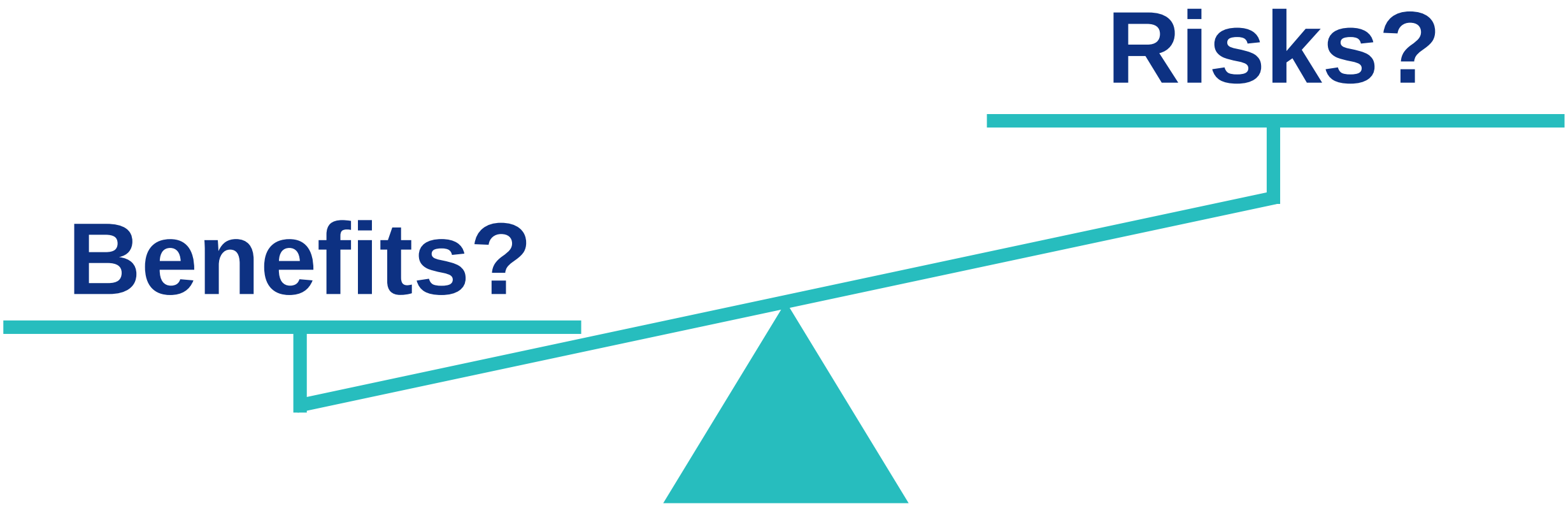
Prone positioning of nonintubated hypoxemic respiratory failure patients

Stephan EHRMANN

Disclosures

- Aerogen Ltd, Galway, Irland
- Fisher & Paykel Healthcare, Auckland, New Zeland
- Open AI, San Francisco, United States

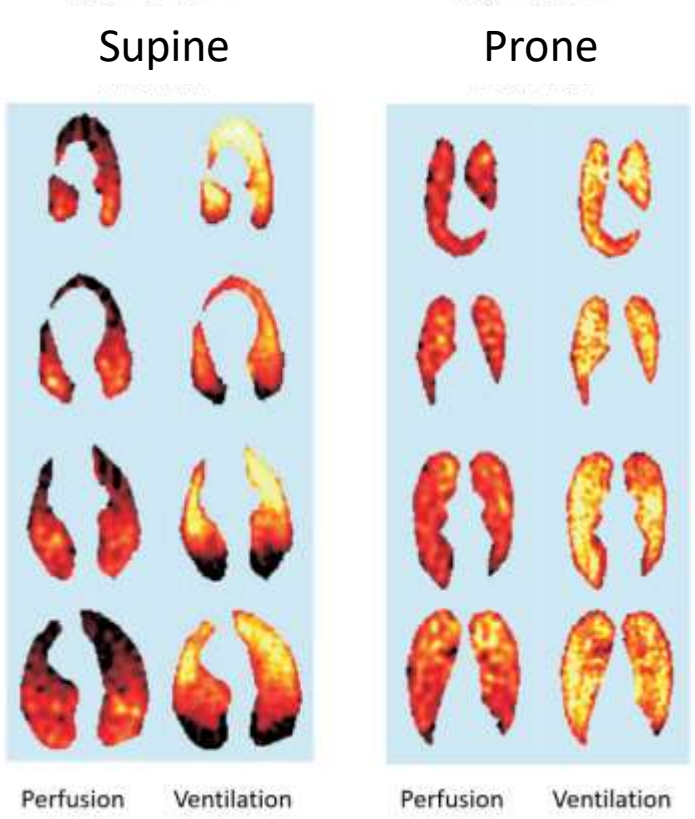
Rational?



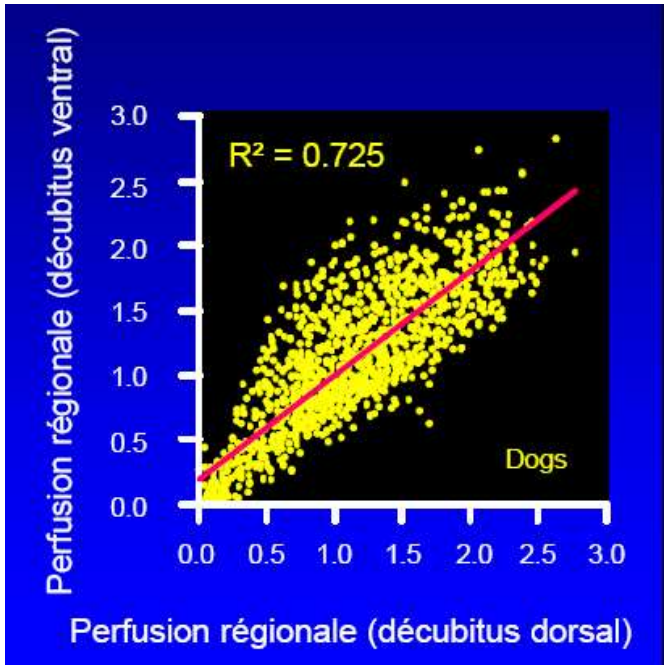
Rational?

Oxygenation / Decarboxylation

- Improved ventilation / perfusion matching



Richter T, Am J Respir Crit Care Med 2005



Glenny RW, J Appl Physiol 1991

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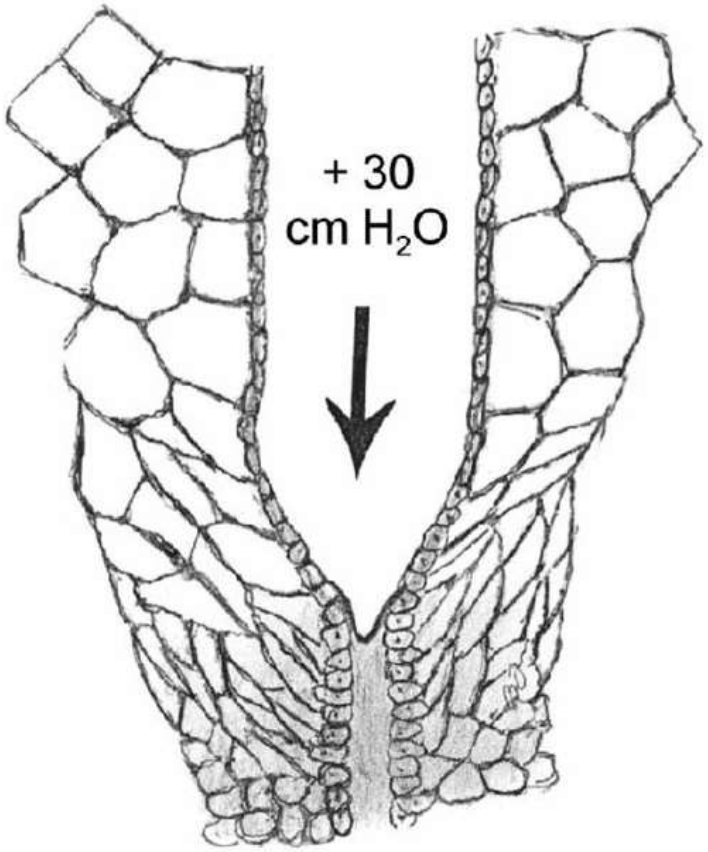
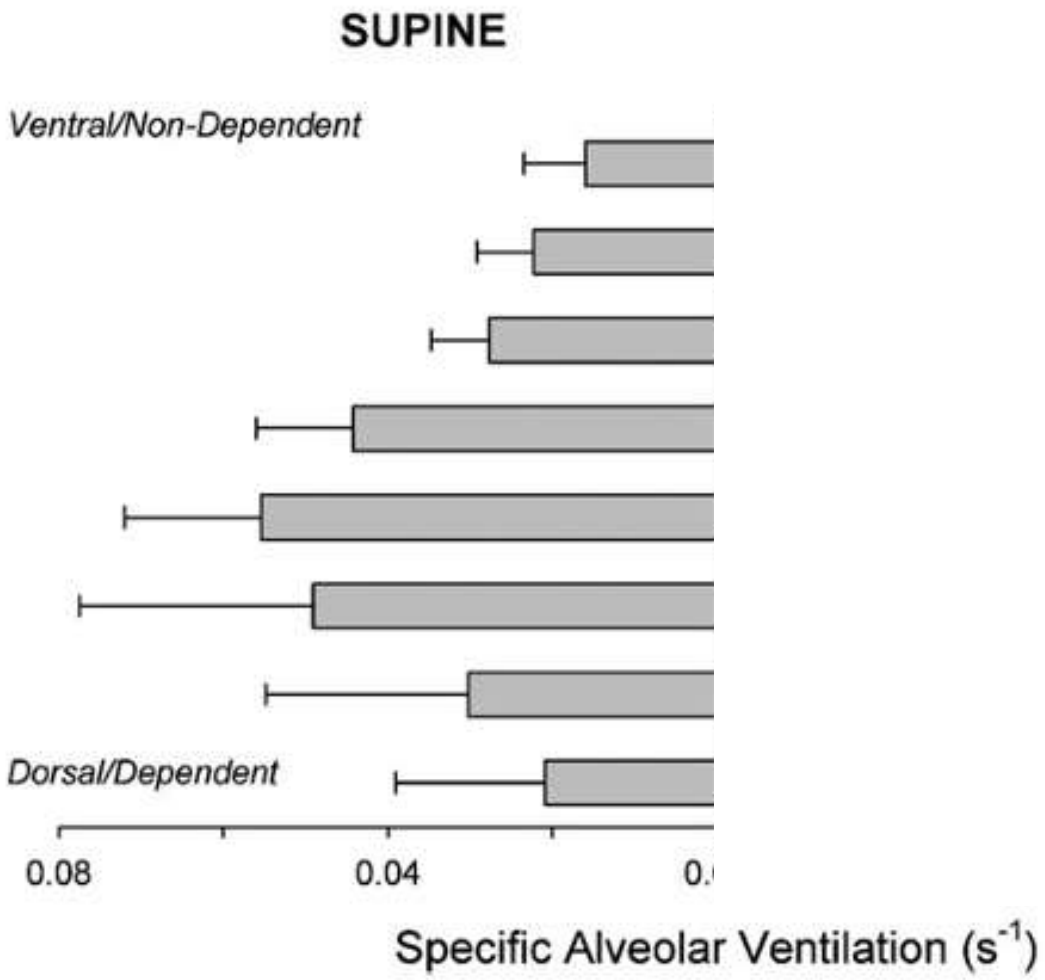


Reduced lung injury

- Pressure gradient homogenization

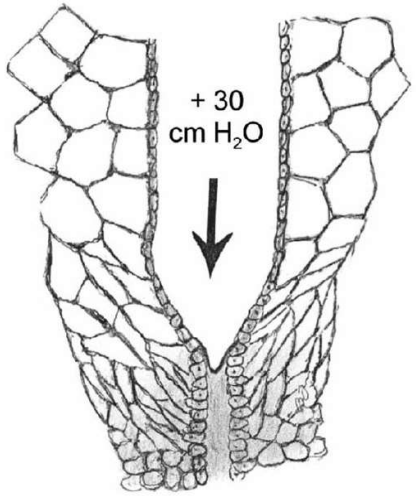
Richter T, Am J Respir Crit Care Med 2005

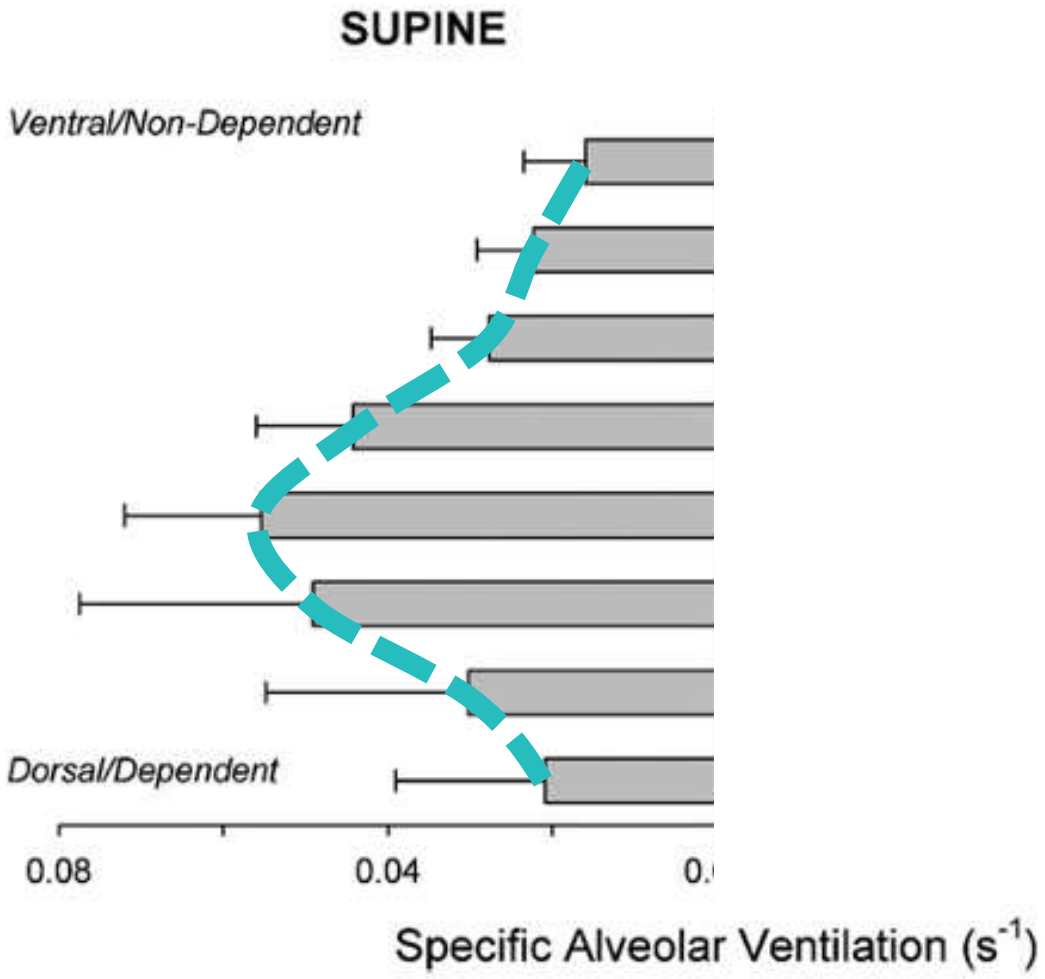
Ventilation homogeneity



Richter T, Am J Respir Crit Care Med 2005

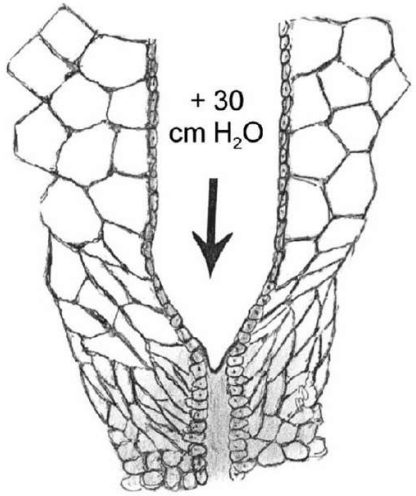
Ventilation homogeneity

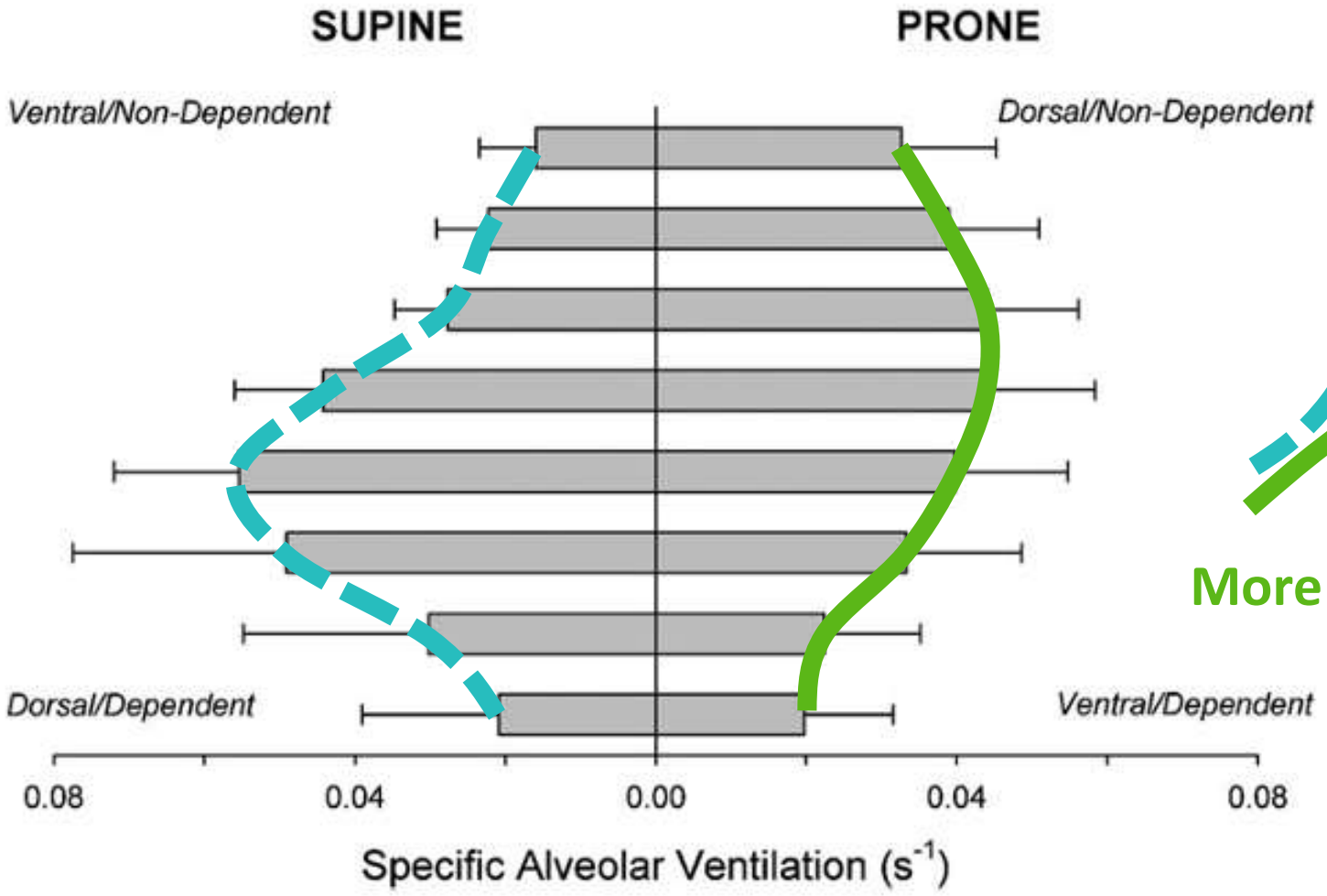




Richter T, Am J Respir Crit Care Med 2005

Ventilation homogeneity





More even ventilation

Richter T, Am J Respir Crit Care Med 2005

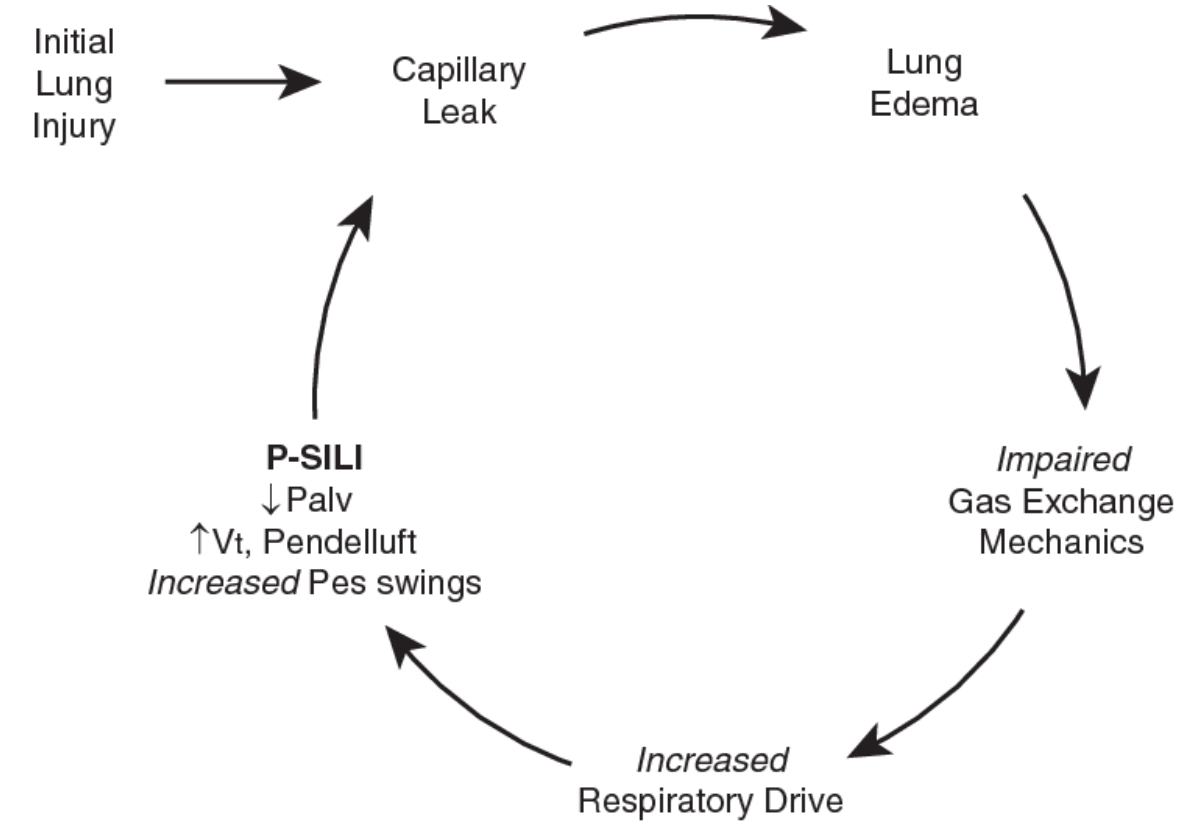
Rational?

Oxygenation / Decarboxylation

- Improved ventilation / perfusion matching

Reduced lung injury

- Pressure gradient homogenization
- Reduced respiratory drive



Brochard L, Am J Respir Crit Care Med 2017

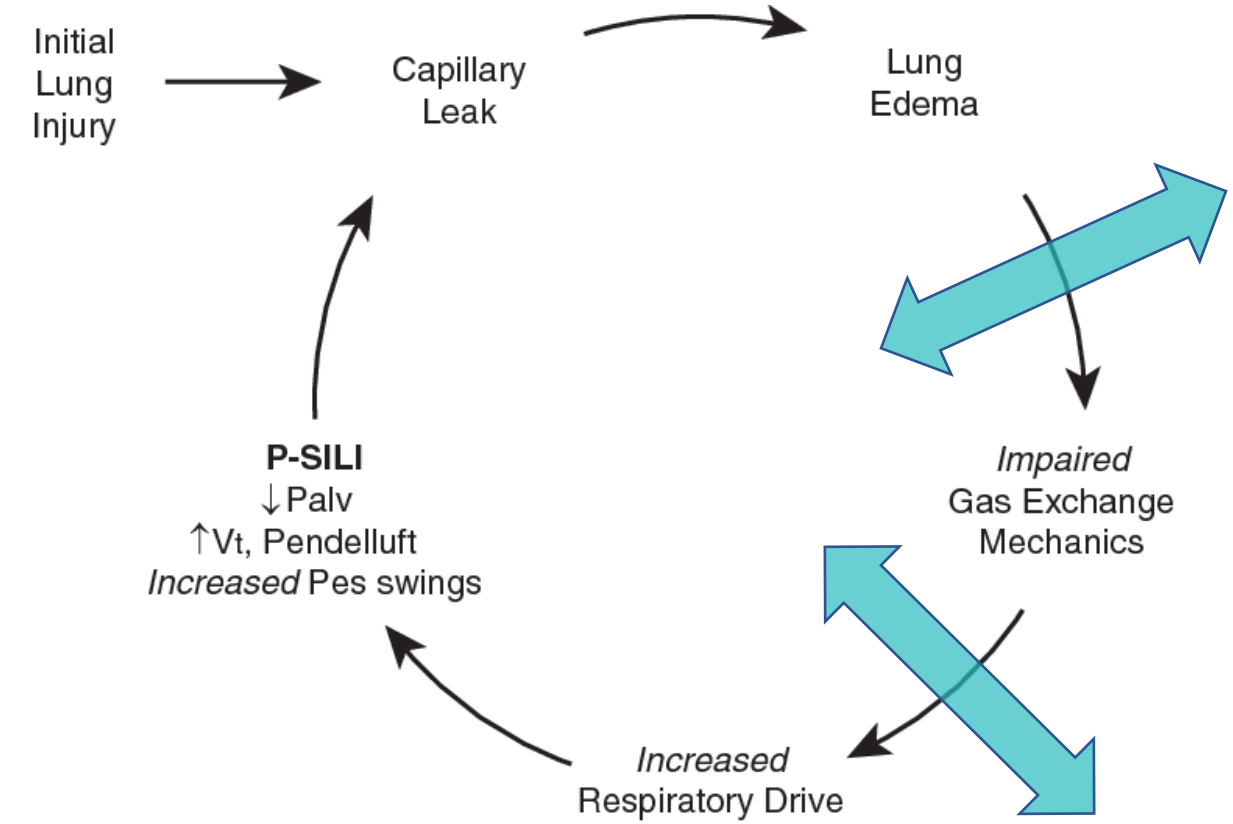
Rational?

Oxygenation / Decarboxylation

- Improved ventilation / perfusion matching

Reduced lung injury

- Pressure gradient homogenization
- Reduced respiratory drive



Brochard L, Am J Respir Crit Care Med 2017

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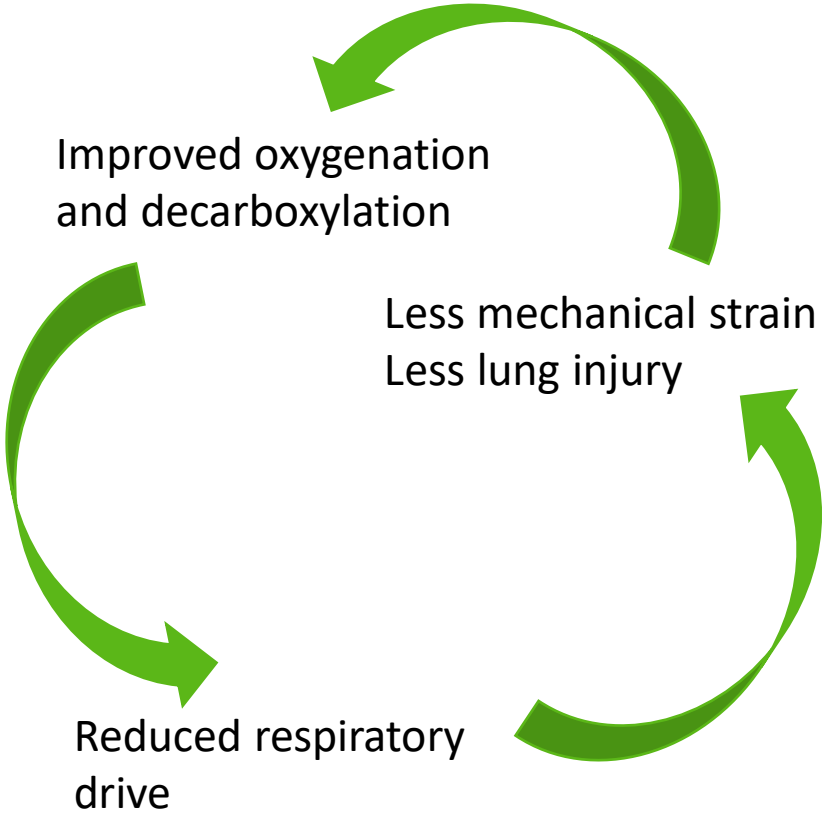

Reduced lung injury

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- Reduced respiratory drive

Rational?

Oxygenation / Decarboxylation

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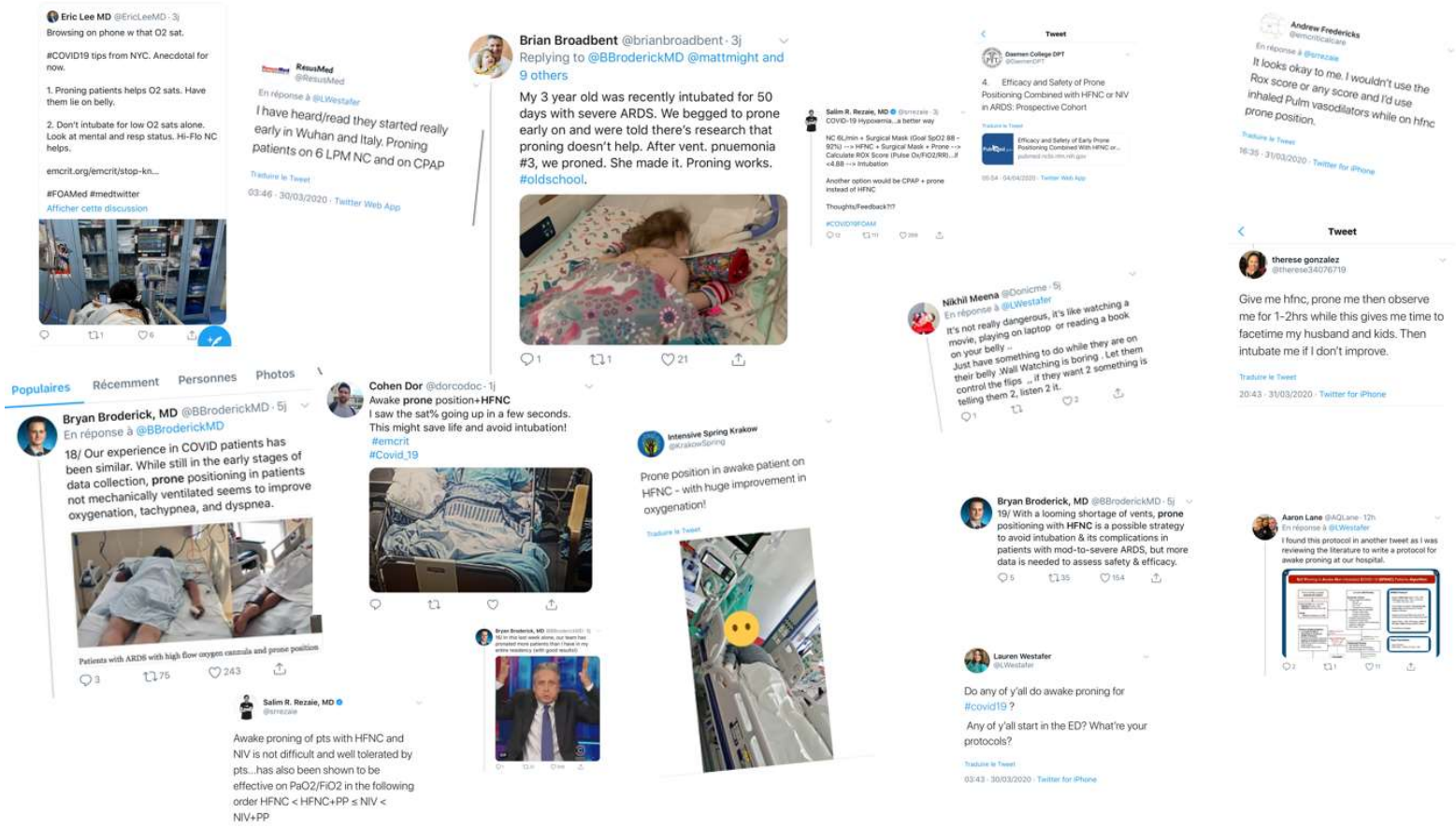
March 2020



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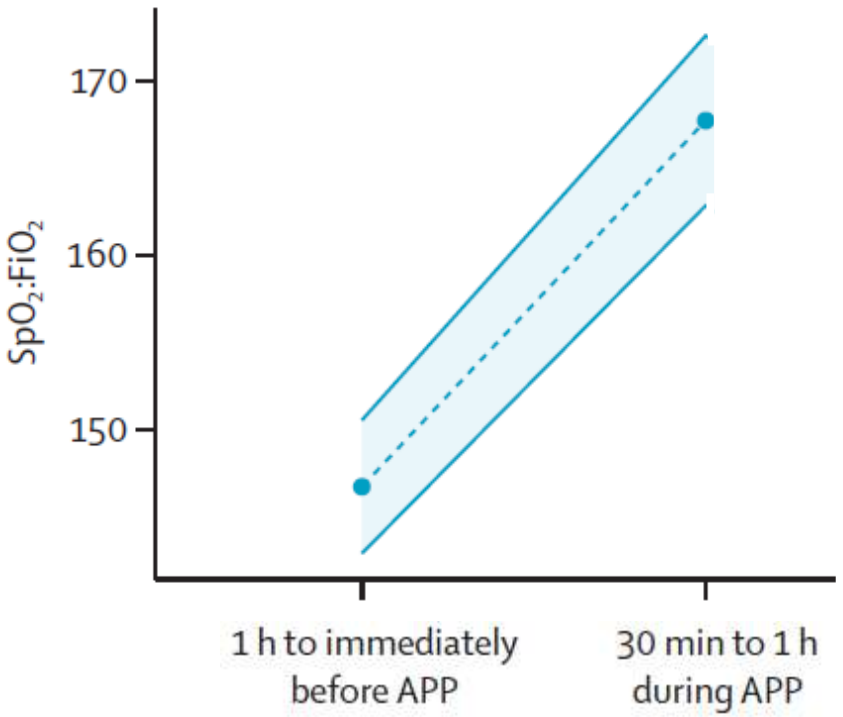
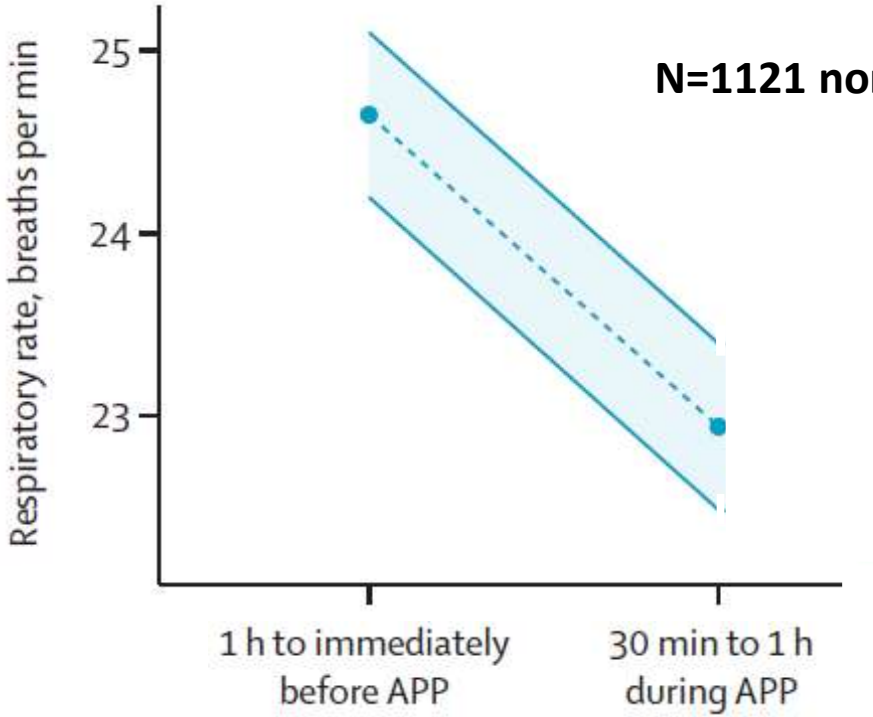




N=1121 non intubated COVID patients

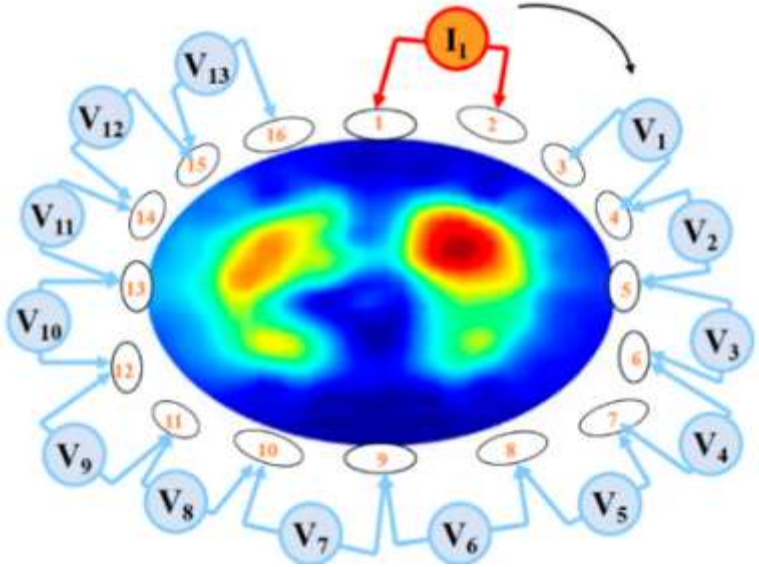
Ehrmann S, Lancet Respir Med 2021

RESEARCH Open Access

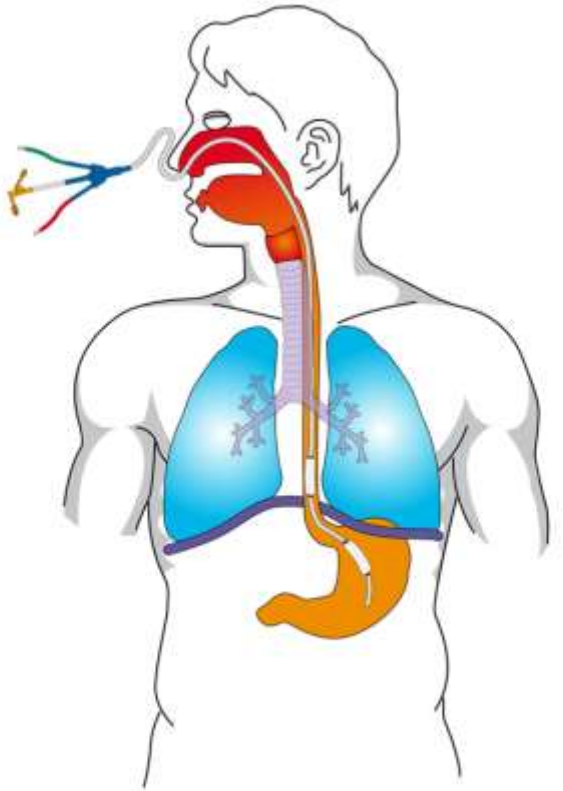
Physiological effects of awake prone position in acute hypoxemic respiratory failure

Domenico Luca Grieco[1,2*], Luca Delle Cese[1,2], Luca S. Menga[1,2], Tommaso Rosà[1,2], Teresa Michi[1,2], Gianmarco Lombardi[1,2], Melania Cesarano[1,2], Valentina Giammatteo[1,2], Giuseppe Bello[1,2], Simone Carelli[1,2], Salvatore L. Cutuli[1,2], Claudio Sandroni[1,2], Gennaro De Pascale[1,2], Antonio Pesenti[3], Salvatore M. Maggiore[4,5] and Massimo Antonelli[1,2]

Grieco et al. Critical Care (2023) 27:315
https://doi.org/10.1186/s13054-023-04600-9



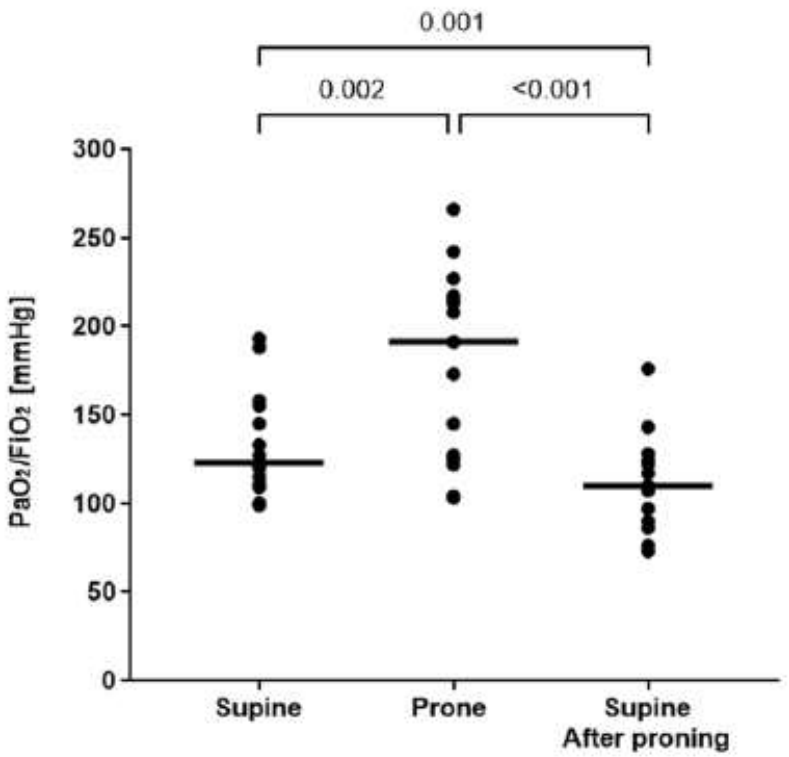
Electric impedance tomography



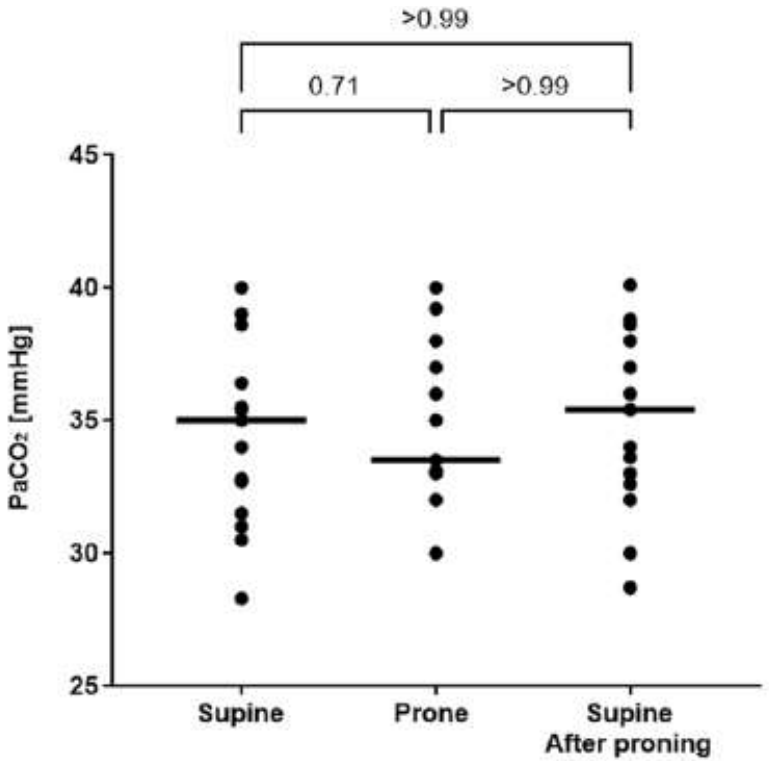
Esophageal pressure monitoring

Grieco D, Crit Care 2023

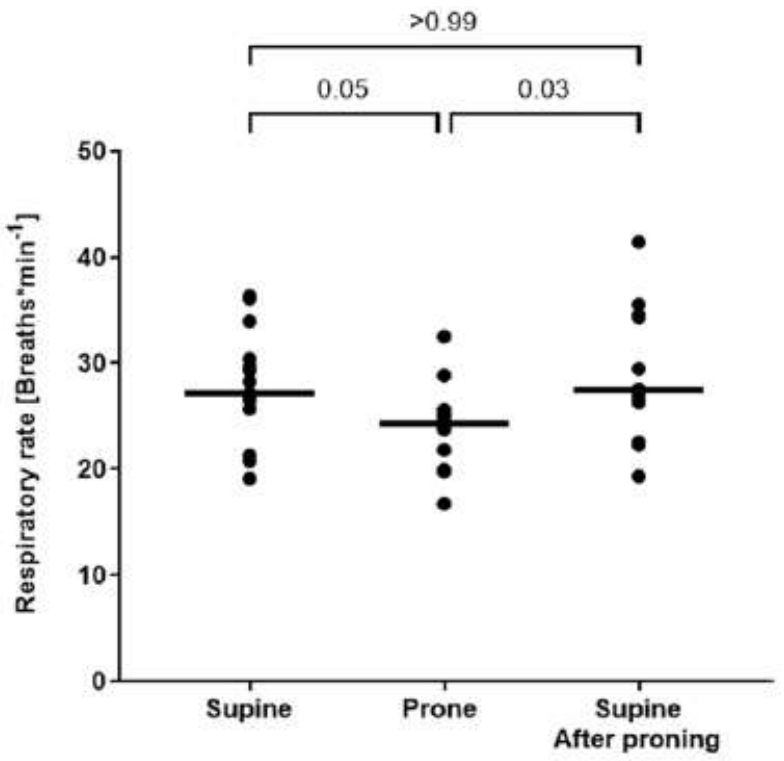
Oxygenation



PCO_2

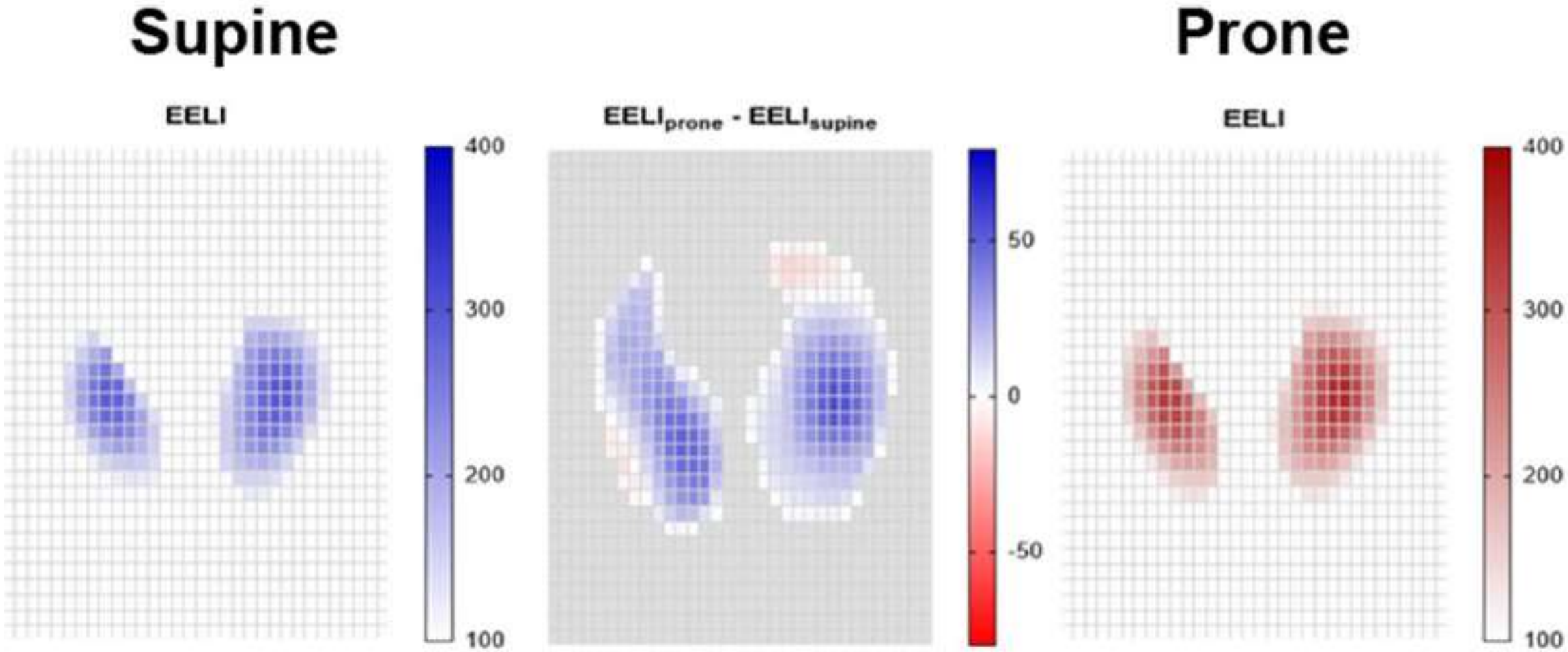


Respiratory Rate



Grieco D, Crit Care 2023

End Expiratory Lung Impedance



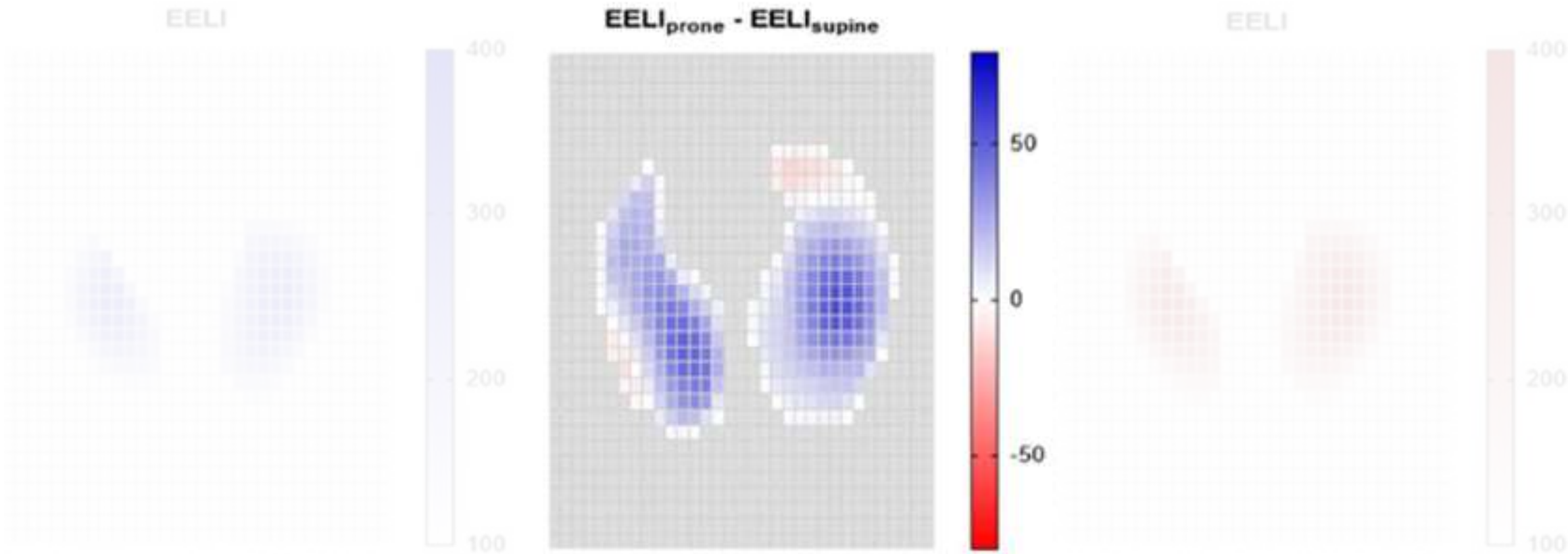
Grieco D, Crit Care 2023

End Expiratory Lung Impedance

Supine

Difference

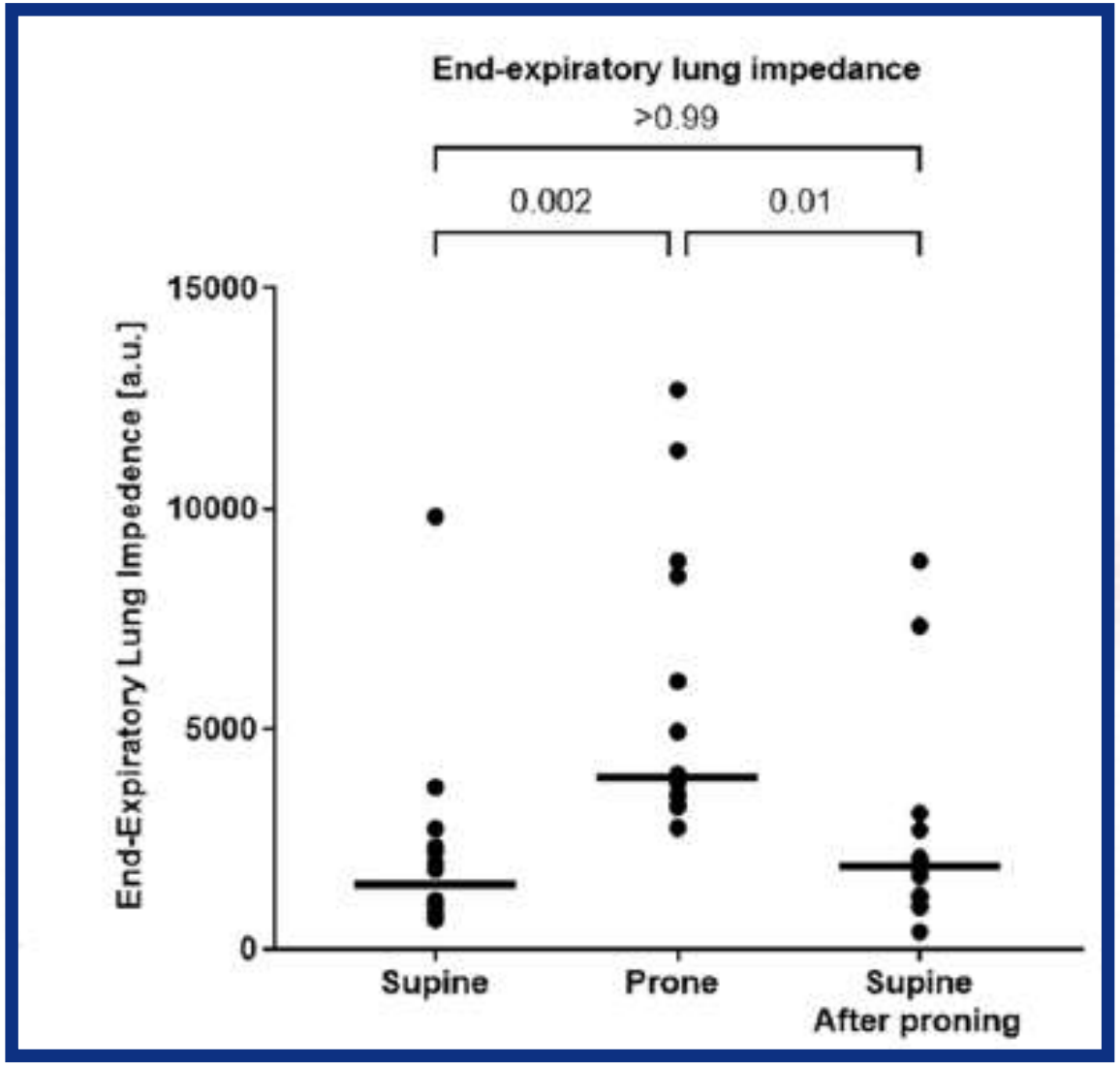
Prone



Grieco D, Crit Care 2023

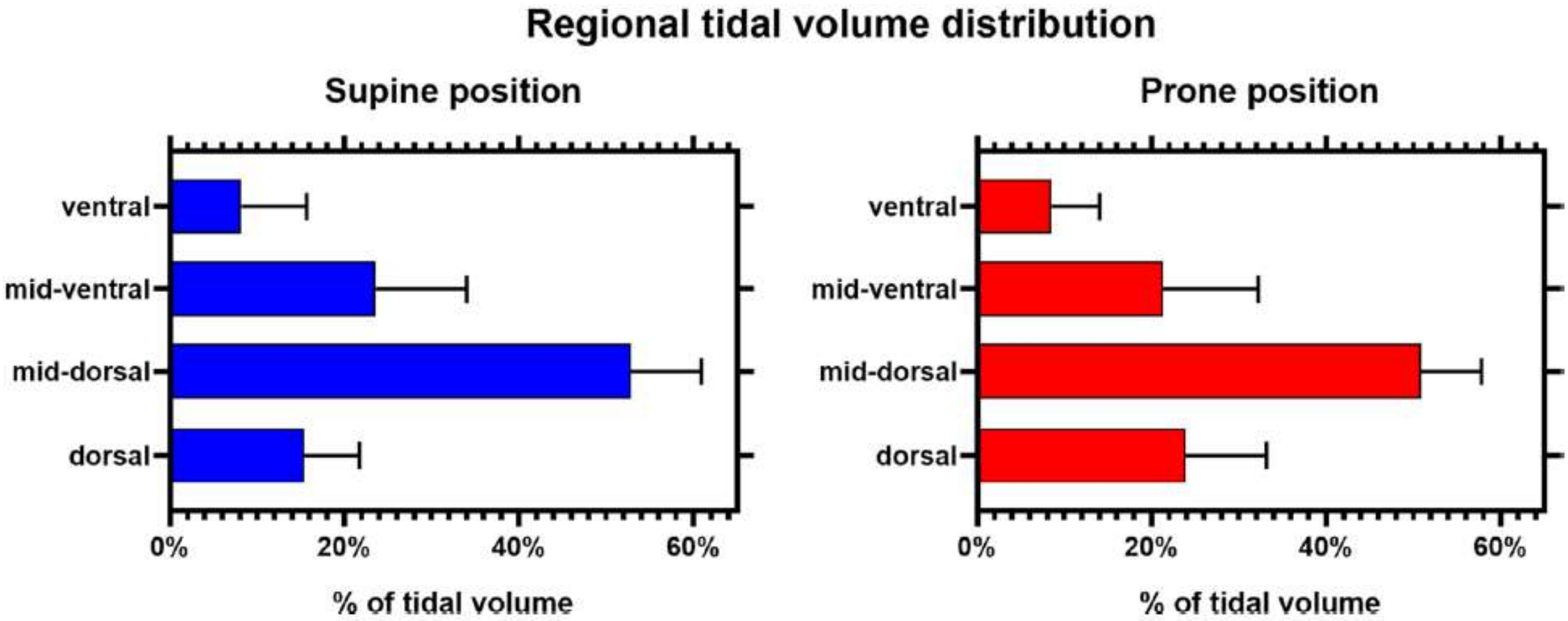
End Expiratory Lung Impedance

Supine



Prone

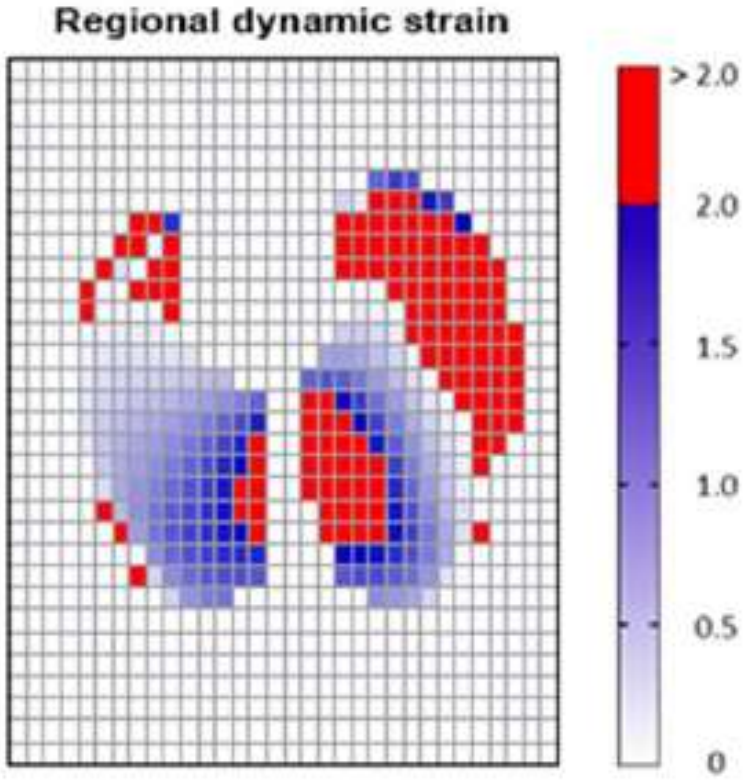
Grieco D, Crit Care 2023



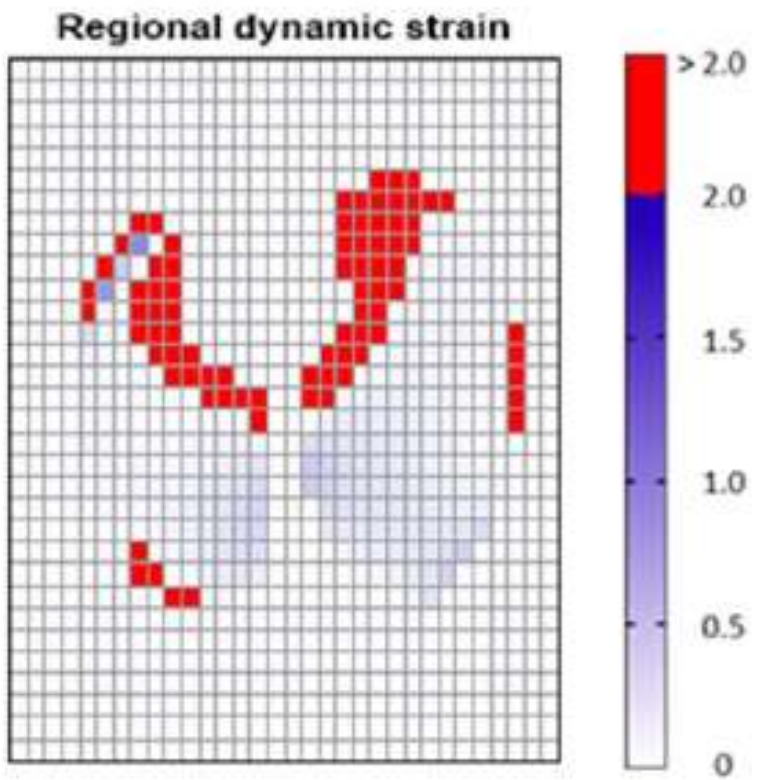
Grieco D, Crit Care 2023

Dynamic strain

Supine

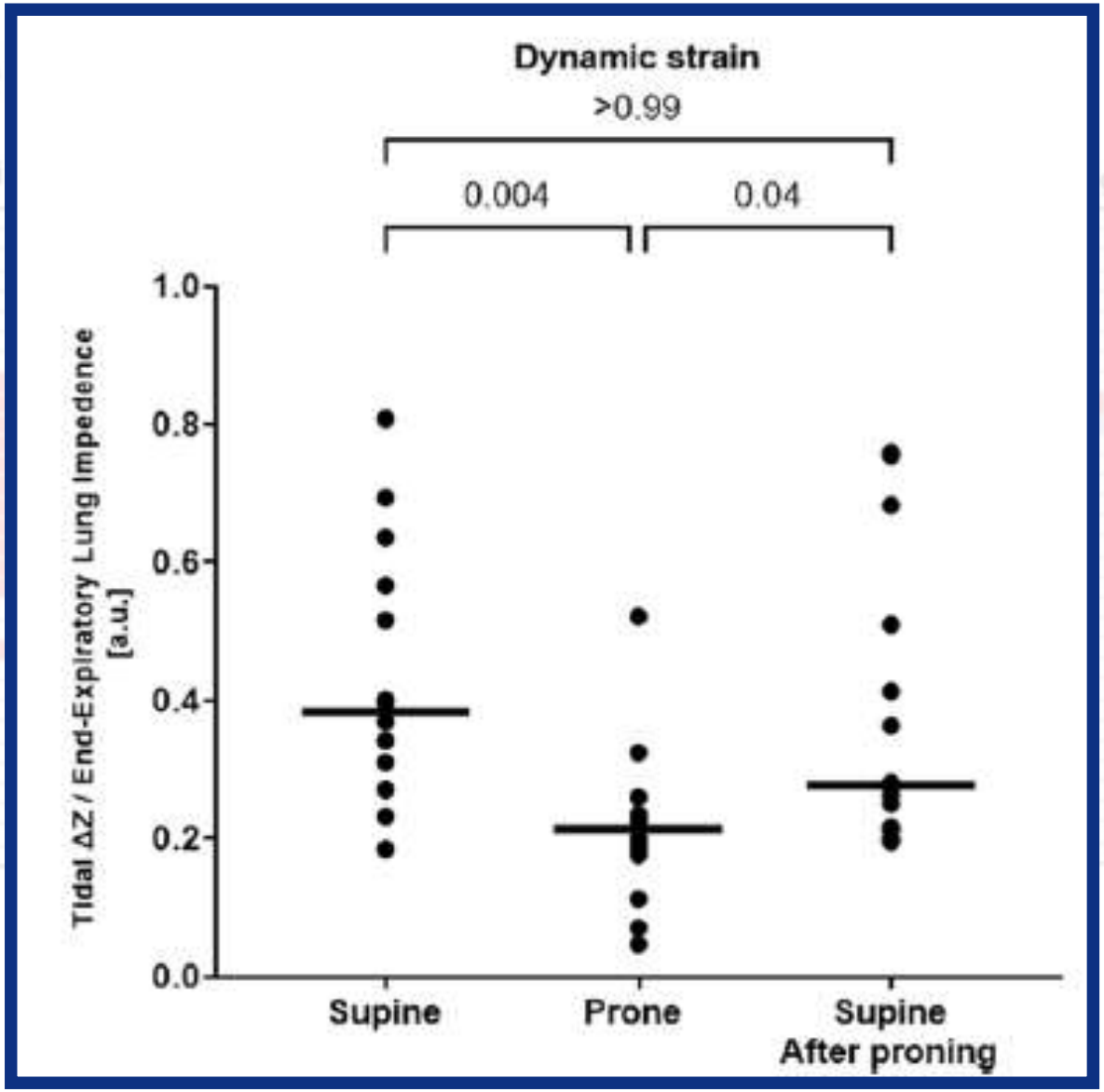


Prone



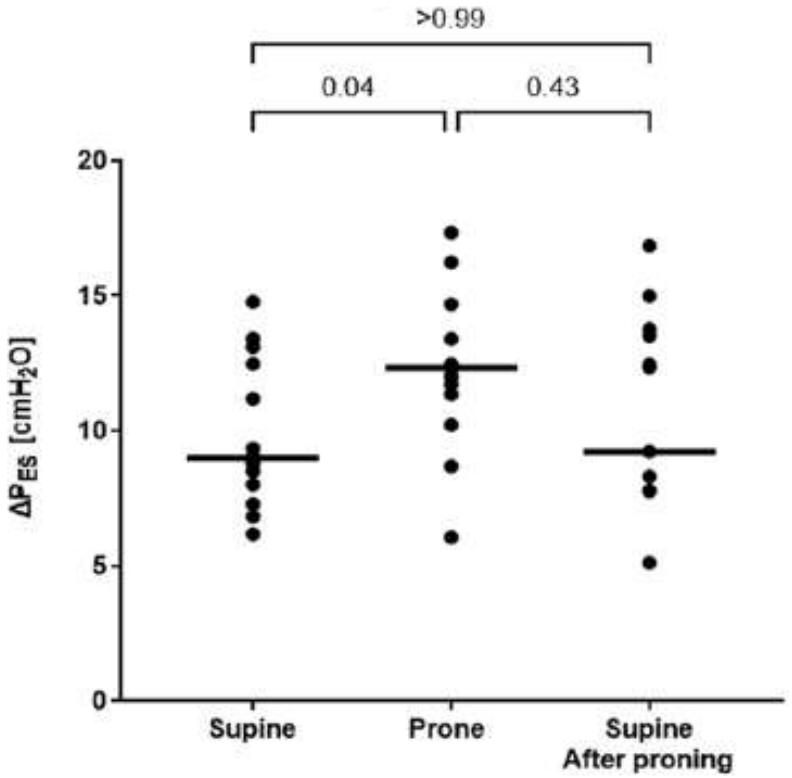
Grieco D, Crit Care 2023

Dynamic strain

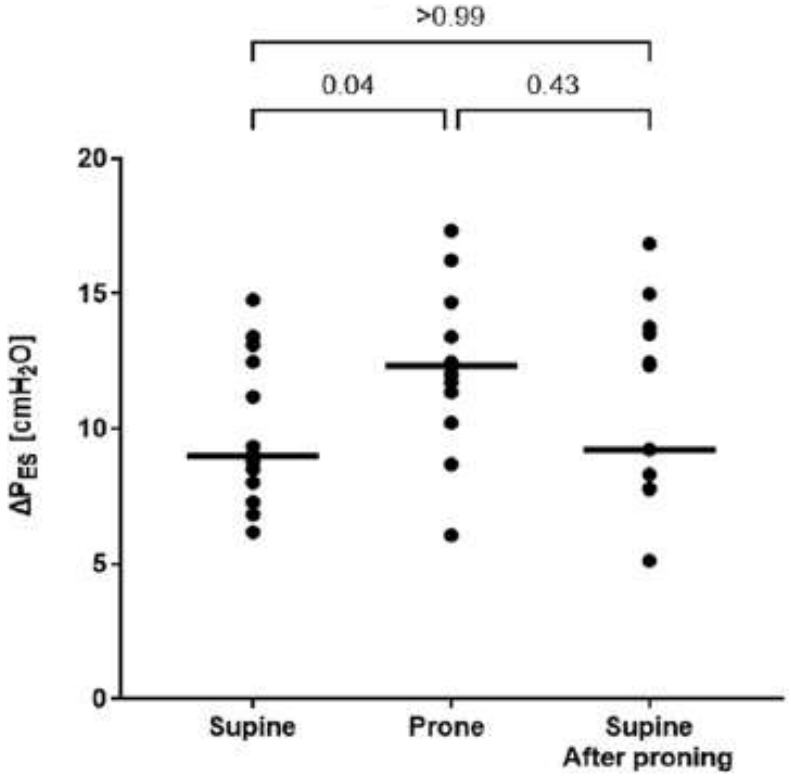


Grieco D, Crit Care 2023

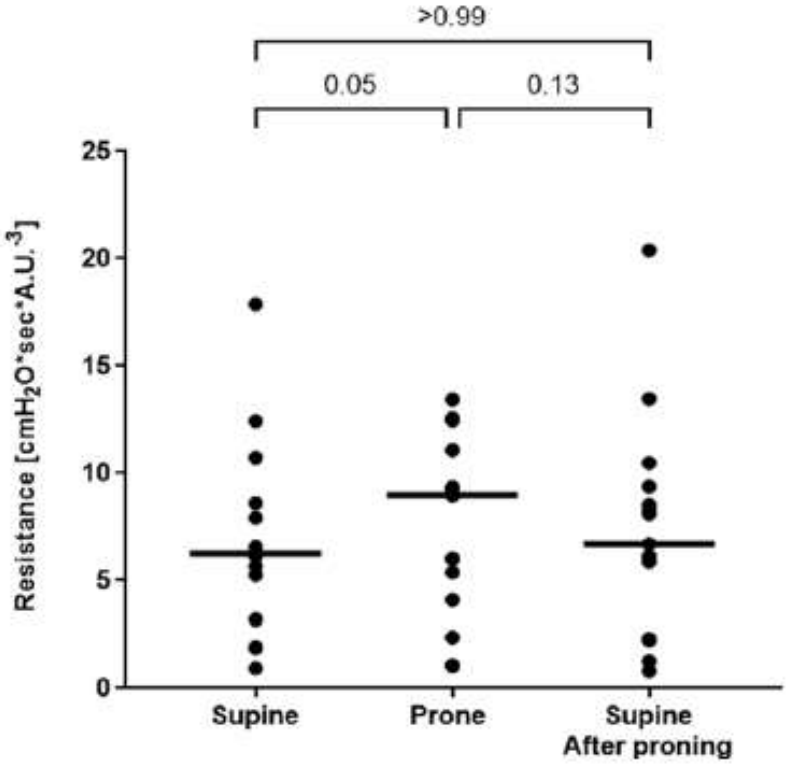
Inspiratory effort



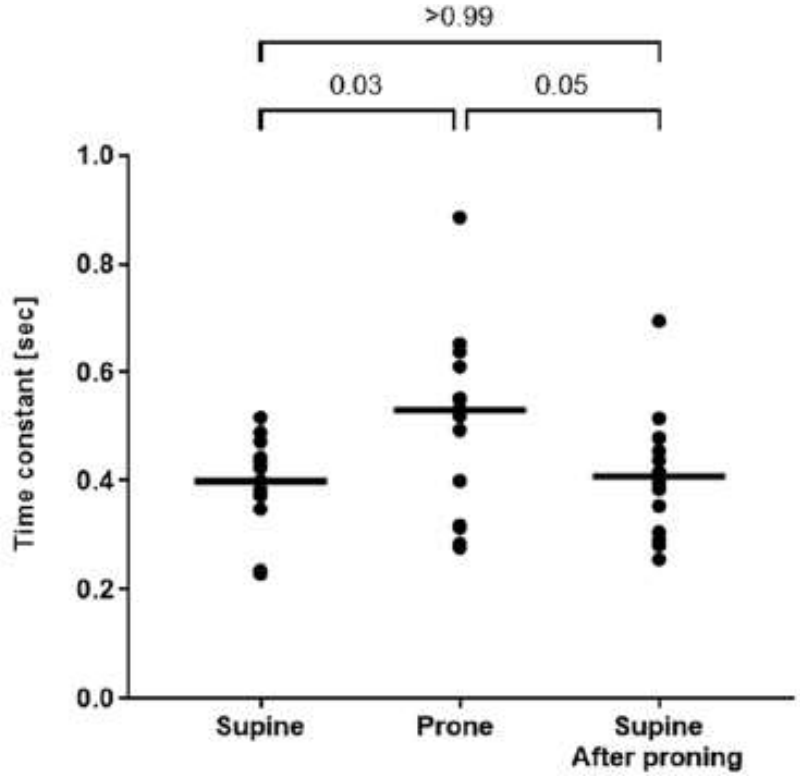
Inspiratory effort



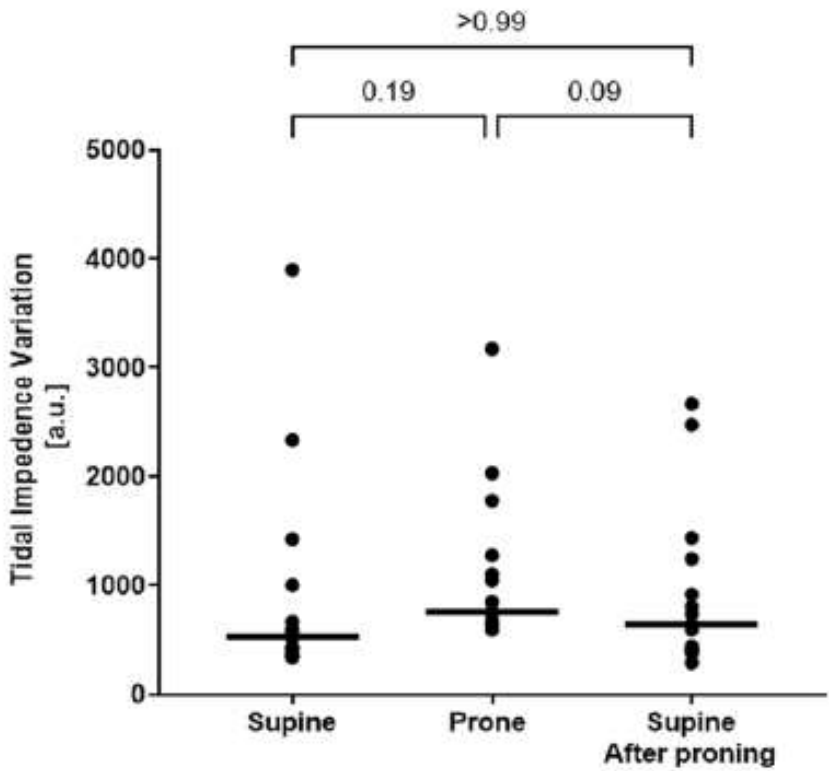
Airway resistances



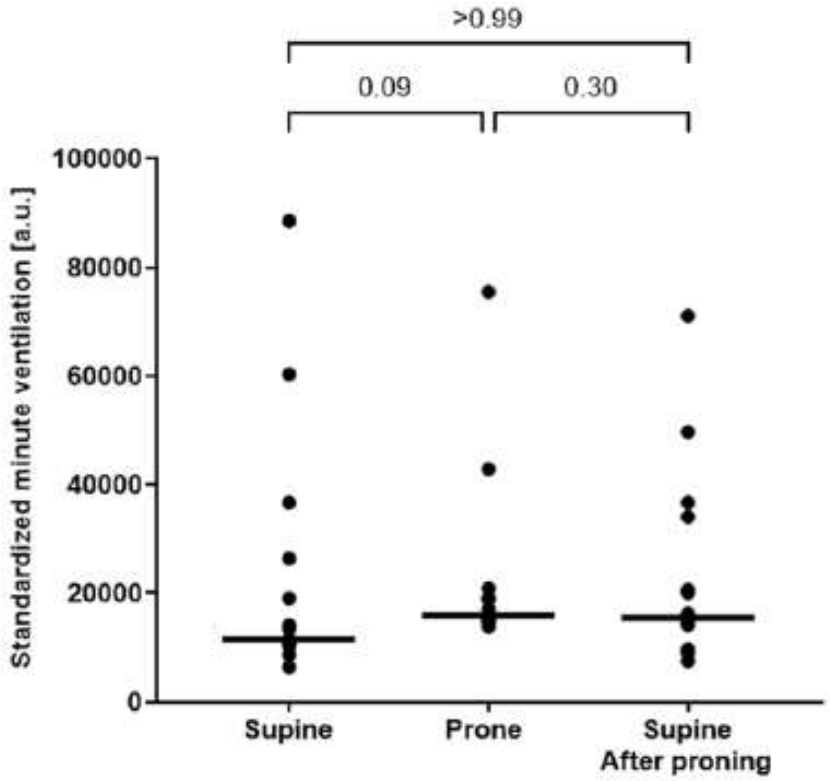
Time constant



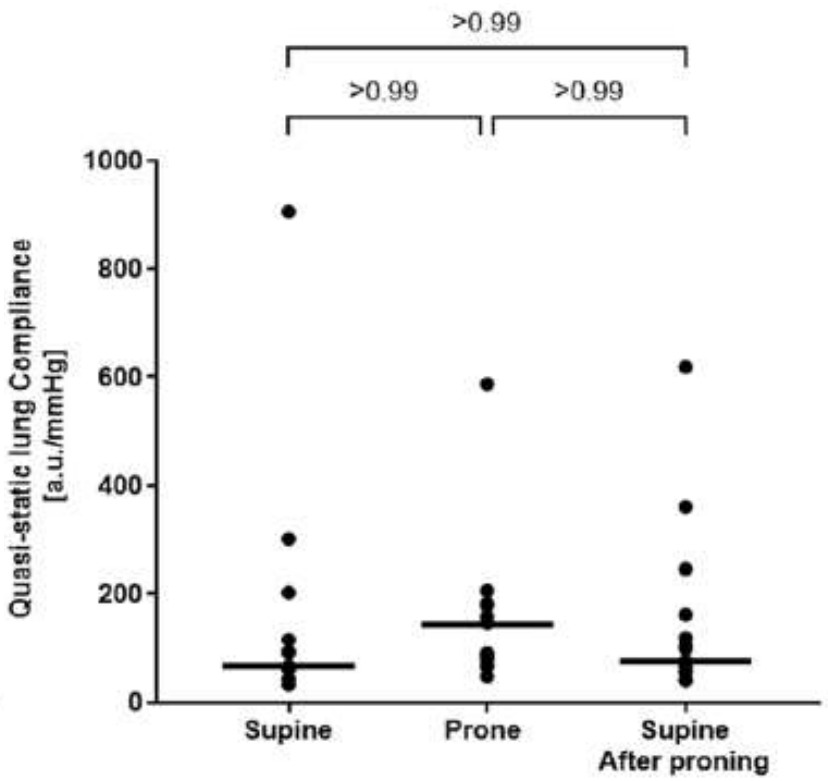
Tidal volume



Minute ventilation



Lung compliance

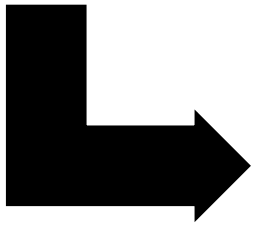


Rational?

Yes

Oxygenation / Decarboxylation

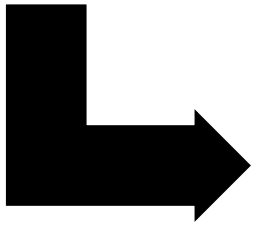
- Improved ventilation / perfusion matching



Hypoxemic patients
High risk of intubation

Reduced lung injury

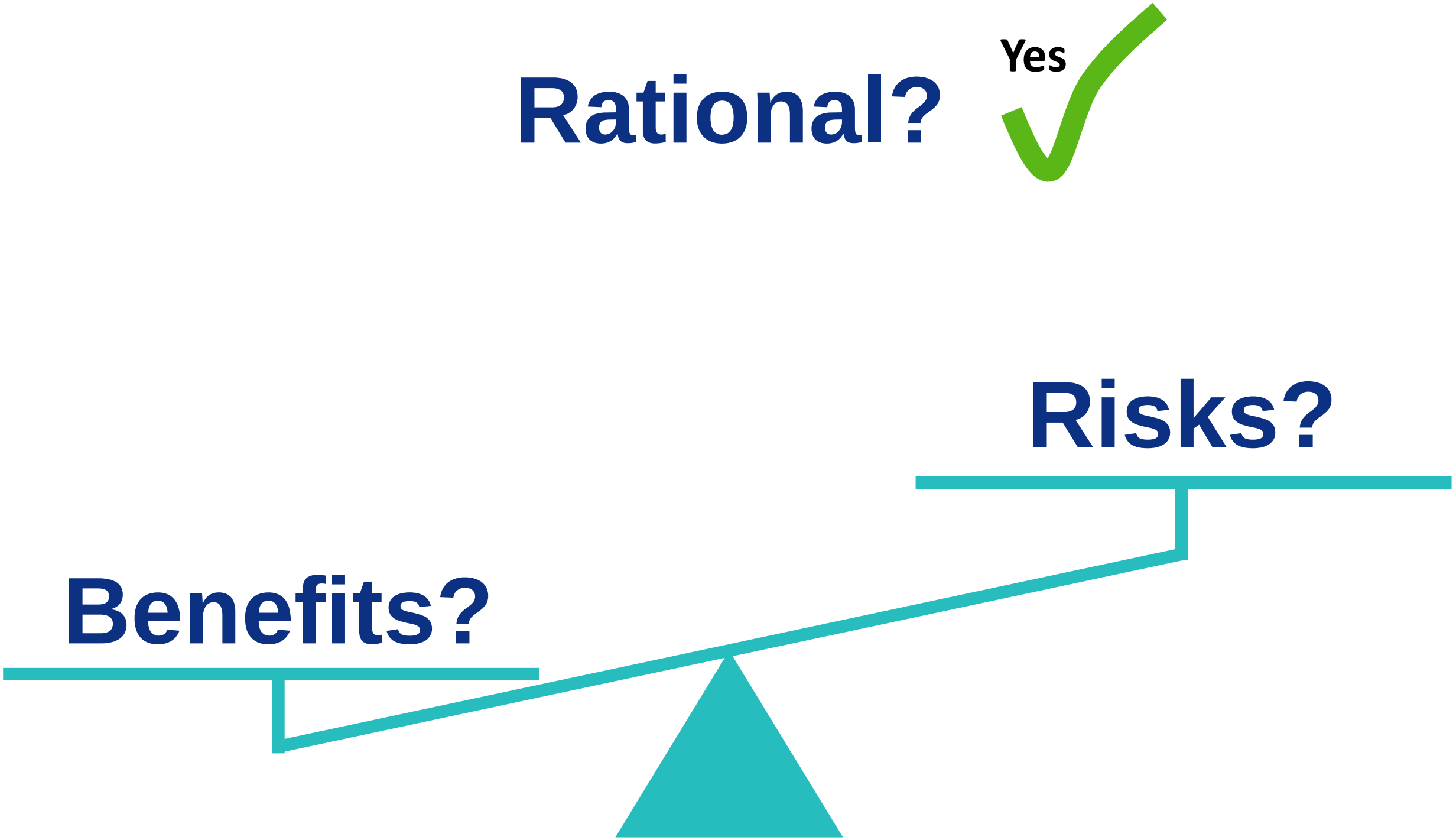
- Pressure gradient homogenization
- Reduced respiratory drive



Alveolar dammage
Baby Lung

Rational?

Yes



Eric Lee MD @EricLeeMD · 3j

Browsing on phone w that O2 sat.

#COVID19 tips from NYC. Anecdotal for now.

1. Proning patients helps O2 sats. Have them lie on belly.

2. Don't intubate for low O2 sats alone. Look at mental and resp status. Hi-Flo NC helps.

emcrit.org/emcrit/stop-kn...

#FOAMed #medtwitter

Afficher cette discussion

1 · 6

ResusMed @ResusMed

En réponse à @LWestafer

I have heard/read they started really early in Wuhan and Italy. Proning patients on 6 LPM NC and on CPAP

Traduire le Tweet

03:46 · 30/03/2020 · Twitter Web App

Brian Broadbent @brianbroadbent · 3j

Replying to @BBroderickMD @mattmight and 9 others

My 3 year old was recently intubated for 50 days with severe ARDS. We begged to prone early on and were told there's research that proning doesn't help. After vent. pnuemonia #3, we proned. She made it. Proning works. #oldschool.

1 · 1 · 21

Tweet

Daemen College DPT @DaemenDPT

4. Efficacy and Safety of Prone Positioning Combined with HFNC or NIV in ARDS: Prospective Cohort

Traduire le Tweet

Efficacy and Safety of Early Prone Positioning Combined With HFNC or...

pubmed.ncbi.nlm.nih.gov

05:54 · 04/04/2020 · Twitter Web App

Salim R. Rezaie, MD @srrezaie · 3j

COVID-19 Hypoxemia...a better way

NC 6L/min + Surgical Mask (Goal SpO2 88 - 92%) --> HFNC + Surgical Mask + Prone --> Calculate ROX Score (Pulse Ox/FiO2/RR)...if <4.88 --> Intubation

Another option would be CPAP + prone instead of HFNC

Thoughts/Feedback?!?

#COVID19FOAM

12 · 111 · 288

Andrew Fredericks @emcriticalcare

En réponse à @srrezaie

It looks okay to me. I wouldn't use the Rox score or any score and I'd use inhaled Pulm vasodilators while on hfnc prone position.

Traduire le Tweet

16:35 · 31/03/2020 · Twitter for iPhone

Tweet

therese gonzalez @therese34076719

Give me hfnc, prone me then observe me for 1-2hrs while this gives me time to facetime my husband and kids. Then intubate me if I don't improve.

Traduire le Tweet

20:43 · 31/03/2020 · Twitter for iPhone

Nikhil Meena @Donicme · 5j

En réponse à @LWestafer

It's not really dangerous, it's like watching a movie, playing on laptop or reading a book on your belly .. Just have something to do while they are on their belly .Wall Watching is boring . Let them control the flips .. if they want 2 something is telling them 2, listen 2 it.

1 · 2

Populaires Récemment Personnes Photos

Bryan Broderick, MD @BBroderickMD · 5j

En réponse à @BBroderickMD

18/ Our experience in COVID patients has been similar. While still in the early stages of data collection, **prone** positioning in patients not mechanically ventilated seems to improve oxygenation, tachypnea, and dyspnea.

Patients with ARDS with high flow oxygen cannula and prone position

3 · 75 · 243

Cohen Dor @dorcodoc · 1j

Awake **prone** position+**HFNC**

I saw the sat% going up in a few seconds. This might save life and avoid intubation!

#emcrit

#Covid_19

Intensive Spring Krakow @KrakowSpring

Prone position in awake patient on HFNC - with huge improvement in oxygenation!

Traduire le Tweet

Salim R. Rezaie, MD @srrezaie

Awake proning of pts with HFNC and NIV is not difficult and well tolerated by pts...has also been shown to be effective on PaO2/FiO2 in the following order HFNC < HFNC+PP ≤ NIV < NIV+PP

Bryan Broderick, MD @BBroderickMD · 5j

19/ With a looming shortage of vents, **prone** positioning with **HFNC** is a possible strategy to avoid intubation & its complications in patients with mod-to-severe ARDS, but more data is needed to assess safety & efficacy.

5 · 35 · 154

Lauren Westafer @LWestafer

Do any of y'all do awake proning for #covid19 ?

Any of y'all start in the ED? What're your protocols?

Traduire le Tweet

03:43 · 30/03/2020 · Twitter for iPhone

Aaron Lane @AQLane · 12h

En réponse à @LWestafer

I found this protocol in another tweet as I was reviewing the literature to write a protocol for awake proning at our hospital.

2 · 1 · 11

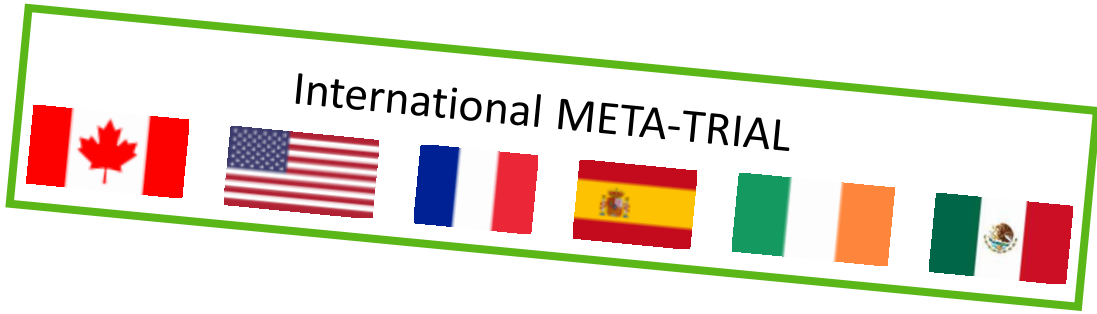
Benefits?

Intubation ?

Lengths of stay ?

Mortality ?

Long term sequelae ?



Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial

Stephan Ehrmann, Jie Li*, Miguel Ibarra-Estrada*, Yonatan Perez*, Ivan Pavlov*, Bairbre McNicholas*, Oriol Roca*, Sara Mirza, David Vines, Roxana Garcia-Salcido, Guadalupe Aguirre-Avalos, Matthew W Trump, Mai-Anh Nay, Jean Dellamonica, Saad Nseir, Idrees Mogri, David Cosgrave, Dev Jayaraman, Joan R Masclans, John G Laffey, Elsa Tavernier, for the Awake Prone Positioning Meta-Trial Group†*

Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial

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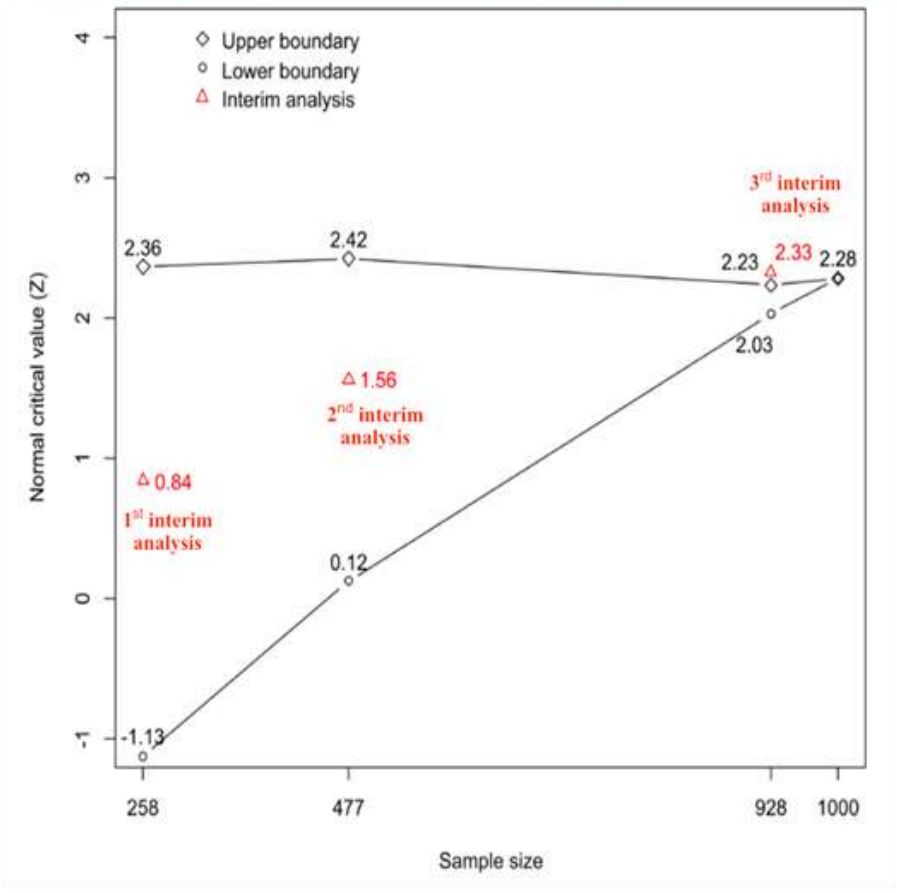


Lancet Respir Med 2021
Published Online
August 20, 2021
https://doi.org/10.1016/
S2213-2600(21)00356-8

France



USA





Mexico

Canada

Spain

Ireland


Patients

➢ INCLUSION CRITERIA

Acute hypoxemic respiratory failure due **to COVID-19 pneumonia**

= **Nasal High Flow** with **$PaO_2/F_IO_2 \leqq 300$** or **$SpO_2/F_IO_2 \leqq 315$**

➢ NON-INCLUSION CRITERIA

- Unable or refuse to provide consent
- Hemodynamically unstable
- BMI >40kg/m^2
- Pregnant
- Contraindication for APP

Ehrmann S, Lancet Respir Med 2021

Procedures

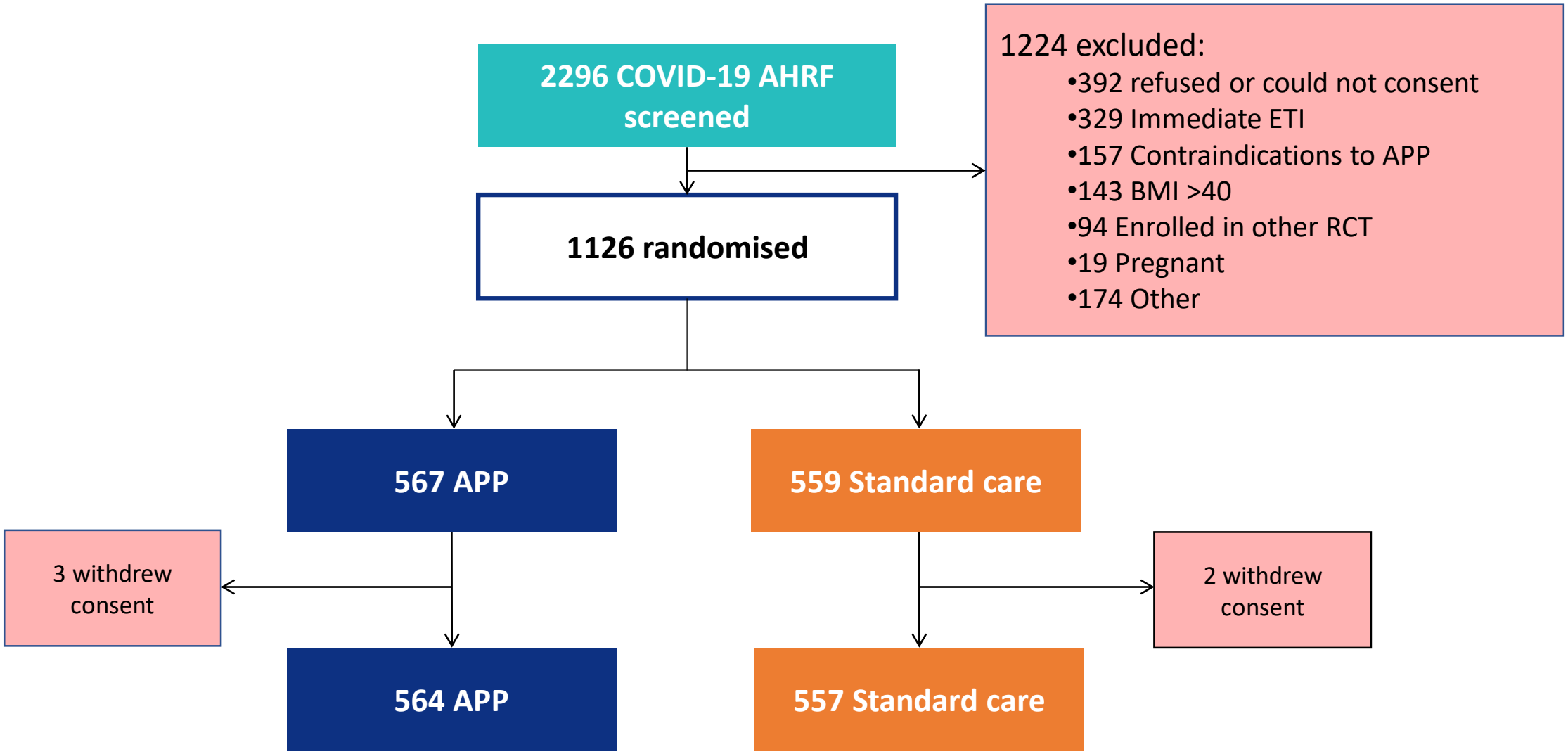
- Prone Positioning :
  - Patients in the prone group were instructed and assisted to **prone as long as frequently as possible** each day.
  - Prone use **as a "rescue" intervention was not allowed** in the standard care group.

- Nasal high flow : initiated **maximum tolerated flow** and F_IO_2 adjusted for an SpO_2 90-95%

- **Predefined criteria for intubation :**
  - Worsening respiratory failure (RR >40bpm, pH <7.25, SpO_2 <90% with F_IO_2 0.8, respiratory muscle fatigue, copious tracheal secretions)
  - Hemodynamic instability
  - Deteriorating mental status

Ehrmann S, Lancet Respir Med 2021

Patient flowchart



Ehrmann S, Lancet Respir Med 2021

Patients' characteristics

Variable		APP (n=564)	Standard care (n=557)
Age, years		61.5 (13.3)	60.7 (14.0)
Female sex		184 (33%)	191 (34%)
BMI, kg/m^2		29.7 (4.6)	29.7 (4.6)
Median time from hospital admission to enrolment, days		1.0 (0.4-1.9)	1.0 (0.4-1.5)
Clinical parameters			
	SpO_2/F_IO_2	147.9 (43.9)	148.6 (43.1)
	RR, bpm	24.7 (5.1)	24.9 (5.6)
Steroids for COVID-19		494 (88%)	492 (88%)
Location at enrolment			
	ICU	336 (60%)	339 (61%)
	Intermediate care	197 (35%)	189 (34%)
	ED	5 (1%)	5 (1%)
	General ward	26 (5%)	24 (4%)

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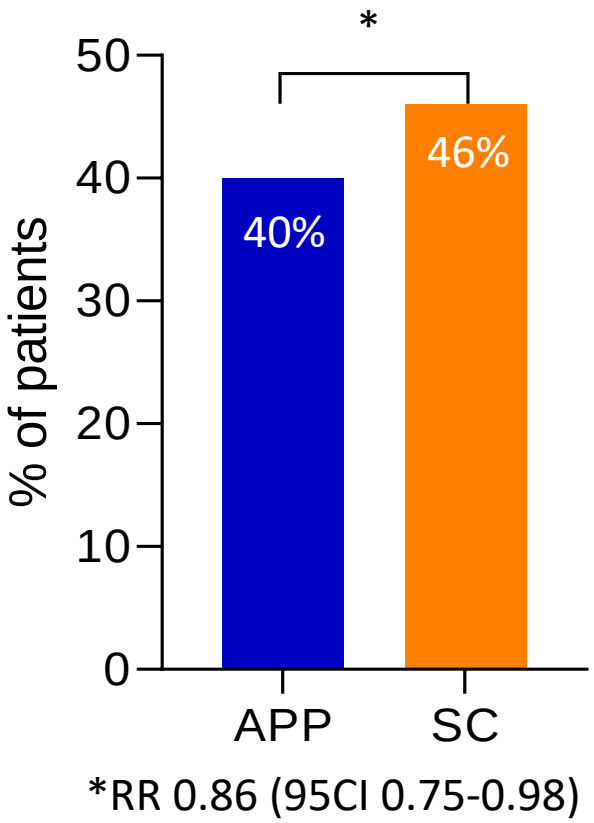
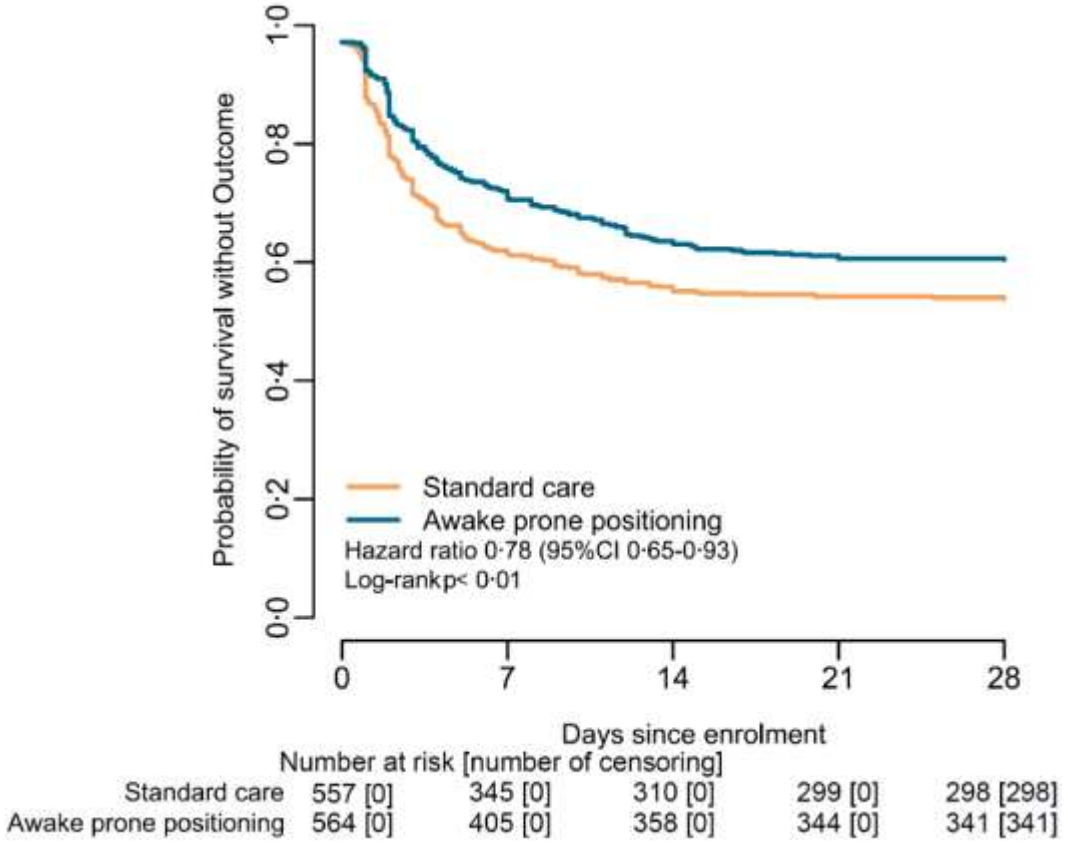
Primary outcome : intubation or death at D28



*RR 0.86 (95CI 0.75-0.98)



NNT to avoid 1 treatment failure = 15 (CI_{95} 8 – 156)

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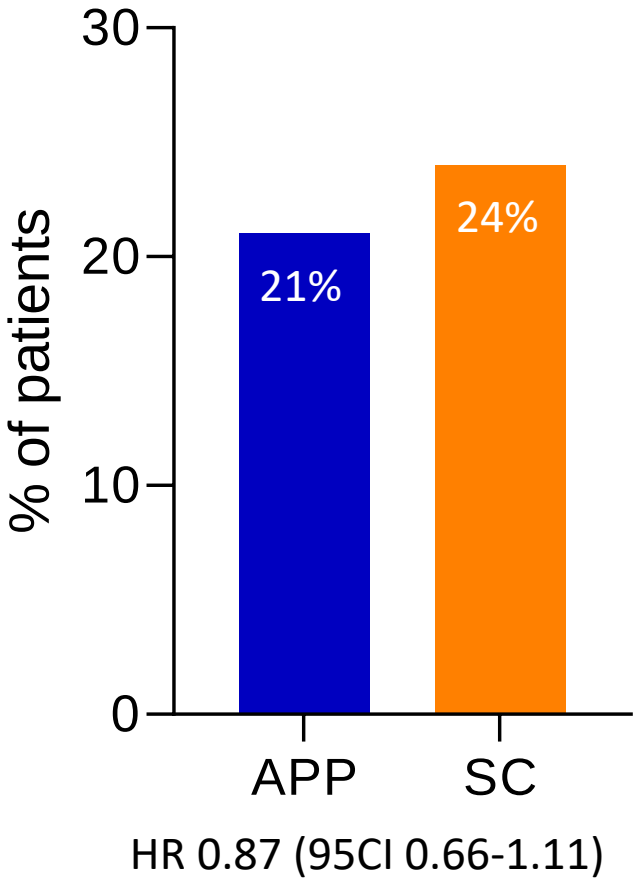
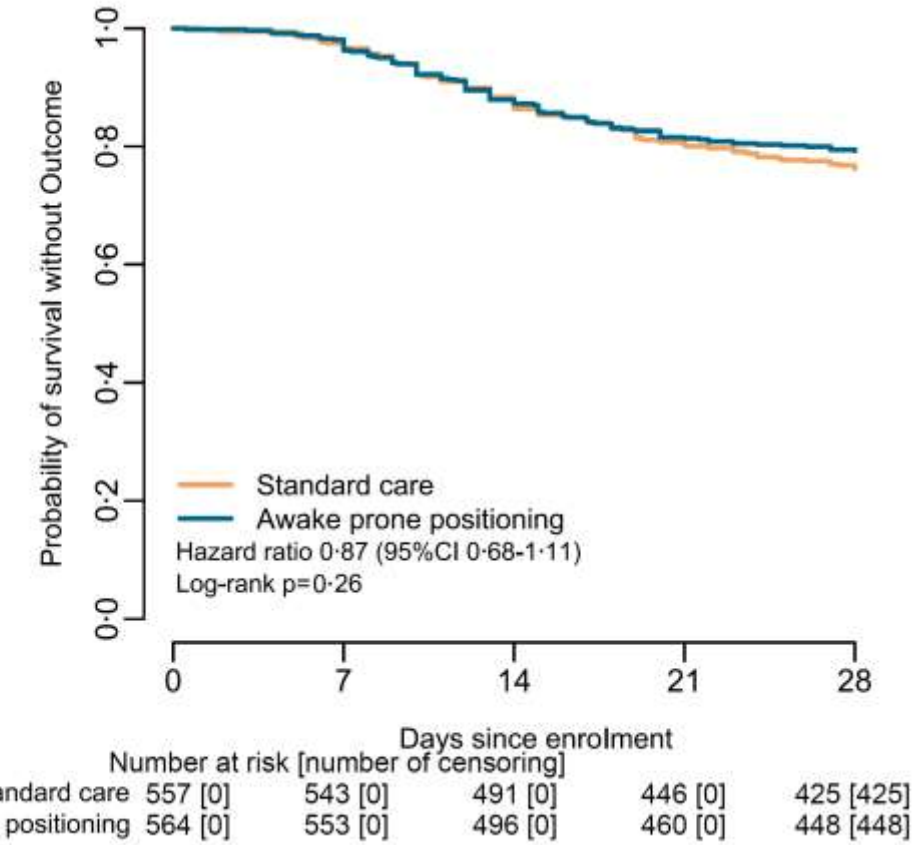
Secondary outcome : death at D28



HR 0.87 (95CI 0.66-1.11)

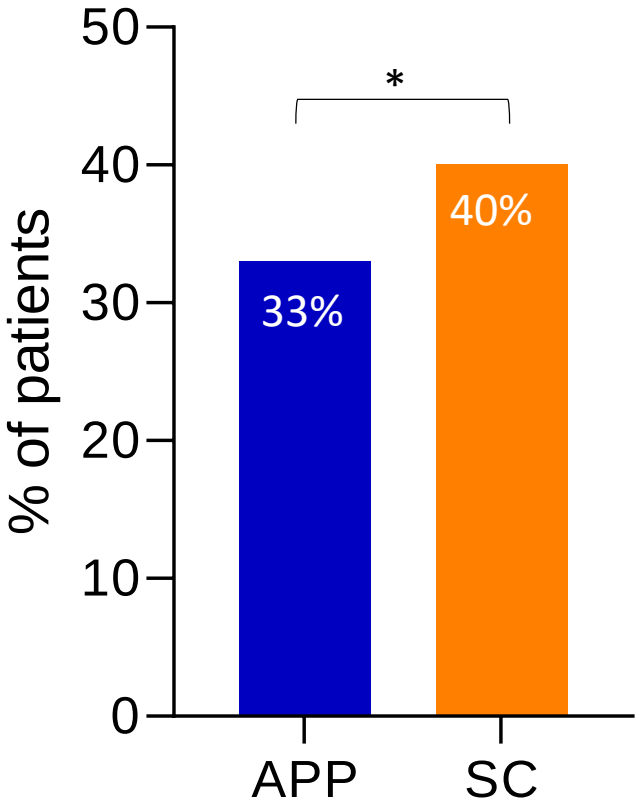


Number at risk [number of censoring]

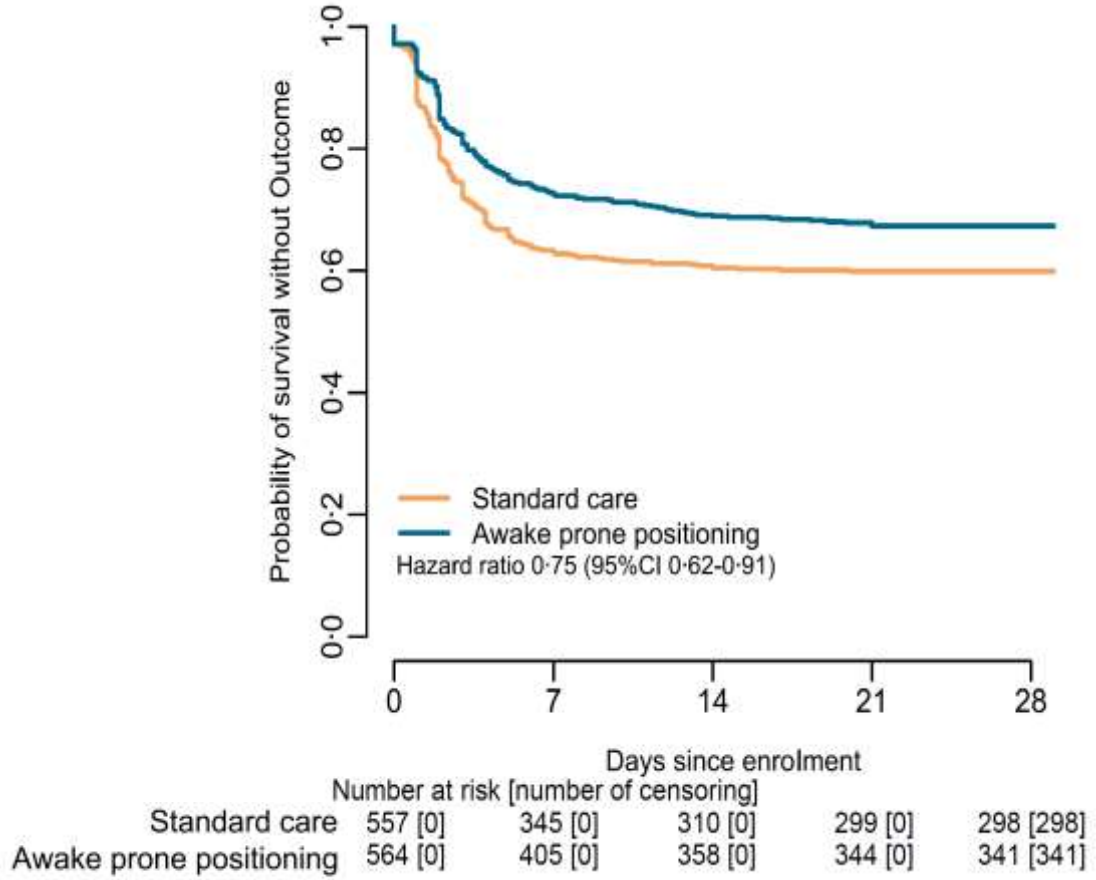
Standard care	557 [0]	543 [0]	491 [0]	446 [0]	425 [425]
Awake prone positioning	564 [0]	553 [0]	496 [0]	460 [0]	448 [448]

Ehrmann S, Lancet Respir Med 2021

Secondary outcome : intubation at D28



*HR 0.75 (95CI 0.62-0.91)



NNT to avoid 1 ETI = 14 (CI_{95} 8 – 69)

Ehrmann S, Lancet Respir Med 2021

Secondary outcome : intubation at D28

N=408 intubated patients

<u>Predefined criteria for intubation</u>:

- Worsening respiratory failure (RR >40bpm, pH <7.25, SpO_2 <90% with F_IO_2 0.8, respiratory muscle fatigue, copious tracheal secretions)
- Hemodynamic instability
- Deteriorating mental status

	Prone positioning	Standard care
Time to intubation (days)	2.3 (1.3-5.0)	2.0 (1.0-3.8)
MV duration (days)	12.4	12.4
Mortality at D28	43%	44%

No impact of delayed intubation

Ehrmann S, Lancet Respir Med 2021

Secondary outcome : intubation at D28

N=408 intubated patients

Predefined criteria for intubation:

- Worsening respiratory failure (RR >40bpm, pH <7.25, SpO_2 <90% with F_IO_2 0.8, respiratory muscle fatigue, copious tracheal secretions)
- Hemodynamic instability
- Deteriorating mental status

	Prone positioning	Standard care
Time to intubation (days)	2.3 (1.3-5.0)	2.0 (1.0-3.8)
MV duration (days)	12.4	12.4
Mortality at D28	43%	44%

→ **No impact of delayed intubation**

Ehrmann S, Lancet Respir Med 2021

Proseva

Mortalité = subjective outcome

« In 30 of the 75 patients (40%) who died in the supine group and 14 of the 38 (36.8%) who died in the prone group, an end-of life decision was made at some time after inclusion. »

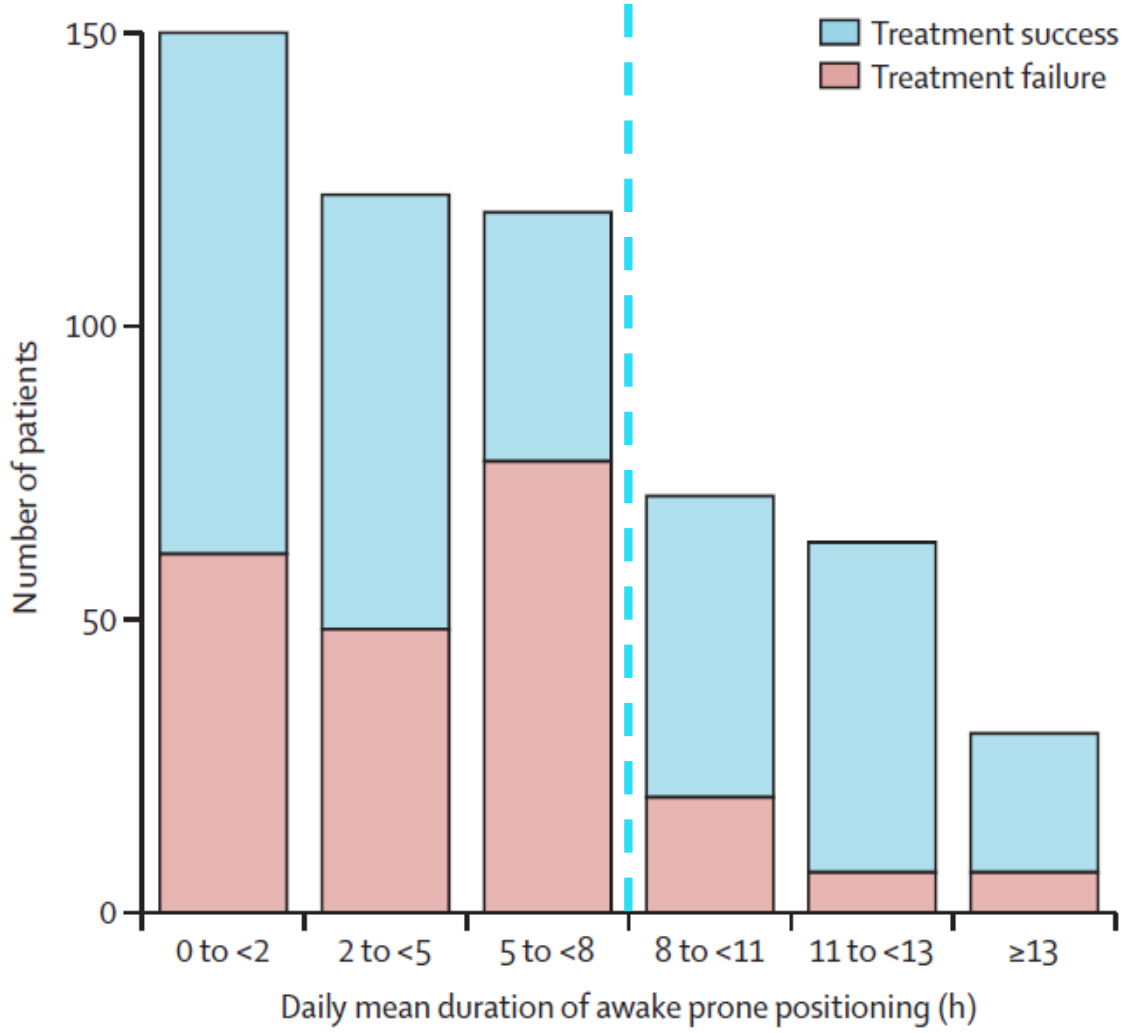
→ 39% DNR among non survivors

Guérin C, N Engl J Med 2013

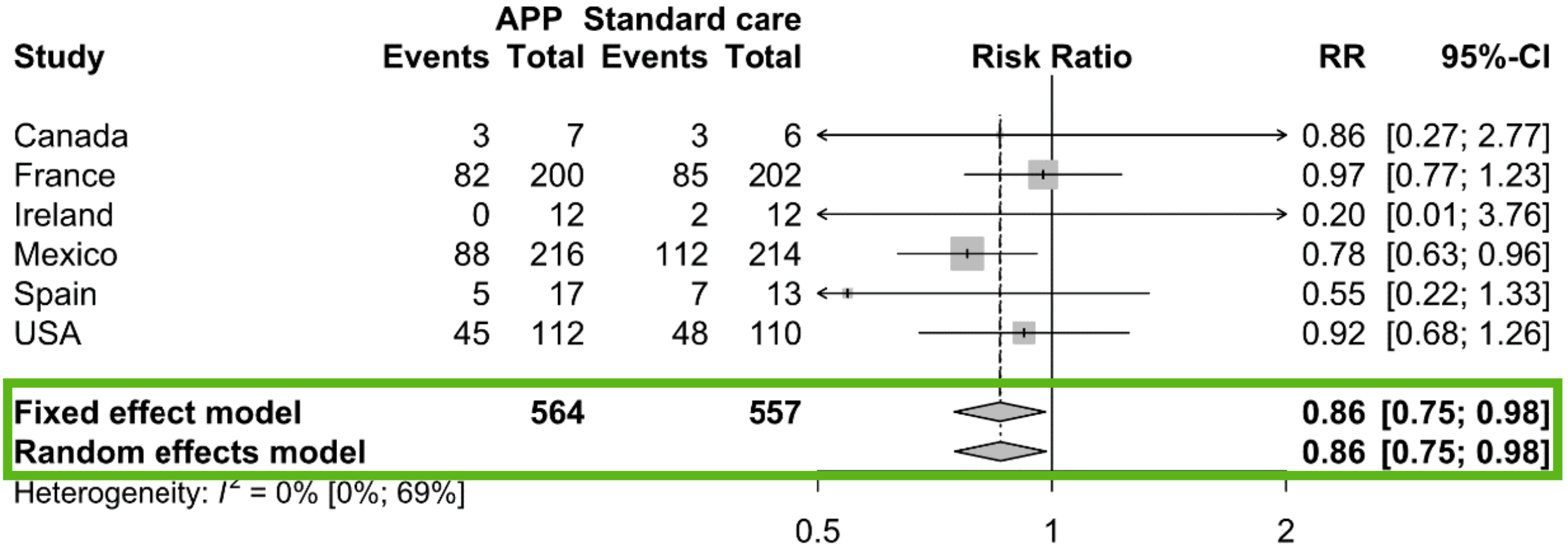
Awake prone : dose – response

- Median daily duration of APP : 5.0h (1.6 – 8.8)

- **Treatment success :**
  - **< 8h : 52%**
  - **> 8h : 83%**

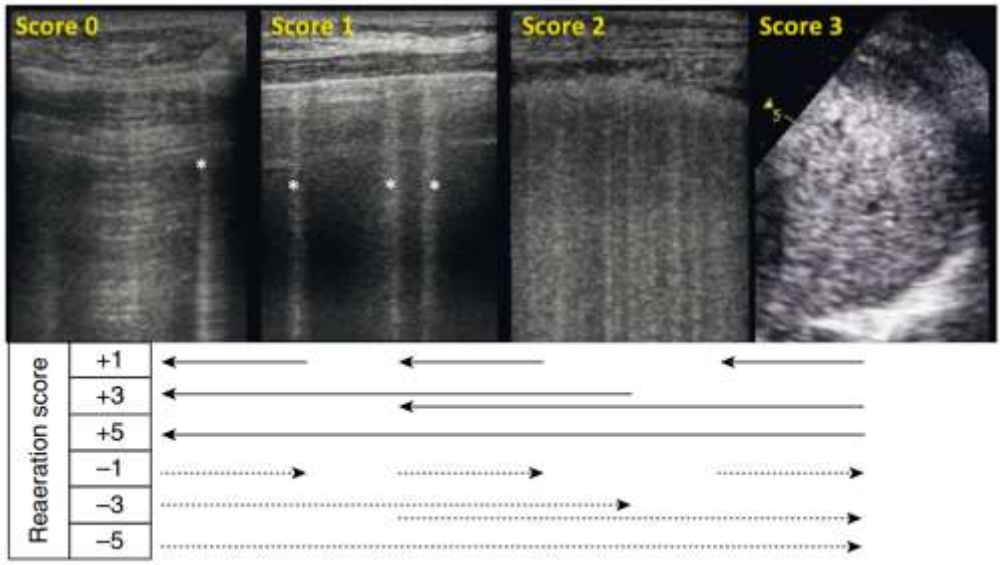


Ehrmann S, Lancet Respir Med 2021



Ehrmann S, Lancet Respir Med 2021

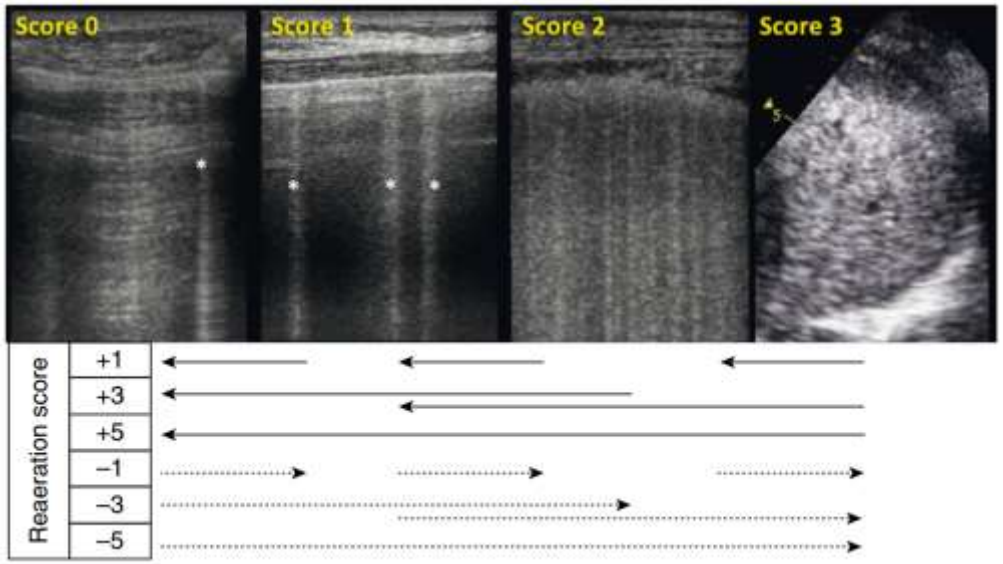
Lung morphology



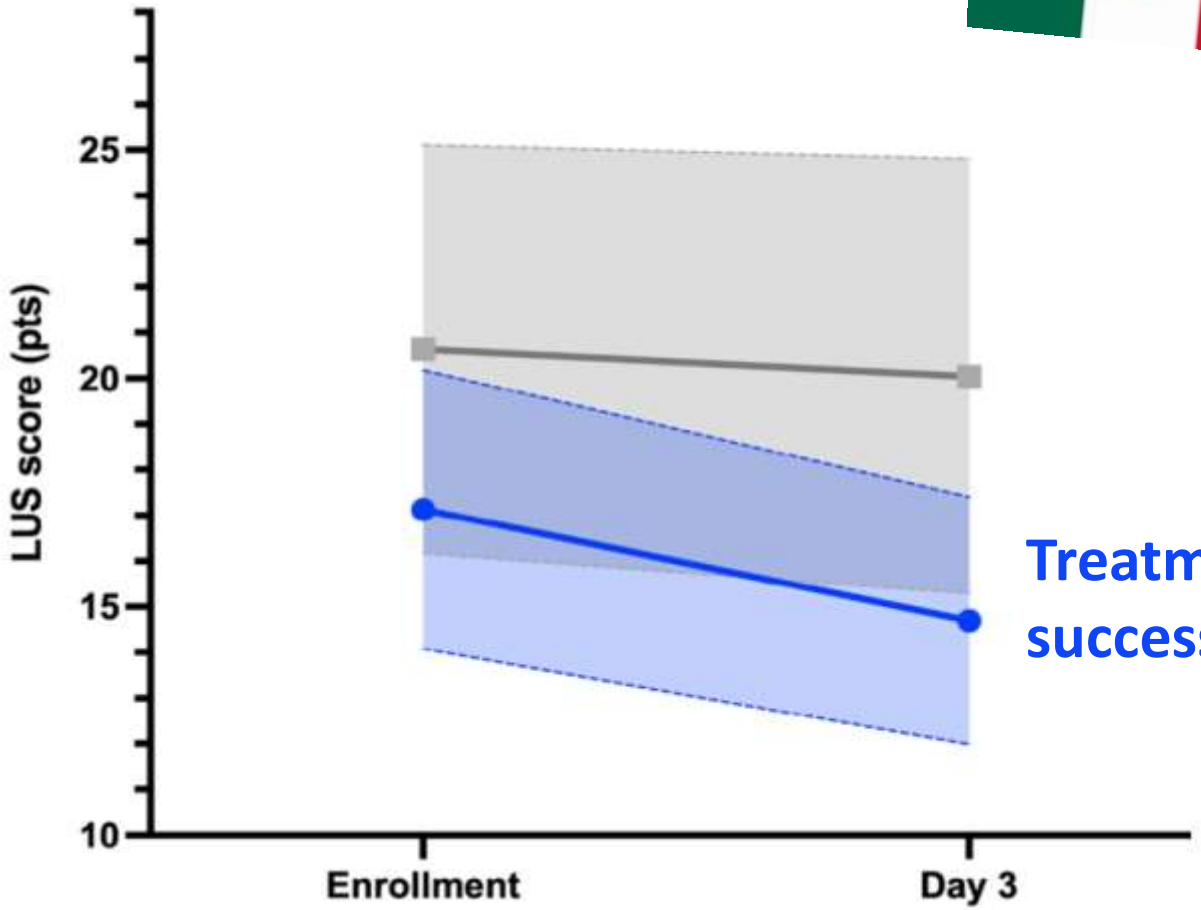
Echographic lung consolidation: 0-36

Ibarra-Estrada M, Crit Care 2022

Lung morphology



Echographic lung consolidation 0-36



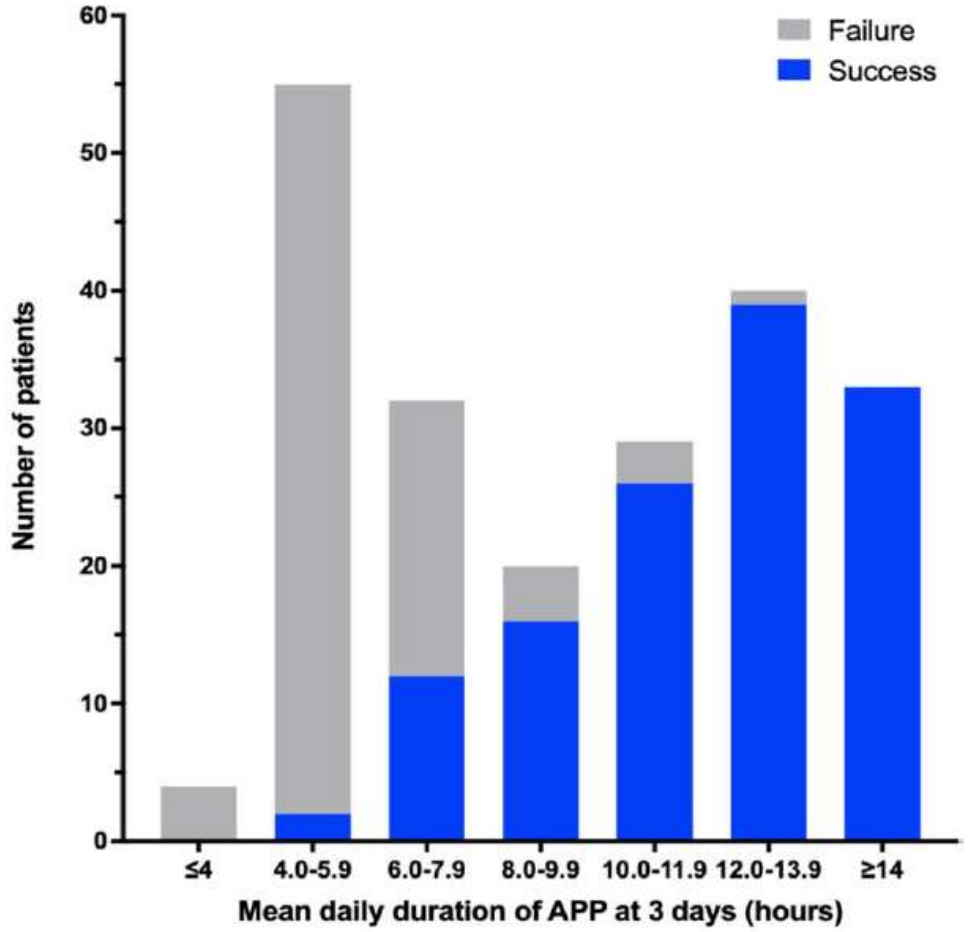
↘ LUS ≥ 2

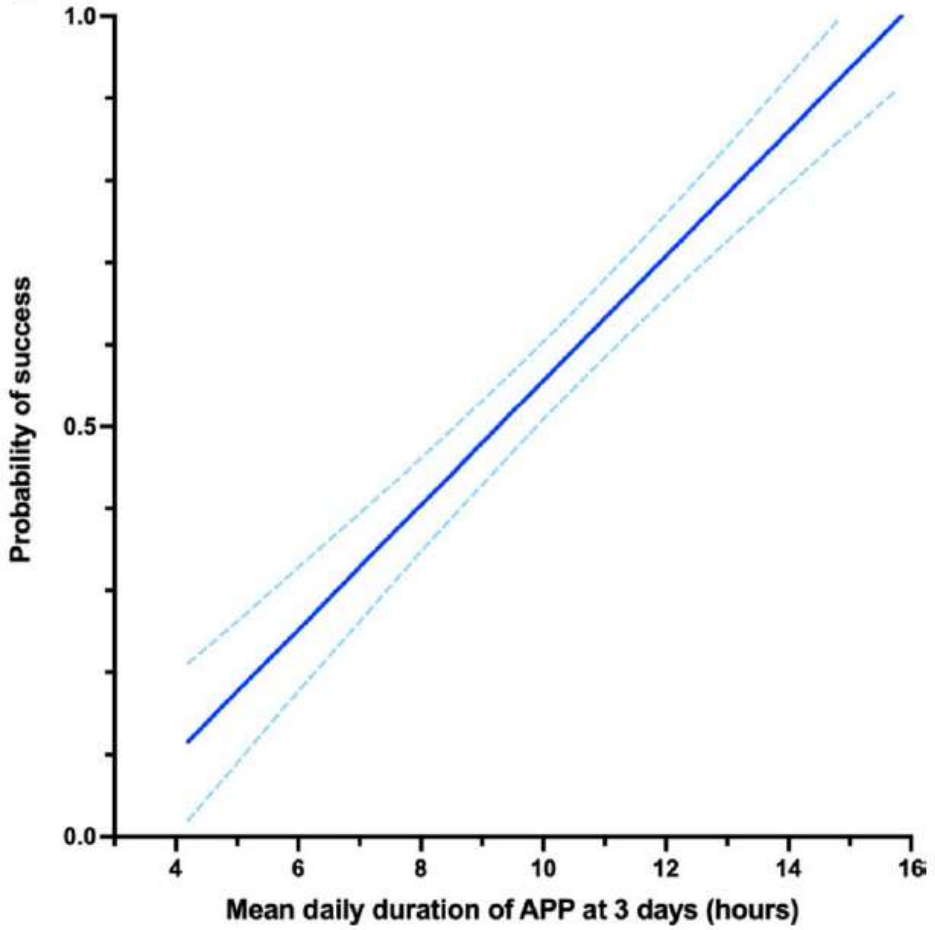
Ibarra-Estrada M, Crit Care 2022

Facteurs de succès : dose de DV

Treatment success :

- < 8h : 15%
- > 8h : 83%





Ibarra-Estrada M, Crit Care 2022

Table 1 In-hospital death and orotracheal intubation in the individual studies by intervention group (aPP vs. not aPP)

Author, year	Death in patients treated by aPP *n/N* (%)	Death in patients not treated by aPP *n/N* (%)	Orotracheal intubation in aPP patients *n/N* (%)	Orotracheal intubation in non-aPP patients *n/N* (%)	RCT	DNR patients (%)
Alhazzani W., 2022 [17]	46/205 (22.4)	46/195 (23.5)	70/205 (34.1)	79/195 (40.5)	Yes	Excluded
Altinay M., 2021 [18]	9/25 (36.0)	16/23 (69.8)	8/25 (32.0)	19/23 (82.6)	No	n.a
Ates I., 2021 [19]	0/97 (0.0)	4/47 (4.12)	7/97 (7.2)	12/47 (25.5)	No	n.a
Bahloul M., 2021 [20]	14/21 (66.7)	12/17 (70.6)	9/21 (42.8)	4/17 (23.5)	No	n.a
Barker J., 2021 [21]	1/10 (10.0)	4/10 (40.0)	6/10 (60.0)	5/10 (50.0)	No	n.a
Burton-Papp HC. 2020 [22]	0/20 (0.0)	0/20 (0.0)	7/20 (35.0)	0/20 (0.0)	No	n.a
Coppo A., 2020 [23]	0/47 (0.0)	0/9 (0.0)	13/47 (27.6)	0/9 (0.0)	No	n.a
Ehrmann S., 2021 [24]	117/564 (20.7)	132/557 (23.7)	185/564 (32.6)	223/557(40.0)	Yes	Included (8)
Ferrando C., 2020 [25]	8/49 (16.3)	17/122 (13.9)	22/55 (40.0)	60/144 (41.7)	No	n.a
Fralick M., 2022 [26]	1/126 (0.80)	1/122 (0.81)	5/126 (3.9)	6/122 (4.9)	Yes	Included
Gad S., 2021 [27]	3/15 (20.0)	3/15 (20.0)	3/15 (20.0)	3/15 (20.0)	No	n.a
Graziani M, 2023 [28]	23/114 (20.1)	102/422(24.1)	39/114 (34.2)	32/422 (7.5)	No	Included (21)
Hallifax RJ, 2020 [29]	12/30 (40.0)	14/18 (77.7)	–	–	No	n.a
Hashemian SM., 2021 [30]	9/45 (20.0)	10/30 (33.3)	10/45 (22.2)	12/30 (40.0)	No	n.a
Hussain HT., 2021 [31]	1/25 (4.0)	2/25 (8.0)	–	–	No	n.a
Imran M., 2021 [32]	2/50 (4.0)	3/50 (6.0)	–	–	No	n.a
Jagan N., 2020 [33]	0/40 (0.0)	16/65 (40.0)	11/40 (27.5)	26/65 (40.0)	No	n.a
Jayakumar D., 2021 [34]	3/30 (10.0)	2/30 (6.7)	4/30 (13.3)	4/30 (13.3)	Yes	n.a
Johnson SA., 2021 [35]	2/15 (13.3)	0/15 (0.00)	2/15 (13.3)	1/15 (6.7)	Yes	n.a
Jouffroy R., 2021 [36]	4/40 (10.0)	94/339 (27.7)	4/40 (10.0)	200/339(58.9)	No	n.a
Liu X., 2020 [37]	0/13 (0.0)	0/16 (0.0)	*n/N* (%)	–	No	n.a
Musso G., 2022 [38]	10/81 (12.3)	59/162 (36.4)	8/81 (9.8)	44/162 (27.1)	No	Excluded
Padrao EMH., 2020 [39]	6/57 (10.5)	22/109 (20.2)	33/57 (57.9)	53/109 (48.6)	No	Excluded
Perez-Nieto OR. 2021 [40]	100/505 (1.9)	120/322 (36.3)	109/505 (21.5)	130/322 (40.4)	No	n.a
Proud'homme E. 2021 [41]	4/48 (8.3)	6/120 (5.0)	7/48 (14.5)	8/120 (6.6)	No	n.a
Qian ET., 2022 [42]	59/239 (24.7)	47/222 (21.1)	–	–	No	n.a
Rosen J., 2021 [43]	6/36 (16.7)	3/39 (7.7)	12/36(33.3)	13/39 (33.3)	Yes	Excluded
Simioli F., 2021 [44]	0/18 (0.0)	3/11 (27.3)	1/18 (5.5)	2/11 (18.1)	No	n.a
Syrma PB., 2021 [45]	2/30 (6.67)	4/15 (26.7)	–	–	No	n.a
Stilma W., 2021 [46]	91/438 (20.8)	62/296 (21.0)	–	–	No	n.a
Thompson A. 2020 [47]	3/25 (12.0)	0/40 (0.0)	13/25 (52.0)	4/40 (10.0)	No	Included
Tonelli R., 2021 [48]	5/38 (13.1)	17/76 (22.4)	7/38 (18.4)	30/76 (39.4)	No	Excluded
Vianello A., 2021 [49]	2/50 (0.0)	7/43 (16.8)	4/50(8.0)	12/43 (27.9)	No	Excluded
Zang X., 2020 [50]	10/23 (43.5)	28/37 (75.6)	8/23 (34.7)	4/37 (10.8)	No	n.a

aPP awake prone positioning, *DNR* do-not resuscitate, *RCT* randomized controlled trial

Clinical studies on awake prone positioning

Graziani M, Internal and Emergency Medicine 2024

Awake prone positioning for patients with COVID-19-related respiratory failure: a systematic review and meta-analysis

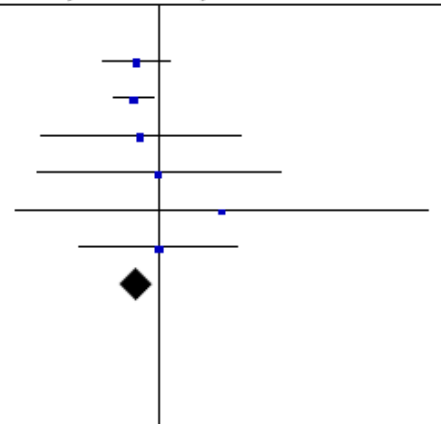
Mara Graziani[1] · Andrea Galeazzo Rigutini[1] · Diletta Bartolini[1] · Laura Traballi[1] · Lorenzo Luzi[1] · Rossana Regina[1] · Francesco Bossi[1] · Carla Caponi[1] · Cecilia Becattini[1]

Received: 7 April 2023 / Accepted: 11 September 2023 / Published online: 5 October 2023

Intubation

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
13.1.1 RCTs						
Alhazzani W.	70	205	79	195	5.2%	0.76 [0.51, 1.14]
Ehrmann S.	185	564	223	557	5.4%	0.73 [0.57, 0.93]
Fralick M.	5	126	6	122	3.7%	0.80 [0.24, 2.69]
Jayakumar D.	4	30	4	30	3.2%	1.00 [0.23, 4.43]
Johnson SA.	2	15	1	15	1.8%	2.15 [0.17, 26.67]
Rosen J.	12	36	13	39	4.2%	1.00 [0.38, 2.61]
Subtotal (95% CI)		**976**		**958**	**23.4%**	**0.76 [0.62, 0.93]**
Total events	278		326			

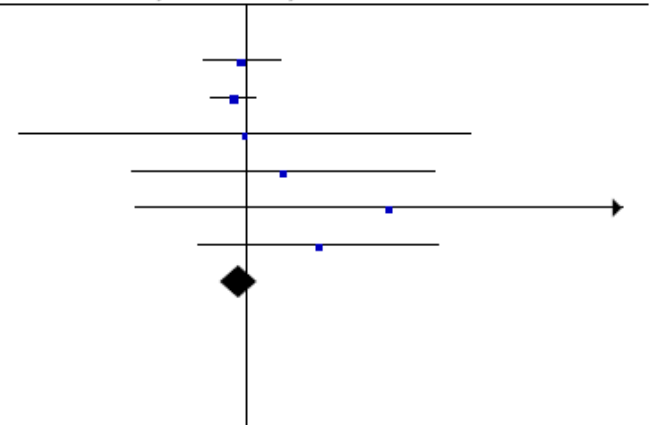
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.21$, df = 5 (P = 0.94); $I^2 = 0\%$
Test for overall effect: Z = 2.71 (P = 0.007)



Mortality

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
5.1.1 RCTs						
Alhazzani W.	46	205	46	195	6.8%	0.94 [0.59, 1.49]
Ehrmann S.	117	564	132	557	7.8%	0.84 [0.64, 1.12]
Fralick M.	1	126	1	122	0.8%	0.97 [0.06, 15.65]
Jayakumar D.	3	30	2	30	1.7%	1.56 [0.24, 10.05]
Johnson SA.	2	15	0	15	0.7%	5.74 [0.25, 130.37]
Rosen J.	6	36	3	39	2.4%	2.40 [0.55, 10.42]
Subtotal (95% CI)		**976**		**958**	**20.1%**	**0.91 [0.72, 1.15]**
Total events	175		184			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.63$, df = 5 (P = 0.60); $I^2 = 0\%$
Test for overall effect: Z = 0.80 (P = 0.42)

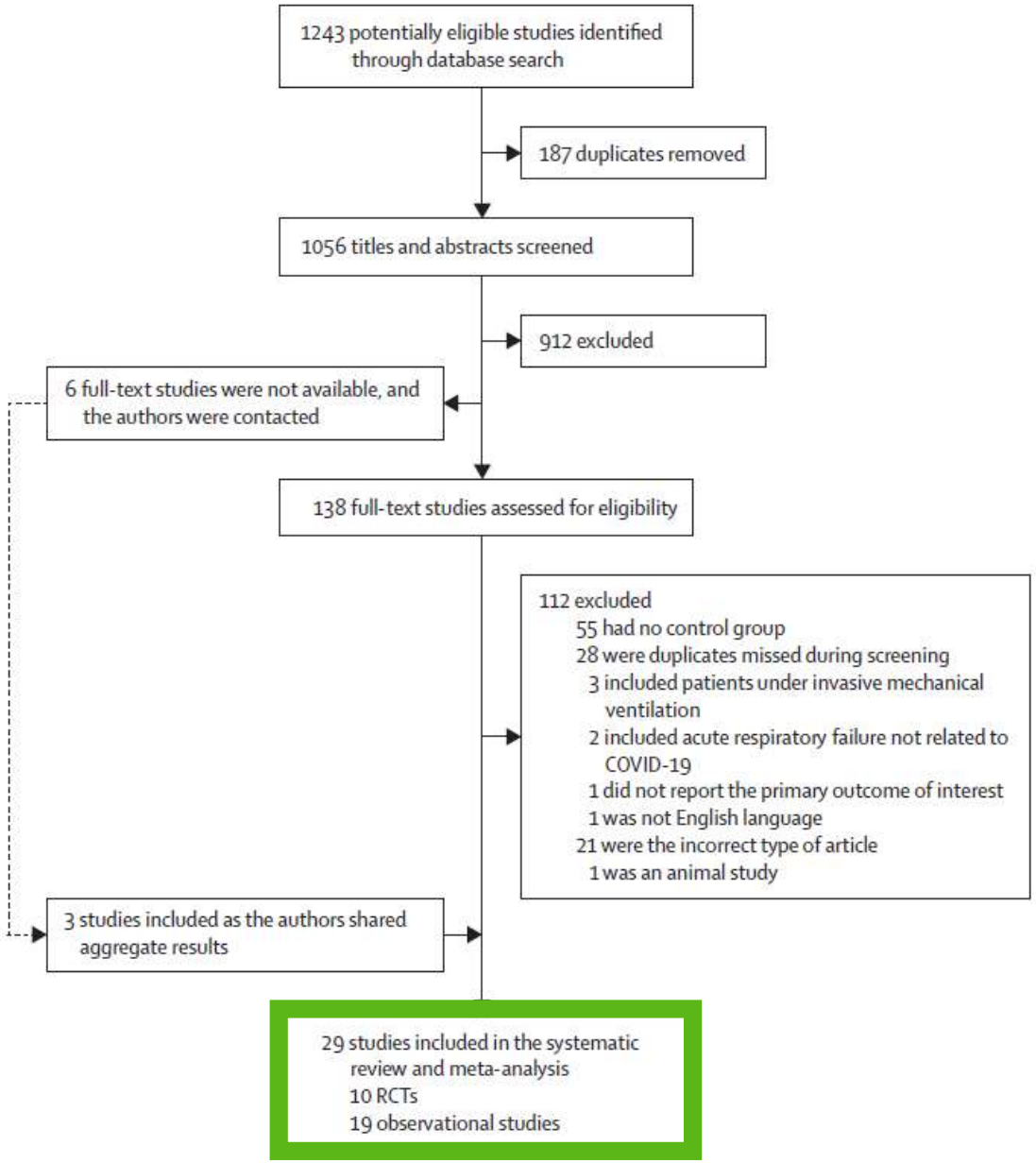


Awake prone positioning for non-intubated patients with COVID-19-related acute hypoxaemic respiratory failure: a systematic review and meta-analysis

Jie Li, Jian Luo*, Ivan Pavlov*, Yonatan Perez*, Wei Tan*, Oriol Roca, Elsa Tavernier, Aileen Kharat, Bairbre McNicholas, Miguel Ibarra-Estrada, David L Vines, Nicholas A Bosch, Garrett Rampon, Steven Q Simpson, Allan J Walkey, Michael Fralick, Amol Verma, Fahad Razak, Tim Harris, John G Laffey†, Claude Guerin†, Stephan Ehrmann†, for the Awake Prone Positioning Meta-Analysis Group‡*

Lancet Respir Med 2022

Published Online
March 16, 2022



- 1 meta-trial
- 6 published RCT
- 3 un published RCT

N=1985 patients

- 19 observational studies with control group

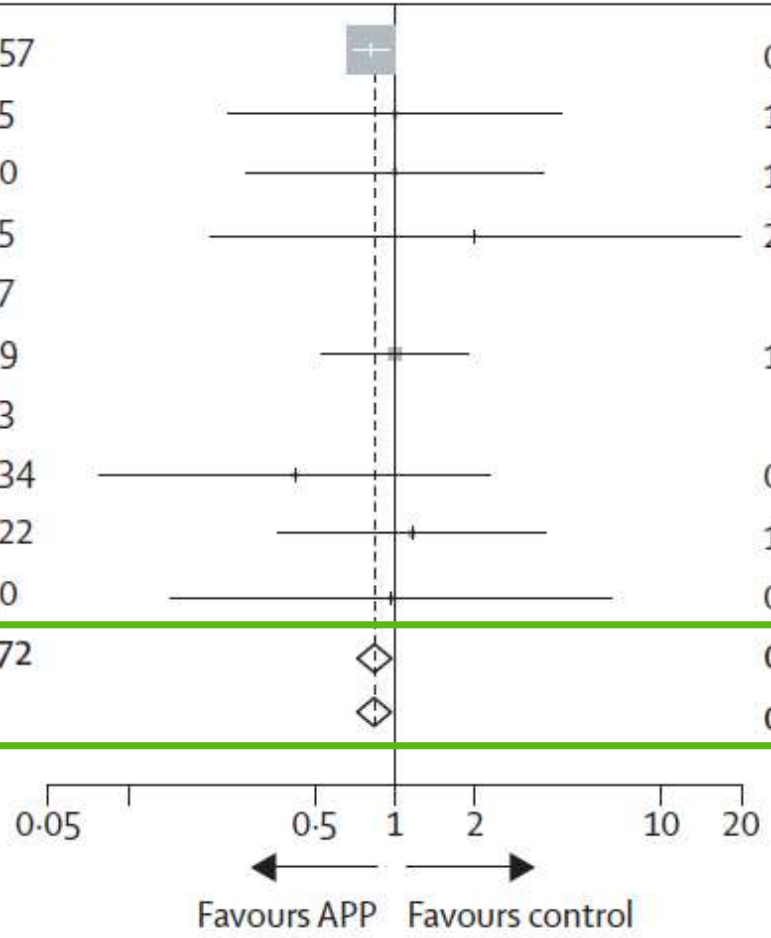
N=2669 patients

Li J, Lancet Respir Med 2022

Intubation

	Awake prone positioning n/N	Control n/N	Risk ratio (95% CI)	Weight (fixed)	Weight (random)
Ehrmann et al[11]	185/564	223/557	0·82 (0·70–0·96)	87·5%	89·0%
Gad et al[17]	3/15	3/15	1·00 (0·24–4·18)	1·2%	1·1%
Jayakumar et al[16]	4/30	4/30	1·00 (0·28–3·63)	1·6%	1·3%
Johnson et al[13]	2/15	1/15	2·00 (0·20–19·78)	0·4%	0·4%
Kharat et al[15]	0/10	0/17		0·0%	0·0%
Rosen et al[14]	12/36	13/39	1·00 (0·53–1·90)	4·9%	5·3%
Taylor et al[12]	0/27	0/13		0·0%	0·0%
Garcia et al[19]	2/159	4/134	0·42 (0·08–2·26)	1·7%	0·8%
Fralick et al[18]	6/126	5/122	1·16 (0·36–3·71)	2·0%	1·6%
Harris et al (NCT04853979)	2/31	2/30	0·97 (0·15–6·44)	0·8%	0·6%
Fixed-effects model	**216/1013**	**255/972**	**0·84 (0·72–0·97)**	**100·0%**	..
Random-effects model			**0·84 (0·72–0·97)**	..	**100·0%**

Heterogeneity: I^2=0%, χ^2_7=2·03 (p=0·96)

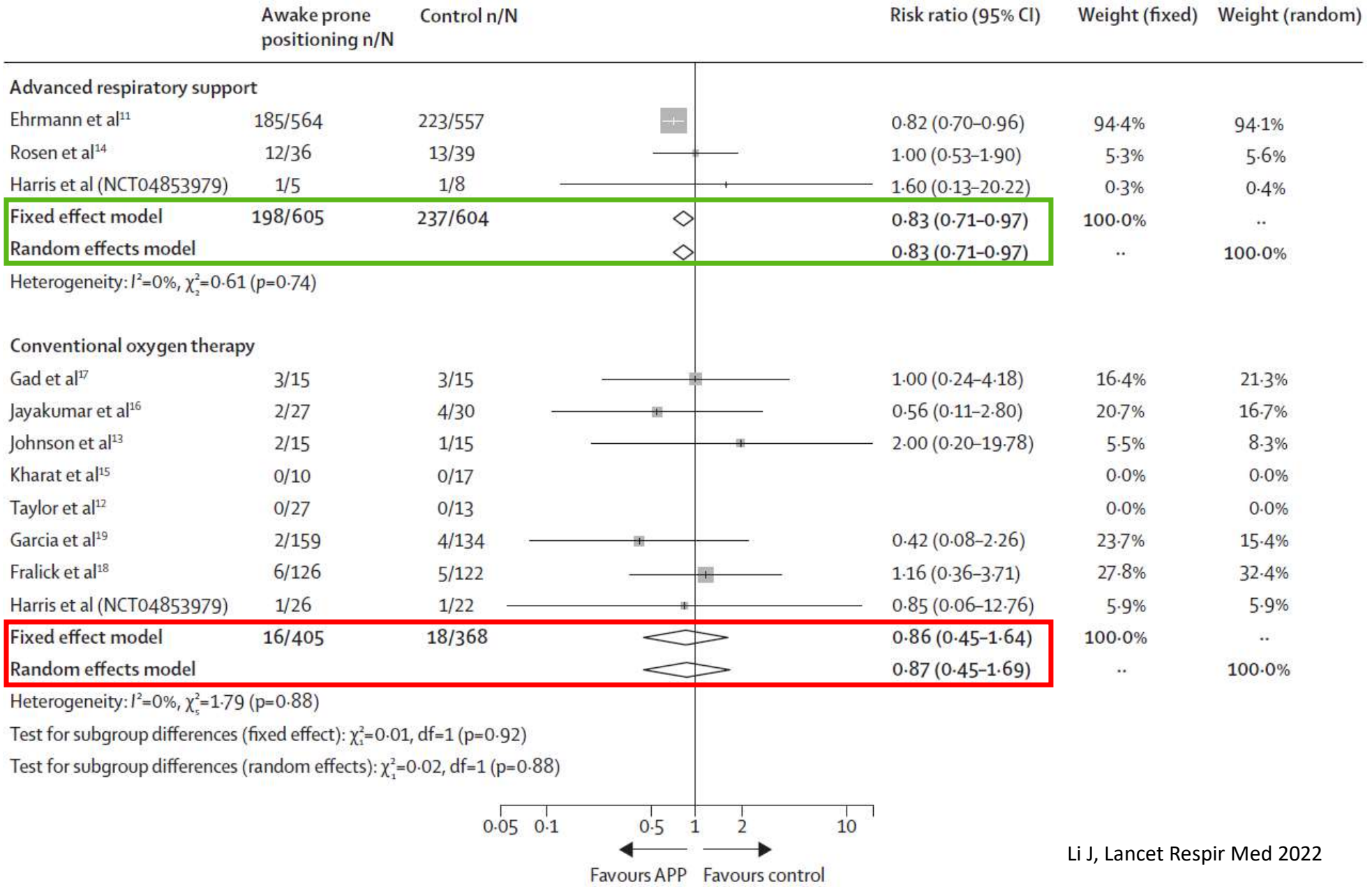


Li J, Lancet Respir Med 2022

Intubation

High Flow
NIV
CPAP

Standard oxygen



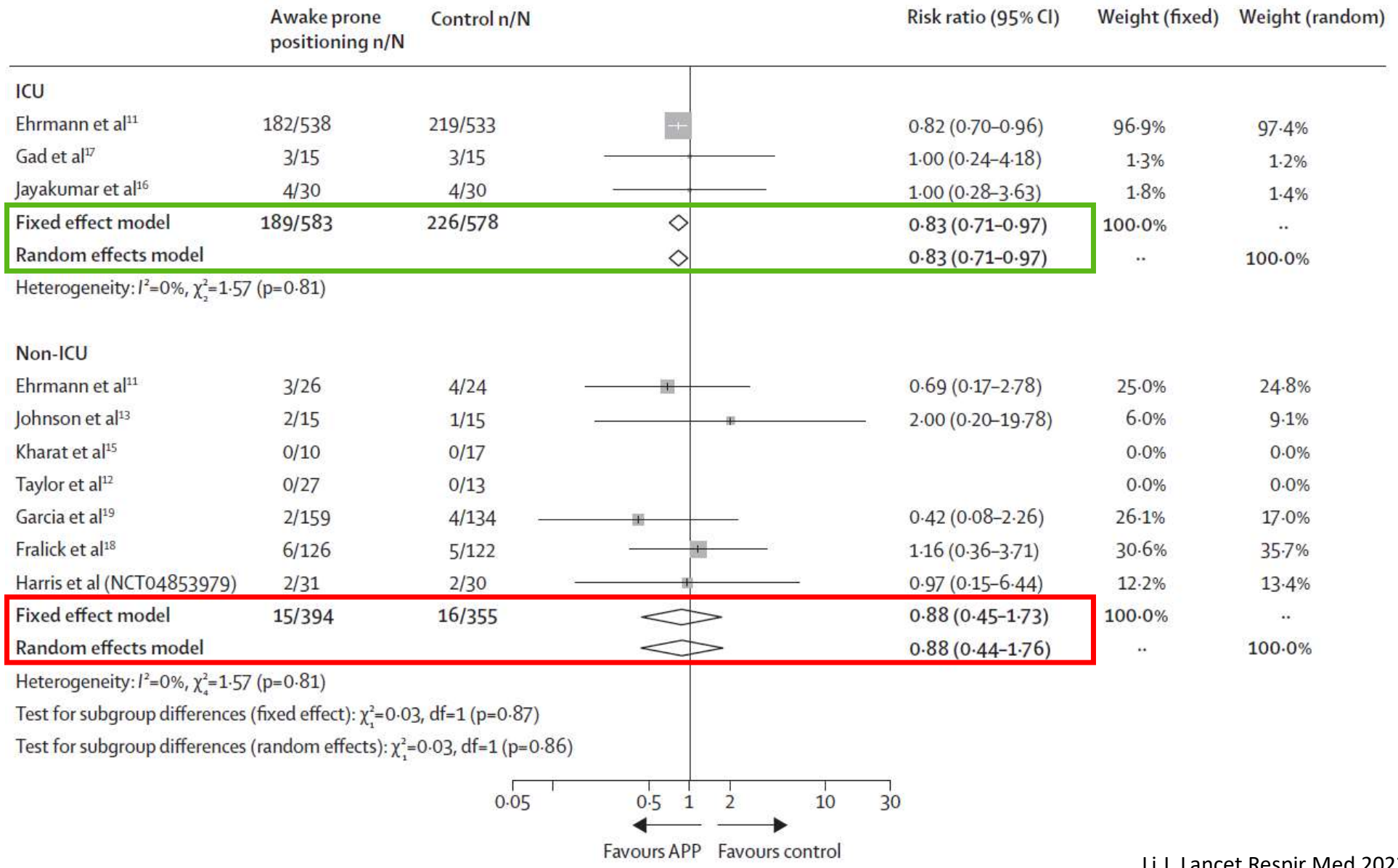
Li J, Lancet Respir Med 2022

Intubation

ICU

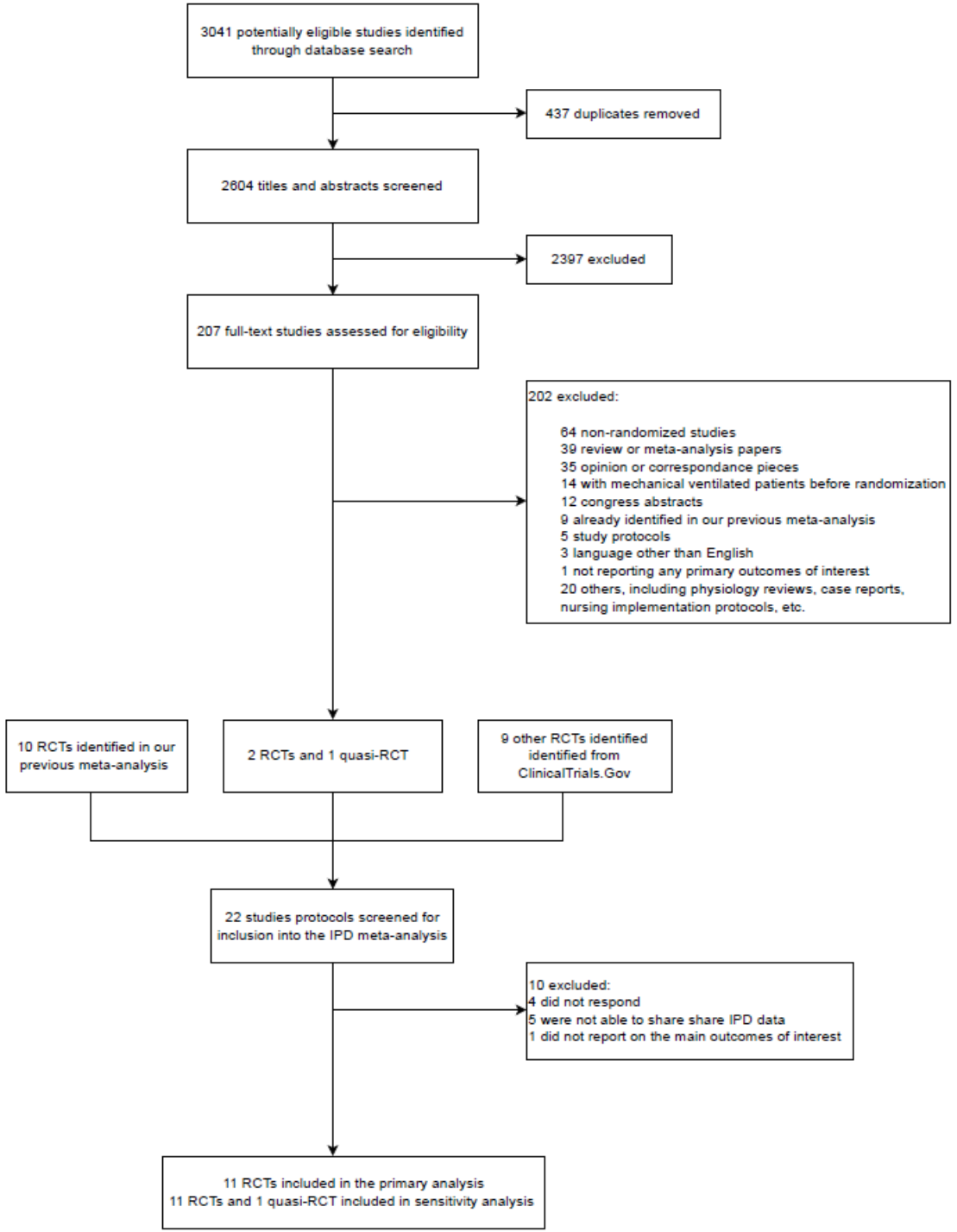
Intermediate care

Ward



Li J, Lancet Respir Med 2022

Individual patient data meta-analysis



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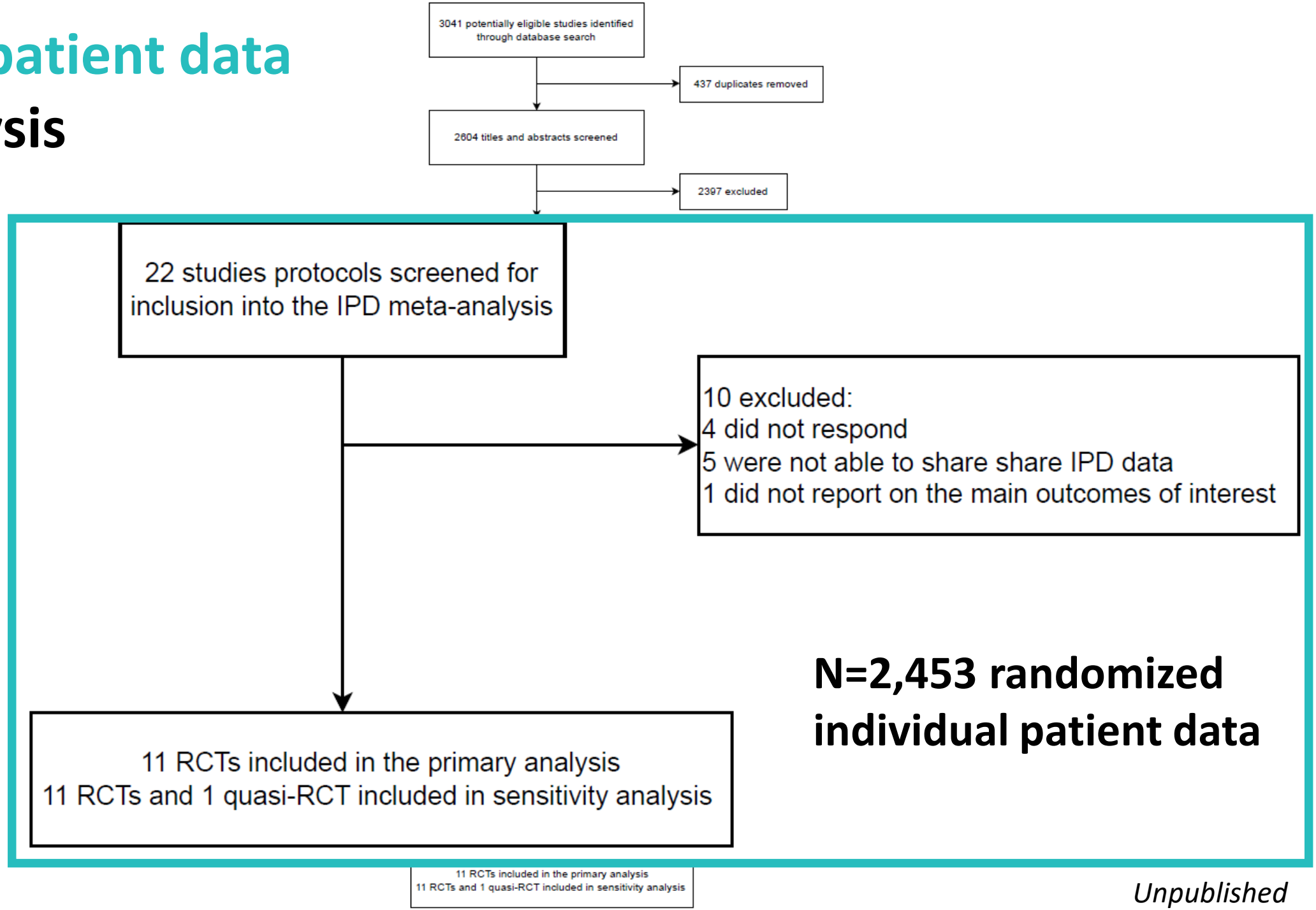
Individual patient data meta-analysis



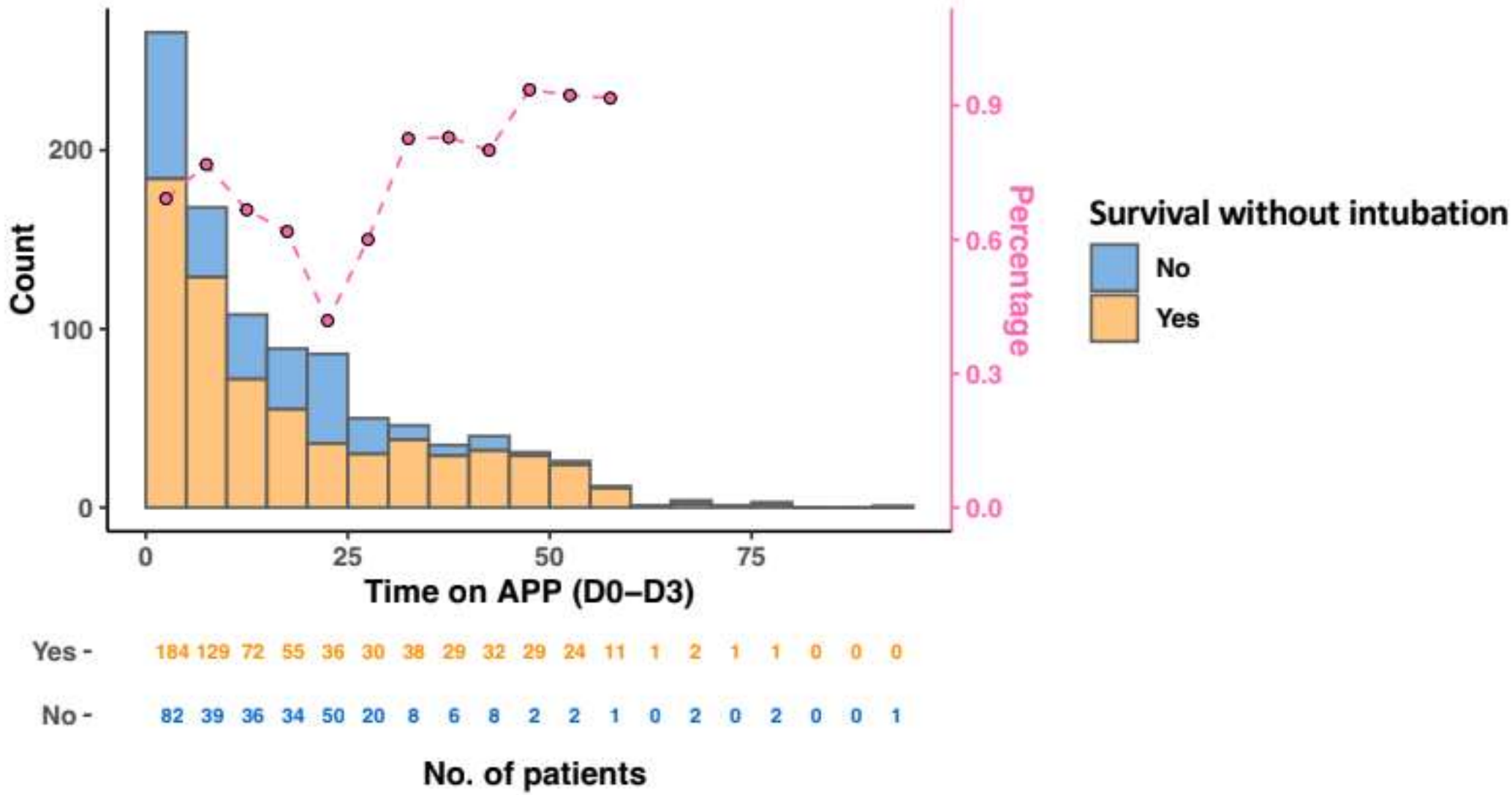
Unpublished

	APP	Control	OR
Intubation or death	27%	32%	4.17 (1.8-9.6)
Intubation	23%	28%	0.27 (0.12-0.59)
Mortality			
Death without intubation			
Death after intubation			

Unpublished

	APP	Control	OR
Intubation or death	73%	68%	4.17 (1.8-9.6)
Intubation	23%	28%	0.27 (0.12-0.59)
Mortality	13%	16%	0.27 (0.10-0.72)
Death without intubation (“DNR”)	3.6%	3.9%	0.21 (0.04-1.05)
Death after intubation	9.8%	11.6%	0.33 (0.13-0.83)

Unpublished



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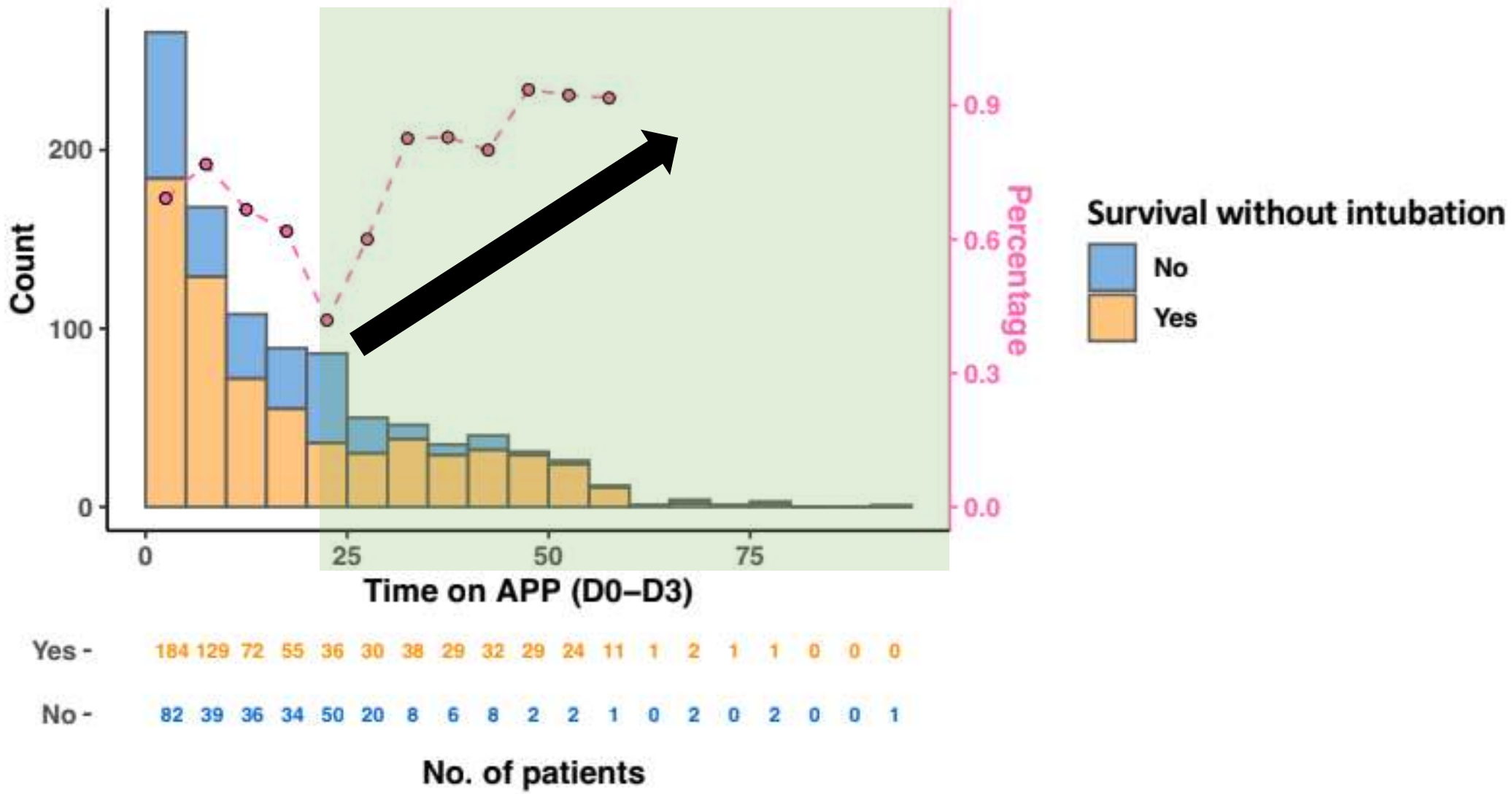
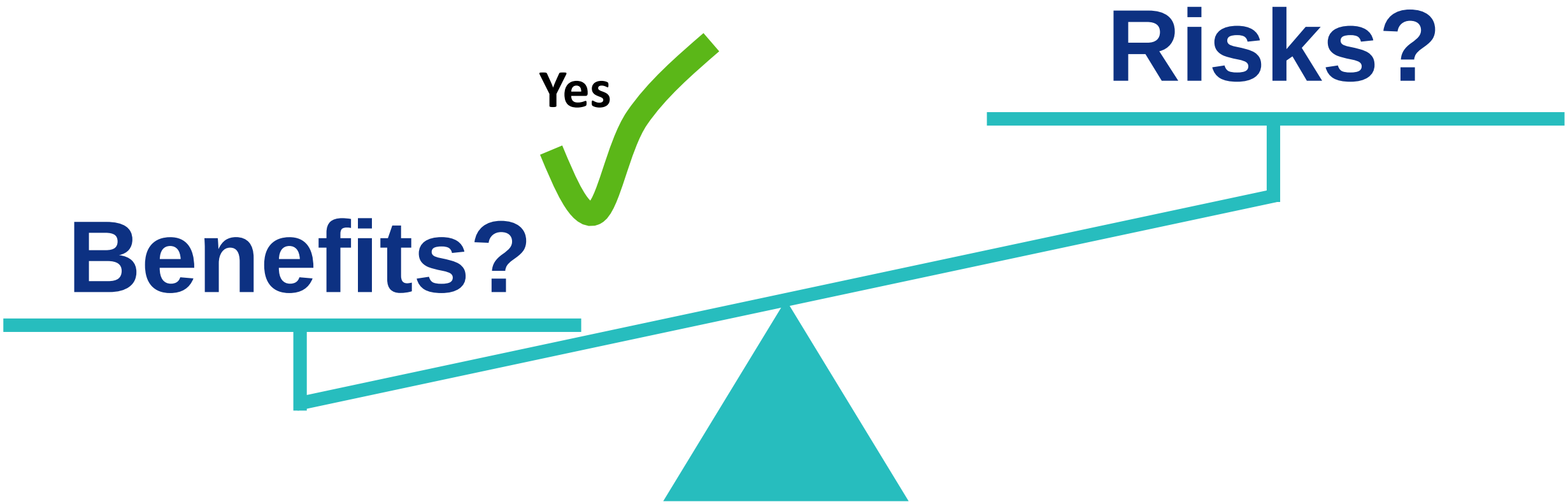


Unpublished

Rational?

Yes



Risks?

Table S6. Adverse events of the included RCTs.

Author, year	Interventions	Population	Skin breakdown (n, %)	Vomiting (n, %)	Central or arterial line dislodgement (n, %)	Cardiac arrest at any time (n, %)	Back pain (n, %)	Bloating sensation (n, %)	Discomfort (n, %)
Appex, Unpublished	COT (Room air/Nasal cannula/Mask/HFNC)	134							28 (20·9)
	COT (Room air/Nasal cannula/Mask/HFNC)+APP	159							14 (8·8)
Ehrmann, 2021	HFNC	557	10 (1·8)	18 (3·2)	17 (3·1)	1 (0·2)			
	HFNC+APP	564	8 (1·4)	15 (2·7)	26 (4·6)	3 (0·5)			
Gad, 2021	NRM	15							
	NRM+APP	15							
Jayakumar, 2021	Standard care (Face mask/NRM)	30	0 (0)	0 (0)					0 (0)
	Standard care (Nasal Prongs/Face mask/NRM/HFNC/NIV) +APP	30	0 (0)	0 (0)					2 (6·7)
Johnson, 2021	Usual care (Room air/ nasal cannula)	15							
	Usual care (Room air/nasal cannula)+APP	15							
Kharat, 2021	Usual care (Nasal cannula)	17	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Usual care (Nasal cannula) +APP	10	0 (0)	0 (0)	0 (0)	0 (0)	6 (60·0)	0 (0)	6 (60·0)
Rosén, 2021	HFNC/NIV	39	9 (23·1)	0 (0)	0 (0)	1 (2·6)			
	HFNC/NIV+APP	36	2 (5·6)	1 (2·8)	0 (0)	2 (5·6)			
Taylor, 2021	Usual care (Room air/ nasal cannula/HFNC/NIV)	13	0 (0)		0 (0)	0 (0)			
	Usual care (Nasal cannula/HFNC/NIV)+APP	27	0 (0)		0 (0)	0 (0)			
Harris, Unpublished	Usual care (Nasal cannula/NRM/HFNC/NIV)	30	0 (0)	0 (0)	0 (0)	0 (0)	1 (3·3)		
	Usual care (Nasal cannula/NRM/HFNC/NIV)+APP	31	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)		
Fralick, Unpublished	Standard care (Nasal cannula/ venturi mask/HFNC)	122							
	Standard care (Nasal cannula/ venturi mask/HFNC)+APP	126							

Missing data was presented as blank. APP, awake prone positioning; COT, conventional oxygen therapy; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; NRM, non-rebreather mask; RCT, randomised controlled trial.

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Risks?

Table S7. Adverse events of the included non-RCTs.

Author, year	Interventions	Population	Skin breakdown (n, %)	Vomiting (n, %)	Central or arterial line dislodgement (n, %)	Cardiac arrest at any time (n, %)	Back pain (n, %)	Bloating sensation (n, %)	Discomfort (n, %)
Alsharif, 2021	Usual care (CPAP)	48							
	Usual care (CPAP)+APP	31							
Altinay, 2021	Usual care (NRM)	23							
	Usual care (NRM)+APP	25							
Barker, 2021	Usual care (NIV)	10							
	Usual care (NIV)+APP	10							
Fazzini, 2021	Usual care (HFNC/Facemask/CPAP)+APP<1h	12							
	Usual care (HFNC/Facemask/CPAP)+APP>1h	34							
Ferrando, 2020	Usual care (HFNC)	144							
	Usual care (HFNC)+APP	55							
Jagan, 2020	APP<1h or <5 occasions per day and for <= 1 continuous hour overnight	65							
	APP>=1h orn >=5 occasions per day and for >= 1 continuous hour overnight	40							
Padrão, 2020	Usual care (Nasal cannula/Venturi mask/NRM)	109				0 (0%)			
	Usual care (Nasal cannula/Venturi mask/NRM) +APP	57				0 (0%)	3 (5·3)		
Jouffroy, 2021	Usual care (COT/HFNC/NIV/CPAP)	339							
	Usual care (COT/HFNC/CPAP)+APP	40							
Loureiro-Amigo, 2021	Usual care	103							
	Usual care+APP	60							
Meredith, 2020	Non-self proning	87							
	Self-proning	26							
Ni, 2021	Usual care	35	0 (0%)						
	Usual care+APP	20	0 (0%)						
Pierucci, 2021	Usual care (HFNC/CPAP/NIV)	16							
	Usual care (HFNC/CPAP/NIV)+APP	16							
Perez-Nieto, 2021	Usual care (Nasal cannula/NRM/HFNC)	322							
	Usual care (Nasal cannula/NRM/HFNC) +APP	505							
Sryma, 2021	Usual care (COT/HFNC/NIV)	15					0 (0%)	0 (0%)	
	Usual care (COT/HFNC/NIV)+APP	30					2 (6·6)	2 (6·7)	
Vianello, 2021	Usual care (HFNC)	43							
	Usual care (HFNC)+APP	50							
Prud'homme, 2021	Usual care (COT/HFNC)	48							
	Usual care (COT/HFNC)+APP	48							
Simioli, 2021	Usual care (HFNC/CPAP)	11							
	Usual care (HFNC/CPAP)+APP	18							
Tonelli, 2021	Usual care (HFNC/NIV)	76							
	Usual care (HFNC/NIV)+APP	38							
Zang, 2020	Usual care (Face mask)	37							
	Usual care (Face mask)+APP	23							

Missing data was presented as blank. APP, awake prone positioning; COT, conventional oxygen therapy; CPAP, continuous positive airway pressure; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; NRM, non-rebreather mask; RCT, randomised controlled trial.

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Risks?

	Awake prone positioning group (n=564)	Standard care group (n=557)
Safety outcomes		
Skin breakdown	8 (1%)	10 (2%)
Vomiting	15 (3%)	18 (3%)
Central or arterial line dislodgement	26 (5%)	17 (3%)
Cardiac arrest at any time†	3 (1%)	1 (0%)

No cardiac arrest related to prone

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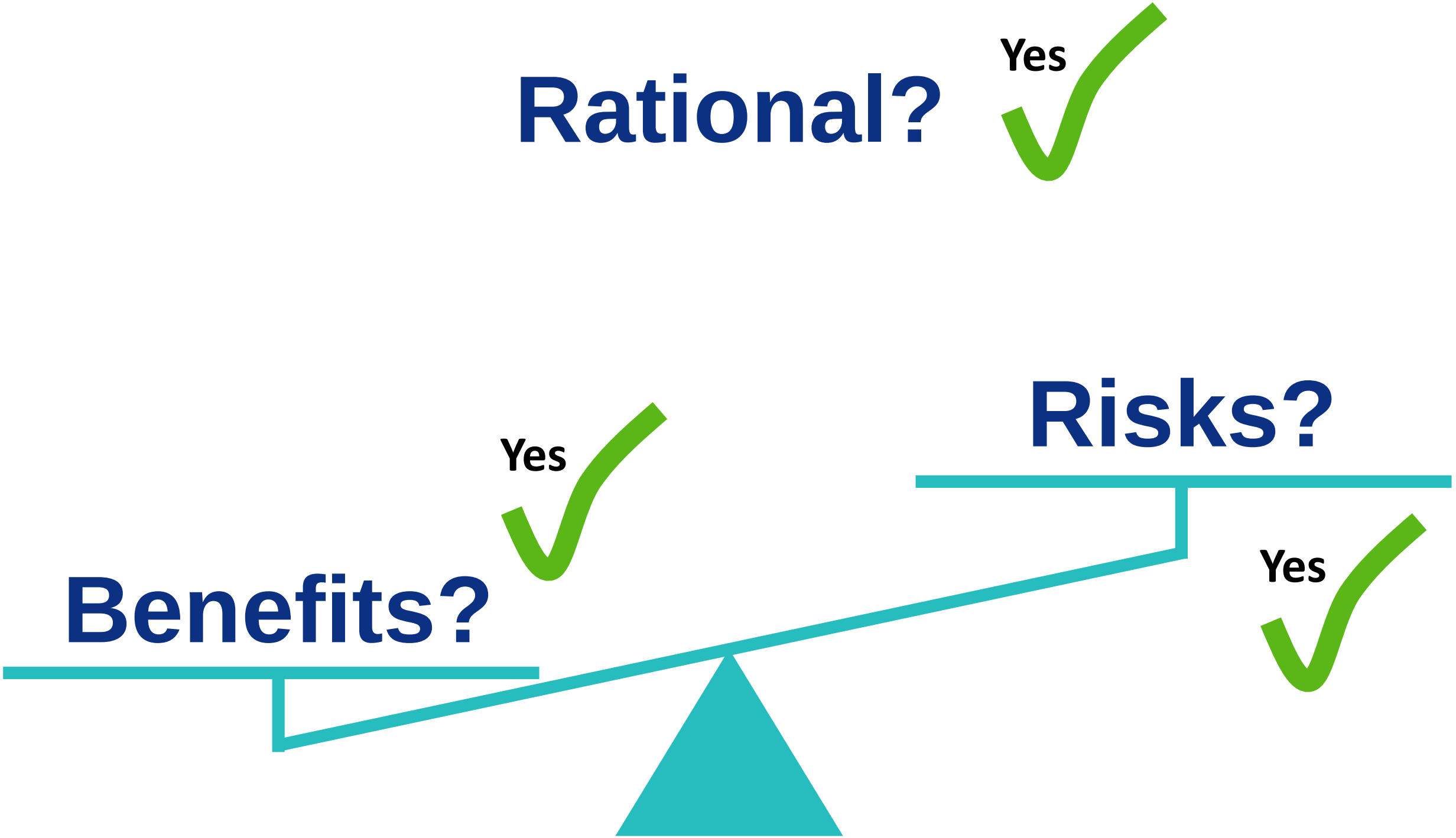
Rational?
Yes
Risks?
Yes
Benefits?
Yes

Thank you very much for your attention

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TOURS

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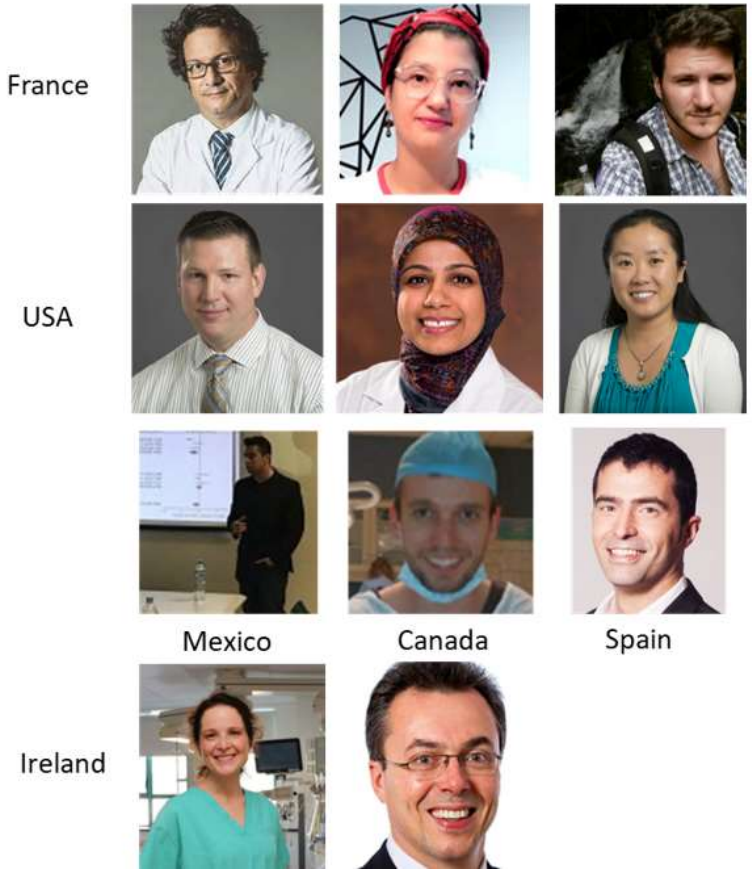

Thank you to the AWP meta-trial core group