Jon Henrik Laake, Akuttklinikken, Rikshospitalet-OUS.

COVID-19: Evidensbaserte retningslinjer for behandling av ARDS og sepsis.

COVID-19

Evidence based

Elegance based

Are there any specific medicines to prevent or treat the new coronavirus?

To date, there is no specific medicine recommended to prevent or treat the new coronavirus (2019-nCoV).

However, those infected with the virus should receive appropriate care to relieve and treat symptoms, and those with severe illness should receive optimized supportive care.

Some specific treatments are under investigation, and will be tested through clinical trials.

WHO is helping to accelerate research and development efforts with a range of partners.

World Health Organization

#Coronavirus

JAMA Insights | CLINICAL UPDATE

Care for Critically Ill Patients With COVID-19

Srinivas Murthy, MD, CM, MHSc; Charles D. Gomersall, MBBS; Robert A. Fowler, MD, CM, MSc

«The critical care community has enormous experience in treating severe acute respiratory infections every year, often from uncertain causes. The foundation for care of severely ill patients with COVID-19 must be grounded in this evidence base and, in parallel, ensure that learning from each patient is maximized to help those who will follow.»

Caring for critically ill patients with COVID-19 is based on the usual management of viral pneumonia with respiratory failure with additional precautions to reduce risk of transmission.

Usual critical care

Many patients with severe COVID-19 develop acute respiratory distress syndrome (ARDS). Evidence-based guidelines for ARDS in the context of COVID-19 include treatments such as

- Conservative intravenous fluid strategies
- Empirical early antibiotics for possible bacterial pneumonia
- Consideration for early invasive ventilation
- Lung-protective ventilation strategies
- Periodic prone positioning during mechanical ventilation
- Consideration of extracorporeal membrane oxygenation

Modifications to usual critical care

- Admission of patients with suspected disease to private rooms when possible
- Use of medical face masks for symptomatic patients during assessment and transfer
- Maintain distancing of at least 2 m between patients
- Caution when using high-flow nasal oxygen or noninvasive ventilation due to risk of dispersion of aerosolized virus in the health care environment with poorly fitting masks
- Clinicians involved with aerosol-generating procedures should use additional airborne precautions including N95 respirators and eye protection

Facility planning

- Ensure staff have updated training in infection prevention and control including personal protective equipment
- Planning at local and regional levels for a potential surge in the need for critical care resources

COVID-19–specific considerations

Antiviral or immunomodulatory therapies are not yet proven effective for treatment of COVID-19. Patients should be asked to participate in clinical trials of supportive or targeted therapies.

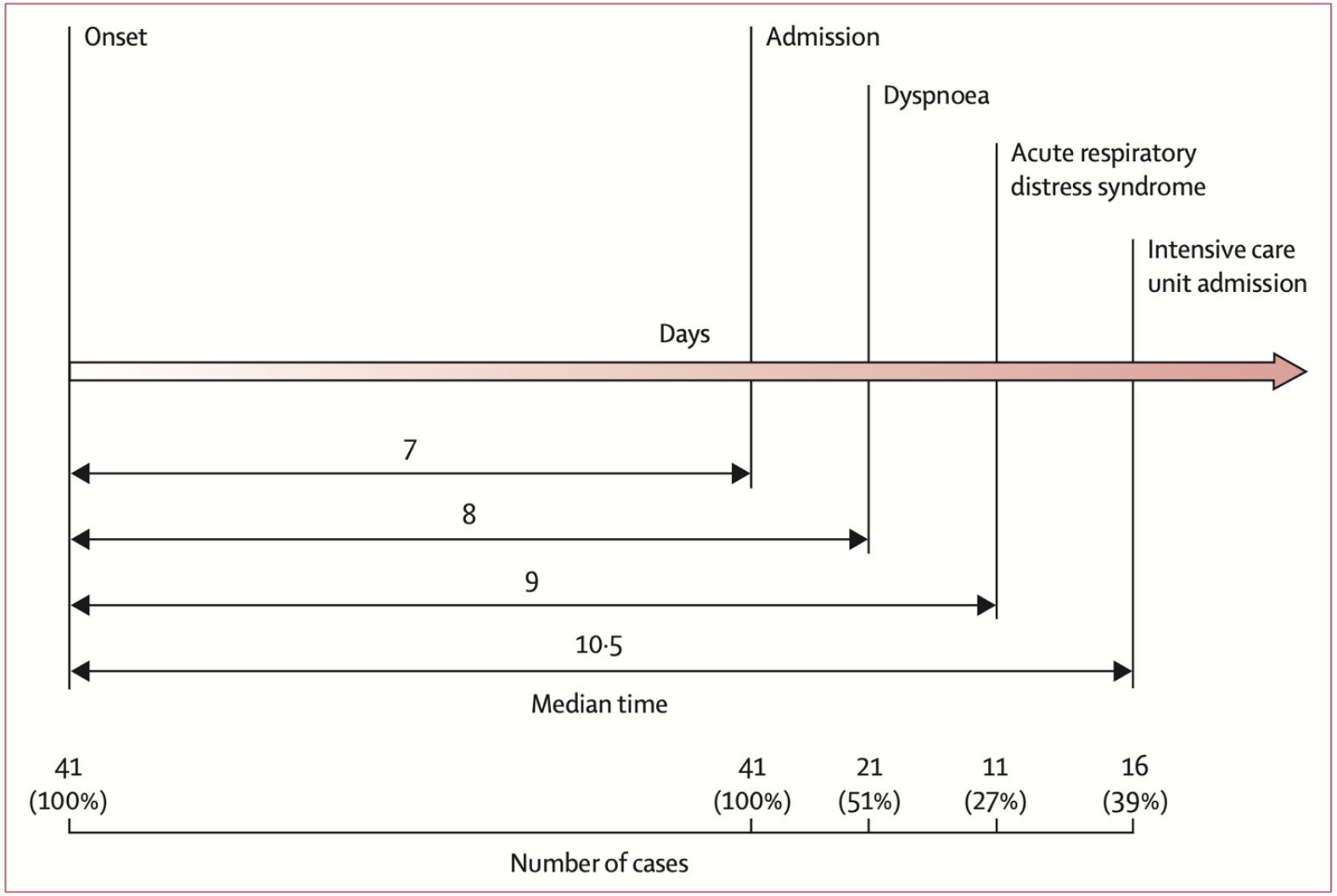


Figure 2: **Timeline of 2019-nCoV cases after onset of illness**

The Lancet Respiratory Medicine
Published: February 24, 2020 DOI:https://doi.org/10.1016/S2213-2600(20)30079-5

COVID-19 ARDS

60-year-old man
(day 8 after symptom onset)

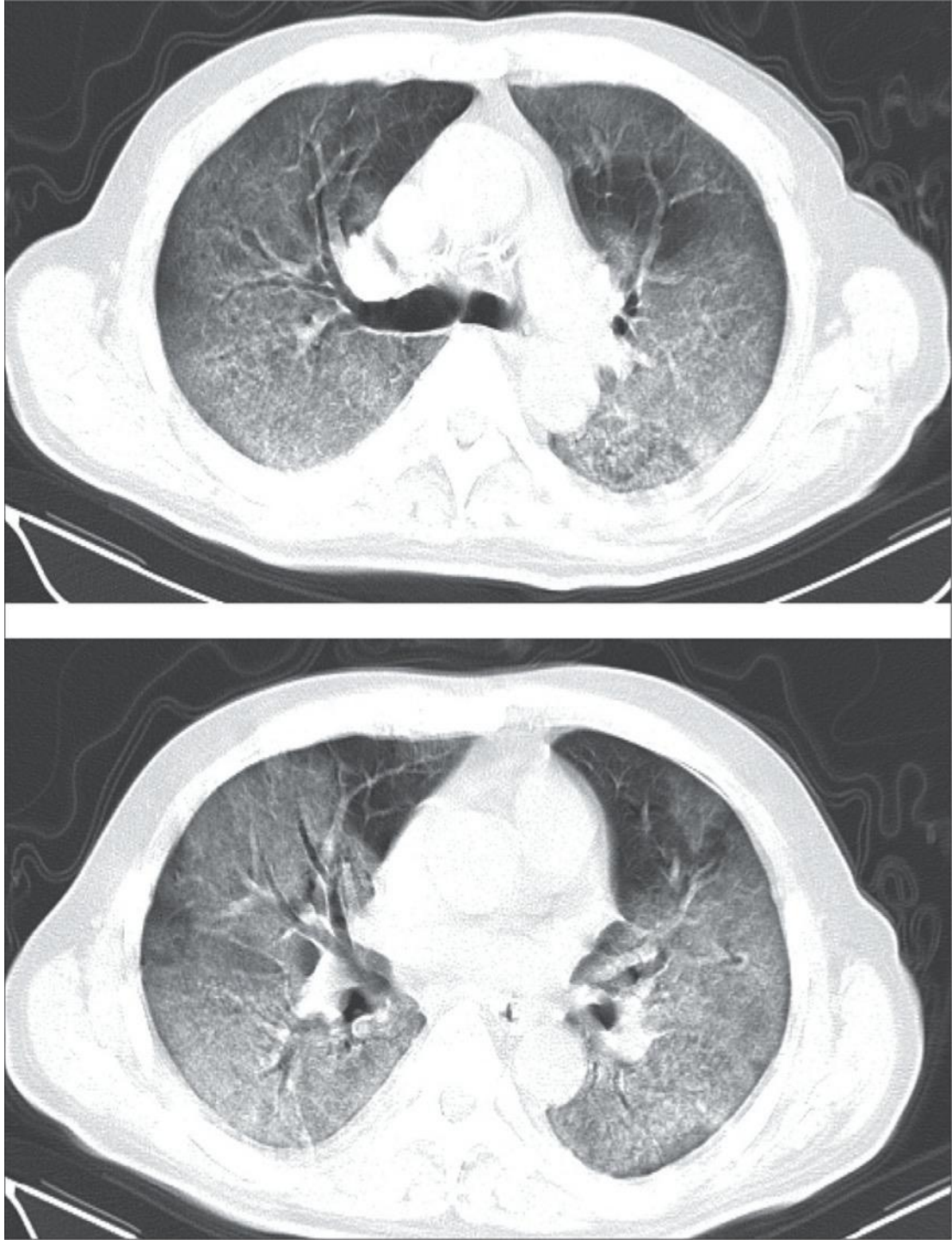
Lancet Infect Dis 2020 Feb 24
DOI:https://doi.org/10.1016/S1473-3099(20)30086-4

ARDS definition (Berlin 2011):

- acute respiratory failure
- bilateral infiltrates
- not explained by heart failure
- p/f ratio <= 40 kPa (300 mm Hg)
- PEEP => 5 cm H2O

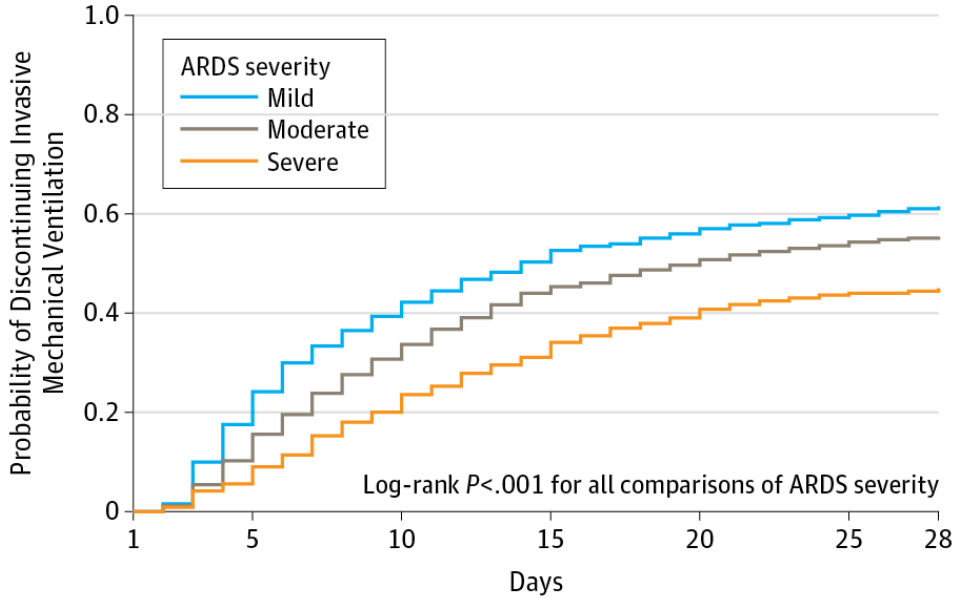
Mild ARDS: p/f 26.6 - 40 kPa
Moderate ARDS: p/f 13.3 – 26.6 kPa
Severe ARDS: p/f <= 13.3 kPa

Mortality: 30-50%



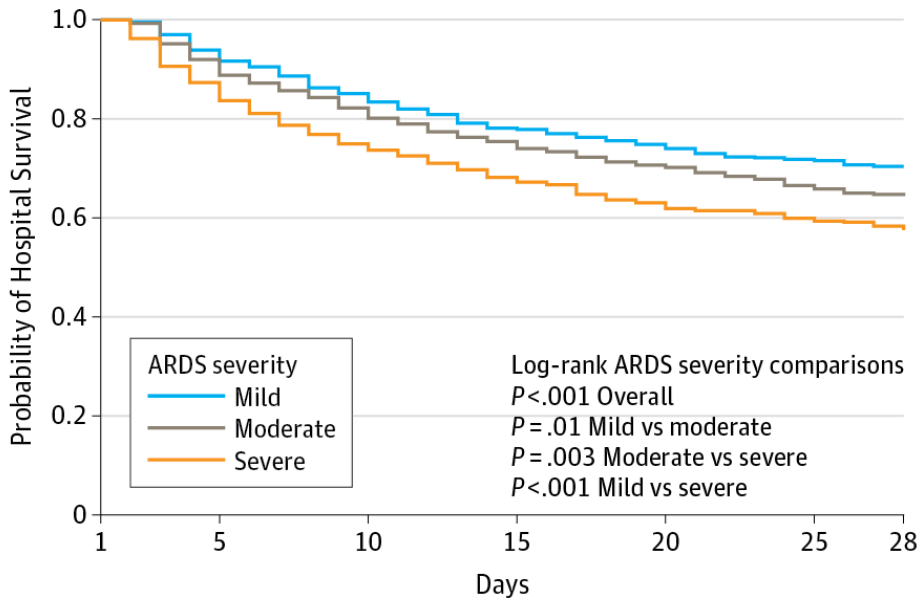
Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries

A Probability of discontinuing mechanical ventilation by ARDS severity



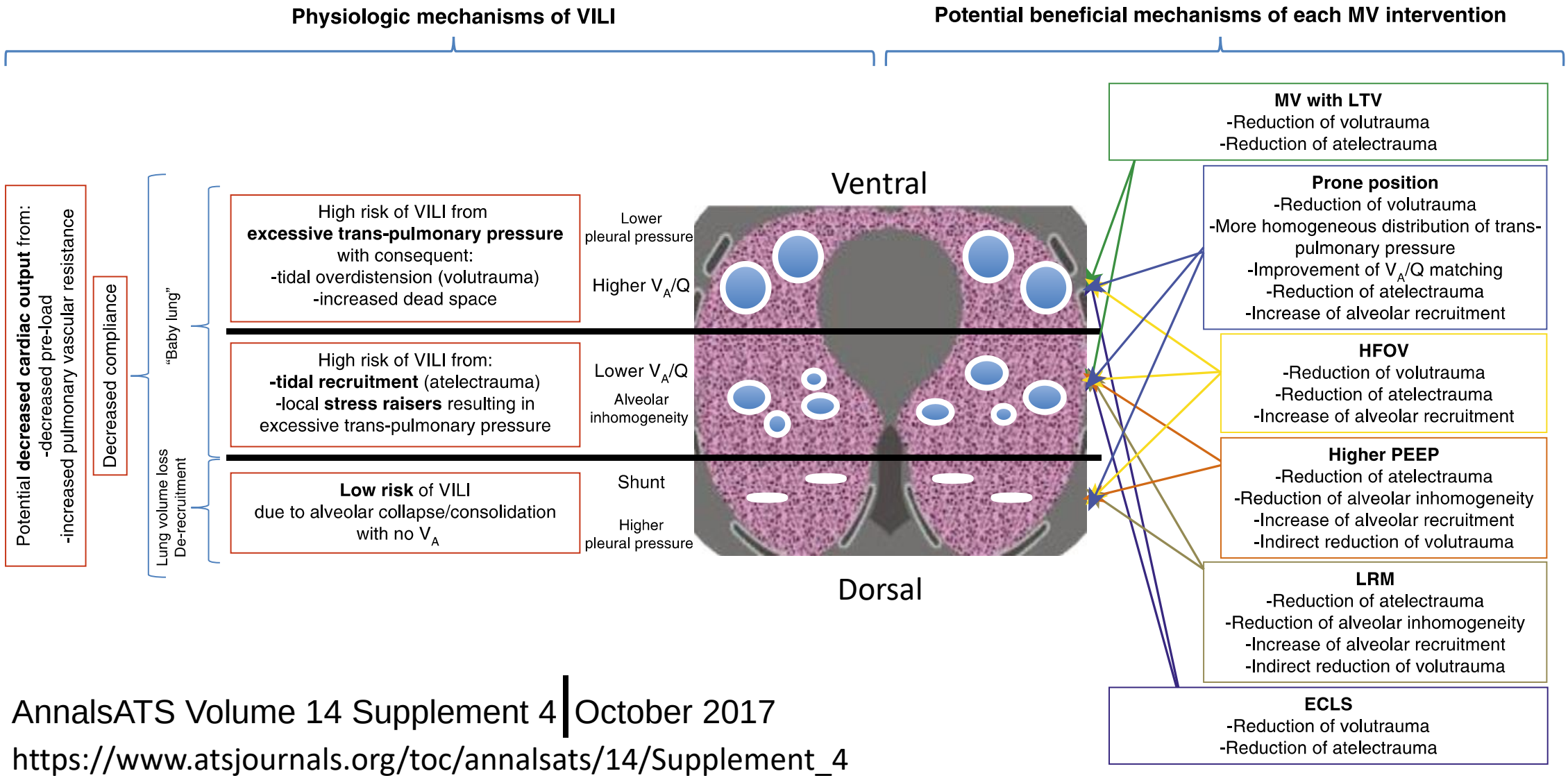
No. at risk, ARDS severity							
Mild	714	585	425	342	298	274	260
Moderate	1106	986	752	599	533	484	467
Severe	557	521	431	365	319	293	287

B Probability of hospital survival by ARDS severity



No. at risk, ARDS severity							
Mild	708	662	599	548	522	501	489
Moderate	1101	1008	892	807	752	708	688
Severe	553	479	401	360	325	304	296

JAMA. 2016;315(8):788-800. doi:10.1001/jama.2016.0291



AnnalsATS Volume 14 Supplement 4 | October 2017
https://www.atsjournals.org/toc/annalsats/14/Supplement_4

Respirator-behandling som ved ARDS

ARDS: Følgende retningslinjer er fritt tilgjengelige:

Nordiske (SSAI):

Scandinavian clinical practice guideline on mechanical ventilation in adults with the acute respiratory distress syndrome
https://onlinelibrary.wiley.com/doi/full/10.1111/aas.12449 (2015)

Scandinavian clinical practice guideline on fluid and drug therapy in adults with acute respiratory distress syndrome
https://onlinelibrary.wiley.com/doi/full/10.1111/aas.12713 (2016)

(flere relevante nordiske retningslinjer her: https://www.ssai.info/guidelines/)

Transatlantiske:

Mechanical Ventilation in Adults with Acute Respiratory Distress Syndrome. Summary of the Experimental Evidence for the Clinical Practice Guideline
https://www.atsjournals.org/doi/full/10.1164/rccm.201703-0548ST (2017)

Britiske:

Guidelines on the management of acute respiratory distress syndrome
https://bmjopenrespres.bmj.com/content/6/1/e000420 (2019)

Sepsis

Sepsis: Følgende retningslinjer er fritt tilgjengelige:

Transatlantiske:

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock
https://link.springer.com/article/10.1007%2Fs00134-017-4683-6

Nordiske (SSAI):

Scandinavian SSAI clinical practice guideline on choice of inotropic agent for patients with acute circulatory failure
https://onlinelibrary.wiley.com/doi/full/10.1111/aas.13089

Scandinavian SSAI clinical practice guideline on choice of first-line vasopressor for patients with acute circulatory failure
https://onlinelibrary.wiley.com/doi/full/10.1111/aas.12780

Scandinavian clinical practice guideline on choice of fluid in resuscitation of critically ill patients with acute circulatory failure
https://onlinelibrary.wiley.com/doi/full/10.1111/aas.12429

(flere relevante nordiske retningslinjer her: https://www.ssai.info/guidelines/)

Guidelines

Early recognition of ARDS, evidence-based practices:

All patients:

- **pressure and volume limitation** (PVL) in MV (strong recommendation) **(5-8 mL/kg PBW; PIP < 30 cm H2O)**
- **fluid restriction** (weak recommendation)

Moderate to severe ARDS:

- higher positive end-expiratory pressure (PEEP) (weak recommendation)
- ventilation of patients in the prone position (weak recommendation)
- utilisation of neuromuscular blocking agents (NMBAs) (weak recommendation).
- recruitment manoeuvres (not recommended) **
- Nitric-oxide (NO) (bridge to ECMO, **only**)
- HFOV (not recommended)
- Corticosteroids (not recommended)

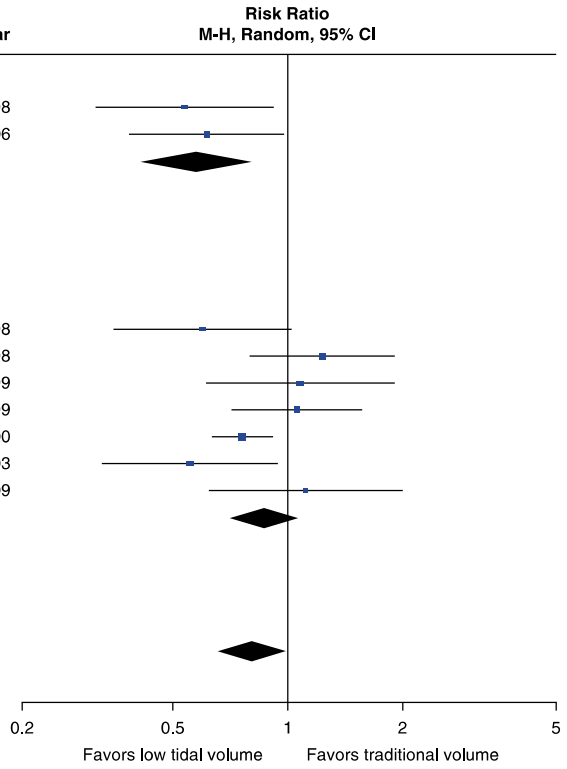
Unable to provide evidence-based recommendations:

- ventilator mode (volume-controlled vs pressure-controlled ventilation, modes allowing spontaneous vs fully controlled ventilation),
- FiO2 or oxygenation target, due to a lack of data from clinical trials.

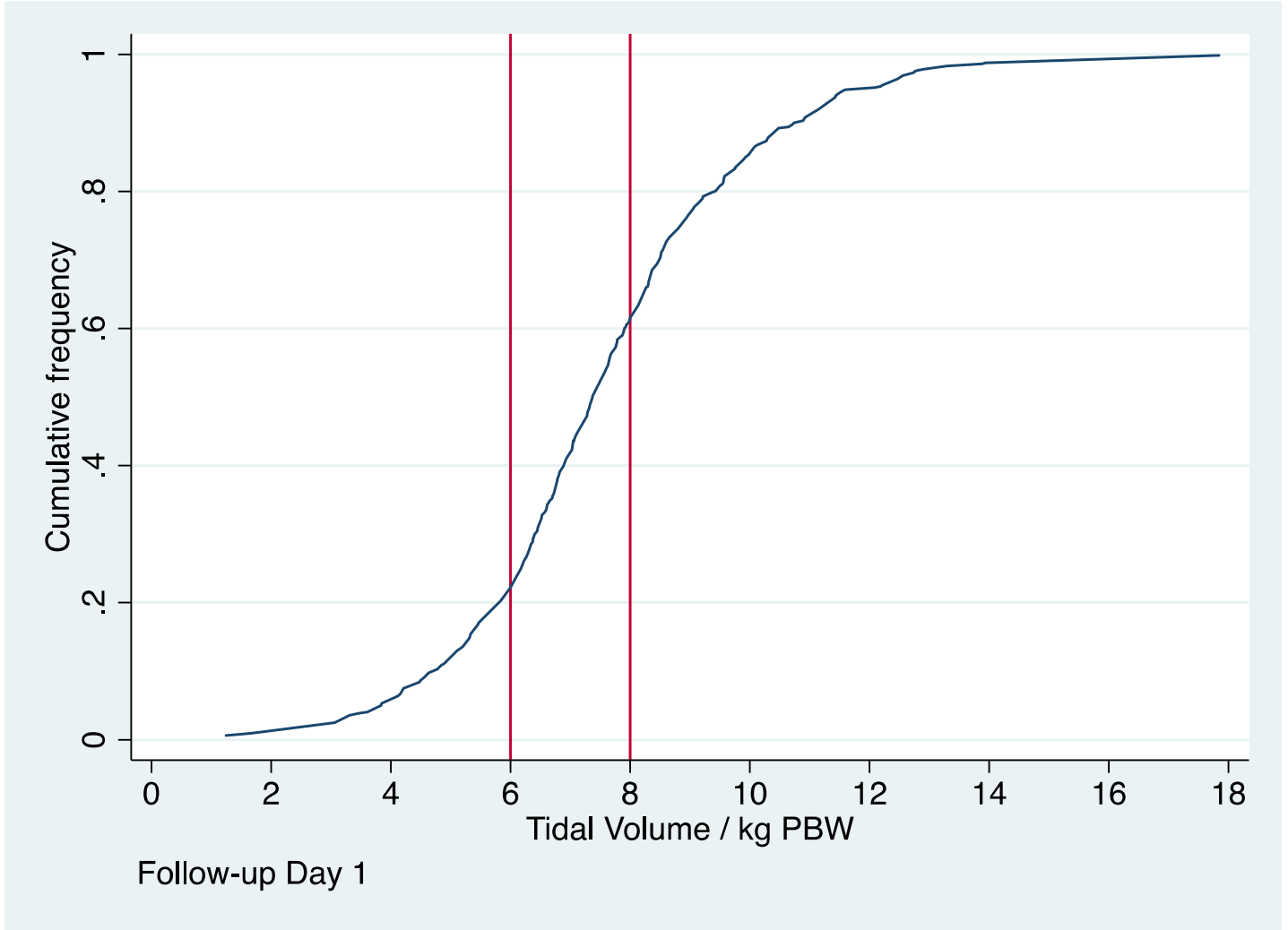
COVID-19 Non-invasive ventilation (not recommended), High-flow nasal cannula (not recommended)

Low Tidal Volume ventilation

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); $I^2 = 73.8\%$							



LUNG SAFE: N/SE/DK:



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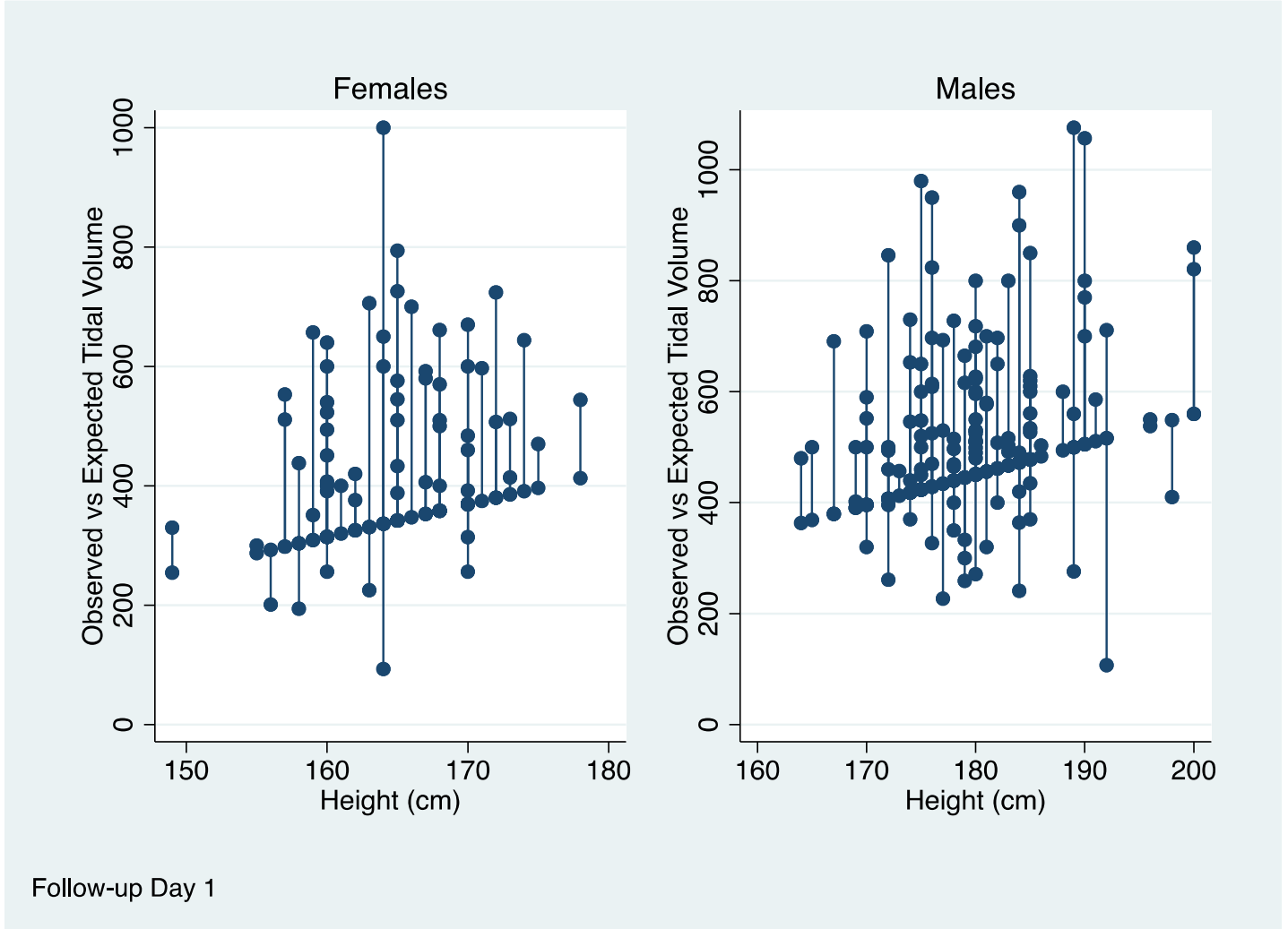
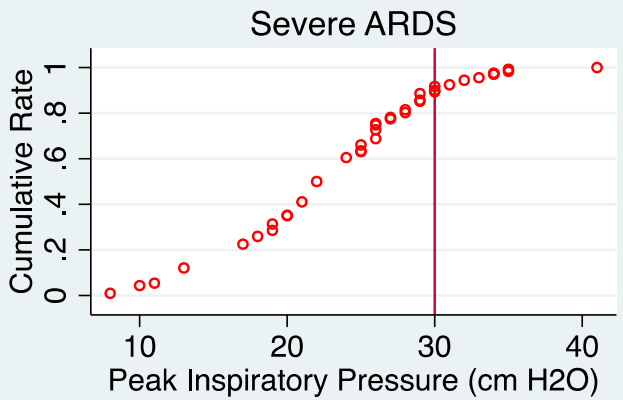
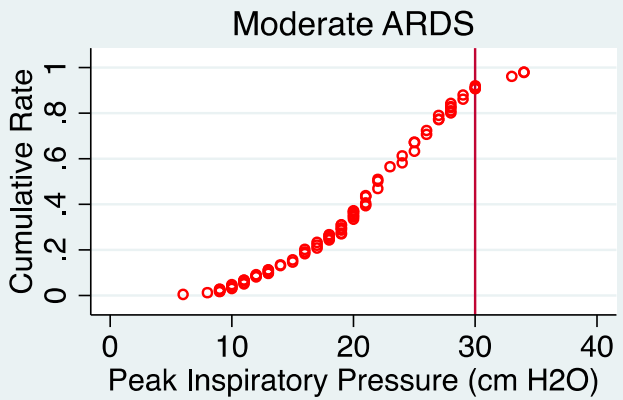
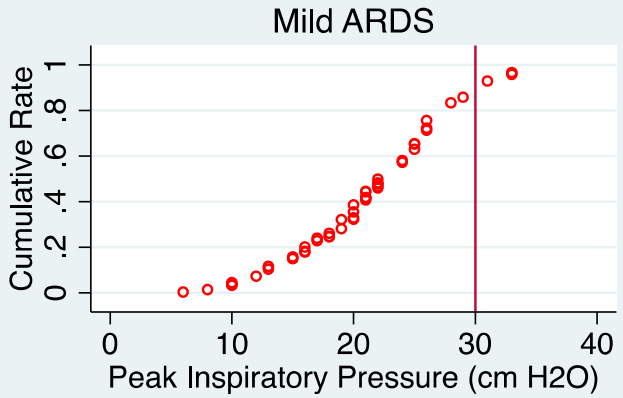


LUNG SAFE: N/SE/DK:

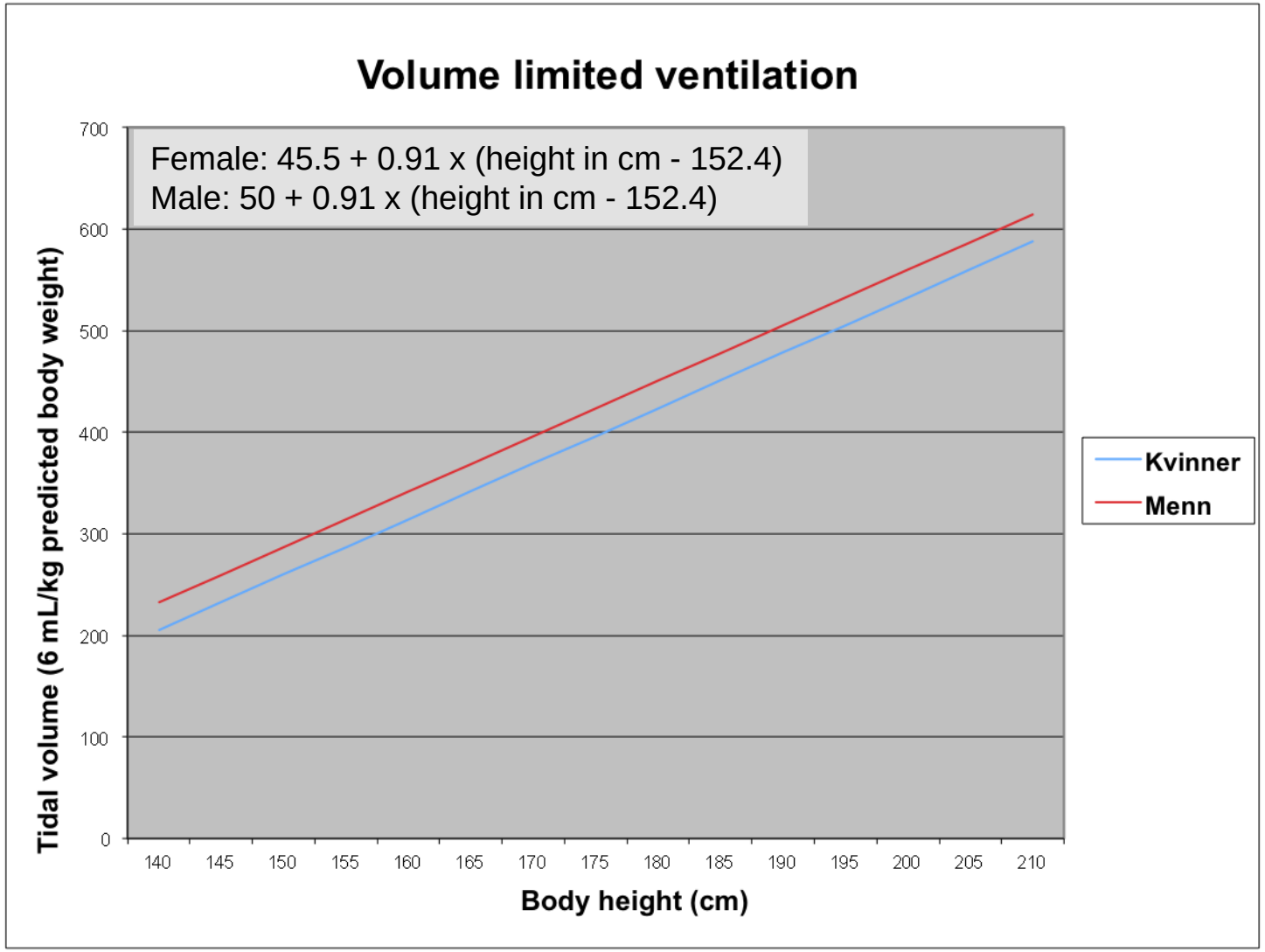






Follow-up Day 1

«6 mL/kg PBW»



	Female		Male	
Height	Predicted body weight	TV	Predicted body weight	TV
140	34	205	39	232
145	39	233	43	260
150	43	260	48	287
155	48	287	52	314
160	52	314	57	341
165	57	342	61	369
170	62	369	66	396
175	66	396	71	423
180	71	424	75	451
185	75	451	80	478
190	80	478	84	505
195	84	506	89	533
200	89	533	93	560
205	93	560	98	587
210	98	587	102	614

Female: 45.5 + 0.91 x (height in cm - 152.4)
Male: 50 + 0.91 x (height in cm - 152.4)

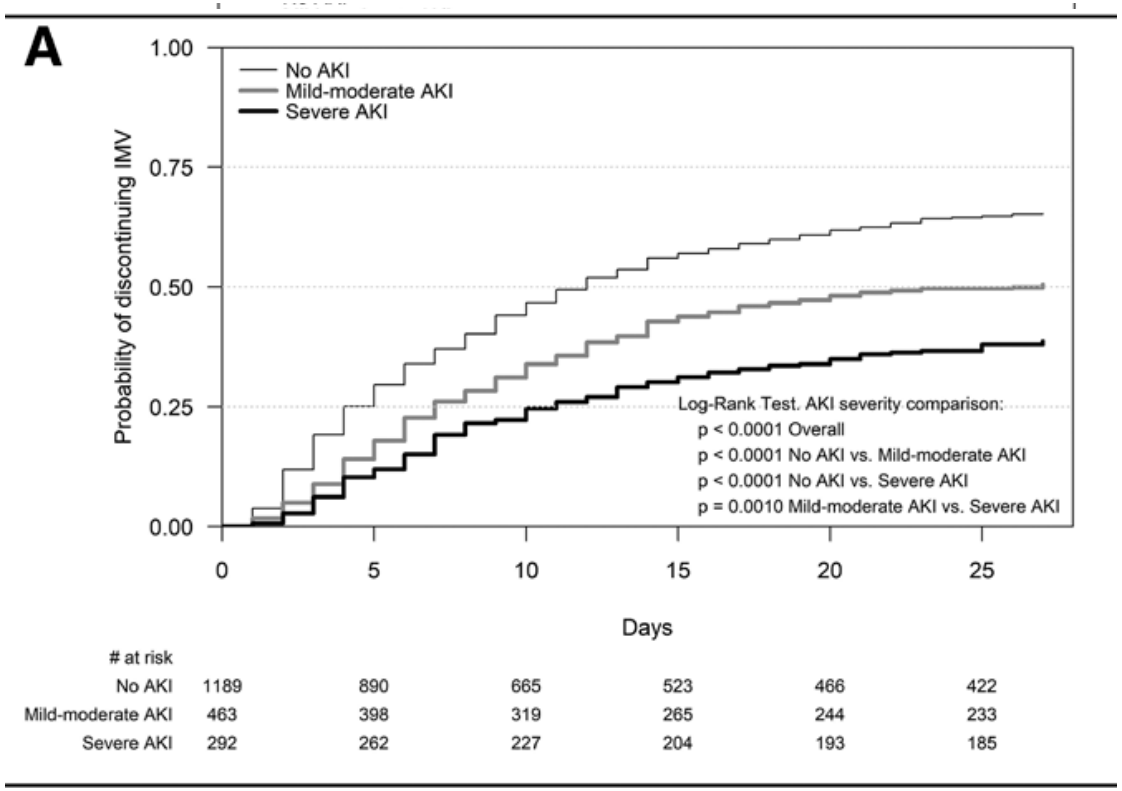
Impact of Early Acute Kidney Injury on Management and Outcome in Patients With Acute Respiratory Distress Syndrome

Any degree of kidney injury impoacts on probability of survival in patients with ARDS

«What of pharmacological manipulations? Apart from avoiding nephrotoxins such as aminoglycosides and iodinated radiocontrast agents, there is little to recommend.»

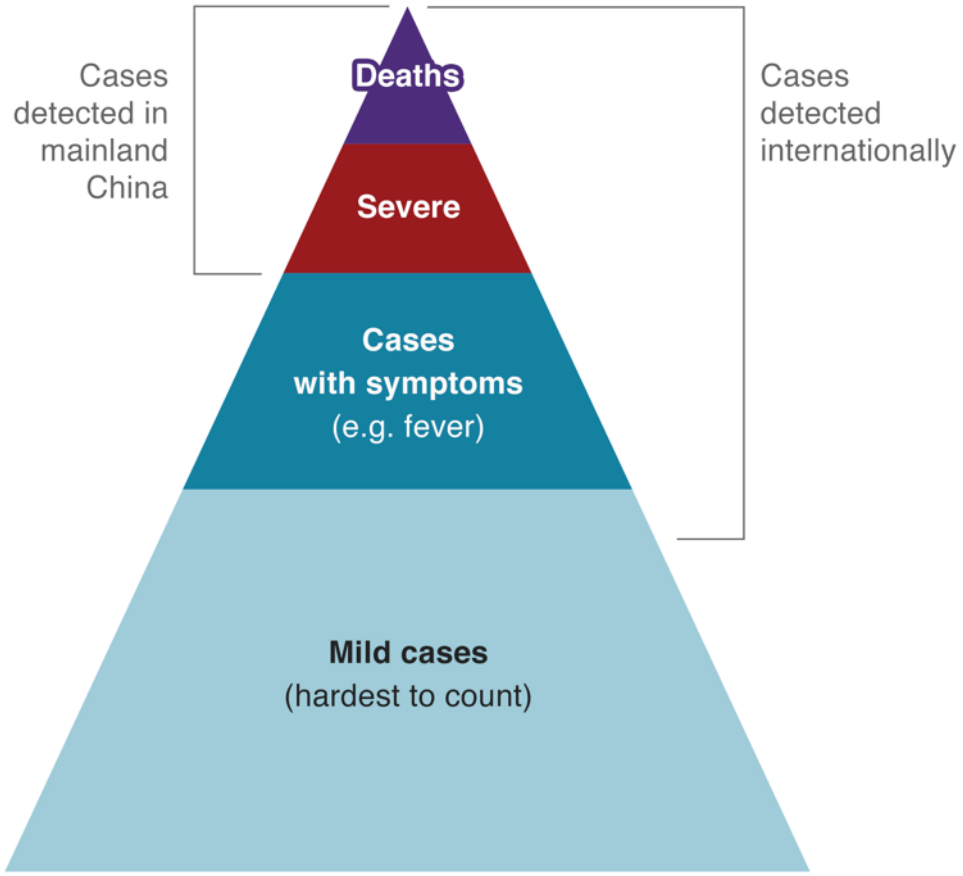
(Michael J O'Leary and David J Bihari)

Preventing renal failure in the critically ill There are no magic bullets—just high quality intensive care. BMJ. 2001 Jun 16; 322(7300): 1437–1439.

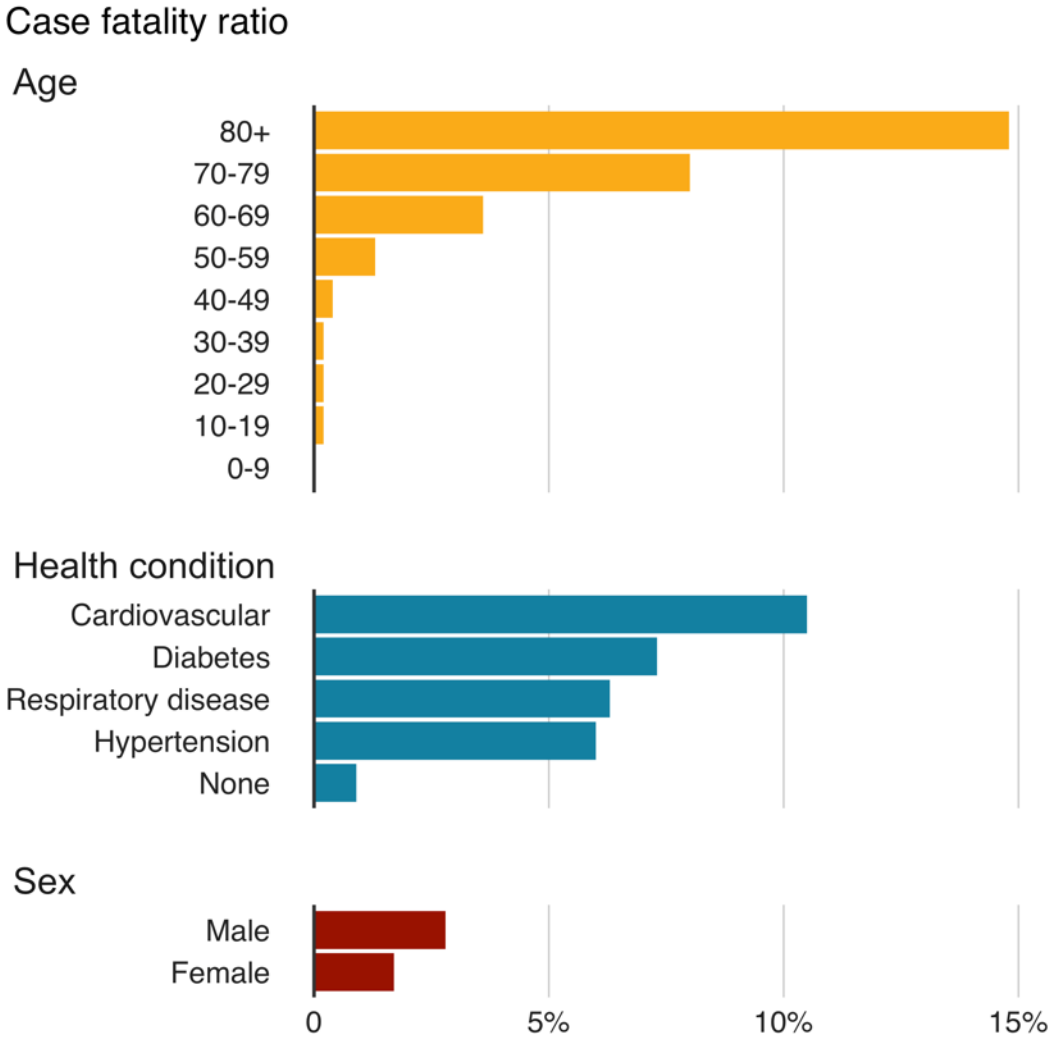


Crit Care Med 47 (9), 1216-1225. Sep 2019.
DOI: 10.1097/CCM.0000000000003832

Most cases are never counted



Death rate varies by age, health and sex



Kilde: BBC

- We **recommend against** the routine use of an NMBA infusion in adults with ARDS before optimising mechanical ventilation and assessing ARDS severity.

- In adults with moderate or severe ARDS who are ventilated using a lighter sedation strategy we **suggest** against using an NMBA infusion (Suggestion, low certainty of evidence).

- If neuromuscular blockade is required to facilitate lung protective ventilation; we **suggest** using intermittent NMBA boluses with judicious deep sedation over an NMBA infusion with deep sedation (Suggestion, low certainty in the evidence).

- In adults with moderate or severe ARDS who clinicians determine require ongoing deep sedation, and neuromuscular blockade to facilitate lung protective ventilation, we **suggest** using an NMBA infusion for up to 48 hours, over intermittent boluses of NMBA (Suggestion, low certainty of evidence).

Remarks: This recommendation may apply to facilitate lung protective ventilation in adults who are persistently hypoxemic, ventilated in the prone position, or at risk for injurious ventilation (i.e. dyssynchronous with the ventilator or elevated plateau pressures).

Alhazzani et al, Intensive Care Medicine, *in press*

Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury

	Outcomes of corticosteroid therapy*	Comment
MERS-CoV	Delayed clearance of viral RNA from respiratory tract[2]	Adjusted hazard ratio 0·4 (95% CI 0·2–0·7)
SARS-CoV	Delayed clearance of viral RNA from blood[5]	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis[6]	Associated with higher cumulative dose, 10 975 mg *vs* 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes[7]	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors[8]	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality[9]	Risk ratio for mortality 1·75 (95% CI 1·3–2·4) in a meta-analysis of 6548 patients from ten studies
RSV	No clinical benefit in children[10,11]	No effect in largest randomised controlled trial of 600 children, of whom 305 (51%) had been treated with corticosteroids

CoV=coronavirus. MERS=Middle East respiratory syndrome. RSV=respiratory syncytial virus. SARS=severe acute respiratory syndrome. *Hydrocortisone, methylprednisolone, dexamethasone, and prednisolone.

Table: **Summary of clinical evidence to date**

https://doi.org/10.1016/ S0140-6736(20)30317-2

Slutt

survival benefit ?

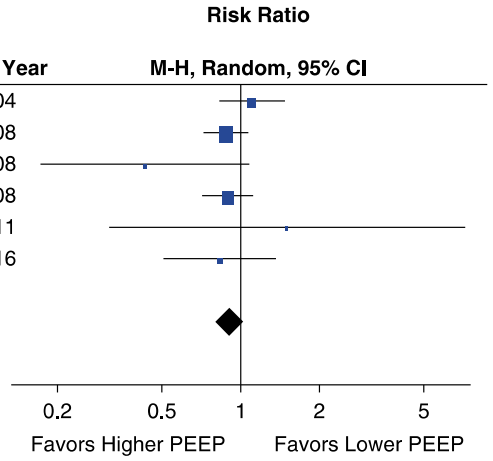
PEEP
> 5 cm H2O

oxygenation ✓

but...

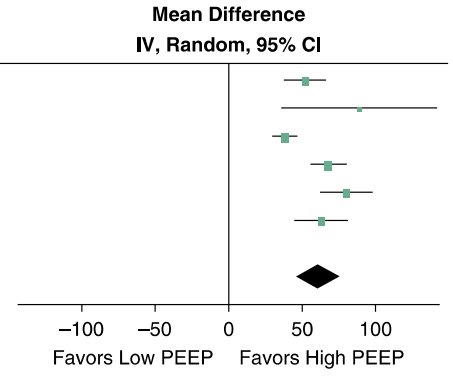
Study or Subgroup	High Mortality Events	High Total Patients	Low Mortality Events	Low Total Patients	Weight	Risk Ratio M-H, Random, 95% CI	Year
Brower *et al.*, 2004	76	276	68	273	19.2%	1.11 [0.83, 1.46]	2004
Meade *et al.*, 2008	135	475	164	508	40.8%	0.88 [0.73, 1.06]	2008
Talmor *et al.*, 2008	5	30	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)



Study or Subgroup	High PEEP Mean	High PEEP SD	High PEEP Total	Low PEEP Mean	Low PEEP SD	Low PEEP Total	Weight	Mean Difference IV, Random, 95% CI	Year
Brower *et al.*, 2004	220	89	244	168	66	230	18.8%	52.00 [37.95, 66.05]	2004
Talmor *et al.*, 2008	280	126	29	191	71	29	6.1%	89.00 [36.36,141.64]	2008
Meade *et al.*, 2008	187.4	68.8	464	149.1	60.6	498	21.0%	38.30 [30.08, 46.52]	2008
Mercat *et al.*, 2008	218	97	378	150	69	371	19.6%	68.00 [55.96, 80.04]	2008
Hodgson *et al.*, 2011	220	20	10	140	20	10	17.3%	80.00 [62.47, 97.53]	2011
Kacmarek *et al.*, 2016	198.5	78.6	94	135.6	43.5	101	17.1%	62.90 [44.89, 80.91]	2016
Total (95% CI)			**1219**			**1239**	**100.0%**	**61.24 [45.92, 76.57]**	

Heterogeneity: $Tau^2 = 273.32$; $Chi^2 = 30.33$, df = 5 (P < 0.0001); $I^2 = 84\%$
Test for overall effect: Z = 7.83 (P < 0.00001)

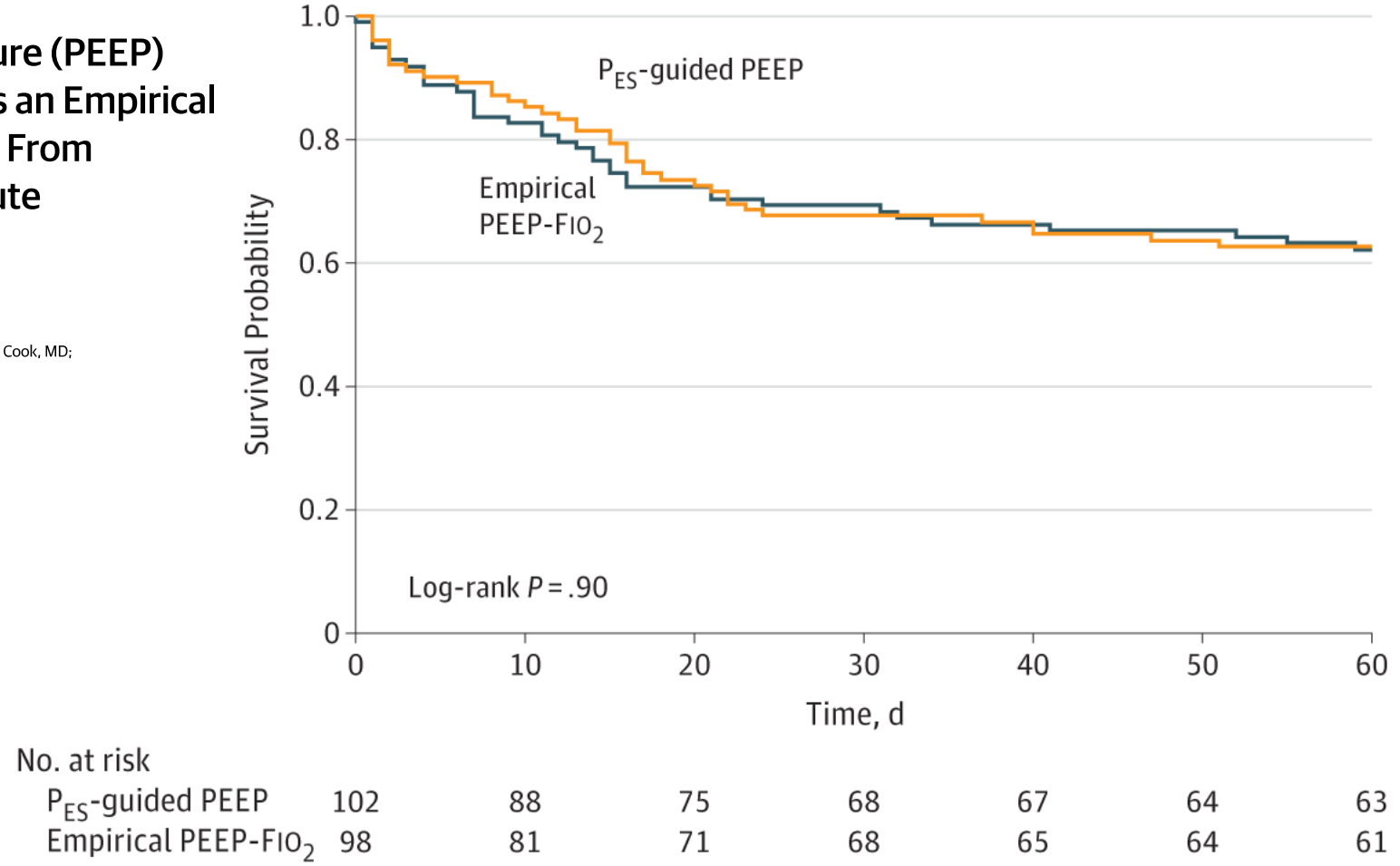


JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure–Guided Strategy vs an Empirical High PEEP-FIO_2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Jeremy R. Beitler, MD, MPH; Todd Sarge, MD; Valerie M. Banner-Goodspeed, MPH; Michelle N. Gong, MD, MSc; Deborah Cook, MD; Victor Novack, MD, PhD; Stephen H. Loring, MD; Daniel Talmor, MD, MPH; for the EPVent-2 Study Group



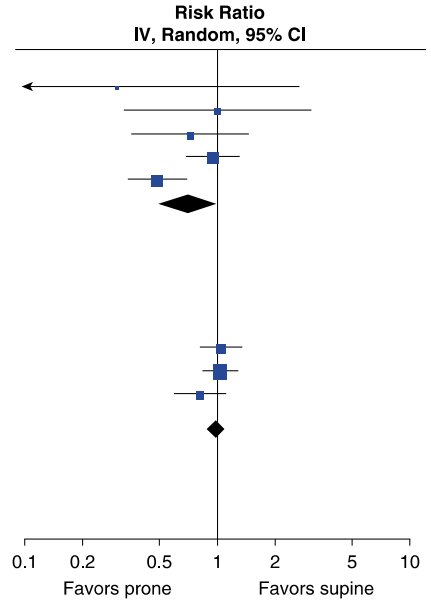
JAMA. 2019;321(9):846-857. doi:10.1001/jama.2019.0555

survival benefit if combined with LTV ✓

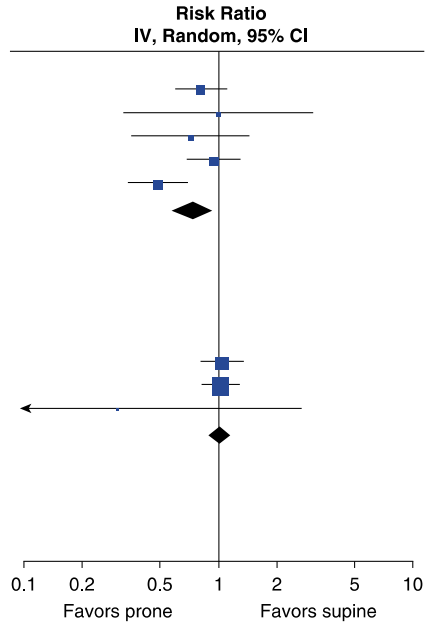
Prone positioning

survival benefit if > 12 h / day ✓

Study or Subgroup	Prone Events	Prone Total	Supine Events	Supine Total	Weight	Risk Ratio IV, Random, 95% CI
Lung Protective Ventilation Studies						
Voggenreiter *et al.* 2005	1	21	3	19	3.1%	0.30 [0.03, 2.66]
Chan *et al.* 2007	4	11	4	11	9.9%	1.00 [0.33, 3.02]
Fernandez *et al.* 2008	8	21	10	19	18.8%	0.72 [0.36, 1.45]
Taccone *et al.* 2009	52	166	57	172	35.0%	0.95 [0.69, 1.29]
Guerin *et al.* 2013	38	237	75	229	33.3%	0.49 [0.35, 0.69]
Subtotal (95% CI)		**456**		**450**	**100.0%**	**0.70 [0.47, 1.04]**
Total events	103		149			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 8.70$, df = 4 (P = 0.07); $I^2 = 54\%$						
Test for overall effect: Z = 1.76 (P = 0.08)						
Non-Lung Protective Ventilation Studies						
Gattinoni *et al.* 2001	70	152	67	152	31.6%	1.04 [0.82, 1.34]
Guerin *et al.* 2004	134	413	119	378	46.8%	1.03 [0.84, 1.26]
Mancebo *et al.* 2006	38	76	37	60	21.6%	0.81 [0.60, 1.10]
Subtotal (95% CI)		**641**		**590**	**100.0%**	**0.98 [0.85, 1.13]**
Total events	242		223			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.02$, df = 2 (P = 0.37); $I^2 = 1\%$						
Test for overall effect: Z = 0.24 (P = 0.81)						
Test for subgroup differences: $Chi^2 = 2.50$, df = 1 (P = 0.11), $I^2 = 60.0\%$						



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), $I^2 = 74.5\%$						



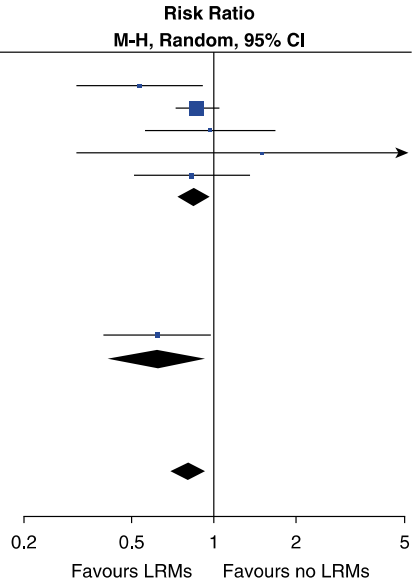
survival benefit ✓

Lung recruitment

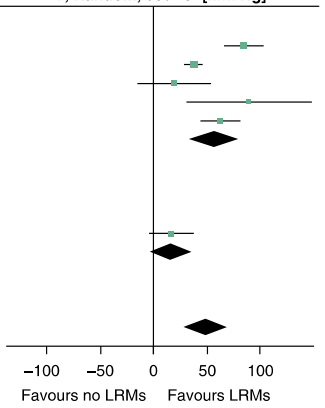
oxygenation ✓

but...

Study or Subgroup	LRMs Events	LRMs Total	No LRMs Events	No LRMs Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Co-intervention with higher PEEP							
Amato 1998	11	29	17	24	8.9%	0.54 [0.31, 0.91]	1998
Meade 2008	145	475	178	508	59.3%	0.87 [0.73, 1.04]	2008
Huh 2009	14	30	13	27	8.4%	0.97 [0.56, 1.68]	2009
Hodgson 2011	3	10	2	10	1.1%	1.50 [0.32, 7.14]	2011
Kacmarek 2016	22	99	27	101	10.4%	0.83 [0.51, 1.36]	2016
Subtotal (95% CI)		**643**		**670**	**88.0%**	**0.84 [0.72, 0.98]**	
Total events	195		237				
Heterogeneity: Tau^2 = 0.00; Chi^2 = 3.71, df = 4 (P = 0.45); I^2 = 0%							
Test for overall effect: Z = 2.16 (P = 0.03)							
No co-intervention with higher PEEP							
Xi 2010	18	55	29	55	12.0%	0.62 [0.39, 0.98]	2010
Subtotal (95% CI)		**55**		**55**	**12.0%**	**0.62 [0.39, 0.98]**	
Total events	18		29				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.06 (P = 0.04)							
Total (95% CI)		**698**		**725**	**100.0%**	**0.81 [0.69, 0.95]**	
Total events	213		266				
Heterogeneity: Tau^2 = 0.00; Chi^2 = 5.30, df = 5 (P = 0.38); I^2 = 6%							
Test for overall effect: Z = 2.57 (P = 0.01)							
Test for subgroup differences: Chi^2 = 1.58, df = 1 (P = 0.21), I^2 = 36.7%							



Study or Subgroup	LRMs Mean [mm Hg]	LRMs SD [mm Hg]	LRMs Total	No LRMs Mean [mm Hg]	No LRMs SD [mm Hg]	No LRMs Total	Weight	Mean Difference IV, Random, 95% CI [mm Hg]	Year
Co-intervention with higher PEEP									
Amato 1998	220	38	29	135	29	24	18.9%	85.00 [66.95, 103.05]	1998
Meade 2008	187	69	464	149	61	498	21.1%	38.00 [29.75, 46.25]	2008
Huh 2009	160	82	30	140	47	27	14.2%	20.00 [–14.28, 54.28]	2009
Hodgson 2011	230	70	10	140	63	10	8.6%	90.00 [31.63, 148.37]	2011
Kacmarek 2016	199	79	94	136	44	104	18.9%	63.00 [44.93, 81.07]	2016
Subtotal (95% CI)			**627**			**663**	**81.7%**	**57.01 [32.72, 81.30]**	
Heterogeneity: Tau^2 = 578.07; Chi^2 = 28.97, df = 4 (P < 0.00001); I^2 = 86%									
Test for overall effect: Z = 4.60 (P < 0.00001)									
No co-intervention with higher PEEP									
Xi 2010	142	61	55	125	46	55	18.3%	17.00 [–3.19, 37.19]	2010
Subtotal (95% CI)			**55**			**55**	**18.3%**	**17.00 [–3.19, 37.19]**	
Heterogeneity: Not applicable									
Test for overall effect: Z = 1.65 (P = 0.10)									
Total (95% CI)			**682**			**718**	**100.0%**	**49.67 [27.75, 71.59]**	
Heterogeneity: Tau^2 = 575.99; Chi^2 = 37.15, df = 5 (P < 0.00001); I^2 = 87%									
Test for overall effect: Z = 4.44 (P < 0.00001)									
Test for subgroup differences: Chi^2 = 6.16, df = 1 (P = 0.01), I^2 = 83.8%									

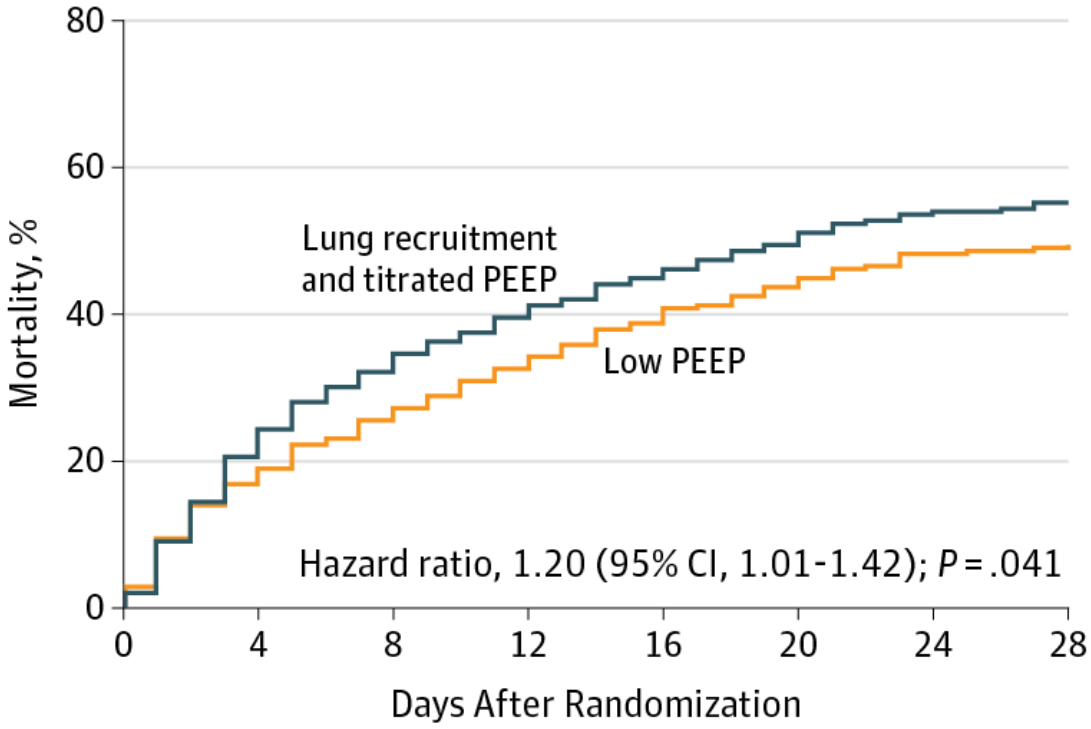


JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Lung Recruitment and Titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on Mortality in Patients With Acute Respiratory Distress Syndrome

A Randomized Clinical Trial

Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators



No. at risk

Lung recruitment and titrated PEEP	501	397	340	303	276	254	233	225
Low PEEP	509	423	378	343	312	286	264	260

JAMA. 2017;318(14):1335-1345. doi:10.1001/jama.2017.14171

INITIAL

IN ITA

COVID-19

Continuously increas
organization to cope
just O_2, or NIV/IMV; ne
involving sub-intens
conventional surgica

KE

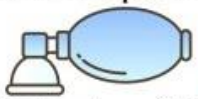
you n
know
alterr
know/

Take care of you
practice donning and
quarantine personnel
Be properly organized
patients, transferring
and eventually diverg

(EARLY) DIAGNOSIS

Patients similar to one another easy to diagnose: CXR interstitiopathy, bilateral infiltrates common (rarely asymmetrical), with gravitational distribution. ABG/blood tests: initially moderate hypoxemia, mild acidosis with normal lactates, severe base deficit, high anion gap, elevated LDH, very high CRP, elevated CK, negative procalcitonin.

Early diagnosis mandatory to properly manage patients & respect pre-defined pathways: in area involved by outbreak, interstitial pneumonia/respiratory failure &/or flu like syndrome = treat as COVID positive unless proven otherwise... using swab to exclude more than to confirm?? be careful, do not blindly trust negative swab if symptoms/pneumonia with suggestive CXR, CT scan, LUS: go for bronchoalveolar lavage/deep bronchial aspirate/ bronchoaspirate (prefer closed suction systems!).



MV & WEANING

Respiratory failure take time to improve, usually need a phase of controlled MV with high PEEP (15-20 cmH20) before assisted breathing: check whole clinical conditions, not only P/F. Often patients are easy to ventilate, with high compliance and acceptable driving P, but be prepared to accept low pH to avoid excessive AW pressures; be cautious with Vt to avoid overdistension. Consider (early & prolonged) NMBAS. Be careful with early spontaneous ventilation due to the risk of derecruitment, particularly in posterior lung fields. Very long time needed to wean; due to delayed weaning, (early) think to tracheostomy: MV/sedation management easier/proning still feasible.

LUNG ULTRASOUND

Couple of LUS pattern reported:

- sonographic sign of pulmonary interstitial syndrome with diffuse, multiple B-lines involving both anterior & posterior lung fields, maybe coalescent, with bilateral distribution = probably PEEP responders: titrate PEEP (check if pattern disappears as increasing PEEP);
- normal anterior lung fields (= risk of overdistension if high PEEP) + tissue like pattern in posterior lung fields, probably not recruitable with PEEP alone = maybe need prone positioning to be recruited.

Consider daily LUS (as feasible due to high number of patients), to guide MV settings/management (ie PEEP titration, prone positioning) & monitor evolution: loss of aeration/re-aeration, early detect complications ie consolidation suggesting superinfections, barotrauma due to high MV settings/recruitment manoeuver (ie PTX/subcutaneous emphysema).

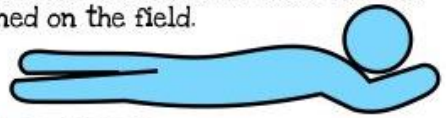
FLUIDS

Keep negative fluid balance, with minimal volemia requested to avoid hypoperfusion (inotropes/ vasopressors generally better vs fluid replacement, if no indicators of hypovolemia).

Due to high right pressures MV induced, often IVC fixed/dilated. Heart involved frequently with hypo/dyskinesia. Strictly control temperature; consider eventual severe glicemic/metabolic derangement (antivirals? inflammation??), and eventual hypoalbuminemia (both reported).

PRONING

To improve prone positioning effectiveness keep patient proned for 18 if no instability/ complications; then 6h supine if feasible, otherwise early re-proning. Consider longer PP (ie 20-22h) if severe hypoxemia persists, until stable P/F>80. Due to lung injury, repeated PP usually required, not easy for staff due to PPE, particularly if inexperienced nurses enrolled from not ICU areas, trained on the field.



ECMO ??

Patients are hypoxemic but really compliant to MV, and prone positioning responders. So, to date, most do not need rescue VV-ECMO vs H1N1 pneumonia (and this is good as patients admission massive...). Consider eventual need for veno-arterial support due to myocarditis/hypoxic cardiac arrest, or veno-arterial-venous ECMO if hemodynamic impairment + no responders to MV.

ID-19

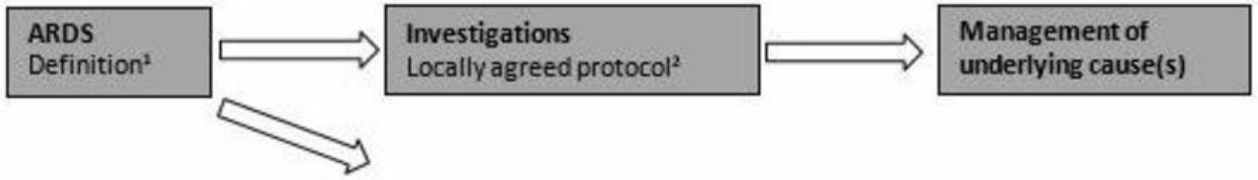
with intensivists
20

be ready to find
s.

amount of critical
eed to be managed.

UK Guidelines on the management of acute respiratory distress syndrome

BMJ Open Resp Res 2019;6:e000420. doi:10.1136/ bmjresp-2019-000420



ARDS specific management		
Mild 27kPaO_2 /FIO_2 ≤ 40kPa with PEEP or CPAP 5 cmH_2O	**Moderate** 13 PaO_2/FIO_2 ≤ 27kPa with PEEP 5 cmH_2O	**Severe** PaO_2/FIO_2 < 13 kPa with PEEP 5 cmH_2O
Conservative fluid balance target		
Low tidal volume ventilation (≤6 ml/Kg IBW[3]; Plateau pressure <30cmH_2O)		
	Higher PEEP[4]	
	Prone positioning (≥12 hr/day)	
	Neuro-muscular blockade (first 48 hour)	
		ECMO centre referral[5]
Non ARDS-specific support		
Rehabilitation: early mobilisation, NICE CG83[6]		
Nutrition: enteral where possible, trophic feeding acceptable initially, consider naso-jejunal tube after pro-kinetics for absorption failure		
Transfusion of blood products: avoid unless absolutely indicated		
Sedation: avoid associated adverse effects		

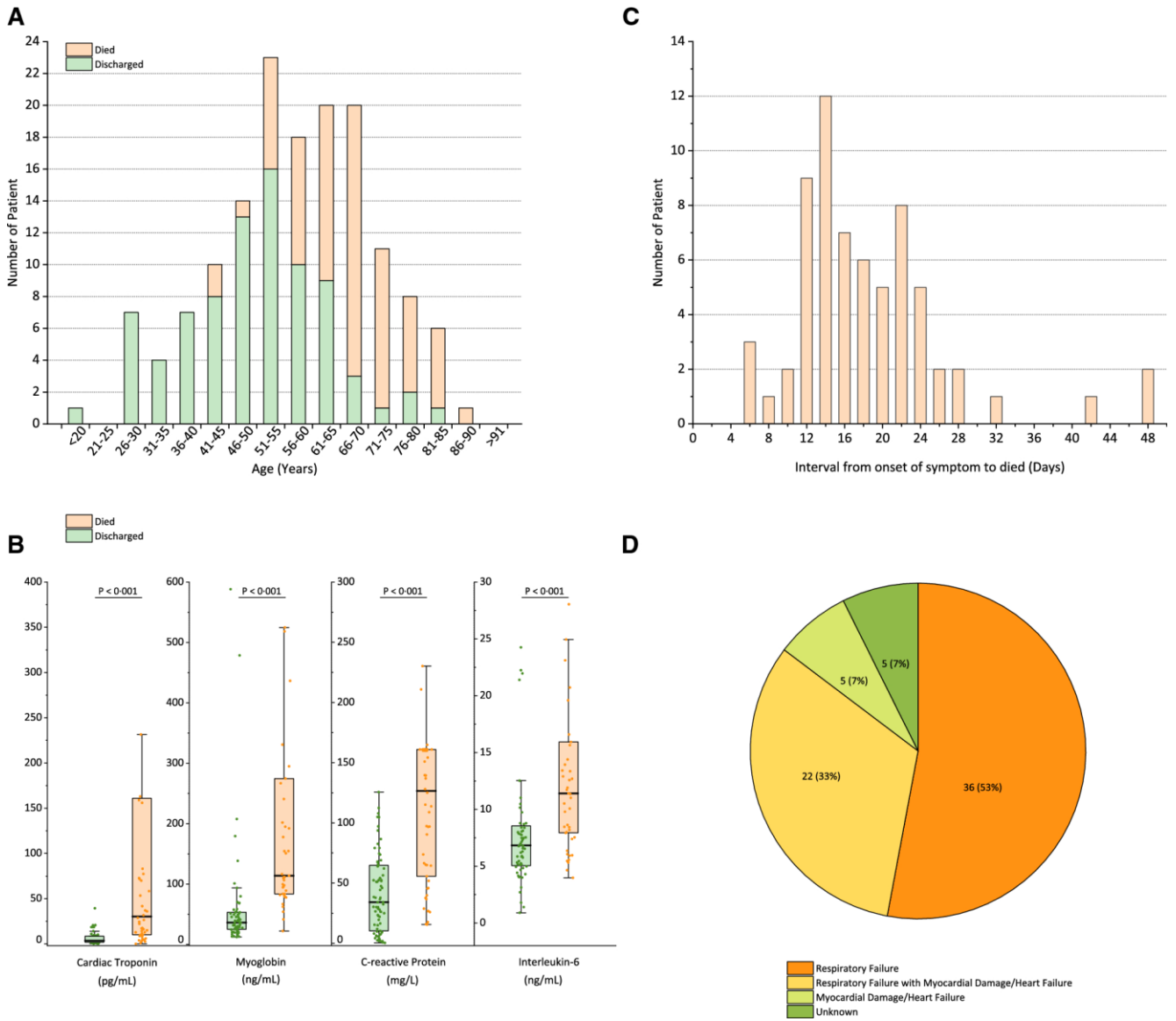
1	**ARDS Definition**	**Timing**	Acute: onset within a week of onset of a known insult, or new or worsening respiratory symptoms
		Respiratory failure	PaO_2/FIO_2 ≤ 20kPa with PEEP (or CPAP 5 cmH_2O for mild ARDS)
		Radiology Chest radiograph or CT scan	Bilateral opacities, not fully accounted for by pleural effusions, collapse or nodules
		Origin of oedema	Not likely to be caused by left sided heart failure or fluid over-load. Echocardiography indicated to assess cardiac function and to detect right-to-left shunts
2	**Investigations**	To diagnose under-lying conditions and complications, to monitor progress and aid prognostication (see appendix B)	
3	**Ideal Body Weight (IBW)**	Male = 50 + 2.3 x ((height cm/2.54)-60) Female = 45.5 + 2.3 x ((height cm/2.54)-60)	
4	**High PEEP**	Individual titration of PEEP recommended. Mean PEEP levels in 'High PEEP' groups in randomised trials was approximately 15 cmH_2O on day 1	
5	**Referral to local ECMO Centre UK**	Potentially reversible respiratory failure Murray Lung Injury Score > 2.5	

Points	0	1	2	3	4
P/F ratio (kPa)	240	30-39.9	23.3-29.9	13.3-23.2	<13.3
PEEP (cmH_2O)	≤5	6-8	9-11	11-14	≥15
Compliance (ml/cmH_2O)	≥80	60-79	40-59	20-39	≤19
CXR quadrants infiltrated	0	1	2	3	4

Murray Score = Total Points / 4

pH < 7.2
FiO_2 not > 0.8 for 7 days
Plateau pressure not > 30 cmH_2O for 7 days
No contraindication to anticoagulation

6	**NICE CG83**	https://www.nice.org.uk/guidance/cg83/evidence/full-guideline-242292349



Intensive Care Med (2020).
https://doi.org/10.1007/s00134-020-05991-x

ECDC TECHNICAL REPORT

Guidance for wearing and removing personal protective equipment in healthcare settings for the care of patients with suspected or confirmed COVID-19

February 2020

Figure 1. Suggested minimal PPE set for the management of suspected or confirmed cases of COVID-19: FFP2 or FFP3 respirators, goggles, long-sleeved water-resistant gown and gloves