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.

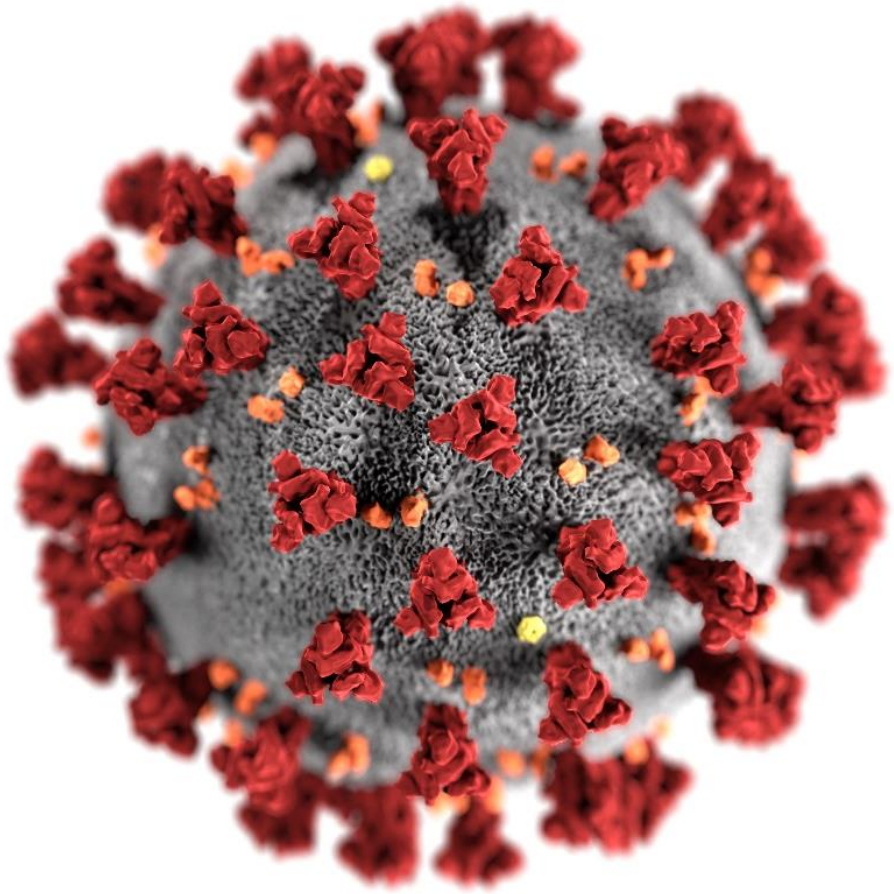
Today's Presenters

- **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

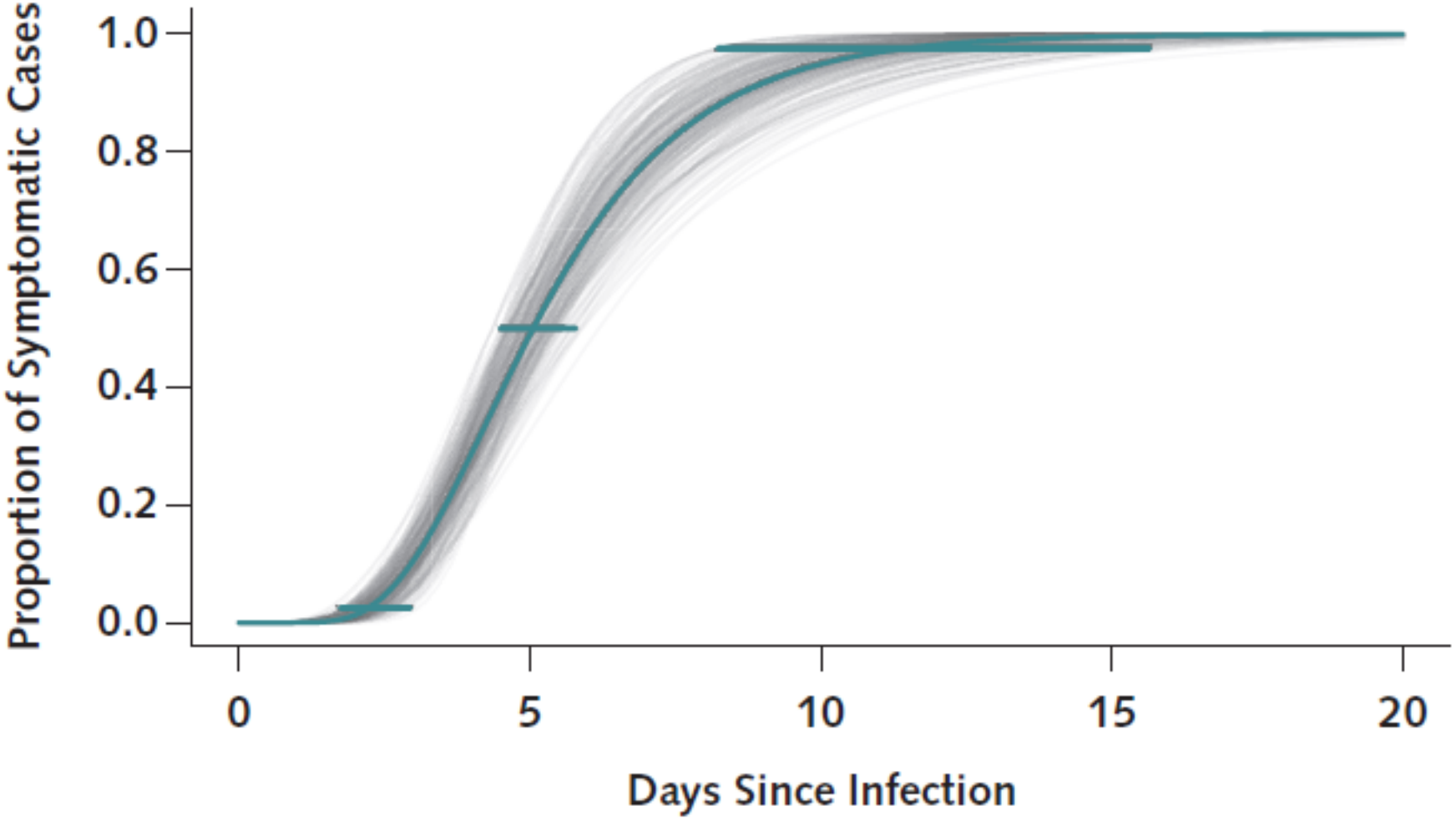
COVID-19 Overview for Clinicians



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*

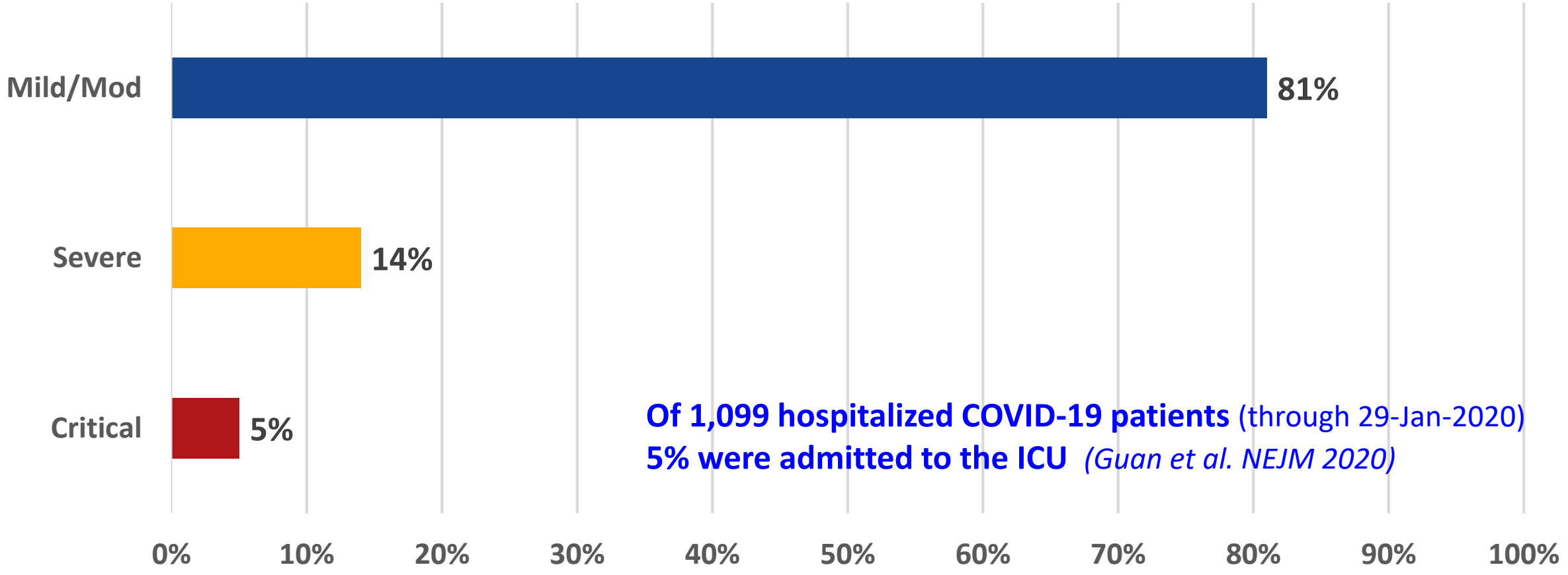
COVID-19: Wide spectrum of disease

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)



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)

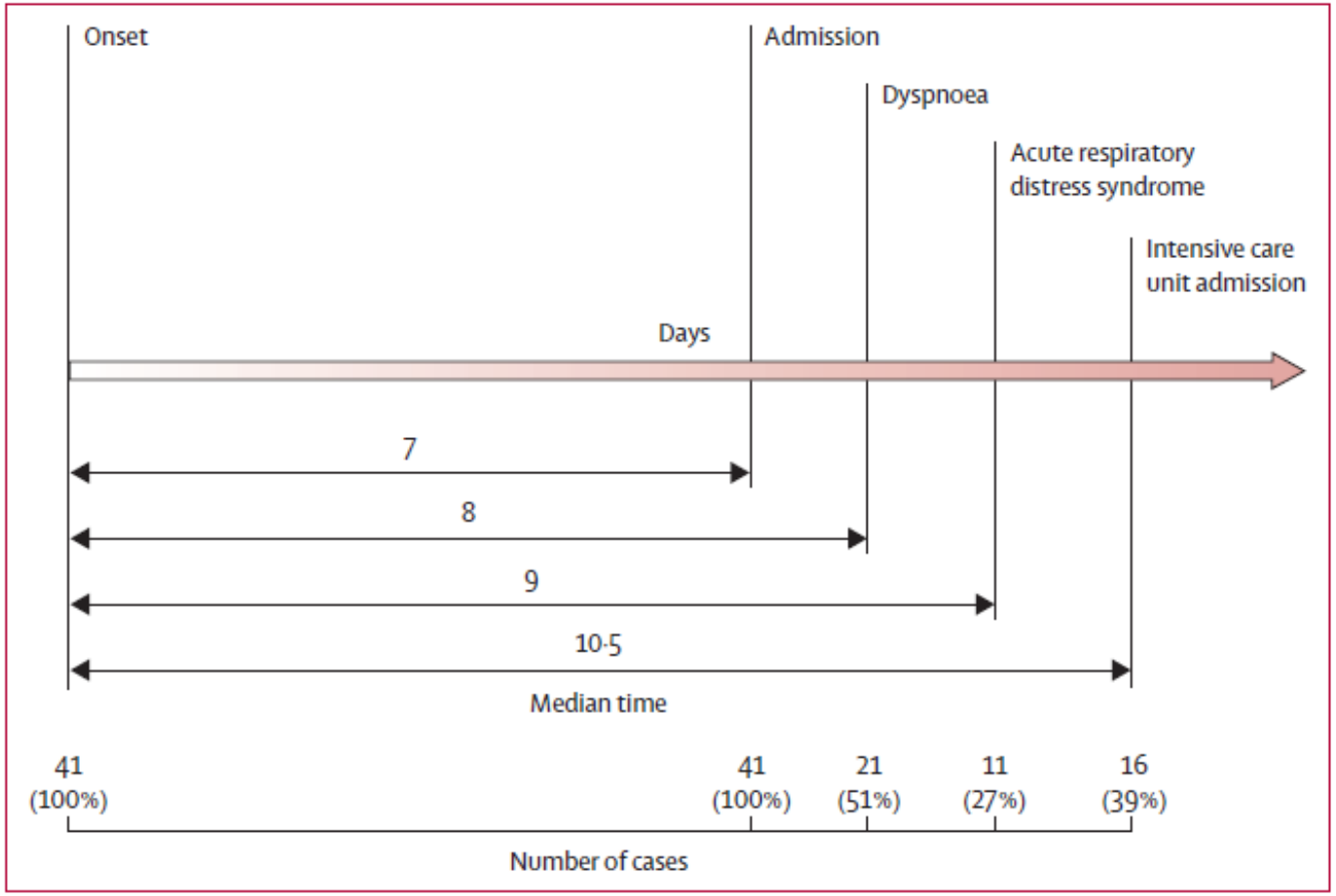
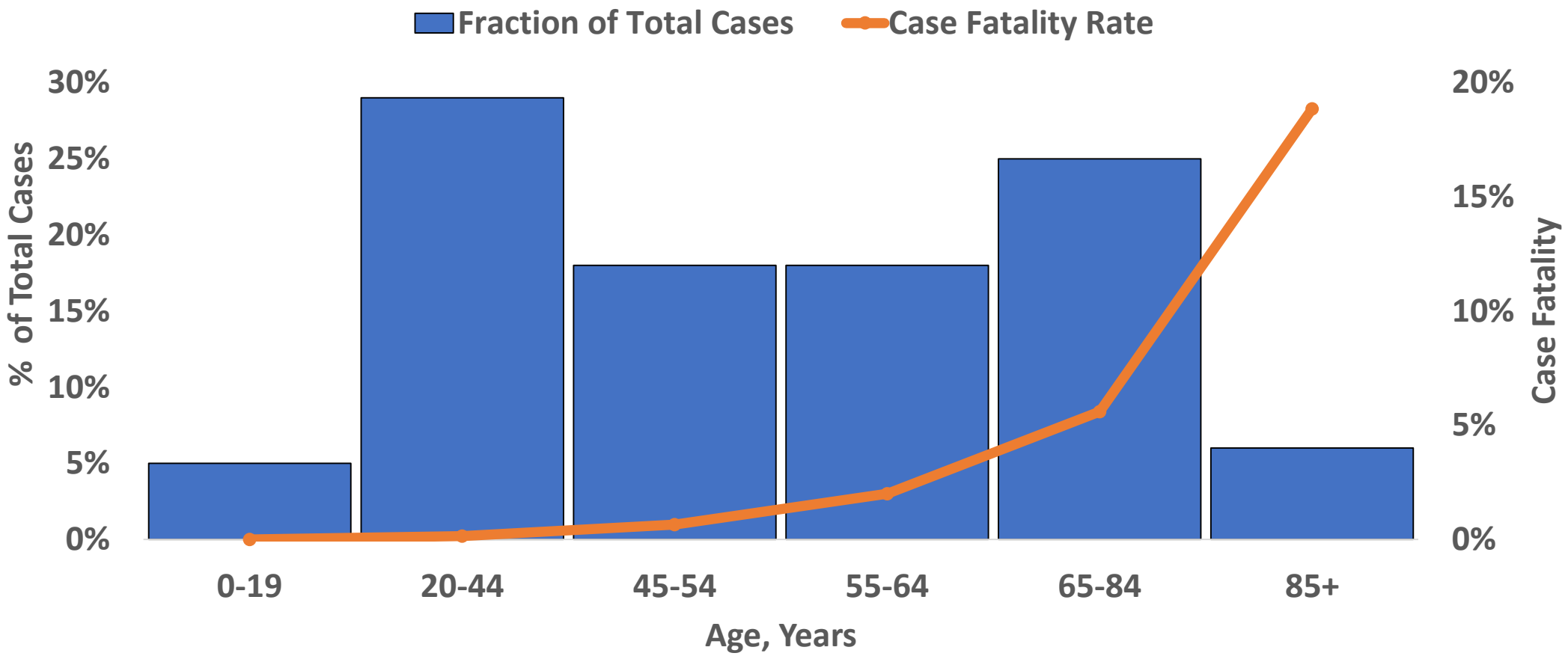


Figure 2: Timeline of 2019-nCoV cases after onset of illness

Link: *Huang Lancet 2020*

But the case-fatality is disproportionately higher among older adults

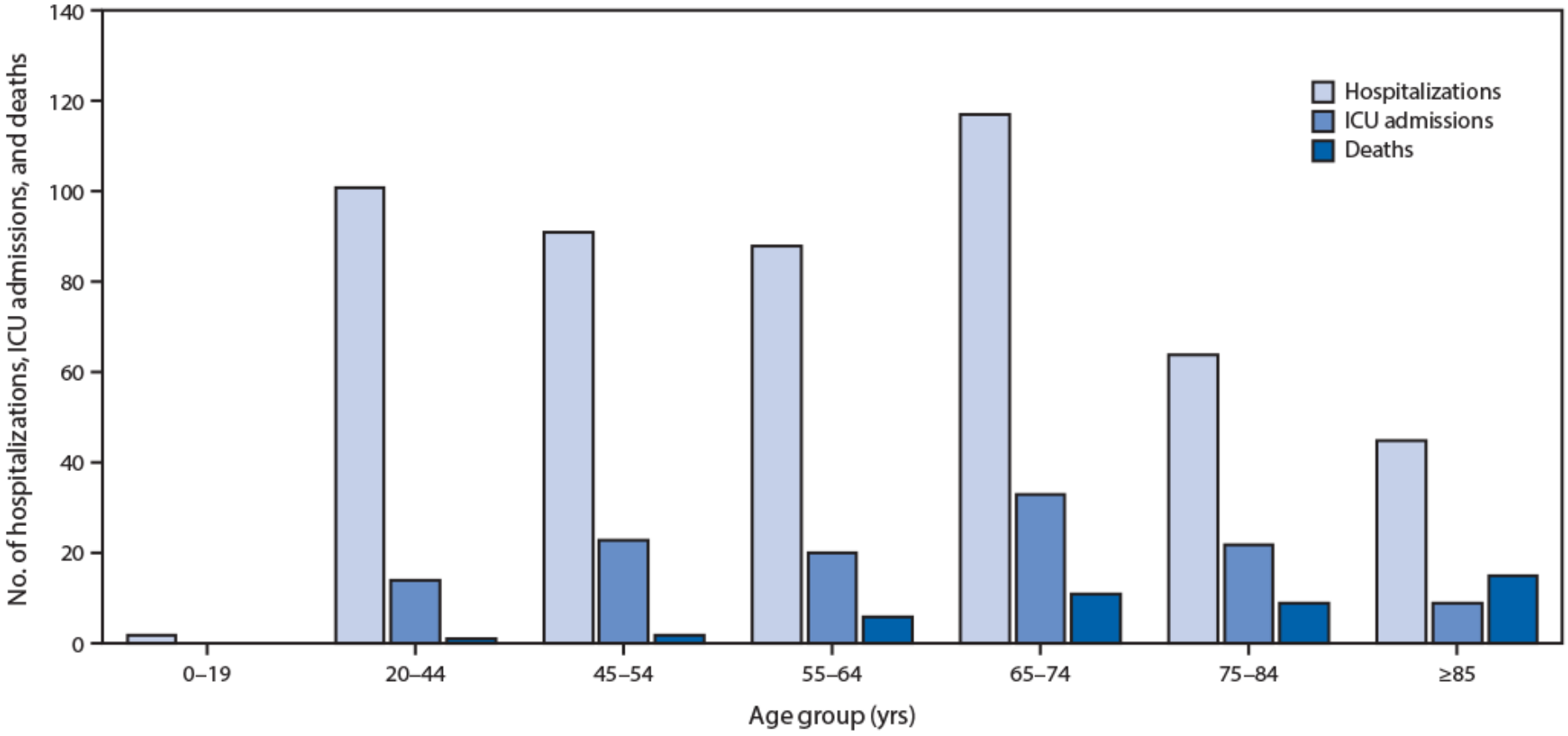
COVID-19 - United States, February 12–March 16, 2020 (N = 4,226)



Links: *MMWR 2020*

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

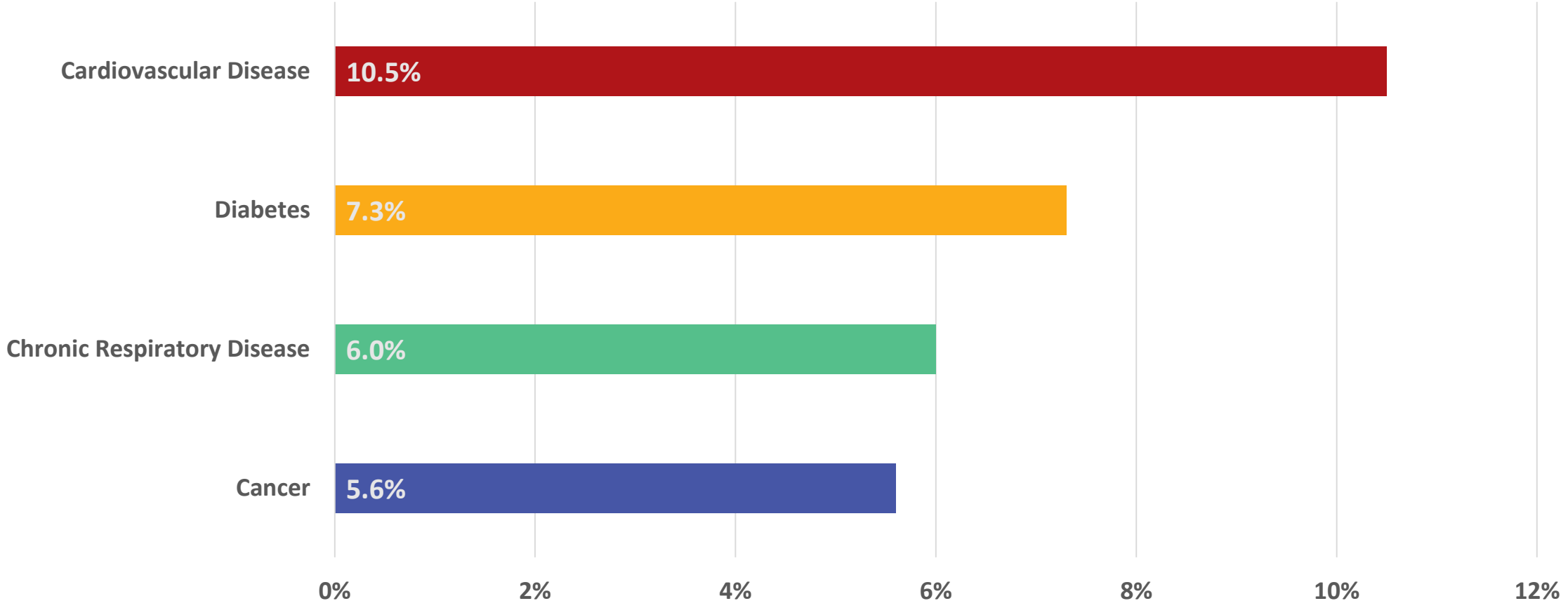
COVID-19 United States, February 12–March 16, 2020 (N = 4,226)



Links: *MMWR 2020*

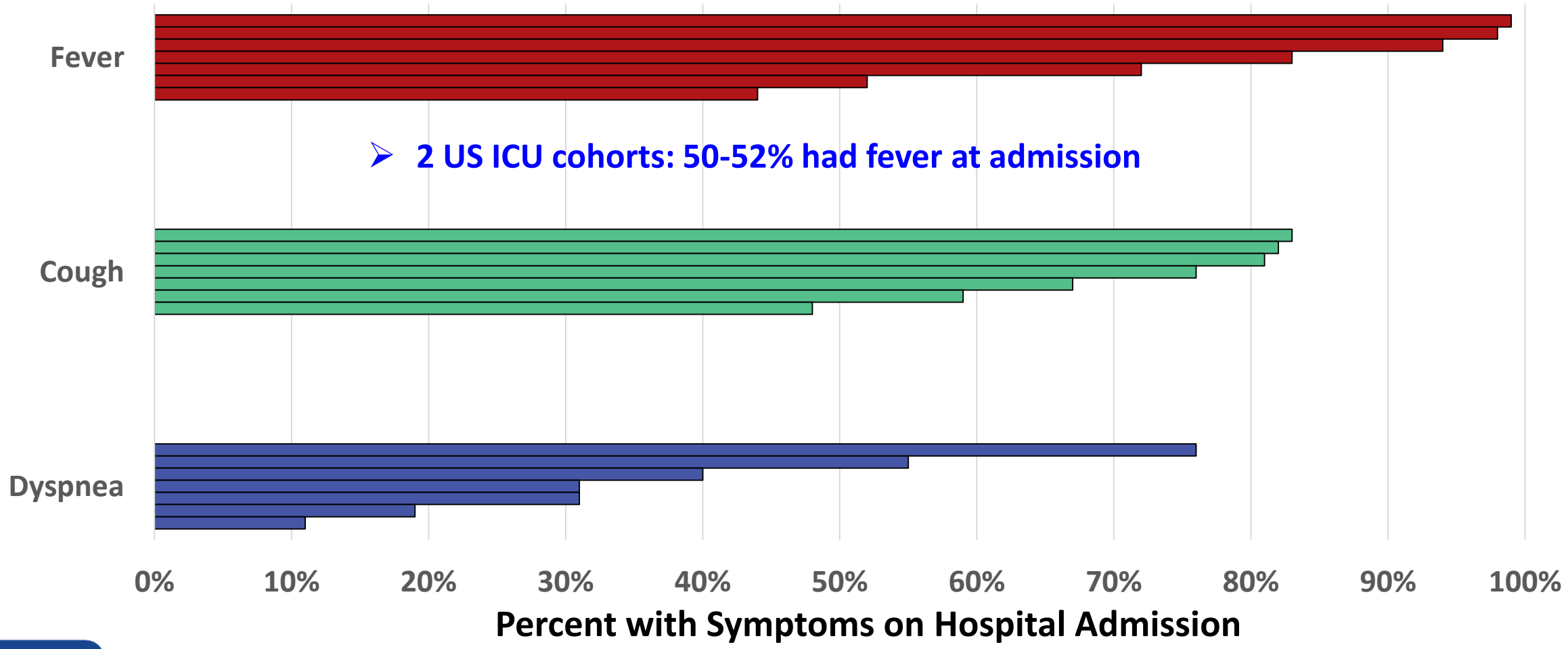
Mortality from COVID-19 is highest among persons with underlying medical conditions

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

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

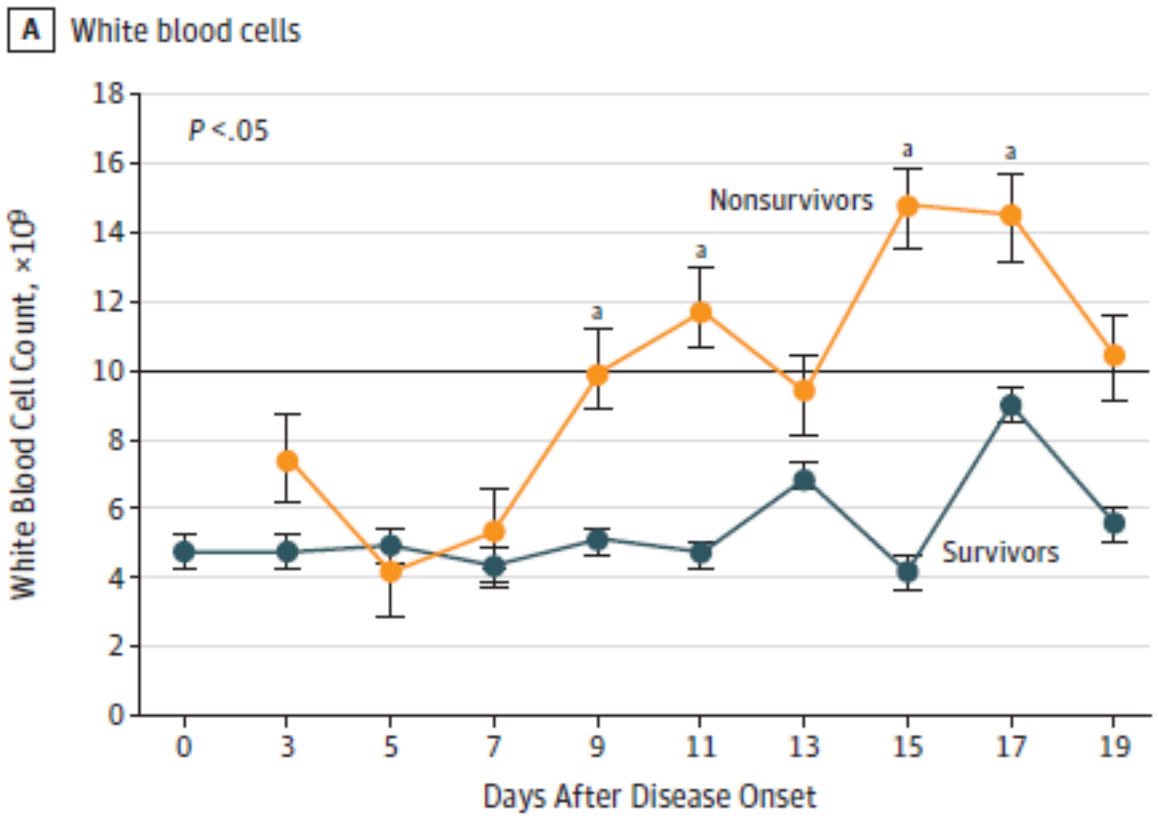
  ↑serum levels of pro-inflammatory cytokines and chemokines

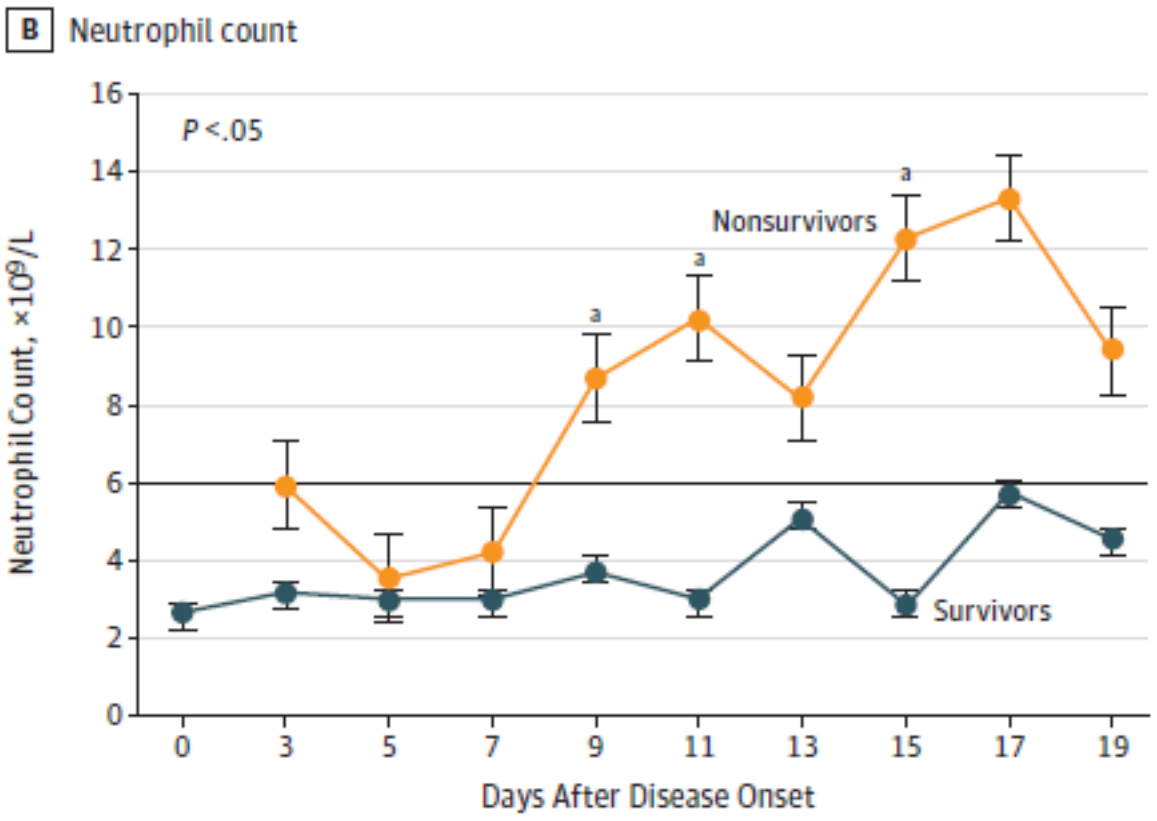
  - Evidence of immune dysregulation: Higher plasma levels of pro-inflammatory cytokines (TNFα, IL-1, IL-6) and chemokines (IL-8) in severe/critically ill patients vs less severely ill patients

- **Associated with mortality:** ↑D-dimers and lymphopenia

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

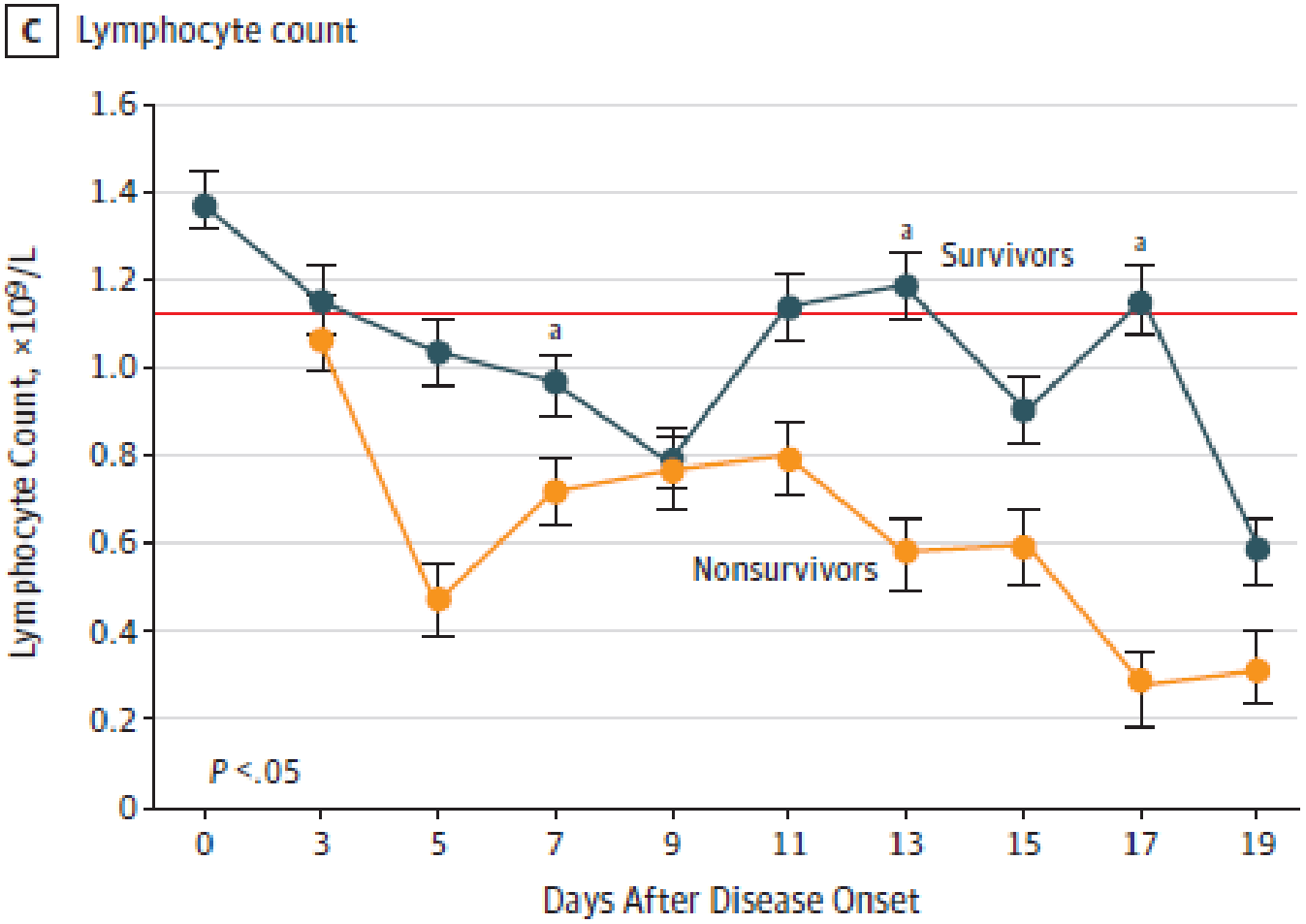
Leukocytosis, specifically neutrophilia, during hospitalization is associated with death (N = 138, China, Jan 1-28, 2020)





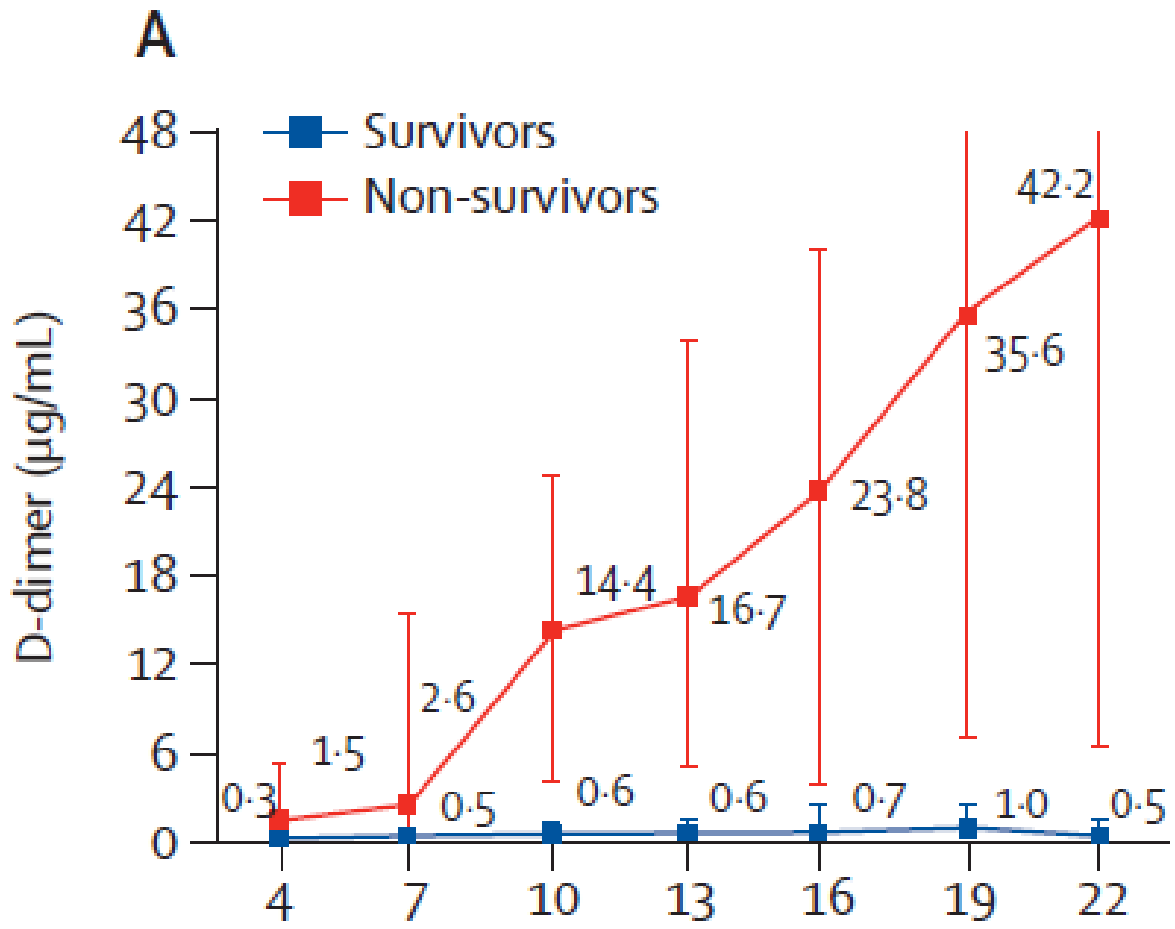
Link: *Wang JAMA 2020*

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



Link: *Wang JAMA 2020*

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



	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%)

Arentz JAMA 2020; Bhatraju NEJM 2020

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

MICHAEL BUNDESMANN, MD, FCCP

MEDICAL DIRECTOR OF RESPIRATORY THERAPY

PULMONARY AND CRITICAL CARE MEDICINE

EVERGREEN HEALTH, KIRKLAND, WA

CDC COCA CALL, APRIL 2, 2020

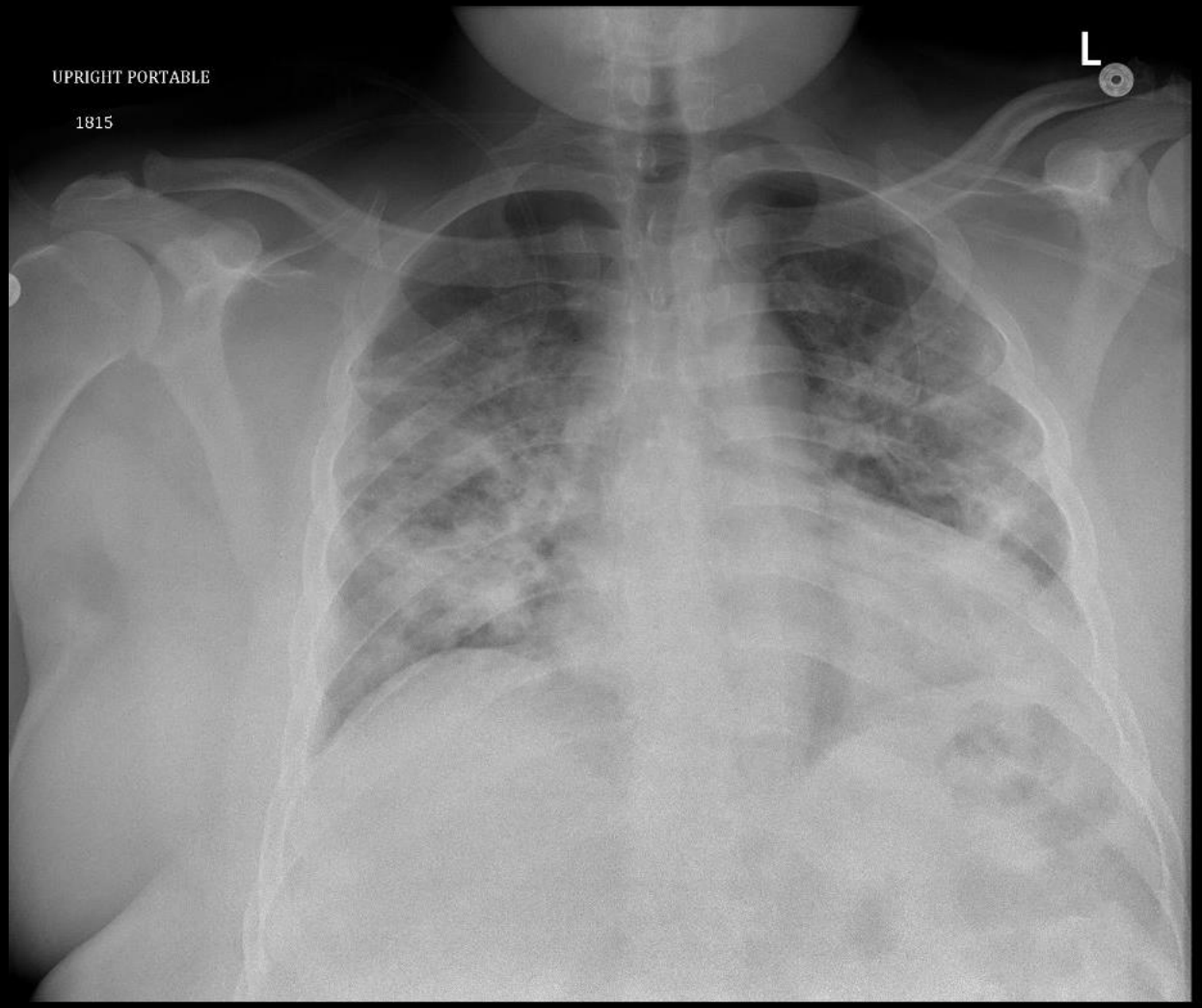
Disclaimer

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.

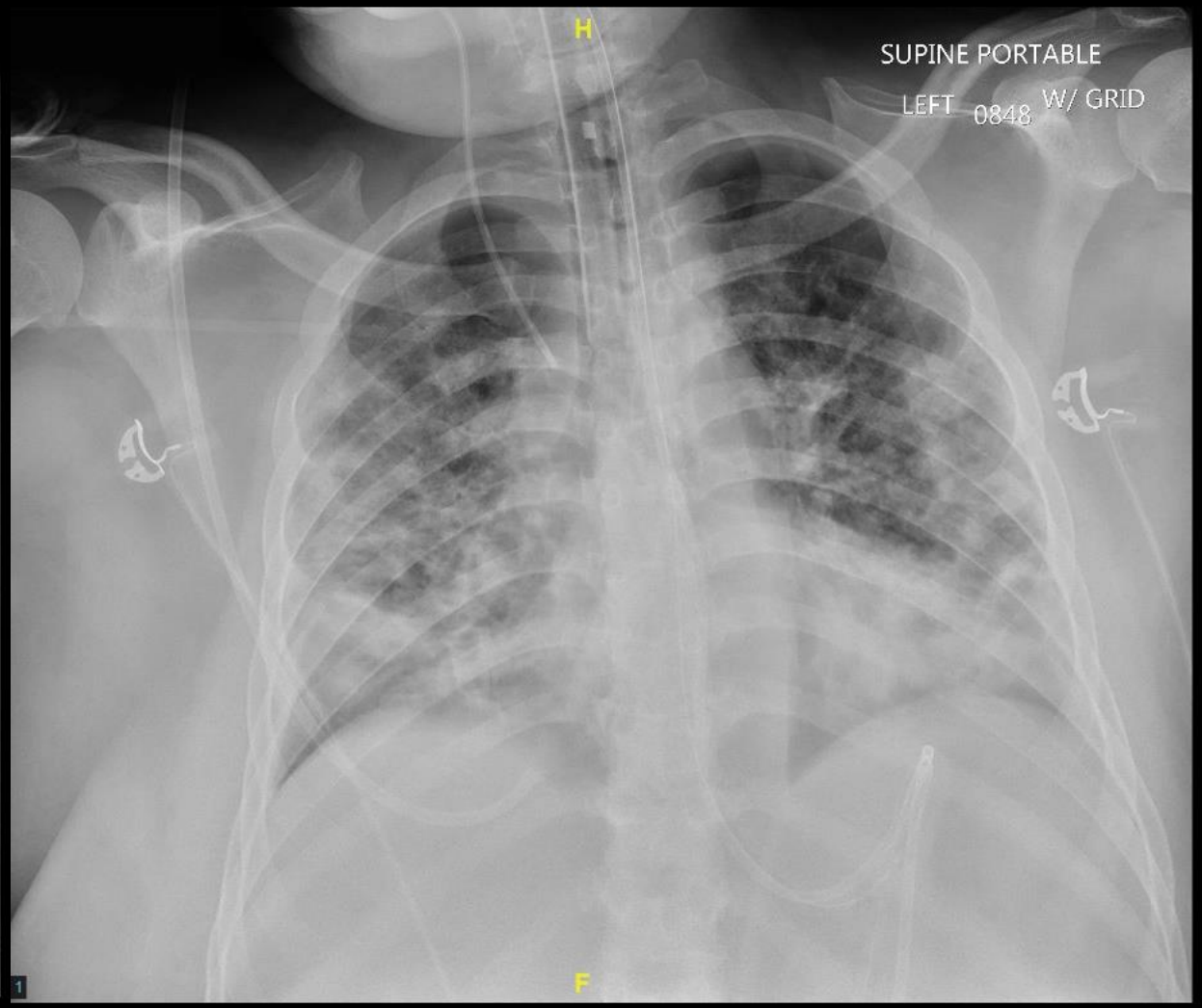
Case 1

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

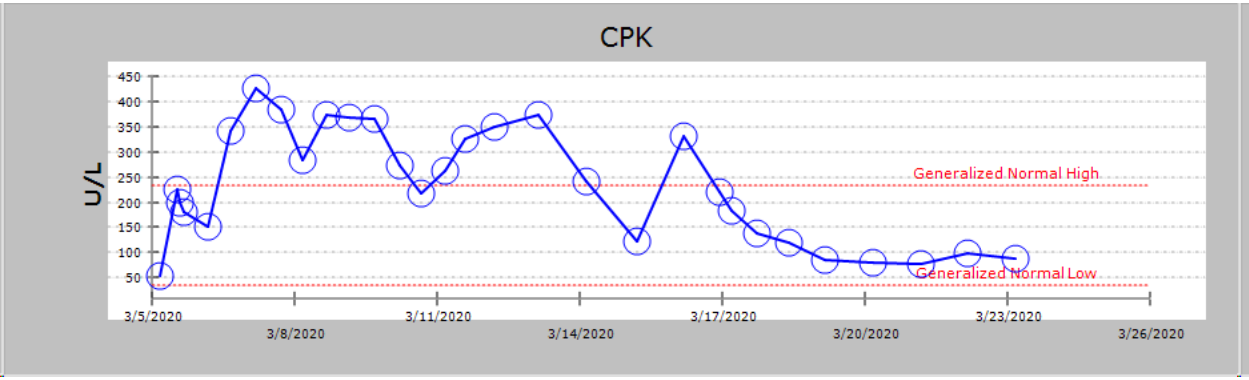
Hospital Course

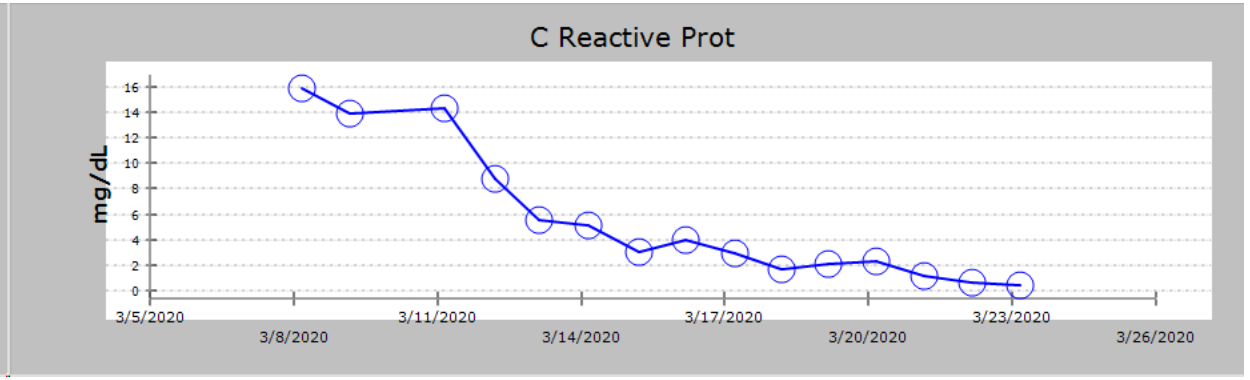
- Intubation and institution of lung protective ventilation from day 2 through day 14
- Proned days 2-13 of hospitalization
  - Inhaled epoprostenol and NMB were not given’
  - Extubated to HFNC
- Ceftriaxone and azithromycin discontinued after 7 days (no initial procalcitonin checked)
- On day 6, compassionate use Remdesivir was given for 10-day course
- On day 10, hydroxychloroquinine 400 BID, then daily x 5 days
- On day 21, weaned to room air, significant neuromuscular weakness

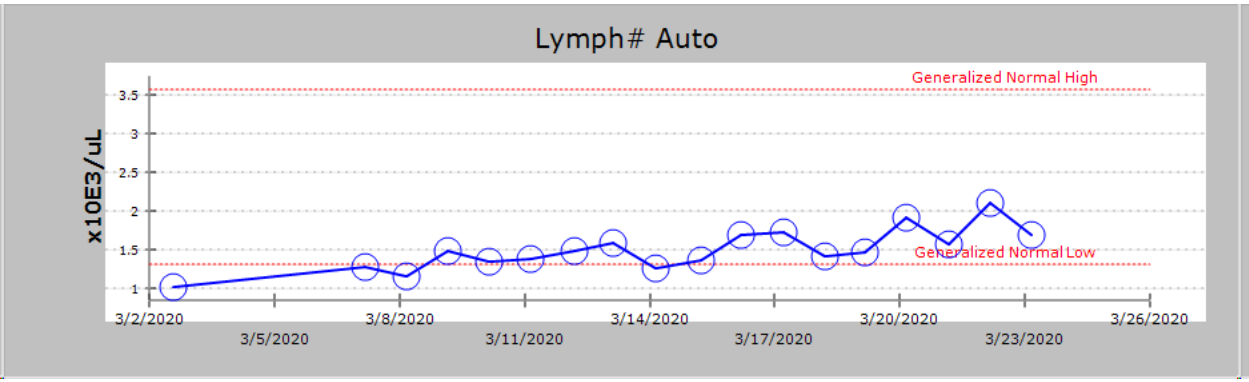
Notable Findings

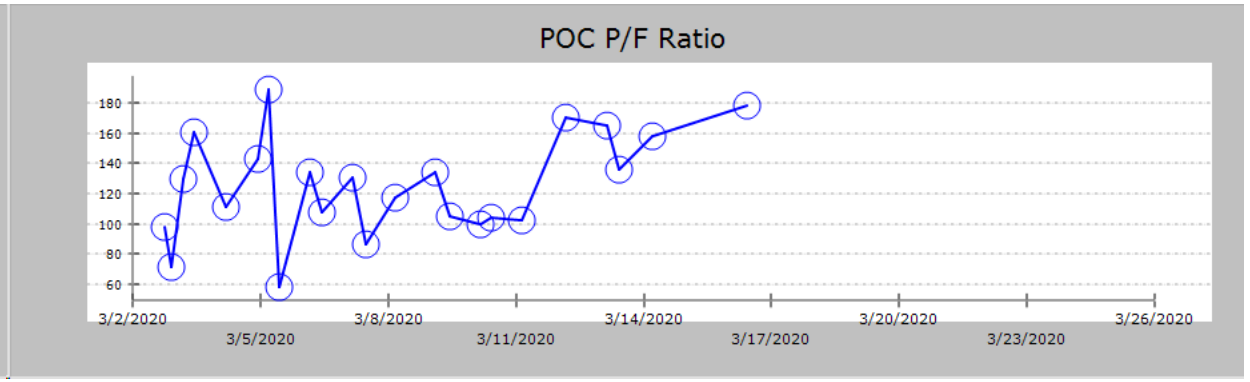
- 3/2 Respiratory pathogen panel negative
- 3/2 NP sample drawn, SARS-CoV-2 detected 3/6
- 3/2 Bronchoscopy BAL 62% Ly, 13% PMN
- Abs lymphocyte 1.0×10^3/uL
- AST/ALT < 2x ULN
- CRP 15.93 on 3/8 decreased to 1.11
- Normal NT-proBNP, TnI
- SARS-CoV-2 remains positive 3 weeks into hospitalization

Lab Trends


CPK
U/L
450
400
350
300
250
200
150
100
50
Generalized Normal High
Generalized Normal Low
3/5/2020
3/8/2020
3/11/2020
3/14/2020
3/17/2020
3/20/2020
3/23/2020
3/26/2020


C Reactive Prot
mg/dL
16
14
12
10
8
6
4
2
0
3/5/2020
3/8/2020
3/11/2020
3/14/2020
3/17/2020
3/20/2020
3/23/2020
3/26/2020


Lymph# Auto
x10E3/uL
3.5
3
2.5
2
1.5
1
Generalized Normal High
Generalized Normal Low
3/2/2020
3/5/2020
3/8/2020
3/11/2020
3/14/2020
3/17/2020
3/20/2020
3/23/2020
3/26/2020


POC P/F Ratio
180
160
140
120
100
80
60
3/2/2020
3/5/2020
3/8/2020
3/11/2020
3/14/2020
3/17/2020
3/20/2020
3/23/2020
3/26/2020

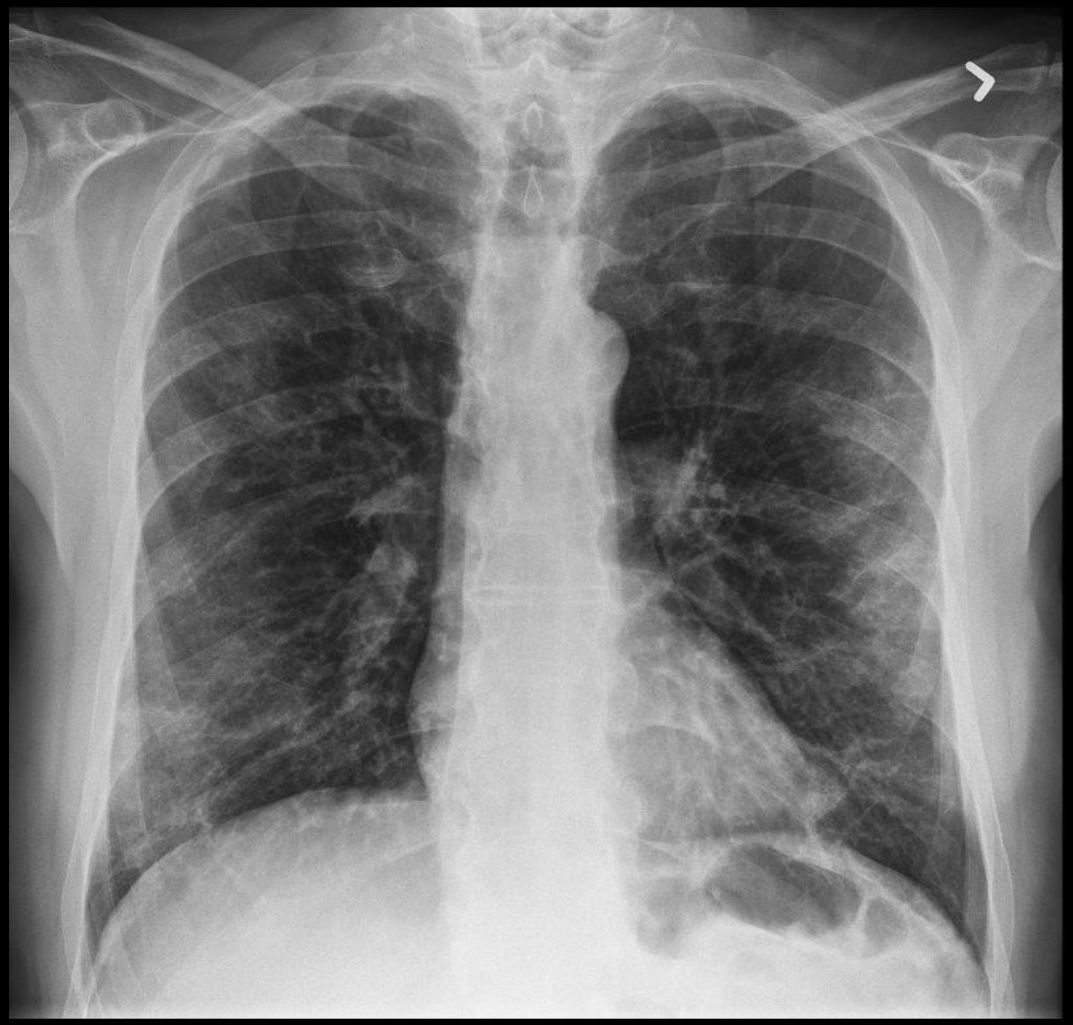
Transthoracic Echocardiogram

- Day 1 – normal LVEF, notable for estimated PASP 45. Normal RVSF. Mildly dilated RV.
- Day 10 – limited echo with estimated RVSP 65

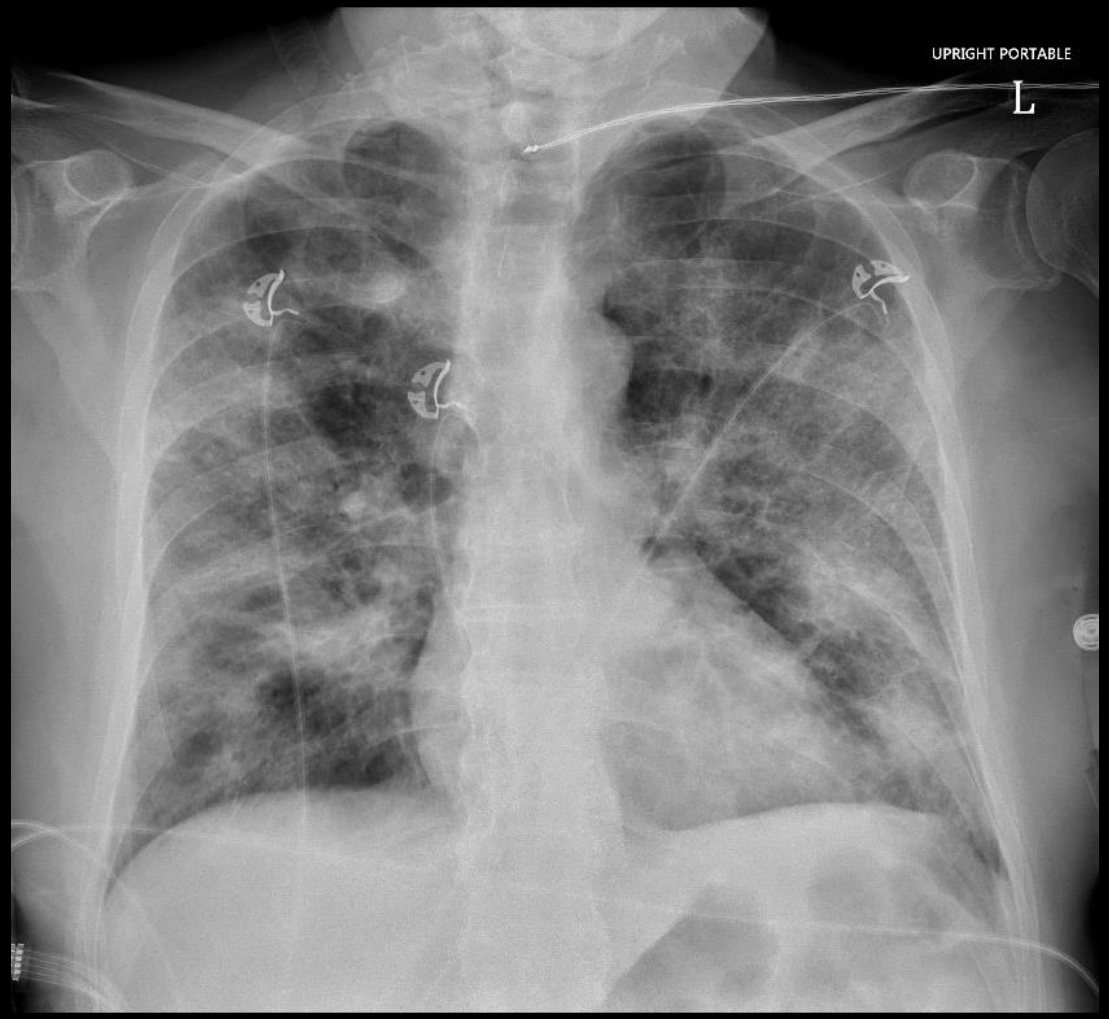
Case 2

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

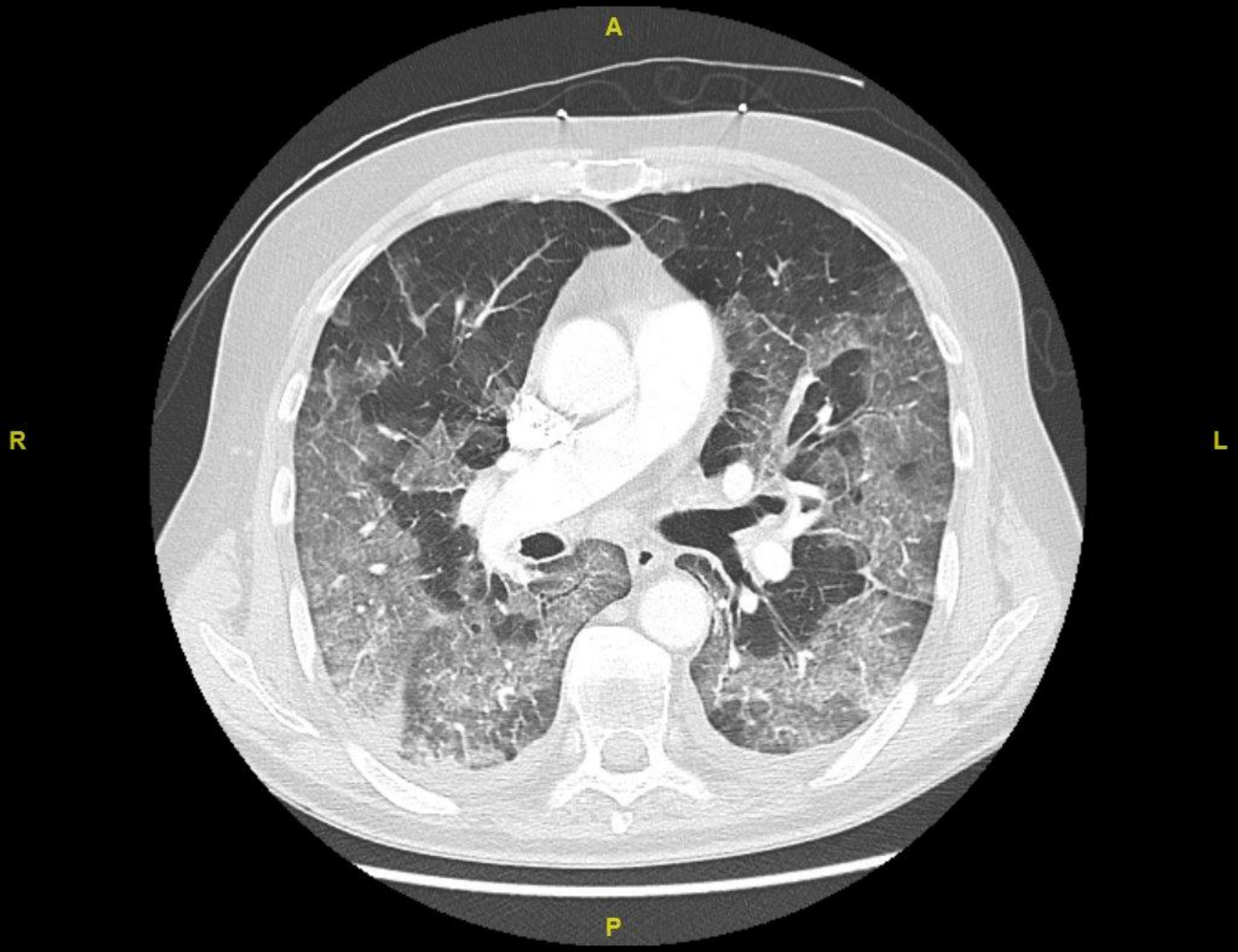
- 4 days prior to admit was seen in urgent care for 7 days of cough, fever, fatigue
- 2/27 – presents to ED with SpO2 82%. Placed on HFNC, intubated within 24 hrs
- At the time of admission, RF for COVID-19 were not identified. He was not tested for COVID-19.



4 days prior to admission



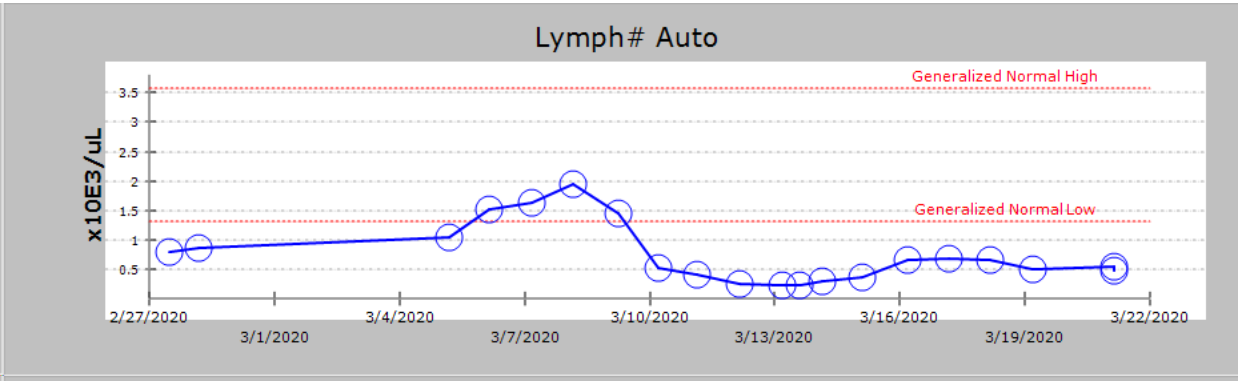
Day of admission

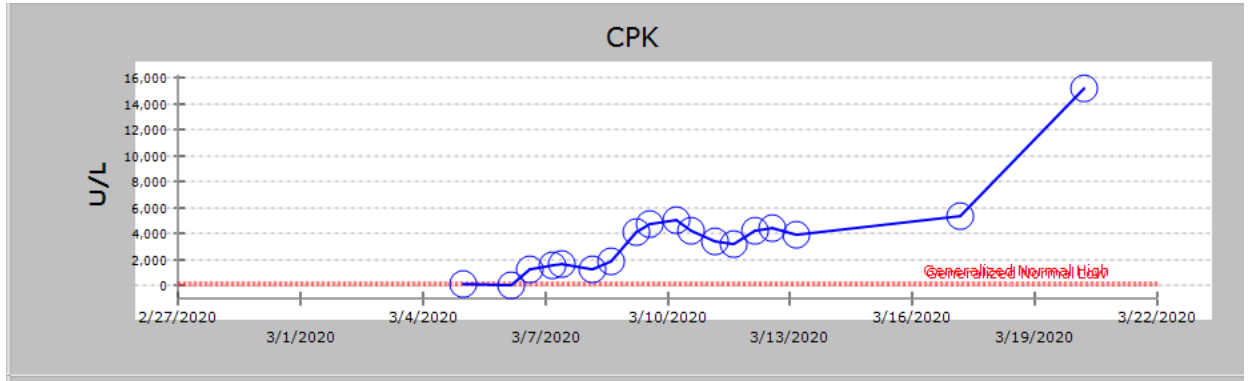

A
R
L
P

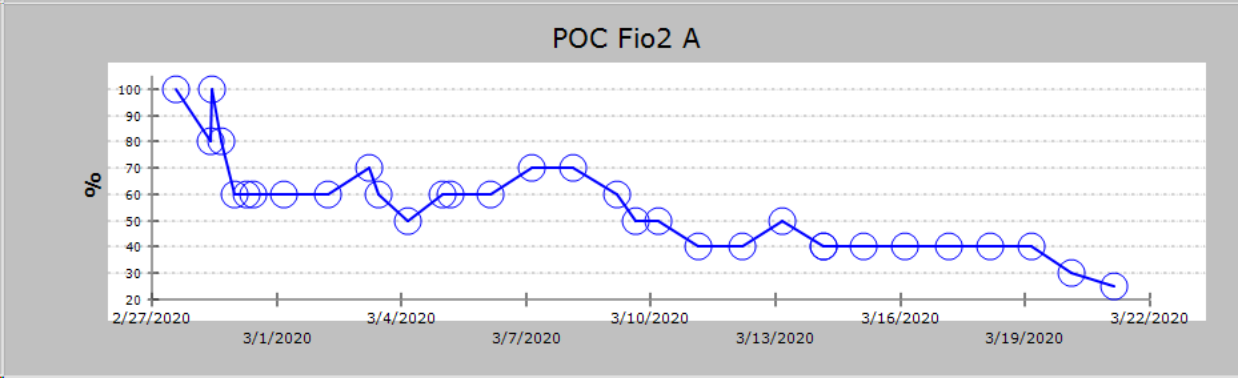
Hospital Course

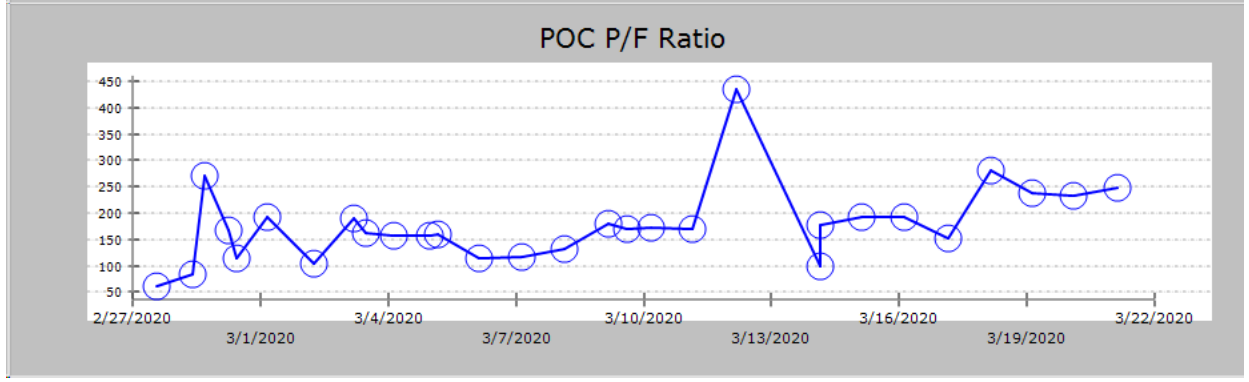
- Cefepime, Vancomycin
- Paralyzed, prone x 4 days
- Day 7 compassionate use remdesivir was added
- Weaned off vasopressors by day 7
- Day 11 worsening acute kidney injury
- Day 11 worsening shock and LVEF (normal troponin)
- CRRT started day 14
- Comatose on day 24, failing SBT, remains on HD. MRI, CT, LP negative
- Goals changed to comfort-care and patient expired

Lab Trends


Lymph# Auto
Generalized Normal High
Generalized Normal Low
x10E3/uL
3.5
3
2.5
2
1.5
1
0.5
2/27/2020
3/1/2020
3/4/2020
3/7/2020
3/10/2020
3/13/2020
3/16/2020
3/19/2020
3/22/2020


CPK
U/L
16,000
14,000
12,000
10,000
8,000
6,000
4,000
2,000
0
2/27/2020
3/1/2020
3/4/2020
3/7/2020
3/10/2020
3/13/2020
3/16/2020
3/19/2020
3/22/2020


POC Fio2 A
%
100
90
80
70
60
50
40
30
20
2/27/2020
3/1/2020
3/4/2020
3/7/2020
3/10/2020
3/13/2020
3/16/2020
3/19/2020
3/22/2020


POC P/F Ratio
450
400
350
300
250
200
150
100
50
2/27/2020
3/1/2020
3/4/2020
3/7/2020
3/10/2020
3/13/2020
3/16/2020
3/19/2020
3/22/2020

Bronchoscopy & Laboratory Results

- Day 1 Bronchoscopy with lavage - 32% Ly, 34% PMN
- Procalcitonin 0.97
- Day 9 Bronch due to suspected VAP – negative cultures. PMN 63%

Echocardiogram Results

- Day 1 – normal transthoracic echocardiogram
- Day 4 – limited TTE remains normal
- Day 9 – LVEF 30% with global dysfunction

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

Surviving Sepsis Campaign

Waleed Alhazzani MD, FRCP, MSc
Associate Professor of Medicine
McMaster University

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
European Society of Intensive Care Medicine
The Intensive Connection

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.

Surviving Sepsis Campaign

SSC COVID Guidelines Panel Members

Morten Hylander Møller
Yaseen M. Arabi
Mark Loeb
Michelle Ng Gong
Eddy Fan
Simon Oczkowski
Mitchell M. Levy
Lennie Derde
Amy Dzierba
Bin Du
Michael Aboodi
Hannah Wunsch
Maurizio Cecconi
Younsuck Koh
Daniel S. Chertow
Kathryn Maitland
Fayez Alshamsi
Emilie Belley-Cote
Massimiliano Greco
Matthew Laundy
Jill S. Morgan
Jozef Kesecioglu
Allison McGeer
Leonard Mermel
Manoj J. Mammen
Paul E. Alexander
Amy Arrington
John Centofanti
Giuseppe Citerio
Bandar Baw
Ziad A. Memish
Naomi Hammond
Frederick G. Hayden
Laura Evans
Andrew Rhodes

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

PICO question

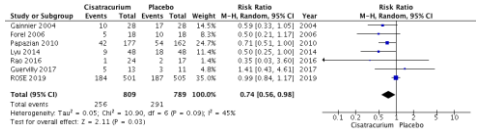
COVID-19

Systematic reviews
ARDS, MERS, SARS, shock

Expert Identified evidence

Assess quality

Summarize the evidence



Study or Subgroup	Cisatracurium Events	Cisatracurium Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Gainner 2004	10	28	17	28	14.5%	0.59 [0.33, 1.05]	2004
Forel 2006	5	18	10	18	8.3%	0.50 [0.21, 1.17]	2006
Papazian 2010	42	177	54	162	24.7%	0.71 [0.51, 1.00]	2010
Lee 2014	9	48	18	48	11.4%	0.50 [0.25, 1.00]	2014
Rao 2016	1	24	2	17	1.4%	0.35 [0.03, 3.60]	2016
Guervilly 2017	5	13	3	11	4.8%	1.41 [0.43, 4.61]	2017
ROSE 2019	184	501	187	505	35.0%	0.99 [0.84, 1.17]	2019
Total (95% CI)		**809**		**789**	**100.0%**	**0.74 [0.56, 0.98]**	
Total events	256		291				

Heterogeneity: Tau² = 0.05; Chi² = 10.90, df = 6 (P = 0.09); I² = 45%
Test for overall effect: Z = 2.11 (P = 0.03)

Risk Ratio M-H, Random, 95% CI
0.1 0.2 0.5 1 2 5 10
Cisatracurium Placebo

Evidence Profile
Certainty of Evidence

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[intervention]	[comparison]	Relative (95% CI)	Absolute (95% CI)		
Outcome B												
8	randomised trials	serious [a]	not serious	not serious	serious [b]	none	43/1022 (4.2%)	47/1108 (4.2%)	**RR 0.99** (0.66 to 1.49)	**0 fewer per 1.000** (from 14 fewer to 21 more)	⊕⊕◯◯ LOW	CRITICAL
Outcome D												
6	observational studies	not serious	not serious	serious [c]	not serious	strong association [d]	689	645	-	MD **18 [unit] lower** (22 lower to 14 lower)	⊕⊕◯◯ LOW	IMPORTANT

New evidence

Panel Discussion

Recommendation

Expedited Review & Publication

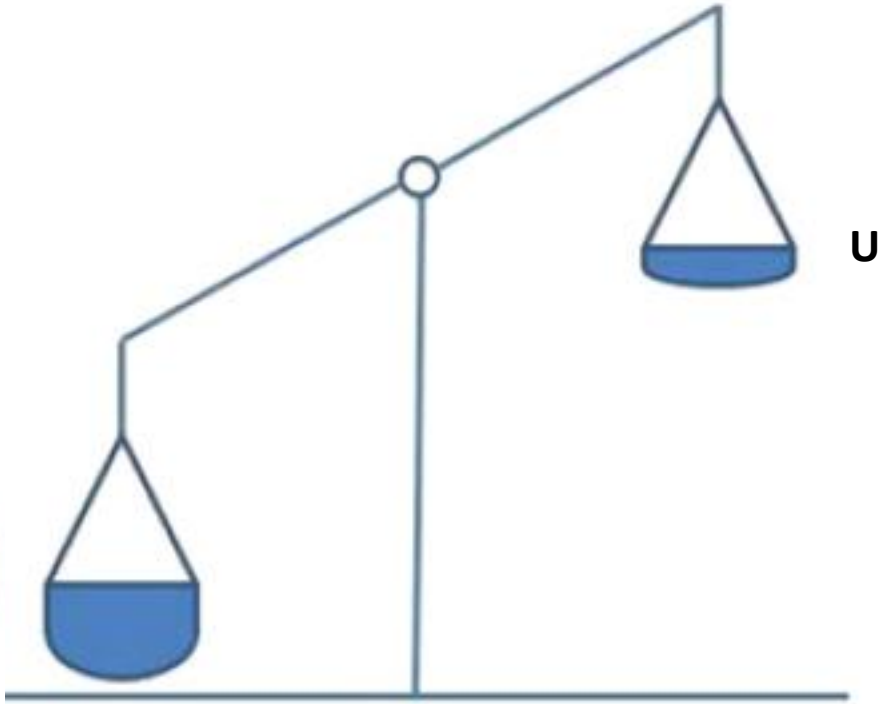
AMERICAN GASTROENTEROLOGICAL ASSOCIATION

Colorectal Cancer Screening and Surveillance: Clinical Guidelines and Rationale—Update Based on New Evidence

Dissemination

Society of Critical Care Medicine
The Intensive Care Professionals

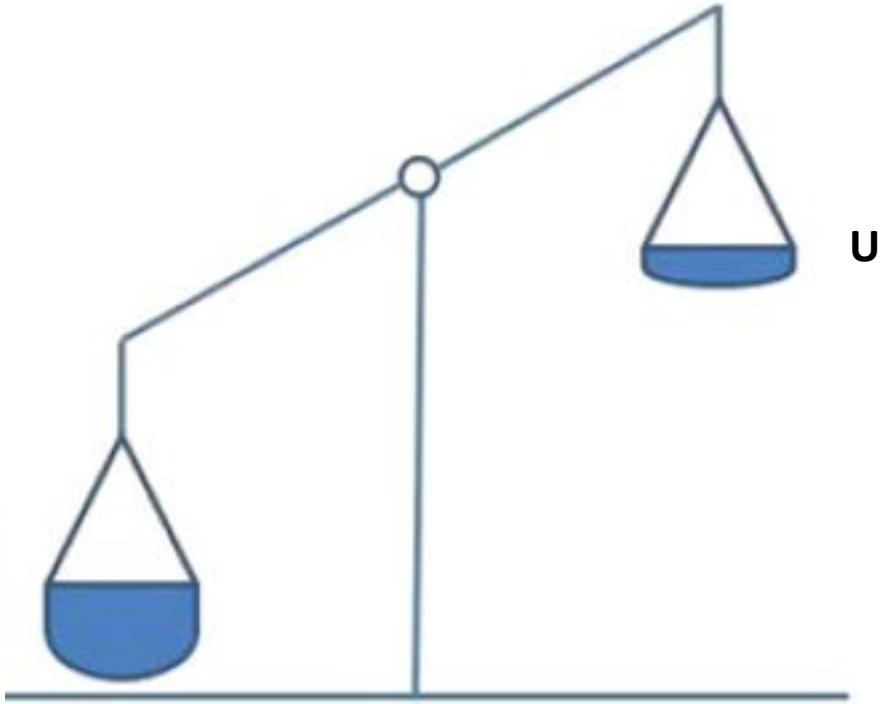
ESICM EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE



Undesirable consequences

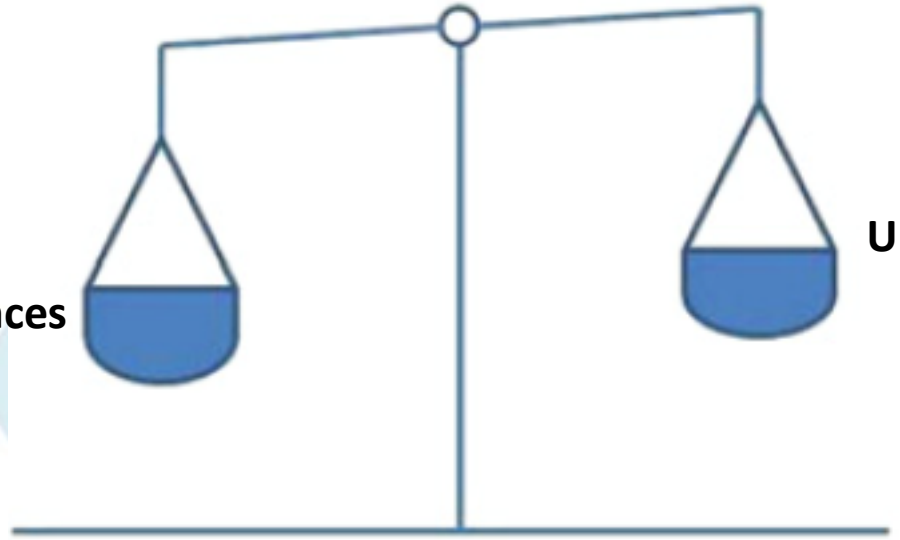
Desirable consequences

Strong Recommendation for the Intervention

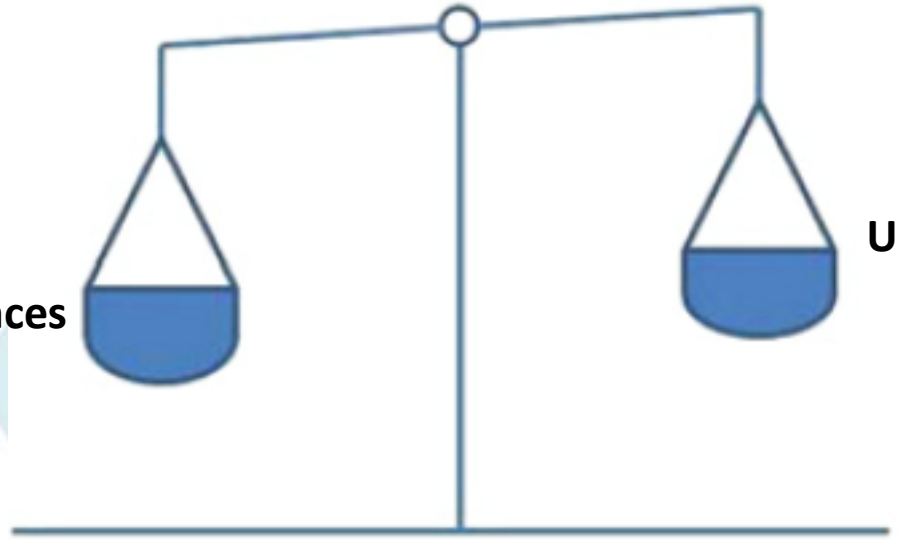


Undesirable consequences

Desirable consequences


Desirable consequences
Undesirable consequences

Weak Recommendation for the Intervention



Desirable consequences

Undesirable consequences

Surviving Sepsis Campaign

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

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

Clinicians

	Strong Recommendation	Weak Recommendation
For Clinicians	**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

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

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

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Infection control

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

Surviving Sepsis Campaign

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)

PLoS One. 2012;7(4):e35797.

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

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

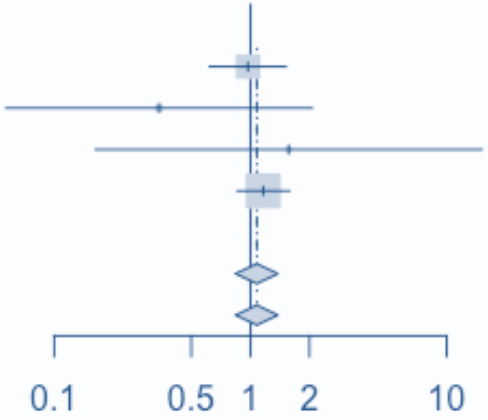
We **suggest** using surgical/medical masks, as compared to respirator masks, in addition to other personal protective equipment.

Surviving Sepsis Campaign

Laboratory Confirmed Influenza Infection

Study	N95 Events	N95 Total	Face Mask Events	Face Mask Total	OR	95%-CI	Weight (fixed)	Weight (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: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.55$



Society of Critical Care Medicine
The Intensive Care Professionals

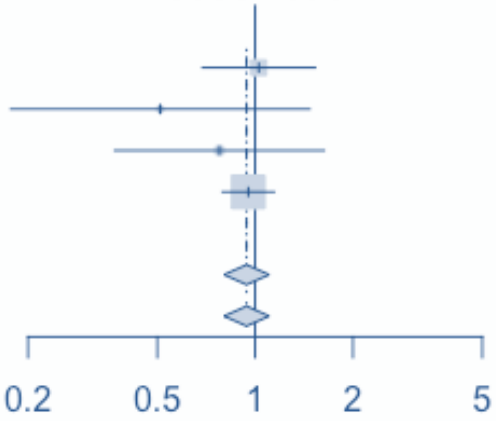
ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

Laboratory Confirmed Respiratory Infection

Study	N95 Events	N95 Total	Face Mask Events	Face Mask Total	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: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.63$



Society of Critical Care Medicine
The Intensive Care Professionals

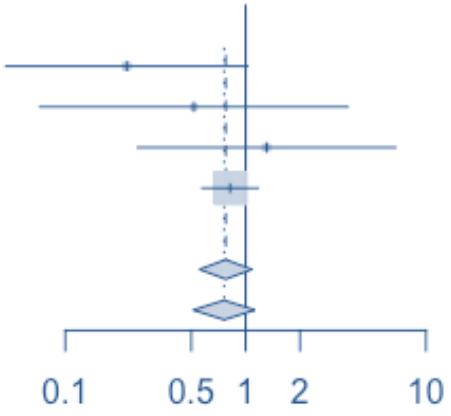
ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

influenza-like illness

Study	N95 Events	N95 Total	Face Mask Events	Face Mask Total	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: $I^2 = 7\%$, $\tau^2 = 0.0153$, $p = 0.36$

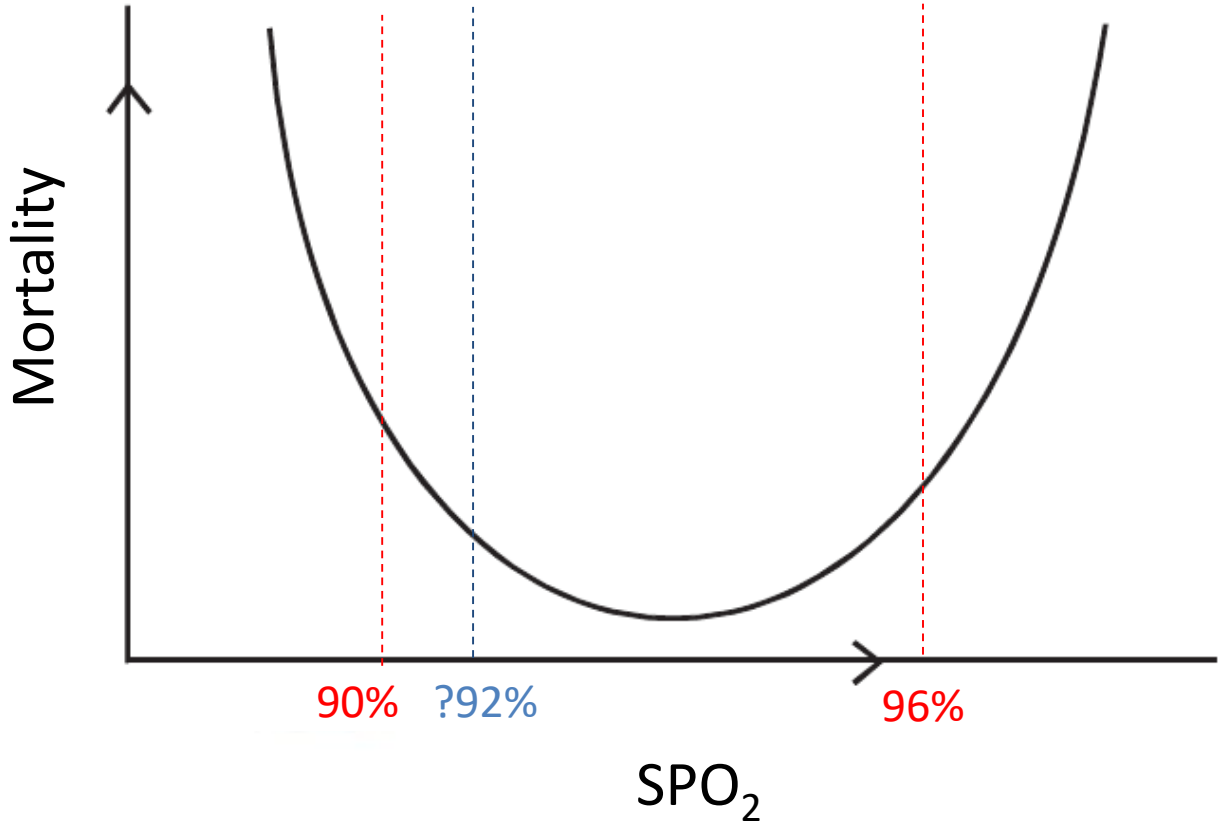


Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

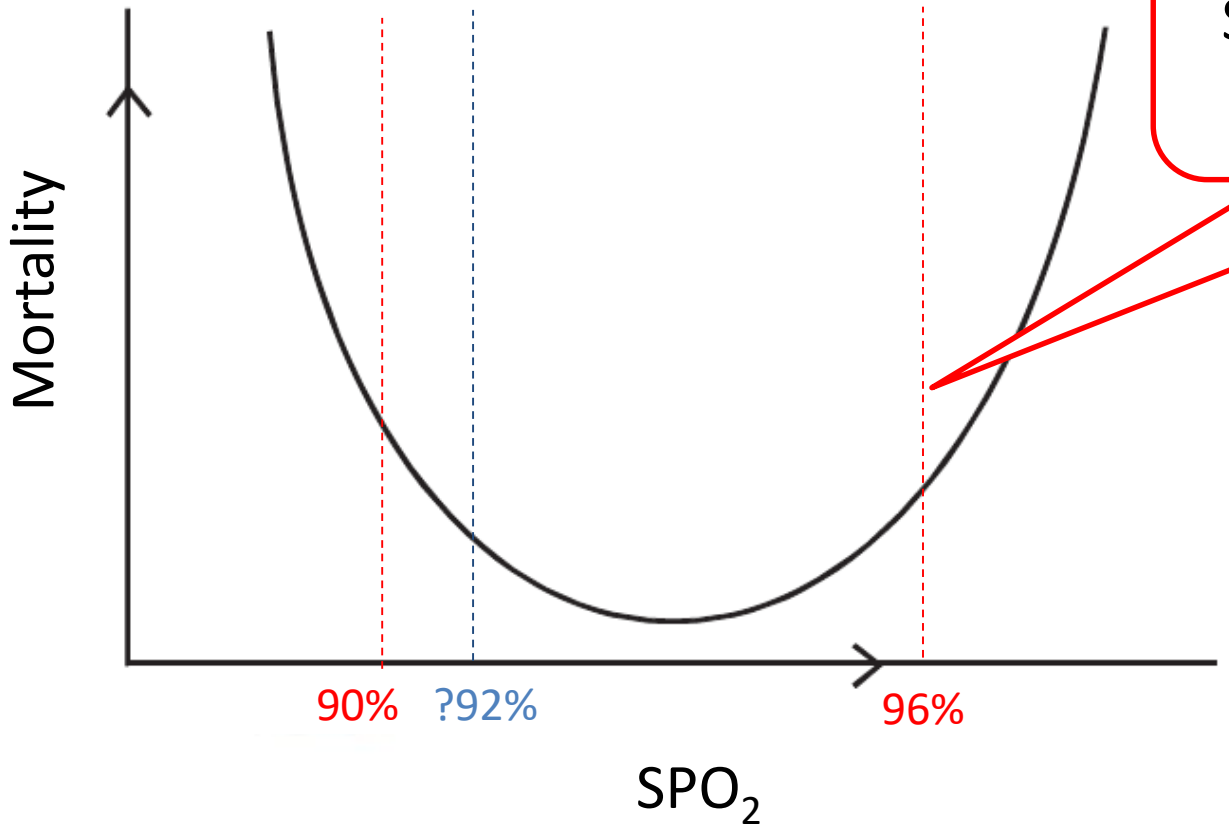
Oxygen Targets



Society of Critical Care Medicine
The Intensive Care Professionals

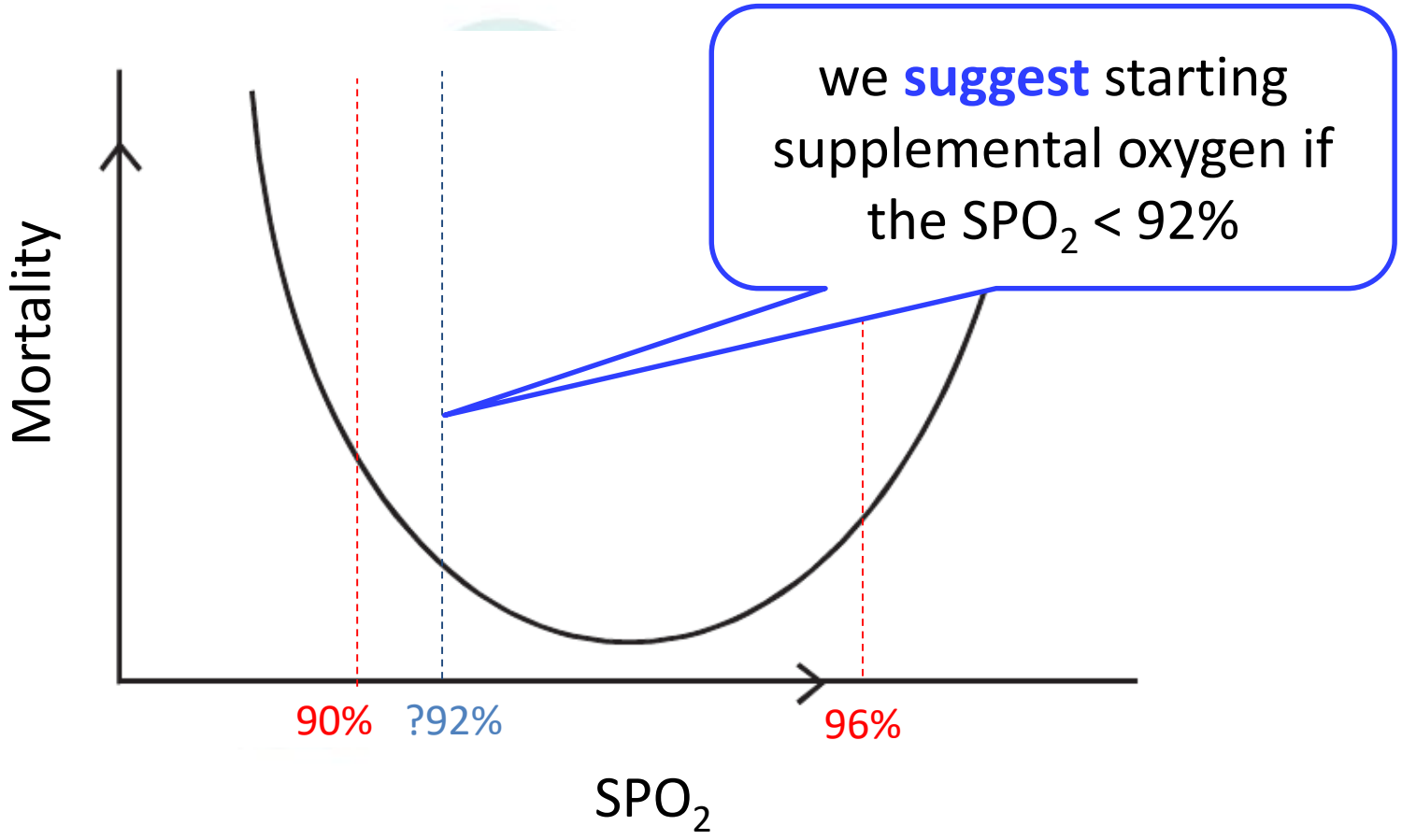
ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Oxygen Targets

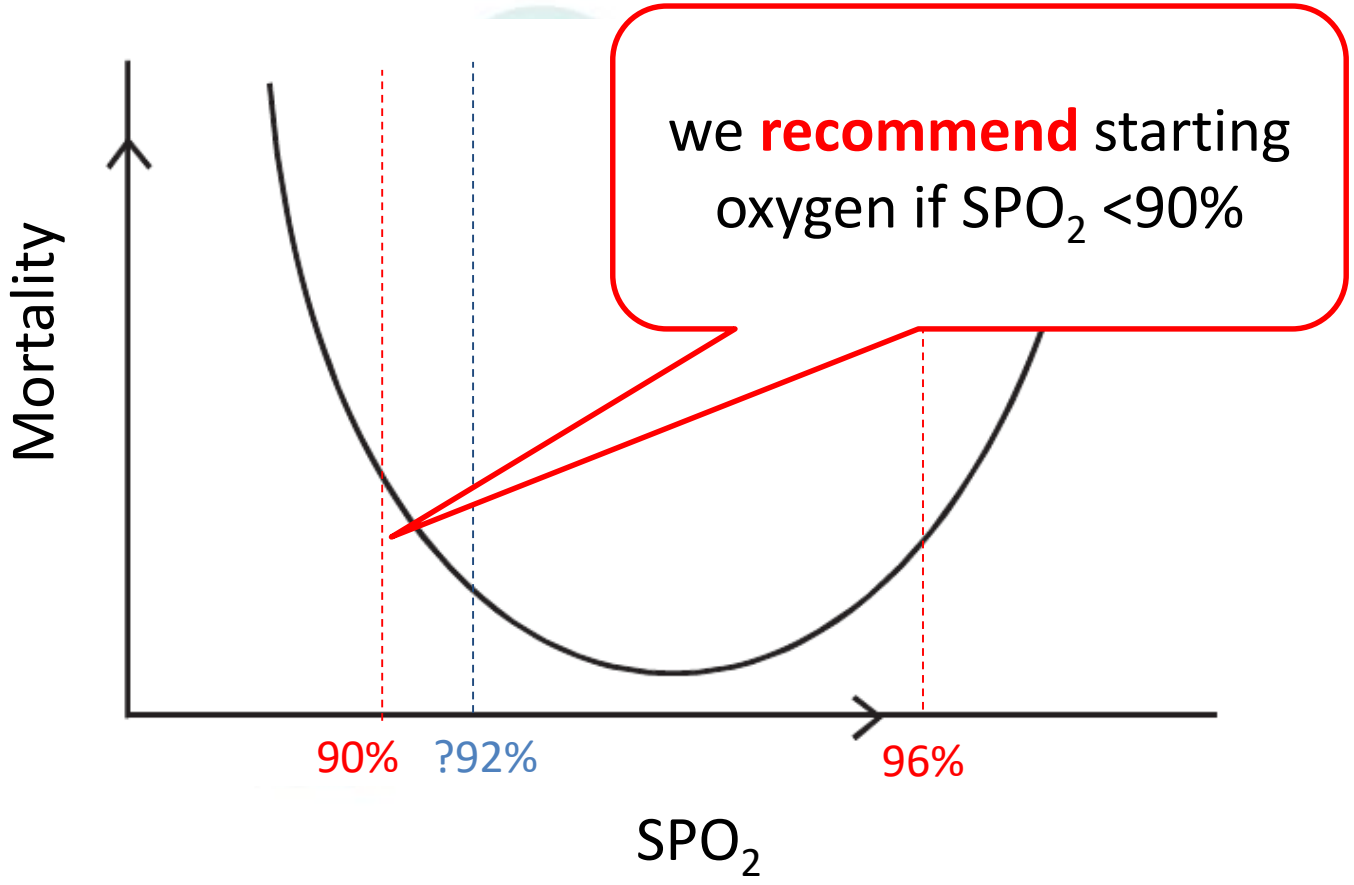


we **recommend** that SPO_2 be maintained no higher than 96%

Oxygen Targets

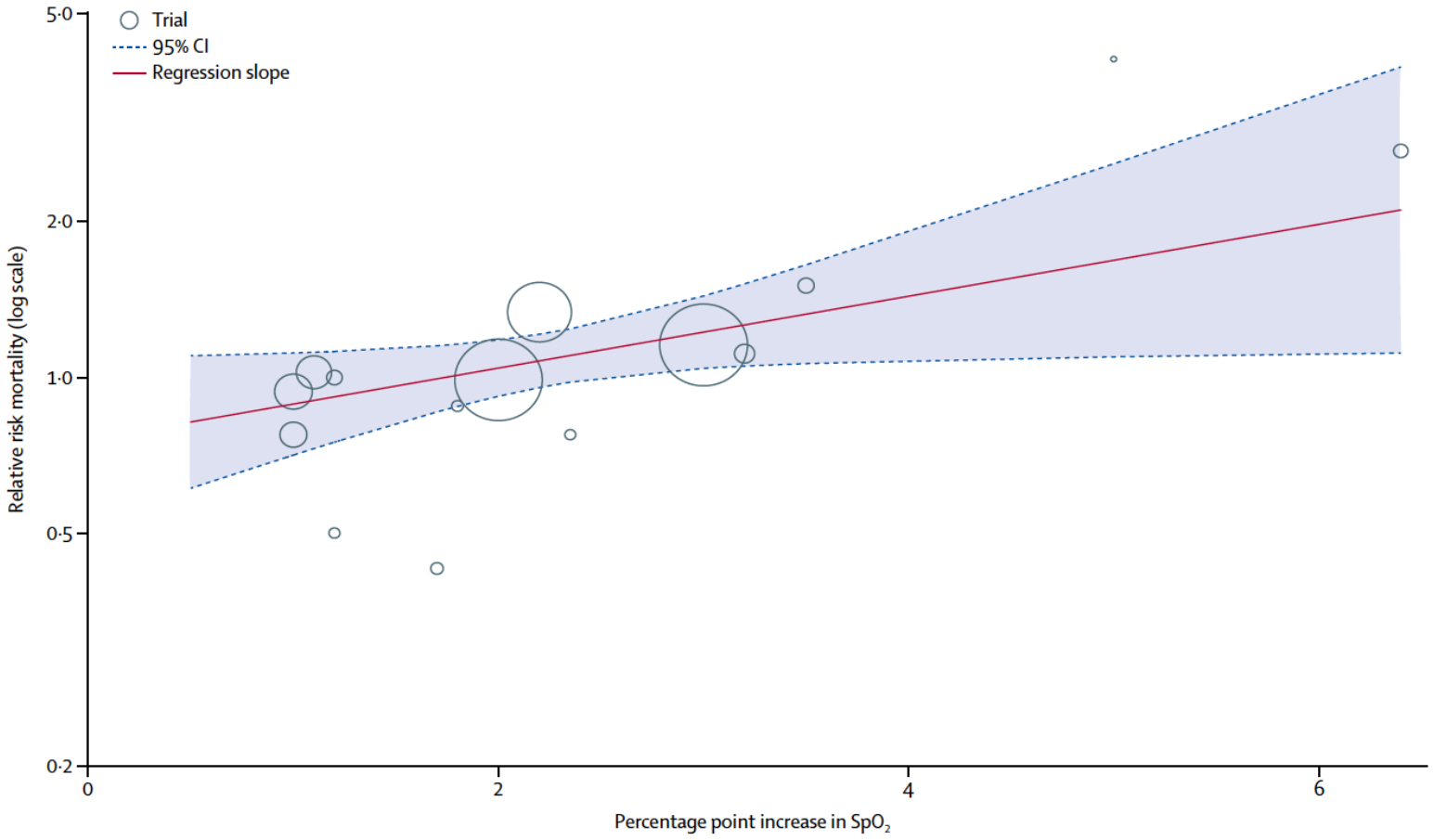


Oxygen Targets



Surviving Sepsis Campaign

SPO_2 and Mortality



Lancet. 2018 Apr 28;391(10131):1693-1705.

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

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.

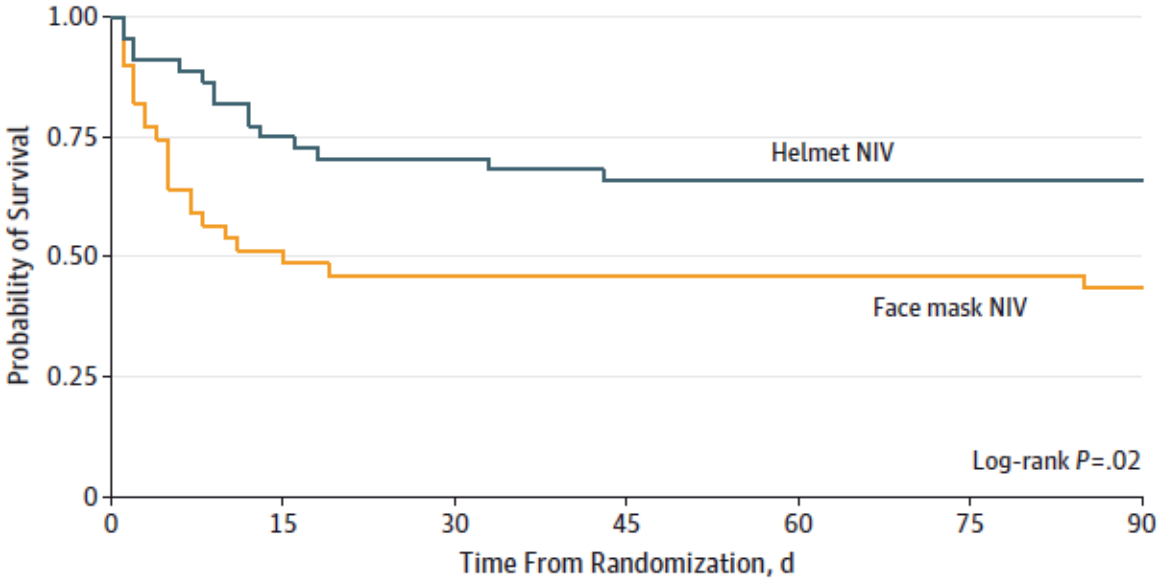
We were not able to make a recommendation regarding the use of helmet NIPPV compared to mask NIPPV, it is an option, but we are not certain about its safety or efficacy for COVID-19 patients.

Surviving Sepsis Campaign

Preliminary Communication | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial



No. at risk							
Face mask	39	20	18	18	18	18	17
Helmet	44	33	31	29	29	29	29

JAMA. 2016 Jun 14;315(22):2435-41

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

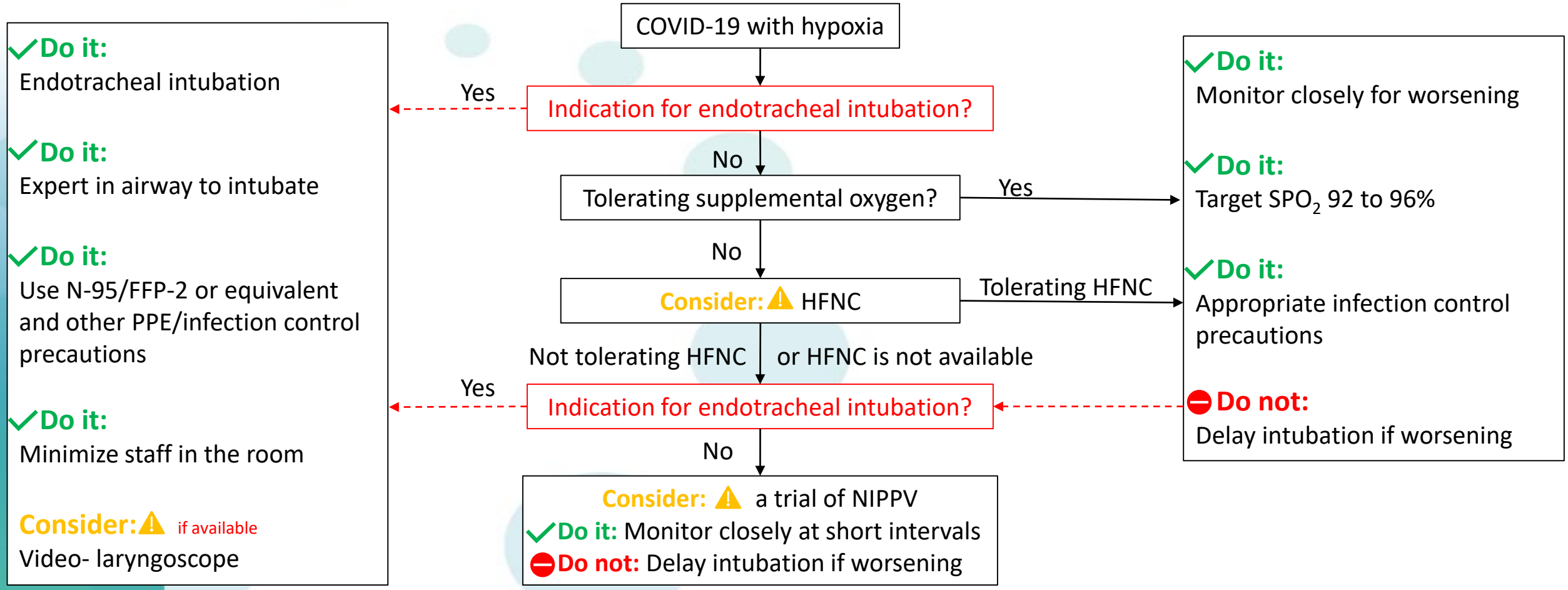
Endotracheal Intubation

- 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.

Surviving Sepsis Campaign



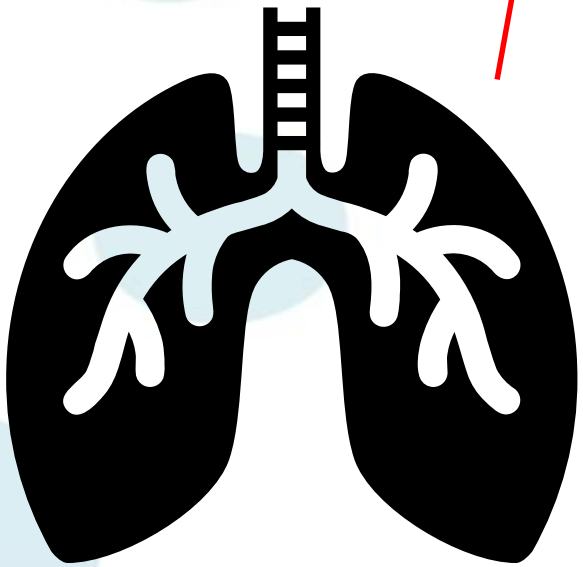
Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Acute Respiratory Distress Syndrome

Surviving Sepsis Campaign

We **recommend** using low Vt (4-8 mL/kg) and
Targeting Pplat <30 cmH_2O



ARDS

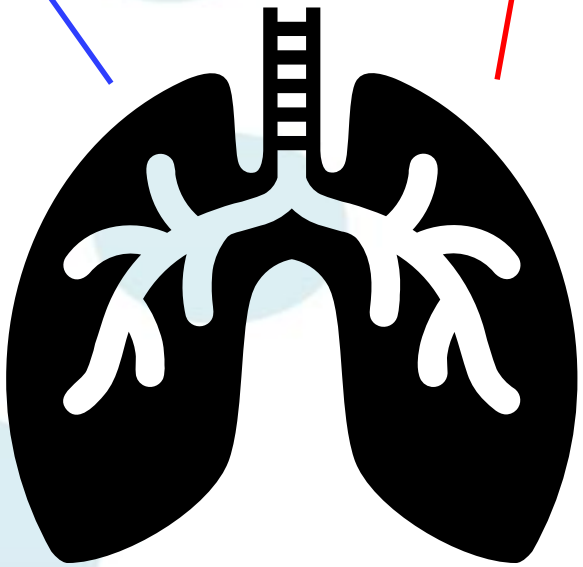
Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

we **suggest** using a higher PEEP strategy

We **recommend** using low Vt (4-8 mL/kg) and
Targeting Pplat <30 cmH_2O



Mod-Severe ARDS

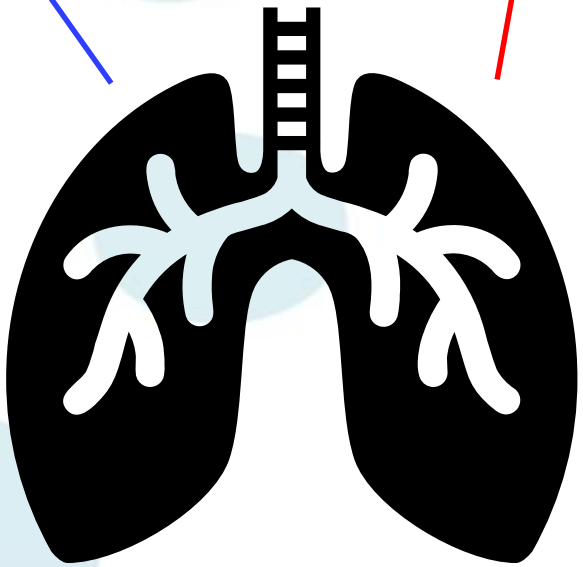
Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Surviving Sepsis Campaign

we **suggest** using a higher PEEP strategy

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



Mod-Severe ARDS

We **recommend** using low Vt (4-8 mL/kg) and
Targeting Pplat <30 cmH_2O

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

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

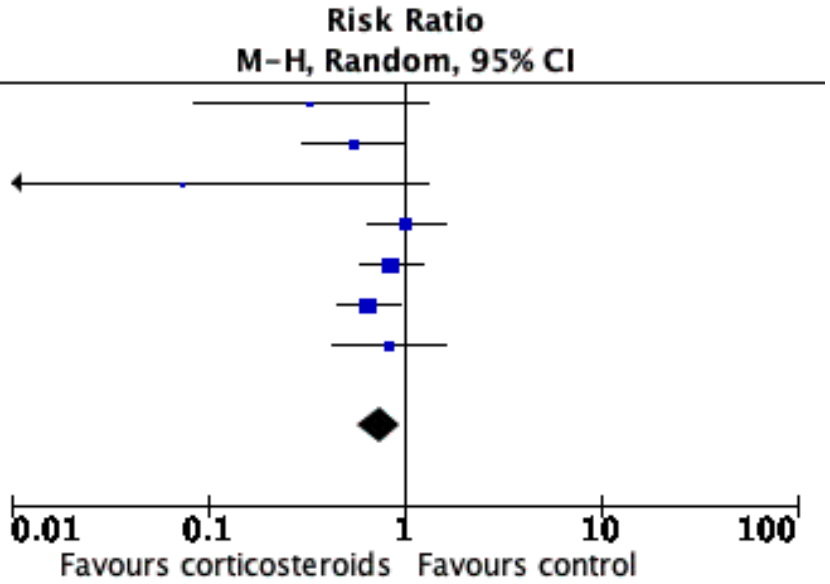
Surviving Sepsis Campaign

Steroids in ARDS - Mortality Outcome

Study or Subgroup	Corticosteroids Events	Corticosteroids Total	Control Events	Control 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: $Tau^2 = 0.02$; $Chi^2 = 7.69$, df = 6 (P = 0.26); $I^2 = 22\%$

Test for overall effect: Z = 2.36 (P = 0.02)



Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

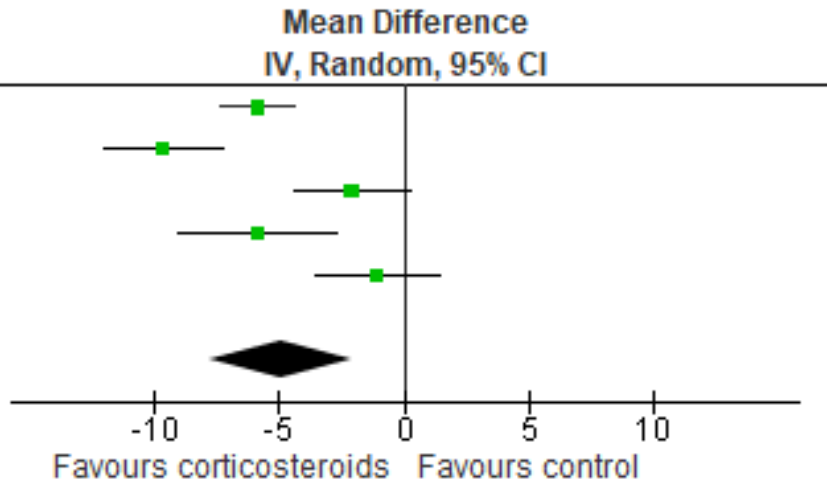
Surviving Sepsis Campaign

Steroids in ARDS - DMV

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Meduri 2007	5.25	1.46	63	11.1	3.9	28	21.9%	-5.85 [-7.34, -4.36]
Rezk 2013	10.6	4.4	18	20.3	1.9	9	20.1%	-9.70 [-12.08, -7.32]
Tongyoo 2016	11.8	7.8	98	13.9	9	99	20.1%	-2.10 [-4.45, 0.25]
Villar 2020	14.3	13.3	139	20.2	14	138	18.0%	-5.90 [-9.12, -2.68]
Zhao 2014	10.5	4.6	24	11.6	4.6	29	19.8%	-1.10 [-3.59, 1.39]
Total (95% CI)			**342**			**303**	**100.0%**	**-4.93 [-7.81, -2.06]**

Heterogeneity: Tau² = 9.22; Chi² = 31.72, df = 4 (P < 0.00001); I² = 87%

Test for overall effect: Z = 3.37 (P = 0.0008)



Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

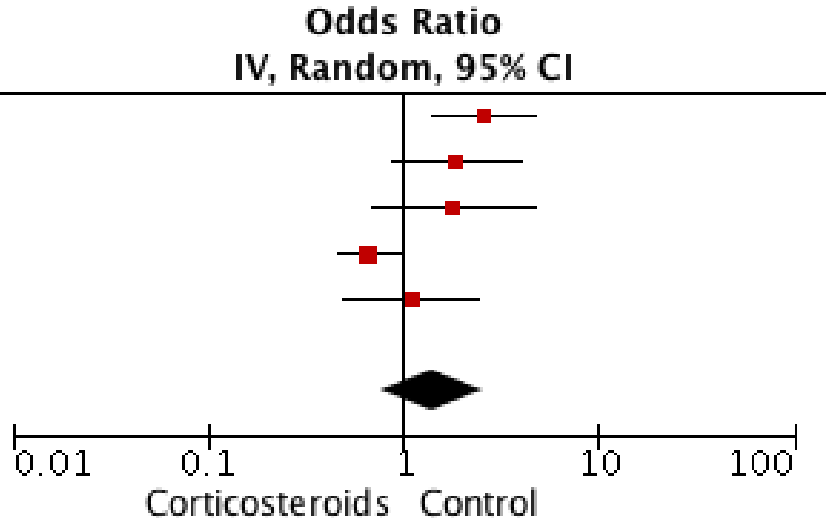
Surviving Sepsis Campaign

Steroids for Viral ARDS - Mortality

All observational studies

Study or Subgroup	log[Odds Ratio]	SE	Weight	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]**

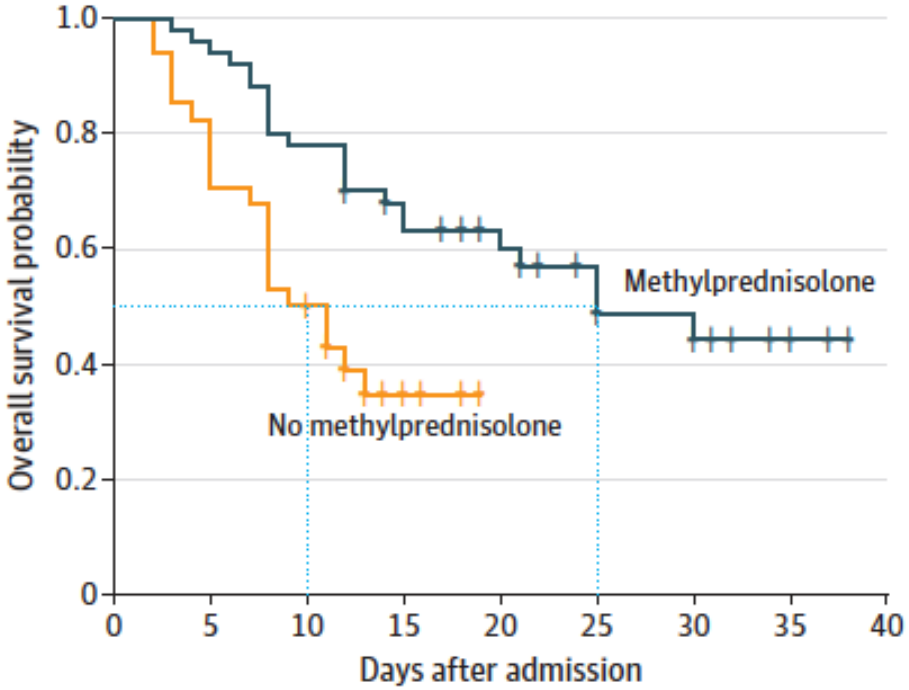
Heterogeneity: Tau² = 0.35; Chi² = 17.29, df = 4 (P = 0.002); I² = 77%
Test for overall effect: Z = 1.09 (P = 0.28)



Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

Direct Evidence



No. at risk									
No methylprednisolone	34	28	17	4	0	0	0	0	0
Methylprednisolone	50	48	39	29	20	14	11	4	0

Retrospective study
N=201
with COVID-19 pneumonia

JAMA Intern Med. 2020 Mar 13.

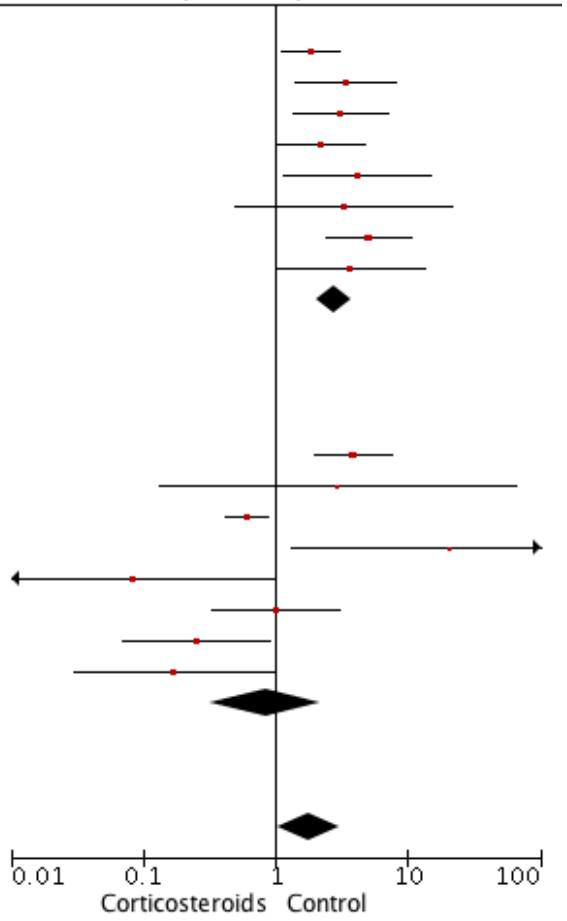
Corticosteroids

- 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.

Surviving Sepsis Campaign

Steroids for Viral Pneumonia - Mortality

Study or Subgroup	log[Odds Ratio]	SE	Weight	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-Rodtriguez 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

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

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

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

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

Surviving Sepsis Campaign

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

Surviving Sepsis Campaign

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

Society of Critical Care Medicine
The Intensive Care Professionals

ESICM
EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

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

To Ask a Question

- **Using the Webinar System**
  - Click on the **Q&A** button in the Zoom webinar system.
  - Type your question in the **Q&A** box.
  - Submit your question.
  - You may also email your question to 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.

Today's COCA Call Will Be Available On-Demand

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

COCA Products & Services

COCA Call Announcements contain all information subscribers need to participate in COCA Calls. COCA Calls are held as needed.

Monthly newsletter that provides information on CDC training opportunities, conference and training resources, the COCA Partner Spotlight, and the Clinician Corner.

As-needed messages that provide specific, immediate action clinicians should take. Contains comprehensive CDC guidance so clinicians can easily follow recommended actions.

COCA Products & Services

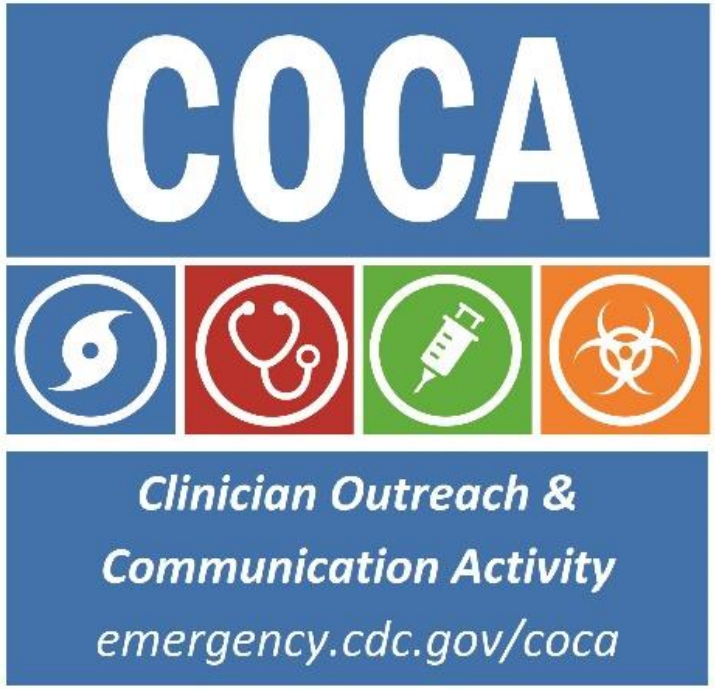
Monthly newsletter providing updates on emergency preparedness and response topics, emerging public health threat literature, resources for health professionals, and additional information important during public health emergencies and disasters.

Informs clinicians of new CDC resources and guidance related to emergency preparedness and response. This email is sent as soon as possible after CDC publishes new content.

CDC's primary method of sharing information about urgent public health incidents with public information officers; federal, state, territorial, and local public health practitioners; clinicians; and public health laboratories.

Join COCA's Mailing List

- **Receive information about:**
  - Upcoming COCA Calls
  - Health Alert Network (HAN) messages
  - CDC emergency response activations
  - Emerging public health threats
  - Emergency preparedness and response conferences and training opportunities



emergency.cdc.gov/coca

Join Us on Facebook

Thank you for joining us today!

emergency.cdc.gov/coca