COVID-19 and Pediatric Patients

Julie C. Fitzgerald, MD PhD MSCE
Attending Physician
Pediatric Intensive Care Unit
Children's Hospital of Philadelphia
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Disclosures

- No financial conflicts of interest
- Research support via NIH NIDDK K23 DK119463

Disclaimers

- Very little primary pediatric/neonatal evidence exists on COVID-19
  - This is especially true with regard to mechanical ventilation practices
- Case reports/small case series generally not included in this talk
- Most of the treatment practices are extrapolated from adult data and data on other etiologies of respiratory failure in pediatric patients
- Evidence continues to accumulate at a rapid pace
- As much as possible, I will focus on the active disease caused by infection with SARS-CoV-2, i.e. COVID-19, rather than the post-infectious inflammatory process MIS-C

Case Presentation

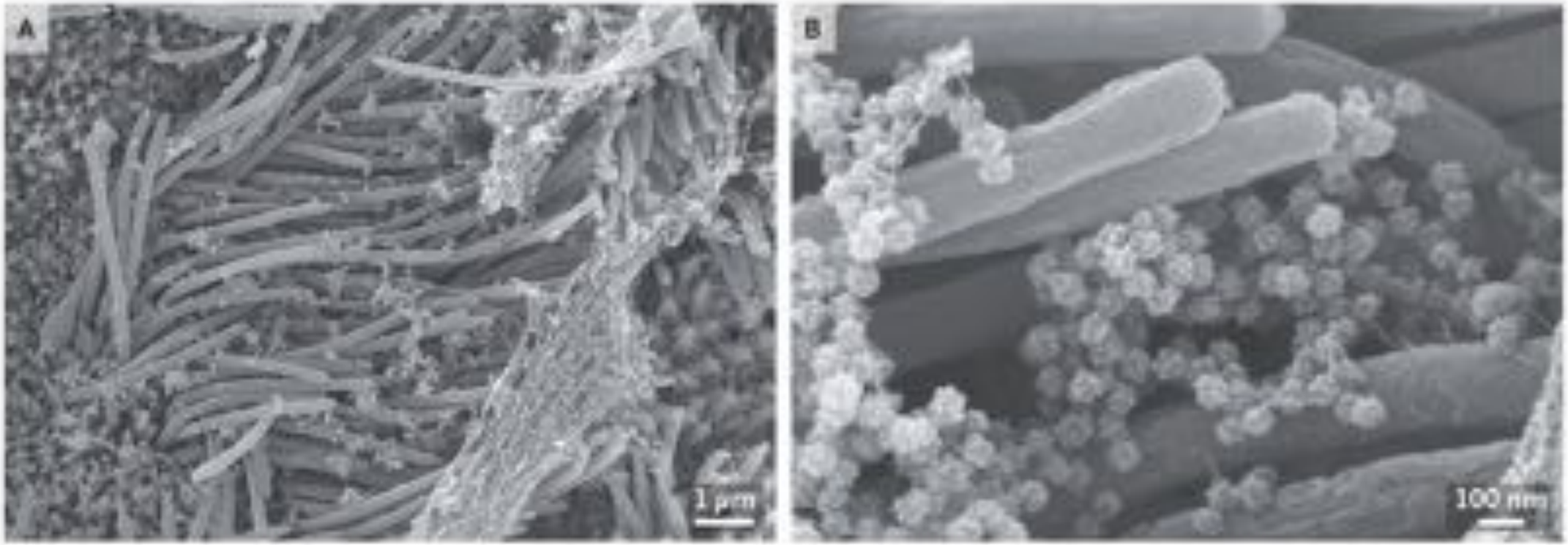
- 15yo female with chronic neurological disorder, neuromuscular scoliosis, nighttime BiPAP dependence (16/6, 2L O_2), difficult airway
- 4 days of cough, respiratory distress, increased secretions, fever
- SARS-CoV-2 positive, other pathogens negative
- ED course: moderate respiratory distress, T 40ºC
  - 7.15/78/27/-4, lactate 4.9
  - BiPAP increased to 20/10, FiO2 0.55 -> 7.27/50/23/-5, lactate 3.4, SpO2 94%
- Admitted to PICU
  - Initial exam: moderate respiratory distress, RR 65, tachycardic HR 128

Objectives

- Discuss landscape of what is known about pediatric COVID-19
- Understand best practices for intubation and mechanical ventilation in children with respiratory failure related to COVID-19
- Review indications for advanced modes of ventilation and ECMO for children with COVID-19
- Identify risks and benefits of potential medications for management of critical COVID-19 in children

SARS-CoV-2 Infection of Airway Cells

Camille Ehre, Ph.D.



Scanning electron microscope images of SARS-CoV-2 96h after inoculation into human bronchial epithelial cells

A. Infected ciliated cell with strands of mucous attached to cilia tips
B. Higher magnification shows structure and density of virions

DOI: 10.1056/NEJMicm2023328

RESEARCH LETTER

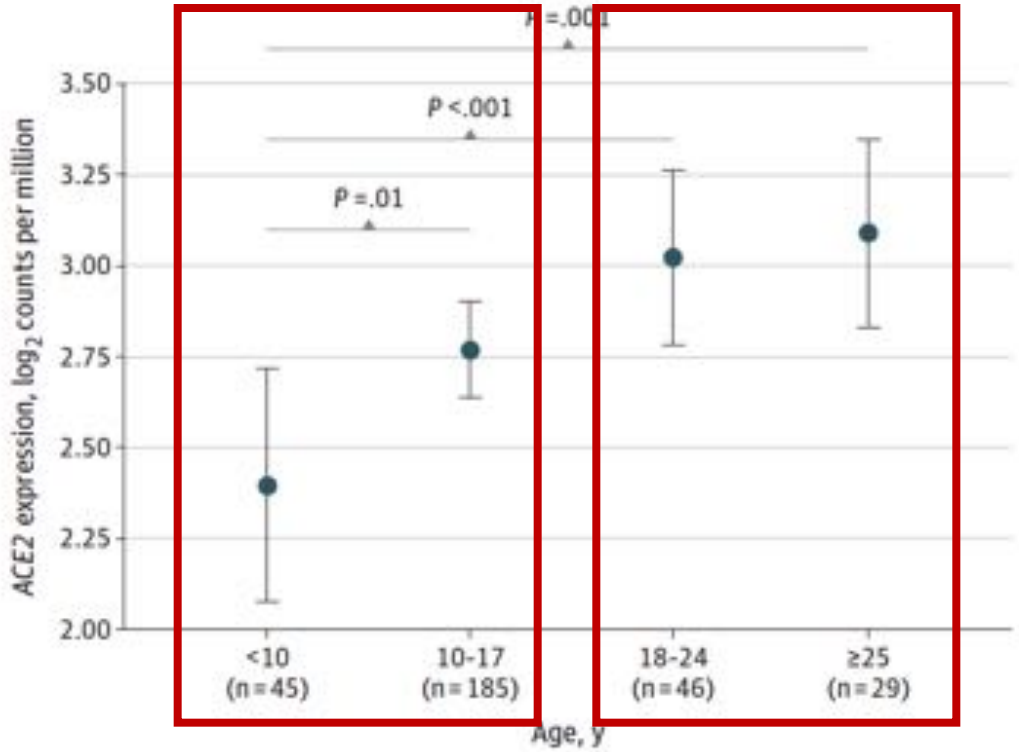
Nasal Gene Expression of Angiotensin-Converting Enzyme 2 in Children and Adults

Supinda Bunyavanich, MD, MPH
Anh Do, PhD
Alfin Vicencio, MD

JAMA Published online May 20, 2020

Tested ACE2 expression in nasal epithelium of patients of different ages

Figure. Nasal Gene Expression of *ACE2* in Different Age Groups



Pediatric Cases of COVID-19 in the ICU

Reference	Region	Period of Study	Total cases	Maximum Support			
				HFNC	NIPPV	IMV	ECMO
Liu et al, NEJM	Wuhan	January	6				
Lu et al, NEJM	Wuhan	February	171			3	
Guo et al, BMC Medicine	China	January-March	341			1	
Tagarro et al, JAMA Pediatr	Spain	March	41	1	2	1	
Garcia-Salido et al, PCCM	Spain	March-April	7	1	3	1	1
Parri et al, NEJM	Italy	March	100	3	1	1	
MMWR	US	February-March	2572	15 ICU admissions, data limited			
Kim et al, MMWR	US	March-July	208	5	8	12	
Shekerdanian et al, JAMA Pediatr	North America	March	48	11	4	18	1
					2 prone, 3 iNO		

Blue shading indicates dedicated ICU study

COVID-19 and Neonatal Respiratory Care: Current Evidence and Practical Approach

Wissam Shalish, MD[1] Satyanarayana Lakshminrusimha, MD[2] Paolo Manzoni, MD[3]
Martin Keszler, MD[4] Guilherme M. Sant'Anna, MD, PhD, FRCPC[1]

[1] Neonatal Division, Department of Pediatrics, McGill University Health Center, Montreal, Quebec, Canada
[2] Department of Pediatrics, UC Davis, Sacramento, California
[3] Department of Pediatrics and Neonatology, University Hospital Degli Infermi, Biella, Italy
[4] Department of Pediatrics, Women and Infants Hospital, Brown University, Providence, Rhode Island

Address for correspondence Guilherme FRCPC, Neonatal Division, Department of Health Center, 1001 Décarie Boulevard, Montreal H4A 3J1, Canada (e-mail: guilh

Am J Perinatol 2020;37:780–791.

Table 2 Characteristics of neonates and infants less than 1 year of age with positive COVID-19 testing

Study	n	Region, country	Age range	Need for respiratory support	Symptoms/outcomes
Cai et al[32]	2	Shanghai and Haikou, China	3 and 7 mo	None	Fever and mild URTI symptoms
Canarutto et al[33]	1	Milan, Italy	32 d	None	Fever and mild URTI symptoms
CDC[31]	398	United States	0–1 y	Not specified	59 out of 96 infants with known hospitalization status were hospitalized, of which 5 required intensive care
Cui et al[34]	1	Guiyang, China	55 d	Oxygen therapy	Pneumonia, increased myocardial/liver enzymes
Dong et al[35]	379	Mainland China	0–1 y	Not specified	7 (2%) asymptomatic 205 (54%) mild 127 (34%) moderate 33 (9%) severe 7 (2%) critical
ISN-SIN[9]	5	Northern Italy	2–44 d	Oxygen therapy (1/5)	Fever and/or mild URTI symptoms conjunctivitis
Kam et al[36]	1	Singapore, Singapore	6 mo	None	Fever
Kamali et al[37]	1	Zanjan, Iran	15 d	Oxygen therapy	Fever, mild tachypnea
Le et al[38]	1	Hanoi, Vietnam	3 mo	None	Mild URTI symptoms
Li et al[39]	1	Zhuhai, China	10 mo	No	Asymptomatic
Liu et al[15]	2	Shanghai, China	2 and 11 mo	Not specified	Both had mild pneumonia, one infant also had pleural effusion and was RSV positive
Lu et al[40]	31	Wuhan, China	0–1 y	1 infant required IMV due to intussusception and multiorgan failure (4 weeks after admission)	0 asymptomatic 6 (19%) URTI symptoms 25 (81%) pneumonia 1 (3%) death
Qiu et al[41]	10	Zhejiang, China	0–5 y	Oxygen therapy (1/10)	4 (40%) asymptomatic/mild 6 (60%) moderate
Su et al[42]	2	Jinan, China	11 mo	None	Mild pneumonia (1/2)
Wei et al[43]	9	Mainland China	28 d–1 y	None	Fever or mild URTI symptoms
Xia et al[44]	9	Wuhan, China	0–1 y	Not specified	Neonates: asymptomatic (3/3) Others: asymptomatic or mild pneumonia
Zeng et al[45]	1	Wuhan, China	17 d	None	Mild symptoms (fever, vomiting, diarrhea)
Zhang et al[46]	1	Haikou, China	3 mo	None	Mild URTI symptoms

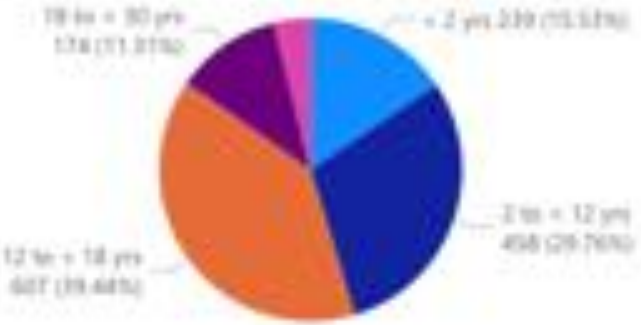
Only 86 confirmed cases in this study

COVID-19 Data: North American Pediatric ICUs

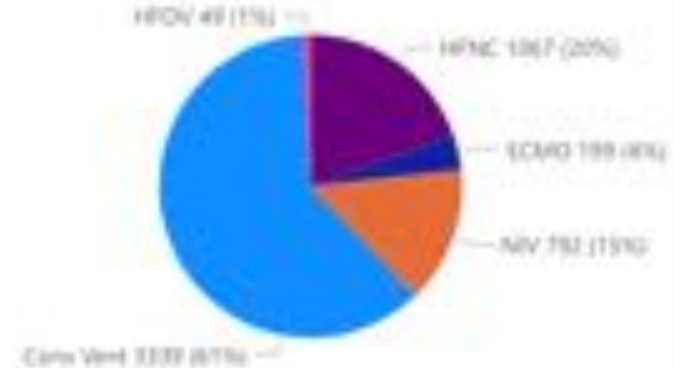
VPS
www.myvps.org

1539	51	22K	344	8888	185
COVID-19 Positive	Confirmed Deaths	Tested*	MIS-C Diagnosed	PICU Days	Sites Submitted Data*

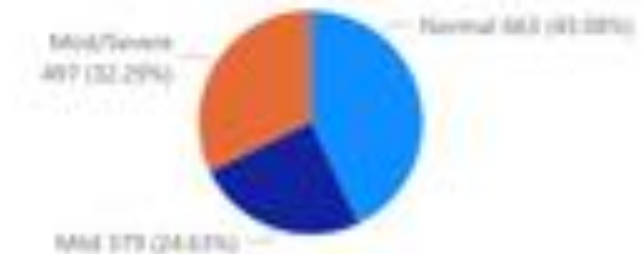
Age Distribution



Therapies Used (as Cumulative PICU Days) *



Comorbidity of Patients



COVID-19 Confirmed Patients BY STATE / PROVINCE

Timeline Dashboard

Clinical Summary I Dashboard

Clinical Summary II Dashboard

State

All

6/14/2020 9/2/2020

COVID-19 BY STATE / PROVINCE

State	Positive	Deaths
Tx	313	8
NY	154	6
CA	147	5
FL	110	2
SC	63	1
NJ	60	15
PA	56	2
NC	44	1
Total	**1539**	**51**

North American PICUs can submit data for this dashboard by contacting covid@myvps.org. Data submission is voluntary. Do not submit PHI; no PHI will be displayed on the dashboard. Please refer to the FAQ section for supportive details behind each component including update frequency. The dashboard and data are for information purposes only, not suitable for research publication. The veracity of the data has not been confirmed by VPS.

Last Updated
9/3/2020 9:23:19 PM

FAQ

COVID-19 Timeline: North American Pediatric ICUs

1539	51	175
Total COVID-19 Positive	Confirmed Deaths	COVID-19 Positive PICU Staff *

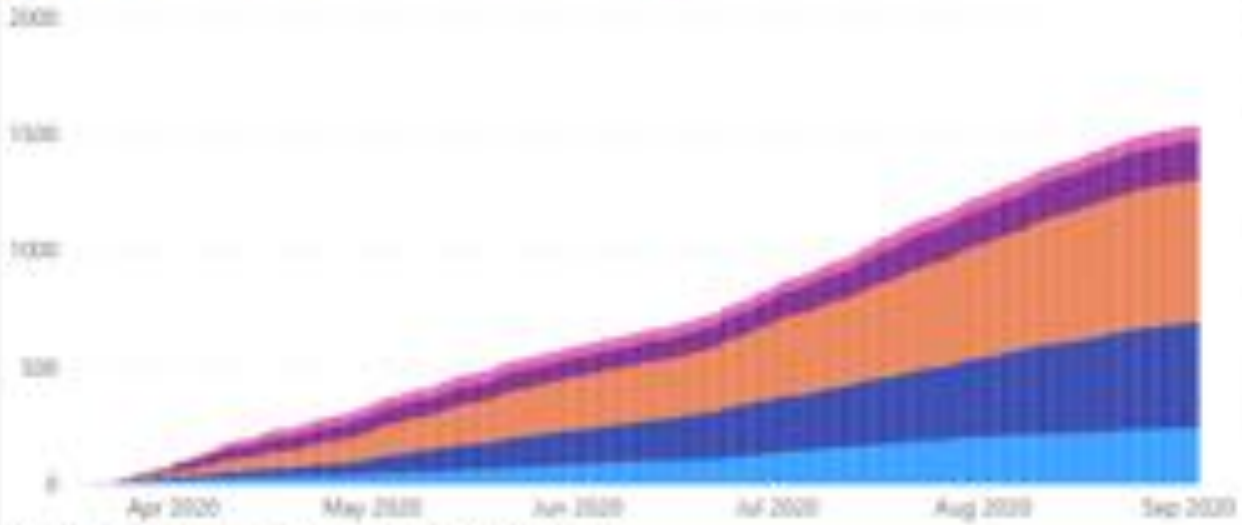
VPS
www.myvps.org

Main Dashboard
Clinical Summary I Dashboard
Clinical Summary II Dashboard

Cumulative COVID-19 Positive PICU Admissions (by Age Group)

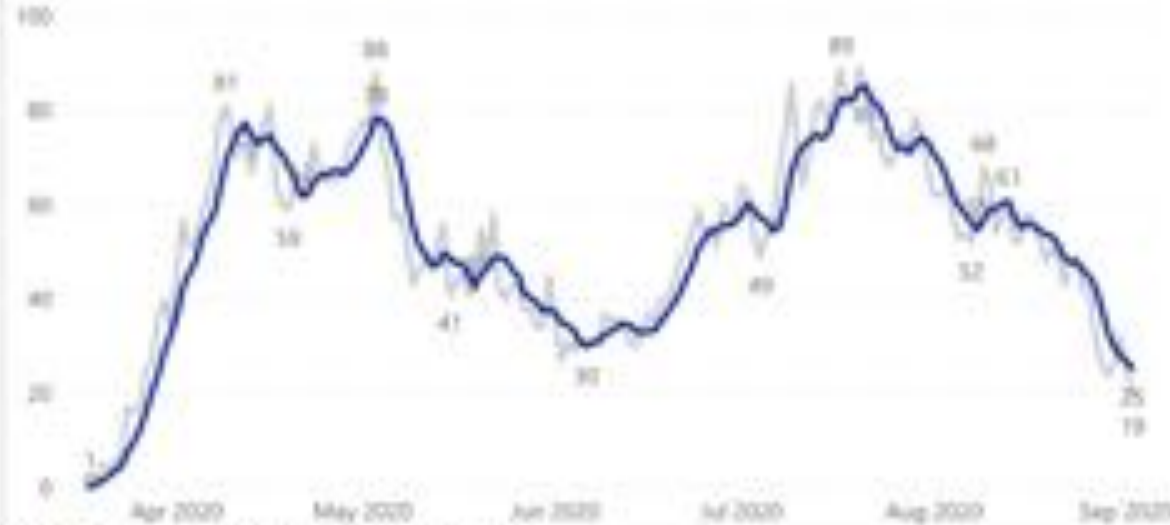
Hover over a day to see daily total

< 2 yrs | 2 to < 12 yrs | 12 to < 18 yrs | 18 to < 30 yrs | >= 30 yrs

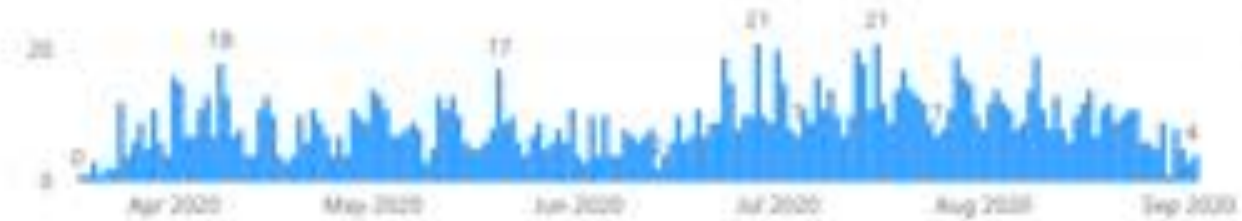


COVID-19 Positive Daily Census

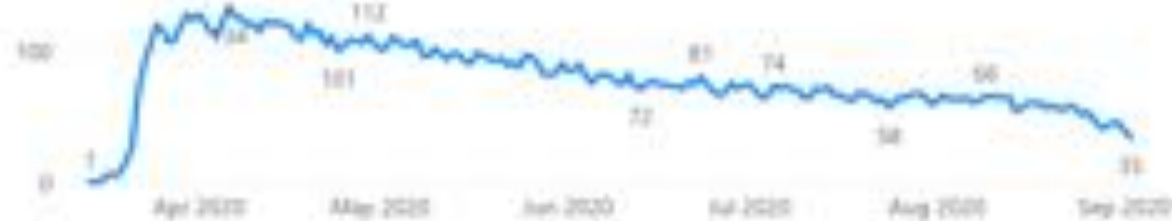
COVID-19 Positive Daily Census | Rolling 5-Day Average Daily Census



COVID-19 Positive PICU Admissions Per Day



Number of Sites Submitting per Day



Data submission by sites can lag behind by 1-3 days (particularly after weekends).

North American PICUs can submit data for this dashboard by contacting covid@myvps.org. Data submission is voluntary. Do not submit PHI; no PHI will be displayed on the dashboard. Please refer to the FAQ section for supportive details behind each component including update frequency. The dashboard and data are for information purposes only, not suitable for research publication. The veracity of the data has not been confirmed by VPS.

*FAQ

As of 9/3/2020

COVID-19 Clinical Summary II: North American Pediatric ICUs

www.myvps.org

892
Patients Reported

857
Discharged

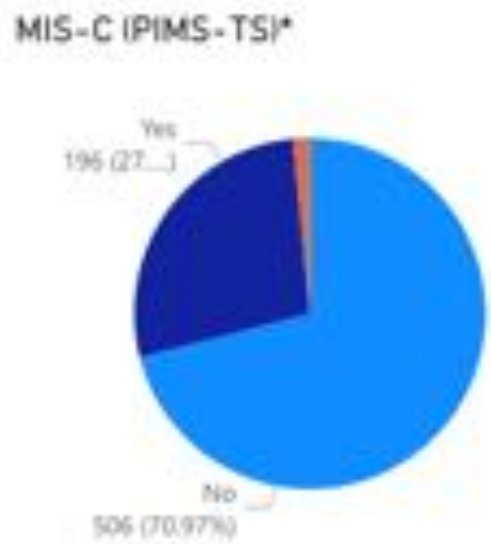
35
Confirmed Deaths

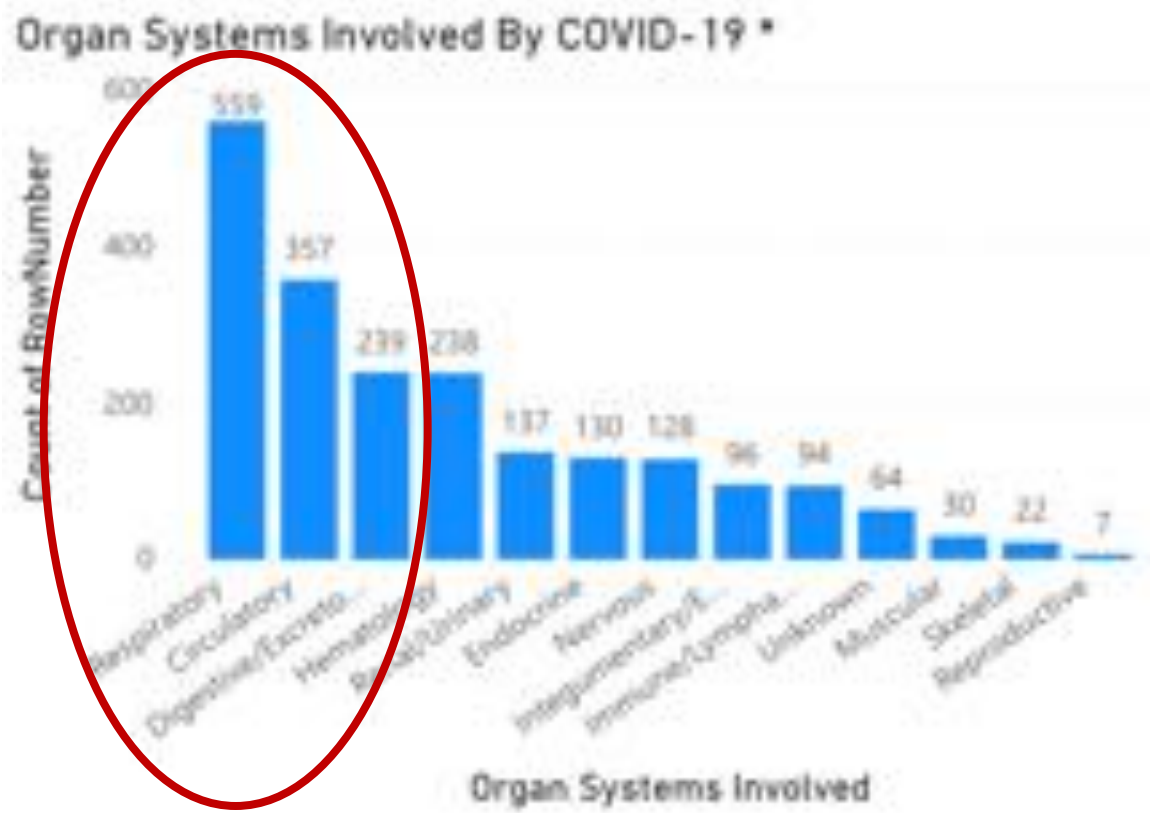
This dashboard is based on a discharge survey. Not all sites that submit data to the primary survey submit to the discharge survey.

Filter by Pt Age

All

Data based on 892 patients who have been discharged

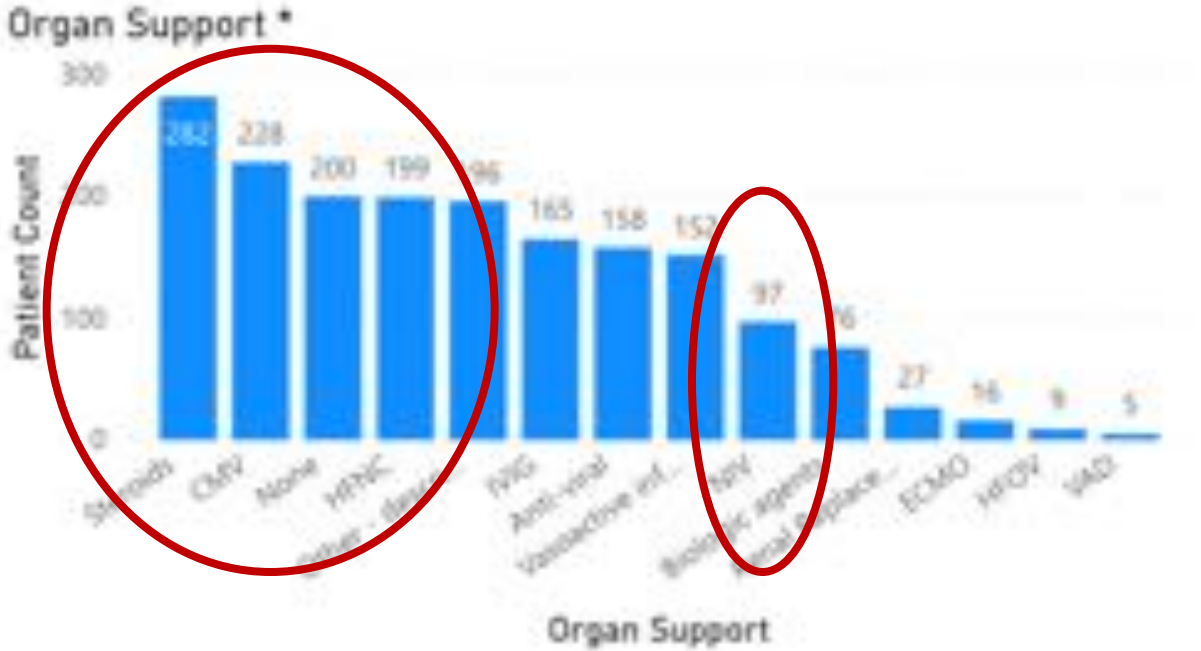


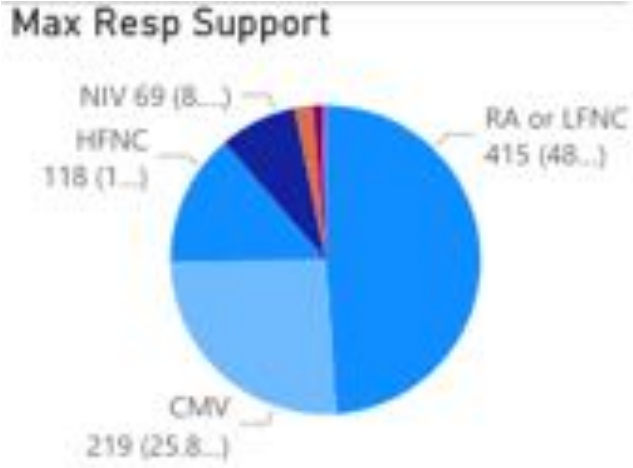


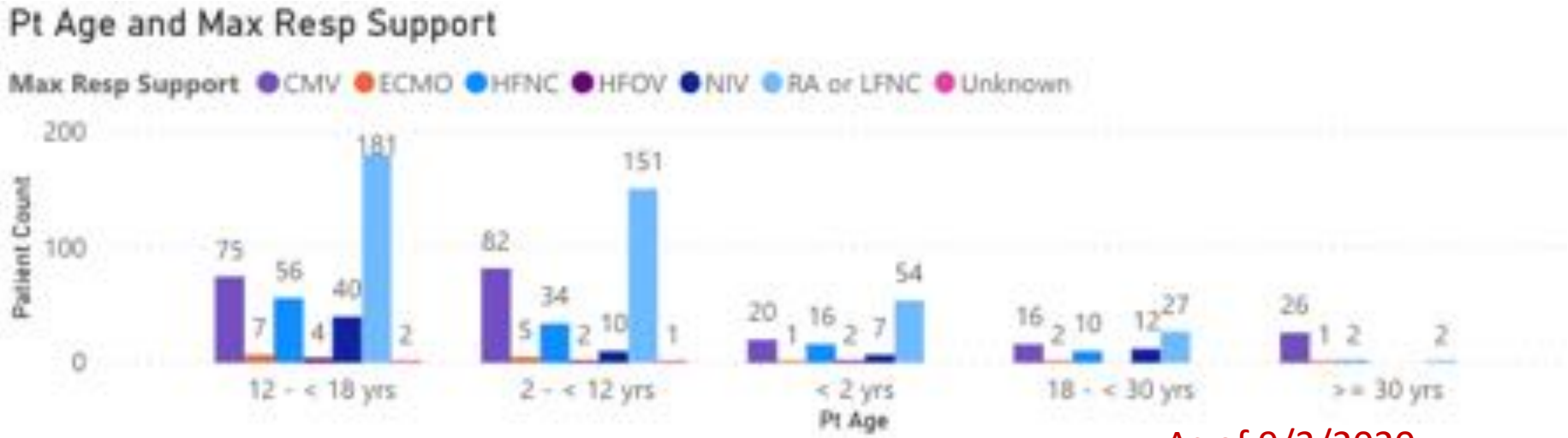
As of 9/3/2020

COVID-19 Clinical Summary II: North American Pediatric ICUs

www.myvps.org







As of 9/3/2020

Respiratory Support for COVID-19

Adult evidence and treatment guidelines

Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19

N Engl J Med 2020;383:120-8.
DOI: 10.1056/NEJMoa2015432

Maximilian Ackermann, M.D., Stijn E. Verleden, Ph.D., Mark Kuehnel, Ph.D., Axel Haverich, M.D., Tobias Welte, M.D., Florian Laenger, M.D., Arno Vanstapel, Ph.D., Christopher Werlein, M.D., Helge Stark, Ph.D., Alexandar Tzankov, M.D., William W. Li, M.D., Vincent W. Li, M.D., Steven J. Mentzer, M.D., and Danny Jonigk, M.D.

- Comparison of autopsy specimens
  - 7 lungs from COVID-19 patients
  - 7 lungs from Influenza A (H1N1) patients
  - 10 matched, uninfected controls
- Histologic pattern in peripheral lung showed diffuse alveolar damage with perivascular T-cell infiltrates in COVID and H1N1
- COVID lungs had severe endothelial injury and thromboses
  - 9x more alveolar capillary microthrombi vs. H1N1

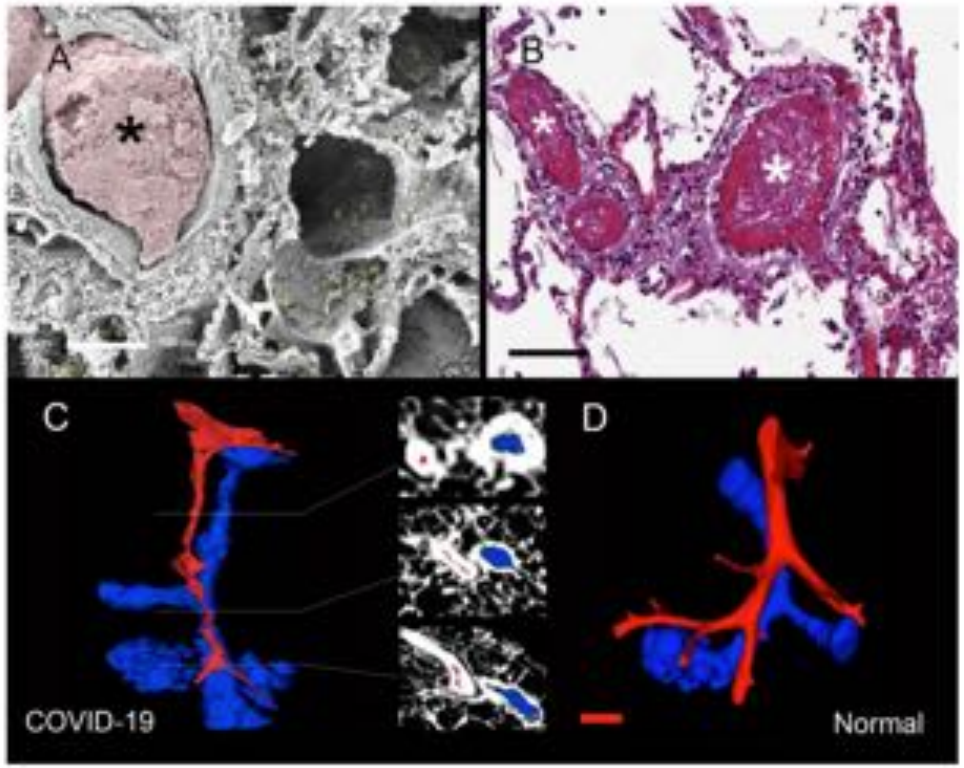


Figure S3. COVID-19-associated thrombosis. (A,B): In the inflamed vessels, there were multifocal thrombi (*) with (sub) total vascular occlusion of both pulmonary arteries and veins as visualized by scanning electron microscopy (A) and conventional histopathology (B) (scale bar = 100um). In the scanning electron microscopy image, the thrombus is pseudocolored pink and the infiltrating lymphocytes pseudocolored yellow. (C, D): µCT-based 3D reconstruction of subsegmental pulmonary arteries (red) and airways (blue) demonstrated (sub)total occlusion of the arteries in COVID-19-lungs (C), as compared to uninfected controls (D) (scale bar = 300 µm).

JAMA Insights | CLINICAL UPDATE

Management of COVID-19 Respiratory Distress

John J. Marini, MD; Luciano Gattinoni, MD

- Standard ARDS characterized by
  - Noncardiogenic pulmonary edema
  - Shunt-related hypoxemia
  - Reduced aerated lung size
  - Response to recruiting collapsed lung units (high PEEP, low VT)
- COVID-19 ARDS
  - Component of injury to the vascular endothelium, activated coagulation cascade, micro- and macrothromboses
  - Good lung compliance in early stages with high minute ventilation
  - Poor oxygenation
  - Low elastance, high compliance, low response to PEEP
  - Deterioration in some patients with transition to more typical ARDS

JAMA Insights | CLINICAL UPDATE

Management of COVID-19 Respiratory Distress

John J. Marini, MD; Luciano Gattinoni, MD

- Proposed approach by Marini & Gattinoni

Table. Time Course and Treatment Approach to Ventilation Support for Patients With CARDS

Time period	Objective	Respiratory support options	Rationale
Before intubation	Adequate gas exchange Avoid P-SILI	Supplemental oxygen, CPAP, NIV, HFNC Awake prone positioning, Target nonvigorous breathing	Powerful respiratory effort can cause reinforcing lung and vascular stress, resulting in injury
During mechanical ventilation	Avoid pulmonary deterioration and VILI vortex	Minimize PEEP, frequency and tidal volume Adjust to acceptable gas exchange Maintain fluid balance Reduce O_2 demand Consider ECMO	Minimize transpulmonary and vascular stresses
After intubation	Minimize pulmonary stress Optimize O_2 Avoid VILI vortex	Type L[a]: use lower PEEP (<10 cm H_2O) Use more liberal tidal volume (7-9 mL/kg) as needed Reduce O_2 demand Consider prone positioning	Lower tidal volumes are unnecessary Higher PEEP is ineffective, creates dead space, and adversely redirects blood flow
	Reduce and evenly distribute lung and vascular stresses Optimize O_2 Avoid VILI vortex	Type H[a]: use higher PEEP (<15 cm H_2O) Lower tidal volume (5-7 mL/kg) Reduce O_2 demand Implement prone positioning	More closely behaves and responds like typical ARDS
Weaning phase	Avoid reversion to previously worsened pulmonary state by causing VILI and worsening edema	Make transitions cautiously Avoid abrupt changes Spontaneous trials only at the very end of the weaning process	Strong spontaneous efforts raise O_2 demand, increase edema, and promote P-SILI

Abbreviations: ARDS, acute respiratory distress syndrome; CARDS, COVID-19 with ARDS; CPAP, continuous positive airway pressure; ECMO, extracorporeal membrane oxygenation; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; P-SILI, patient self-inflicted lung injury; PEEP, positive end-expiratory pressure; VILI, ventilator-induced lung injury.

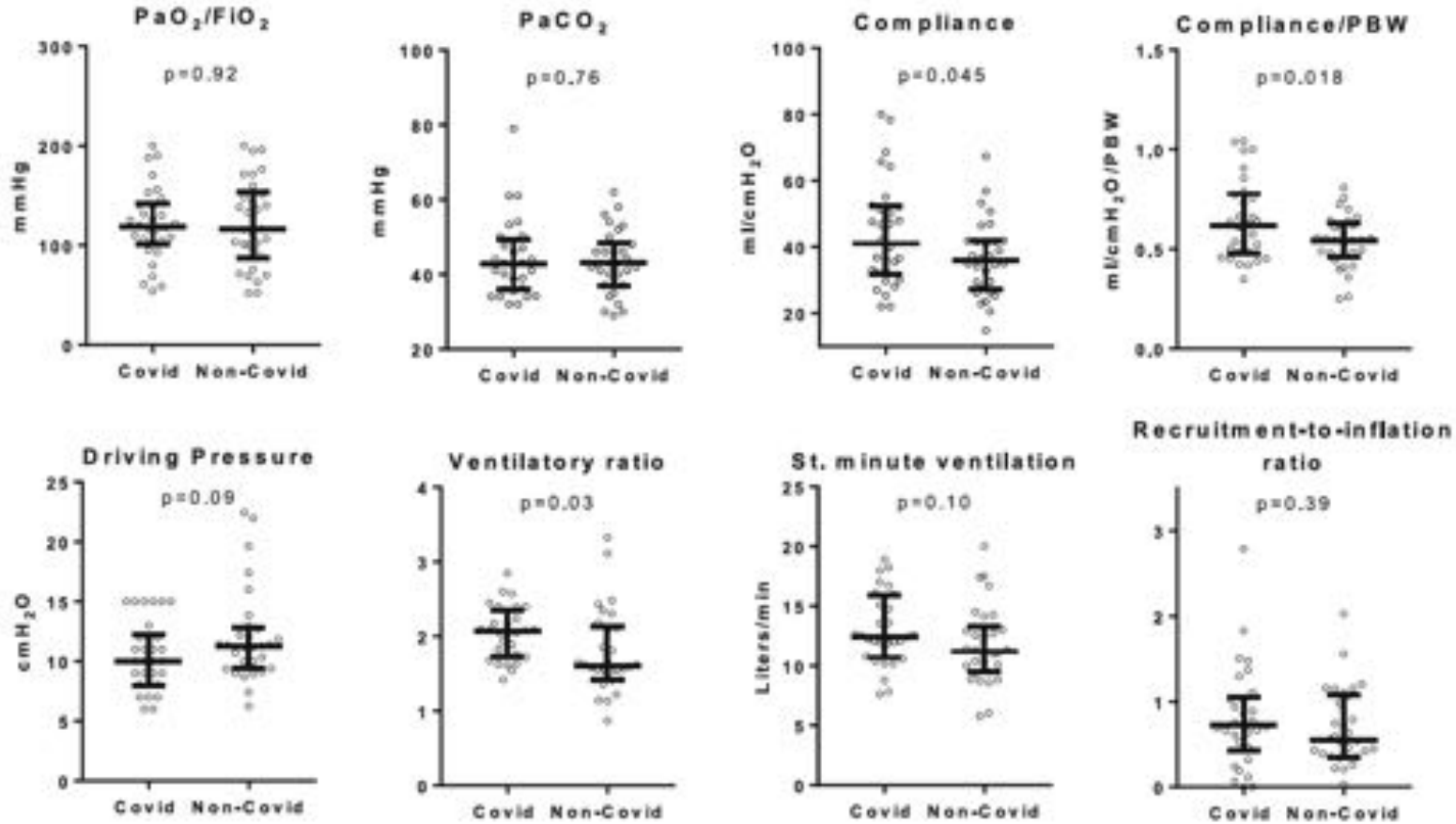
[a] Type L: Scattered ground-glass infiltrates, higher compliance (>50 mL/cm H_2O), not PEEP responsive, less dyspnea. Type H: Extensive infiltrates of atelectasis and edema, lower compliance, PEEP responsive, overtly dyspneic.

Respiratory physiology of COVID-19-induced respiratory failure compared to ARDS of other etiologies

Grieco *et al. Critical Care* (2020) 24:529
https://doi.org/10.1186/s13054-020-03253-2

Domenico Luca Grieco[1,2*], Filippo Bongiovanni[1,2], Lu Chen[3,4], Luca S. Menga[1,2], Salvatore Lucio Cutuli[1,2], Gabriele Pintaudi[1,2], Simone Carelli[1,2], Teresa Michi[1,2], Flava Torrini[1,2], Gianmarco Lombardi[1,2], Gian Marco Anzellotti[1,2], Gennaro De Pascale[1,2], Andrea Urbani[5,6], Maria Grazia Bocci[1,2], Eloisa S. Tanzarella[1,2], Giuseppe Bello[1,2], Antonio M. Dell'Anna[1,2], Salvatore M. Maggiore[7], Laurent Brochard[3,4] and Massimo Antonelli[1,2]

30 COVID-19 ARDS patients matched to 30 ARDS controls in Italy



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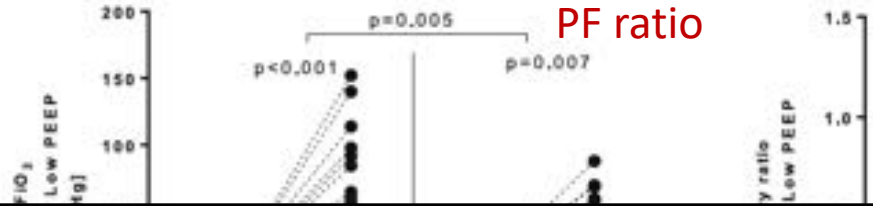
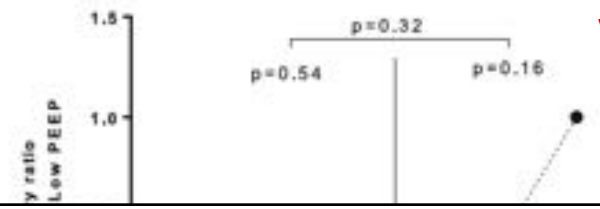
30 COVID-19 ARDS patients matched to 30 ARDS controls in Italy

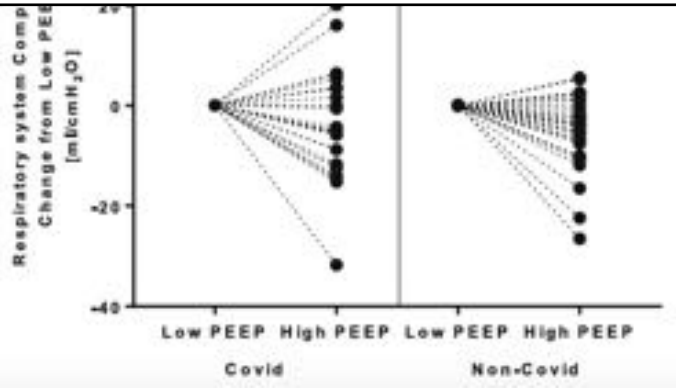
PF ratio

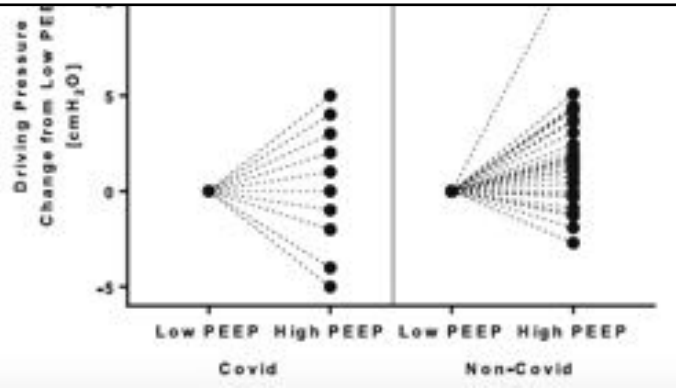


Ventilatory ratio



Conclusions: Early after establishment of mechanical ventilation, COVID-19 patients follow ARDS physiology, with compliance reduction related to the degree of hypoxemia, and inter-individually variable respiratory mechanics and recruitability. Physiological differences between ARDS from COVID-19 and other causes appear small.

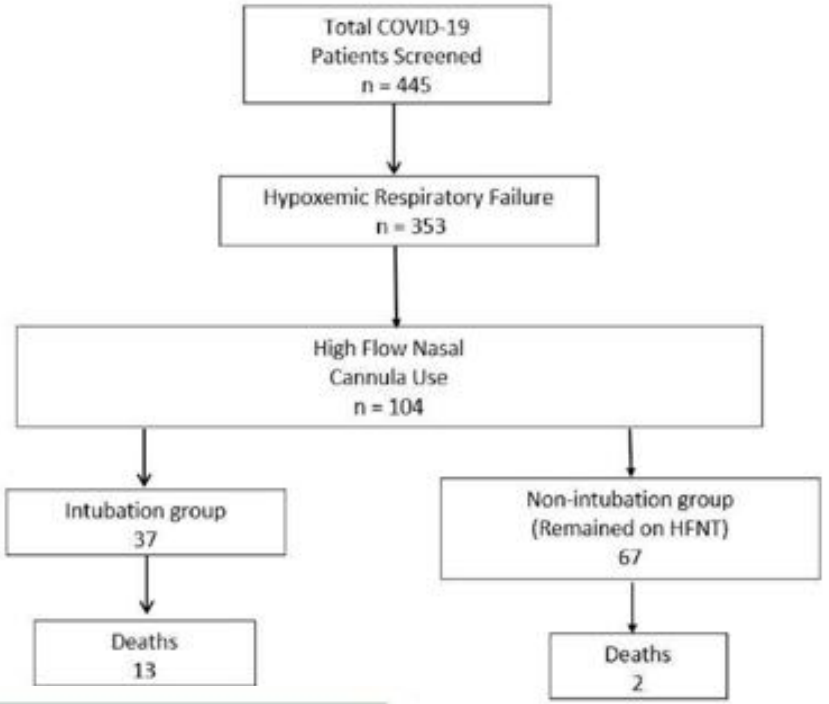




BMJ Open Respiratory Research

Retrospective analysis of high flow nasal therapy in COVID-19-related moderate-to-severe hypoxaemic respiratory failure

Maulin Patel,[1] Andrew Gangemi,[1] Robert Marron,[1] Junad Chowdhury,[1] Ibraheem Yousef,[1] Matthew Zheng,[1] Nicole Mills,[1] Lauren Tragesser,[2] Julie Giurintano,[2] Rohit Gupta,[1] Matthew Gordon ,[1] Parth Rali,[1] Gilbert D'Alonso,[1] David Fleece,[3] Huaqing Zhao,[1] Nicole Patlakh,[1] Gerard Criner[1]



Retrospective study of adults with COVID-19 receiving HFNC at Temple U

Table 4 Comparing outcomes between intubation and non-intubation groups

Outcomes	Intubation	Non-intubation	P value
Mortality	13 (35.1%)	2 (2.9%)	0.0018
Hospital LOS (days)	13.67 (±7.97)	9.7 (±4.6)	0.03
ICU LOS (days)	10.45 (±6.12)	4.05 (±2.64)	0.0008
HAP/VAP incidence	3 (8.57%)	0	0.017
Change in SF ratio	40.5 (±67.90)	141.4 (±117.14)	0.0001
Change in CXR RALES	−0.13 (±11.18)	−3.2 (±8.50)	0.09
Change in HR (beats/min)	−7.65 (±20.69)	−7.95 (±19.19)	0.94
Change in RR (breaths/min)	−2.32 (±9.32)	−4.4 (±8.39)	0.27

Timing of Intubation and Mortality Among Critically Ill Coronavirus Disease 2019 Patients: A Single-Center Cohort Study

DOI: 10.1097/CCM.0000000000004600

Alfonso C. Hernandez-Romieu, MD, MPH[1]; Max W. Adelman, MD, MSc[1]; Maxwell A. Hockstein, MD[2,3]; Chad J. Robichaux, MPH[4,5]; Johnathan A. Edwards, MSPH[4,5]; Jane C. Fazio, MD[6]; James M. Blum, MD[2,3,4,5]; Craig S. Jabaley, MD[2,3]; Mark Caridi-Scheible, MD[2,3]; Greg S. Martin, MD, MSc[3,7]; David J. Murphy, MD, PhD[3,7,8]; Sara C. Auld, MD, MSc[3,7,8]; and the Emory COVID-19 Quality and Clinical Research Collaborative

- Retrospective study of adults with COVID-19 in 4 ICUs in Atlanta
  - 109 of 231 treated with HFNC: 78 of 109 intubated
  - 97 patients intubated without HFNC trial
- Mortality did not differ by time to intubation (≤8h, 8-24h, or ≥24h)
- No difference in duration of MV or ICU LOS by timing of intubation
- HFNC use was not associated with mortality

RESEARCH LETTER

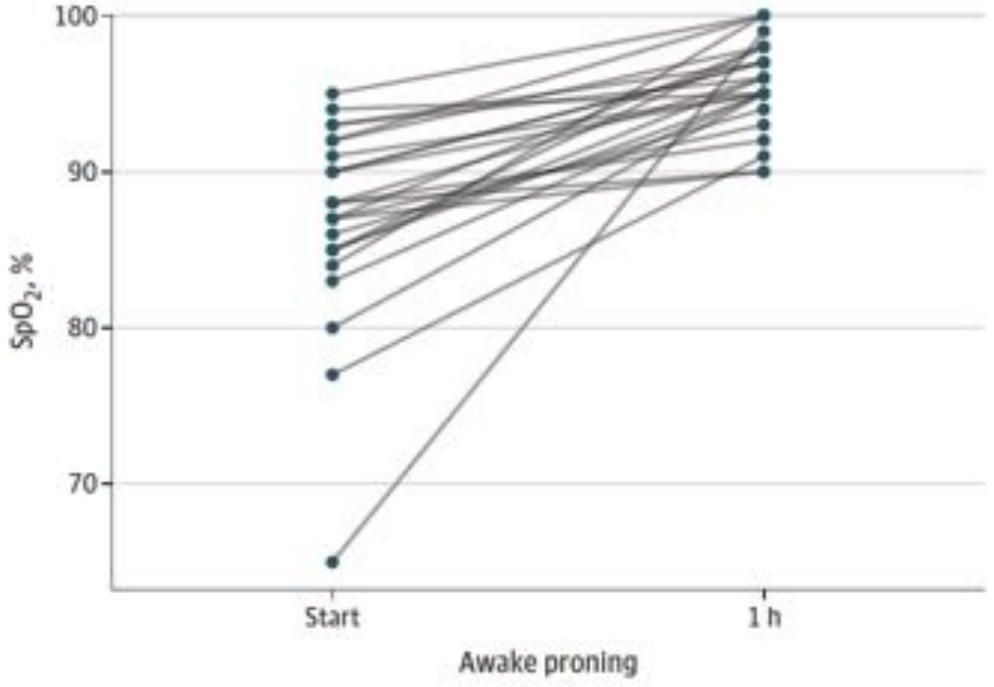
JAMA Internal Medicine Published online June 17, 2020

Prone Positioning in Awake, Nonintubated Patients With COVID-19 Hypoxemic Respiratory Failure

Alison E. Thompson, MD
Benjamin L. Ranard, MD
Ying Wei, PhD
Sanja Jelic, MD

- Cohort study of adults with COVID-19 at Columbia Univ in step-down unit
- 29 eligible patients – 4 refused prone positioning and were intubated
- After 1hr of prone positioning, 19 patients had SpO2≥95%
- 7 patients (37%) intubated after proning
- 5 of 6 with SpO2<95% after 1h were intubated

Figure. Oxyhemoglobin Saturation (Spo_2) 1 Hour After Initiation of the Prone Position in Awake, Nonintubated Patients With COVID-19



Spo_2 before and 1 h after initiation of the prone position in awake, nonintubated patients with COVID-19 severe hypoxemic respiratory failure (n = 25).

Extracorporeal Membrane Oxygenation Support in Severe COVID-19

Annals of Thoracic Surgery 2020

Running Head: ECMO Support in Severe COVID-19

*Zachary N. Kon MD[1], *Deane E. Smith MD[1], Stephanie H. Chang MD[1], Ronald M. Goldenberg MD[2], Luis F. Angel MD[2], Julius A. Carillo MD[1], Travis C. Geraci MD[1], Robert J. Cerfolio MD MBA[1], Robert A. Montgomery MD PhD[3], Nader Moazami MD[1], Aubrey C. Galloway MD[1]

- Retrospective study of critical COVID-19 adults at NYU Langone Health
- 77 of 321 intubated patients evaluated for ECMO, 27 (8.4%) placed on ECMO
- All 27 treated with VV-ECMO support
- 48% remain on ECMO, 48% successfully decannulated, 1 death
- Cannulation in the ICU
  - Percutaneous R femoral venous drainage and RIJ venous return cannulae
  - PIP<25, PEEP 10-14, RR≤16, vent FiO2≤0.40, oxygenator FiO2 = 1.0
  - BAL used for secretion clearance
  - Early tracheostomy within 3d of ECMO cannulation

NIH COVID-19 Treatment Guidelines: Infection Control

- Recommend use of N95 or PAPR plus gloves, gown, eye protection for HCWs performing AGPs on patients with COVID-19
- Recommend endotracheal intubation is performed by HCWs with extensive airway management experience, if possible
- Recommend intubation performed using video laryngoscopy, if possible

NIH COVID-19 Treatment Guidelines: Ventilatory Support

- Recommend HFNC over NIPPV for acute hypoxemic respiratory failure despite conventional O2 therapy
  - Trial of NIPPV if no indication for intubation and HFNC not available
- Recommend trial of awake prone positioning for persistent hypoxemia if no other indication for intubation
  - Recommend AGAINST awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise require intubation/IMV
- Recommend low VT ventilation (4-8mL/kg predicted body weight)
- Recommend prone for 12-16h/day for mechanically ventilated patients
- Recommend using an inhaled pulmonary vasodilator as rescue therapy
- Insufficient data to recommend for or against routine use of ECMO

Position Paper for the State-of-the-Art Application of Respiratory Support in Patients with COVID-19

Respiration
DOI: 10.1159/000509104

Received: May 29, 2020
Accepted: May 29, 2020
Published online: June 19, 2020

German Respiratory Society

Michael Pfeifer[a–c] Santiago Ewig[d] Thomas Voshaar[e]
Winfried Johannes Randerath[f, g] Torsten Bauer[h] Jens Geiseler[i]
Dominic Dellweg[j] Michael Westhoff[k, l] Wolfram Windisch[l, m]
Bernd Schönhofer[n] Stefan Kluge[o] Philipp M. Lepper[p]

- Key statement 3.1: Open or vented systems can increase release of respiratory particles, closed systems are safe/do not increase aerosol formation
- Key statement 3.2: Closed suction should be used for ETT or trach tube, exhaled air should be filtered with filter in expiratory limb
- Finding 3.2: HFNC extends aerosol reach by several centimeters. Relevant increased release of infectious aerosols has not been demonstrated.
- Finding 3.3: Nebulizers increase amount of aerosol in air, but do not increase risk of infection for staff. Inhalation of saline reduces aerosol release from lungs.

Position Paper for the State-of-the-Art Application of Respiratory Support in Patients with COVID-19

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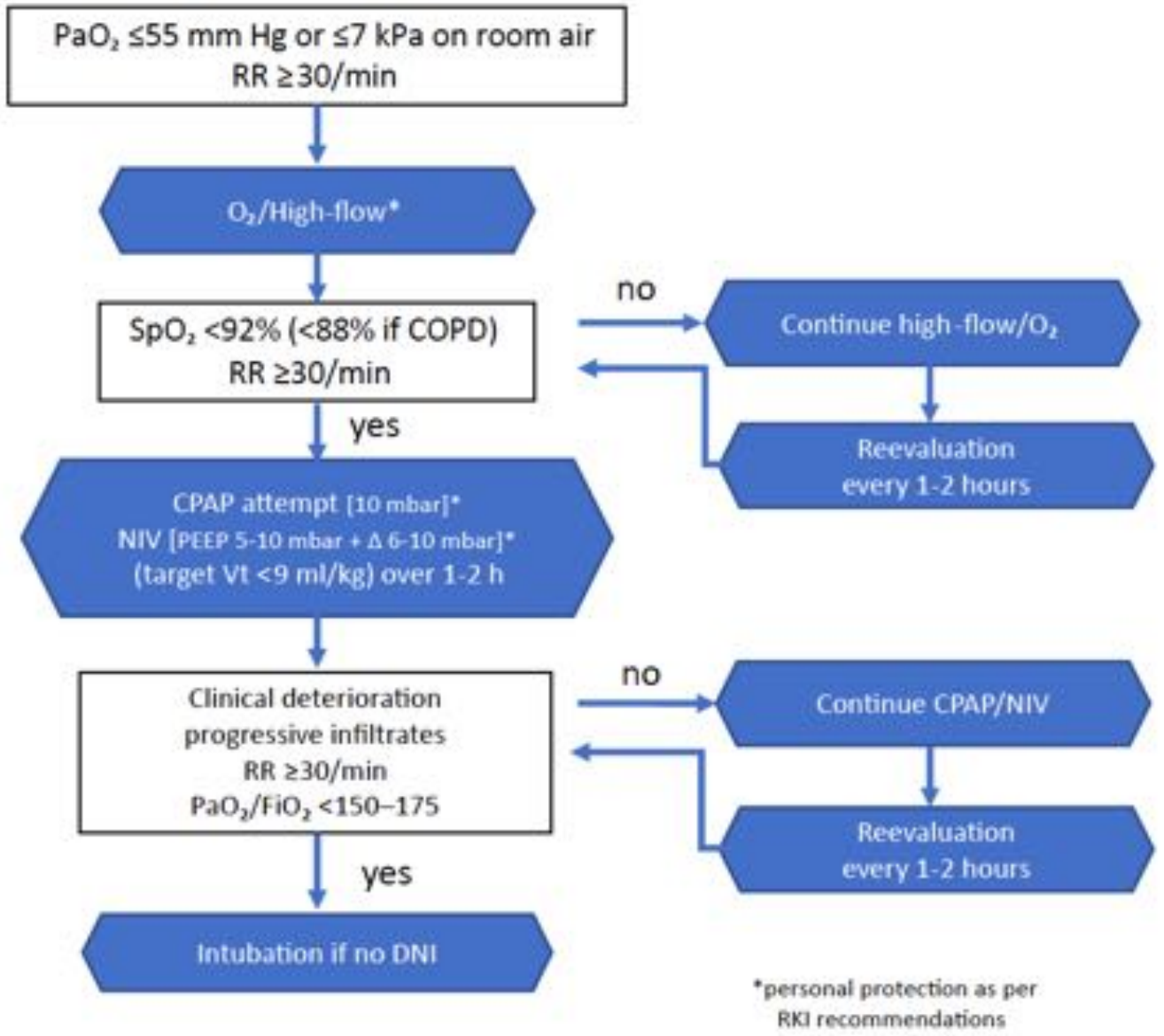
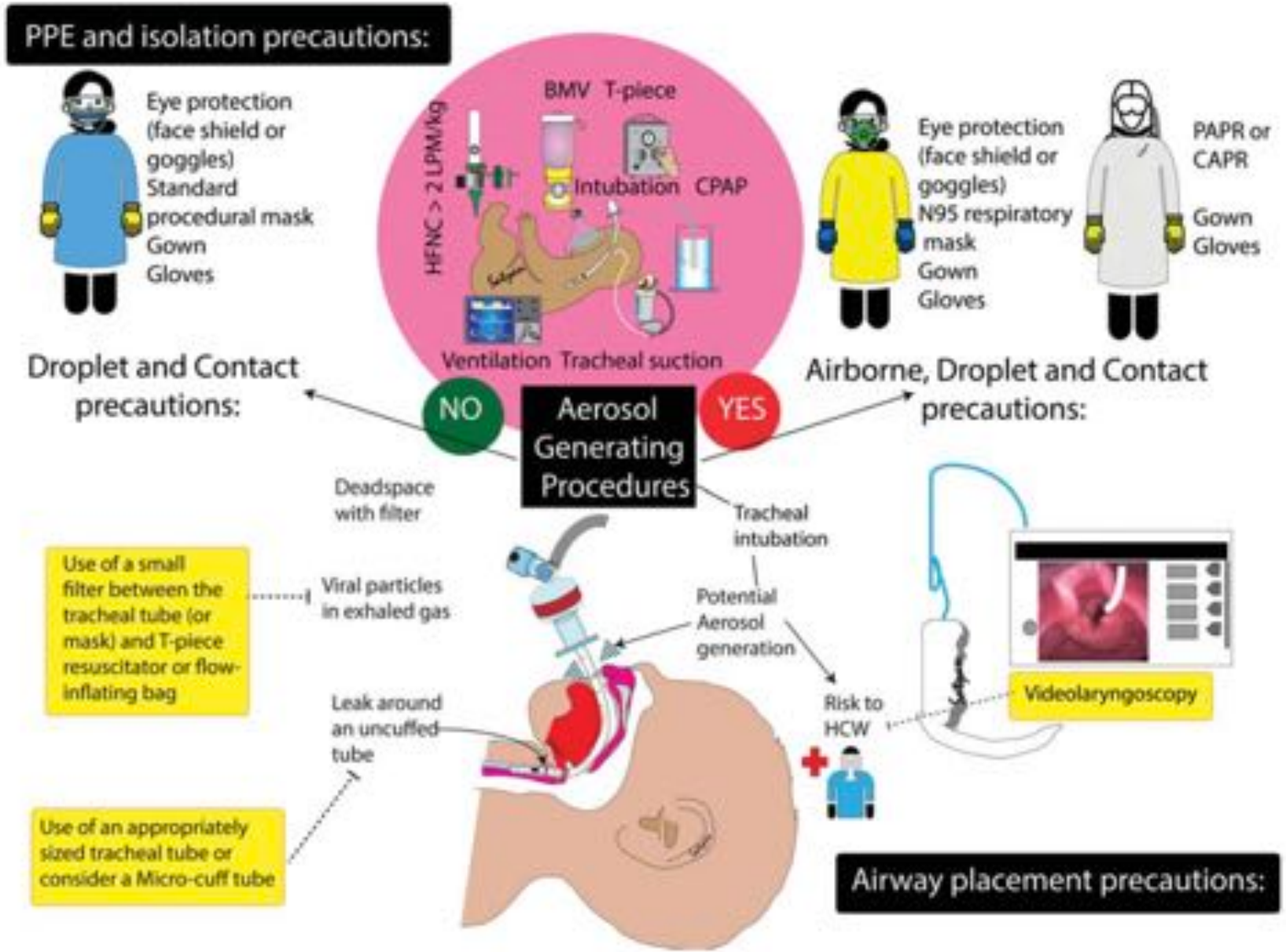


COVID-19 and Neonatal Respiratory Care: Current Evidence and Practical Approach

Wissam Shalish, MD[1]



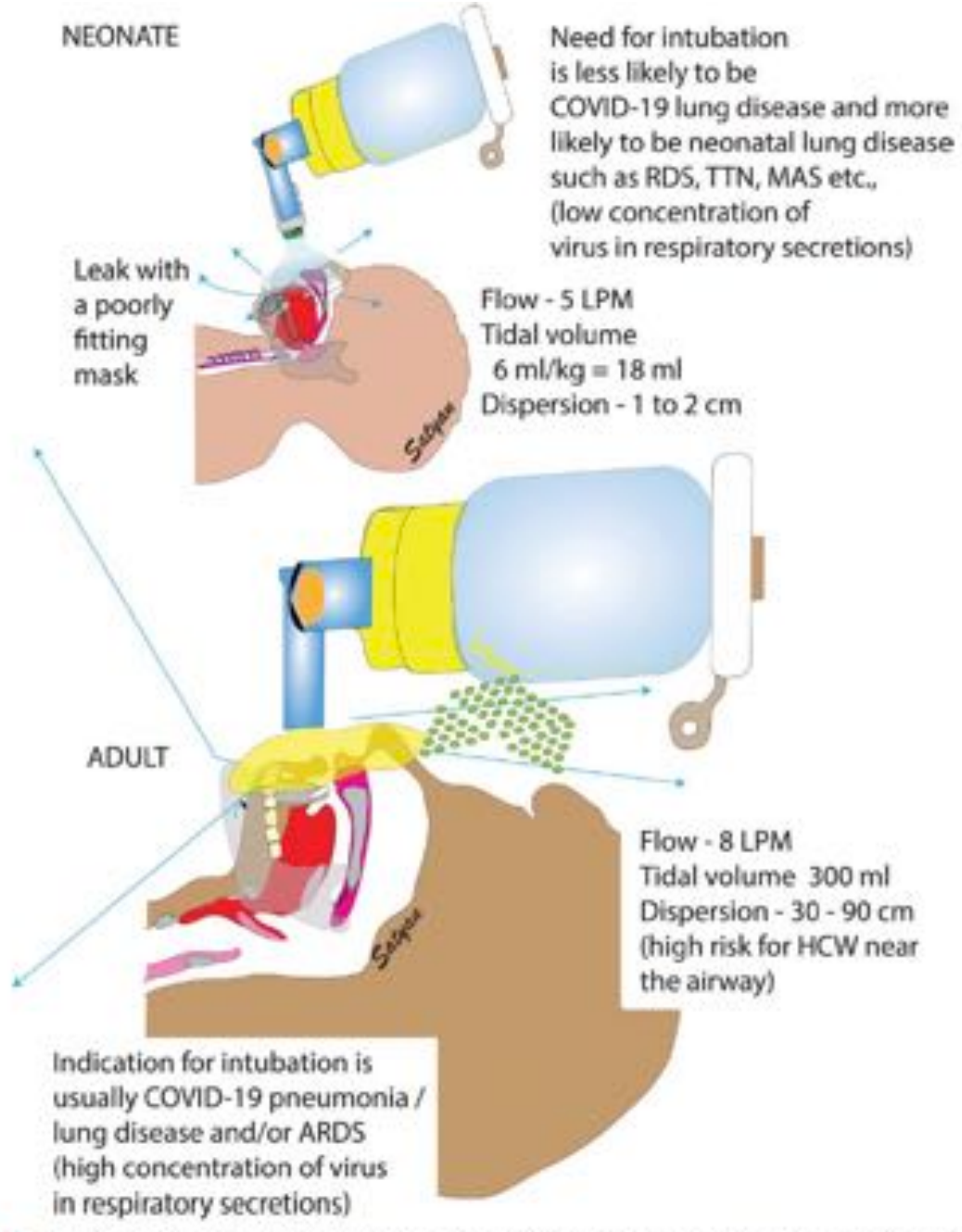


Fig. 3 Differences between neonatal and adult aerosol dispersion during bag-mask ventilation. The area of dispersion is much lower in neonates due to lower airflow and smaller tidal volumes. However, a poorly fitting mask can enhance air-leak. ARDS, acute respiratory distress syndrome; COVID-19, novel coronavirus disease 2019; HCW, health care workers; LPM, liters per minute; MAS, Meconium aspiration syndrome; RDS, respiratory distress syndrome; TTN, transient tachypnea of the newborn. (*Image courtesy*: Satyan Lakshminrusimha)

Pharmacologic Therapies

Focus on remdesivir and corticosteroids

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

- NIH-funded randomized, double blind, placebo controlled trial
- Hospitalized adults
- Primary outcome: time to recovery (category 1-3 on ordinal scale)

Definition of Recovery:

1-not hospitalized, no activity limits

2-not hospitalized, activity limits or home O2 requirement

3-hospitalized, not requiring O2 or ongoing medical care

4-hospitalized, not requiring supplemental oxygen but requiring ongoing medical care

5-hospitalized, receiving any supplemental oxygen

6-hospitalized, receiving non-invasive mechanical ventilation or HFNC

7-hospitalized, receiving invasive mechanical ventilation or ECMO

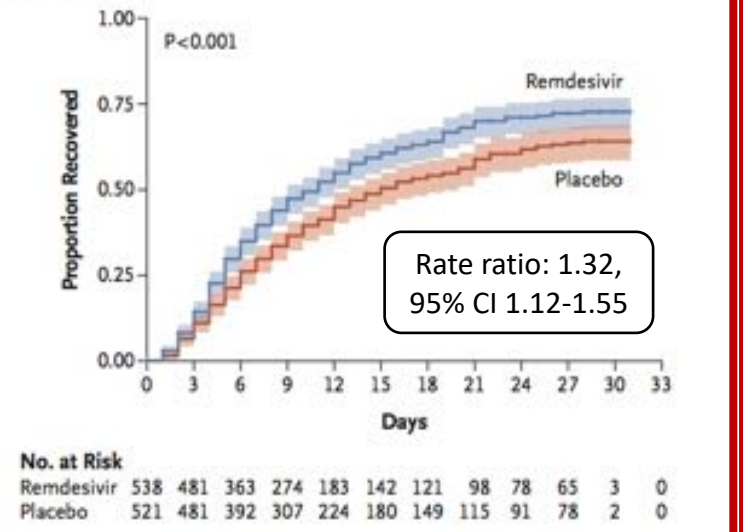
8-death

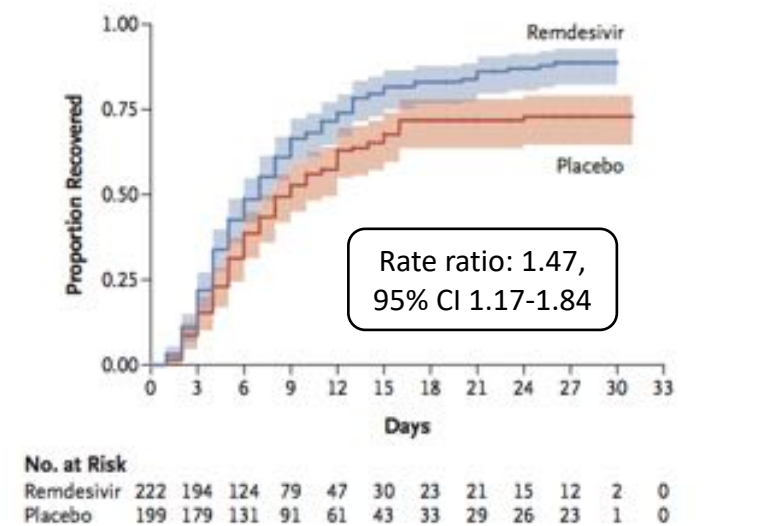
Beigel JH, et al. *New Engl J Med;* epub.

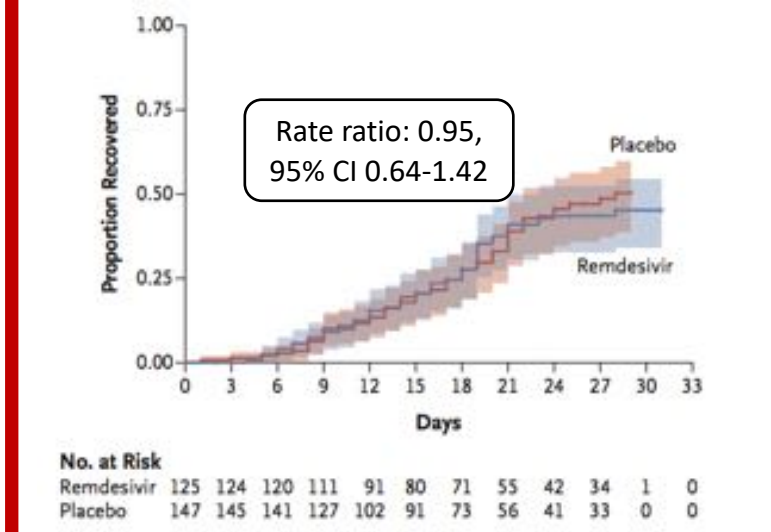
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report







Beigel JH, et al. *New Engl J Med;* epub.

Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report

DOI: 10.1056/NEJMoa2021436

The RECOVERY Collaborative Group*

Open label randomized trial

Intervention: dexamethasone 6 mg daily for up to 10 days + usual care (n=2104)

Control: Usual care only (n=4321)

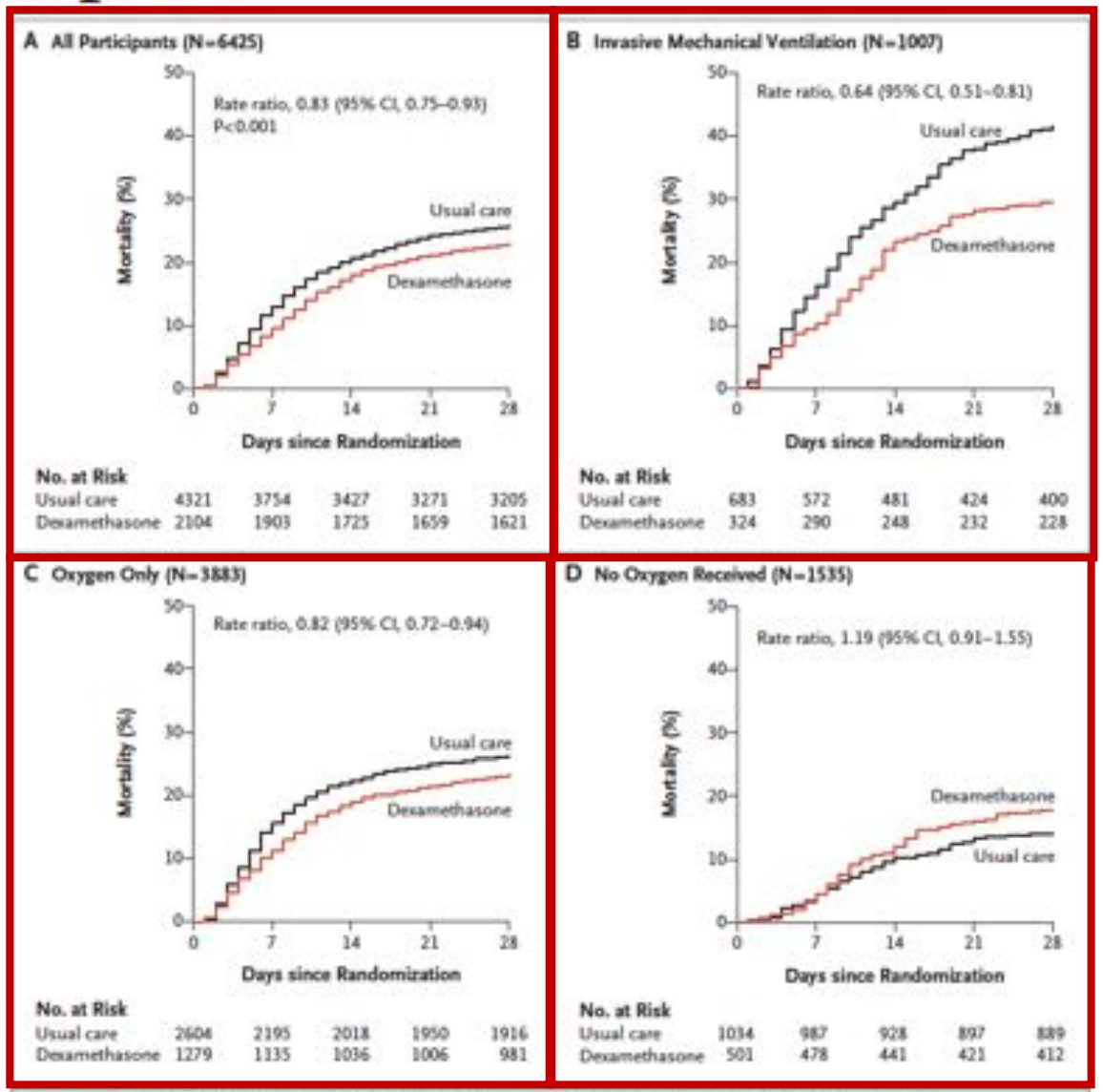


Figure 2. Mortality at 28 Days in All Patients and According to Respiratory Support at Randomization.

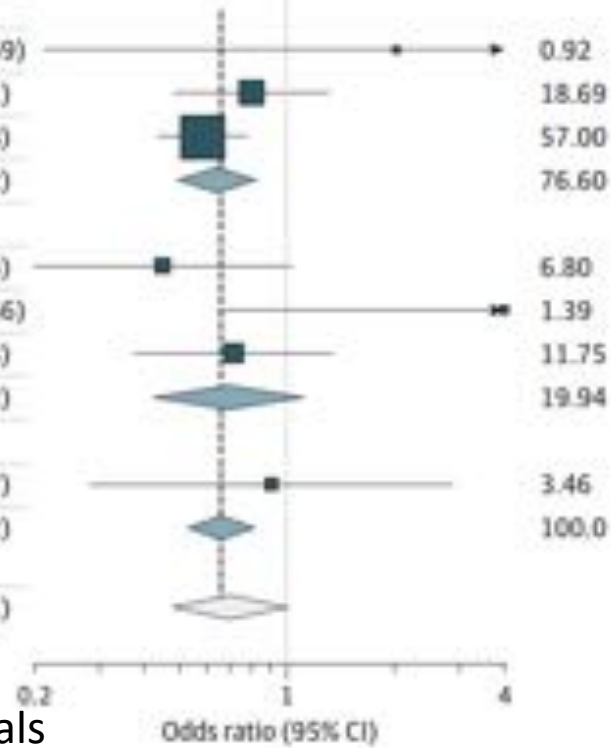
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19
A Meta-analysis

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

Figure 2. Association Between Corticosteroids and 28-Day All-Cause Mortality in Each Trial, Overall, and According to Corticosteroid Drug

Drug and trial	ClinicalTrials.gov identifier	Initial dose and administration	No. of deaths/total No. of patients: Steroids	No. of deaths/total No. of patients: No steroids	Odds ratio (95% CI)	Weight, %
Dexamethasone						
DEXA-COVID 19	NCT04325061	High: 20 mg/d intravenously	2/7	2/12	2.00 (0.21-18.69)	0.92
CoDEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)	18.69
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/324	283/683	0.59 (0.44-0.78)	57.00
Subgroup fixed effect			166/459	361/823	0.64 (0.50-0.82)	76.60
Hydrocortisone						
CAPE COVID	NCT02517489	Low: 200 mg/d intravenously	11/75	20/73	0.46 (0.20-1.04)	6.80
COVID STEROID	NCT04348305	Low: 200 mg/d intravenously	6/15	2/14	4.00 (0.65-24.66)	1.39
REMAP-CAP	NCT02735707	Low: 50 mg every 6 h intravenously	26/105	29/92	0.71 (0.38-1.33)	11.75
Subgroup fixed effect			43/195	51/179	0.69 (0.43-1.12)	19.94
Methylprednisolone						
Steroids-SARI	NCT04244591	High: 40 mg every 12 h intravenously	13/24	13/23	0.91 (0.29-2.87)	3.46
Overall (fixed effect)			222/678	425/1025	0.66 (0.53-0.82)	100.0
$P = .31$ for heterogeneity; $I^2 = 15.6\%$						
Overall (random effects[a])			222/678	425/1025	0.70 (0.48-1.01)	



Overall improved mortality with steroids, primary effect from dexamethasone trials

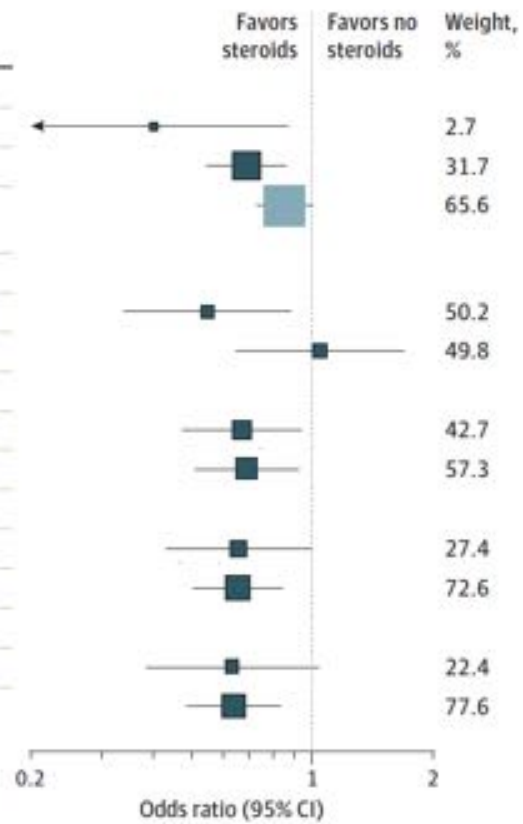
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19
A Meta-analysis

The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

Figure 3. Association Between Corticosteroids and 28-Day All-Cause Mortality Within Subgroups Defined by Patient Characteristics at the Time of Randomization

Subgroup	No. of deaths/total No. of patients: Steroids	No. of deaths/total No. of patients: No steroids	Odds ratio (95% CI)	Weight, %
Invasive mechanical ventilation (IMV)				
No (I^2 = 0%)	14/70	28/74	0.41 (0.19-0.88)	2.7
Yes (I^2 = 44.1%)	208/608	397/951	0.69 (0.55-0.86)	31.7
Oxygen treatment without IMV (RECOVERY)	298/1279	682/2604	0.86 (0.73-1.00)	65.6
Taking vasoactive medication				
No (I^2 = 0%)	51/184	68/184	0.55 (0.34-0.88)	50.2
Yes (I^2 = 0%)	76/169	74/158	1.05 (0.65-1.69)	49.8
Age, y				
≤60 (I^2 = 0%)	72/338	141/483	0.67 (0.48-0.94)	42.7
>60 (I^2 = 49.7%)	150/339	284/541	0.69 (0.51-0.93)	57.3
Sex				
Female (I^2 = 0%)	60/202	106/286	0.66 (0.43-0.99)	27.4
Male (I^2 = 14.7%)	162/476	319/739	0.66 (0.51-0.84)	72.6
Symptomatic, d				
≤7 (I^2 = 69.1%)	51/130	99/211	0.63 (0.39-1.04)	22.4
>7 (I^2 = 0%)	139/418	293/693	0.64 (0.49-0.83)	77.6



Higher impact in IMV vs. O2 group, and perhaps those symptomatic for >7d

How do we apply this to the pediatric patient with COVID-19?

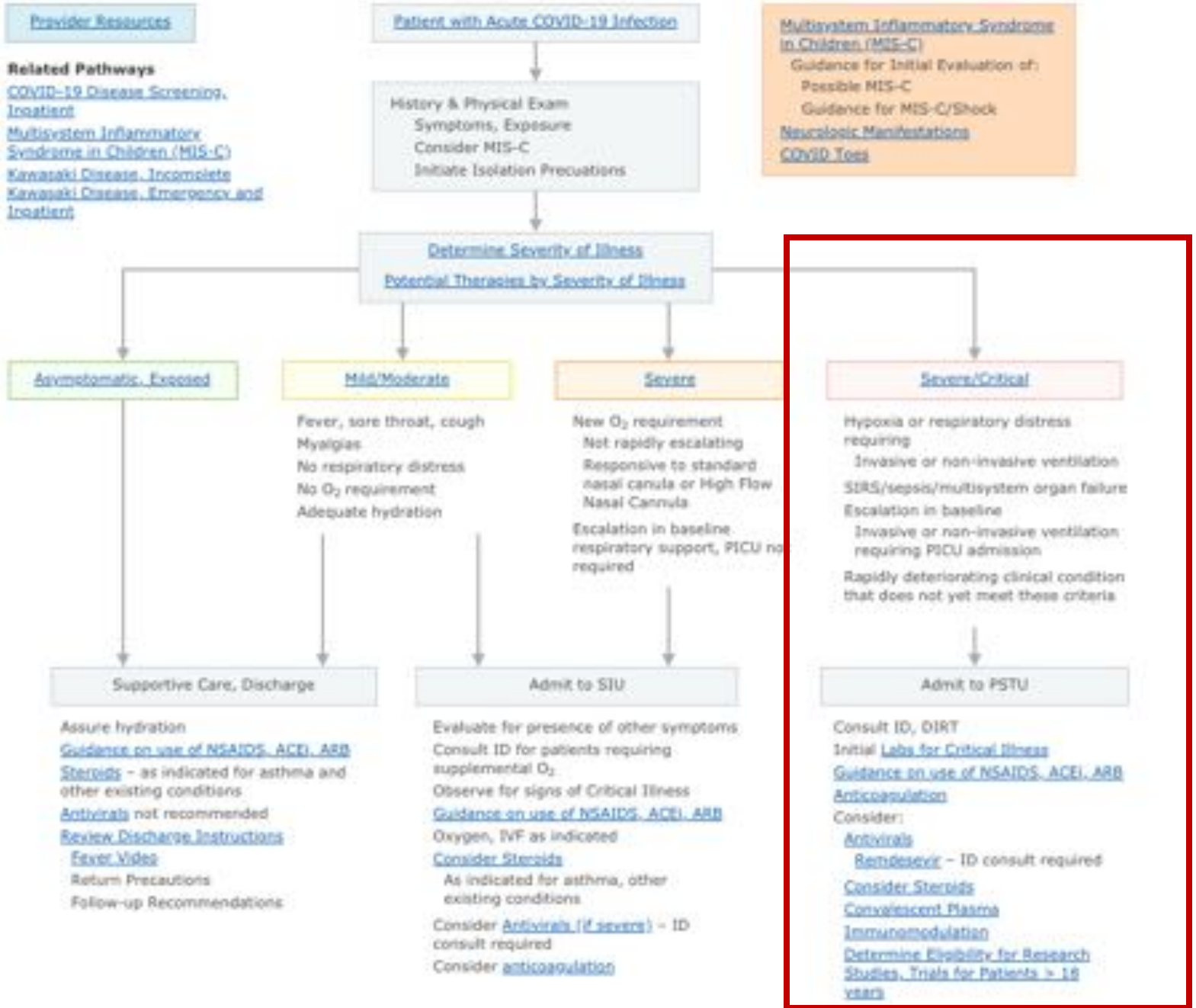
Supportive Care for the Critically Ill Pediatric Patient with COVID-19 (Disclaimer)

- Recommended cornerstone of treatment of COVID-19 in children is supportive care.

- There are no high-quality data supporting the efficacy of any antiviral medication, immunomodulatory agent, or convalescent plasma in children with COVID-19.

- The overwhelming majority of children with COVID-19 recover with supportive care alone.

Clinical Pathway for Evaluation and Treatment of Patients with Active COVID-19 Infection



Our Institutional Guidance on AGPs and Application of Filters

- We have developed internal guidance on how to mitigate aerosol generating procedures
- The following graphics are an example of one institution's approach to managing patients with (or suspected of having) COVID-19 and requiring mechanical ventilation and other respiratory therapies
- Please use this information as an example for your reference
- Please do not disseminate these graphics

AGP Mitigation

AGPs	Recommendations to Decrease Risk in these Areas
Tracheal Intubation	☐ RSI (induction and NMB given simultaneously) minimizing duration of bag mask ventilation ☐ Most experienced provider ☐ Use of cuffed endotracheal tubes ☐ Use of video laryngoscopy ☐ Minimize personnel in the room. Establish clear roles for those present ☐ Early connection to ventilator
Extubation	☐ Increase the FiO_2 on the ventilator prior to procedure ☐ Avoid manual ventilation prior to removing the endotracheal tube ☐ If the plan is to extubate to NIV, refer to NIV as AGP (see below) ☐ Minimize personnel in the room. Establish clear roles for those present
Elective airway manipulation and airway care (tracheostomy care and securement of airway)	☐ Avoid routine tracheostomy tube and endotracheal tube changes ☐ If patient has uncuffed tracheostomy tube, consider replacement with cuffed tube ☐ Tighten all connections to airway prior to performing routine care
Bronchoscopy	☐ COVID-19 Testing should be completed before bronchoscopy ☐ Routine bronchoscopy should not be performed unless there is a high likelihood of therapeutic benefit (e.g. identification of bacterial superinfection)
Deep Suctioning (defined as the passing of a suction catheter beyond the naso- or oropharynx) in non-tracheostomy dependent patients	☐ Avoid induced sputum techniques
Manual ventilation with mask or artificial airway with or without chest compressions	☐ Place filter in line with the flow-inflating or self-inflating bag ☐ Minimize duration of bag mask ventilation and consider early endotracheal intubation and connection to a ventilator
NIV (CPAP,BiPAP, mouthpiece ventilation)	☐ If using NIV strongly recommend placement of filter between patient interface and ventilator circuit ☐ Use non-vented, full face (e.g., scuba, nose/mouth covered) masks when possible (assess tolerance). ☐ Consider using disposable exhalation valve with side port for filtering in single limb circuits in smaller patients (< 10kg) where a filter between patient interface and circuit may impair triggering or cause excessive dead space

Summary:

Minimize personnel in room

Minimize time providing bag ventilation

- RSI
- Early connection to ventilator

Minimize tube changes

Use filters

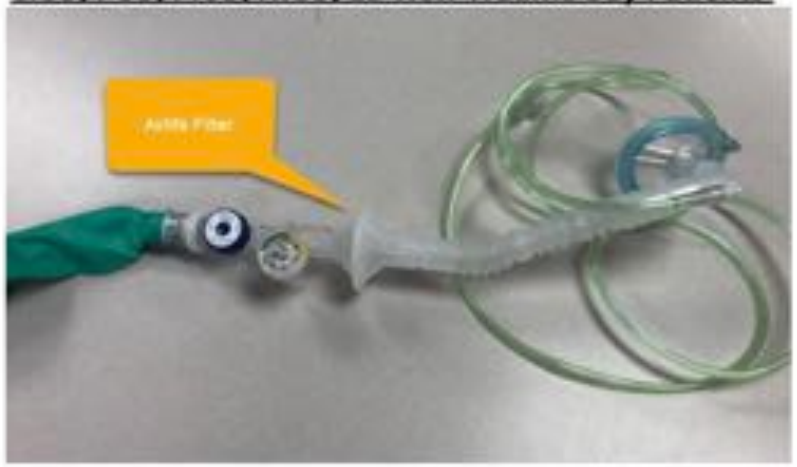
Use cuffed tubes

Use non-vented, full face masks for NIV

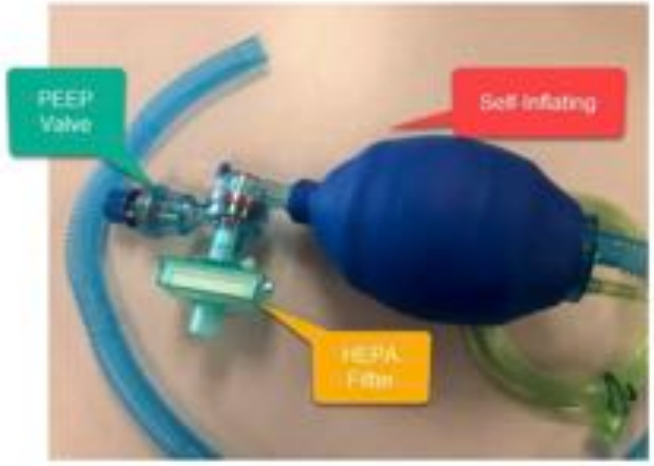
Filter Placement for Bag Mask Ventilation

ED Trauma Bay, SDU

CICU, PCU, PICU, NICU, ED Non-Trauma Bay Patients

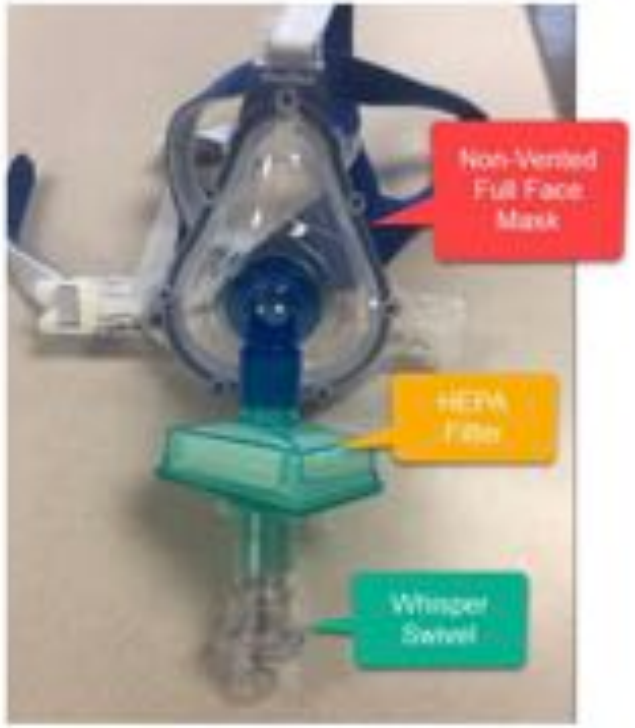


If ventilating with a self-inflating bag, use an expiratory filter.



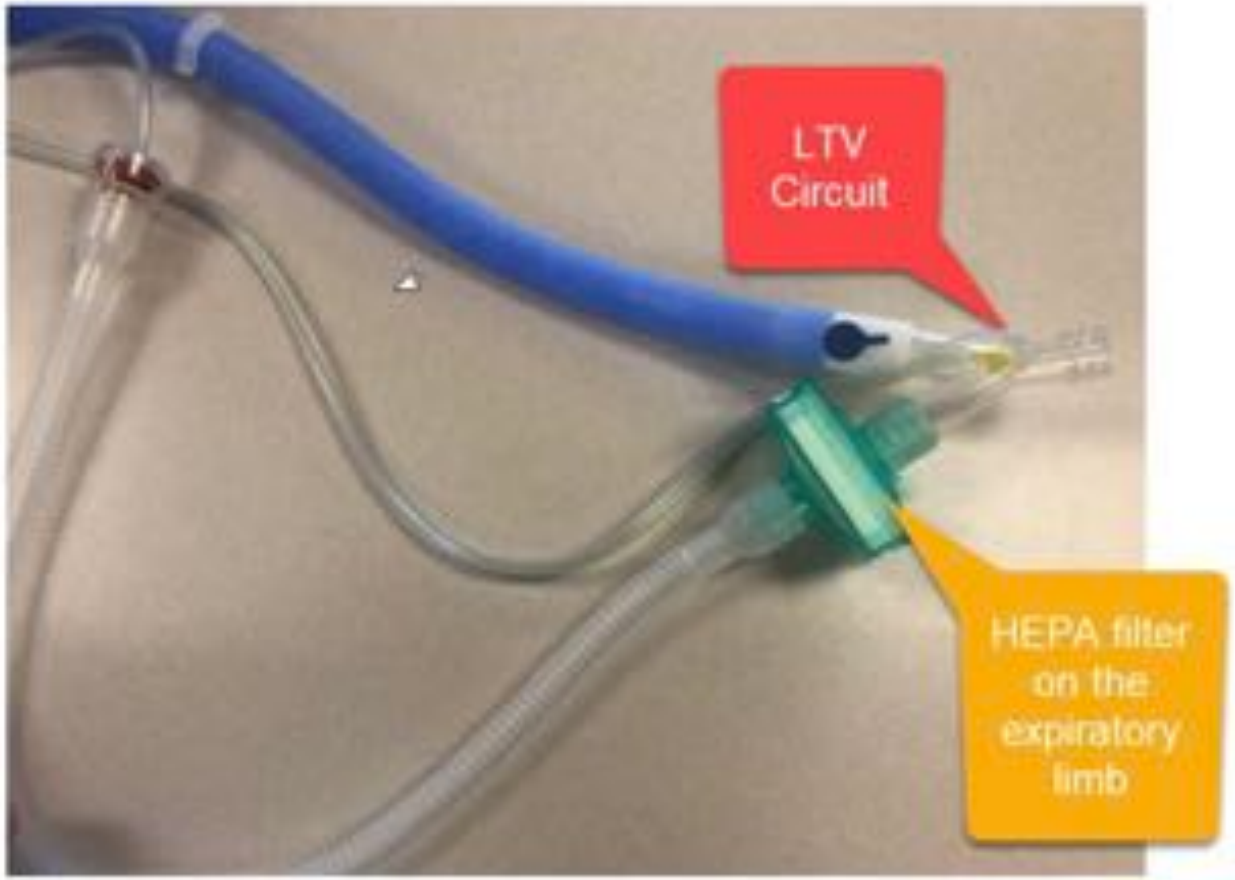
Filter Placement for NIV Interfaces

- Use non-vented, full face (e.g., scuba, nose/mouth covered) masks.
- The delivery of continuous albuterol requires a dual-limb circuit (V500).
- Consider using ICU ventilator for NIV (V500, Hamilton) with dual-limb circuit in smaller patients (< 10 kg) where a filter between patient interface and circuit may impair triggering or cause excessive dead space re-breathing. Alternatively, a NIV exhalation port that allows for filtration of exhaled gases may be placed in line with a single limb circuit.

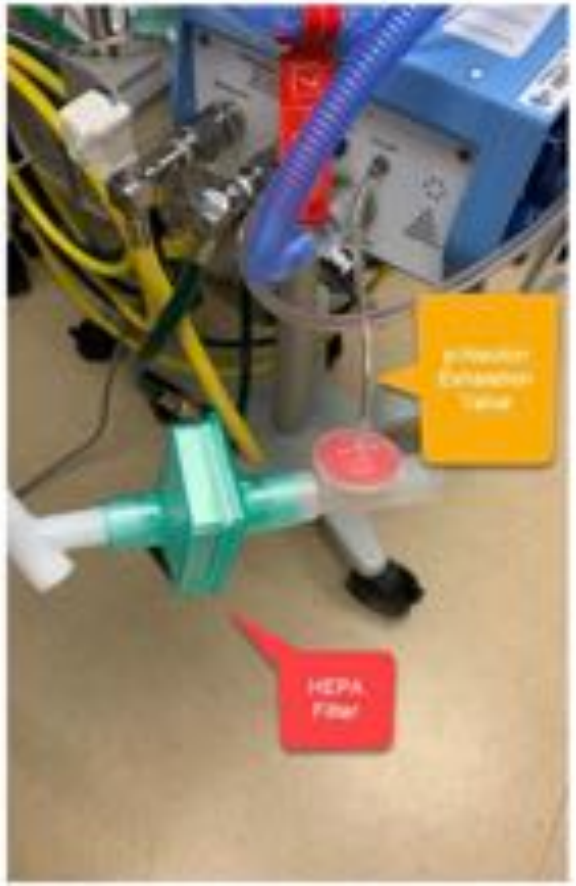


Filter Placement for LTV or HFJV

LTV

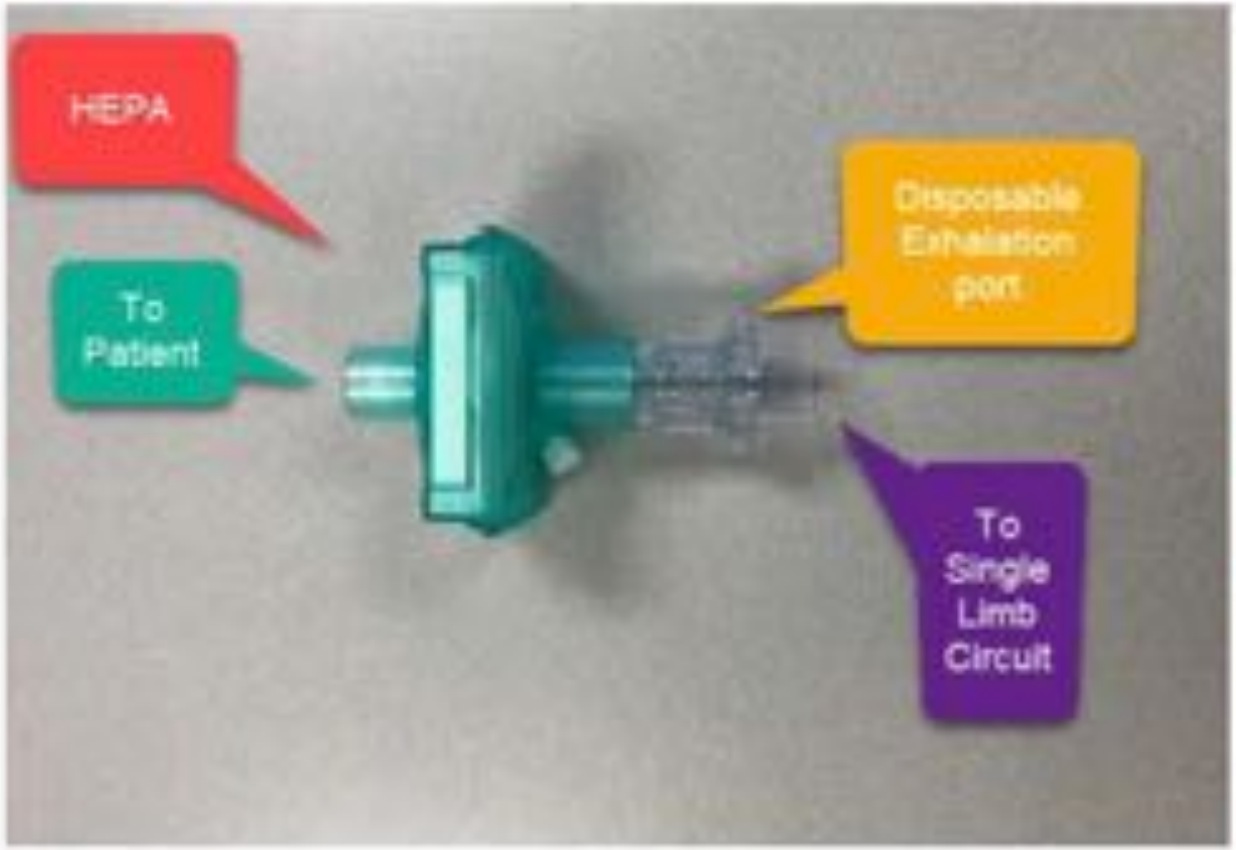


HFJV



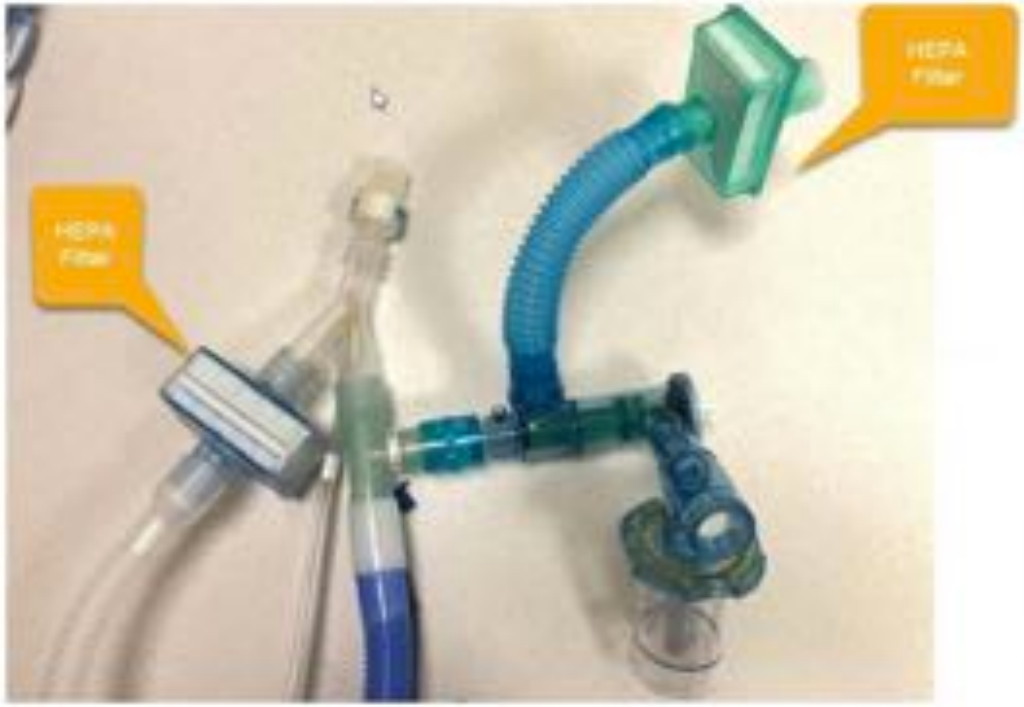
Filter Placement for Astral or Trilogy Vents

Filtering Single Limb Circuit for Astral or Trilogy



Filter Placement for IPV and Cough Assist Device

IPV

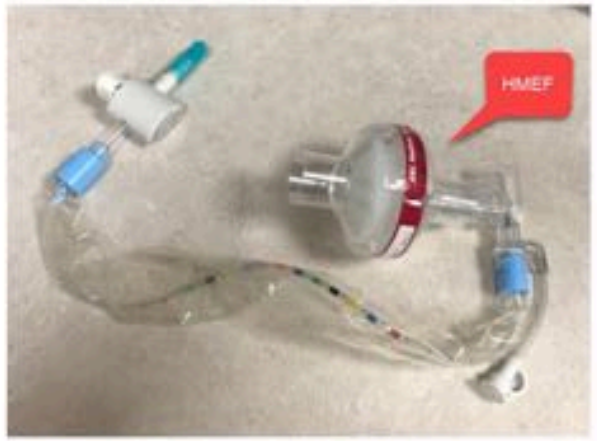


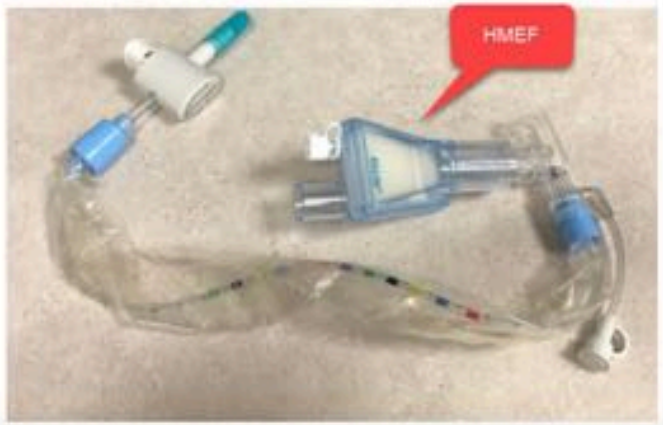
Cough Assist

Filter Placement for Tracheostomy T-Piece

If patient requires humidification via tracheostomy recommend use of t-piece setup. Alternatively, use inline suction with HMEF (HME with filtering).

- A filter is placed on the expiratory side of the t-piece setup as shown below.
- Trach collar should not be used.





Airway Bundle Checklist (FRONT and BACK) FOR COVID-19

Date: _____ [Place patient sticker/stamp here]

Time: _____

Front page completed (check all that apply):

☐ On admission ☐ During/after rounds ☐ Prior to intubation ☐ After intubation

Assessment for ANTICIPATED Airway Management

Intubation Risk Assessment

Difficult Airway	**History** of difficult airway?	YES	NO
	Physical? (e.g. small mouth, small jaw, large tongue, or short neck)	YES	NO
At Risk For:	High risk for rapid **desaturation** during intubation	YES	NO
	Increased ICP, pulmonary hypertension, need to avoid **hypercarbia**	YES	NO
	Unstable hemodynamics (e.g. hypovolemia, potential need for fluid bolus, vasopressor, CPR)	YES	NO
	Other risk factors? _____	YES	NO

Planning (all risk noted above should be considered in plan)

Who will intubate? (Specify primary provider who will perform **first** laryngoscopy):

☐ Fellow ☐ Attending ☐ Anesthesiologist ***Most experienced provider to intubate and minimal providers in the room ***

How will we intubate? *** Recommend oral intubation with a cuffed ETT ***

ETT Size: ☐ 3.0 ☐ 3.5 ☐ 4.0 ☐ 4.5 ☐ 5.0 ☐ 5.5 ☐ 6.0 ☐ 6.5 ☐ 7.0 ☐ 7.5 ☐ 8.0 ☐Other: ____

*** Stylette BOTH the primary and ½ size smaller ETT prior to intubation***

Air-Q LMA at Bedside : ☐ 1.0 ☐ 1.5 ☐ 2.0 ☐ 2.5 ☐ 3.5 ☐ 4.5

Device: ☐CMAC ☐ Laryngoscope ☐ Glidescope _____ ☐Other: _____

Blade: ☐ Mac _____ ☐ Miller _____ ☐ Wis-Hipple

Meds: ☐ Atropine ☐ Glycopyrrolate
☐ Fentanyl ☐ Midazolam ☐ Ketamine ☐ Propofol
☐ Rocuronium ☐ Vecuronium

*** Use of RSI recommended - Have 10 mcg/ml Epinephrine and extra doses of all meds drawn up and in room ***

Apneic Oxygenation: YES / NO _____ L/min (<1y = 5L; 1-7y = 10L; ≥ 8y = 15L)

When will we intubate? (Describe the timing of airway management):

☐ Prior to procedure at:_____ ☐ Mental Status Changes ☐ Hypoxemia refractory to CPAP: SpO2 < _____%

☐ Ventilation failure refractory to NIV ☐ Loss of Airway Protection ☐Other: _____

Pharmacologic therapies for pediatric COVID-19

Recommend	
Suggest	
Should consider	Remdesivir for patients requiring supplemental O2, mechanical ventilation, or ECMO Steroids in mechanically ventilated patients Prophylactic dosing anticoagulation
Could consider	Steroids in patients requiring supplemental oxygen Convalescent plasma IL-6 blockade, IL-1 blockade
Suggest against	Hydroxychloroquine or chloroquine* Hydroxychloroquine or chloroquine with or without azithromycin* Lopinavir-ritonavir* **Steroids in patients not requiring oxygen (unless there is another indication)*** JAK inhibitors*
Recommend against	

*If used, use should be limited to clinical trials

These recommendations are based on expert opinion, primarily derived from adult data.

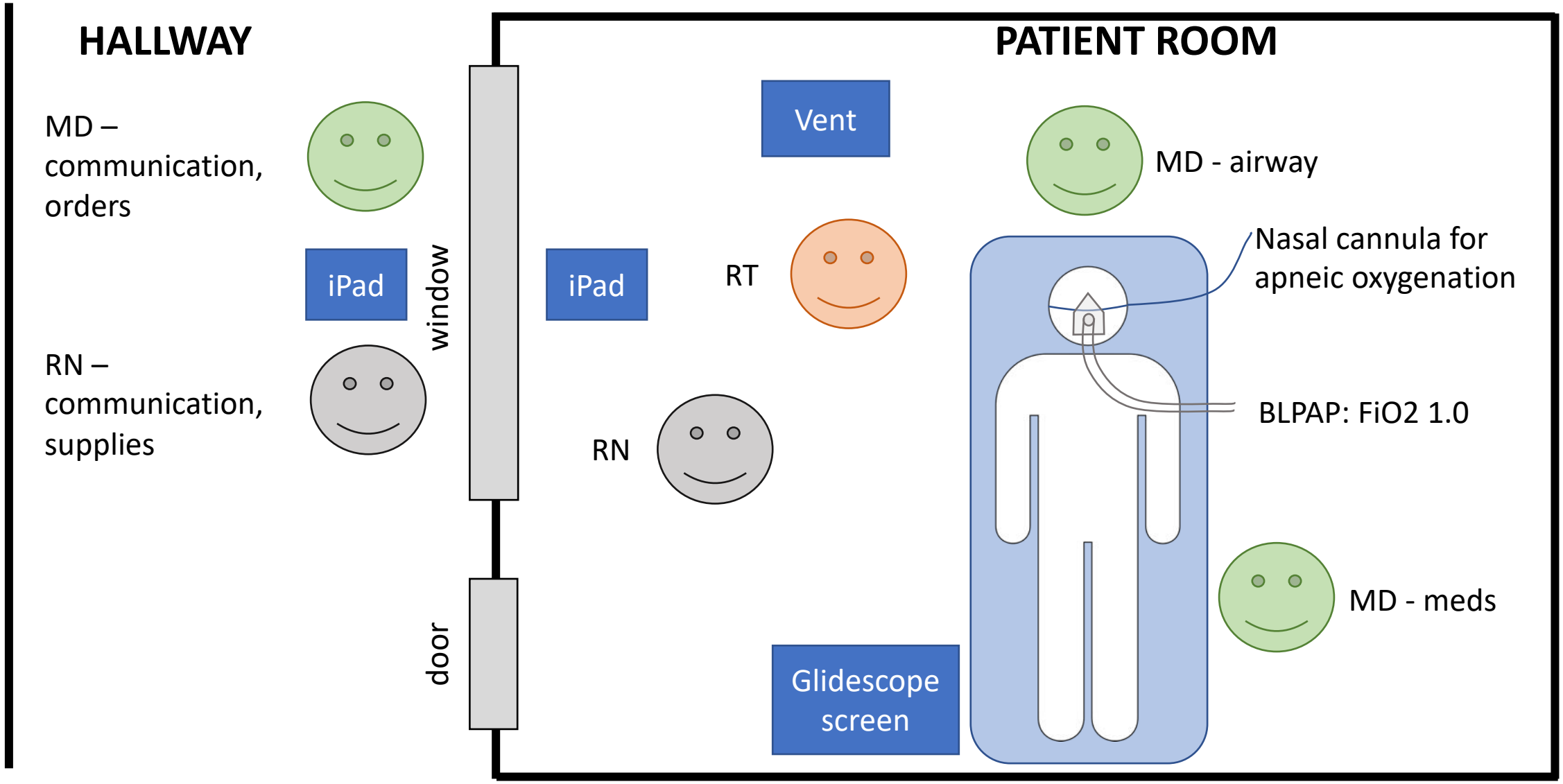
Case Presentation 1

- 15yo female with chronic neurological disorder, neuromuscular scoliosis, nighttime BiPAP dependence (16/6, 2L O_2), difficult airway
- 4 days of cough, respiratory distress, increased secretions, fever
- SARS-CoV-2 positive, other pathogens negative
- ED course: moderate respiratory distress, T 40ºC
  - 7.15/78/27/-4, lactate 4.9
  - BiPAP increased to 20/10, FiO2 0.55 -> 7.27/50/23/-5, lactate 3.4, SpO2 94%
- Admitted to PICU
  - Initial exam: moderate respiratory distress, RR 65, tachycardic HR 128

Initial Supportive Care for Case 1

- PICU arrival: BiPAP 20/10, FiO2 0.55, SpO2 94%, VBG 7.27/50/23/-5, lactate 3.4, POC glucose 308
- Intubated with glidescope, CVL, arterial line placed
  - Intubator – Anesthesia/CCM provider
  - In room personnel: Airway MD, RT, RN, medication MD
- Vent support: 30/12, exhaled tidal volumes ~6ml/kg, FiO2 weaned to 21% by morning
- Epinephrine infusion for hypotension
- Insulin infusion for hyperglycemia

Case 1 Intubation Room Diagram



Hospital Course for Case 1

- 10d remdesivir started HD1
- Enoxaparin at therapeutic dosing range (changed to prophylaxis after multiple weeks)
- No corticosteroids (met criteria for moderate ARDS in first 24hr, but FiO2 rapidly weaned)
  - Treated before steroid RCTs completed
- Multiple extubation failures (deconditioning), tracheostomy performed (after PCR negative several weeks after presentation)

Case Presentation 2

- 14yo female, ex-27wk prematurity, transferred with COVID-19 ARDS for ECMO evaluation
- Fevers 1 week prior to presentation, followed by cough, then respiratory distress prompting ED visit, hospitalized 2d prior to transfer
- Intubated at referring hospital, managed with iNO and FiO2 1.0, proning, neuromuscular blockade
  - Oxygenation index 40, PCV 40/18 x 20
  - Vasoactive infusions for hypotension
  - Increasing creatinine, fluid overload

Hospital Course for Case 2

- Attempted trial of HFOV – worsened hypoxemia
- Cannulated onto VV-ECMO (DL-RIJ cannula) – 6 day run
- Methylprednisolone for ARDS
- Convalescent plasma and tocilizumab administered
  - Not a candidate for remdesivir due to renal and hepatic dysfunction
- Heparin during ECMO, enoxaparin after ECMO decannulation
- BAL on ECMO day 2 with minimal mucous plugging
- Extubated to BLPAP 4 days after ECMO decannulation, off respiratory support 1 day later

Summary

- Little pediatric data on best practices for ventilation in COVID-19
- Standardize care with pathways/protocols
- Minimize personnel and exposure risks
- Manage according to standard ARDS treatment protocols
- HFNC slightly preferred to NIPPV

Thank you!

Questions?