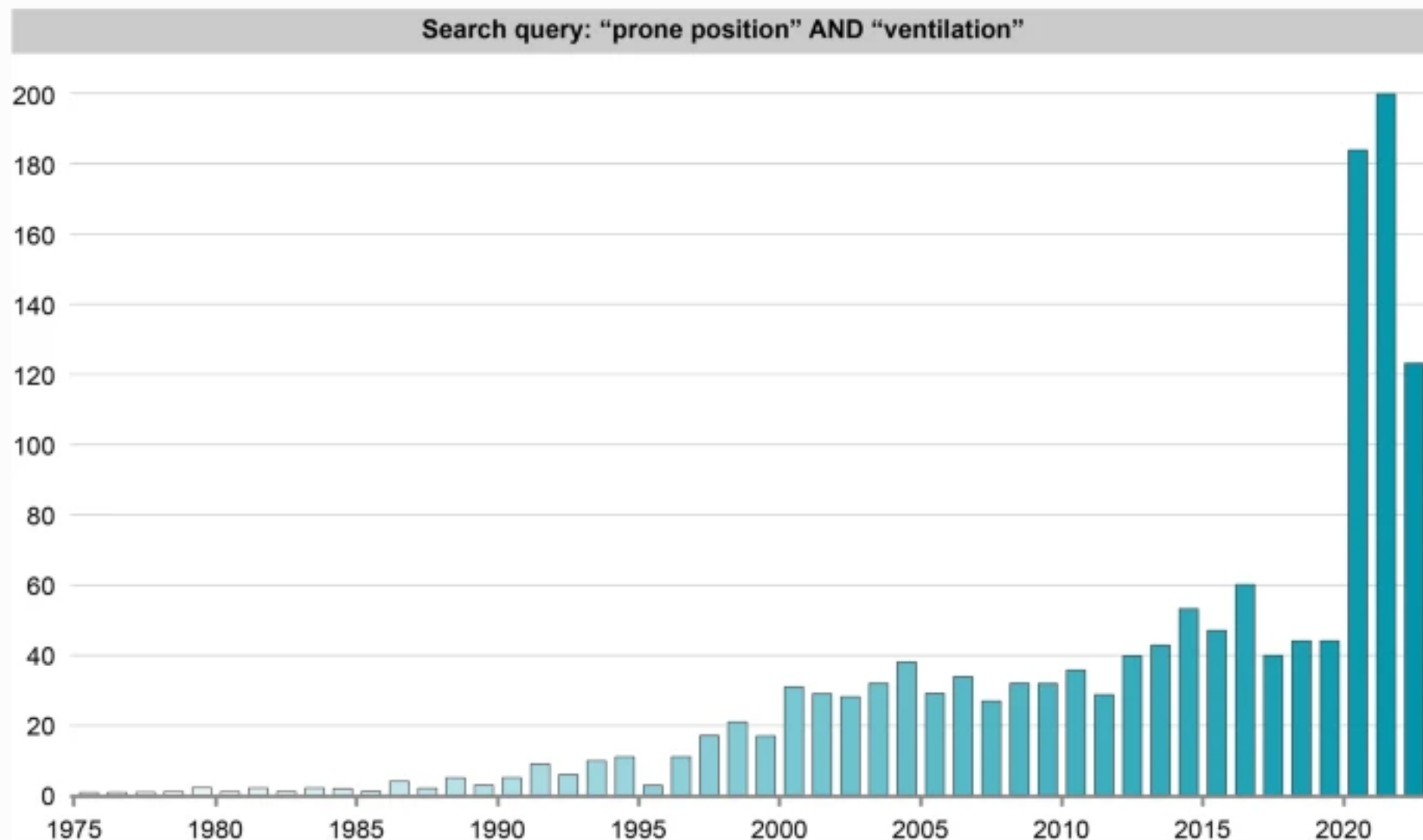


Awake prone positioning in covid-19 respiratory failure

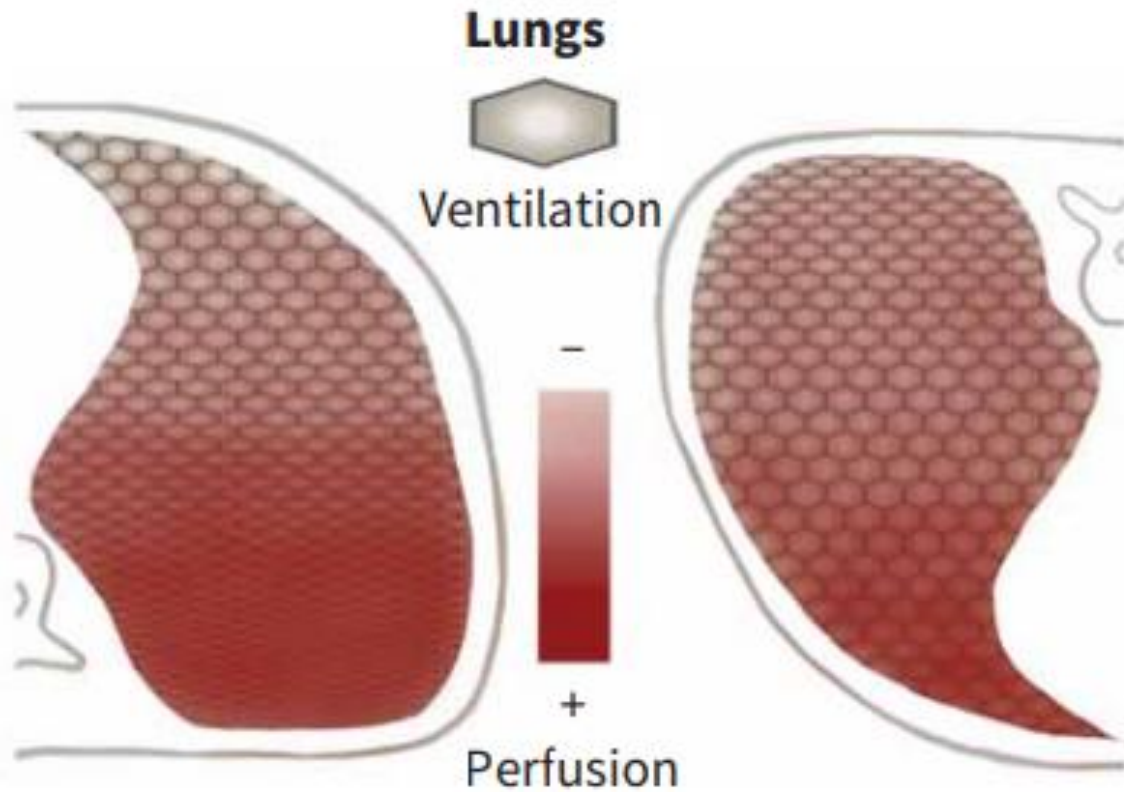
정원재

Fig. 1

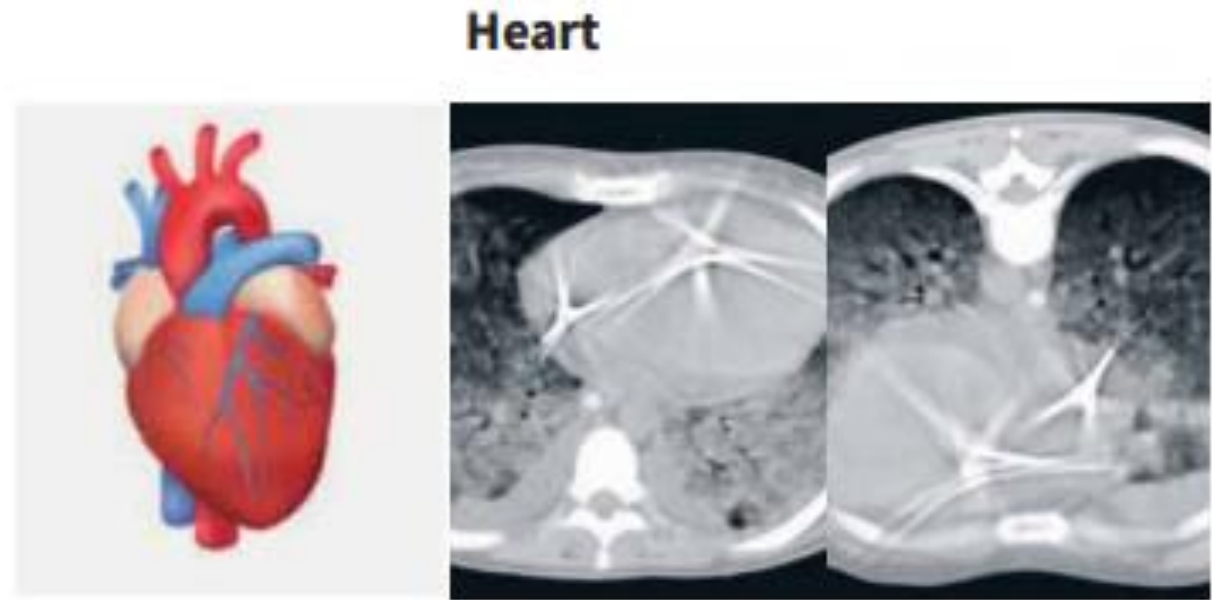


Number of studies per year about "prone position" and "ventilation". The research was conducted in PubMed, using as search query: "prone position" AND "ventilation"

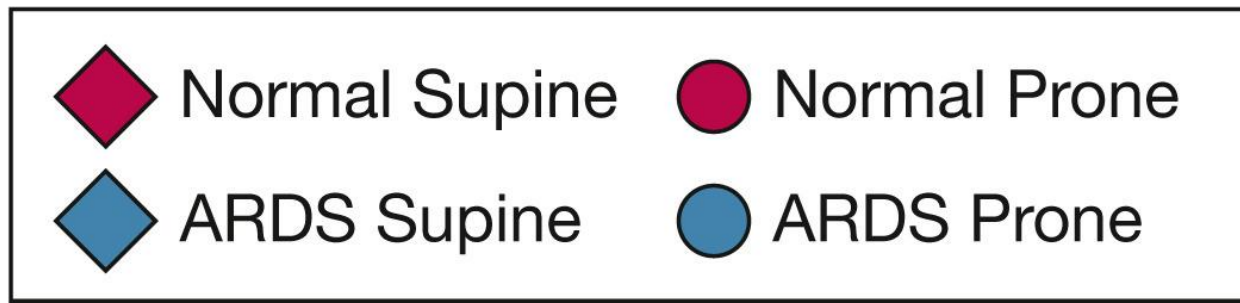
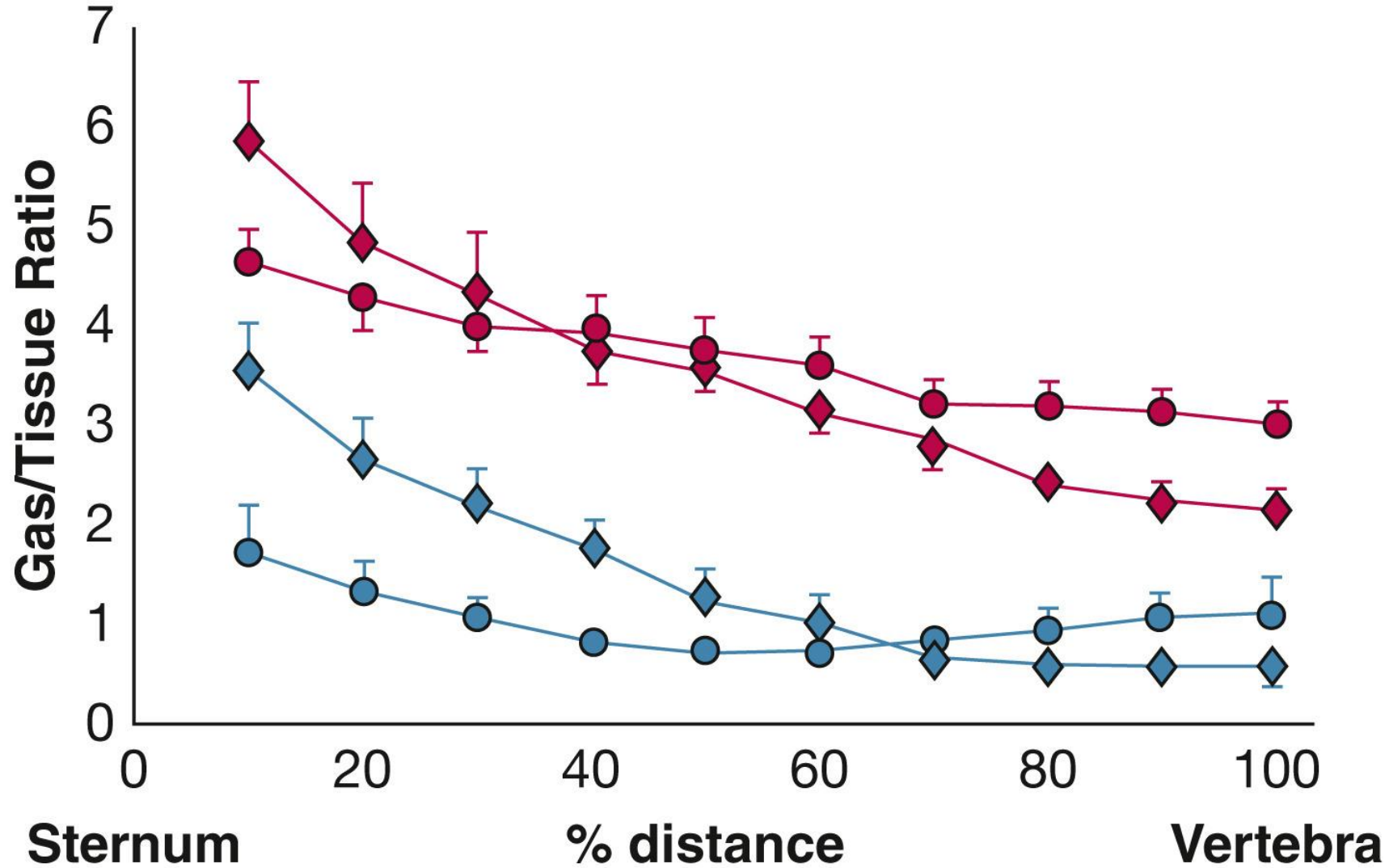
Physiologic effects of Prone position



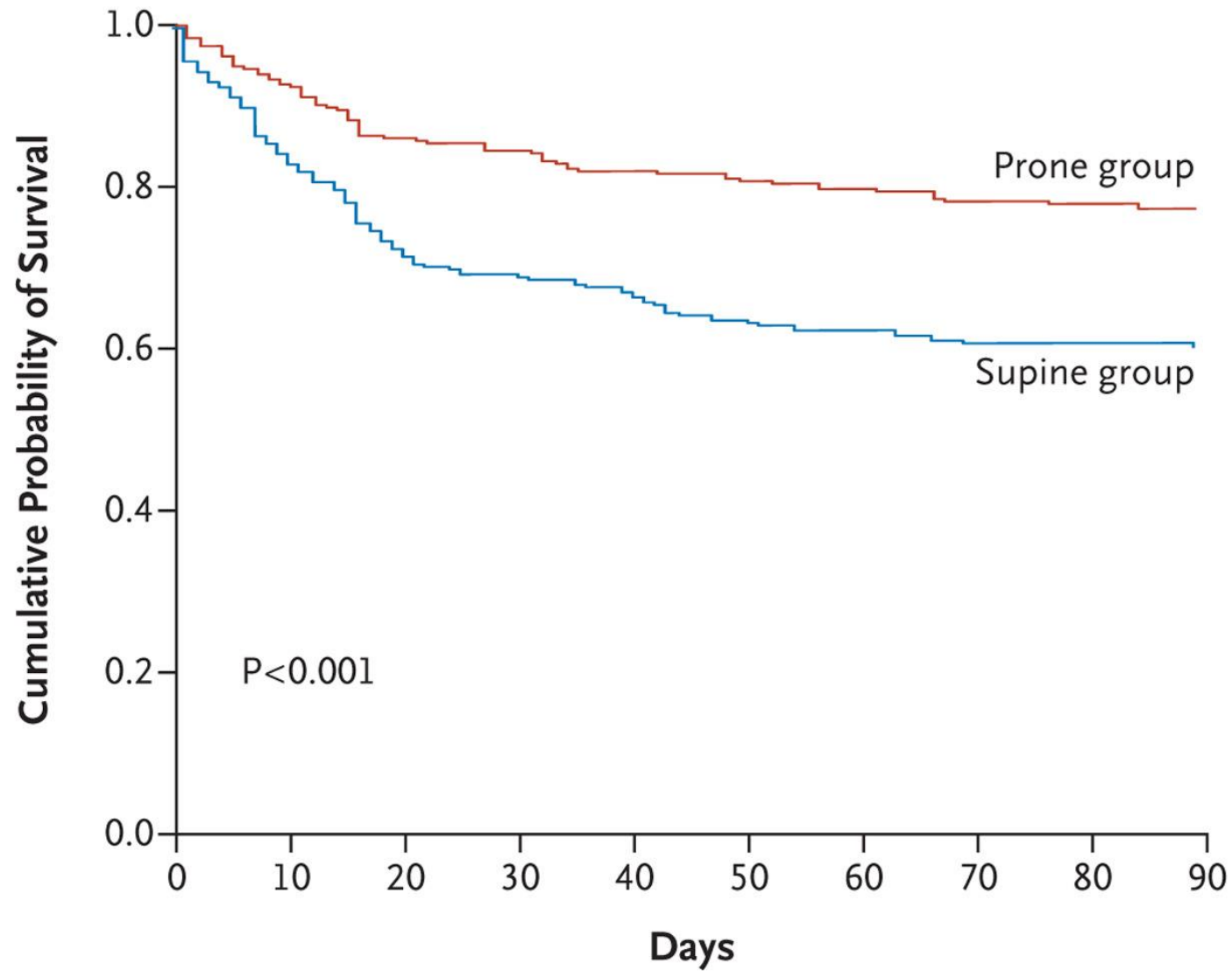
- ↑ Regional ventilation in dependent lung regions
- ↑ Matching of ventilation and perfusion
- ↓ Airway closure in dorsal lung regions
- ↑ Secretion removal
- ↑ Functional residual capacity
- ↑ Regional diaphragm movement



- ↑ Cardiac output
- ↑ Systemic venous return
- ↑ Right ventricular preload
- ↓ Right ventricular afterload



Prone position in ARDS



No. at Risk

Prone group	237	202	191	186	182
Supine group	229	163	150	139	136

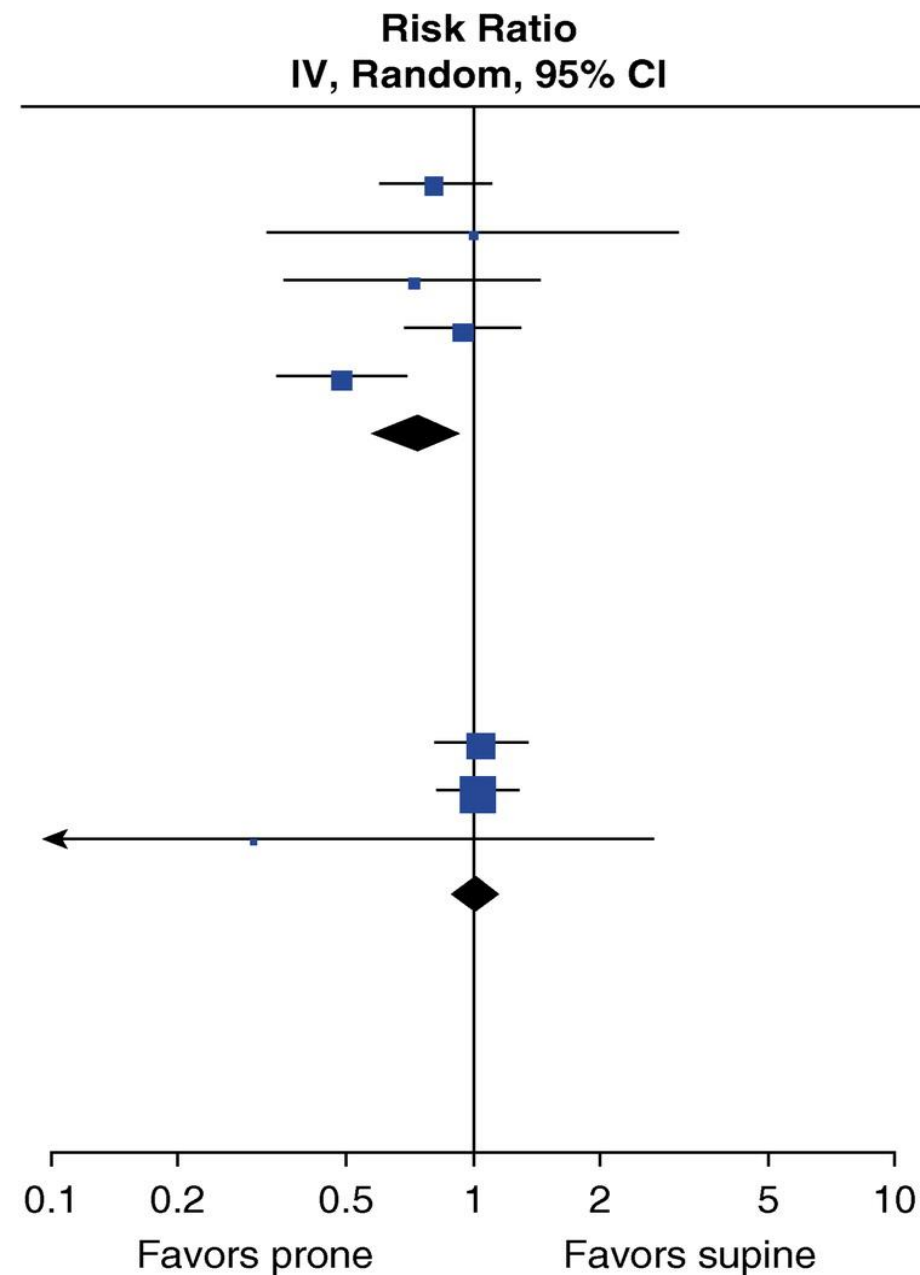
Study or Subgroup	Prone		Supine		Weight	Risk Ratio IV, Random, 95% CI
	Events	Total	Events	Total		
≥12h Prone						
Mancebo <i>et al.</i> 2006	38	76	37	60	28.5%	0.81 [0.60, 1.10]
Chan <i>et al.</i> 2007	4	11	4	11	5.7%	1.00 [0.33, 3.02]
Fernandez <i>et al.</i> 2008	8	21	10	19	12.0%	0.72 [0.36, 1.45]
Taccone <i>et al.</i> 2009	52	166	57	172	27.9%	0.95 [0.69, 1.29]
Guerin <i>et al.</i> 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 <i>et al.</i> 2001	70	152	67	152	40.0%	1.04 [0.82, 1.34]
Guerin <i>et al.</i> 2004	134	413	119	378	59.5%	1.03 [0.84, 1.26]
Voggenreiter <i>et al.</i> 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: $\chi^2 = 3.92$, $df = 1$ ($P = 0.05$), $I^2 = 74.5\%$



Awake prone positioning (APP)



ELSEVIER

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Journal of Critical Care

journal homepage: www.jccjournal.org



Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: A retrospective study ☆☆☆☆



Vittorio Scaravilli ^{a,*}, Giacomo Grasselli ^b, Luigi Castagna ^a, Alberto Zanella ^a, Stefano Isgrò ^b, Alberto Lucchini ^b, Nicolò Patroniti ^{a,b}, Giacomo Bellani ^{a,b}, Antonio Pesenti ^{a,b}

RESEARCH

Open Access

Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study



Lin Ding ^{1,2,3,4†}, Li Wang ^{1,2,3†}, Wanhong Ma ^{5†} and Hangyong He ^{1,2,3*} 



CORONAVIRUS
PANDEMIC

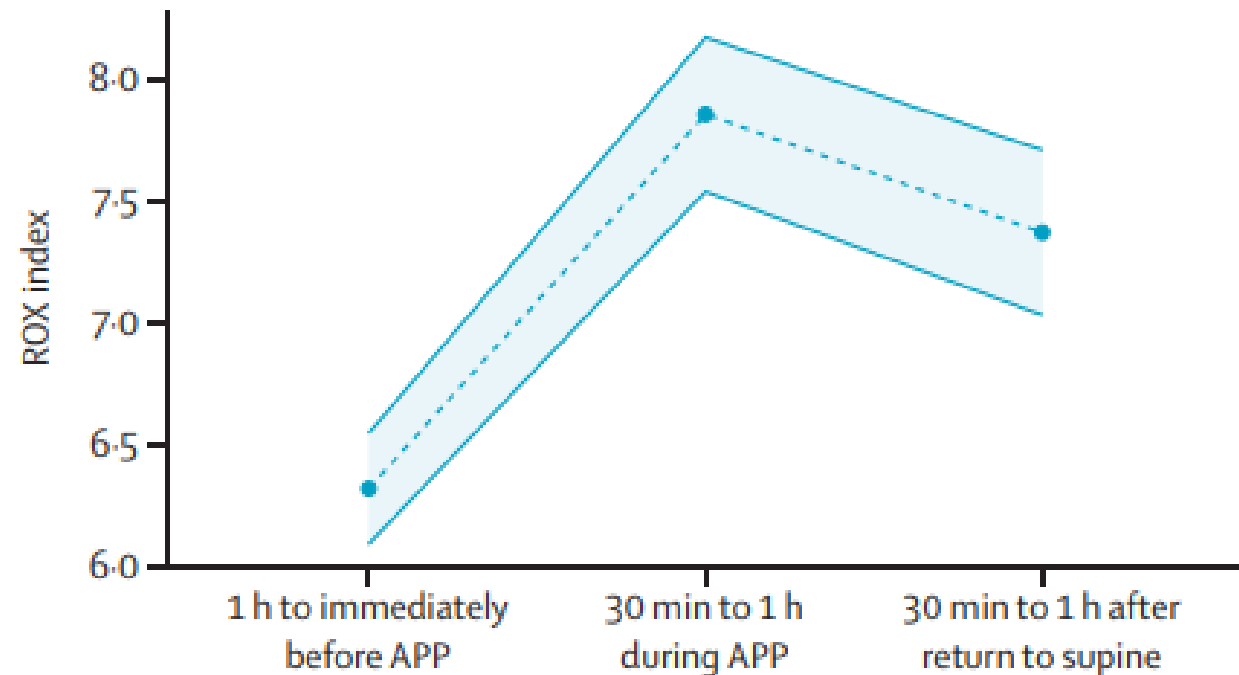
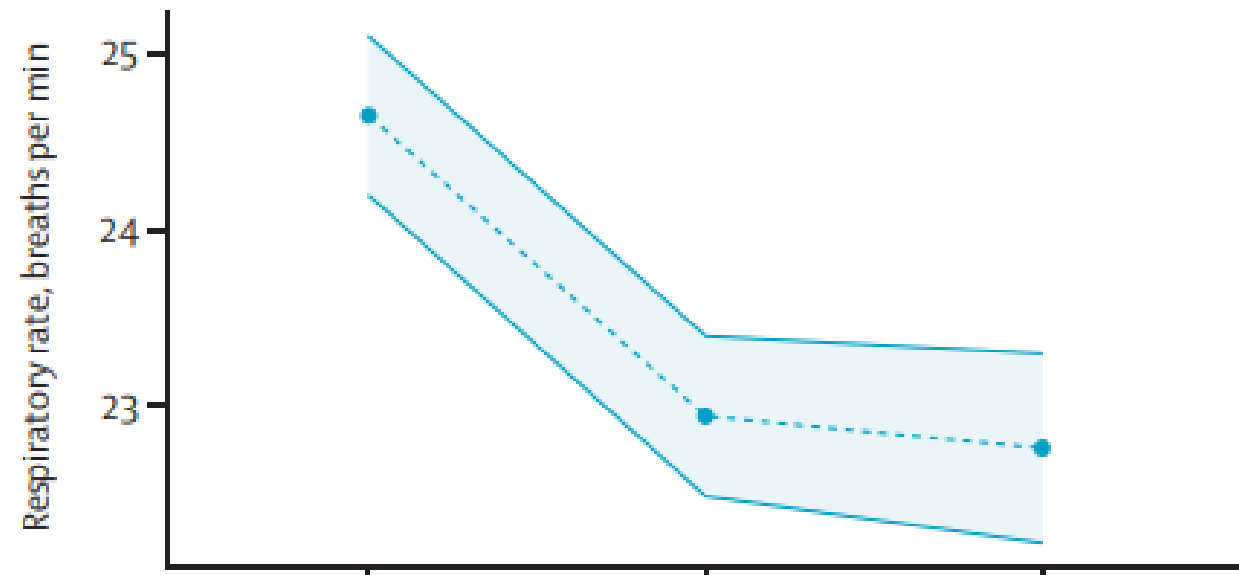
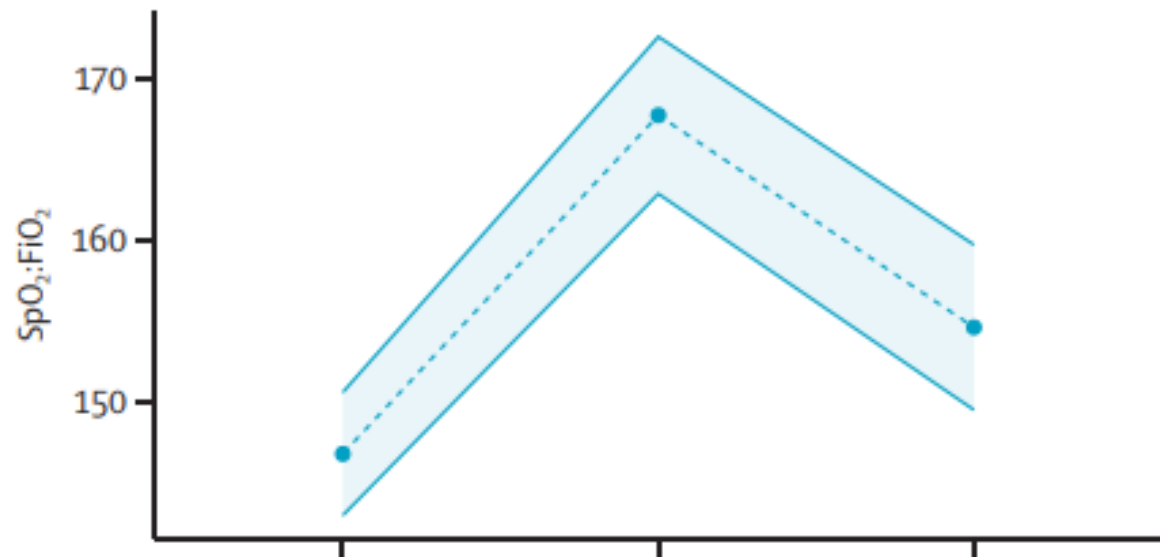


Safety of APP

- catheter dislodgement 2.5 % (37/1469)
- N/V 1.2%
- skin breakdown 0.7% (10/469)

Study	Reported Adverse Events	Awake proning Group no. (%)	Control Group no. (%)
Alhazzani 2022	Pain or discomfort	16 (8)	0 (0)
	Accidental removal of vascular access	1 (1)	0 (0)
	Desaturation	4 (2)	0 (0)
	Hypotension	1 (1)	0 (0)
	Nausea	1 (1)	0 (0)
	Other	3 (2)	0 (0)
Ehrmann 2021^a	Skin breakdown	8 (1)	10 (2)
	Vomiting	15 (3)	18 (3)
	Central or arterial line dislodgement	26 (5)	17 (3)
	Cardiac arrest	3 (1)	1 (0)
Fralick 2021	Aspiration pneumonia	2 (2)	1 (1)
	Venous thromboembolism	3 (2)	2 (2)
Rampon 2022	Positioning related discomfort	14 (9)	28 (21)
	Accidental removal of vascular access	9 (6)	12 (9)
	Accidental removal of urinary catheter	1 (0.6)	0 (0)
Harris 2022	Positioning related discomfort	0 (0)	1 (3)
Hashemian 2021	None reported	-	-
Jayakumar 2021	None reported	-	-
Johnson 2021	None reported	-	-
Kharat 2021	Positioning related discomfort	None reported	5 (50)
Qian 2022	None reported	-	-
Rosén 2021	Pressure sores	2 (6)	9 (23)
	Vomiting	1 (3)	0 (0)
	Central or arterial line dislodgement	0 (0)	0 (0)
	Cardiac arrest	2 (6)	1 (3)
Taylor 2021	Pressure sore	0 (0)	0 (0)
	Accidental removal of vascular access	1 (4)	0 (0)
	Emergent intubation outside of the ICU	0 (0)	0 (0)

Physiological effects of AAP



The efficacy of APP for clinical outcome

- Treatment failure
- Intubation
- Mortality

QUESTION Does prone positioning reduce endotracheal intubation in adults who were awake and not intubated and who had hypoxemic respiratory failure from COVID-19?

CONCLUSION Although the findings do not support prone positioning in this setting, the effect size for the primary study outcome was imprecise and does not exclude a clinically important benefit.

POPULATION

283 Men
117 Women



Adults hospitalized with COVID-19, but not intubated, who required $\geq 40\%$ oxygen or noninvasive ventilation

Mean age: 57.6 years

LOCATIONS

21 Hospitals
in Canada, Kuwait,
Saudi Arabia, and the US



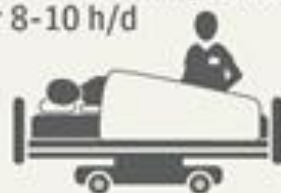
INTERVENTION

400 Patients randomized

205

Prone positioning

Usual care with awake prone positioning sessions for 8-10 h/d



195

Control treatment

Usual care without awake prone positioning



PRIMARY OUTCOME

Endotracheal intubation by day 30

FINDINGS

Patients receiving endotracheal intubation

Prone positioning

70 of 205 patients



34.1%

Control treatment

79 of 195 patients



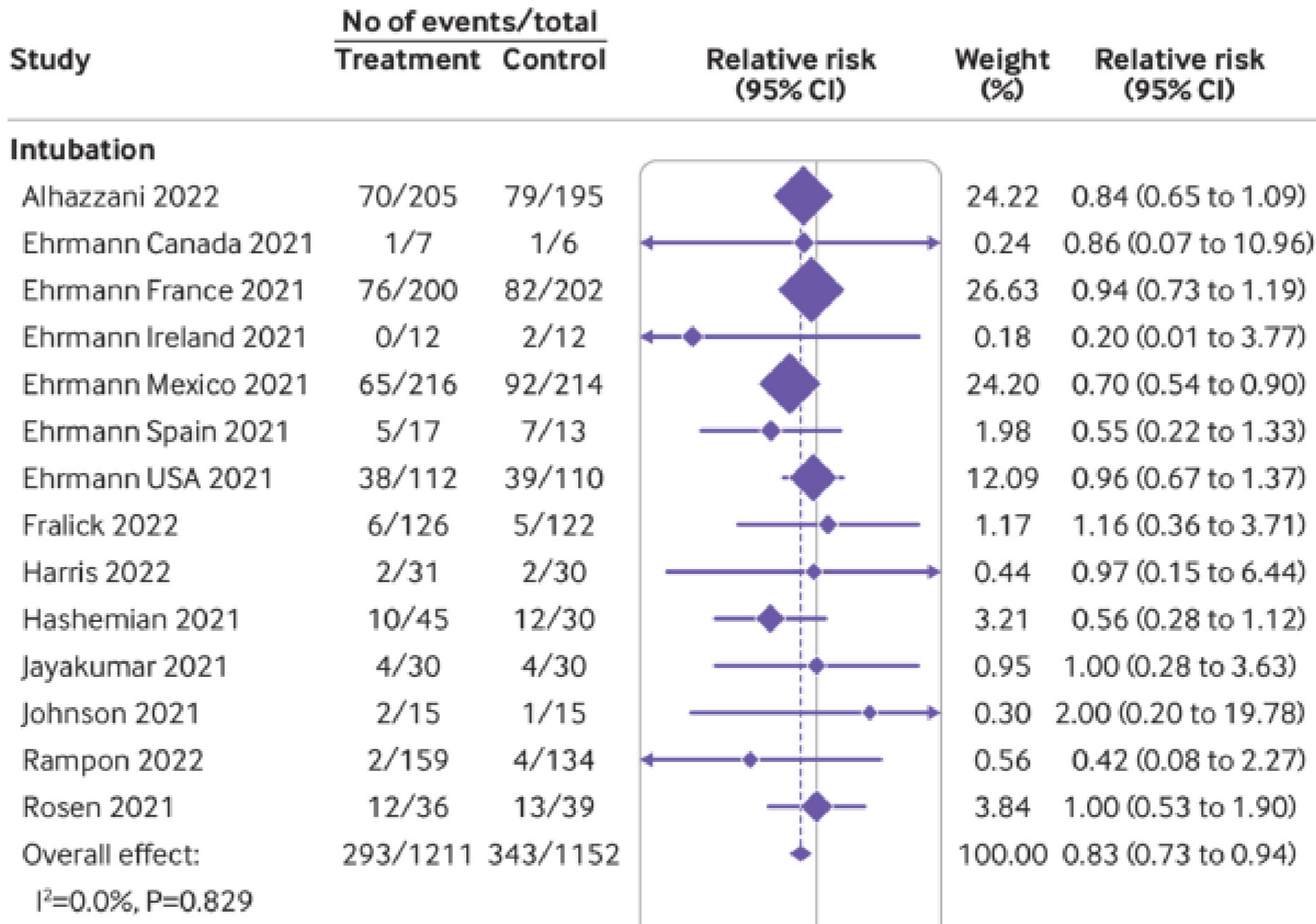
40.5%

Hazard ratio, **0.81**

(95% CI, 0.59 to 1.12); $P = .20$

Absolute difference, **-6.37%**

(95% CI, -15.83% to 3.10%)



Mortality

Alhazzani 2022	46/205	46/195		23.16	0.95 (0.67 to 1.36)
Ehrmann Canada 2021	2/7	2/6		1.12	0.86 (0.17 to 4.37)
Ehrmann France 2021	21/200	20/202		8.84	1.06 (0.59 to 1.90)
Ehrmann Mexico 2021	71/216	79/214		44.45	0.89 (0.69 to 1.15)
Ehrmann Spain 2021	2/17	1/13		0.57	1.53 (0.16 to 15.09)
Ehrmann USA 2021	21/112	30/110		12.32	0.69 (0.42 to 1.12)
Fralick 2022	1/126	1/122		0.39	0.97 (0.06 to 15.31)
Harris 2022	1/31	0/30		0.30	2.91 (0.12 to 68.66)
Hashemian 2021	9/45	10/30		4.98	0.60 (0.28 to 1.30)
Jayakumar 2021	3/30	2/30		1.01	1.50 (0.27 to 8.34)
Johnson 2021	2/15	0/15		0.34	5.00 (0.26 to 96.13)
Rampon 2022	2/159	2/134		0.79	0.84 (0.12 to 5.90)
Rosen 2021	6/36	3/39		1.74	2.17 (0.59 to 8.03)
Overall effect:	189/1199	196/1140		100.00	0.90 (0.76 to 1.07)

$I^2=0.0\%$, $P=0.873$

0.1 1 5
 Favours APP Favours control

What is matter?

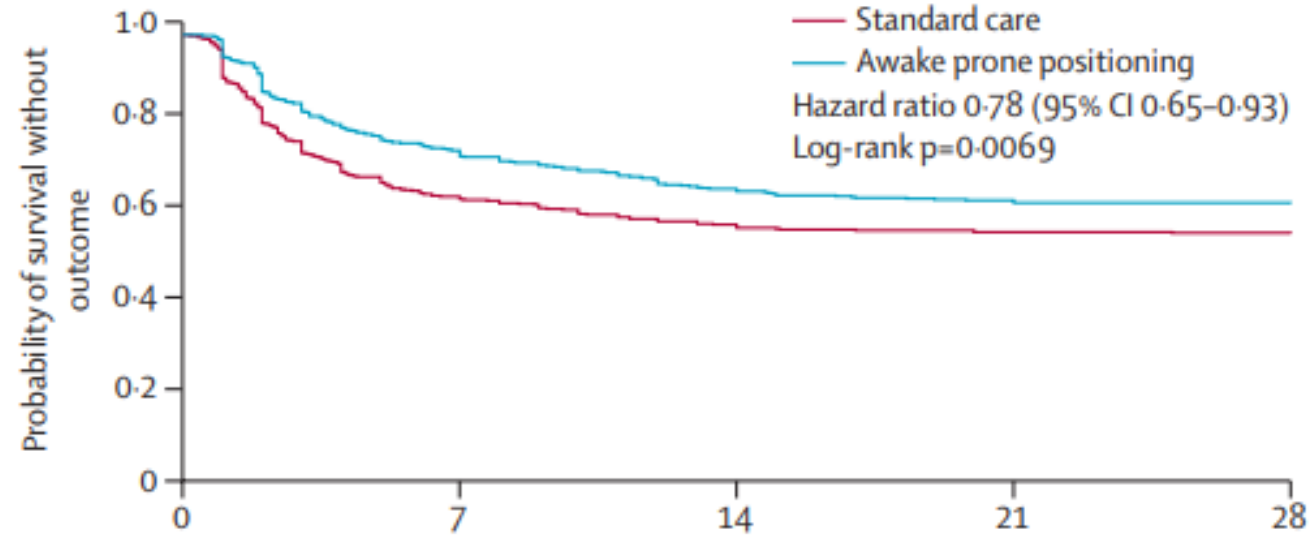
- Kind of respiratory support & disease severity
- Duration of APP

Influence of type of respiratory support

- Respiratory support through HFNC reduces work of breathing , homogenously increases the end-expiratory lung volume in PP and reduces dead space and PaCO₂
- The increased positive end-expiratory pressure and end-expiratory lung volume could be synergistic with APP and could theoretically reduce the risk of P-SILI

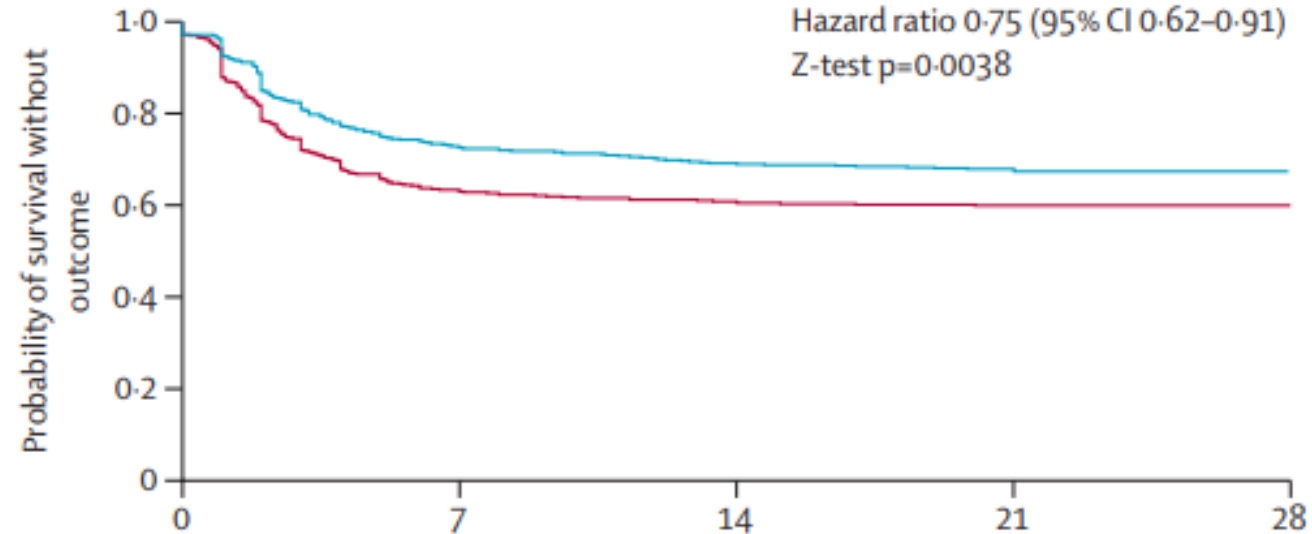
RCT in HFNC

A Treatment failure



	0	7	14	21	28
Number at risk					
(number censored)					
Standard care	557 (0)	345 (0)	310 (0)	299 (0)	298 (298)
Awake prone positioning	564 (0)	405 (0)	358 (0)	344 (0)	341 (341)

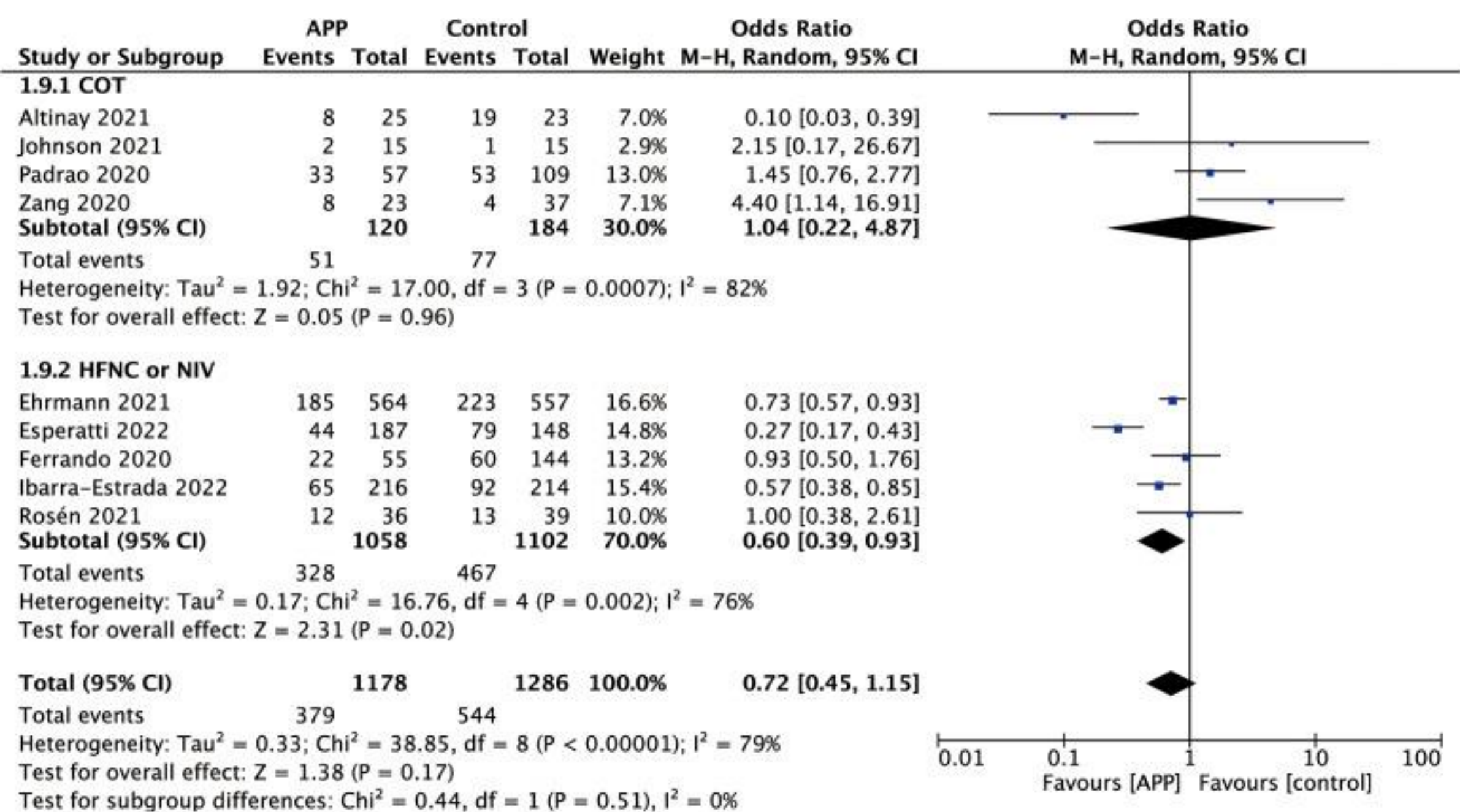
B Intubation



Subgroup analysis (only HFNC)

eTable 9. Subgroup analyses for endotracheal intubation outcome

Subgroup	Awake Prone Events/total	Control Events/total	Hazard Ratio (95% CI)	Absolute difference (95% CI)	P- Interaction	FDR%
Severity of hypoxia at baseline					0.03	12
SpO ₂ FiO ₂ >150	13/84 (15)	25/78 (32)	0.44 (0.23 to 0.87)	-16.58% (-29.50 to -3.65)		
SpO ₂ FiO ₂ ≤150	57/121 (47)	54/117 (46)	1.02 (0.70 to 1.48)	0.95% (-11.72 to 13.63)		
Respiratory Support at baseline					0.54	73
Low flow oxygen	14/45 (31)	10/43 (23)	1.35 (0.60 to 3.05)	7.86% (-10.65 to 26.36)		
High flow oxygen	49/148 (33)	65/132 (49)	0.61 (0.42 to 0.88)	-16.13% (-27.55 to -4.72)		
NIPPV	7/12 (58)	4/20 (20)	3.69 (1.07 to 12.70)	38.33% (5.39 to 71.28)		



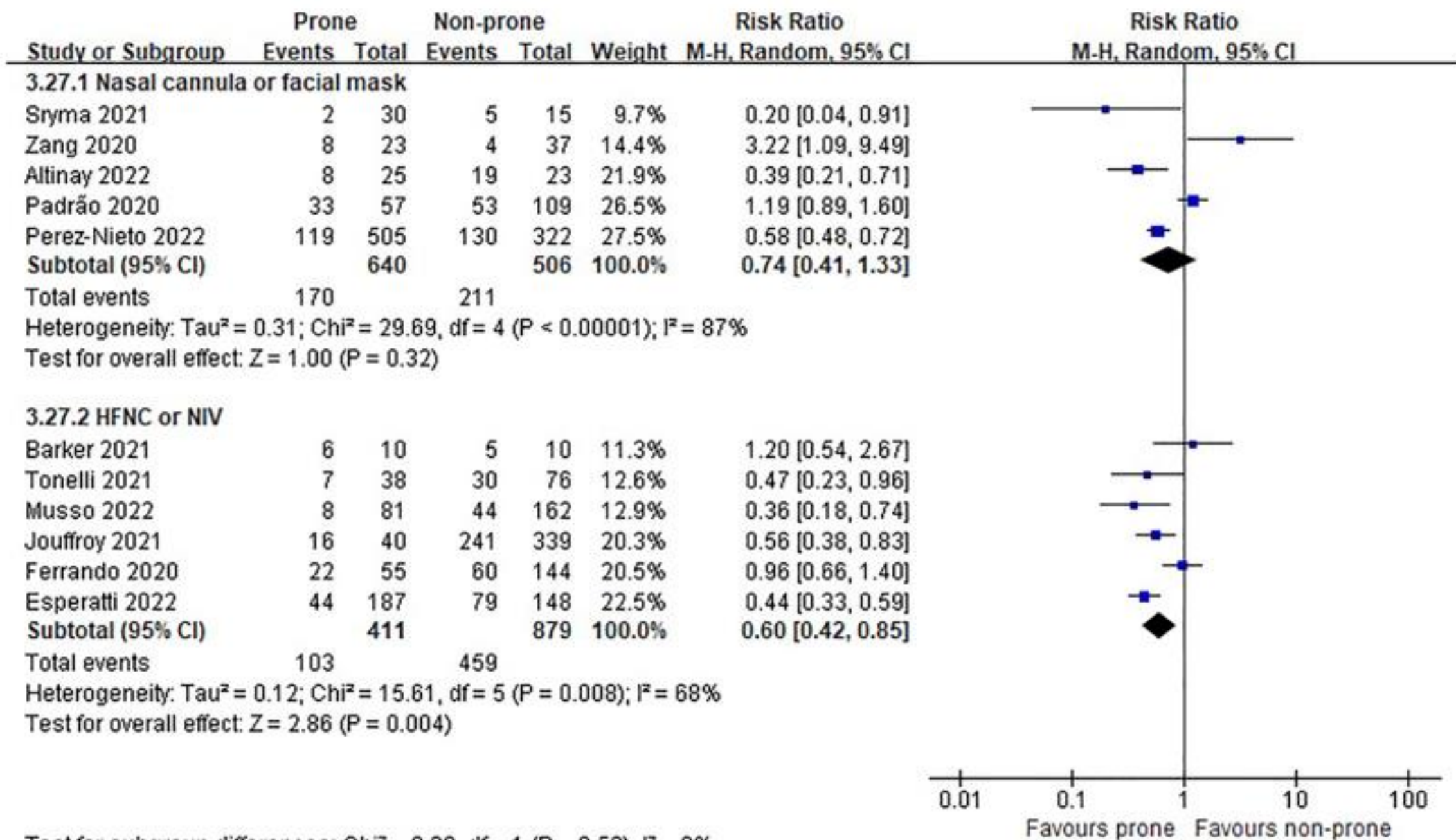


Fig. 7 Subgroup analysis of intubation rate by oxygen delivery methods in non-intubated patients of non-randomized studies

1.13.2 HFNC or NIV

Gad 2021	3	15	3	15	1.1%	1.00 [0.24, 4.18]
Rosén 2021	6	36	3	39	1.3%	2.17 [0.58, 8.03]
Alhazzani 2022	46	205	46	195	17.5%	0.95 [0.66, 1.36]
Ibarra-Estrada 2022	71	216	79	214	33.5%	0.89 [0.69, 1.15]
Ehrmann 2021	117	564	132	557	46.6%	0.88 [0.70, 1.09]
Subtotal (95% CI)		1036		1020	100.0%	0.91 [0.78, 1.05]

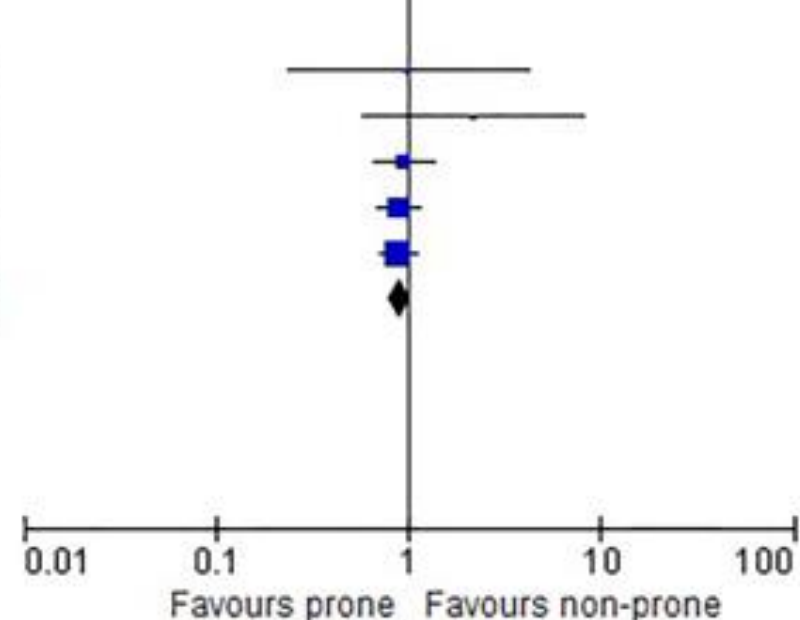
Total events

243

263

Heterogeneity: $\text{Tau}^2 = 0.00$; $\text{Chi}^2 = 1.91$, $\text{df} = 4$ ($P = 0.75$); $I^2 = 0\%$

Test for overall effect: $Z = 1.30$ ($P = 0.19$)



Test for subgroup differences: $\text{Chi}^2 = 0.26$, $\text{df} = 1$ ($P = 0.61$), $I^2 = 0\%$

3.22.2 HFNC or NIV

Barker 2021	1	10	4	10	3.8%	0.25 [0.03, 1.86]
Tonelli 2021	5	38	17	76	13.7%	0.59 [0.23, 1.47]
Jouffroy 2021	5	40	98	339	15.5%	0.43 [0.19, 1.00]
Ferrando 2020	8	49	17	122	17.1%	1.17 [0.54, 2.54]
Musso 2022	10	81	59	162	22.0%	0.34 [0.18, 0.63]
Esperatti 2022	21	187	47	148	27.9%	0.35 [0.22, 0.56]
Subtotal (95% CI)		405		857	100.0%	0.47 [0.31, 0.71]

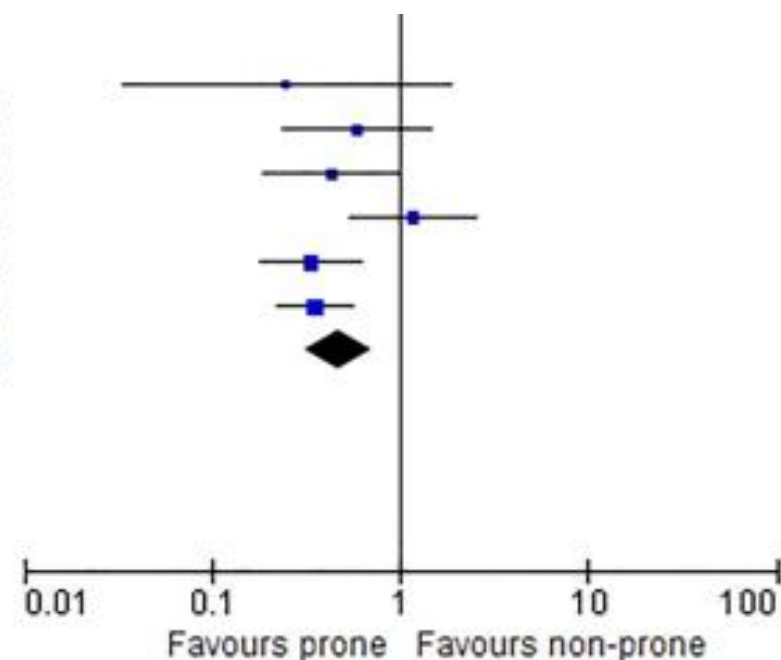
Total events

50

242

Heterogeneity: $\text{Tau}^2 = 0.10$; $\text{Chi}^2 = 8.42$, $\text{df} = 5$ ($P = 0.13$); $I^2 = 41\%$

Test for overall effect: $Z = 3.61$ ($P = 0.0003$)



Test for subgroup differences: $\text{Chi}^2 = 0.70$, $\text{df} = 1$ ($P = 0.40$), $I^2 = 0\%$

Fig. 4 Subgroup analysis of mortality by oxygen delivery methods in non-intubated patients of non-randomized studies

It's matter of time

- Duration of APP is important

Research

Prone positioning of patients with moderate hypoxaemia due to covid-19: multicentre pragmatic randomised trial (COVID-PRONE)

BMJ 2022 ; 376 doi: <https://doi.org/10.1136/bmj-2021-068585> (Published 23 March 2022)

Cite this as: *BMJ* 2022;376:e068585

	Prone (n=126)	Control (n=122)	Effect estimate (95% CI)
Primary outcome			
Composite of death, mechanical ventilation, and FiO ₂ >60	18 (14)	17 (14)	OR [*] : 0.92 (0.44 to 1.92)
Components of composite:			
Death	1 (1)	1 (1)	-
Mechanical ventilation	6 (5)	5 (4)	-
FiO ₂ >60%	18 (14)	17 (14)	-

Research | [Open Access](#) | [Published: 28 March 2022](#)

Factors for success of awake prone positioning in patients with COVID-19-induced acute hypoxemic respiratory failure: analysis of a randomized controlled trial

[Miguel Ibarra-Estrada](#) , [Jie Li](#), [Ivan Pavlov](#), [Yonatan Perez](#), [Oriol Roca](#), [Elsa Tavernier](#), [Bairbre McNicholas](#),

- 216 APP vs 214 usual care
- intubation rate (30% vs 43%, relative risk [RR] 0.7, $P = 0.006$)
- Mean duration 9.4 (5.6-12.9) hr/day, 4 sessions

duration of APP

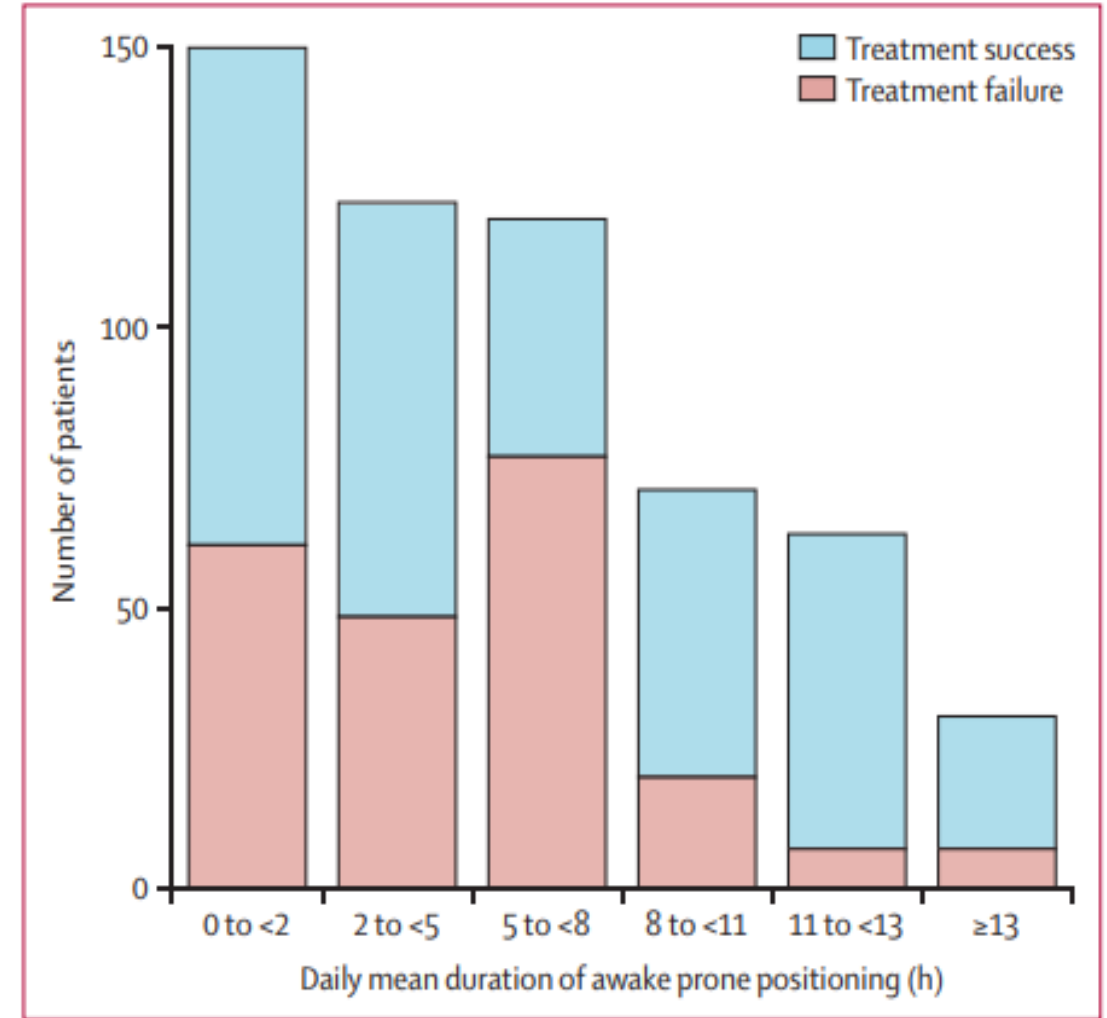
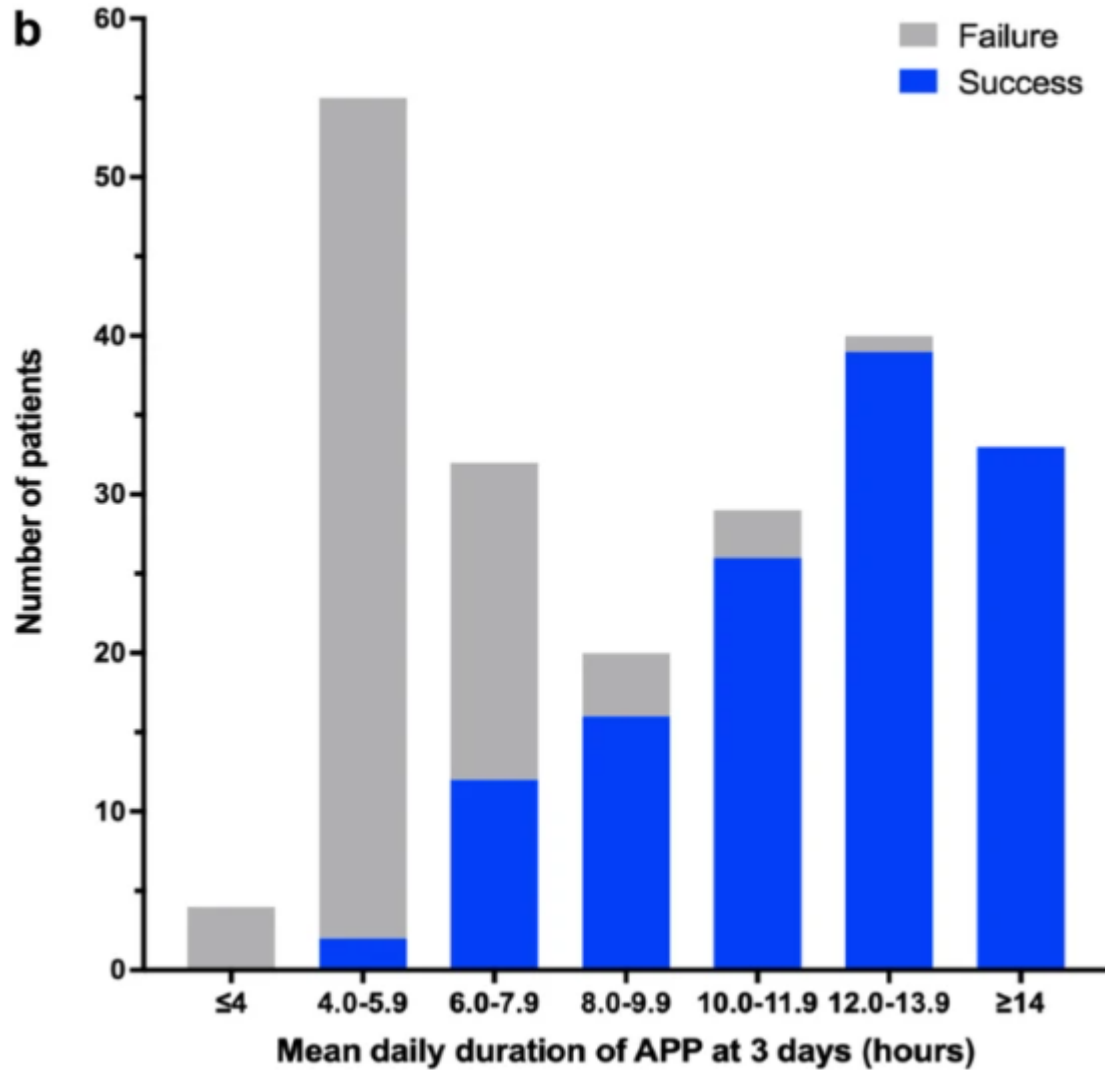
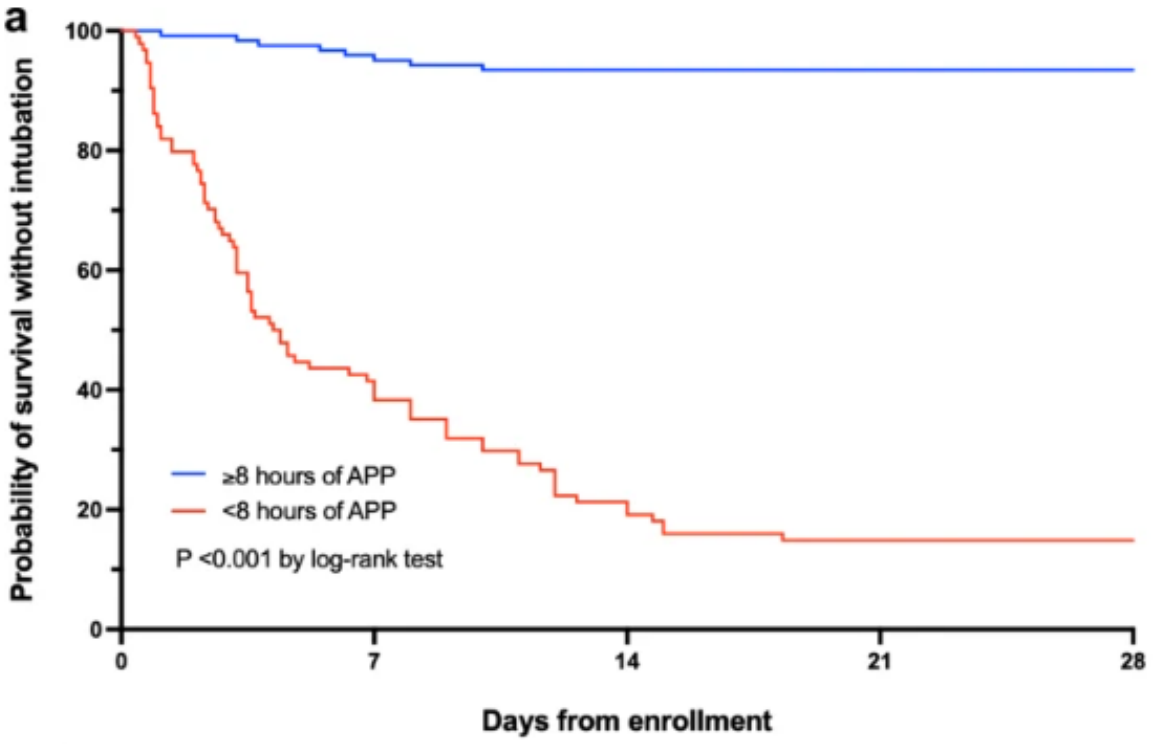


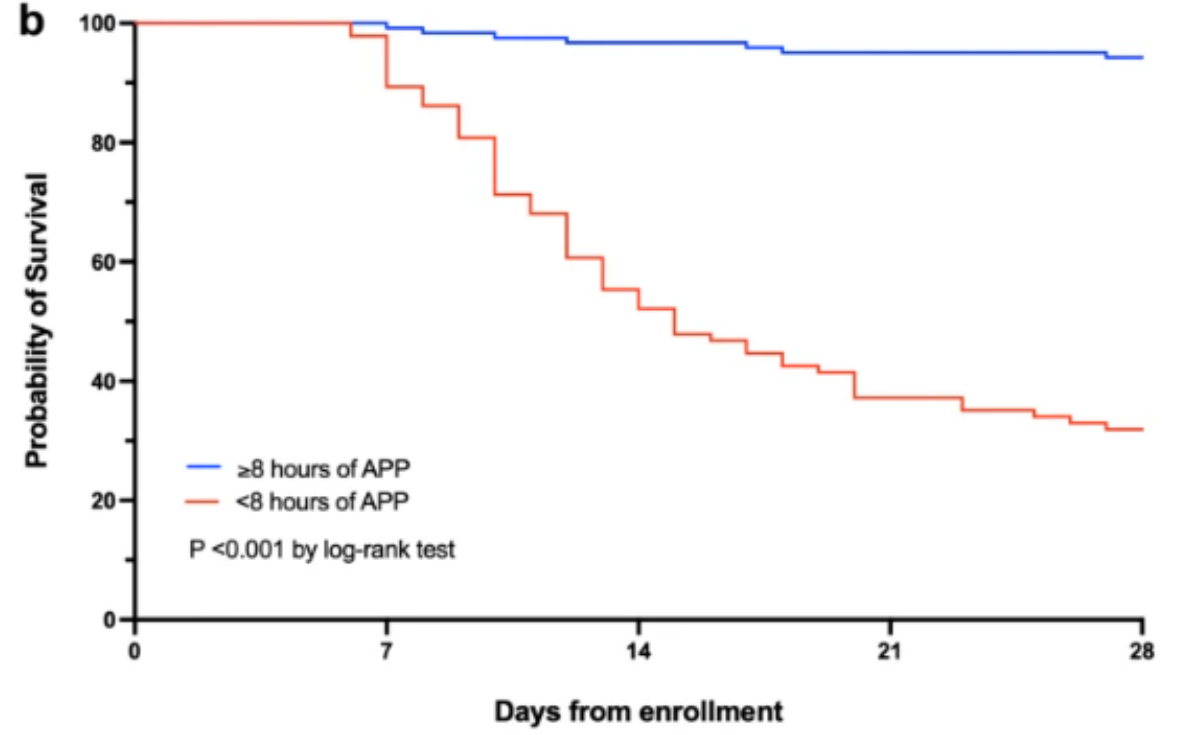
Figure 4: Daily mean duration of prone positioning and outcomes in patients allocated to awake prone positioning

Fig. 5



Number at risk:

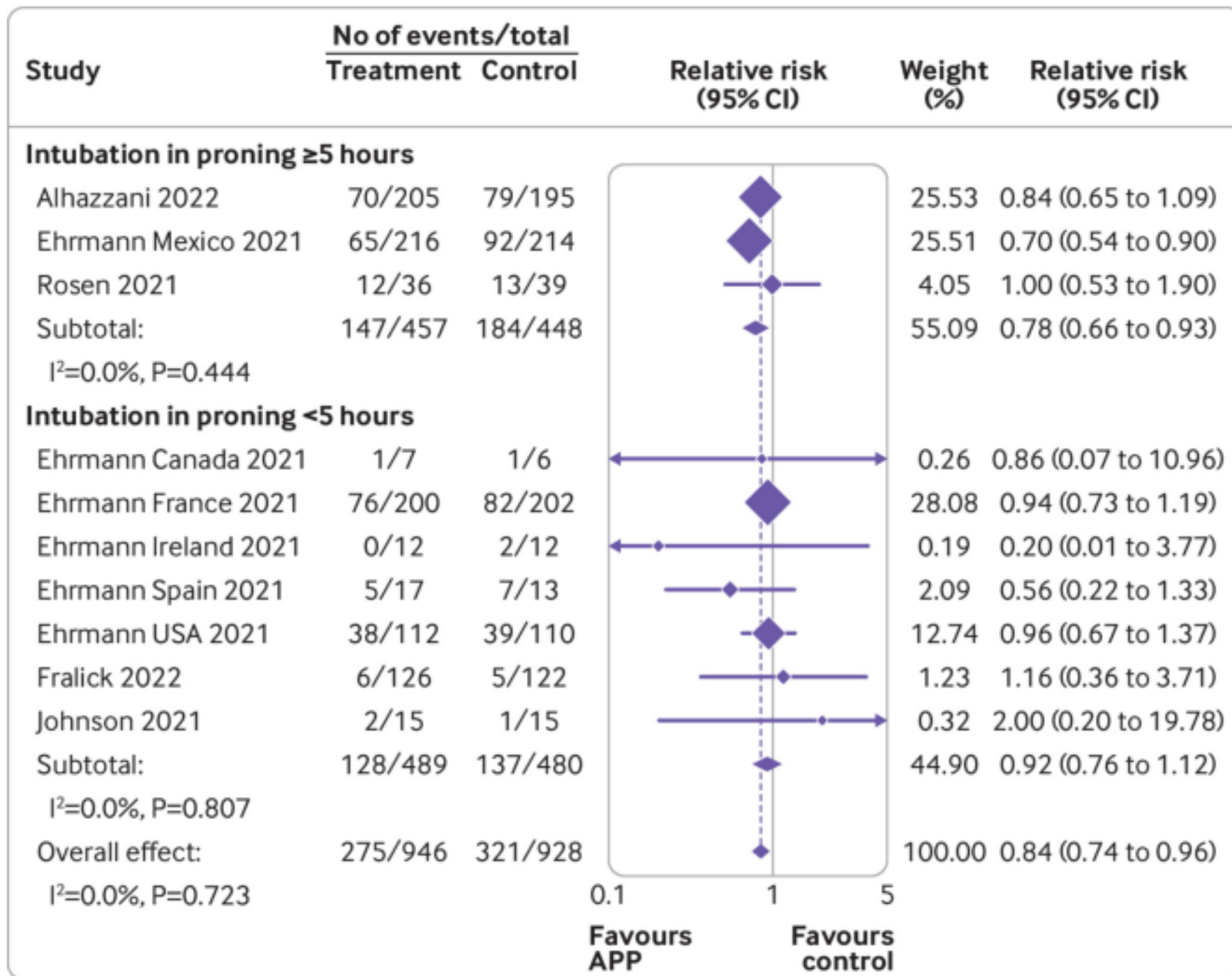
Days from enrollment	≥ 8 hours	< 8 hours
0	122	94
7	116	36
14	114	18
21	114	14
28	114	14

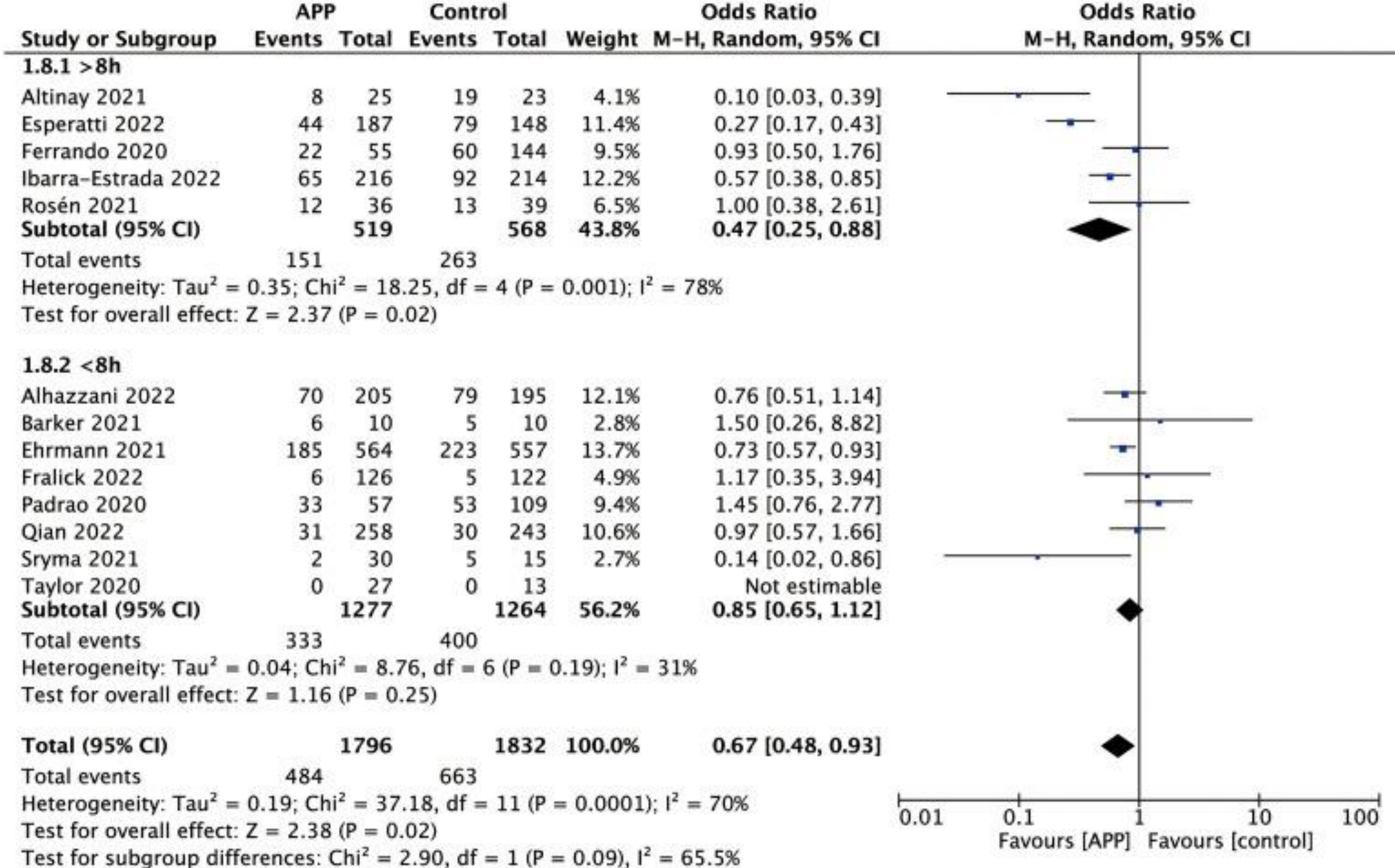


Number at risk:

Days from enrollment	≥ 8 hours	< 8 hours
0	122	94
7	121	84
14	118	49
21	116	35
28	115	30

Kaplan–Meier plots of the cumulative incidence of treatment success (a) and death (b) (APP, awake prone positioning)





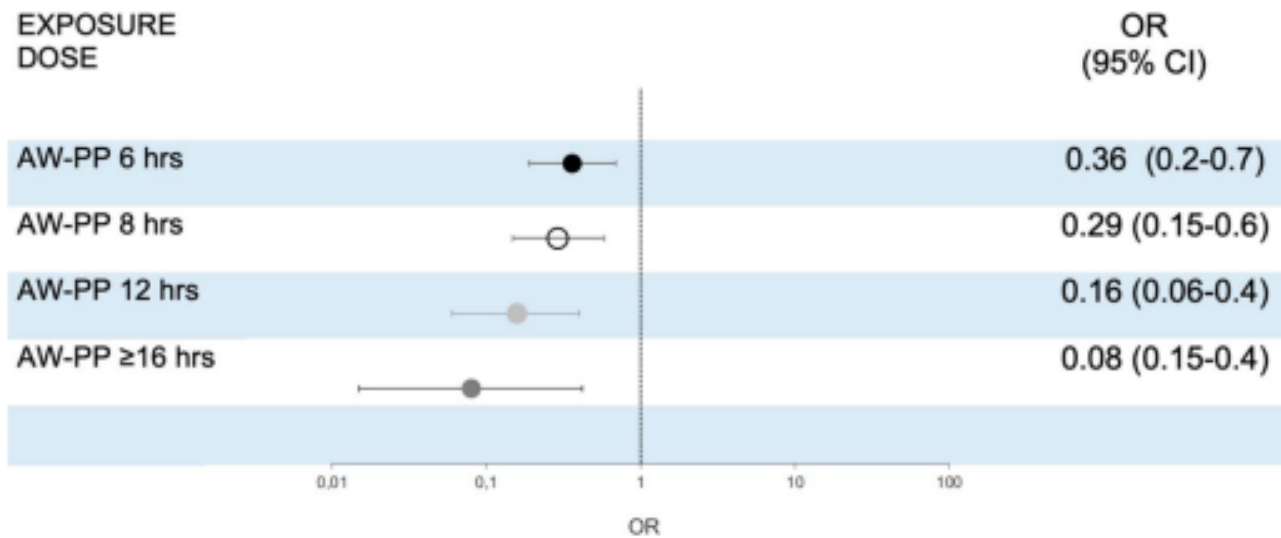


Fig. 2 Risk of intubation between groups in awake prone position and non-prone position. OR indicates odds ratio; 95% CI indicates confidence interval. Non-awake prone positioning group (supine or lateral) as reference. Abbreviations. AW-PP: awake prone positioning. Weighted population and adjusted by center and pandemic time

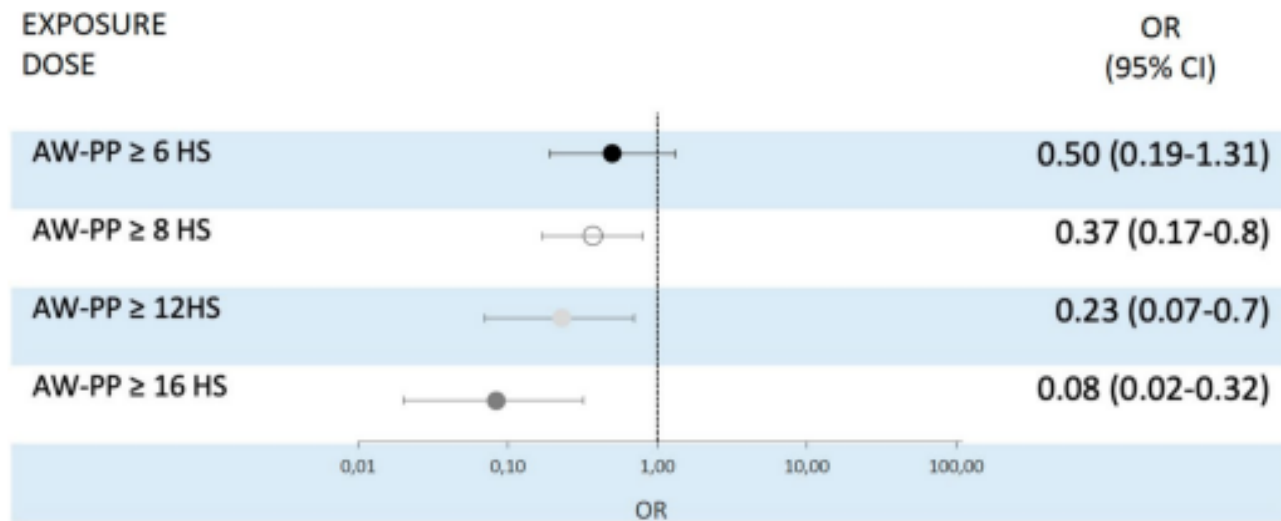
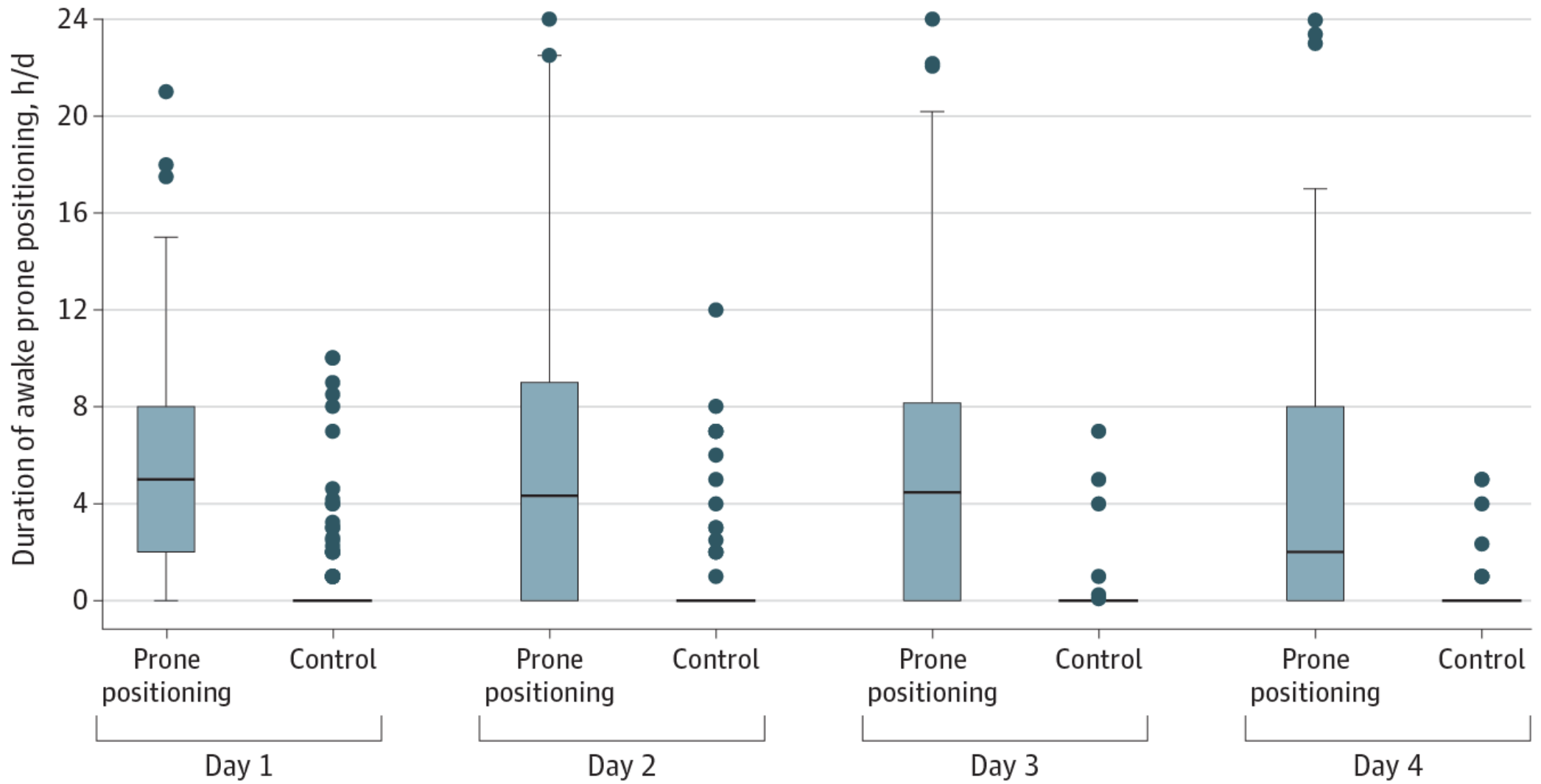


Fig. 3 Risk of hospital mortality between groups in the awake prone position versus non-prone position. OR indicates odds ratio; 95% CI indicates confidence interval. Non-prone positioning group (supine or lateral) as reference. Abbreviations. AW-PP: awake prone positioning. Weighted population and adjusted by center and pandemic time



No. of participants
 Prone positioning
 Control

205
 195

193
 160

160
 137

145
 105

TABLE 2] Summary of Major Trials of APP in Respiratory Failure

Variable	Ehrmann et al ⁴⁰ (2021)	Jayakumar et al ⁴³ (2021)	Rosen ⁴⁷ (2021)	Qian et al ⁴⁵ (2022)	Fralick et al ⁴⁶ (2022)	Rampon et al ⁴⁴ (2022)	Alhazzani et al ⁴² (2022)
No. of patients	1,121	60	75	501	248	293	400
Enrollment location	ICU, intermediate care, general ward	ICU	ICU, general ward	ICU, intermediate care, general ward	General ward	General ward	ICU, monitored acute care unit
Average time prone, h/d	5.0	Averages not reported ^a	3.4 (usual care), 9.0 (APP)	4.2	0.0 (usual care), 2.5 (APP)	Averages not reported ^b	5.0
Baseline Pao ₂ to Fio ₂ ratio	117.3 (usual care) 119.3 (APP)	185 (usual care) 201 (APP)	115.5	Unavailable	293 ^c	396	134 ^c
Primary outcome	Treatment failure, defined as intubation or death	Protocol adherence	Intubation within 30 d	Highest level of oxygen support on day 5	Composite of respiratory deterioration, mechanical ventilation, and death	Composite of respiratory deterioration and transfer to an ICU	Endotracheal intubation within 30 d
Key secondary outcomes	Intubation, mortality, use of NIV, length of hospital stay, others	Escalation of respiratory support, ICU mortality, length of ICU stay	Mortality, clinical improvement at 7 and 30 d, ventilator-free days, length of ICU stay	Daily oxygen support device and maximum Fio ₂	Respiratory deterioration, mechanical ventilation, death, time in prone position, improved oxygenation	Time spent in prone position, subjective dyspnea, mortality, hospital length of stay, development of ARDS	Mortality at 60 d, ventilator-free days, ICU-free days, hospital-free days
Results	Treatment failure occurred in 223 patients (40%) in prone group and 257 patients (46%) in usual care group (<i>P</i> = .02)	43% of patients were able to prone > 6 h/d; no difference in secondary outcomes between groups	No difference in rates of primary or secondary outcomes	No difference in rates of intubation or mortality	No difference in primary or secondary outcomes; low rates of self-prone positioning	No difference in primary or secondary outcomes; low rates of self-prone positioning	No difference in primary or secondary outcomes

APP = awake prone positioning; NIV = noninvasive ventilation.

Limitation and unsolved problem of APP

- Insufficient patients cooperation, tolerance
- Variable and short duration of position time
- Usually below 5 hours per day

- 24/7 on-site clinician & team assist & encourage by Estrada in Mexico

- optimal means of maintaining awake prone positioning ?

Summary

- Reduce intubation rate
- Time (duration) is matter