

Supplementary Information No 5 Risk of bias assessment

Table 1 Risk of bias analysis for 28-day mortality

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
28-day mortality	Declercq 2021	Low	Low	Low	Low	Low	Low
	Derde 2021	Low	Low	Low	Low	Low	Low
	Kyriazopoulou 2021	Some concerns due to baseline differences	Low	Low	Low	Low	Some concerns
	Tharaux 2021	Low	Low	Low	Low	Low	Low

Table 2 Risk of bias analysis for 60-day mortality

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
60-day mortality	Declercq 2021	Low	Low	Low	Low	Low	Low

Table 3 Risk of bias analysis for mortality time-to-event at day 28

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Mortality time-to-event, 28 day	Tharaux 2021	Low	Low	Low	Low	Low	Low
	Kyriazopoulou 2021	Some concerns due to baseline differences	Low	Low	Low	Low	Some concerns

Table 4 Risk of bias analysis for mortality time-to-event at day 90

Outcome	Study	Risk of Bias					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Mortality time-to-event, 90 day	Tharoux 2021	Low	Low	Low	Low	Low	Low
	Derde 2021	Low	Low	Low	Low	Low	Low

Table 5 Risk of bias analysis for mortality at hospital discharge

Outcome	Study	Risk of Bias					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Mortality at hospital discharge	Derde 2021	Low	Low	Low	Low	Low	Low
	Declercq 2021	Low	Low	Low	Low	Low	Low

Table 6 Risk of bias analysis for clinical worsening: new need for invasive mechanical ventilation or death at day 28

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Clinical worsening: new need for invasive mechanical ventilation	Declercq 2021	Low	Low	Low	Low	Low	Low
	Kyriazopoulou 2021	Some concerns due to baseline differences	Low	Low	Low	Low	Some concerns

Table 7 Risk of bias analysis for clinical improvement: patients discharged alive

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Clinical improvement: patients discharged alive	Declercq 2021	Low	Low	Low	Low	Low	Low
	Kyriazopoulou 2021	Some concerns due to baseline differences	Low	Low	Low	Low	Some concerns
	Tharaux 2021	Low	Low	Low	Low	Low	Low

Table 8 Risk of bias analysis for serious adverse events

Bias							
Outcome	Study	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Serious adverse events	Declercq 2021	Low	Low	Low	Low	Low	Low
	Kyriazopoulou 2021	Some concerns due to baseline differences	Low	Low	Low	Low	Some concerns
	Tharoux 2021	Low	Low	Low	Low	Low	Low

Table 9 Risk of bias analysis for any adverse events

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Adverse events, any	Declercq 2021	Low	Low	Low	Some concerns due to lack of blinding	Low	Some concerns
	Tharaux 2021	Low	Low	Low	Some concerns due to lack of blinding	Low	Some concerns

Table 10 Risk of bias analysis for adverse events, grade 3-4

Outcome	Study	Risk of Bias Domain					
		Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Adverse events, grade 3-4	Declercq 2021	Low	Low	Low	Some concerns due to lack of blinding	Low	Some concerns