ARDS: Unlocking the Eight Key Components to Care

Kathleen Vollman
ADVANCING NURSING THROUGH KNOWLEDGE & INNOVATION

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Disclosures

- Consultant-Michigan Hospital Association Keystone Center
- Subject matter expert on CAUTI, CLABSI, HAPI, Sepsis, Safety culture for HRET/AHA
- Consultant and speaker bureau
  - Stryker's Sage business
  - Potrero Medical
- Baxter Advisory Board

Objectives

- Discuss strategies for early recognition of patients with ARDS and explain the pathophysiologic manifestations seen in ARDS
- Apply the 8 P's of supportive evidence-based care practices for patients with ARDS
- Summarize the latest research that demonstrate an impact on short- and long-term outcomes for the ARDS patient.

Surviving **Thriving**

Post Intensive Care Syndrome/ Post COVID Long Haulers

Harvey M, Davidson J. Crit Care Med, 2016;44(2):381-385

The Berlin ARDS Definition

TIMING	Within 1 week of a known clinical insult
CHEST IMAGING (X-RAY OR CAT SCAN)	Bilateral opacities
ORIGIN OF EDEMA	Respiratory failure not fully explained by cardiac failure or fluid overload

	MILD	MODERATE	SEVERE
OXYGENATION	<200 PaO_2/FiO_2 or ≤300 with PEEP/CPAP ≥5 cm H_2O	<100 PaO_2/FiO_2 or ≤200 with PEEP ≥5 cm H_2O	≤100 PaO_2/FiO_2 with PEEP ≥5 cm H_2O
MORTALITY	27% (24% to 30%)	32% (29% to 34%)	45% (42% to 48%)

Ferguson ND, et al. *Intensive Care Med*. 2012;38(10):1573-1582.
Dharia A, et al. *ICU Director*. 2012;3(6):287-292.

A New Global Definition of ARDS

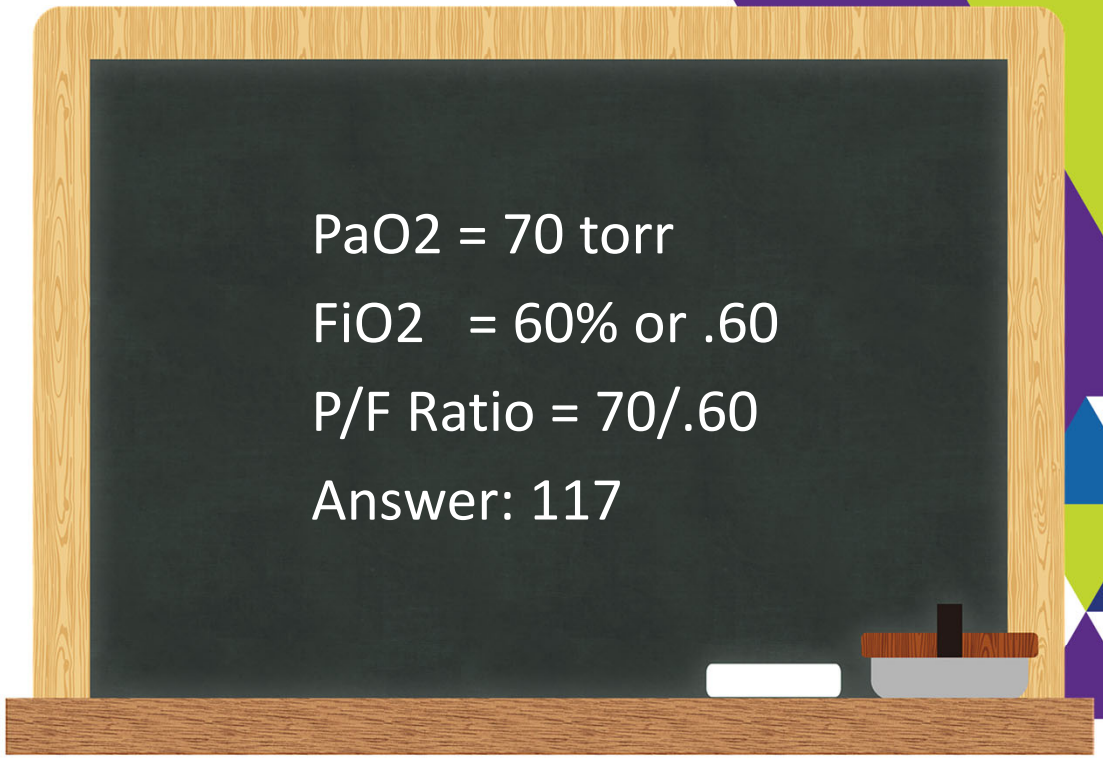
ARDS New Global Definition 2023

new definition criteria	Classification		
	Mild	**Moderate**	**Severe**
Time to instalation	Up to seven days - known risk fator(s)		
Pulmonary edema	Not explained by cardiogenic edema or intravascular volume overload		
Radiologic features	Bilateral infiltrates on chest X-ray or CT or lung ultrasound (by a trained professional) (not explained by nodules, pleural effusion or atelectasis)		
Hypoxemia PaO_2/FIO_2**	201-300 with NIV/CPAP PEEP ≥ 5* **or HFNO > 30l/min**	101 - 200 com PEEP ≥ 5	≤ 100 com PEEP ≥ 5
Hypoxemia SpO_2/FIO_2	**≤ 315 with SpO_2 ≤ 97%**		

Am J Respir Crit Care Med 2023;207:A6229

PaO_2/FiO_2 Ratio

- User friendly tool
- Crude assessment of the severity of lung injury
- Used in the definition of ARDS
  - Mild
  - Moderate
  - Severe



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Am J Respir Crit Care Med 2023;207:A6229

Sub Phenotypes-Help Direct Therapy

- Hypoinflammatory
- Hyperinflammatory

Sub-Phenotypes:
Hypoinflammatory
Hyperinflammatory: ↑ mortality/Vent days

Matthay MA, 2019; Primer 5;18. www.nature.com

Epidemiology, Patterns of Care & Mortality in ICU's in 50 Countries

- Large observational study to understand the global impact of severe acute respiratory failure (LUNG SAFE)
- Winter 2014: Four consecutive weeks
- 459 ICUs from 50 countries across 5 continents
- Primary outcome measure: ARDS incidence
  - Secondary measures: assessment of clinical recognition, application of vent management, use of adjunct interventions and outcomes for ARDS

Bellaini G, et al. JAMA, 2016;315(8):788-800

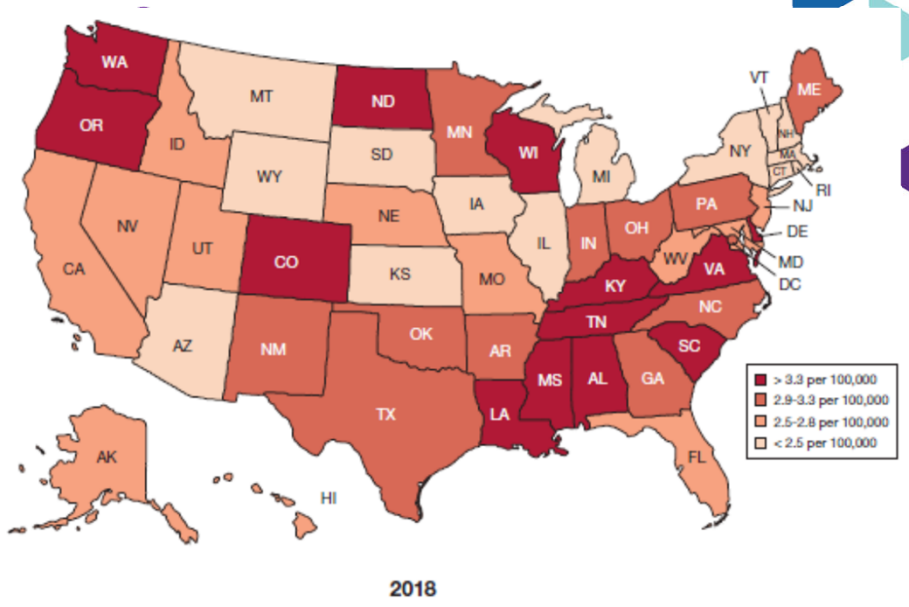
ARDS Prevalence & Mortality By

Type of ARDS	Prevalence	Hospital Mortality
Mild	30%	34.9%
Moderate	46.6%	40.3%
Severe	23.4%	46.1%

Greater incidence, 10% of ICU admissions and, under recognized and higher mortality

ARDS occurs in 1 of every 10 patients in ICU's around the world & 23% of all mechanically ventilated patients

Bellaini G, et al. JAMA, 2016;315(8):788-800



Mortality for ARDS in US stagnate

Higher rates:

↑in Blacks & Hispanics

↑Males and low-income patients

Parcha V, et al. Chest 2020 22:s0012-3692

Predisposing Conditions Associated with ARDS

Direct Injury

- Inhalation injuries
- Pneumonitis
- Virus
- Pulmonary Contusion
- Oxygen Toxicity
- Drugs:
- Radiation

Indirect Injury

- Sepsis
- Hyperinflammatory
- Multiple Transfusions (TRALI)
- Shock
- Multisystem Trauma
- Pulmonary Embolism
- Fat Embolism
- Pancreatitis
- Intracranial Hypertension
- Burns
- Bypass Surgery
- DIC

Sub-Phenotypes:
Hypoinflammatory
Hyperinflammatory: ↑ mortality/Vent days

Matthay MA, 2019; Primer 5;18. www.nature.com

Pathophysiologic Characteristics in ARDS

- A permeability defect described as a diffuse, non-uniform injury to the alveolar epithelium and alveolar capillary membrane (mediator/biotrauma & ventilator induced)
- Ventilator induced lung injury: overdistenison injury caused by higher tidal volumes and higher transpulmonary pressures. This may induce cytokine release
- Direct injury to pulmonary circulation (mediator/biotrauma & ventilator induced)
- Defect in the body's ability to transport and utilize O_2 at tissue level

Blondonnet R, e tal. Disease Markers, 2016; open access
Manimala R, et al. Current Respiratory Medicine Reviews, 2015;11(3):231-235
Walkey AJ, et al. AnnalsATS, 2017;14(Supp 4): s271-s279

The Eight P's of ARDS Treatment

- PREVENTION
- PEEP
- PUMP
- PIPES
- PARALYSIS
- POSITION
- PROTEIN
- PROTOCOL

9th : PHARMACOLOGY

PREVENTION

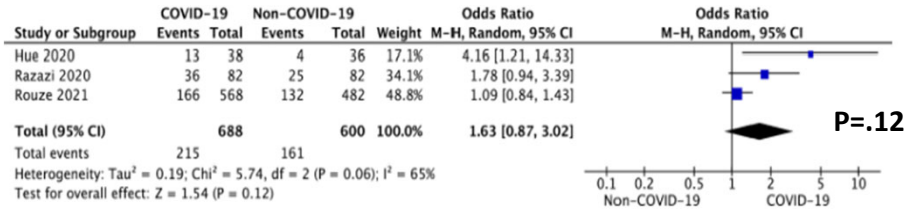
Preventing the Invasion

- VAE/VAC/IVAC & Probable VAP-Increase risk of death in COVID
- CLA-BSI-higher rates seen nationally with COVID
- SSI
- CA-UTI

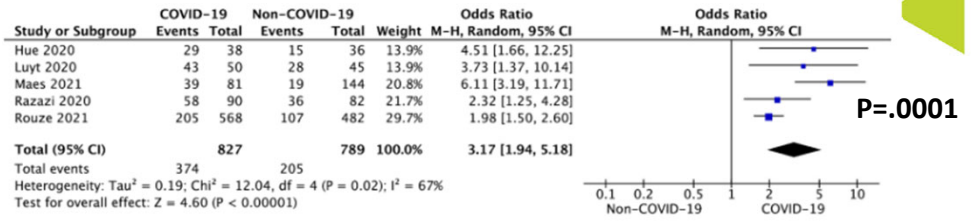
Pickens CO, et al. *medRxiv.* 2021:2021.2001.2012.20248588
https://www.tarrn.org/covid
Rouze A, et al. Intensive Care Med. 2021 Feb;47(2):188-198
Buetti N, et al. Intensive Care Med. 2021 https://link.springer.com/article/10.1007/s00134-021-06346-w

Significance of VAP in COVID Patients: A Systematic Review and Case Series

- Case series & systematic review (5 studies)
- COVID and Non COVID studies that measured VAP using the same methodology
- Outcome measures
  - △ Mortality during hospitalization
  - △ Secondary
    - Mortality at ICU
    - LOS
    - VAP
- Results: Mortality at 28 days

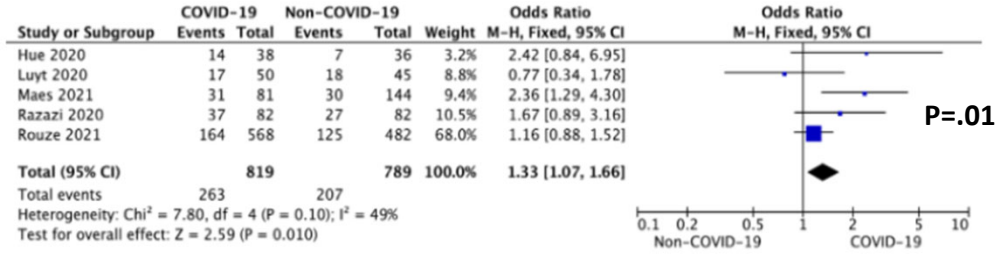


VAP Rates



26% **45%**

ICU Mortality



26.3% **32.1%**

Szarpak L., TRC Journal of Medicine, 2022;1(1)

Impact of COVID on HAI's in 2020 Compared to 2019: Data from NHSN

	2020 Q1	2020 Q2	2020 Q3	2020 Q4
CLABSI	↓ -11.8%	↑ 27.9%	↑ 46.4%	↑ 47.0%
CAUTI	↓ -21.3%	No Change[1]	↑ 12.7%	↑ 18.8%
VAE	↑ 11.3%	↑ 33.7%	↑ 29.0%	↑ 44.8%
SSI: Colon surgery	↓ -9.1%	No Change[1]	↓ -6.9%	↓ -8.3%
SSI: Abdominal hysterectomy	↓ -16.0%	No Change[1]	No Change[1]	↓ -13.1%
Laboratory-identified MRSA bacteremia	↓ -7.2%	↑ 12.2%	↑ 22.5%	↑ 33.8%
Laboratory-identified CDI	↓ -17.5%	↓ -10.3%	↓ -8.8%	↓ -5.5%

Weiner-Lastinger LM, Pattabiraman V, Konnor RY, et al. The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections in 2020: A summary of data reported to the National Healthcare Safety Network. *Infection Control & Hospital Epidemiology*. 2021:1-14. doi:10.1017/ice.2021.362

PEEP

POSITIVE END EXPERIATORY PRESSURE

Strategies for Ventilating the ARDS Lung: Protect From Injury

- Oxygen exposure
- Pressure (Barotrauma)
- Volume (Volutrauma & Biotrauma)
- Shear forces (Reopening & closing of alveoli) (Atelectrauma & Biotrauma)

ATS & SCCM Guidelines for Mechanical Ventilation of ARDS Patients

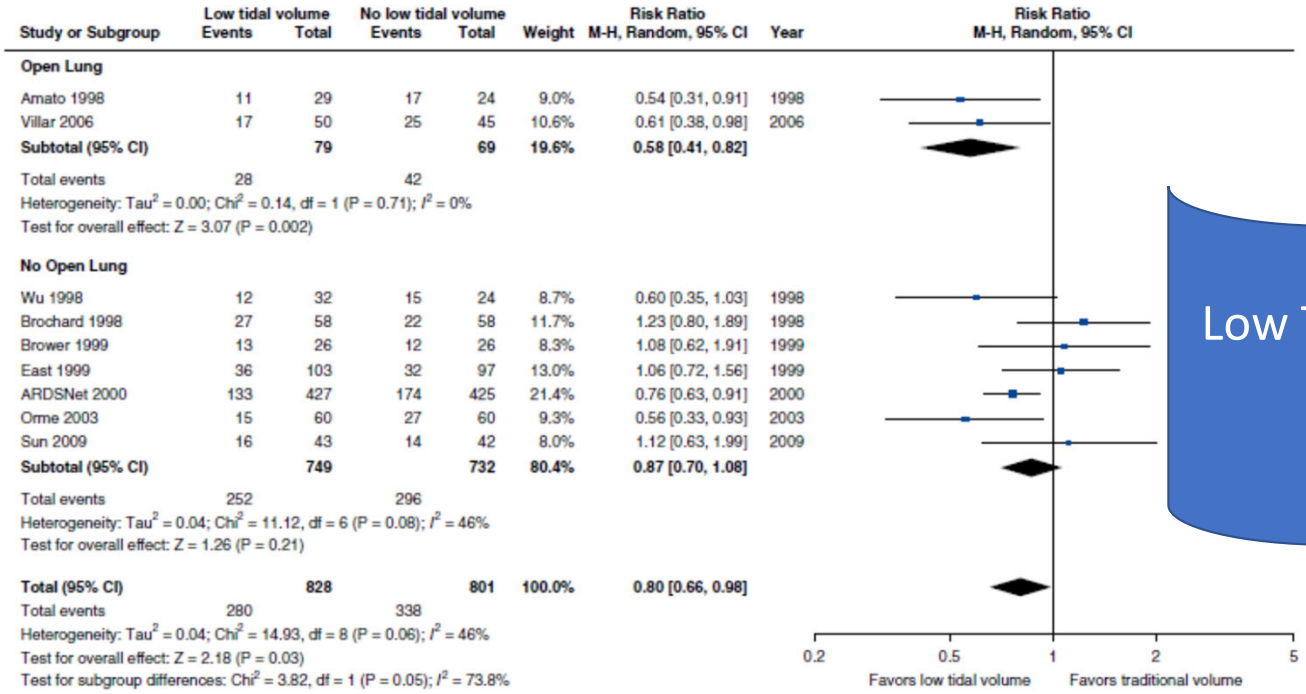
- Strong recommendation for:
  - Using lower tidal volumes (4-8ml/kg PBW) & lower inspiratory pressures (plateau pressures < 30 cm H2O
  - Severe ARDS prone positioning for > 12 h/d
  - Against the routine use of HFOV
- Conditional recommendation
  - Higher PEEP's
  - Recruitment maneuvers

Additional evidence needed for ECMO

Amer J of Respir & Crit Care Med, 2017:195(9):1253-1263

Low Tidal Volume

- 7 RCT's
- 1481 patients



Study or Subgroup	Low tidal volume Events	Total	No low tidal volume Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Open Lung							
Amato 1998	11	29	17	24	9.0%	0.54 [0.31, 0.91]	1998
Villar 2006	17	50	25	45	10.6%	0.61 [0.38, 0.98]	2006
Subtotal (95% CI)		**79**		**69**	**19.6%**	**0.58 [0.41, 0.82]**	
Total events	28		42				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.14$, df = 1 (P = 0.71); $I^2 = 0\%$							
Test for overall effect: Z = 3.07 (P = 0.002)							
No Open Lung							
Wu 1998	12	32	15	24	8.7%	0.60 [0.35, 1.03]	1998
Brochard 1998	27	58	22	58	11.7%	1.23 [0.80, 1.89]	1998
Brower 1999	13	26	12	26	8.3%	1.08 [0.62, 1.91]	1999
East 1999	36	103	32	97	13.0%	1.06 [0.72, 1.56]	1999
ARDSNet 2000	133	427	174	425	21.4%	0.76 [0.63, 0.91]	2000
Orme 2003	15	60	27	60	9.3%	0.56 [0.33, 0.93]	2003
Sun 2009	16	43	14	42	8.0%	1.12 [0.63, 1.99]	2009
Subtotal (95% CI)		**749**		**732**	**80.4%**	**0.87 [0.70, 1.08]**	
Total events	252		296				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 11.12$, df = 6 (P = 0.08); $I^2 = 46\%$							
Test for overall effect: Z = 1.26 (P = 0.21)							
Total (95% CI)		**828**		**801**	**100.0%**	**0.80 [0.66, 0.98]**	
Total events	280		338				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 14.93$, df = 8 (P = 0.06); $I^2 = 46\%$							
Test for overall effect: Z = 2.18 (P = 0.03)							
Test for subgroup differences: $Chi^2 = 3.82$, df = 1 (P = 0.05); $I^2 = 73.8\%$							

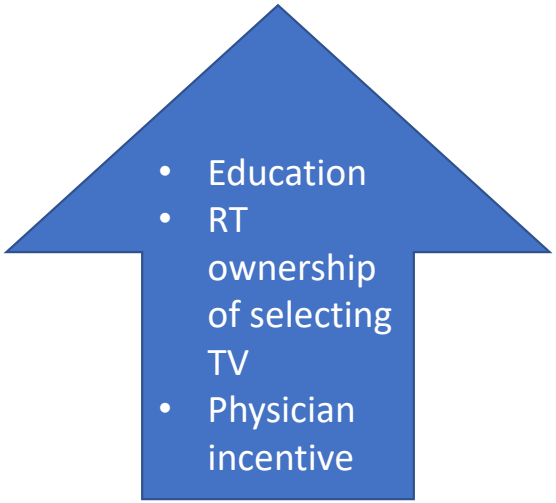
Low TV achieved in < 2/3 of ARDS patients

Bellaini G, et al. JAMA, 2016;315(8):788-800

Walkey AJ, et al Ann Am Thorac Soc. 2017 Oct;14(Supplement_4):S271-S279.

Improving Delivery of Low Tidal Volume

- QI project-4 PDSA cycles
- 10 ICU's, 3 Hospitals
- Initial compliance rate: 40%-60%



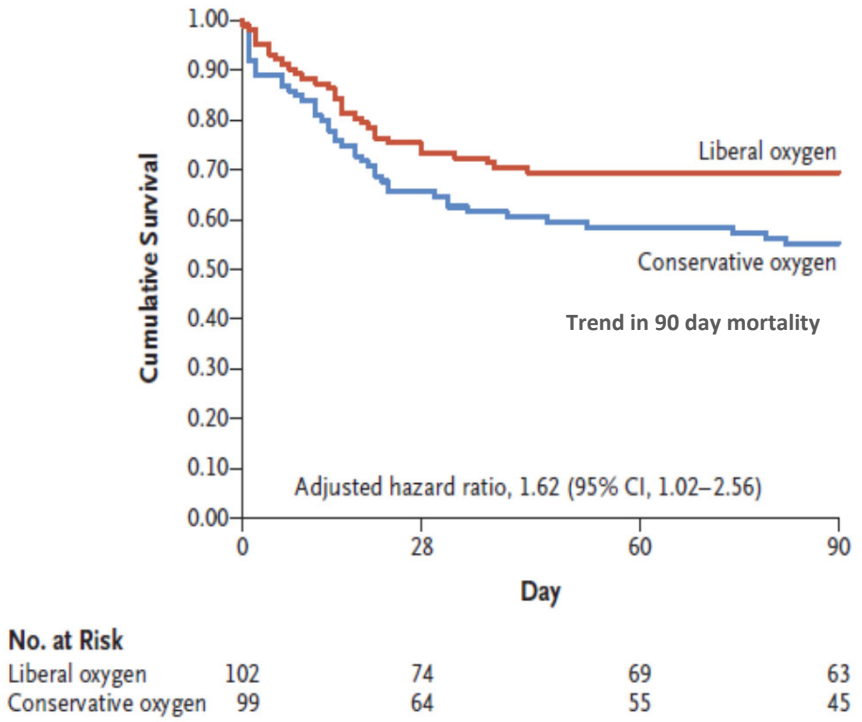
91%-96%

Donadee C. BMJ Open Quality, 2022;11:e001343

Liberal vs. Conservative O2 therapy in ARDS

- RCT-13 ICU's, 205 patients
- Intubated/Ventilated with ARDS < 12hrs
- Randomized:
  - Conservative O2: 55 -70 mmhg
  - Liberal O2: 90-105mmhg
- Targets maintained for first 7days or extubation

Mesenteric ischemia in conservative O2 group



No. at Risk				
Liberal oxygen	102	74	69	63
Conservative oxygen	99	64	55	45

Barrot J, et al. N Engl J Med. 2020;382:999-1008

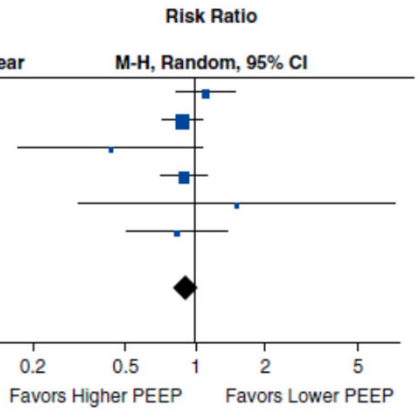
EBR & Meta-analysis: High Peep vs. Low PEEP

- 8 trials, 2,728 patients
- Mean PEEP in higher 15.1 (±3.6 cm)
- Mean PEEP in lower 9.1 (± 2.7cm)
- No difference in mortality, barotrauma, new organ failure or VFD's

	High		Low			Risk Ratio		Risk Ratio
Study or Subgroup	Mortality Events	Total Patients	Mortality Events	Total Patients	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Brower *et al.*, 2004	76	276	68	273	19.2%	1.11 [0.83, 1.46]	2004	
Meade *et al.*, 2008	135	475	164	508	40.8%	0.88 [0.73, 1.06]	2008	
Talmor *et al.*, 2008	5	30	12	31	1.9%	0.43 [0.17, 1.07]	2008	
Mercat *et al.*, 2008	107	385	119	382	31.1%	0.89 [0.72, 1.11]	2008	
Hodgson *et al.*, 2011	3	10	2	10	0.6%	1.50 [0.32, 7.14]	2011	
Kacmarek *et al.*, 2016	22	99	27	101	6.4%	0.83 [0.51, 1.36]	2016	
Total (95% CI)		**1275**		**1305**	**100.0%**	**0.91 [0.80, 1.03]**		
Total events	348		392					

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.09$, df = 5 (P = 0.41); $I^2 = 2\%$

Test for overall effect: Z = 1.46 (P = 0.14)

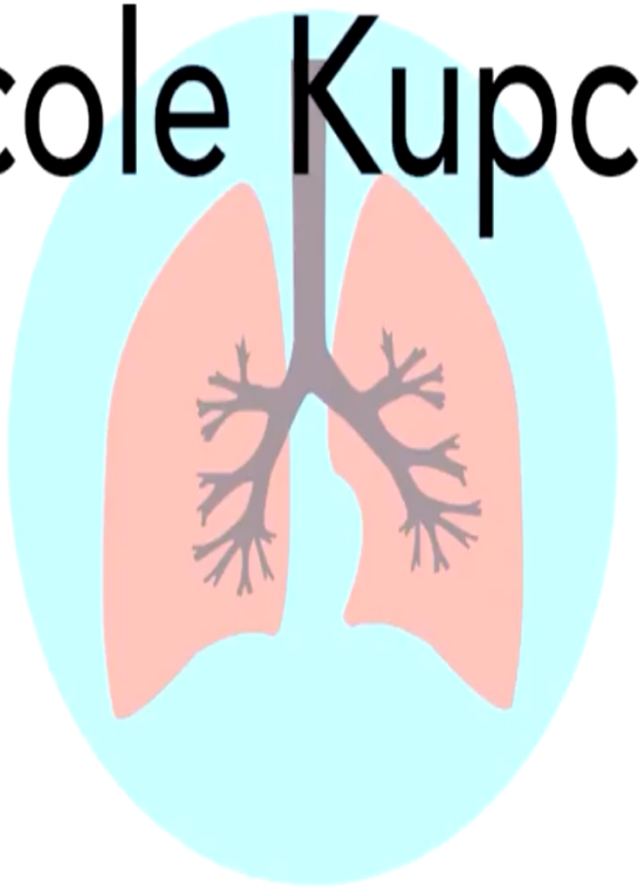


Walkey AJ, et al. AnnalsATS, 2017;14(Supp 4):s297-s303

Nicole Kupchik

How do you know what PEEP to start with post intubation?

- Gattinoni Method
- ARDSnet PEEP/FiO_2 table



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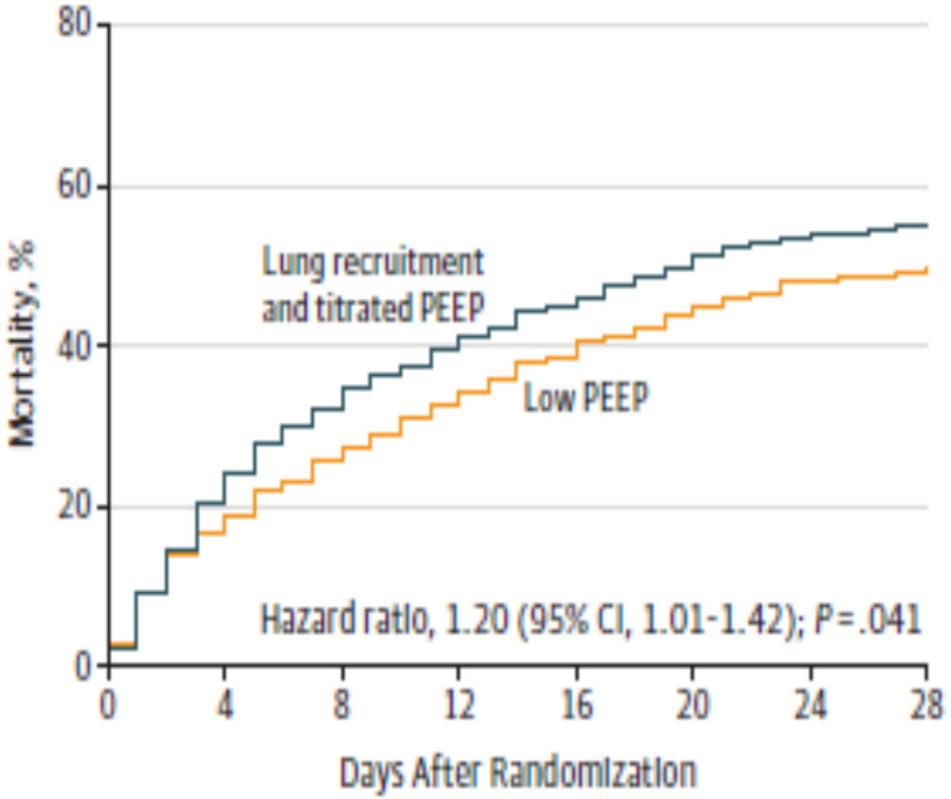
Titrating PEEP—No difference seen between using Esophageal pressure guided strategy versus the PEEP/FIO2 strategy (Beitler JR, et al. JAMA, 2019;321:646-857

Effect of Lung Recruitment & Titrated PEEP vs Low PEEP on Mortality (ART Trial)

- Multi-center RCT, 120 ICU's, 9 countries, 1010 patients
- Maneuver: RM with incremental PEEP titration, then PEEP set at 23cm and ↓ by 3cm till 11cm based on compliance.
- Results
  - Small # didn't received RM due to hypotension
  - Higher # with barotrauma in RM group
  - PEEP diff was 3-4 cm



Cavalcanti AB, et al. JAMA, 2017;318(14):13351345

PHARLAP:
An Open Lung Strategy including Permissive Hypercapnia, Alveolar Recruitment and Low Airway Pressure in ARDS patients

- A Multi-center RCT in 5 countries/Phase II trial
- Objective: Determine whether maximal lung recruitment strategies reduce VFD versus Low V_t and moderate PEEP
- Enrollment stopped after publication of ART trial

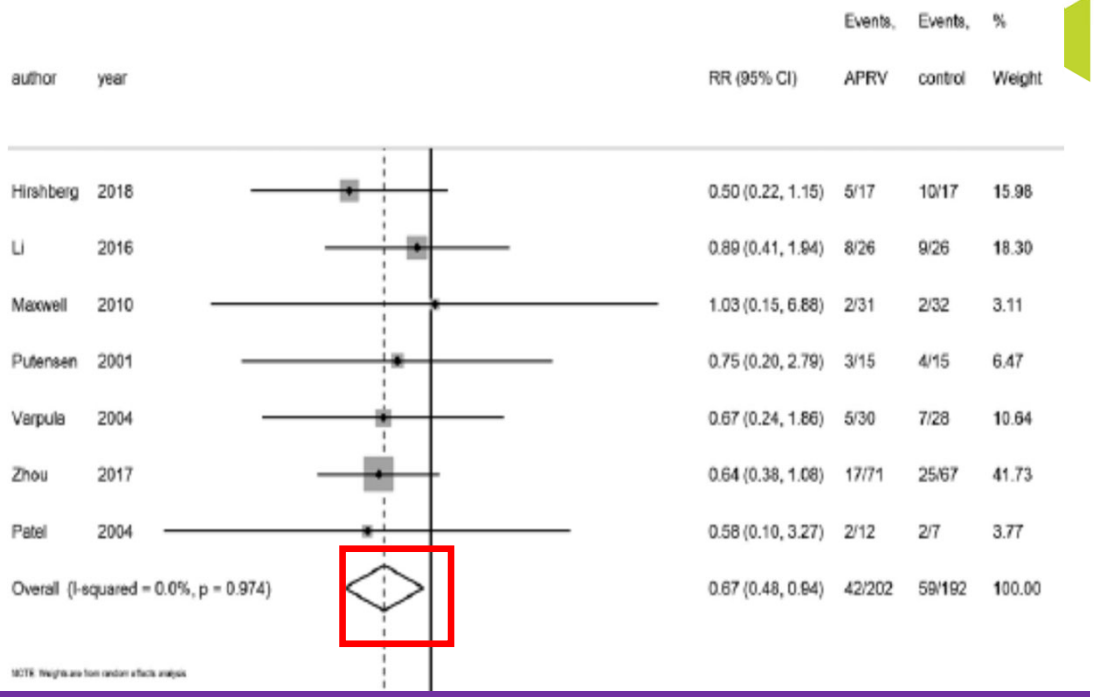
Hodgson CL, et al. Am J Respir Crit Care Med. 2019 Dec 1;200(11):1363-1372.

Adjunctive Strategies

- APRV
- HFOV
- ECMO
- $ECCO_2$ (experimental)
  - The strategy of altar protective lung ventilation with extracorporeal CO2 removal for new onset moderate to severe ARDS (SUPERNOVA) trial
  - Protective ventilation with veno-venous lung assist in respiratory failure (REST) trial

APRV:
Airway Pressure Release Ventilation vs any Ventilator Mode

- 7 RCT's, 412 patients
- Mean measured TV in APRV group: 7.47 ml/kg, vs. 7.45 ml/kg
- Improvement in day 3 PaO2/FiO2 ratio
- No difference in:
  - Initial rescue treatments
    - inhaled pulmonary vasodilators
    - prone positioning
    - ECMO
- Barotrauma only reported in three studies (no difference)

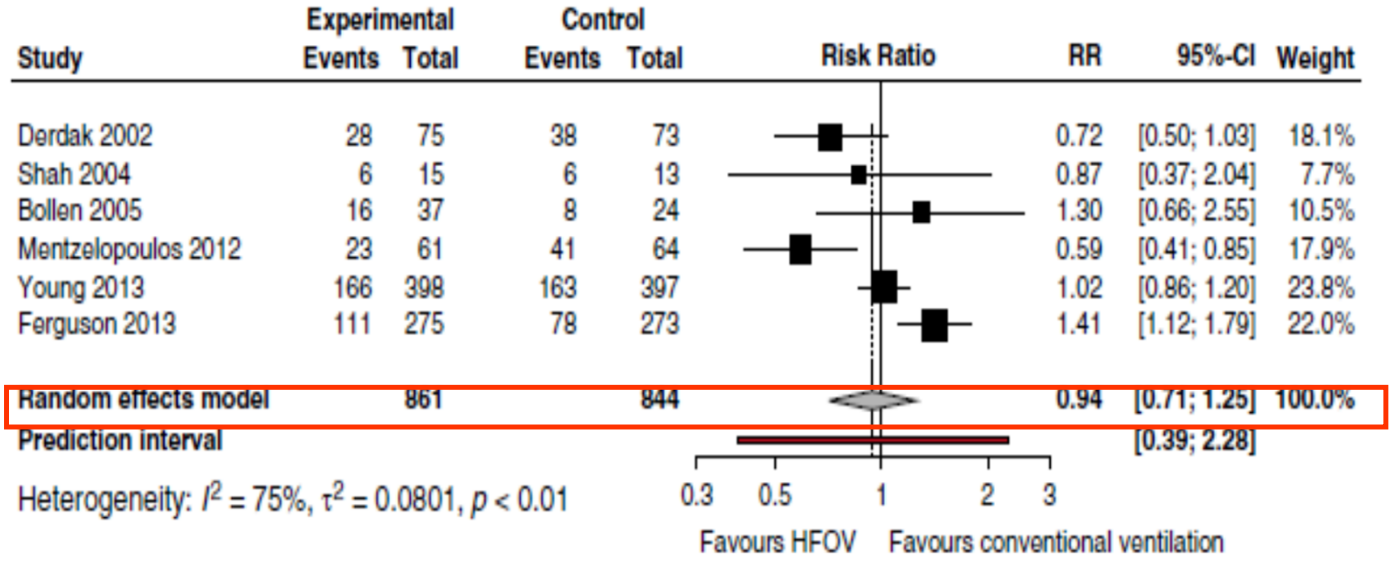


Needed a larger sample to prevent false positive in primary outcomes (614 patients)

Lim J, et al. Crit Care Med. 2019 Dec;47(12):1794-1799.

High Frequency Oscillation: EBR & Meta-analysis

- Six trials with 1715 patients
- No difference in barotrauma rates



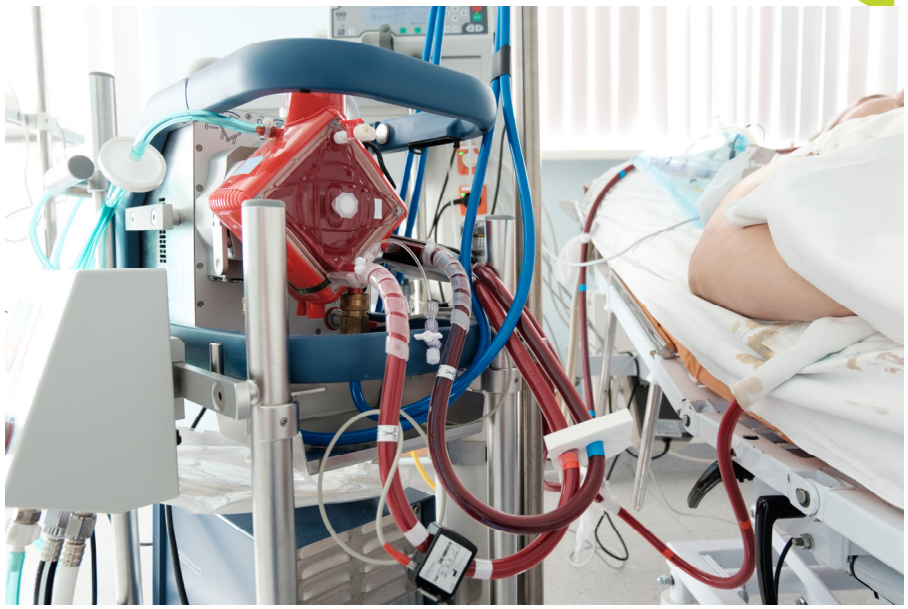
In an individual patient meta-analysis, those with ARDS with P/F ratios < 65mmhg may see a benefit.

Meade MO, et al. AJRCCM,2017;196(6):727-733

Goligher EC, et al. AnnalsATS, 2017;14(suppl 4):s289-s296

EOLIA Trial

- Multicenter, International, RCT
- Method: Compared early VV ECMO or continued conventional ventilator therapy and measure 60-day mortality in patients with severe forms of ARDS
- Cross over to ECMO was possible for conventional group who had refractory hypoxemia
- Results:
  - Mortality: 35% in ECMO versus 46% in control ($p < 0.09$)
  - Crossover to ECMO avg 6.5 days-28% of control / Mortality 57%



Purchased Shutterstock image

Combes A, et al. New Engl J of Med. 2018;378(21):1965-75

Discoveries with COVID

- Candidacy of Patients
  - Previous scoring tools were no longer accurate
  - Younger patients (<50 yrs) single organ dysfunction had best outcomes
- Shorten the interval from intubation to cannulation
  - Less than 3 days of MV, P/F ratio <70 mmHg
- Adjunctive therapies
  - Monoclonal antibodies, cytoreductive techniques
- Early Extubation
  - Allows for Physical Therapy, Ambulation, decreases resources, Nutrition

Slide courtesy of Lisa Soltis

PIPES
&
PUMP

Measures to Improve Oxygen Delivery

Measures to Improve O_2 Delivery

- Fluid Management
  - Balanced fluids vs. Saline
  - Dry vs. Wet

Balanced Fluids vs .9 % Normal Saline

HEMODYNAMIC MANAGEMENT

Fluid Management

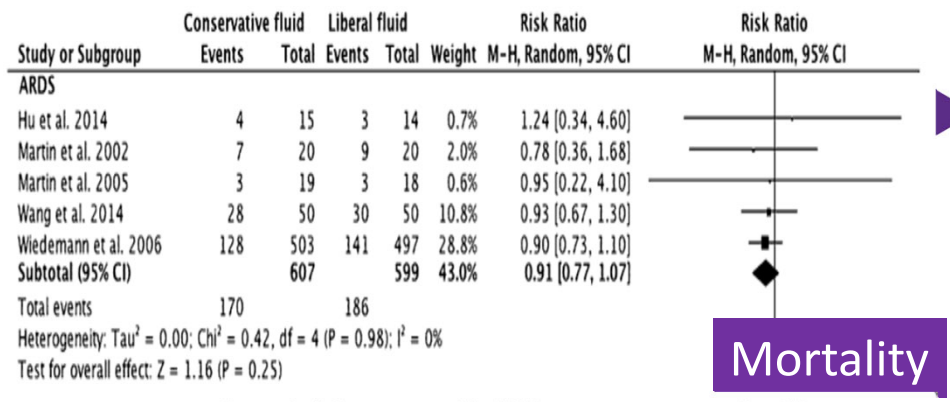
Recommendations
32. For adults with sepsis or septic shock, we **recommend** using crystalloids as first-line fluid for resuscitation. *Strong recommendation, moderate quality of evidence.*
33. For adults with sepsis or septic shock, we **suggest** using balanced crystalloids instead of normal saline for resuscitation. *Weak recommendation, low quality of evidence.*
34. For adults with sepsis or septic shock, we **suggest** using albumin in patients who received large volumes of crystalloids over using crystalloids alone. *Weak recommendation, moderate quality of evidence.*
35. For adults with sepsis or septic shock, we **recommend against** using starches for resuscitation. *Strong recommendation, high quality of evidence.*
36. For adults with sepsis and septic shock, we **suggest against** using gelatin for resuscitation. *Weak recommendation, moderate quality.*

With a high probability, the average effect of using balance fluids is to reduce mortality

Surviving Sepsis Campaign: International Guidelines for the Management of Sepsis and Septic Shock 2021. Evans Hammond NE, et al. Evidence. 2022;1(2):EVIDoa2100010.,

Conservative/ Deresuscitation vs. Liberal Fluid For ARDS Following Critical Phase

- 11 RCT's
- 2051 patients
- Results:
  - No difference in mortality
  - ↑ VFD 1.82 days
  - ↓ LOS 1.9 days



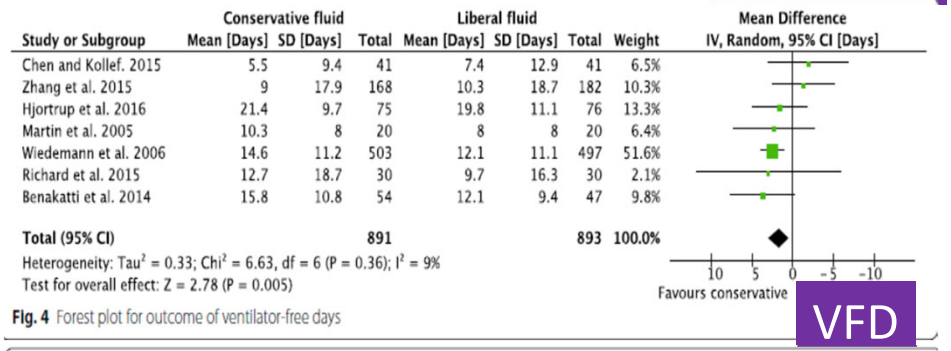


Fig. 4 Forest plot for outcome of ventilator-free days

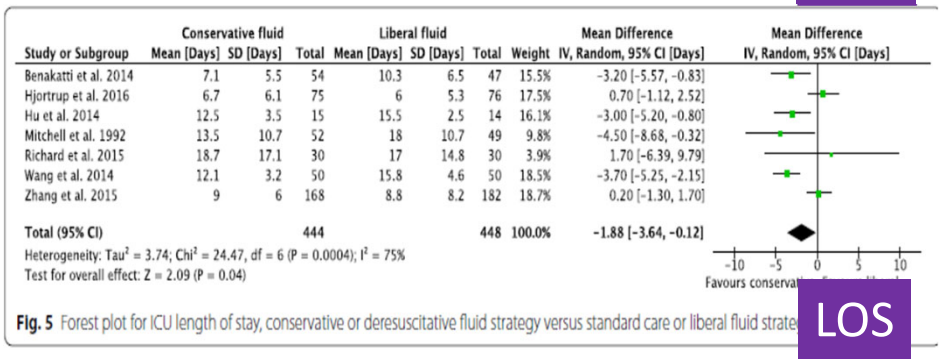
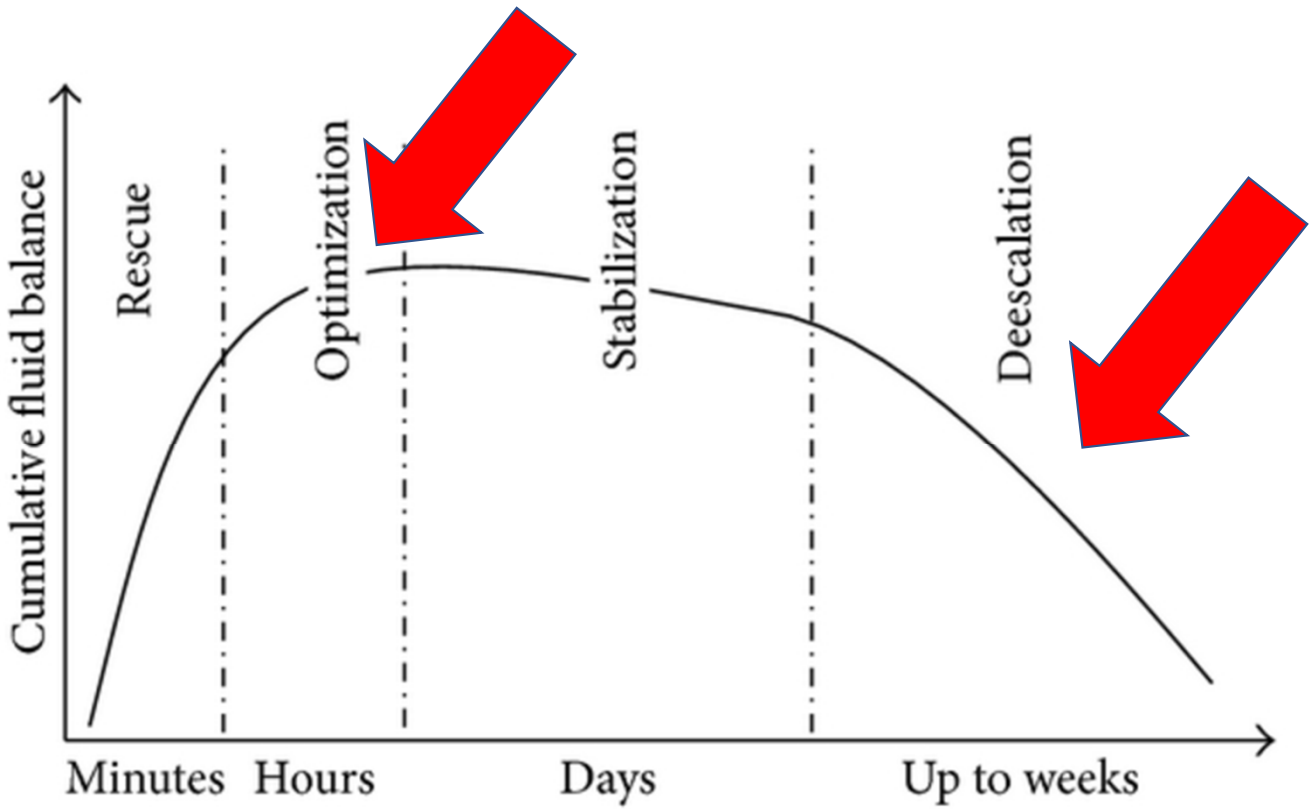


Fig. 5 Forest plot for ICU length of stay, conservative or deresuscitative fluid strategy versus standard care or liberal fluid strate

Silversides JA, et al. Intensive Care Med, 2017;43:155-170

4 Phases of Fluid Resuscitation



https://www.researchgate.net/figure/Four-phases-of-hemodynamic-treatment-in-relation-to-cumulative-fluid-balance_fig1_287977953

Timing & Amount of Fluid Administration is Key

- Start as early as possible the administration of volume if warranted-more conservative for patients not in shock
- Control the efficacy of volume expansion with predefined goal-oriented therapy
- More fluid early if needed, less fluid later
- Consider deresuscation if warranted after hemodynamically stable

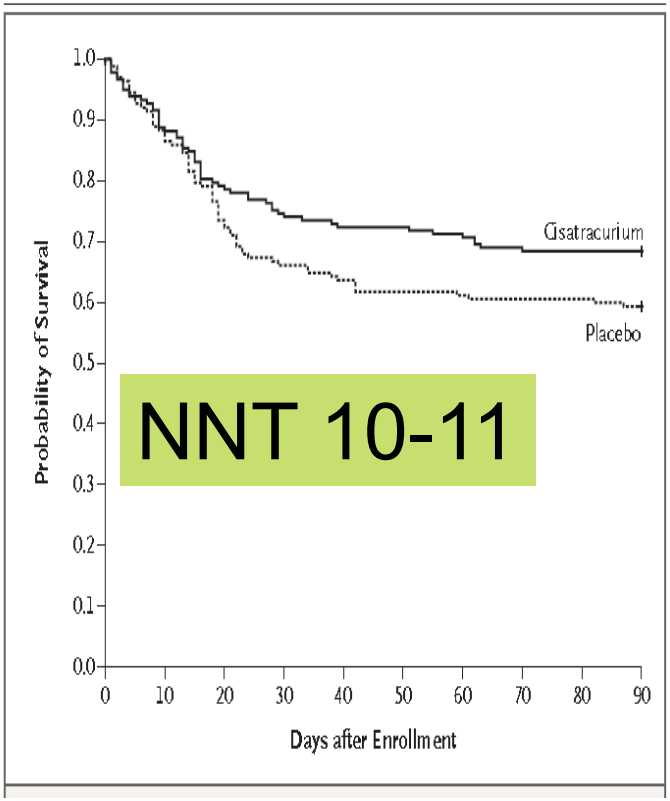
PARALYSIS

Neuromuscular Blockade in Early ARDS

- Multicenter, double blind trial
- 340 patients with ARDS within 48hrs of admitted to ICU
- ARDS defined as P/F ratio of < 150 ≥ PEEP 5cm & Vt of 6-8 ml/kg PBW
- Randomized to receive 48hrs of cisatracurium or placebo
- Study did not use train of 4

Results:

- After risk adjustment NMB group showed improved mortality at 90 days (31.6% vs. 40.7%)
- Also significant at 28 days
- ↑time off vent
- No difference in muscle weakness



NNT 10-11

Papazian L, et al. N Engl J Med. 2010;363(12):1107-16

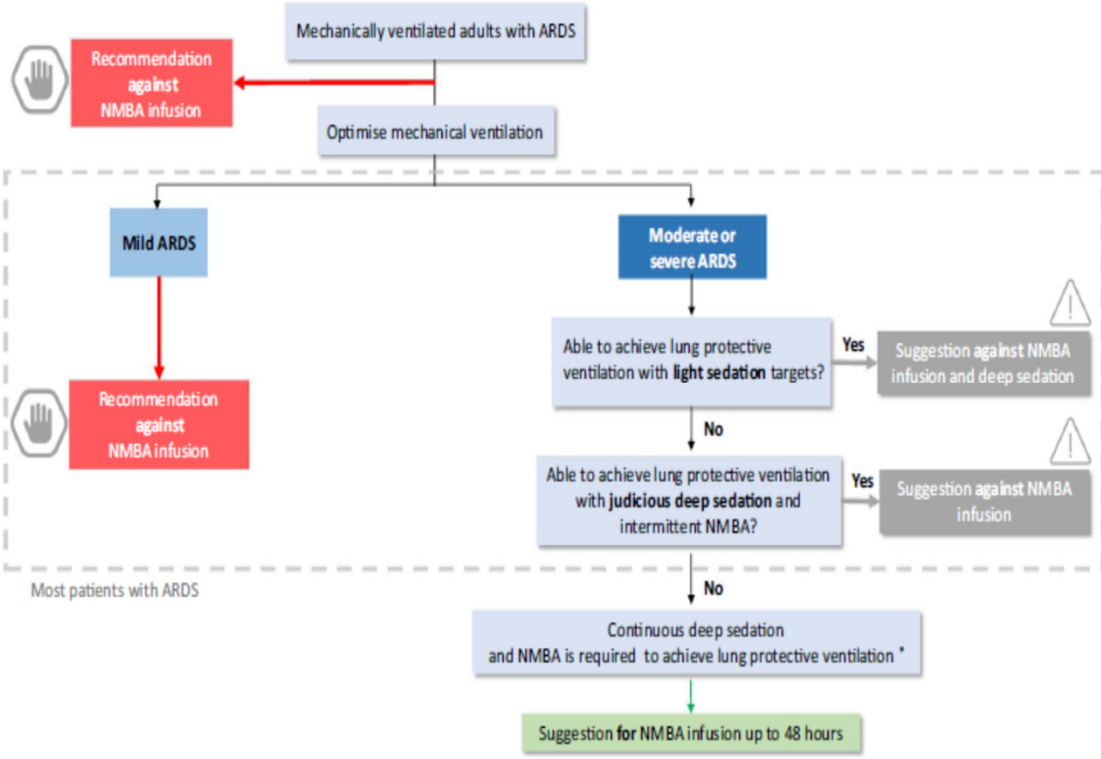
ROSE Trial

- 1006 moderate to severe ARDS patients
- Randomized to 48hrs Cisatracurium/deep sedation or usual care
- Vent strategies similar in both group (use of higher PEEP)
- Trial stopped for futility at 2nd analysis
- Results:
  - 90-day follow-up
  - Mortality: 42.5% vs. 42.8% (0.3%, 95% CI -6.4 to 5, *P*=0.93)
  - During hospital stay intervention group had more;
    - Adverse cardiovascular events
    - Less active

Moss M, et al. Petal Network. NEJM, 2019;380(21):1997-2008

Rapid Practice Guideline: NMBA in ARDS Patients

- 20 international experts/12 countries
- Overall certainty in the evidence was low
- 1 Recommendation:
  - Against routine use of NMBA infusions before optimizing mechanical ventilation & assessing ARDS severity
- 2 suggestions:
  - If NMBA required to facilitate LPV, suggest intermittent doses with judicious deep sedation over NMBA infusion & deep sedation
  - If clinician determines continued need for NMBA and deep sedation, suggest continuous for 48hrs over intermittent



Alhazzani W, et al. Intensive Care Medicine 2020;46:1977-1986-PMC free text

POSITION

ATS & SCCM Guidelines for Mechanical Ventilation of ARDS Patients

- Strong recommendation for:
  - Using lower tidal volumes (4-8ml/kg PBW) & lower inspiratory pressures (plateau pressures < 30 cm H2O
  - Severe ARDS prone positioning for > 12 h/d
  - Against the routine use of HFOV
- Conditional recommendation
  - Higher PEEP's
  - Recruitment maneuvers

Amer J of Respir & Crit Care Med, 2017:195(9):1253-1263

Prone Positioning Incidence

Prone positioning (PP) was only used in 16.3% of patients with severe ARDS in the LUNG SAFE study

Bellaini G, et al. JAMA, 2016;315(8):788-800

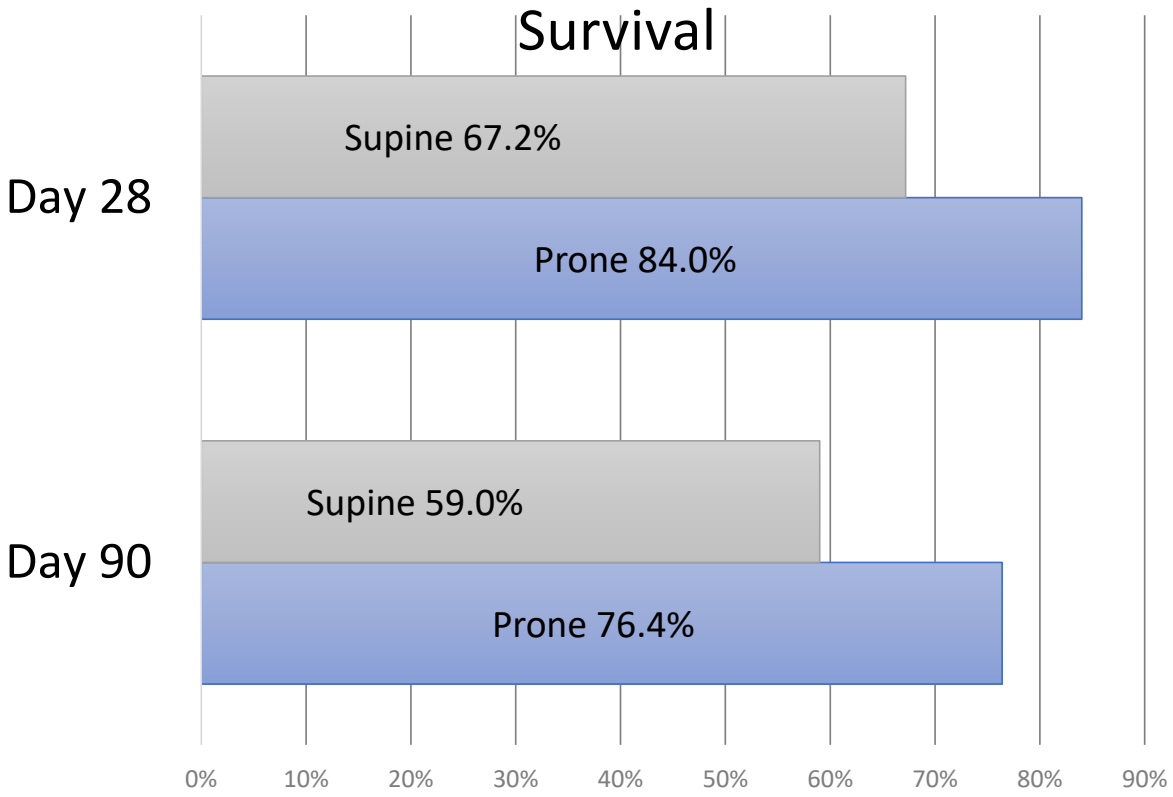
European Prevalence Study (APRONET): Use of PP in mild 5.9%, moderate 10.3%, severe 32.9% ARDS

Guerin C, et al. Intensive Care Med, 2018;44(1):22-37

Italy and Netherlands—60% of Mechanical Ventilated ARDS COVID 19 patient were proned, 50% in the US

Stilma W, et al. *J Clin Med*. 2021;10(20):4783.
Langer T, et al. *Crit Care* 2021; **25:**128
Mathews KS, et al. Crit Care Med. 2021;49(7):1026-1037.

Proning Severe ARDS Patients



In a randomized, controlled trial of 466 patients with severe ARDS, survival was significantly higher at 28 and 90 days in the prone position group

NNT=6

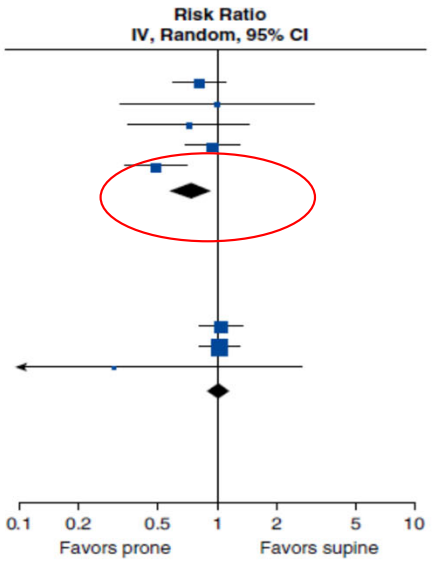
Guerin C, et al. *N Engl J Med*. 2013368(23):2159-2168.

Prone Meta-Analysis

- 8 RCT's
- 2129 total adult patients
- Subgroup analyses: Lower mortality with > 12 hours

Study or Subgroup	Prone Events	Prone Total	Supine Events	Supine Total	Weight	Risk Ratio IV, Random, 95% CI
≥12h Prone						
Mancebo *et al.* 2006	38	76	37	60	28.5%	0.81 [0.60, 1.10]
Chan *et al.* 2007	4	11	4	11	5.7%	1.00 [0.33, 3.02]
Fernandez *et al.* 2008	8	21	10	19	12.0%	0.72 [0.36, 1.45]
Taccone *et al.* 2009	52	166	57	172	27.9%	0.95 [0.69, 1.29]
Guerin *et al.* 2013	38	237	75	229	25.8%	0.49 [0.35, 0.69]
Subtotal (95% CI)		**511**		**491**	**100.0%**	**0.74 [0.56, 0.99]**
Total events	140		183			
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 8.53$, df = 4 (P = 0.07); $I^2 = 53\%$						
Test for overall effect: Z = 2.06 (P = 0.04)						
<12h Prone						
Gattinoni *et al.* 2001	70	152	67	152	40.0%	1.04 [0.82, 1.34]
Guerin *et al.* 2004	134	413	119	378	59.5%	1.03 [0.84, 1.26]
Voggenreiter *et al.* 2005	1	21	3	19	0.5%	0.30 [0.03, 2.66]
Subtotal (95% CI)		**586**		**549**	**100.0%**	**1.03 [0.88, 1.20]**
Total events	205		189			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.24$, df = 2 (P = 0.54); $I^2 = 0\%$						
Test for overall effect: Z = 0.36 (P = 0.72)						

Test for subgroup differences: $Chi^2 = 3.92$, df = 1 (P = 0.05), $I^2 = 74.5\%$



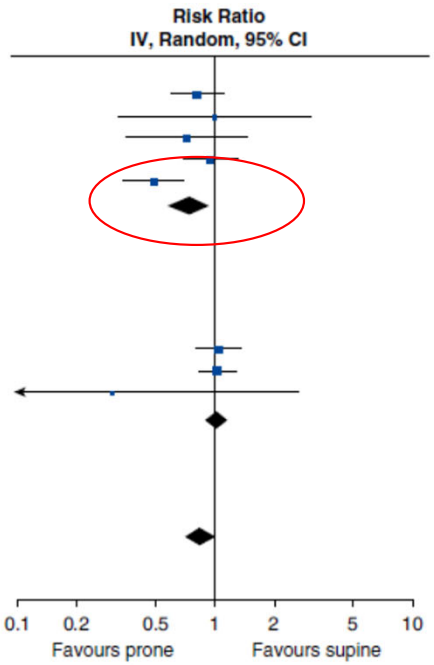
Overall Mortality

Munshi L, et al. AnnalATS, 2017;14(4):s280-s288

Prone Meta-Analysis: Sub-Groups

- Moderate to Severe ARDS vs. Mild ARDS

Study or Subgroup	Prone Events	Prone Total	Supine Events	Supine Total	Weight	Risk Ratio IV, Random, 95% CI
Moderate to Severe ARDS						
Mancebo *et al.* 2006	38	76	37	60	17.0%	0.81 [0.60, 1.10]
Chan *et al.* 2007	4	11	4	11	3.2%	1.00 [0.33, 3.02]
Fernandez *et al.* 2008	8	21	10	19	6.9%	0.72 [0.36, 1.45]
Taccone *et al.* 2009	52	168	57	174	16.6%	0.94 [0.69, 1.29]
Guerin *et al.* 2013	38	237	75	229	15.3%	0.49 [0.35, 0.69]
Subtotal (95% CI)		**513**		**493**	**59.1%**	**0.74 [0.56, 0.99]**
Total events	140		183			
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 8.51$, df = 4 (P = 0.07); $I^2 = 53\%$						
Test for overall effect: Z = 2.06 (P = 0.04)						
All ARDS						
Gattinoni *et al.* 2001	70	152	67	152	19.1%	1.04 [0.82, 1.34]
Guerin *et al.* 2004	134	413	119	378	20.9%	1.03 [0.84, 1.26]
Voggenreiter *et al.* 2005	1	21	3	19	0.9%	0.30 [0.03, 2.66]
Subtotal (95% CI)		**586**		**549**	**40.9%**	**1.03 [0.88, 1.20]**
Total events	205		189			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.24$, df = 2 (P = 0.54); $I^2 = 0\%$						
Test for overall effect: Z = 0.36 (P = 0.72)						
Total (95% CI)		**1099**		**1042**	**100.0%**	**0.84 [0.68, 1.04]**
Total events	345		372			
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 16.94$, df = 7 (P = 0.02); $I^2 = 59\%$						
Test for overall effect: Z = 1.60 (P = 0.11)						
Test for subgroup differences: $Chi^2 = 3.93$, df = 1 (P = 0.05), $I^2 = 74.6\%$						

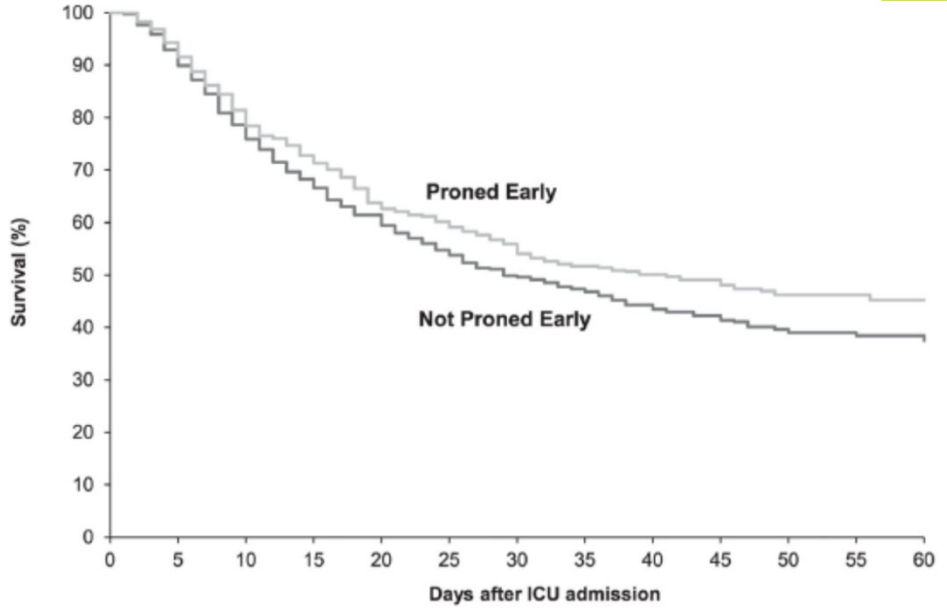


Greater incidence of pressure injuries and ET tube obstruction in prone vs supine.

Munshi L, et al. AnnalATS, 2017;14(4):s280-s288

Prone Positioning in COVID 19 Patients

- Data from study & treatment of outcomes in critical ill patients with COVID
- 68 hospitals
- Patients with p/f ratio < 200mmHg initiated prone positioning or not within first 2 days of ICU admission
- Results
  - 2338 eligible pts: 30% proned
  - Lower in-hospital mortality if proned early



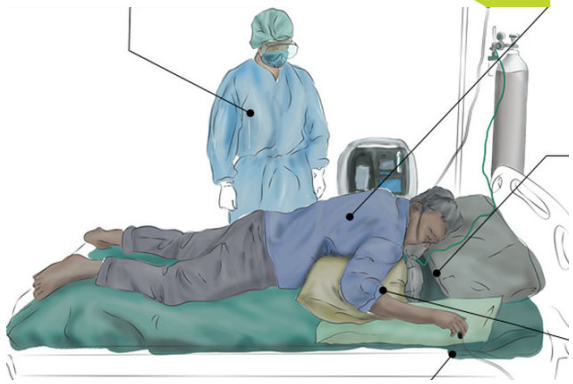
No. at risk

	Day 0	Day 10	Day 20	Day 30	Day 40	Day 50	Day 60
Proned	702	566	387	243	126	59	22
Not Proned	1636	1258	755	421	215	105	52

Mathews KS, et al. *Crit Care Med*. 2021;49(7):1026-1037.

Awake Prone Positioning with COVID: Open Label RCT

- Efficacy of awake proning to prevent intubation or death
- International open label RCT
- COVID 19 hypoxemic respiratory failure defined as: requiring respiratory support with HFNC & P/F ratio of $\leq$ 315 randomized to awake prone positioning or standard care
  - Awake prone (567)
  - Standard care (559)
- Patient instructed to lie in PP as frequent and as long as can be tolerated each day
- Pre-defined criteria for intubation was used in both group
- Outcomes:
  - Tx failure define as intubation or dying within 28 days of enrolment
  - Secondary outcome: intubation, mortality, use of non-invasive vent, time to intubation, time to death, Hospital LOS

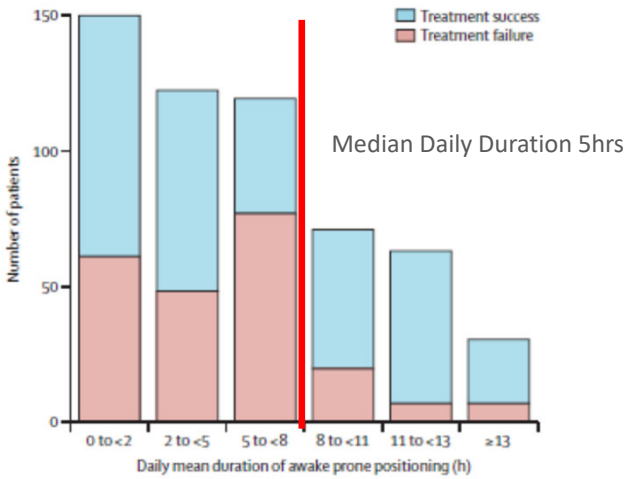


6 Countries: Mexico, US, Spain, Canada, France & Ireland

Ehrmann S, et al. *Lancet Respir Med*. 2021;9(12):1387-1395.

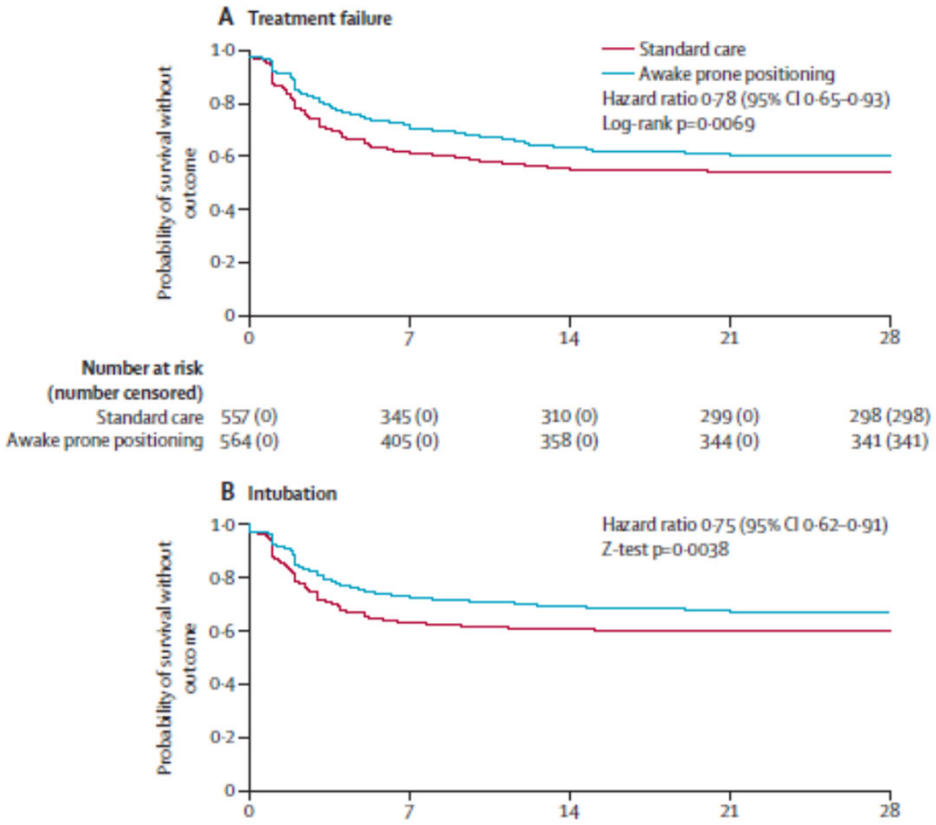
Awake Prone Positioning with COVID: Open Label RCT

Time Spent in Prone Position



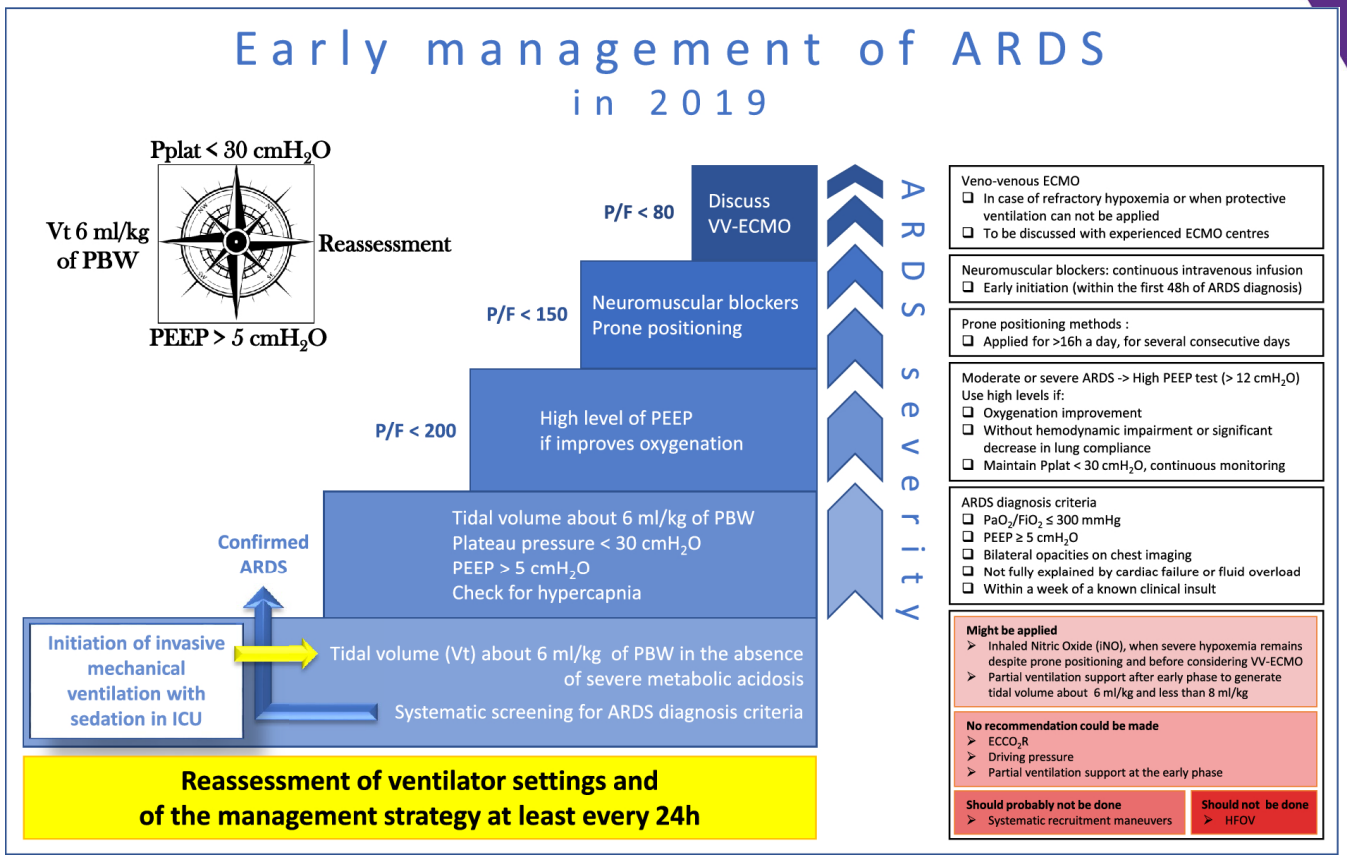
NNT 14

Outcomes



Ehrmann S, et al. *Lancet Respir Med*. 2021;9(12):1387-1395.

Sample ARDS Treatment Algorithm



Papazian, L., Formal guidelines: management of acute respiratory distress syndrome. *Ann. Intensive Care* **9,** 69 (2019) Springer Open Journal

PROTEIN (NURTITION)

SSCM Nutritional Guidelines (2016)

- Initiate enteral nutrition (EN) within 24−48 hours following the onset of critical illness and admission to the ICU and increase to goals over the first week of ICU stay. For ARDS-either trophic or full EN
- Take steps as needed to reduce risk of aspiration or improve tolerance to gastric feeding
- Do not use gastric residual volumes as part of routine care to monitor ICU patients on EN
- Start parenteral nutrition early when EN is not feasible or sufficient in high-risk or poorly nourished patients
- No specific recommendation for ARDS/Severe ALI=EN formula with anti-inflammatory lipid

Taylor B, et al. Crit Care Med, 201644(2):390-438

Recommended for COVID 19 Requiring ICU

Early EN is always preferred –exceptions escalating vasopressors , high positive respiratory support , GI symptoms or bowel ischemia

Feeding via nasogastric tube is in easy to execute method that requires minimal expertise

A prokinetic agent can be used as a second step in case of GI intolerance

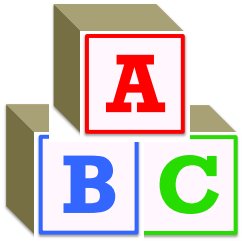
Postpyloric delivery route is only used in cases when above strategies have failed

Continuous rather than bolus is recommended

Initiate at low dose (tropic) slowly advancing to full dose over first week

Journal of Parenteral and Enteral Nutrition, Volume: 44, Issue: 8, Pages: 1439-1446, First published: 16 August 2020, DOI: (10.1002/jpen.1996)

PROTOCOL/ BUNDLE DRIVEN CARE



Assess & Manage Pain, Awake and Breathing Coordination:

- ↓Duration of mechanical ventilation
- ↓Duration of coma
- ↓Mortality

Manage pain first, Choose light sedation & avoid benzos

- ↓Duration of mechanical ventilation
- ↓Mortality
- ↓Delirium

Delirium monitoring & management

- ↑ Delirium detection

Early Mobility & Environment

- ↓Duration of delirium
- ↓Disability
- ↓ICU Length of Stay
- ↓Rehospitalization/Mortality

Family Engagement

Morandi et al Curr Opin Crit Care 2011;17:43-9
Vasilevskis et al Crit Care Med 2010;38:S683-91
Vasilevskis et al Chest 2010;138:1224-1233
Zaal et al, ICM 2013;39:481-88
Colombo et al, Minerva Anest 1012;78:1026-33
Chanques G, et al. Intensive Care Medicine. 2020 Dec;46(12):2342-2356.

PHARMACOLOGICAL TREATMENT

Dexamethasone in ARDS: RCT

- Multicenter randomized RCT
- 17 ICU's in Spain/277 pts
- Enrolled mod-severe ARDS patients <200 P/F ratio
- Treatment group: 139 patient
  - 20mg IV x1 daily from day 1 to day 5
  - 10mg IV x1 daily from day 6 to day 10
- Control group: 138
  - Usual care
- Underpowered by 37pts

	Dexamethasone group (n=139)	Control group (n=138)	Between-group difference (95% CI)	p value
Ventilator-free days at 28 days	12·3 (9·9)	7·5 (9·0)	4·8 (2·57 to 7·03)	<0·0001
All-cause mortality at day 60	29 (21%)	50 (36%)	−15·3% (−25·9 to −4·9)	0·0047
ICU mortality	26 (19%)	43 (31%)	−12·5% (−22·4 to −2·3)	0·0166
Hospital mortality	33 (24%)	50 (36%)	−12·5% (−22·9 to −1·7)	0·0235
Actual duration of mechanical ventilation in ICU survivors, days	14·2 (13·2)	19·5 (13·2)	−5·3 (−8·4 to −2·2)	0·0009
Actual duration of mechanical ventilation in survivors at day 60, days	14·3 (13·3)	20·2 (14·0)	−5·9 (−9·1 to −2·7)	0·0004
Adverse events and complications*				
Hyperglycaemia in ICU	105 (76%)	97 (70%)	5·2% (−5·2 to 15·6)	0·33
New infections in ICU	33 (24%)	35 (25%)	1·6% (−8·5 to 11·7)	0·75
Barotrauma	14 (10%)	10 (7%)	2·8% (−4·0 to 9·8)	0·41

Data are n (%) or mean (SD). ICU=intensive care unit. *Data included the period from randomisation to day 10 (for hyperglycaemia) and from randomisation to ICU discharge (for new infections and barotrauma).

Table 2: Outcomes, adverse events, and complications

Villar J, et al. *Lancet Respir Med*. 2020;8(3):267-276.

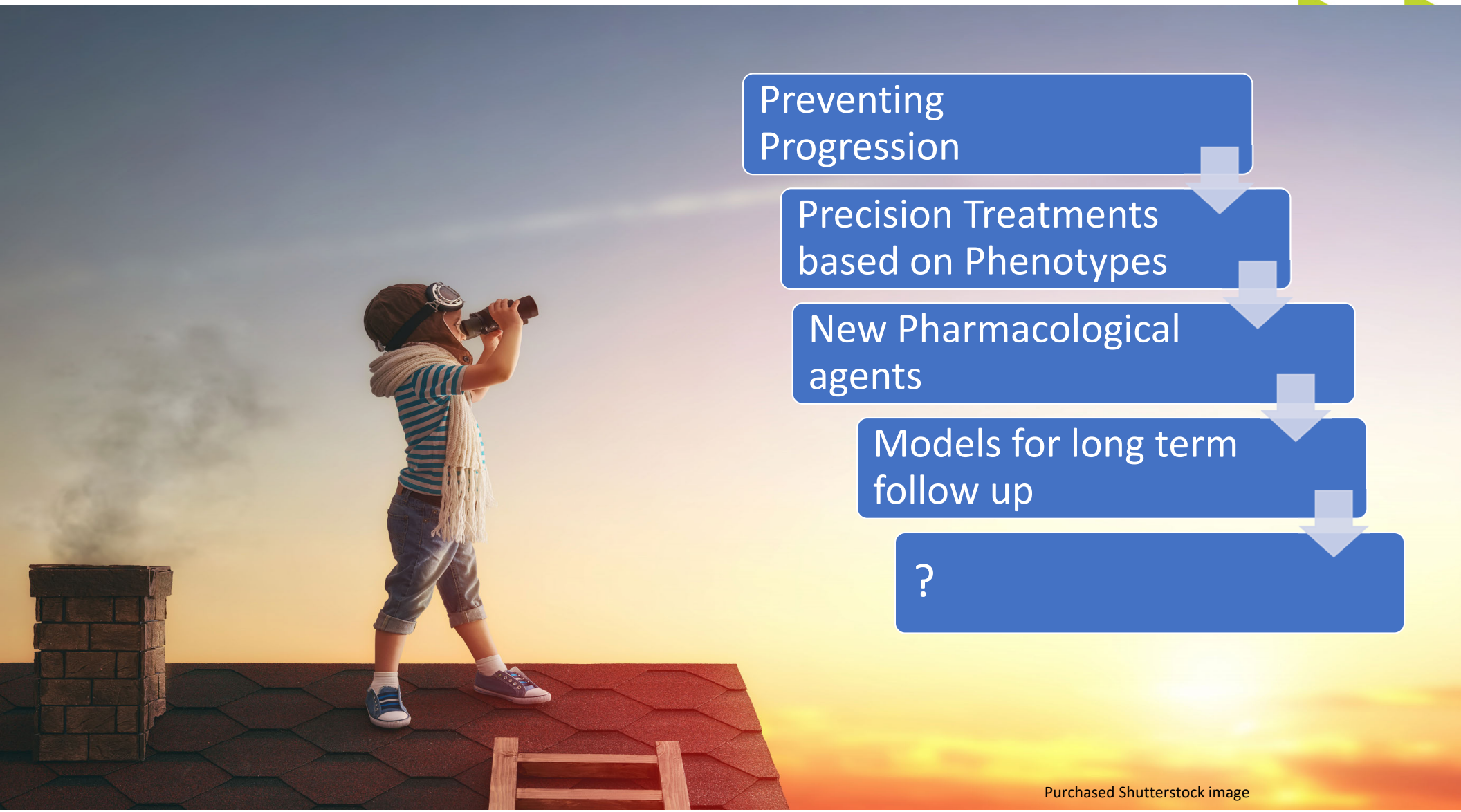
Post ICU Discharge & Long Term: How Do We Help?

Long Term Follow Up: Managing Medical Complexity

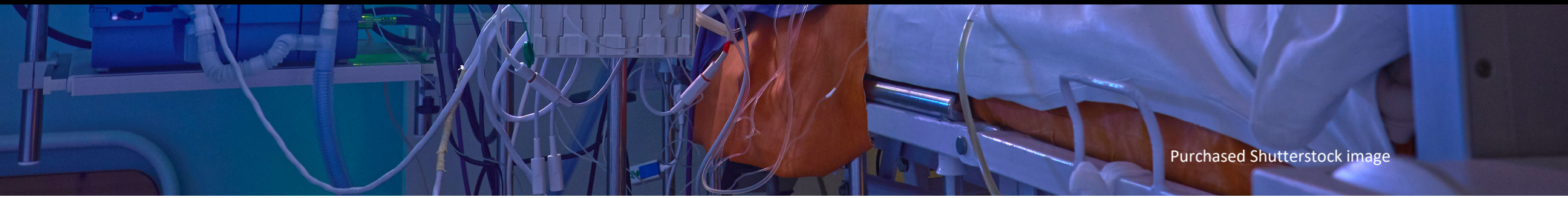
- Cognitive impairment 83.5% at d/c--51.3% at 1yr (ARDS)
- Quality of life scores & exercise intolerance remain lower than average 5 yrs. out. (ARDS)
- Peripheral nerve injuries from positioning, joint contracture from immobility, and oral or laryngeal injuries are common. (COVID)
- Critical illness erodes baseline health and increases medical complexity
- Specialized inpatient and longitudinal interprofessional and multidisciplinary team-based care

Formal Patient/Family Center Follow-Up After ARDS/COVID/Critical Illness

Herridge MS, Am J Respir Crit Care Med, 2017;196(11):1380-1384
Peach BC. Rehabilitation Nursing 2-22;47(2):72-81
Parotto M, *Lancet Respir Med*. 2021;9(8):812-814.



WHAT YOU ARE LEARNING TODAY, IS GOING TO SAVE A LIFE TOMORROW



Purchased Shutterstock image

Questions

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