

THE LANCET

Respiratory Medicine

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Tran A, Fernando SM, Rochweg B, et al. Prognostic factors associated with mortality among patients receiving venovenous extracorporeal membrane oxygenation for COVID-19: a systematic review and meta-analysis. *Lancet Respir Med* 2022; published online Oct 10. [https://doi.org/10.1016/S2213-2600\(22\)00296-X](https://doi.org/10.1016/S2213-2600(22)00296-X).

Title: Prognostic Factors Associated with Mortality among Patients Receiving Venovenous Extracorporeal Membrane Oxygenation for COVID-19 – A Systematic Review and Meta-Analysis

Electronic Search Strategies (April 14th, 2022)

MEDLINE

1. Exp SARS-CoV-2
2. SARS-CoV-2.ti
3. Exp COVID-19
4. COVID-19.ti
5. Exp Coronavirus
6. Coronavirus.ti
7. Exp Extracorporeal membrane oxygenation
8. Extracorporeal membrane oxygenation.ti
9. Exp Extracorporeal life support
10. Extracorporeal life support.ti
11. ECMO.mp
12. ECMO.ti
13. (predict* or model* or utility* or scor* or validat* or risk* or prognos* or associat* or factor* or outcome* or mortality or survival).tw
14. Or/1-6
15. Or/7-12
16. And/13-15

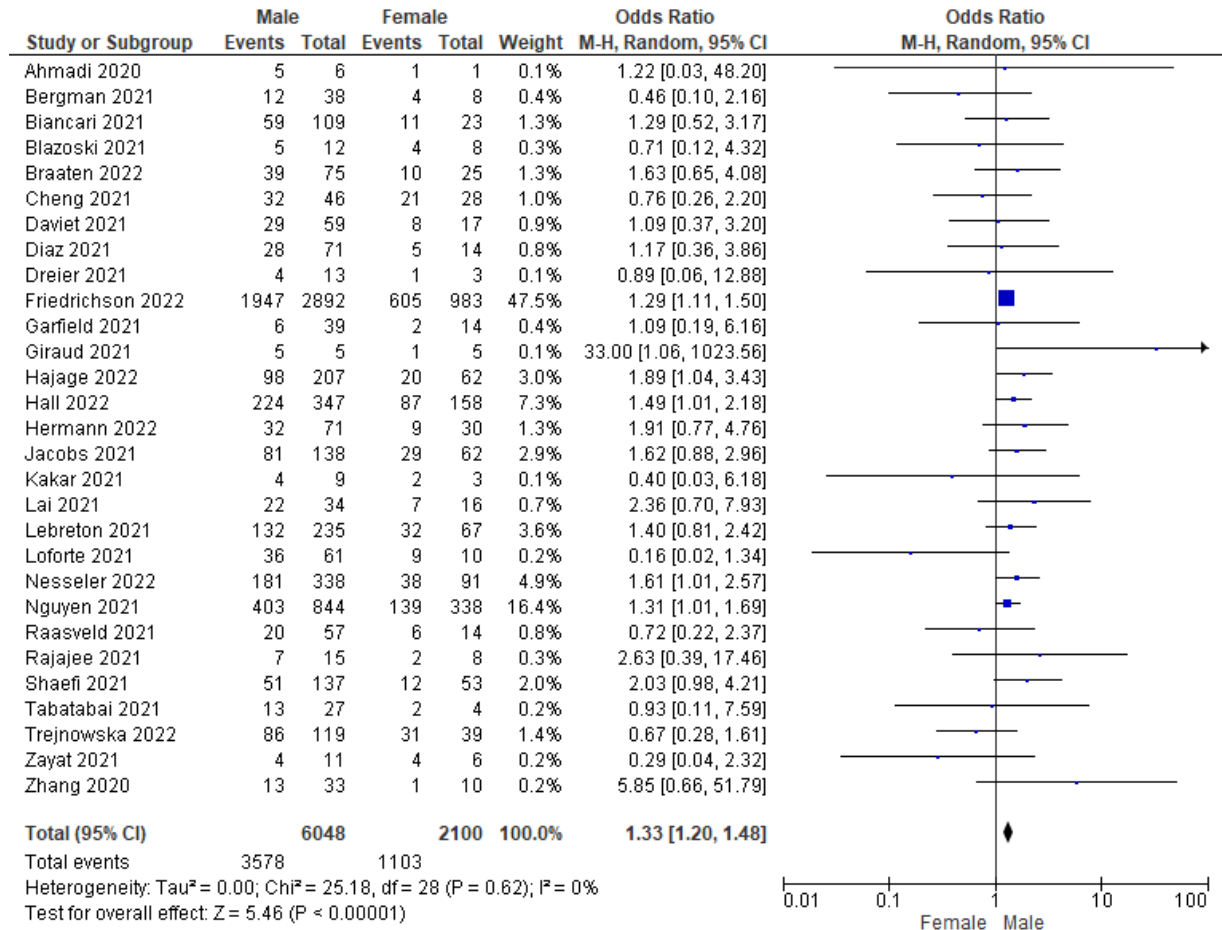
EMBASE

1. Exp SARS-CoV-2
2. SARS-CoV-2.ti
3. Exp COVID-19
4. COVID-19.tiri
5. Exp Coronavirus
6. Coronavirus.ti
7. Exp Extracorporeal membrane oxygenation
8. Extracorporeal membrane oxygenation.ti
9. Exp Extracorporeal life support
10. Extracorporeal life support.ti
11. ECMO.mp
12. ECMO.ti
13. (predict* or model* or utility* or scor* or validat* or risk* or prognos* or associat* or factor* or outcome* or mortality or survival).tw
14. Or/1-6
15. Or/7-12
16. And/13-15

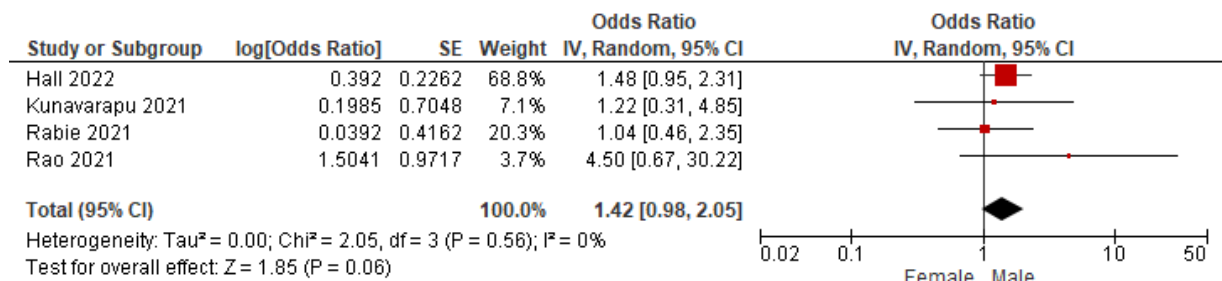
Supplemental Figure 1: Association with Mortality for COVID-19 Patients Requiring VV-ECMO

Patient Factors (Male vs Female Sex)

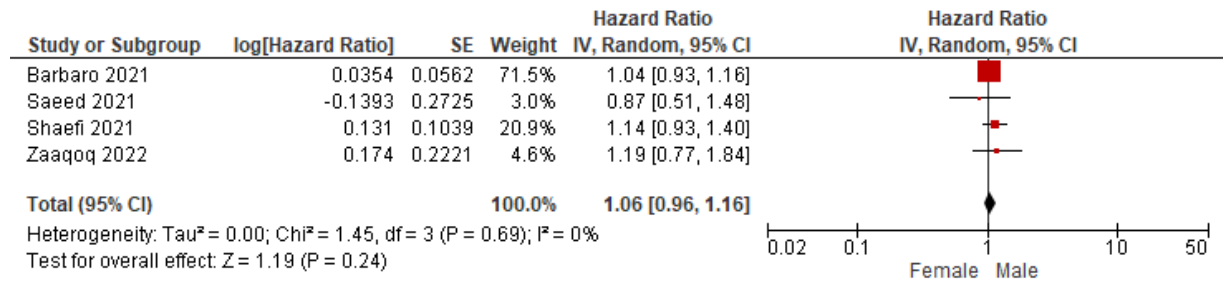
Male vs Female (Unadjusted Odds Ratio)



Male vs Female (Adjusted Odds Ratio)

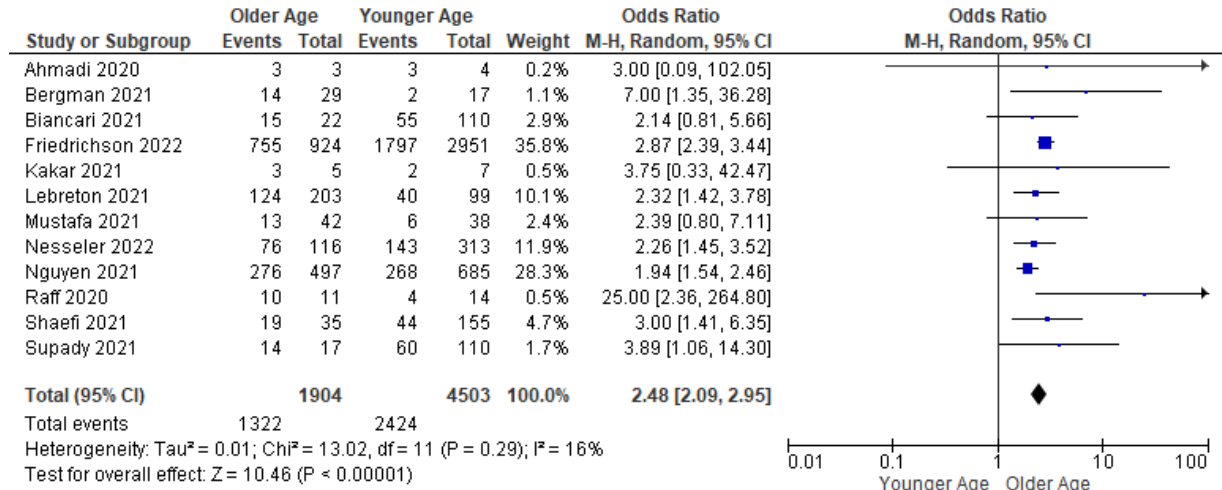


Male vs Female (Adjusted Hazard Ratio)

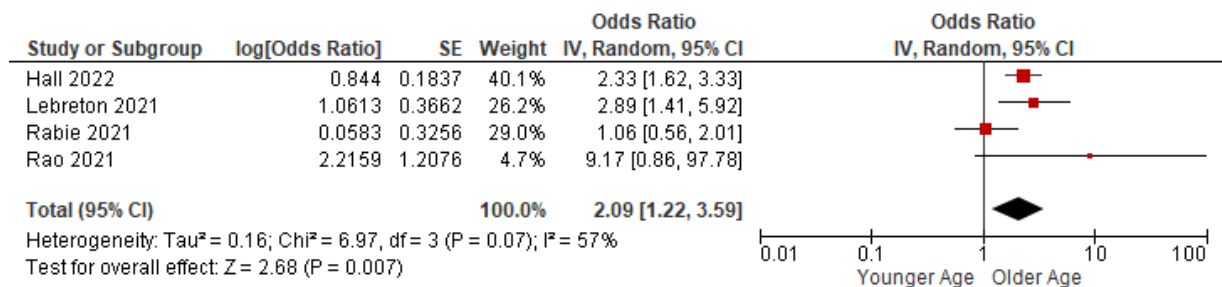


Patient Factors (Older vs Younger Age)

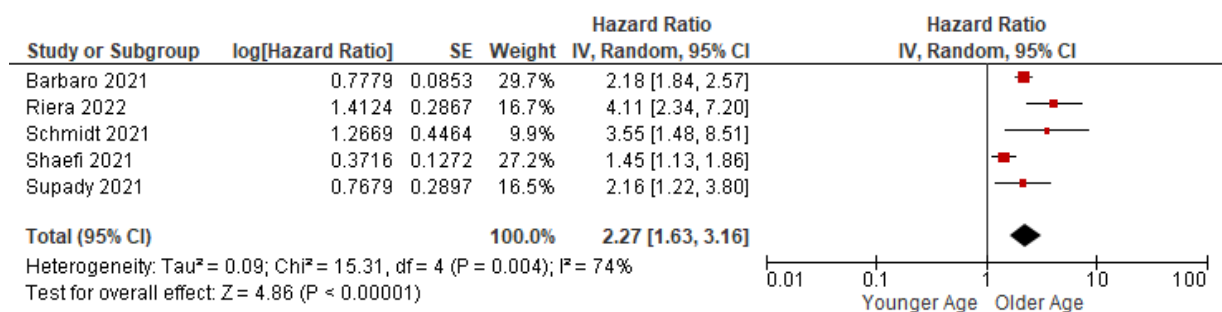
Older Age vs Younger Age (Unadjusted Odds Ratio)



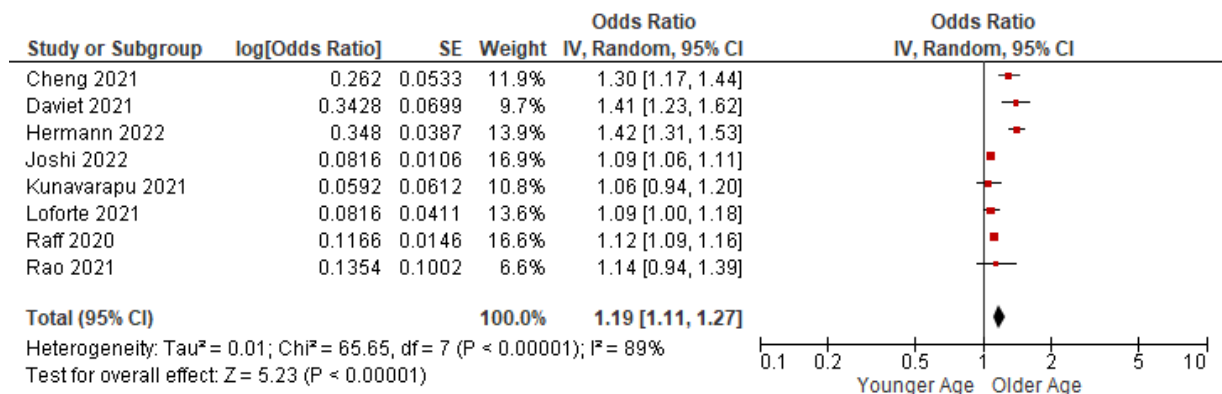
Older Age vs Younger Age (Adjusted Odds Ratio)



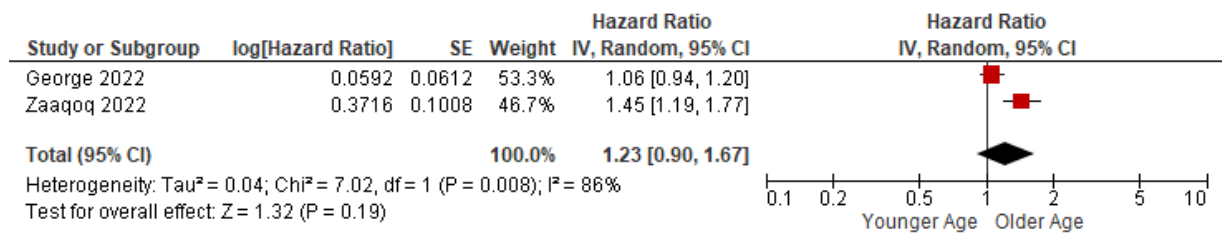
Older Age vs Younger Age (Hazard Odds Ratio)



Older Age vs Younger Age (Per 10 Year Increase, Adjusted Odds Ratio)

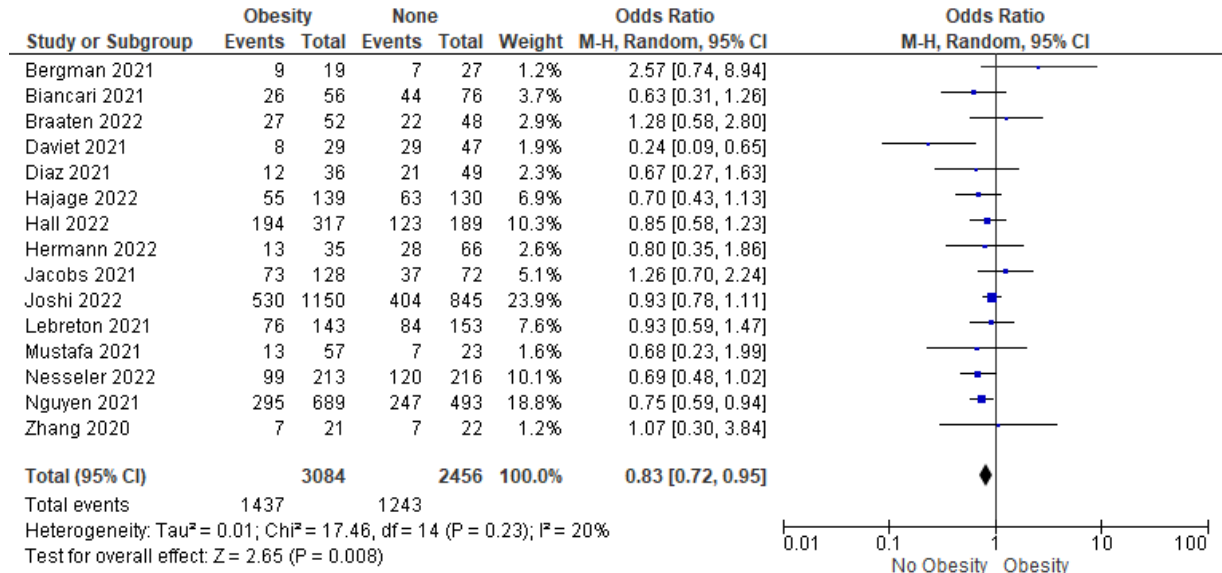


Older Age vs Younger Age (Per 10 Year Increase, Adjusted Hazard Ratio)

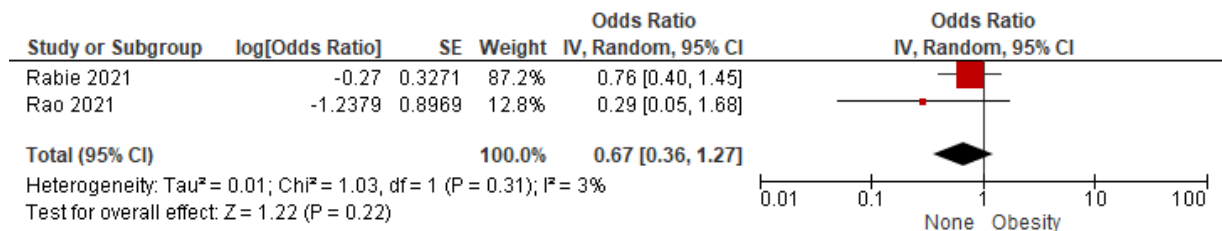


Patient Factors (Obesity vs None)

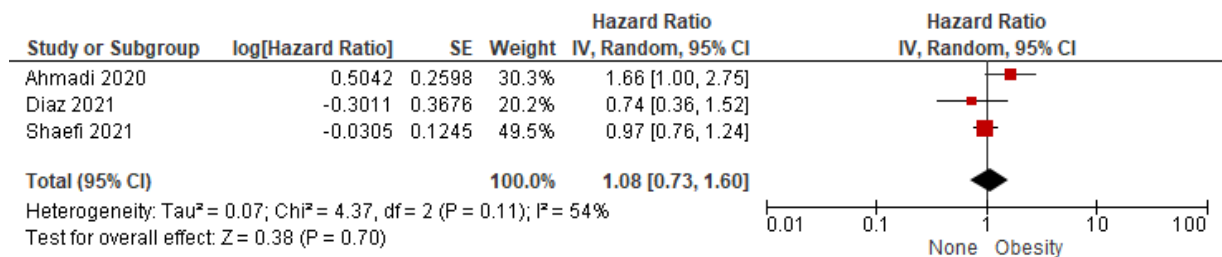
Obesity vs None (Unadjusted Odds Ratio)



Obesity vs None (Adjusted Odds Ratio)

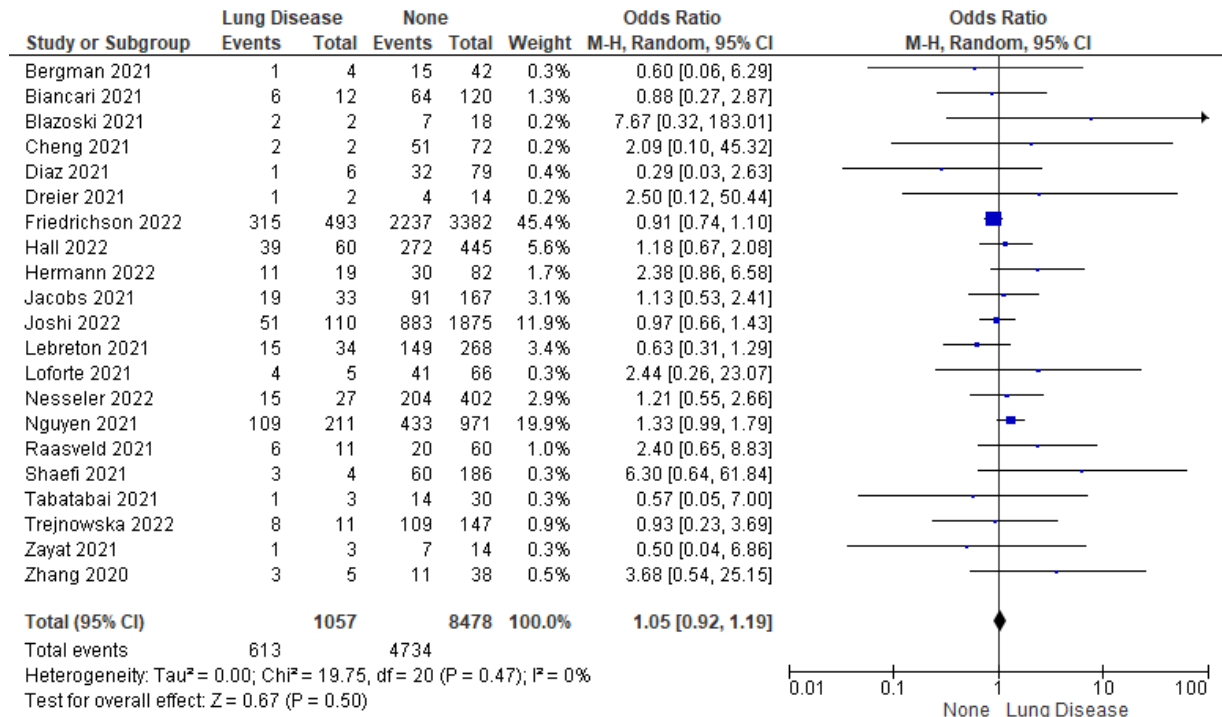


Obesity vs None (Adjusted Hazard Ratio)

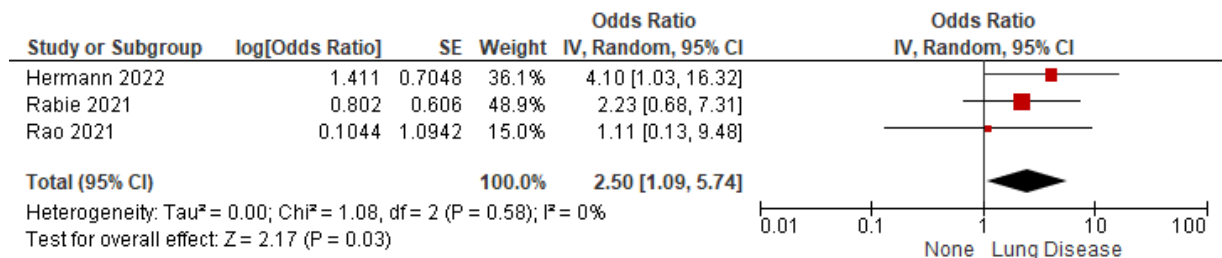


Patient Factors (Chronic Lung Disease vs None)

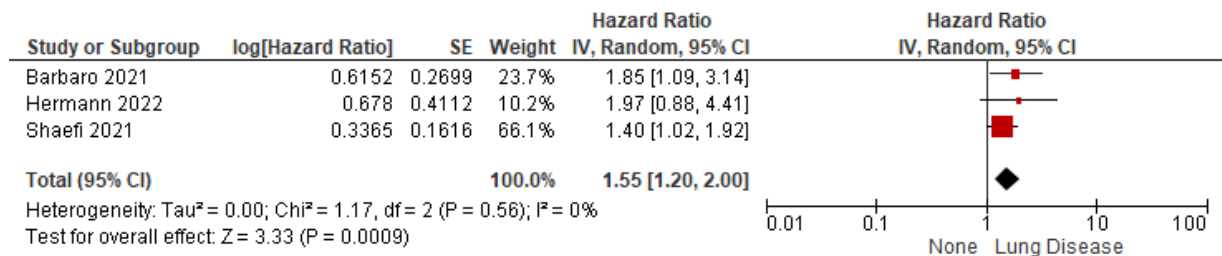
Chronic Lung Disease vs None (Unadjusted Odds Ratio)



Chronic Lung Disease vs None (Adjusted Odds Ratio)

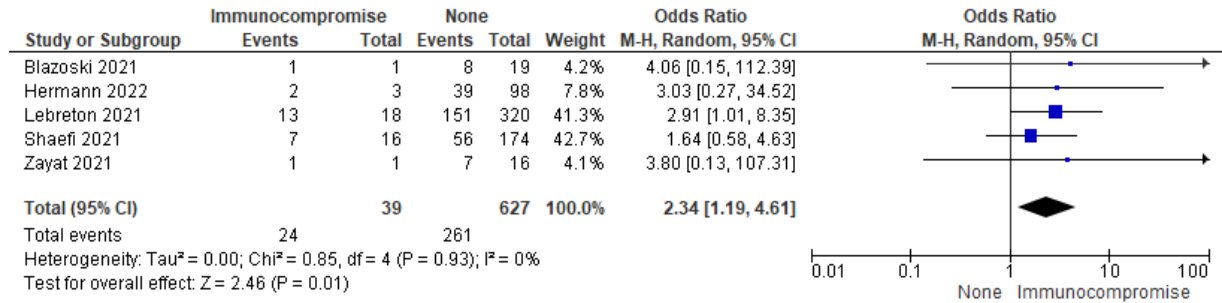


Chronic Lung Disease vs None (Adjusted Hazard Ratio)



Patient Factors (Immunocompromise vs None)

Immunocompromise vs None (Unadjusted Odds Ratio)



Immunocompromise vs None (Adjusted Odds Ratio)

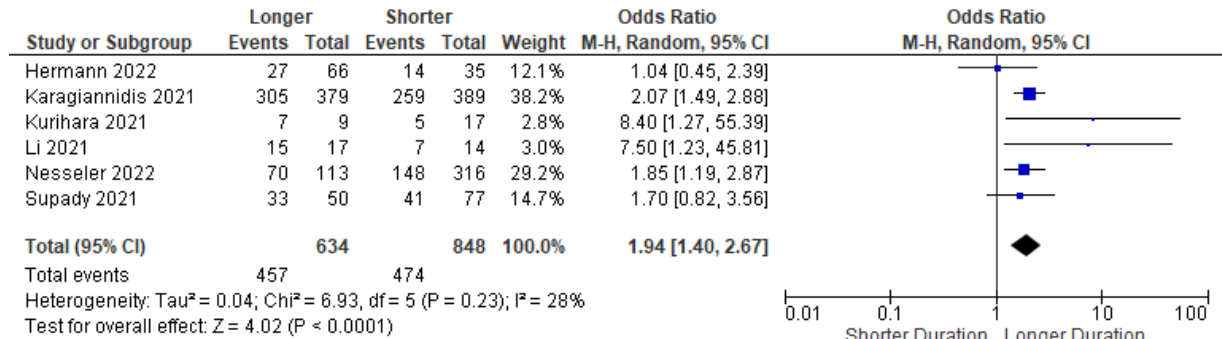
Joshi 2022 – 4.35 (2.46 to 7.69)

Immunocompromise vs None (Adjusted Hazard Ratio)

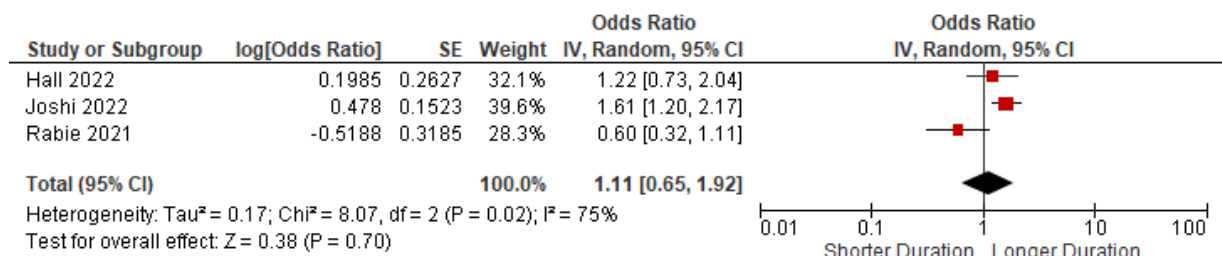
Barbaro 2021 – 1.06 (0.83 to 1.35)

Disease Factors (Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation)

Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation (Unadjusted Odds Ratio)



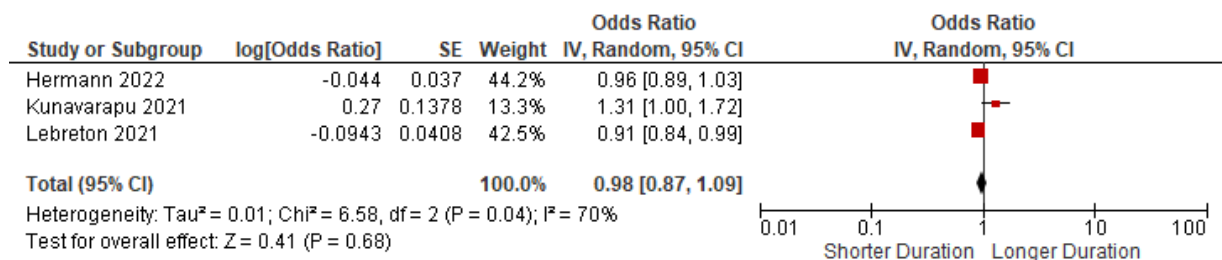
Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation (Adjusted Odds Ratio)



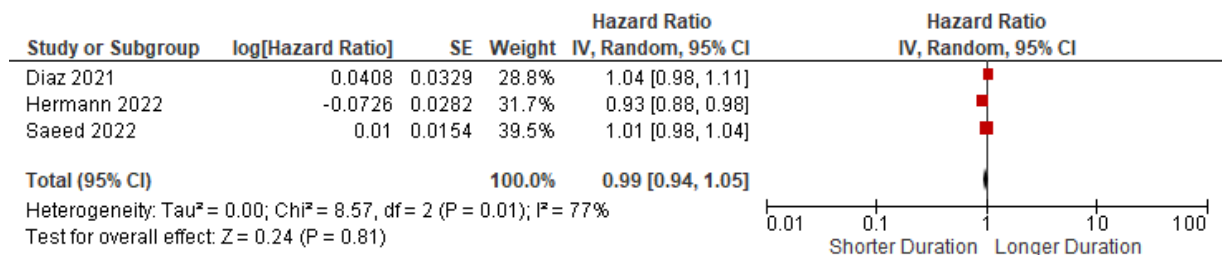
Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation (Adjusted Hazard Ratio)

Supady 2021 – 1.66 (1.00 to 2.75)

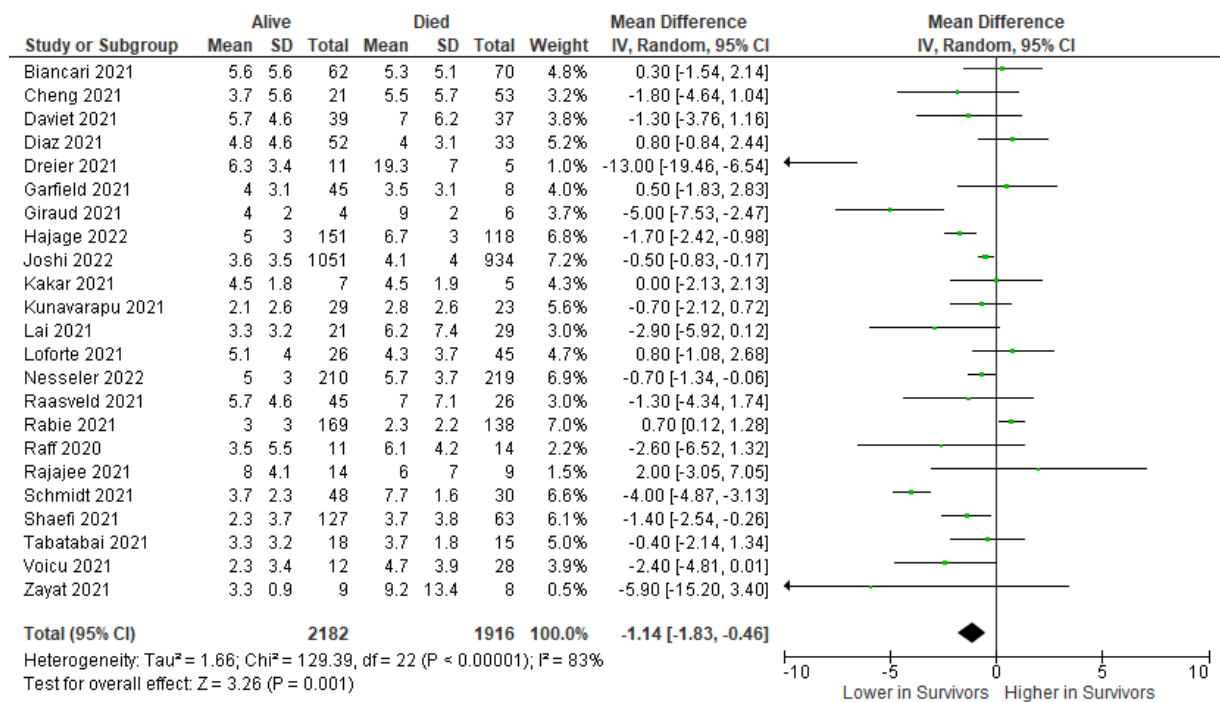
Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation (Per Day Increase, Adjusted Odds Ratio)



Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation (Per Day Increase, Adjusted Hazard Ratio)

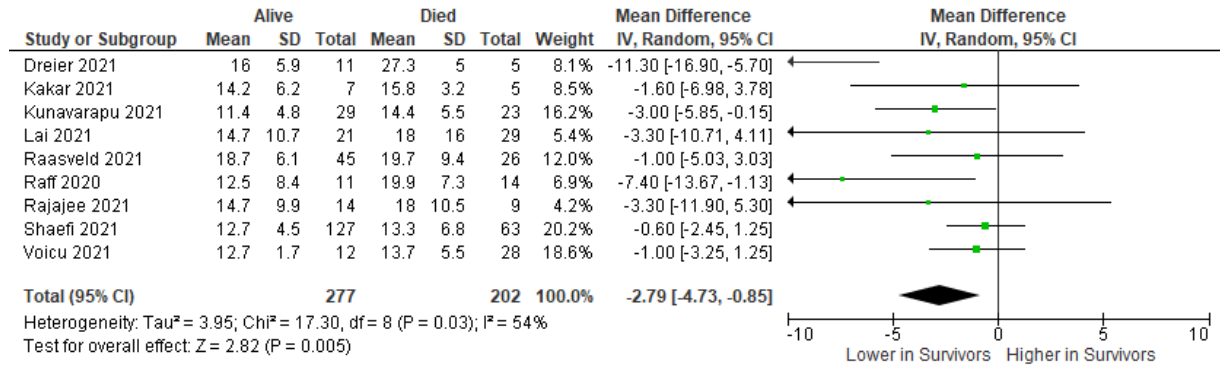


Duration of Pre-ECMO Mechanical Ventilation, Alive vs Died (Mean Difference)



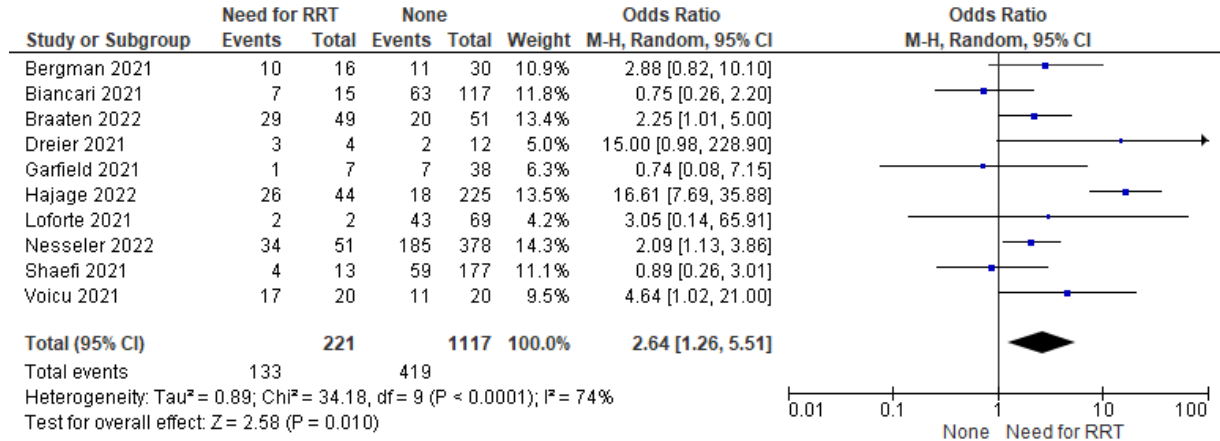
Disease Factors (Longer vs Shorter Pre-ECMO Time from Symptom Onset)

Longer vs Shorter Pre-ECMO Time from Symptom Onset, Alive vs Died (Mean Difference)



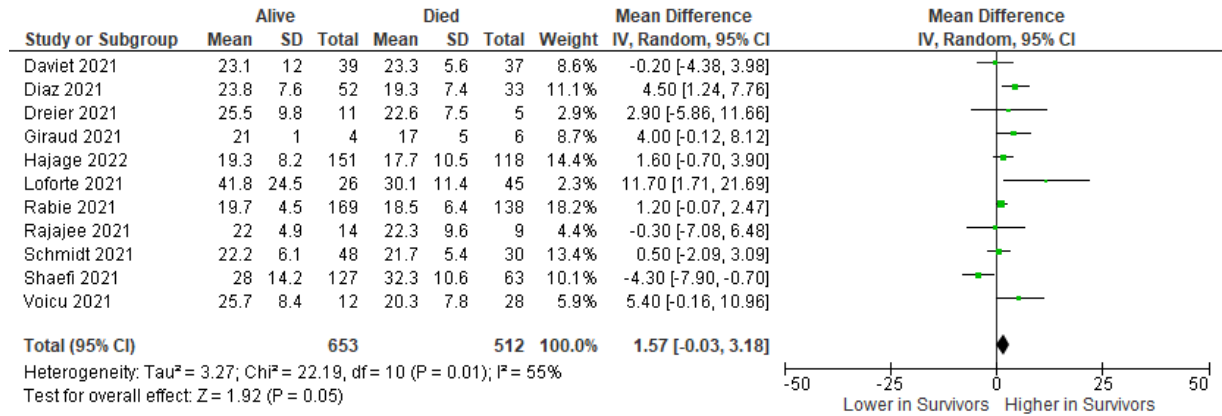
Disease Factors (Need for Pre-ECMO Renal Replacement Therapy vs None)

Need for Pre-ECMO Renal Replacement Therapy vs None (Unadjusted Odds Ratio)



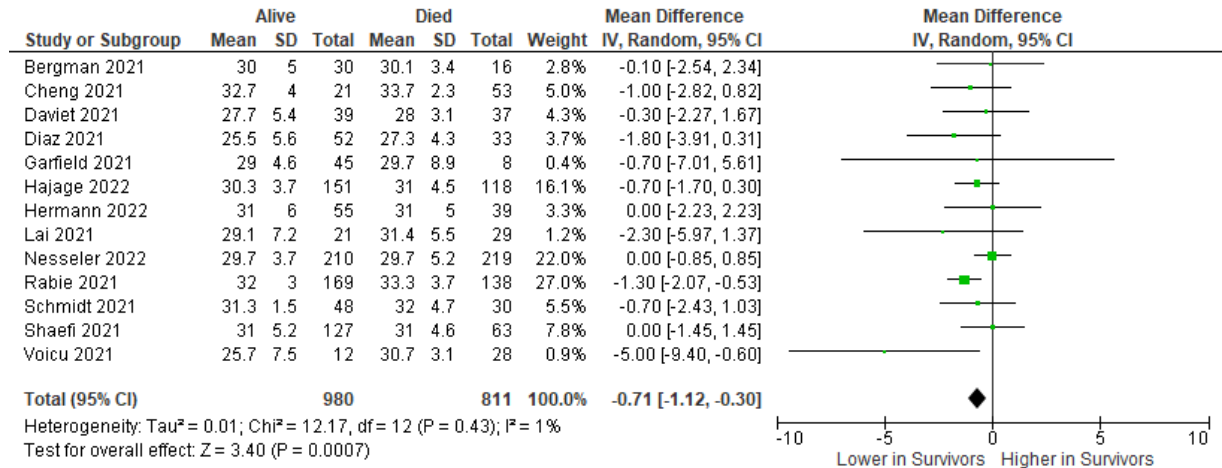
Disease Factors (Lower vs Higher Compliance, cm H2O)

Lower vs Higher Compliance, cm H2O, Alive vs Died (Mean Difference)



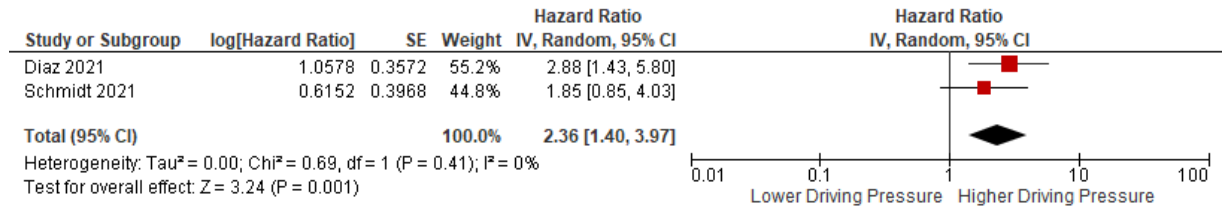
Disease Factors (Higher vs Lower Plateau Pressure, cm H2O)

Higher vs Lower Plateau Pressure, cm H2O, Alive vs Died (Mean Difference)



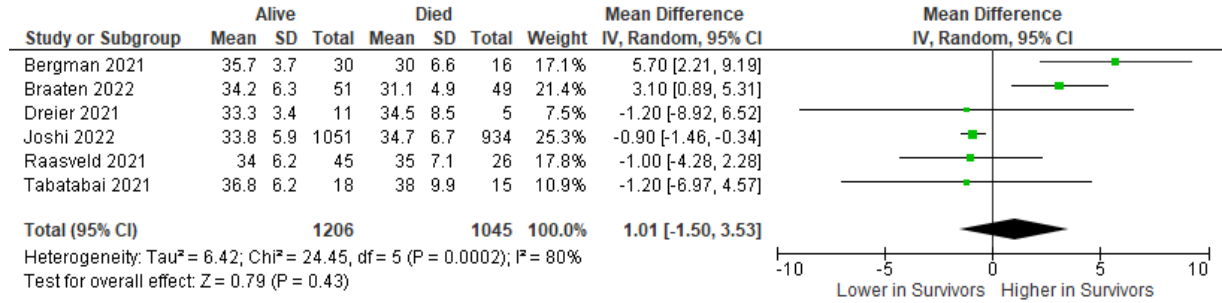
Disease Factors (Higher vs Lower Driving Pressure, cm H2O)

Higher vs Lower Driving Pressure, cm H2O, Alive vs Died (Adjusted Hazard Ratio)



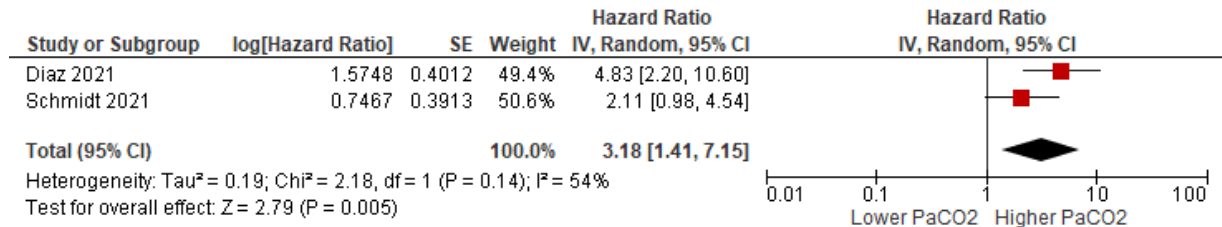
Disease Factors (Peak Pressure, cm H2O)

Peak Pressure, cm H2O, Alive vs Died (Mean Difference)

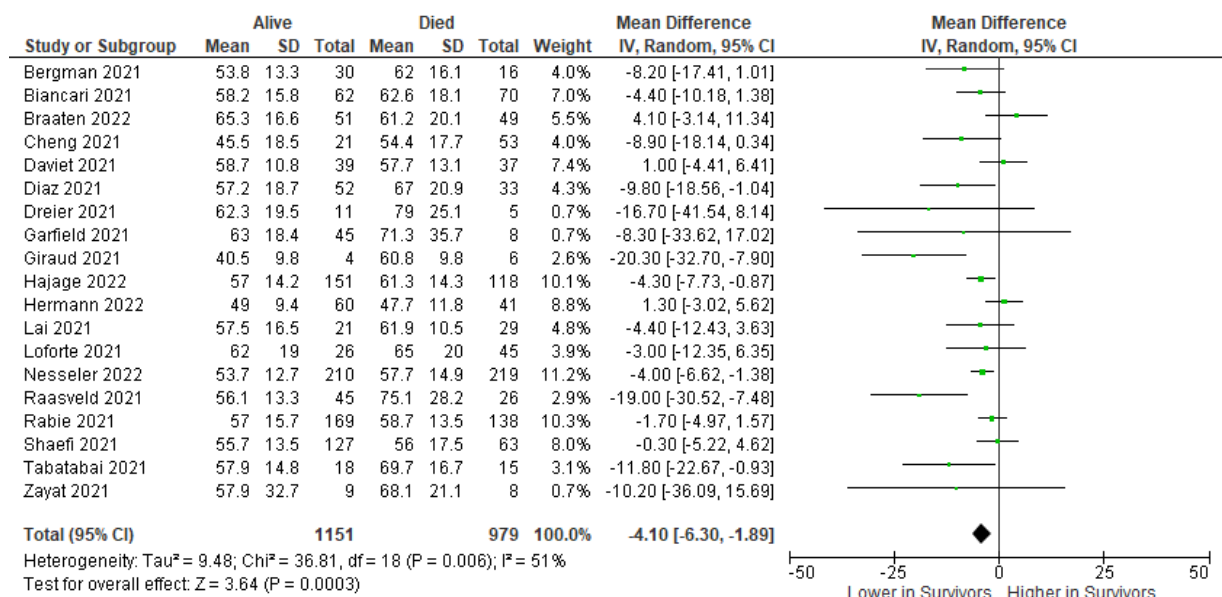


Disease Factors (Higher vs Lower PaCO₂, mmHg)

Higher vs Lower PaCO₂, mmHg (Adjusted Hazard Ratio)

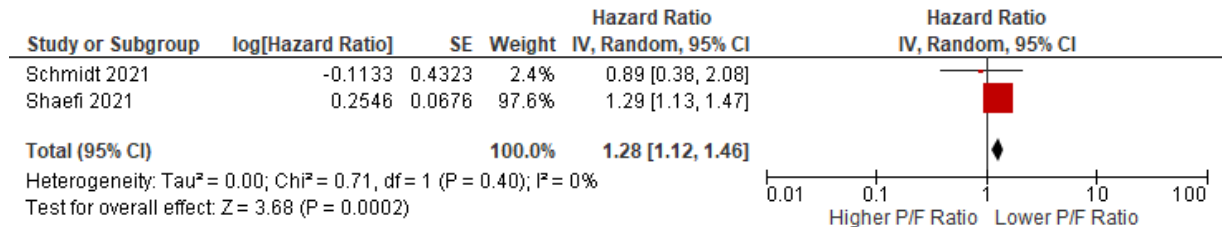


Higher vs Lower PaCO₂, mmHg, Alive vs Died (Mean Difference)

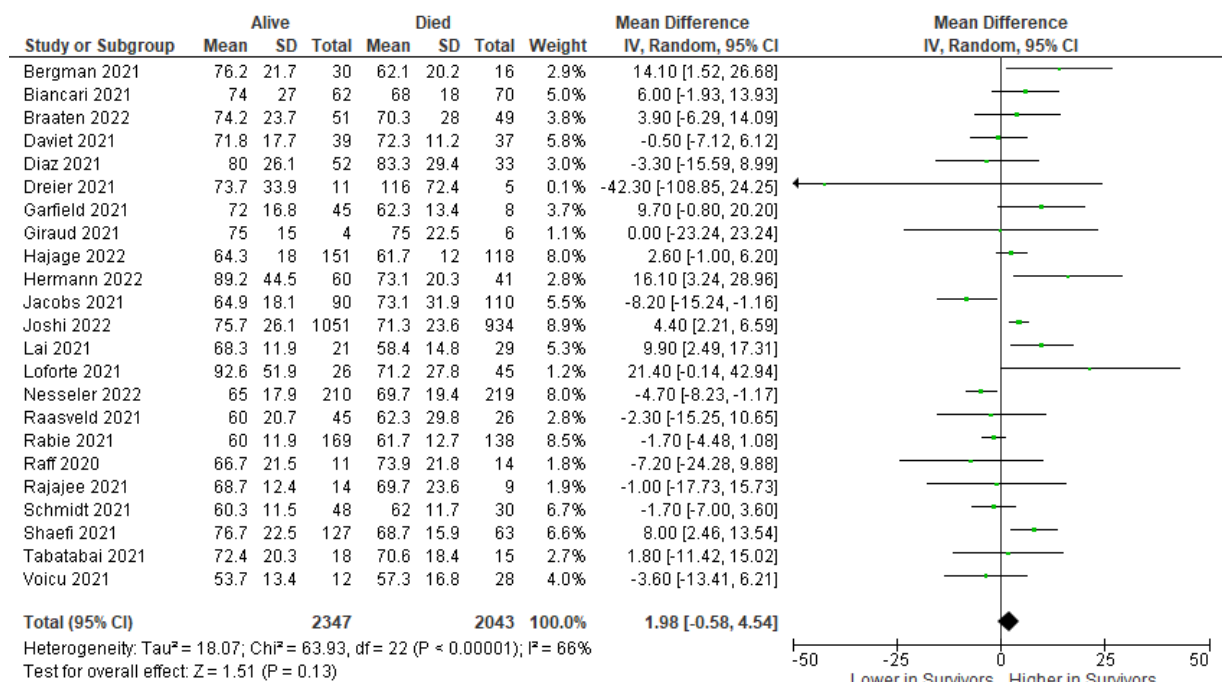


Disease Factors (Lower vs Higher PaO₂/FiO₂ Ratio)

Lower vs Higher PaO₂/FiO₂ Ratio (Adjusted Hazard Ratio)

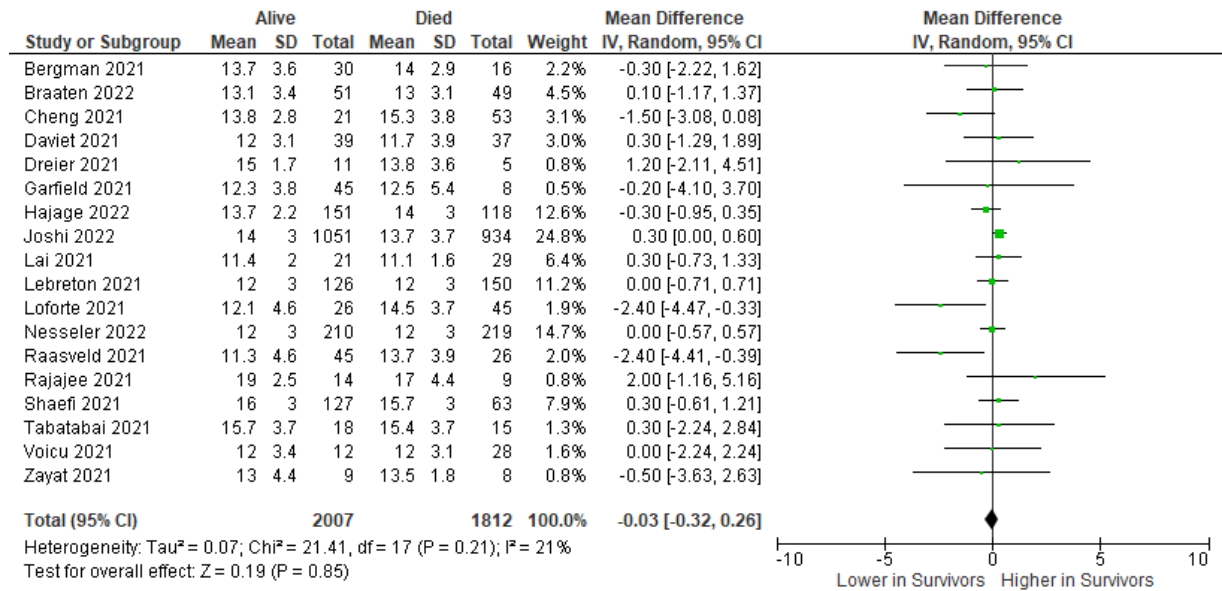


Lower vs Higher PaO₂/FiO₂ Ratio, Alive vs Died (Mean Difference)



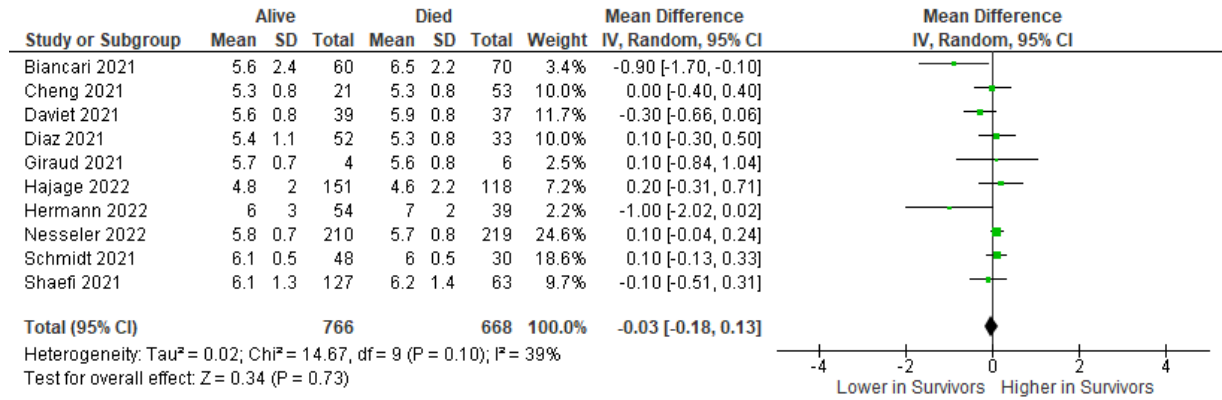
Disease Factors (Higher vs Lower PEEP, cm H2O)

Higher vs Lower PEEP, cm H2O, Alive vs Died (Mean Difference)



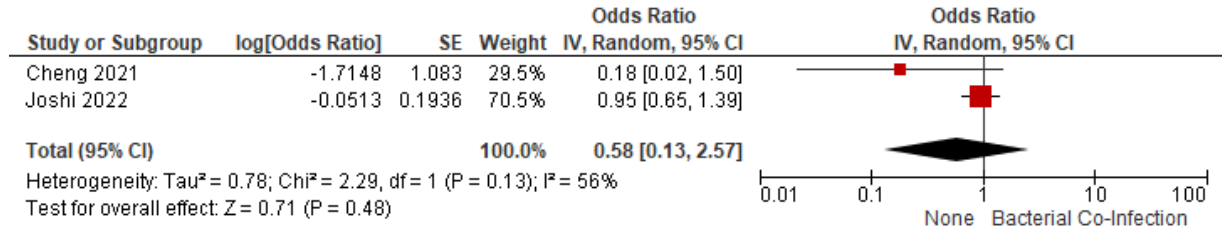
Disease Factors (Higher vs Lower Tidal Volume, mL/kg)

Higher vs Lower Tidal Volume, mL/kg, Alive vs Died (Mean Difference)

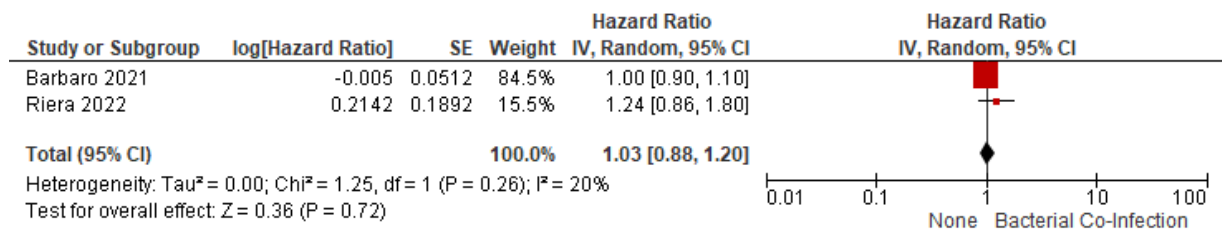


Disease Factors (Bacterial Co-Infection vs None)

Bacterial Co-Infection vs None (Adjusted Odds Ratio)

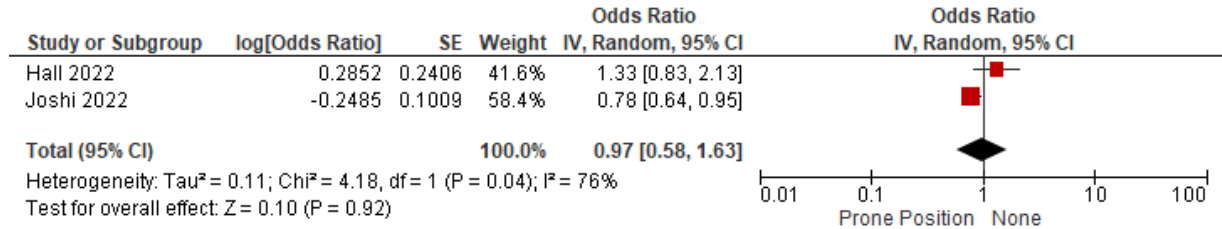


Bacterial Co-Infection vs None (Adjusted Hazard Ratio)

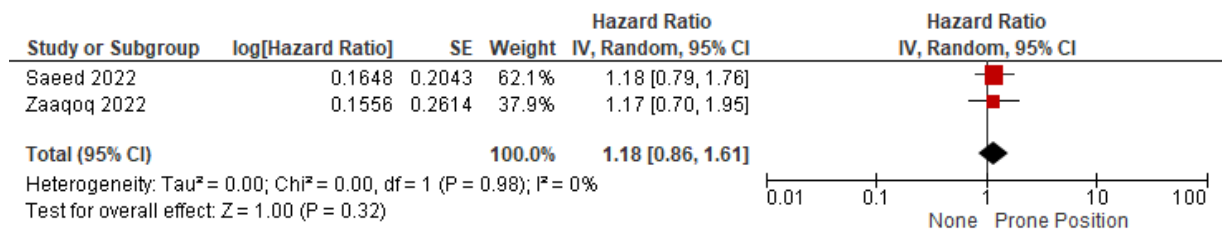


Disease Factors (Pre-ECMO Proning vs None)

Pre-ECMO Proning vs None (Adjusted Odds Ratio)

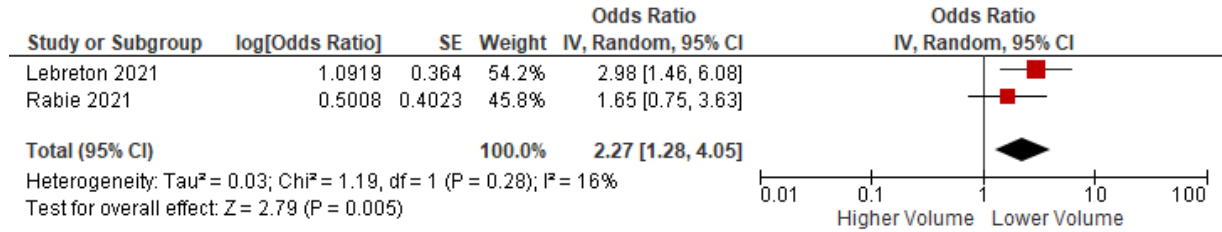


Pre-ECMO Proning vs None (Adjusted Hazard Ratio)

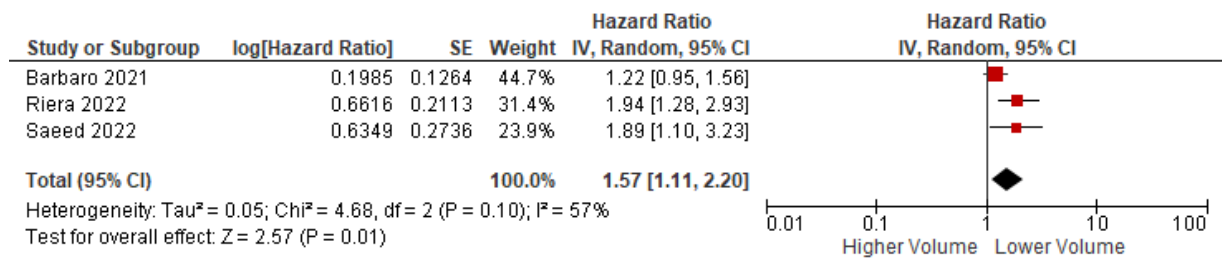


Center Factors (Lower vs Higher Volume)

Lower vs Higher Volume (Adjusted Odds Ratio)



Lower vs Higher Volume (Adjusted Hazard Ratio)



Supplemental Table 1: Risk of Bias Assessments – QUIPS

Study	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Confounding Adjustment	Statistical Analysis & Reporting
Ahmad 2022	😊	😊	😊	😊	😞	😞
Barbaro 2021	😊	😊	😊	😊	😊	😊
Bergman 2021	😊	😊	😊	😊	😞	😞
Blazoski 2021	😊	😊	😊	😊	😞	😞
Braaten 2022	😊	😊	😊	😊	😞	😞
Cheng 2021	😊	😊	😊	😊	😊	😞
Daviet 2021	😊	😊	😊	😊	😊	😞
Diaz 2021	😊	😊	😊	😊	😊	😊
Friedrichson 2022	😊	😊	😊	😊	😞	😞
Giraud 2020	😊	😊	😊	😊	😞	😞
Hajage 2022	😊	😊	😊	😊	😞	😞
Hall 2022	😊	😊	😊	😊	😊	😊
Hermann 2022	😊	😊	😊	😞	😊	😞
Jacobs 2021	😊	😊	😊	😊	😞	😞
Kakar 2021	😊	😊	😊	😊	😞	😞
Karagiannidis 2021	😊	😊	😊	😊	😞	😞
Kunavarapu 2021	😊	😊	😊	😊	😊	😞
Kurihara 2021	😊	😊	😊	😞	😊	😞
Lai 2021	😊	😊	😊	😊	😞	😞
Lebreton 2021	😊	😊	😊	😊	😊	😊
Li 2021	😊	😊	😊	😊	😞	😞
Loforte 2021	😊	😊	😊	😊	😞	😞
Mustafa 2021	😊	😊	😊	😊	😞	😞
Nessler 2022	😊	😊	😊	😊	😊	😊
Nguyen 2021	😊	😊	😊	😊	😞	😞
Raasveld 2021	😊	😊	😊	😞	😊	😞
Rabie 2021	😊	😊	😊	😊	😊	😞
Raff 2020	😊	😊	😊	😊	😊	😊
Rajajee 2021	😊	😊	😊	😊	😞	😞
Rao 2021	😊	😊	😊	😊	😊	😞
Riera 2022	😊	😊	😊	😊	😊	😊
Saeed 2022	😊	😊	😊	😊	😊	😊
Schmidt 2021	😊	😊	😊	😞	😊	😊
Shaefi 2021	😊	😊	😊	😊	😊	😊
Supady 2021	😊	😊	😊	😊	😊	😞
Tabatabai 2021	😊	😊	😊	😊	😞	😞
Trejnowska 2022	😊	😊	😊	😊	😊	😞
Voicu 2021	😊	😊	😊	😊	😞	😞
Zaaqoq 2022	😊	😊	😊	😊	😊	😊
Zayat 2021	😊	😊	😊	😊	😊	😞
Zhang 2020	😊	😊	😊	😊	😞	😞

Low Risk = 😊; Moderate Risk = 😞

Supplemental Table 2: GRADE Assessments

Nº of studies	Certainty assessment						impact	Certainty	Importance
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication Bias			
Sex									
26	observational studies	not serious ^{a,b}	serious ^c	not serious	not serious	none	Pooled unadjusted OR = 1.34 (95% CI 1.20 to 1.49) suggesting higher risk of dying in males. Less data in the adjusted analysis however pooled analysis for aOR and aHR is consistent with unadjusted analysis.	⊕⊕⊕○ Moderate	CRITICAL
Age									
11	observational studies	not serious ^{a,b}	not serious	not serious	not serious	none	Pooled unadjusted OR = 2.51 (95% CI 2.07 to 3.03) suggesting older age associated with mortality. Less data in the adjusted analysis however pooled analysis for aOR and aHR is consistent with unadjusted analysis.	⊕⊕⊕⊕ High	CRITICAL
Obesity									
14	observational studies	serious ^d	not serious	not serious	serious ^e	none	Pooled unadjusted OR = 0.84 (95% CI 0.72 to 0.97) suggesting lower risk of death if not obese.	⊕⊕○○ Low	CRITICAL

Chronic Lung Disease									
19	observational studies	not serious ^{a,b}	not serious	not serious	serious ^f	none	Pooled unadjusted OR = 1.08 (95% CI 0.92 to 1.26) suggesting higher risk of death if presence of chronic lung disease. Less data in the adjusted analysis however pooled analysis for aOR and aHR is consistent with unadjusted analysis.	⊕⊕⊕○ Moderate	CRITICAL
Immunocompromised Status									
5	observational studies	serious ^d	not serious	not serious	serious ^g	none	Pooled unadjusted OR = 2.34 (95% CI 1.19 to 4.61) suggesting high risk of death if immunocompromised. Less data in the adjusted analysis however studies reporting aOR and aHR is consistent with unadjusted analysis.	⊕⊕○○ Low	CRITICAL
Pre-ECMO RRT use									
7	observational studies	serious ^d	not serious	not serious	serious ^{f,g}	none	Pooled unadjusted OR = 3.18 (95% CI 1.41 to 7.17) suggesting higher risk of death with RRT use.	⊕⊕○○ Low	CRITICAL
Duration of MV Pre-ECMO									
6	observational studies	serious ^d	not serious	not serious	not serious	none	Pooled unadjusted OR = 1.94 (95% CI 1.40 to 2.67) suggesting higher risk of death with longer duration. Consistent with unadjusted pooled mean difference = 1.14 days fewer duration of MV pre-	⊕⊕⊕○ Moderate	CRITICAL

							ECMO in those that survived (95% CI 0.46 to 1.83 days fewer). Consistent with longer vs shorter duration adjusted analysis but not with per-day adjusted analysis (likely limited by linear categorization).		
Duration of symptoms									
8	observational studies	serious ^d	not serious ⁱ	not serious	not serious	none	Unadjusted pooled mean difference = 1.51 days shorter duration of symptoms pre-ECMO in those that survived (95% CI 0.36 higher to 2.65 fewer)	⊕⊕⊕○ Moderate	CRITICAL
P:F ratio									
20	observational studies	not serious ^{a,b}	serious ^j	not serious	serious ^f	none	Unadjusted pooled mean difference = 1.52 points higher in those that survived (95% CI 1.16 lower to 4.20 higher). Less data in the adjusted analysis however consistent with the unadjusted analysis.	⊕⊕○○ Low	CRITICAL
PaCO2									
16	observational studies	not serious ^{a,b}	serious ^j	not serious	not serious	none	Unadjusted pooled mean difference = 4.04 mmHg lower in those that survived (95% CI 1.64 to 6.44 lower). Less data in the adjusted analysis however consistent with the unadjusted analysis.	⊕⊕⊕○ Moderate	CRITICAL
Compliance									

10	observational studies	serious ^d	serious ⁱ	not serious	serious ^f	none	Unadjusted pooled mean difference = 1.55 cm H20 higher in those that survived (95% CI 0.12 lower to 3.21 higher).	⊕○○○ Very low	CRITICAL
PEEP									
16	observational studies	serious ^d	not serious	not serious	serious ^k	none	Unadjusted pooled mean difference = 0.05 cmH20 higher in those that survived (95% CI 0.26 lower to 0.37 higher).	⊕⊕○○ Low	CRITICAL
Plateau Pressure									
12	observational studies	serious ^d	not serious	not serious	serious	none	Unadjusted pooled mean difference = 0.71 cmH20 lower in those that survived (95% CI 0.26 lower to 1.15 lower).	⊕⊕○○ Low	CRITICAL
Peak Pressure									
5	observational studies	serious ^d	serious ⁱ	not serious	serious ^l	none	Unadjusted pooled mean difference = 1.20 cmH20 higher in those that survived (95% CI 1.51 lower to 3.90 higher).	⊕○○○ Very low	CRITICAL
Tidal Volume									
9	observational studies	serious ^d	not serious	not serious	serious ^k	none	Unadjusted pooled mean difference = 0.03 ml/kg lower in those that survived (95% CI 0.15 lower to 0.09 higher).	⊕⊕○○ Low	CRITICAL
Centre Volume									

2	observational studies	not serious	not serious	not serious	serious ^g	none	Adjusted odds ratio = 2.27 (95% CI 1.28 to 4.05) suggesting higher mortality in lower volume centres.	⊕⊕⊕○ Moderate	CRITICAL
Driving Pressure									
2	observational studies	not serious	not serious	not serious	not serious	none	Adjusted hazard ratio = 2.36 (95% CI 1.40 to 3.97) suggesting high mortality with higher driving pressure	⊕⊕⊕⊕ High	CRITICAL
Bacterial Co-Infection									
2	observational studies	not serious	not serious	not serious	serious ^k	none	Adjusted hazard ratio = 1.03 (95% CI 0.88 to 1.20) suggesting no impact on mortality with bacterial coinfection.	⊕⊕⊕○ Moderate	CRITICAL
Prone positioning before ECMO									
2	observational studies	not serious	not serious	not serious	very serious ^k	none	Adjusted odds ratio = 0.97 (95% CI 0.58 to 1.63) suggesting no impact on mortality with prone positioning prior to ECMO	⊕⊕○○ Low	CRITICAL

Explanations

- a. Most data comes from unadjusted analysis however adjusted analysis is consistent in demonstrating association.
- b. Most included studies at low risk of bias.
- c. Low I-squared but visual inspection of the forest plot suggests variation amongst included trials.
- d. All unadjusted analysis so residual confounding a concern.
- e. Upper end of the 95% CI does not rule out no association.
- f. Lower end of the 95% CI does not rule out no association.

- g. Small number of events contribute to imprecision.
- h. Visual inspection suggests wide overlap in CIs.
- i. High I-squared but all heterogeneity on the same side of association
- j. High I-squared
- k. Overall rated 'no association' but ends of CI don't rule out association
- l. Very wide confidence intervals.

Supplemental Table 3: Model Composition for Adjusted Analyses

Study	Sex	Age	BMI	Immunocompromise	Lung Disease	Other Comorbidity	COVID Therapies	Co-Infection	MV Duration	Ventilation Metrics	Oxygenation Metrics	Acute Kidney Injury	Centre Experience	Other
Barbaro 2021	😊	😊	😊	😊	😊	😊		😊	😊	😊	😊	😊	😊	Cardiac Arrest, ELSO Chapter, Race, ECMO Configuration, COVID Wave
Cheng 2021		😊						😊		😊				Lymphocyte Count
Daviet 2021		😊	😊	😊			😊		😊	😊				High Flow O2, PRESERVE Score, COVID Wave
Diaz 2021		😊	😊						😊	😊	😊			Lactate, RESP Score, SOFA Score
George 2022		😊				😊								
Hall 2022		😊				😊	😊		😊					
Hermann 2022		😊		😊	😊	😊			😊	😊	😊			SOFA Score, RESP Score
Joshi 2022				😊			😊	😊	😊	😊	😊			
Kunavarapu 2021	😊	😊	😊			😊			😊					
Lebreton 2021		😊							😊			😊		
Loforte 2021		😊								😊				CRP
Rabie 2021	😊	😊	😊		😊					😊	😊		😊	SOFA Score
Raff 2020		😊												
Rao 2021	😊	😊	😊		😊	😊								Race
Riera 2022		😊						😊		😊	😊		😊	Symptom Duration, COVID Wave
Saeed 2022	😊	😊	😊				😊		😊	😊			😊	Cardiac Arrest, Symptom Duration
Schmidt 2021		😊					😊		😊	😊	😊	😊		COVID Wave
Shaefi 2021	😊	😊	😊		😊	😊	😊	😊		😊	😊	😊		SOFA Score

Sensitivity Analyses

Supplemental Table 5: Exclusion of Studies evaluating ICU or 28-day mortality (versus primary outcome of in-hospital)

Prognostic Factor	Unadjusted Odds Ratio Analysis		Adjusted Odds Ratio Analysis		Adjusted Hazard Ratio Analysis		Mean Difference Analysis	
	Studies (N)	uOR (95% CI)	Studies (N)	aOR (95% CI)	Studies (N)	aHR (95% CI)	Studies (N)	MD (95% CI)
Patient Factors								
Older Age	12	2.48 (2.09 to 2.95)	4	2.09 (1.22 to 3.59)	5	2.27 (1.63 to 3.16)	-	-
Male Sex	25	1.33 (1.20 to 1.48)	4	1.42 (0.98 to 2.05)	4	1.06 (0.96 to 1.16)	-	-
Chronic Lung Disease	18	1.02 (0.89 to 1.17)	3	2.50 (1.09 to 5.74)	3	1.55 (1.20 to 2.00)	-	-
Obesity	13	0.84 (0.71 to 0.98)	2	0.67 (0.36 to 1.27)	3	1.08 (0.73 to 1.60)	-	-
Immunocompromised	4	2.29 (1.13 to 4.64)	1	4.35 (2.46 to 7.69)	1	1.06 (0.83 to 1.35)	-	-
Pre-Cannulation Disease Factors								
Higher Driving Pressure	-	-	-	-	2	2.36 (1.40 to 3.97)	-	-
Longer Symptom Duration	-	-	-	-	-	-	8	-3.13 (-5.32 to -0.93) days
Higher PaCO ₂	-	-	-	-	2	3.18 (1.41 to 7.15)	16	-3.97 (-6.29 to -1.65) mmHg
Longer IMV Duration	5	2.07 (1.55 to 2.76)	3	1.11 (0.65 to 1.92)	1	1.66 (1.00 to 2.75)	20	-0.74 (-1.34 to -0.14) days
Lower PaO ₂ /FiO ₂ Ratio	-	-	-	-	1	1.29 (1.13 to 1.47)	19	1.93 (-1.10 to 4.96) points
Higher Plateau Pressure	-	-	-	-	-	-	10	-0.76 (-1.37 to -0.15) cm H ₂ O
Need for Renal Replacement Therapy	9	1.89 (1.23 to 2.90)	-	-	-	-	-	-
Lower Positive End Expiratory Pressure	-	-	-	-	-	-	16	0.15 (-0.06 to 0.37) cm H ₂ O

Higher Tidal Volume	-	-	-	-	-	-	7	-0.06 (-0.24 to 0.13) ml/kg
Lower Compliance	-	-	-	-	-	-	9	1.91 (-0.36 to 4.18)
Higher Peak Pressure	-	-	-	-	-	-	6	1.44 (-1.65 to 4.52)
Bacterial Co-Infection	-	-	2	0.58 (0.13 to 2.57)	2	1.03 (0.88 to 1.20)	-	-
Pre-ECMO Proning	-	-	2	0.97 (0.58 to 1.63)	2	1.18 (0.86 to 1.61)	-	-
Center Factors								
Lower Volume	-	-	2	2.27 (1.28 to 4.05)	3	1.57 (1.11 to 2.20)	-	-

uOR: unadjusted odds ratio; aOR; adjusted odds ratio; aHR; adjusted hazard ratio; MD: mean difference; IMV: invasive mechanical ventilation

Sensitivity Analyses

Supplemental Table 6: Exclusion of Studies with potential risk of bias related to prediction model development

Prognostic Factor	Unadjusted Odds Ratio Analysis		Adjusted Odds Ratio Analysis		Adjusted Hazard Ratio Analysis		Mean Difference Analysis	
	Studies (N)	uOR (95% CI)	Studies (N)	aOR (95% CI)	Studies (N)	aHR (95% CI)	Studies (N)	MD (95% CI)
Patient Factors								
Older Age	12	2.48 (2.09 to 2.95)	2	2.43 (1.76 to 3.35)	4	2.33 (1.57 to 3.45)	-	-
Male Sex	28	1.32 (1.19 to 1.47)	1	1.48 (0.95 to 2.31)	4	1.06 (0.96 to 1.16)	-	-
Chronic Lung Disease	21	1.05 (0.92 to 1.19)	-	-	2	1.51 (1.15 to 1.98)	-	-
Obesity	14	0.84 (0.72 to 0.97)	-	-	3	1.08 (0.73 to 1.60)	-	-
Immunocompromised	5	2.34 (1.19 to 4.61)	1	4.35 (2.46 to 7.69)	1	1.06 (0.83 to 1.35)	-	-
Pre-Cannulation Disease Factors								
Higher Driving Pressure	-	-	-	-	2	2.36 (1.40 to 3.97)	-	-
Longer Symptom Duration	-	-	-	-	-	-	9	-2.79 (-4.73 to -0.85) days
Higher PaCO ₂	-	-	-	-	2	3.18 (1.41 to 7.15)	18	-4.23 (-6.69 to -1.77) mmHg
Longer IMV Duration	6	1.94 (1.40 to 2.67)	2	1.50 (1.16 to 1.95)	1	1.66 (1.00 to 2.75)	22	-1.11 (-1.84 to -0.38) days
Lower PaO ₂ /FiO ₂ Ratio	-	-	-	-	2	1.28 (1.12 to 1.46)	22	1.98 (-0.82 to 4.78) points
Higher Plateau Pressure	-	-	-	-	-	-	12	-0.71 (-1.20 to -0.21) cm H ₂ O
Need for Renal Replacement Therapy	9	1.89 (1.23 to 2.90)	-	-	-	-	-	-
Lower Positive End Expiratory Pressure	-	-	-	-	-	-	17	0.01 (-0.31 to 0.32) cm H ₂ O

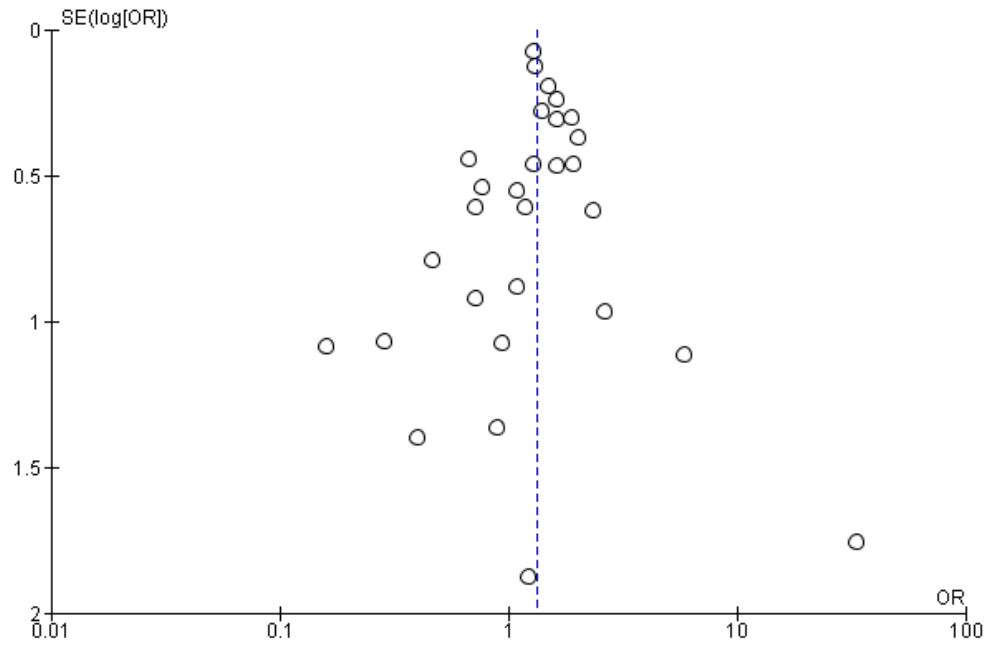
Higher Tidal Volume	-	-	-	-	-	-	9	-0.05 (-0.22 to 0.12) ml/kg
Lower Compliance	-	-	-	-	-	-	10	1.63 (-0.27 to 3.53)
Higher Peak Pressure	-	-	-	-	-	-	6	1.01 (-1.50 to 3.53)
Bacterial Co-Infection	-	-	2	0.58 (0.13 to 2.57)	2	1.03 (0.88 to 1.20)	-	-
Pre-ECMO Proning	-	-	2	0.97 (0.58 to 1.63)	2	1.18 (0.86 to 1.61)	-	-
Center Factors								
Lower Volume	-	-	1	2.98 (1.46 to 6.08)	3	1.57 (1.11 to 2.20)	-	-

uOR: unadjusted odds ratio; aOR; adjusted odds ratio; aHR; adjusted hazard ratio; MD: mean difference; IMV: invasive mechanical ventilation

Supplemental Figure 2: Funnel Plots

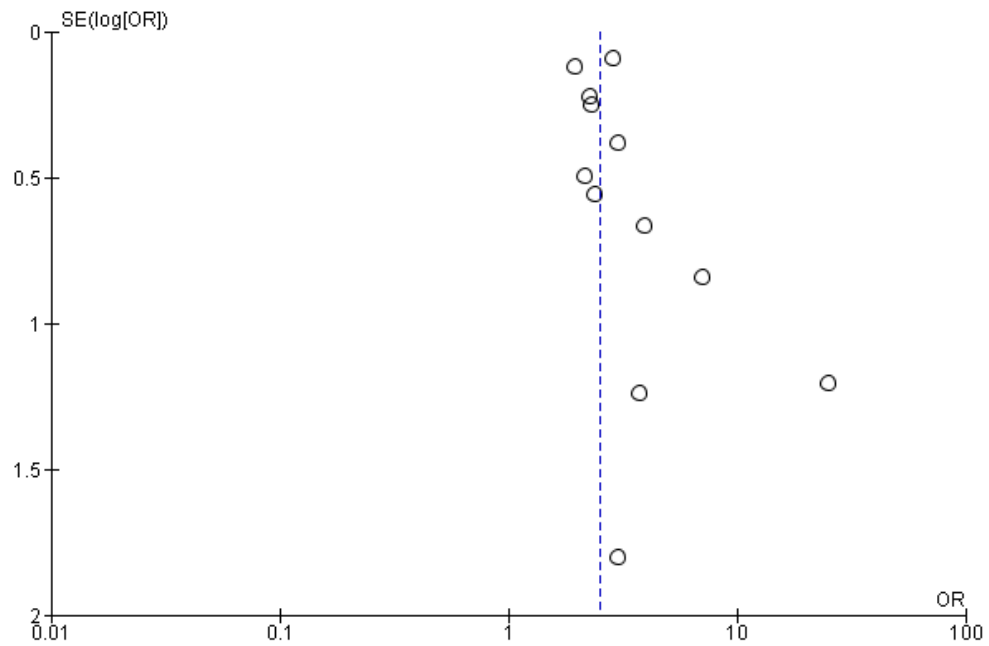
Patient Factors (Male vs Female Sex)

Unadjusted Odds Ratio



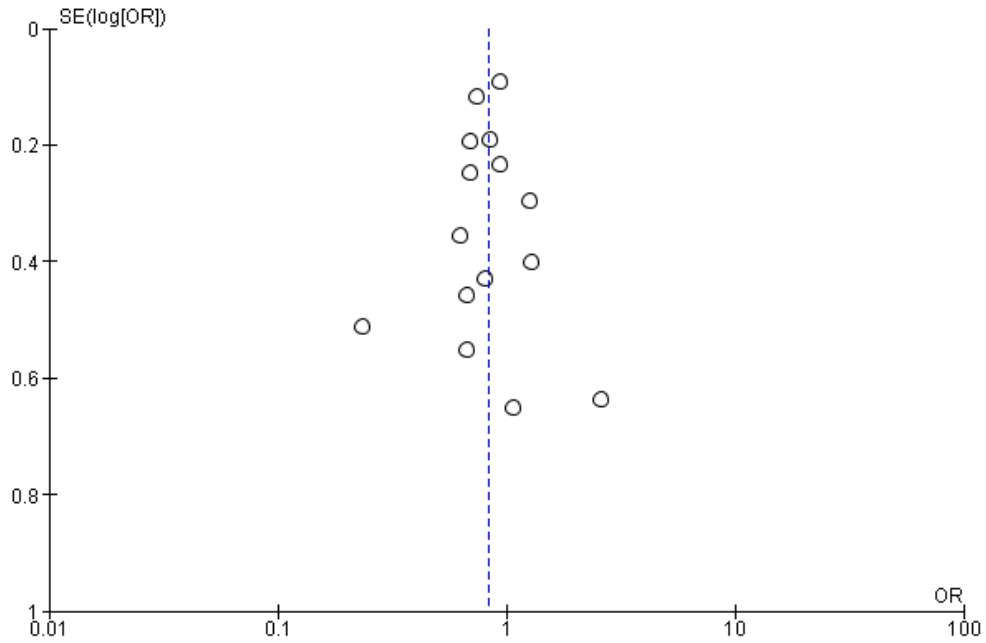
Patient Factors (Older vs Younger Age)

Unadjusted Odds Ratio



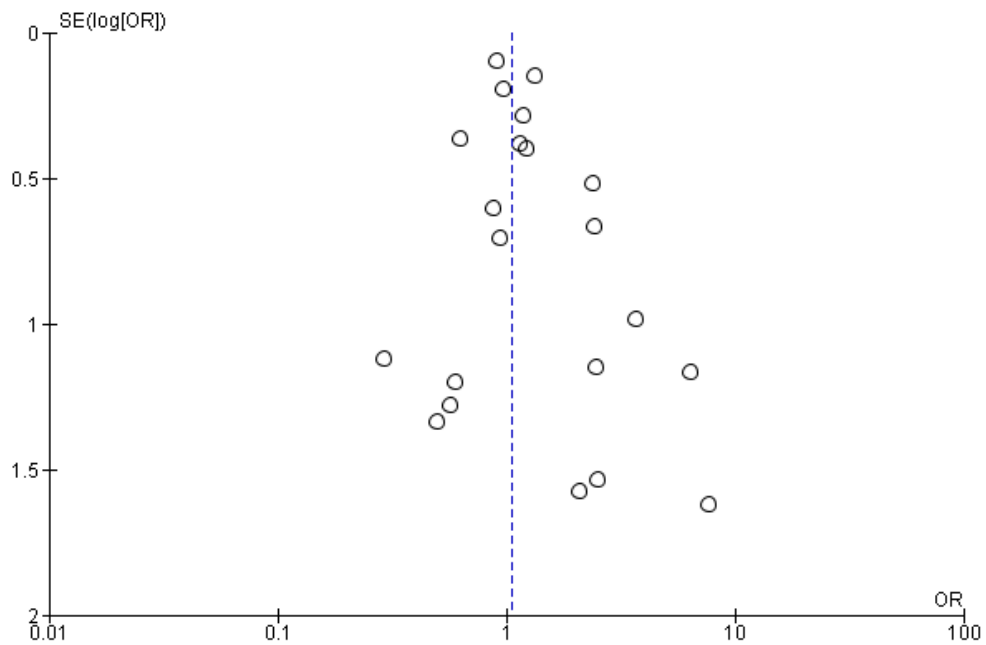
Patient Factors (Obesity vs None)

Unadjusted Odds Ratio



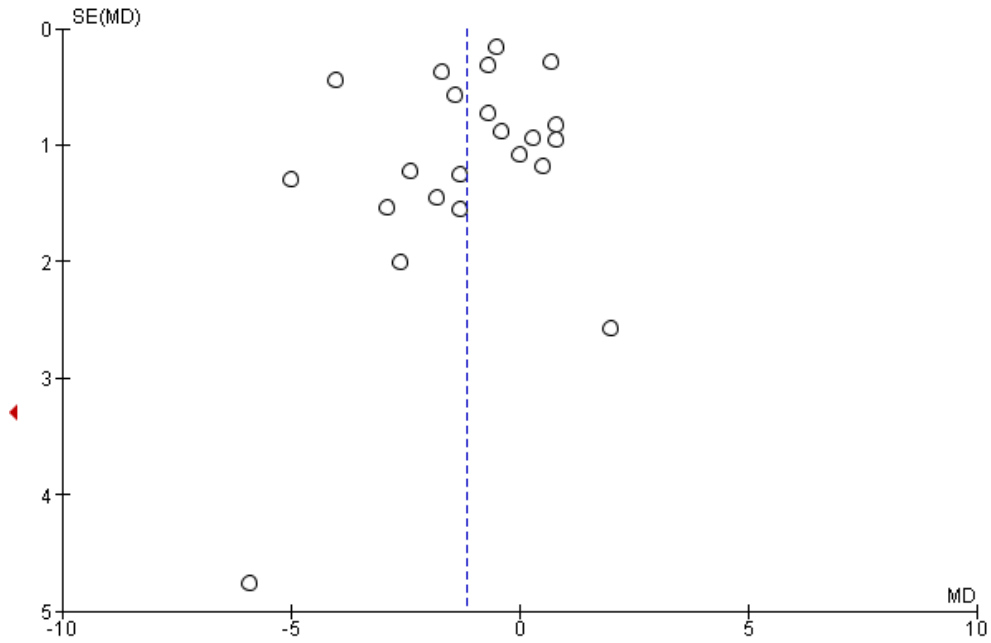
Patient Factors (Lung Disease vs None)

Unadjusted Odds Ratio



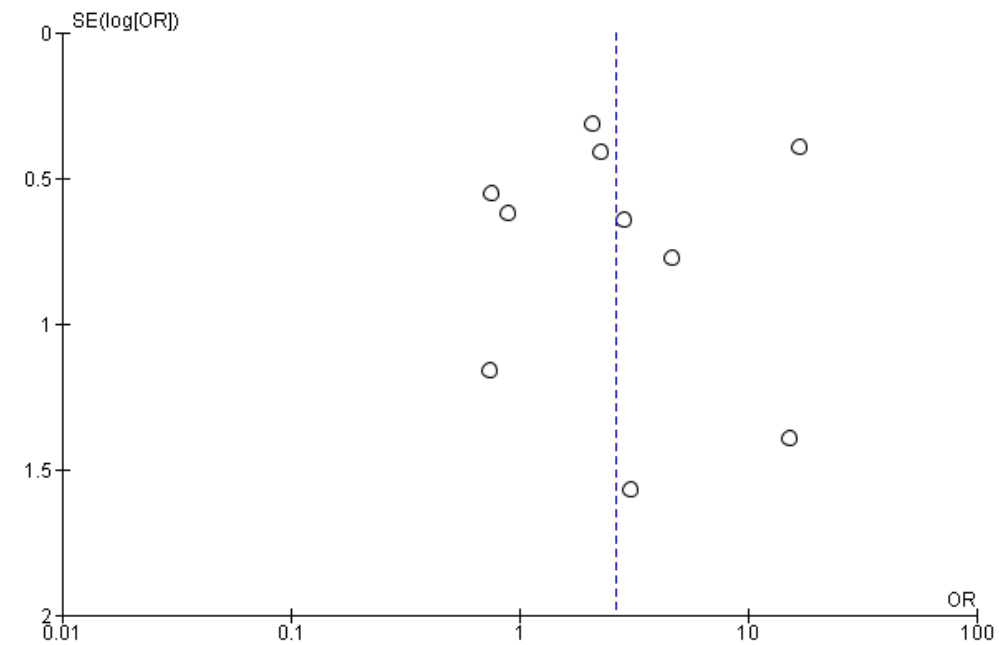
Disease Factors (Longer vs Shorter Duration of Pre-ECMO Mechanical Ventilation)

Duration of Pre-ECMO Mechanical Ventilation, Alive vs Died (Mean Difference)



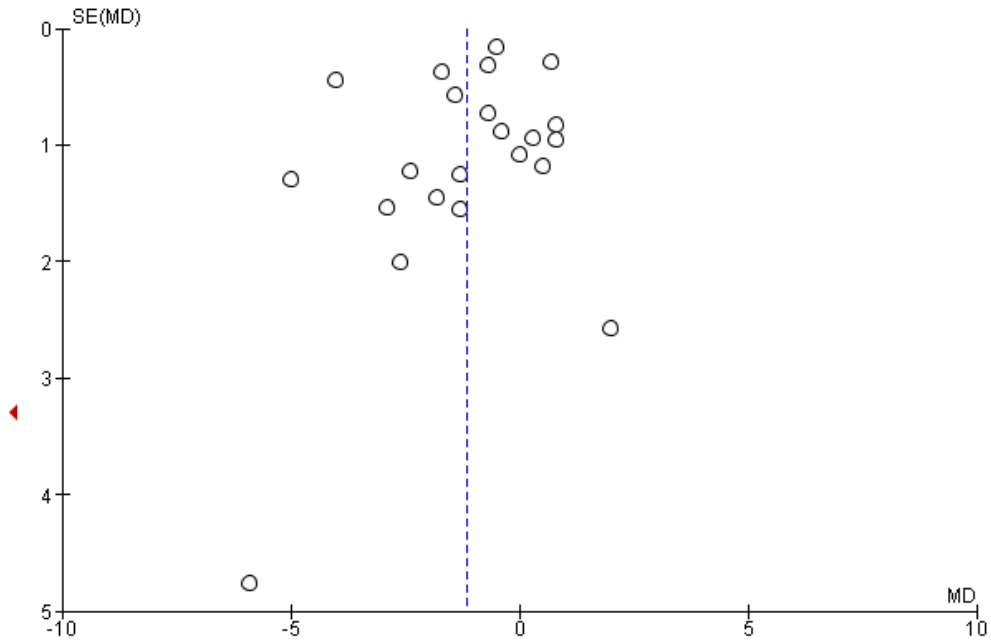
Disease Factors (Need for RRT vs None)

Unadjusted Odds Ratio



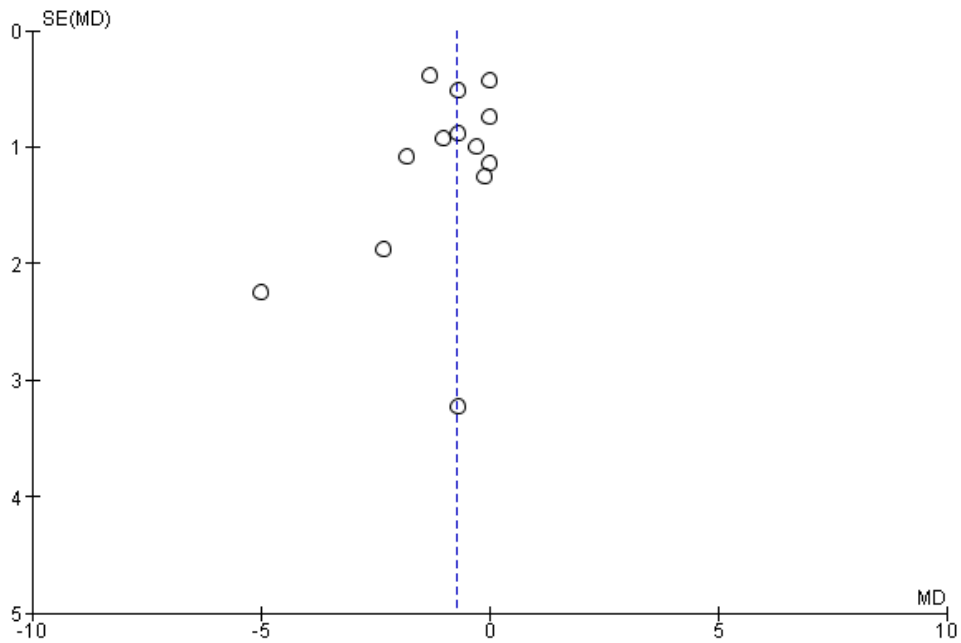
Disease Factors (Lower vs Higher Compliance, cm H2O)

Lower vs Higher Compliance, cm H2O, Alive vs Died (Mean Difference)



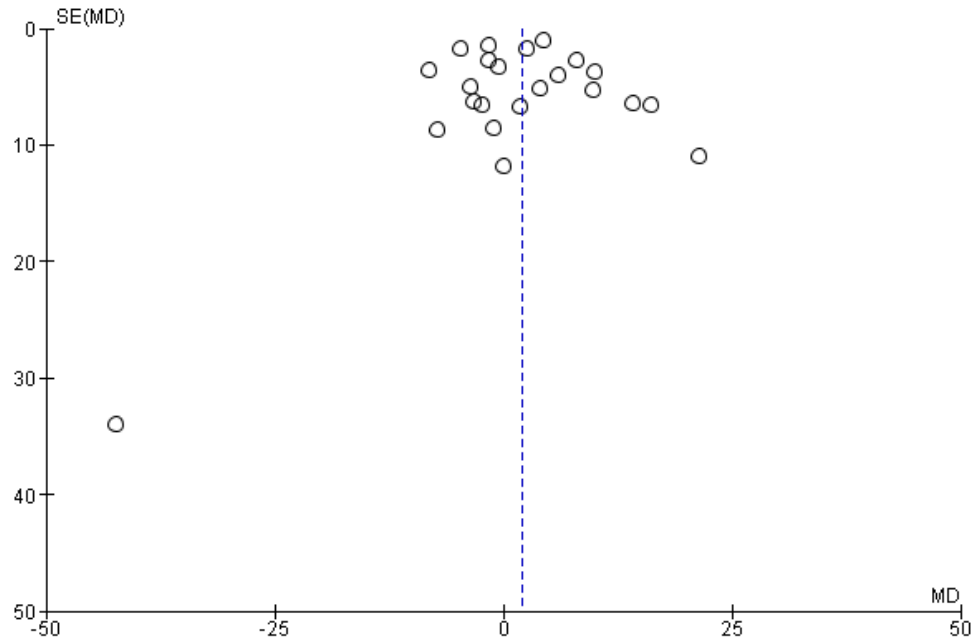
Disease Factors (Higher vs Lower Plateau Pressure, cm H2O)

Higher vs Lower Plateau Pressure, cm H2O, Alive vs Died (Mean Difference)



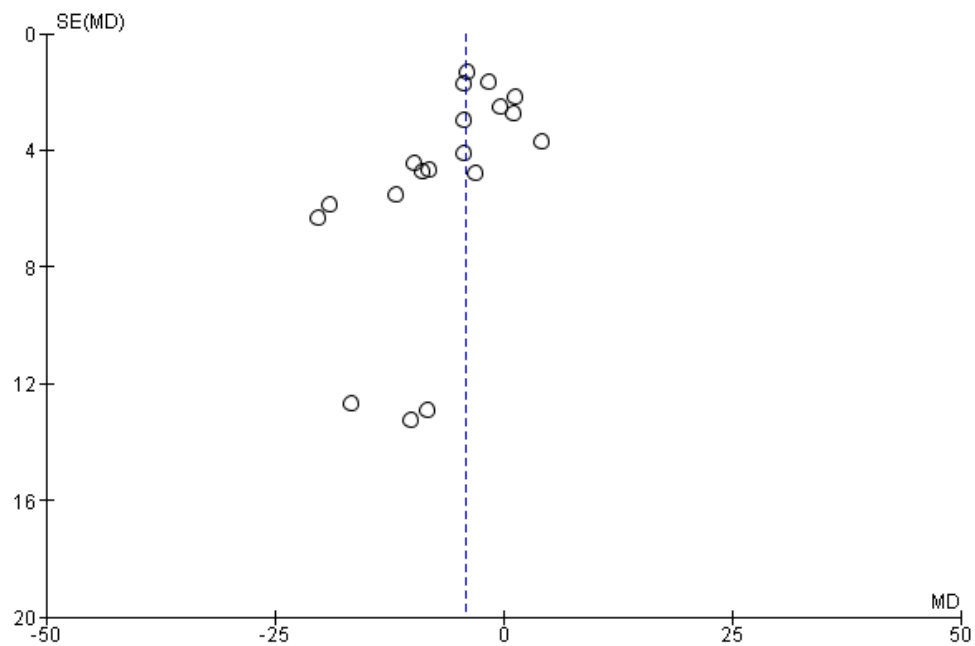
Disease Factors (Lower vs Higher PaO2/FiO2 Ratio)

Lower vs Higher PaO2/FiO2 Ratio, Alive vs Died (Mean Difference)



Disease Factors (Higher vs Lower PaCO2, mmHg)

Higher vs Lower PaCO2, mmHg, Alive vs Died (Mean Difference)



Disease Factors (Higher vs Lower PEEP, cm H2O)

Higher vs Lower PEEP, cm H2O, Alive vs Died (Mean Difference)

