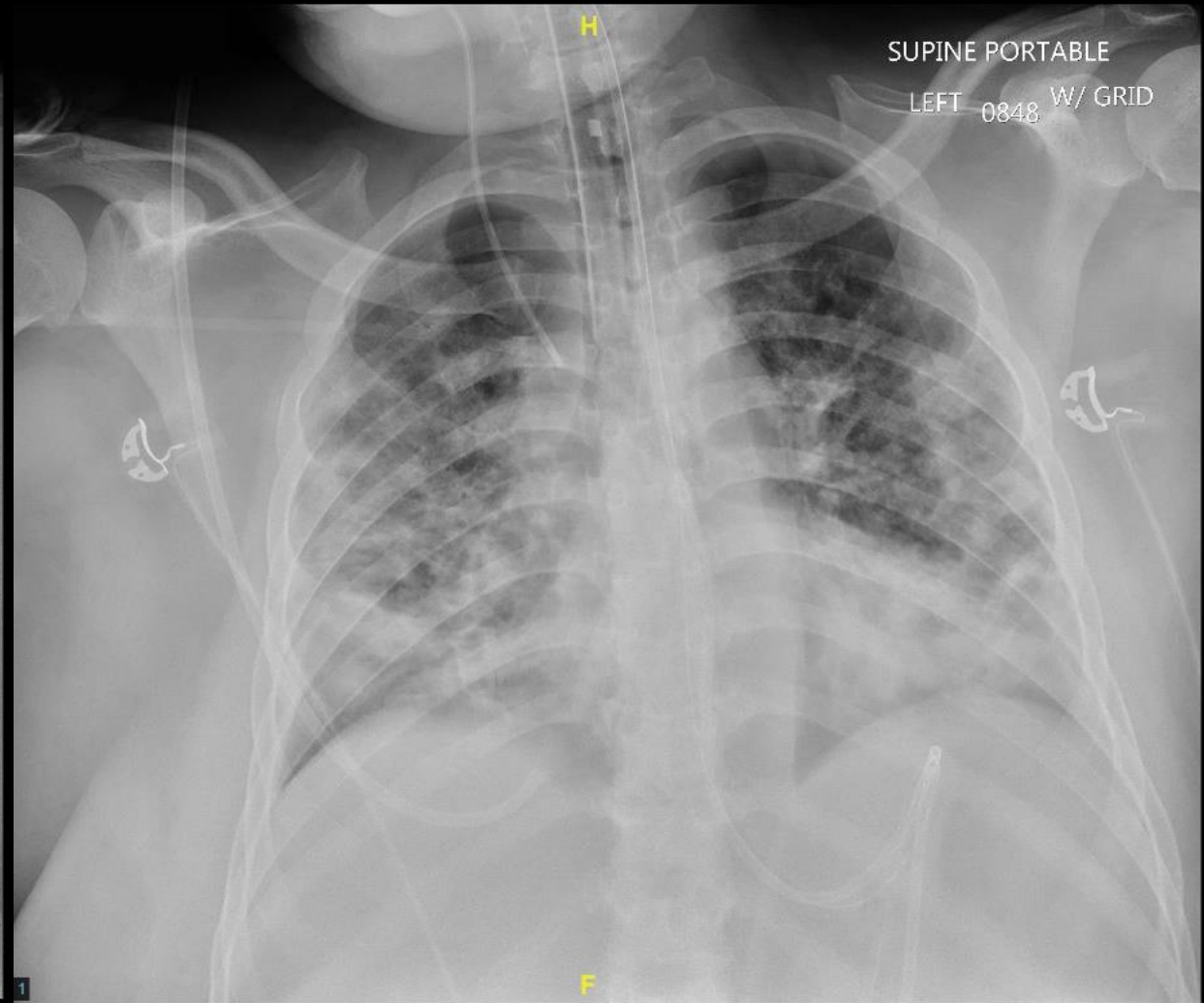
Case 1

47-year-old man with 7 days of URI, 3 days of worsening dyspnea

- ◦ HTN, obesity (BMI 36), untreated DM
- ◦ No tobacco
- ◦ Home medications included lisinopril, HCTZ, carvedilol
- ◦ At time of presentation, he was not tested for COVID-19
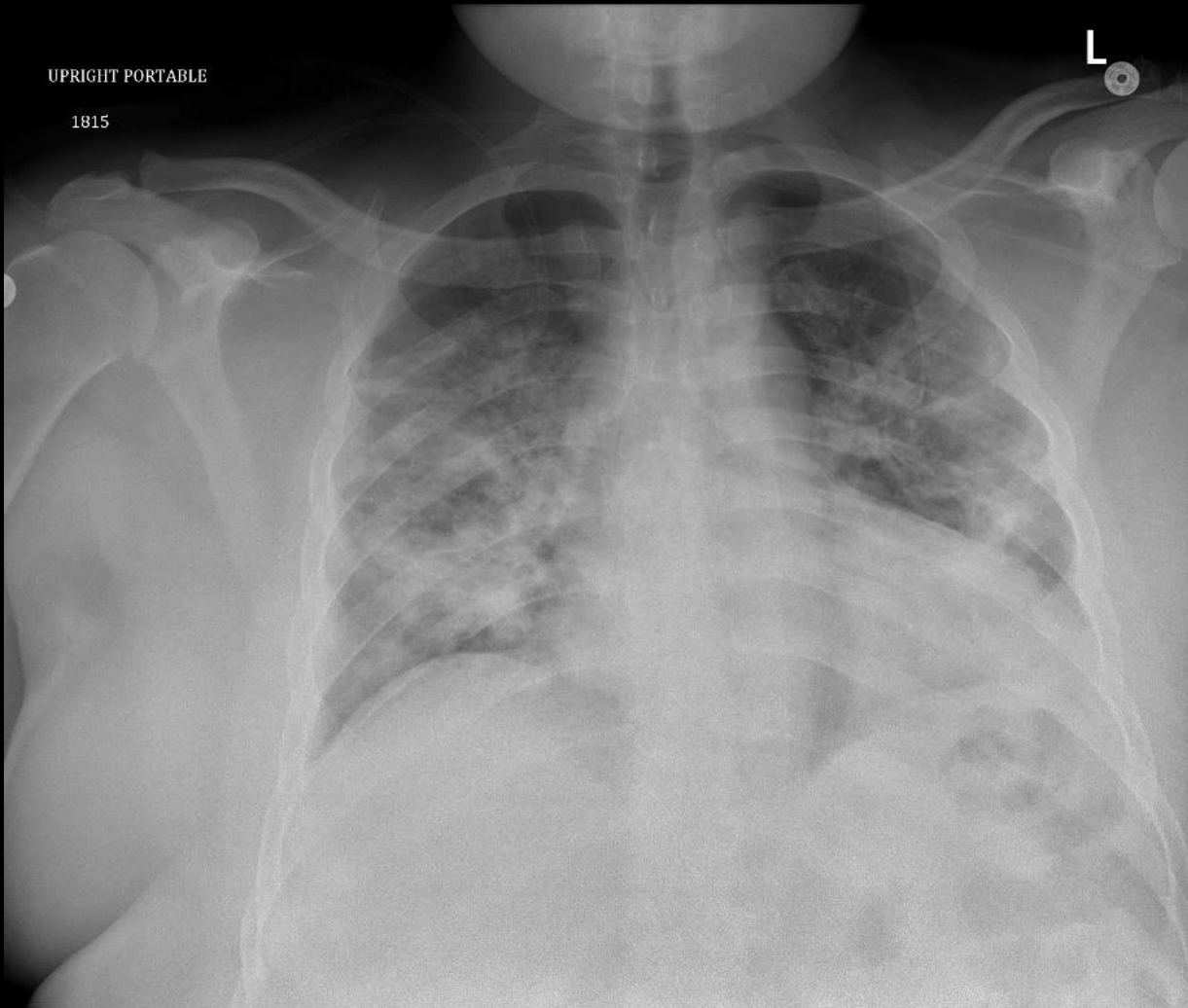
Admission AP CXR

Day 4 AP CXR

Hospital Course

o Intubation and institution of lung protective ventilation from day 2 through day 14

o Proned days 2-13 of hospitalization
   o Inhaled epoprostenol and NMB were not given
   o Extubated to HFNC

o Ceftriaxone and azithromycin discontinued after 7 days (no initial procalcitonin checked)

o On day 6, compassionate use Remdesivir was given for 10-day course

o On day 10, hydroxychloroquinine 400 BID, then daily x 5 days

o On day 21, weaned to room air, significant neuromuscular weakness

Notable Findings

- 3/2 Respiratory pathogen panel negative

- 3/2 NP sample drawn, SARS-CoV-2 detected 3/6

- 3/2 Bronchoscopy BAL 62% Ly, 13% PMN

- Abs lymphocyte 1.0×10^3/uL

- AST/ALT < 2x ULN

- CRP 15.93 on 3/8 decreased to 1.11

- Normal NT-proBNP, TnI

- Normal echocardiogram, except for mild pulmonary HTN

Lab Trends
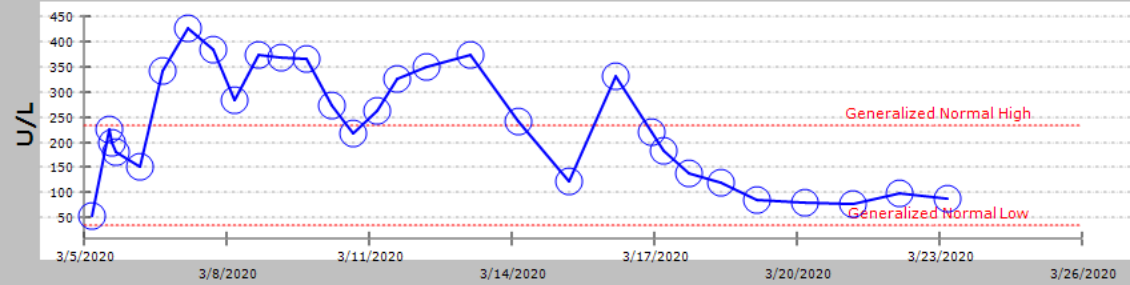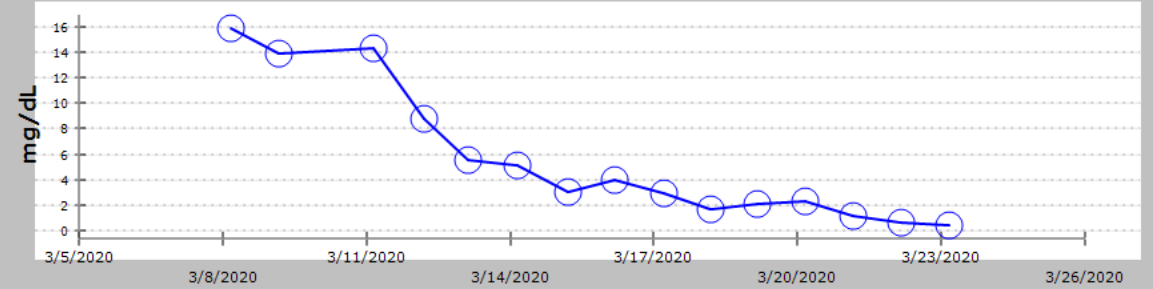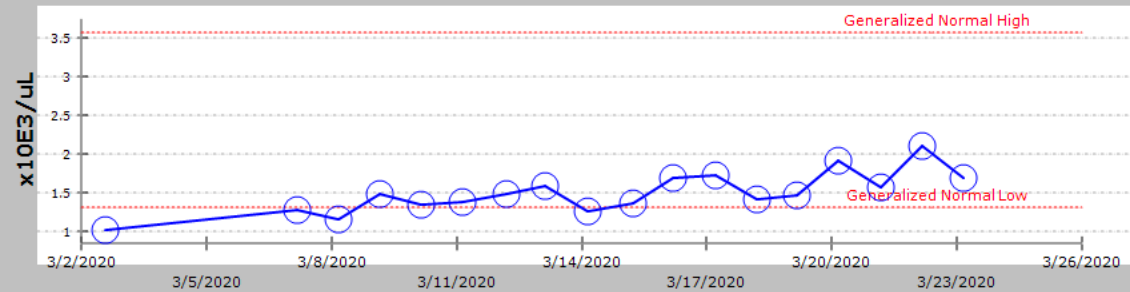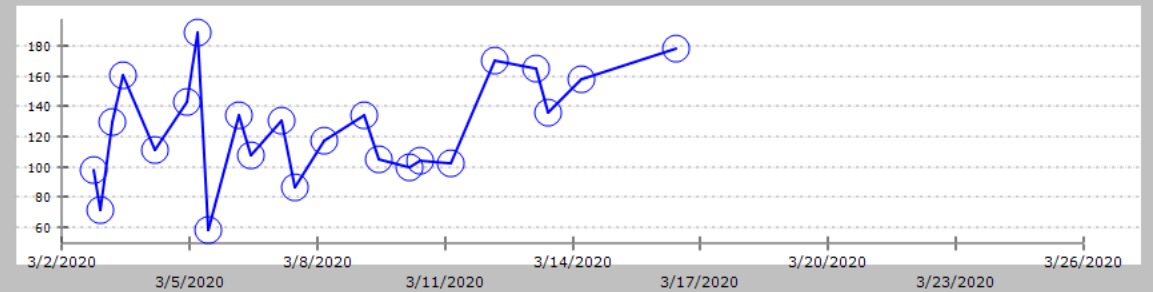
Hospital course

o Significant weakness and myopathy
  o No steroids or NMB were used

o Remains hospitalized more than four weeks after admission
  o Complicated below DVT, then psoas hematoma on anticoagulation

o COVID-19 testing remained positive after 3 weeks

o Repeat COVID-19 testing negative during 4th week

Case 2

73-year-old man with controlled asthma, HL, BPH. Good functional capacity and active.

- 4 days prior to admit was seen in urgent care for 7 days of cough, fever, fatigue
- 2/27 – presents to ED with SpO2 82%. Placed on HFNC, intubated within 24 hrs
- At the time of admission, RF for COVID-19 were not identified.
- COVID-19 testing was positive in 2/29
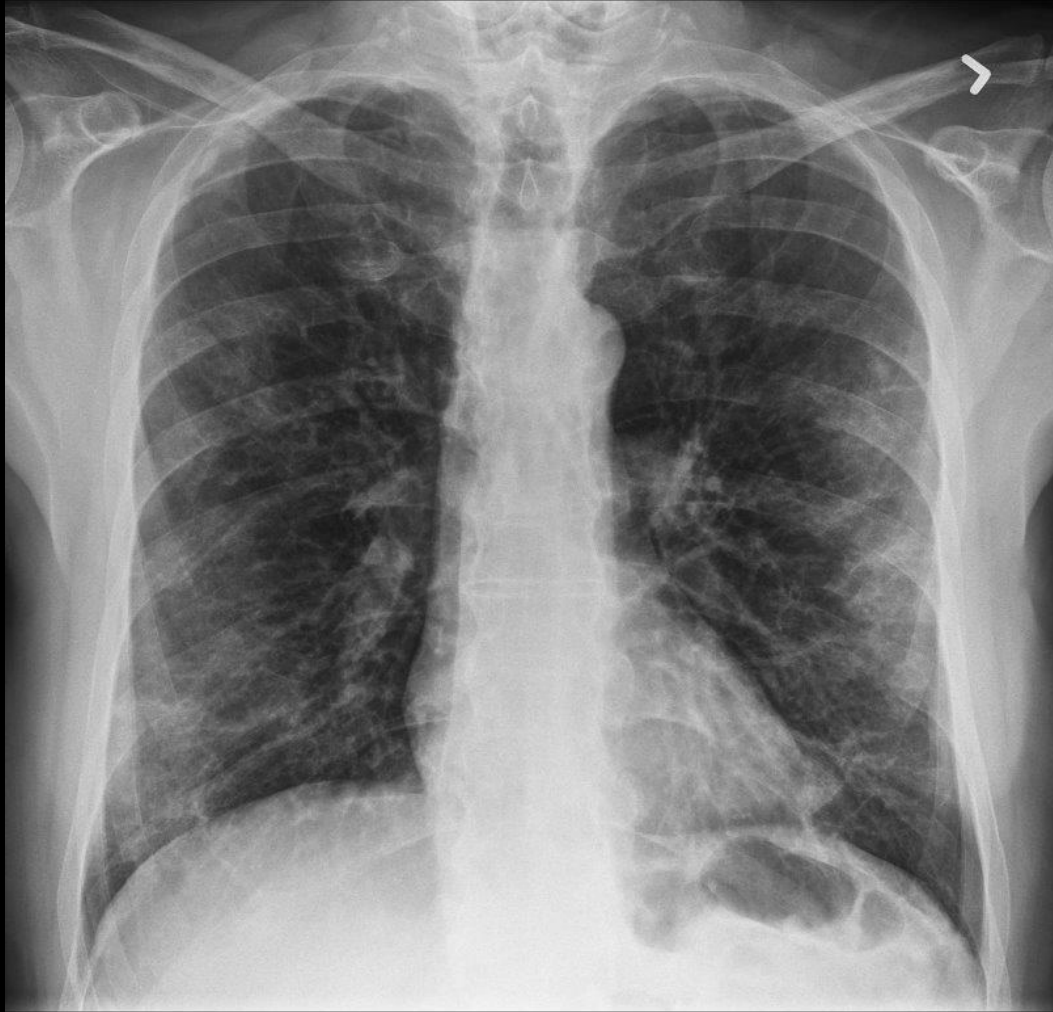
4 days prior to admission   Day of admission
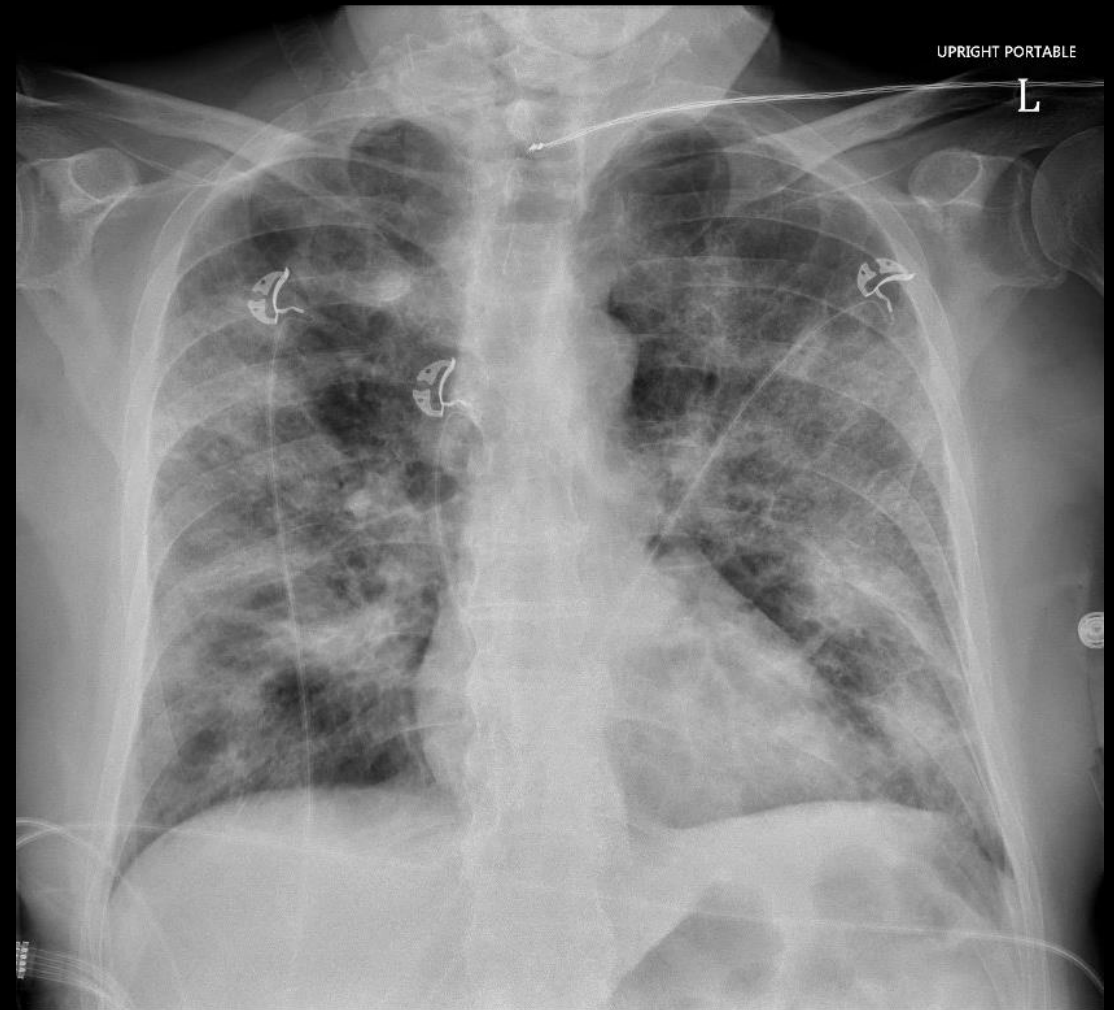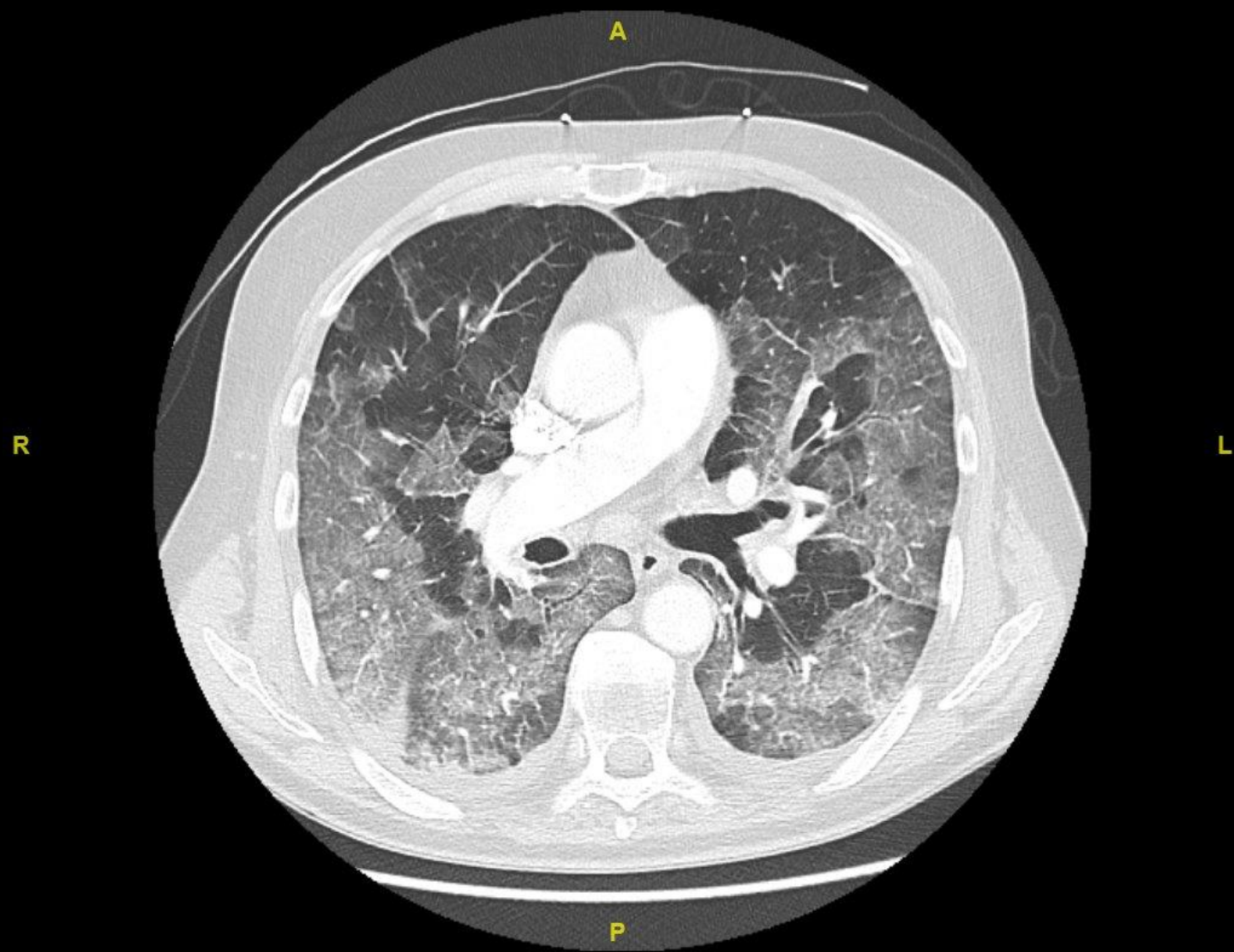
Hospital Course

o Cefepime, Vancomycin

o Paralyzed, prone x 4 days

o Day 7 compassionate use remdesivir was added

o Weaned off vasopressors by day 7

o Day 11 worsening acute kidney injury

o Day 11 worsening shock and LVEF (normal troponin)

o CRRT started day 14

o Comatose on day 24, failing SBT, remains on HD. MRI brain, CT brain and LP negative

o Acutely deteriorated further, goals changed to comfort-care and patient expired

Lab Trends
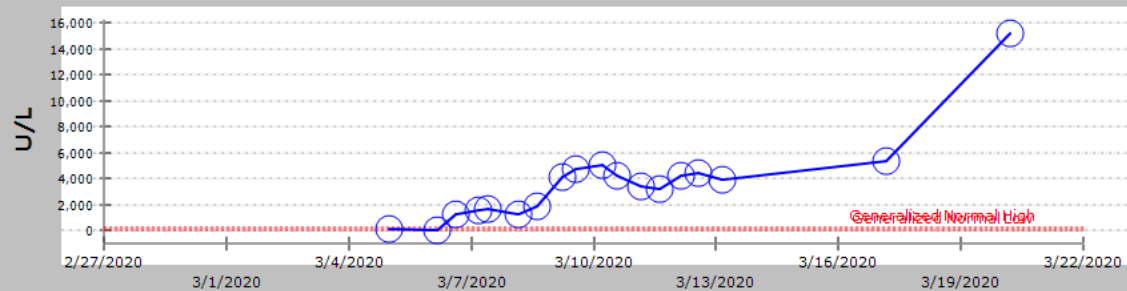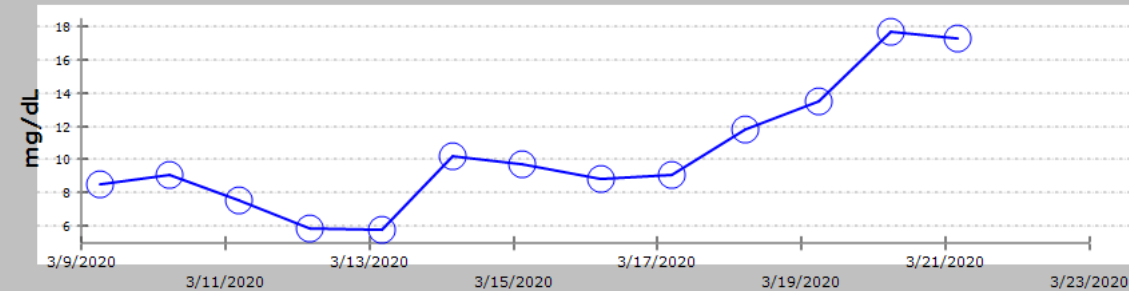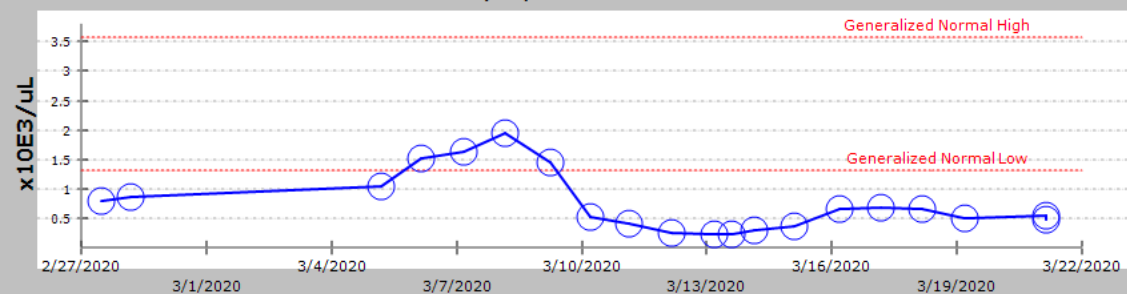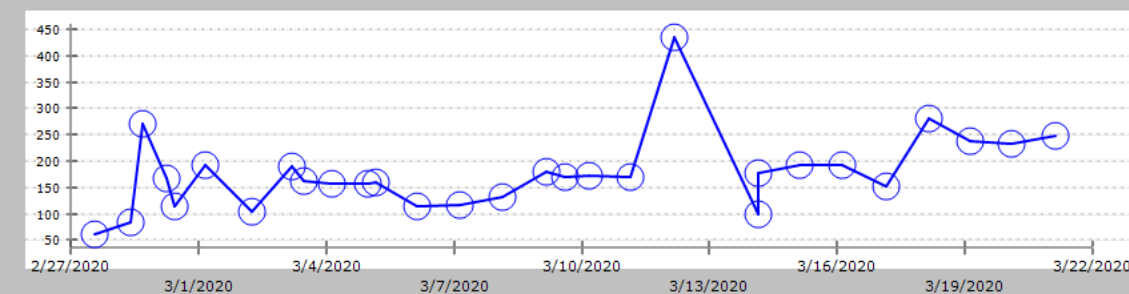
Bronchoscopy & Laboratory Results

o Day 1 Bronchoscopy with lavage - 32% Ly, 34% PMN

o Procalcitonin 0.97

o Day 9 Bronch due to suspected VAP – negative cultures. PMN 63%

Echocardiogram Results

o Day 1 – normal transthoracic echocardiogram

o Day 4 – limited TTE remains normal

o Day 9 – LVEF 30% with global dysfunction

Evergreen ICU Summary

- >45 ICU admits

- >30 Required mechanical ventilation

- 4 Transferred for ECMO (3 were ultimately cannulated)

- 7 extubations (ages 44-84)
  - Includes 44 year old transfer for ECMO and RRT

- Duration of MV in extubated patients has been 5-13 days

- 4 required renal replacement therapy

Approach to care

- Early intubation

- Early use of proning, lung protective ventilation

- Light sedation, early PT

- Avoidance of corticosteroids, unless clear indication

- Enrollment in clinical trial for therapeutics

- Fluid restrictive approach

- Early discontinuation of antibiotics if low procalcitonin, negative cultures

- Consider early consultation for ECMO in young and sickest patients

COI Disclosures

- Chair of GUIDE Group, and

- Member of the GRADE Working Group

The views expressed in this presentation are those of the author and do not necessarily represent the opinion of the Centers for Disease Control and Prevention.

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Undesirable consequences
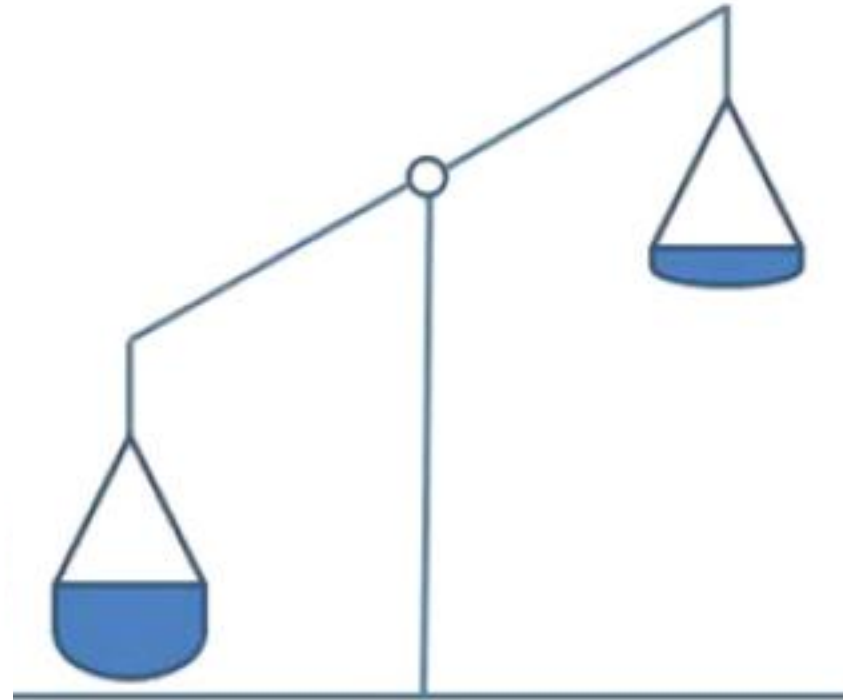
Desirable consequences

Strong Recommendation for the Intervention

Undesirable consequences

Desirable consequences

Weak Recommendation for the Intervention

Desirable consequences

Undesirable consequences
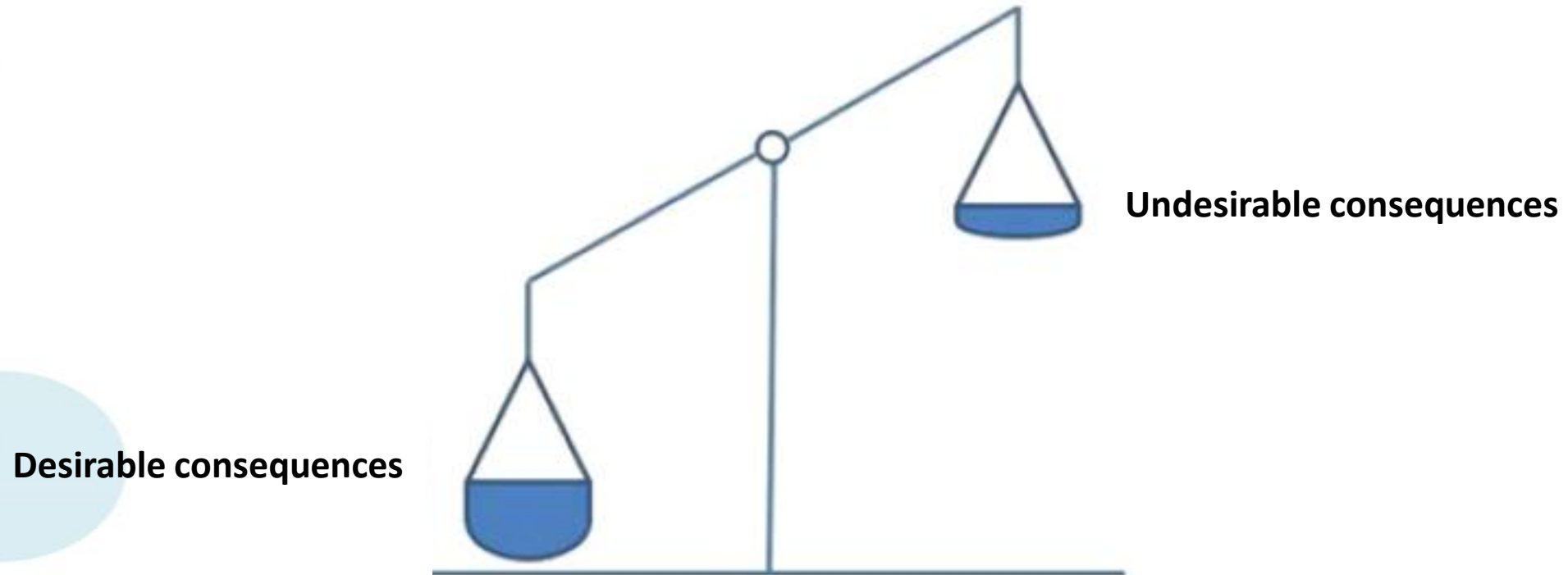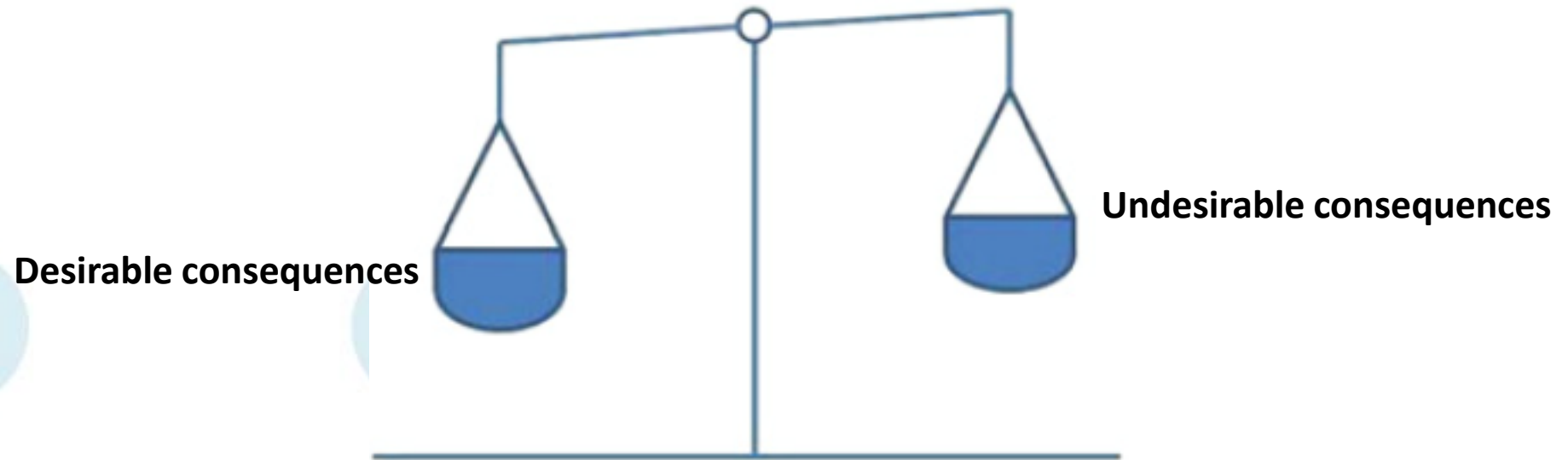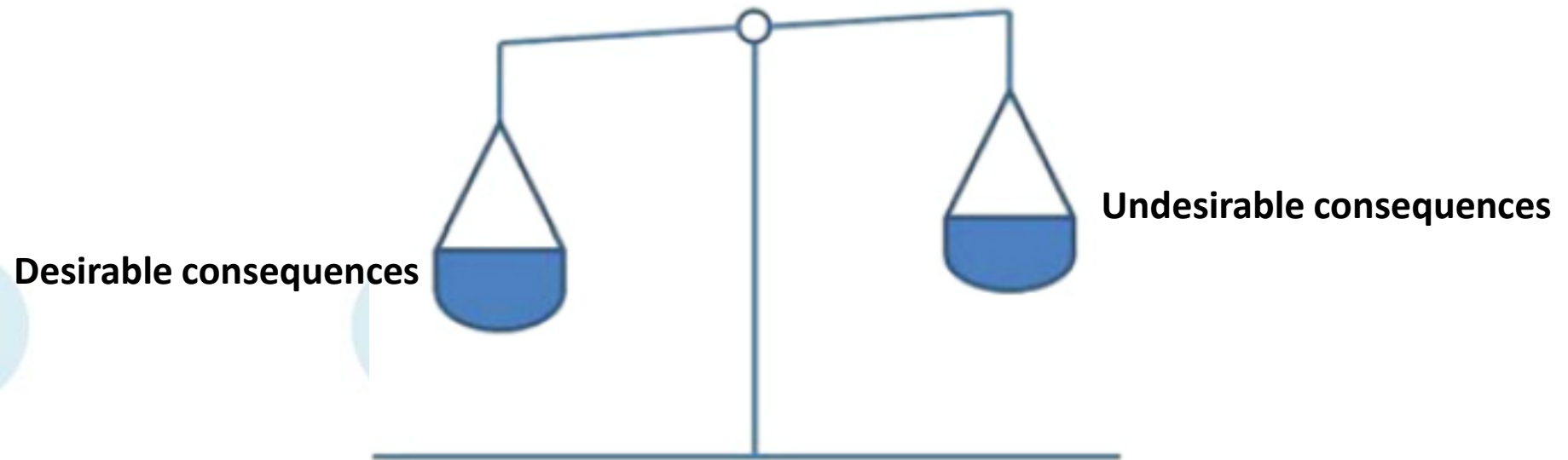
Patients

	Strong Recommendation	Weak Recommendation
For Patients	**Most** individuals in this situation would want the recommended course of action, and only a **small** proportion would not	The **majority** of individuals in this situation would want the suggested course of action, but **many** would not

Clinicians

For Clinicians	Strong Recommendation	Weak Recommendation
	Most individuals **should receive** the recommended course of action. Formal decision aids **are not likely to be needed** to help individuals make decisions consistent with their values and preferences	Different choices are likely to be appropriate for different patients Therapy should be tailored to the individual patient's circumstances, such as patients' or family's values and preferences

Policymakers

	Strong Recommendation	Weak Recommendation
For Policymakers	Can be adapted as policy in most situations, including for use as performance indicators	Policies will likely be variable

Infection control

- Aerosol generating procedure vs not
- Negative pressure room vs regular room
- Surgical masks vs respirator masks

Aerosol Generating Procedures

Procedure	Studies	Estimate
Intubation	4	OR 6.6 (2.3, 18.9)
Manipulation of BiPAP mask	1	OR 6.2 (2.2, 18.1)
CPR	1	OR 4.5 (1.5, 13.8)
Tracheostomy	1	OR 4.2 (1.5, 11.5)
Non-Invasive Ventilation	2	OR 3.1 (1.4, 6.8)
Manual Ventilation	1	OR 2.8 (1.3, 6.4)

Infection Control

- For healthcare workers performing **aerosol generating procedures** on patients with COVID-19 in the ICU, we **recommend** using **fitted respirator masks (N95 respirators, FFP2, or equivalent)**, as compared to surgical/medical masks, in addition to other personal protective equipment.

*FFP3 respirators are more commonly used in many parts of the world

Infection Control

1. Usual care for non-ventilated COVID-19 patients, or
2. Performing **non-AGP** on MV (closed circuit) patients with COVID-19

We **suggest** using surgical/medical masks, as compared to respirator masks, in addition to other personal protective equipment.

Laboratory Confirmed Influenza Infection

| | N95 | | Face Mask | | | | | Weight | Weight |
Study	Events	Total	Events	Total	Odds Ratio	OR	95%-CI	(fixed)	(random)
Loeb 2009	48	221	50	225		0.97	[0.62; 1.52]	30.9%	30.9%
MacIntyre 2011	2	475	3	246		0.34	[0.06; 2.06]	1.9%	1.9%
MacIntyre 2013	3	665	1	347		1.57	[0.16; 15.13]	1.2%	1.2%
Radonovich 2019	92	1112	85	1181		1.16	[0.86; 1.58]	66.0%	66.0%
Fixed effect model		**2473**		**1999**		**1.08**	**[0.84; 1.38]**	**100.0%**	--
Random effects model						**1.08**	**[0.84; 1.38]**	--	**100.0%**

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.55$

0.1 0.5 1 2 10

Laboratory Confirmed Respiratory Infection

Study	N95 Events	N95 Total	Face Mask Events	Face Mask Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Loeb 2009	70	221	70	225		1.03	[0.69; 1.53]	16.2%	16.2%
MacIntyre 2011	7	475	7	246		0.51	[0.18; 1.47]	2.3%	2.3%
MacIntyre 2013	18	665	12	347		0.78	[0.37; 1.63]	4.7%	4.7%
Radonovich 2019	300	1112	330	1181		0.95	[0.79; 1.14]	76.8%	76.8%
Fixed effect model		2473		1999		0.94	[0.80; 1.11]	100.0%	--
Random effects model						0.94	[0.80; 1.11]	--	100.0%

Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.63$

influenza-like illness

Study	N95 Events	N95 Total	Face Mask Events	Face Mask Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Loeb 2009	2	221	9	225		0.22	[0.05; 1.03]	4.7%	6.4%
MacIntyre 2011	2	475	2	246		0.52	[0.07; 3.68]	2.9%	4.0%
MacIntyre 2013	5	665	2	347		1.31	[0.25; 6.77]	4.1%	5.7%
Radonovich 2019	57	1112	73	1181		0.82	[0.57; 1.17]	88.2%	84.0%
Fixed effect model		2473		1999		0.78	[0.55; 1.08]	100.0%	--
Random effects model						0.76	[0.51; 1.13]	--	100.0%

Heterogeneity: $I^2 = 7\%$, $\tau^2 = 0.0153$, $p = 0.36$

Oxygen Targets
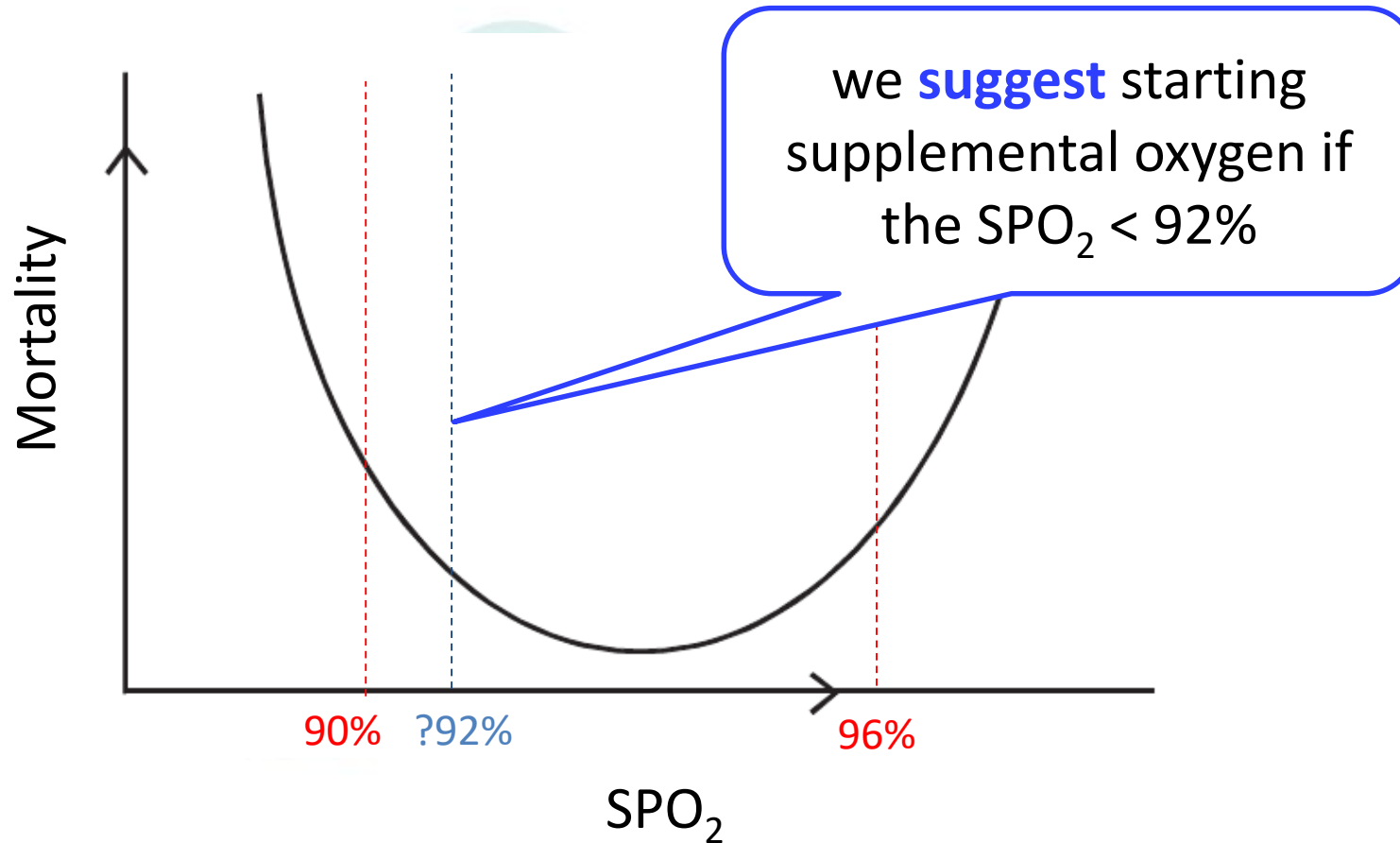
Oxygen Targets
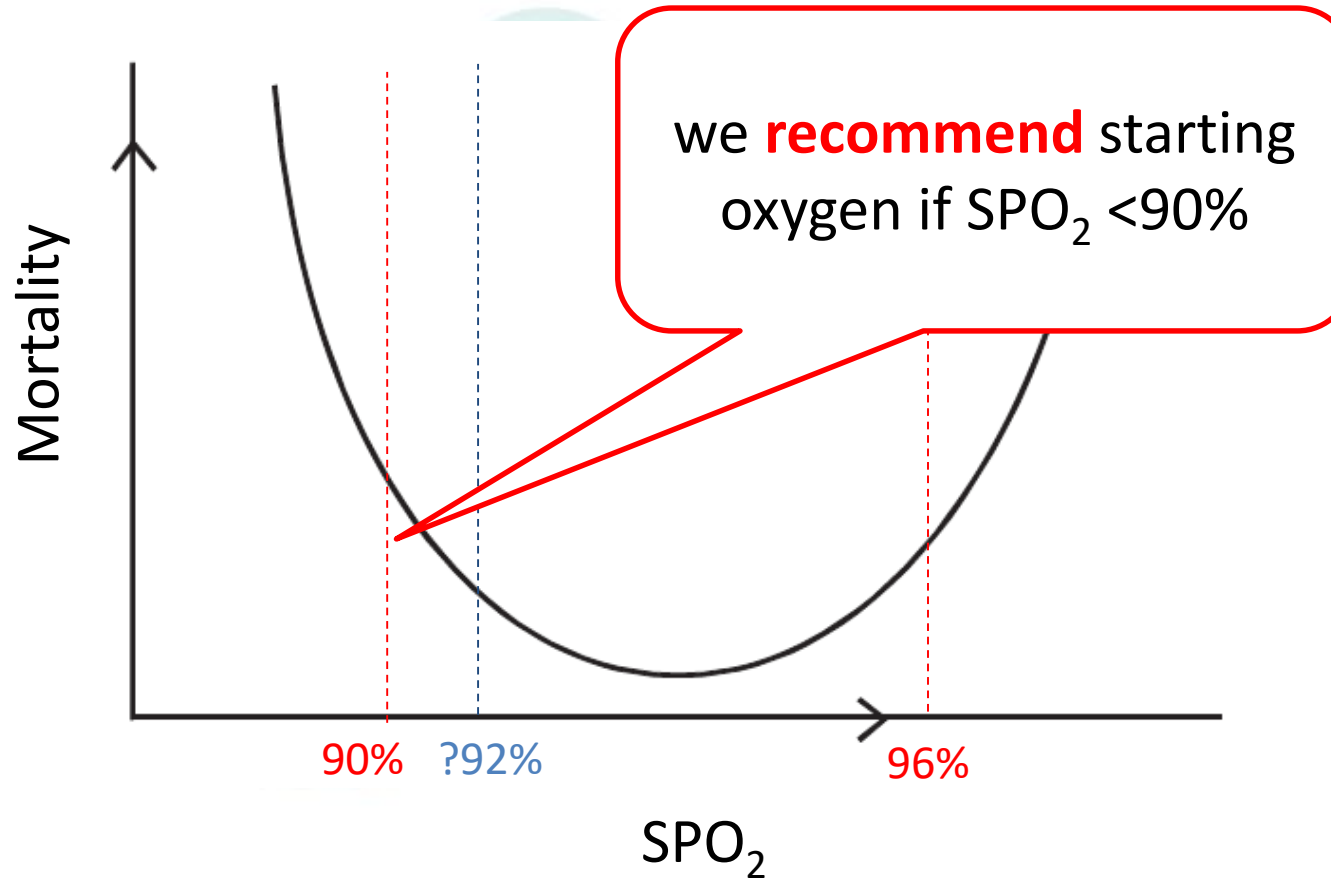
SPO$_2$ and Mortality
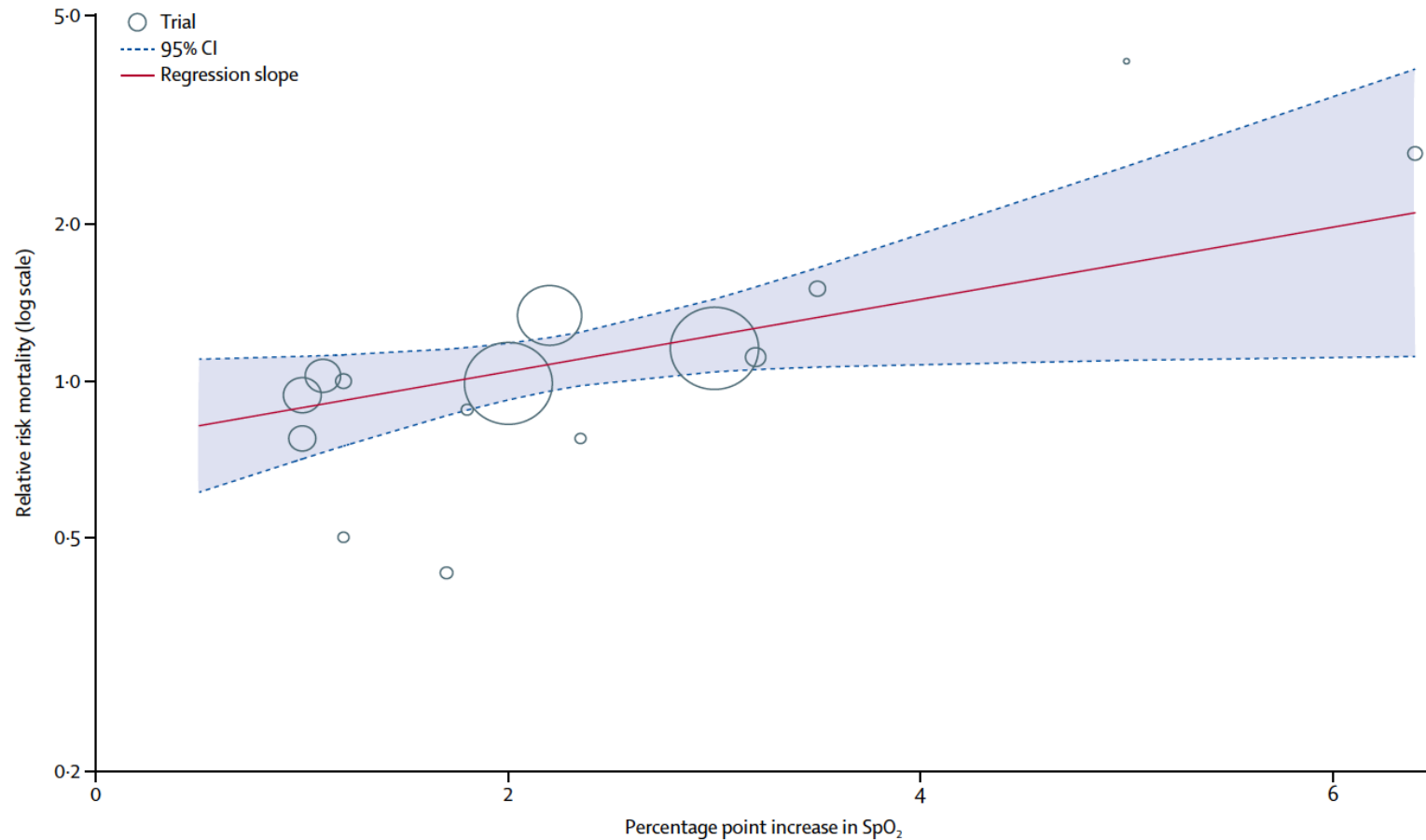
Hypoxemia

- For adults with COVID-19 and **acute hypoxemic respiratory failure** despite conventional oxygen therapy, we **suggest** **using** HFNC over conventional oxygen therapy.

Hypoxemia

- For adults with COVID-19 and **acute hypoxemic respiratory failure**, we **suggest** using HFNC over NIPPV.

Hypoxemia

- For adults with COVID-19 and **acute hypoxemic respiratory failure**, if HFNC is not available and no emergent indication for endotracheal intubation; we **suggest** a trial of NIPPV with close monitoring and short interval assessment for worsening of respiratory failure.

We were not able to make a recommendation regarding the use of helmet NIPPV compared to mask NIPPV, it is an option, but we are not certain about its safety or efficacy for COVID-19 patients.

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Endotracheal Intubation

- For healthcare workers performing **endotracheal intubation** on patients with COVID-19, we **recommend** endotracheal intubation is performed by healthcare worker experienced with airway management, to minimize the number of attempts and risk of transmission.

Endotracheal Intubation

- For healthcare workers performing **endotracheal intubation** on patients with COVID-19, we **suggest** using video guided laryngoscopy, over direct laryngoscopy, if available.

Do it:
Endotracheal intubation

Do it:
Expert in airway to intubate

Do it:
Use N-95/FFP-2 or equivalent and other PPE/infection control precautions

Do it:
Minimize staff in the room

Consider: ⚠ if available
Video- laryngoscope

COVID-19 with hypoxia

↓

Yes ⇠---- Indication for endotracheal intubation?

No ↓

Tolerating supplemental oxygen? ⟶ Yes

No ↓

Consider: ⚠ HFNC ⟶ Tolerating HFNC

Not tolerating HFNC | or HFNC is not available

↓

Yes ⇠---- Indication for endotracheal intubation? ⇠-------

No ↓

Consider: ⚠ a trial of NIPPV
✓**Do it:** Monitor closely at short intervals
⛔**Do not:** Delay intubation if worsening
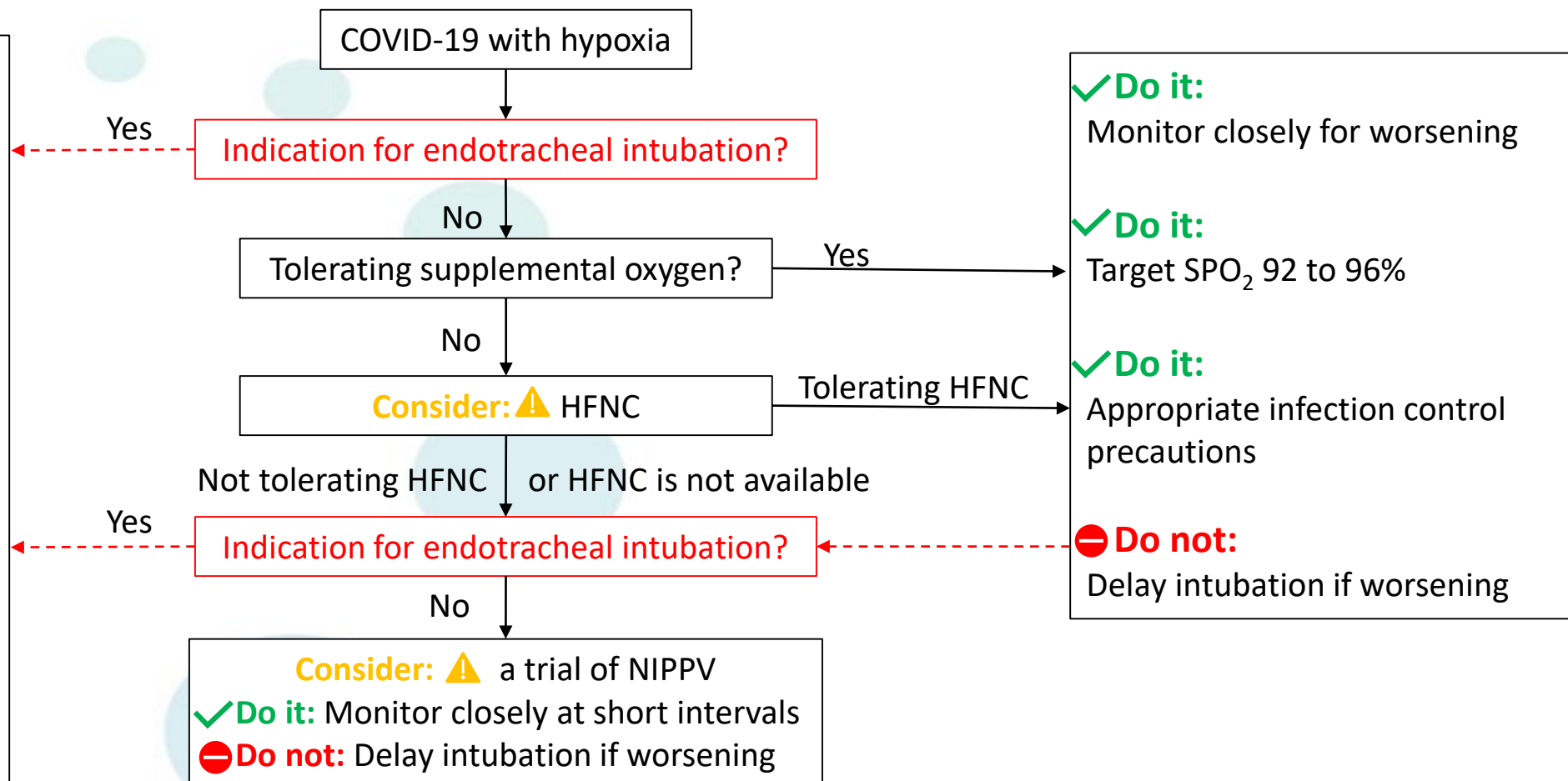
Do it:
Monitor closely for worsening

Do it:
Target SPO$_2$ 92 to 96%

Do it:
Appropriate infection control precautions

⛔**Do not:**
Delay intubation if worsening

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Acute Respiratory Distress Syndrome

We **recommend** using low Vt (4-8 mL/kg) and
Targeting Pplat <30 cmH$_2$O
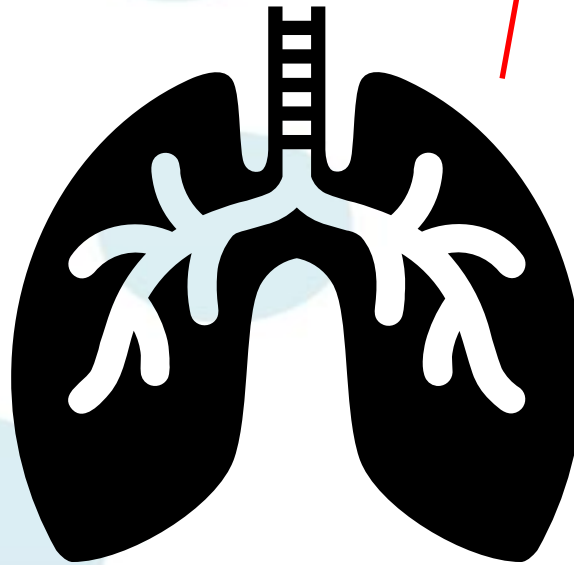
ARDS

We **recommend** using low Vt (4-8 mL/kg) and
Targeting Pplat <30 cmH$_2$O

we **suggest** using a higher PEEP strategy

Mod-Severe
ARDS

We **recommend** using low Vt (4-8 mL/kg) and
Targeting Pplat <30 cmH$_2$O

we **suggest** using a higher PEEP strategy

we **suggest** using a conservative, over a liberal, fluid strategy.

Mod-Severe ARDS

Prone Ventilation

- For mechanically ventilated adults with COVID-19 and **moderate to severe ARDS**, we **suggest** prone ventilation for **12 to 16 hours**, over no prone ventilation.

Neuromuscular Blocking Agents (NMBA)?

NMBA

- For MV adults with COVID-19 and **moderate to severe ARDS**, we **suggest** using as needed intermittent boluses of NMBA, over a continuous NMBA infusion, to facilitate protective lung ventilation.

NMBA

- In case of persistent ventilator dyssynchrony, requirement of ongoing deep sedation, prone ventilation, or persistently high P_{plt}; we **suggest** using a continuous NMBA infusion for up to 48 hours.

Corticosteroids

Steroids in ARDS - Mortality Outcome

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M–H, Random, 95% CI
Liu 2012	2	12	7	14	3.0%	0.33 [0.08, 1.31]
Meduri 2007	15	63	12	28	12.6%	0.56 [0.30, 1.03]
Rezk 2013	0	18	3	9	0.7%	0.08 [0.00, 1.32]
Steinberg 2006	26	89	26	91	19.7%	1.02 [0.65, 1.62]
Tongyoo 2016	34	98	40	99	26.8%	0.86 [0.60, 1.23]
Villar 2020	33	139	50	138	26.0%	0.66 [0.45, 0.95]
Zhao 2014	9	24	13	29	11.3%	0.84 [0.43, 1.61]
Total (95% CI)		443		408	100.0%	0.75 [0.59, 0.95]
Total events	119		151			

Heterogeneity: Tau² = 0.02; Chi² = 7.69, df = 6 (P = 0.26); I² = 22%
Test for overall effect: Z = 2.36 (P = 0.02)

Steroids in ARDS - DMV

Steroids for <mark>Viral ARDS</mark> - Mortality

All observational studies
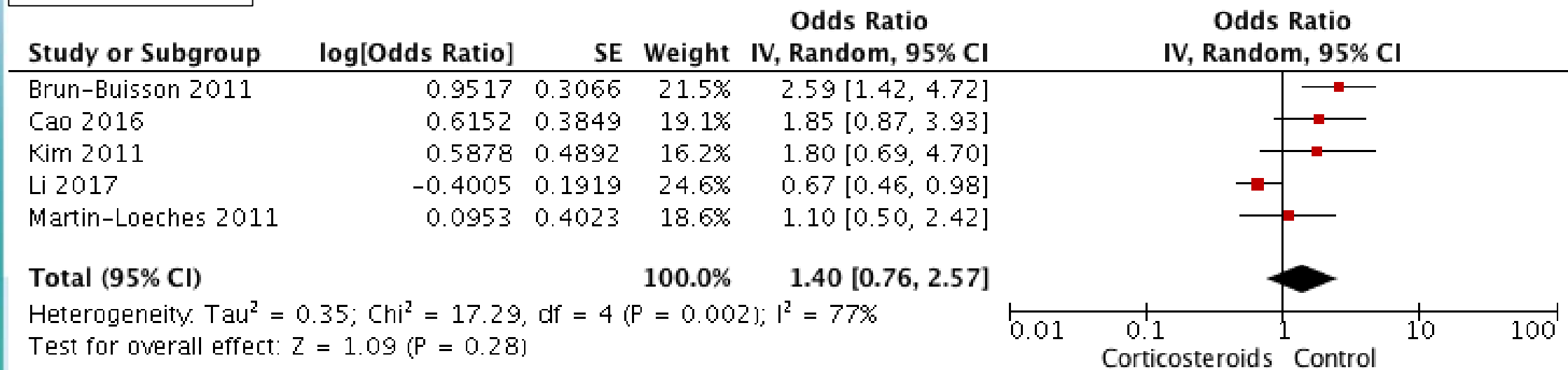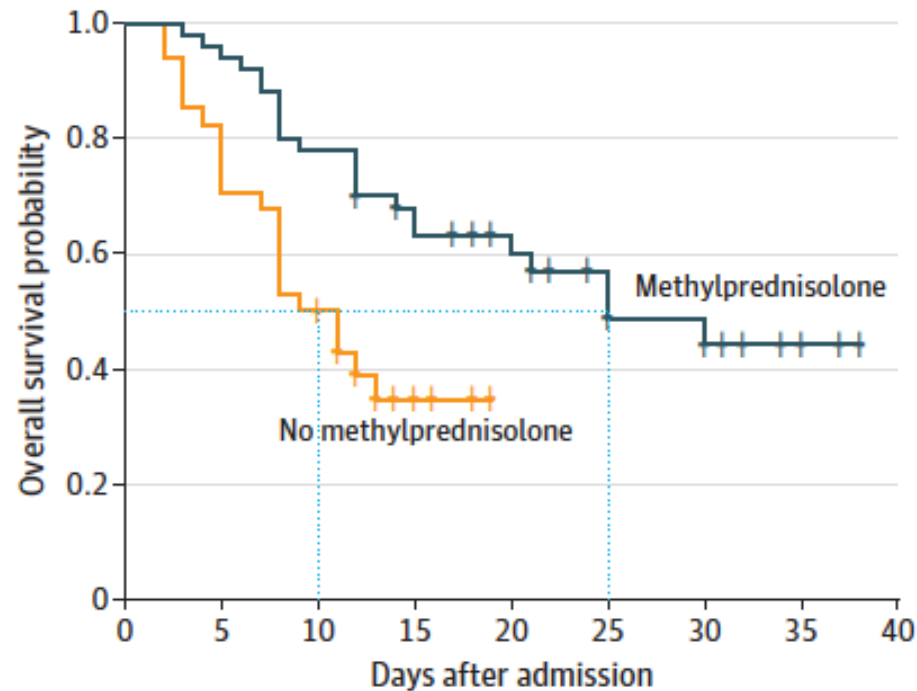
Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
Brun-Buisson 2011	0.9517	0.3066	21.5%	2.59 [1.42, 4.72]	
Cao 2016	0.6152	0.3849	19.1%	1.85 [0.87, 3.93]	
Kim 2011	0.5878	0.4892	16.2%	1.80 [0.69, 4.70]	
Li 2017	−0.4005	0.1919	24.6%	0.67 [0.46, 0.98]	
Martin-Loeches 2011	0.0953	0.4023	18.6%	1.10 [0.50, 2.42]	
Total (95% CI)			100.0%	1.40 [0.76, 2.57]	

Heterogeneity: Tau² = 0.35; Chi² = 17.29, df = 4 (P = 0.002); I² = 77%
Test for overall effect: Z = 1.09 (P = 0.28)

Corticosteroids   Control

Direct Evidence

Retrospective study
N=201
with COVID-19 pneumonia

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Corticosteroids

- For mechanically ventilated adults with COVID-19 **and ARDS**, we **suggest** using systemic corticosteroids over not using corticosteroids.

- **Remark:** The majority of our panel support a weak recommendation (i.e. suggestion) to use steroids in the sickest patients with COVID-19 and ARDS. However, because of the very low quality evidence, some experts on the panel preferred not to issue a recommendation until higher quality direct-evidence is available.

Steroids for <mark>Viral Pneumonia</mark> - Mortality

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
1.1.1 Influenza					
Delaney 2016	0.6152	0.2561	8.8%	1.85 [1.12, 3.06]	
Delgado-Rodriguez 2012	1.2149	0.4518	7.6%	3.37 [1.39, 8.17]	
Jung 2011	1.1282	0.4187	7.8%	3.09 [1.36, 7.02]	
Kim 2011	0.7885	0.3872	8.0%	2.20 [1.03, 4.70]	
Liem 2009	1.4134	0.6543	6.2%	4.11 [1.14, 14.82]	
Linko 2011	1.1939	0.9628	4.4%	3.30 [0.50, 21.78]	
Tsai 2020	1.6134	0.3786	8.0%	5.02 [2.39, 10.54]	
Xi 2010	1.3002	0.6685	6.1%	3.67 [0.99, 13.60]	
Subtotal (95% CI)			56.7%	**2.76 [2.06, 3.69]**	

Heterogeneity: Tau² = 0.00; Chi² = 6.13, df = 7 (P = 0.52); I² = 0%
Test for overall effect: Z = 6.81 (P < 0.00001)

1.1.2 Corona/SARS/MERS					
Alfaraj 2019	1.3455	0.3457	8.2%	3.84 [1.95, 7.56]	
Alghamdi 2016	1.0716	1.5877	2.3%	2.92 [0.13, 65.59]	
Arabi 2017	−0.4943	0.1904	9.1%	0.61 [0.42, 0.89]	
Auyeung 2005	3.0301	1.4122	2.7%	20.70 [1.30, 329.63]	
Chen 2006	−2.4889	1.2617	3.2%	0.08 [0.01, 0.98]	
Yam 2007 HC	0	0.5657	6.8%	1.00 [0.33, 3.03]	
Yam 2007 MP	−1.3863	0.6495	6.2%	0.25 [0.07, 0.89]	
Yam 2007 P	−1.772	0.885	4.8%	0.17 [0.03, 0.96]	
Subtotal (95% CI)			43.3%	**0.83 [0.32, 2.17]**	

Heterogeneity: Tau² = 1.24; Chi² = 38.12, df = 7 (P < 0.00001); I² = 82%
Test for overall effect: Z = 0.37 (P = 0.71)

Total (95% CI)			100.0%	**1.76 [1.03, 3.03]**	

Heterogeneity: Tau² = 0.80; Chi² = 75.61, df = 15 (P < 0.00001); I² = 80%
Test for overall effect: Z = 2.06 (P = 0.04)
Test for subgroup differences: Chi² = 5.48, df = 1 (P = 0.02), I² = 81.8%

All observational studies

Corticosteroids   Control

Corticosteroids

- For mechanically ventilated adults with COVID-19 and respiratory failure (**without ARDS**), we **suggest against** the routine use of systemic corticosteroids

Surviving Sepsis Campaign

COVID-19 with mild ARDS	COVID-19 with Mod to Severe ARDS	Rescue/Adjunctive therapy

COVID-19 with mild ARDS

✓ **Do:**
Vt 4-8 ml/kg and P_{plat} <30 cm H_2O

✓ **Do:**
Investigate for bacterial infection

✓ **Do:**
Target SPO2 92% - 96%

⚠ **CONSIDER:**
Conservative fluid strategy

⚠ **CONSIDER:**
Empiric antibiotics

❓ **Uncertain:**
Systemic corticosteroids

COVID-19 with Mod to Severe ARDS

⚠ **CONSIDER:**
Higher PEEP

⚠ **CONSIDER:**
NMBA boluses to facilitate ventilation targets

⚠ **CONSIDER:** *if PEEP responsive*
Traditional Recruitment maneuvers

⚠ **CONSIDER:**
Prone ventilation 12 -16 h

⚠ **CONSIDER :** *if proning, high P_{plt}, asynchrony*
NMBA infusion for 24 h

⛔ **Don't do:**
Staircase Recruitment maneuvers

⚠ **CONSIDER:**
Short course of systemic corticosteroids

Rescue/Adjunctive therapy

⚠ **CONSIDER :** *if proning, high P_{plt}, asynchrony*
NMBA infusion for 24 h

⚠ **CONSIDER:**
Prone ventilation 12 -16 h

⚠ **CONSIDER :** *STOP if no quick response*
A trial of inhaled Nitric Oxide

⚠ **CONSIDER :** *follow local criteria for ECMO*
V-V ECMO or referral to ECMO center

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Antibiotics

- For mechanically ventilated patients with COVID-19 and respiratory failure, we **suggest** using empiric antimicrobials/antibacterial agents, compared to no antimicrobials.

- **Remark**: if the treating team initiates empiric antimicrobials, they should assess for de-escalation daily, and re-evaluate the duration of therapy and spectrum of coverage based on the microbiology results and the patient's clinical status.

Therapy

For critically ill adults with COVID-19, we **suggest against** the routine use of standard intravenous immunoglobulins.

For critically ill adults with COVID-19, we **suggest against** the routine use of convalescent plasma.

For critically ill adults with COVID-19, we **suggest against** the routine use of lopinavir/ritonavir.

Therapy

- Insufficient evidence to support recommendations for:
  - Antivirals
  - Hydroxychloroquine
  - Immunomodulators

Hemodynamic Support

- For the **acute resuscitation** of adults with **COVID-19 and shock**, we **suggest** using a conservative, over a liberal fluid strategy

Outcomes	№ of participants (studies)	Relative effect (95% CI)	Certainty of the evidence
All-cause Mortality	637 (9 RCTs)	RR 0.87 (0.69–1.10)	VERY LOW
Serious Adverse Events	637 (9 RCTs)	RR 0.91 (0.78–1.05)	VERY LOW

Hemodynamic Support

- For adults with **COVID-19 and refractory shock**, we **suggest** using low-dose corticosteroid therapy ("shock-reversal"), over no corticosteroid therapy.

- Remark: typical corticosteroid regimen in septic shock is intravenous hydrocortisone 200 mg per day either as an infusion or intermittent doses.

Outcomes	№ of participants (studies)	Relative effect (95% CI)	Certainty of the evidence
Short-term Mortality (<90 days)	7297 (22 RCTs)	RR 0.96 (0.91–1.02)	MODERATE
Long-term Mortality (>90 days)	5667 (5 RCTs)	RR 0.96 (0.90–1.02)	MODERATE
Serious Adverse Events	5908 (10 RCTs)	RR 0.98 (0.90–1.08)	LOW

Special Thank You

- Guidelines panelists

- Methodologists

- SCCM and ESICM

- Colleagues around the world caring for patients

CDC COVID-19 Resources

- **Coronavirus Disease 2019 Website**
  https://www.cdc.gov/COVID19

- **Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease**
  https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

- **Information for Clinicians on Therapeutic Options for COVID-19 Patients**
  https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html

- **Healthcare Professionals: Frequently Asked Questions and Answers**
  https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html

- **Discontinuation of Transmission-Based Precautions and Disposition of Patients with COVID-19 in Healthcare Settings**
  https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html

- **What Healthcare Personnel Should Know about Caring for Patients with Confirmed or Possible COVID-19 Infection**
  https://www.cdc.gov/coronavirus/2019-ncov/hcp/caring-for-patients.html

- **Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Patients Under Investigation for COVID-19**
  https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

- **Rapid Guidelines for Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with COVID-19**
  https://www.sccm.org/getattachment/Disaster/SSC-COVID19-Critical-Care-Guidelines.pdf?lang=en-US

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  - You may also email your question to [coca@cdc.gov.](mailto:coca@cdc.gov)
- For media questions, please contact CDC Media Relations at 404-639-3286 or email media@cdc.gov.
- **For more Clinical Care information on COVID-19**
  - **Call** COVID-19 Clinical Call Center at 770-488-7100 (24 hours/day).
  - **Refer** patients to state and local health departments for COVID-19 COVID19 testing and test results.
    - Clinicians should NOT refer patients to CDC to find out where or how to get tested for COVID-19 OR to get COVID-19 test results.
  - **Visit** CDC's Coronavirus (COVID-19) website: https://www.cdc.gov/coronavirus.

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When: Soon after the live call

What: Video recording

Where:

On the COCA Call webpage at

https://emergency.cdc.gov/coca/calls/2020/callinfo_040220.asp

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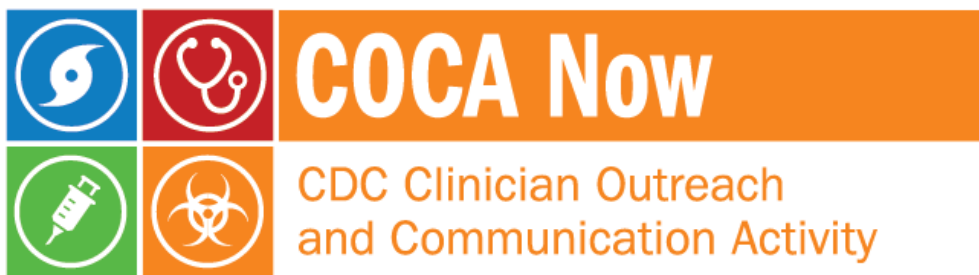
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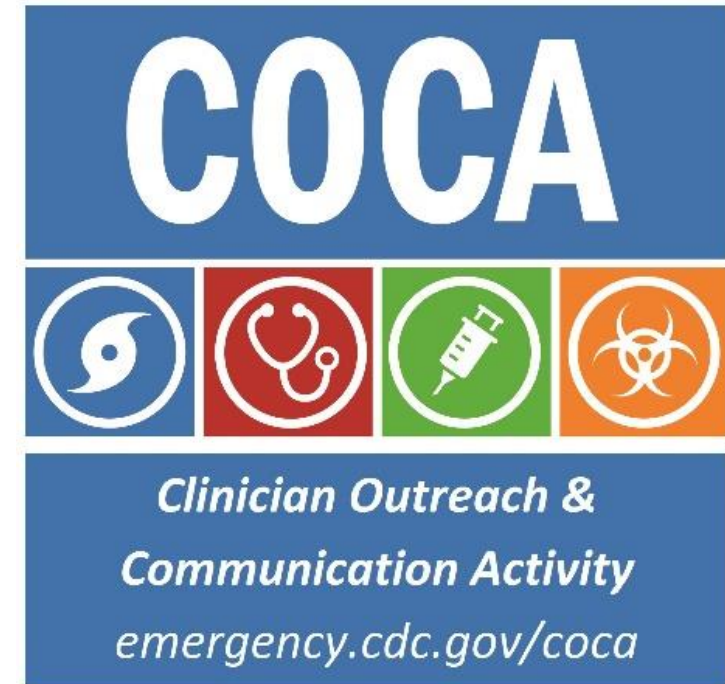
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