Figures and Tables

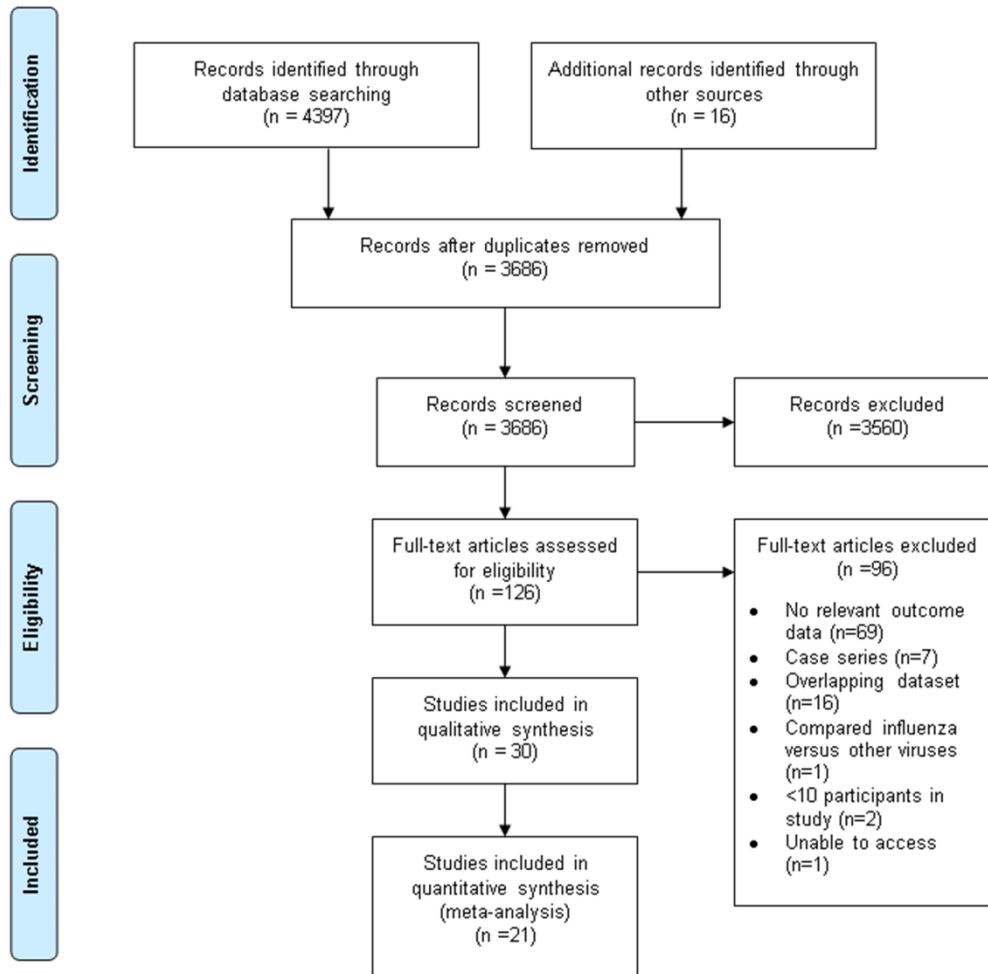**Figure 1** Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA)

flow diagram for the article selection process
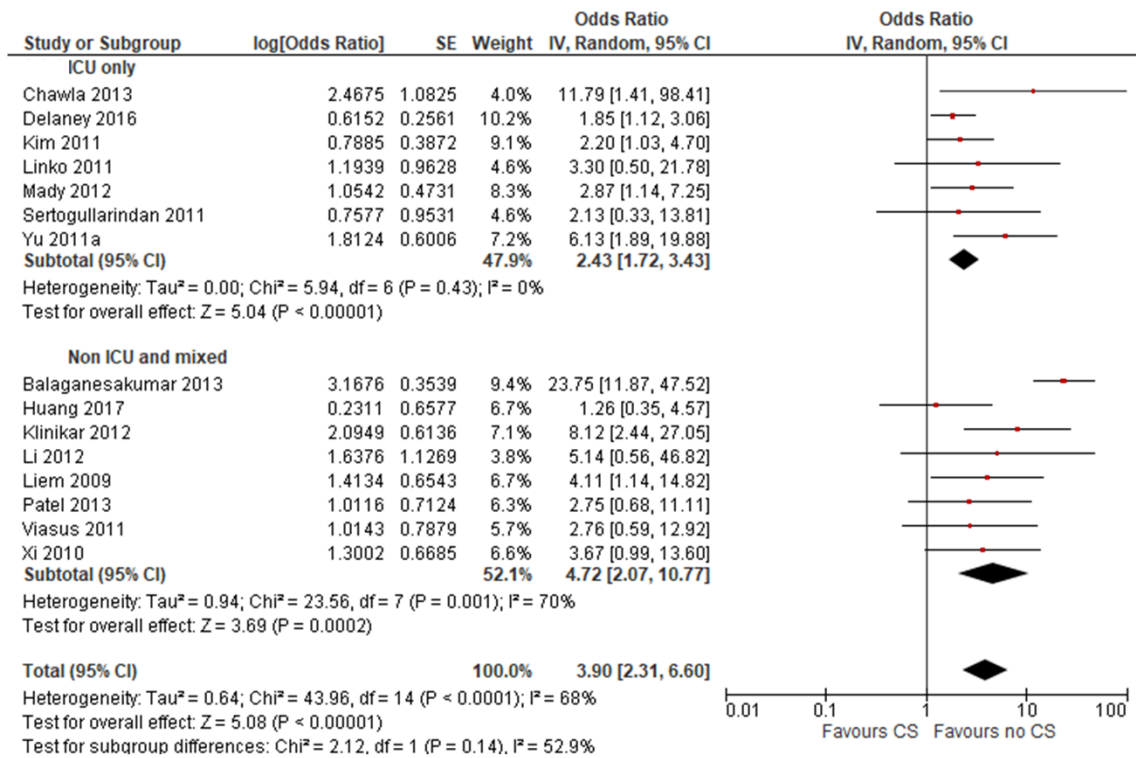
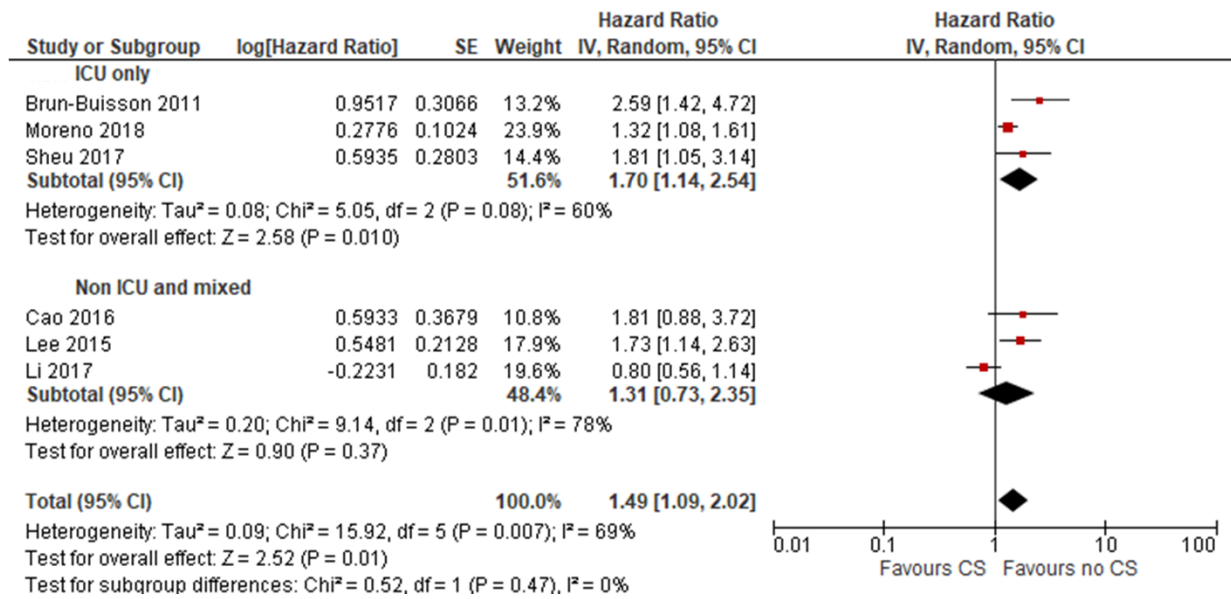| Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI	Odds Ratio IV, Random, 95% CI
ICU only					
Chawla 2013	2.4675	1.0825	4.0%	11.79 [1.41, 98.41]	
Delaney 2016	0.6152	0.2561	10.2%	1.85 [1.12, 3.06]	
Kim 2011	0.7885	0.3872	9.1%	2.20 [1.03, 4.70]	
Linko 2011	1.1939	0.9628	4.6%	3.30 [0.50, 21.78]	
Mady 2012	1.0542	0.4731	8.3%	2.87 [1.14, 7.25]	
Sertogullarindan 2011	0.7577	0.9531	4.6%	2.13 [0.33, 13.81]	
Yu 2011a	1.8124	0.6006	7.2%	6.13 [1.89, 19.88]	
Subtotal (95% CI)			**47.9%**	**2.43 [1.72, 3.43]**	
Heterogeneity: Tau² = 0.00; Chi² = 5.94, df = 6 (P = 0.43); I² = 0%					
Test for overall effect: Z = 5.04 (P < 0.00001)					
Non ICU and mixed					
Balaganesakumar 2013	3.1676	0.3539	9.4%	23.75 [11.87, 47.52]	
Huang 2017	0.2311	0.6577	6.7%	1.26 [0.35, 4.57]	
Klinikar 2012	2.0949	0.6136	7.1%	8.12 [2.44, 27.05]	
Li 2012	1.6376	1.1269	3.8%	5.14 [0.56, 46.82]	
Liem 2009	1.4134	0.6543	6.7%	4.11 [1.14, 14.82]	
Patel 2013	1.0116	0.7124	6.3%	2.75 [0.68, 11.11]	
Viasus 2011	1.0143	0.7879	5.7%	2.76 [0.59, 12.92]	
Xi 2010	1.3002	0.6685	6.6%	3.67 [0.99, 13.60]	
Subtotal (95% CI)			**52.1%**	**4.72 [2.07, 10.77]**	
Heterogeneity: Tau² = 0.94; Chi² = 23.56, df = 7 (P = 0.001); I² = 70%					
Test for overall effect: Z = 3.69 (P = 0.0002)					
Total (95% CI)			**100.0%**	**3.90 [2.31, 6.60]**	
Heterogeneity: Tau² = 0.64; Chi² = 43.96, df = 14 (P < 0.0001); I² = 68%					
Test for overall effect: Z = 5.08 (P < 0.00001)					
Test for subgroup differences: Chi² = 2.12, df = 1 (P = 0.14), I² = 52.9%					

0.01 0.1 1 10 100
Favours CS Favours no CS

Figure 2a

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
ICU only				
Brun-Buisson 2011	0.9517	0.3066	13.2%	2.59 [1.42, 4.72]
Moreno 2018	0.2776	0.1024	23.9%	1.32 [1.08, 1.61]
Sheu 2017	0.5935	0.2803	14.4%	1.81 [1.05, 3.14]
Subtotal (95% CI)			51.6%	1.70 [1.14, 2.54]
Heterogeneity: Tau² = 0.08; Chi² = 5.05, df = 2 (P = 0.08); I² = 60%				
Test for overall effect: Z = 2.58 (P = 0.010)				
Non ICU and mixed				
Cao 2016	0.5933	0.3679	10.8%	1.81 [0.88, 3.72]
Lee 2015	0.5481	0.2128	17.9%	1.73 [1.14, 2.63]
Li 2017	-0.2231	0.182	19.6%	0.80 [0.56, 1.14]
Subtotal (95% CI)			48.4%	1.31 [0.73, 2.35]
Heterogeneity: Tau² = 0.20; Chi² = 9.14, df = 2 (P = 0.01); I² = 78%				
Test for overall effect: Z = 0.90 (P = 0.37)				
Total (95% CI)			100.0%	1.49 [1.09, 2.02]
Heterogeneity: Tau² = 0.09; Chi² = 15.92, df = 5 (P = 0.007); I² = 69%				
Test for overall effect: Z = 2.52 (P = 0.01)				
Test for subgroup differences: Chi² = 0.52, df = 1 (P = 0.47), I² = 0%				

Figure 2b

Figure 2a and 2b Meta-analysis of studies reporting mortality stratified by ICU admission status.

Figure 2a Odds Ratios (ORs)

Figure 2b Hazard Ratios (HRs)

Footnote for figure 2: Mortality estimates determined using random effects modelling.

CI Confidence intervals; CS Corticosteroids; HR Hazard Ratio; OR Odds Ratio; SE Standard Error
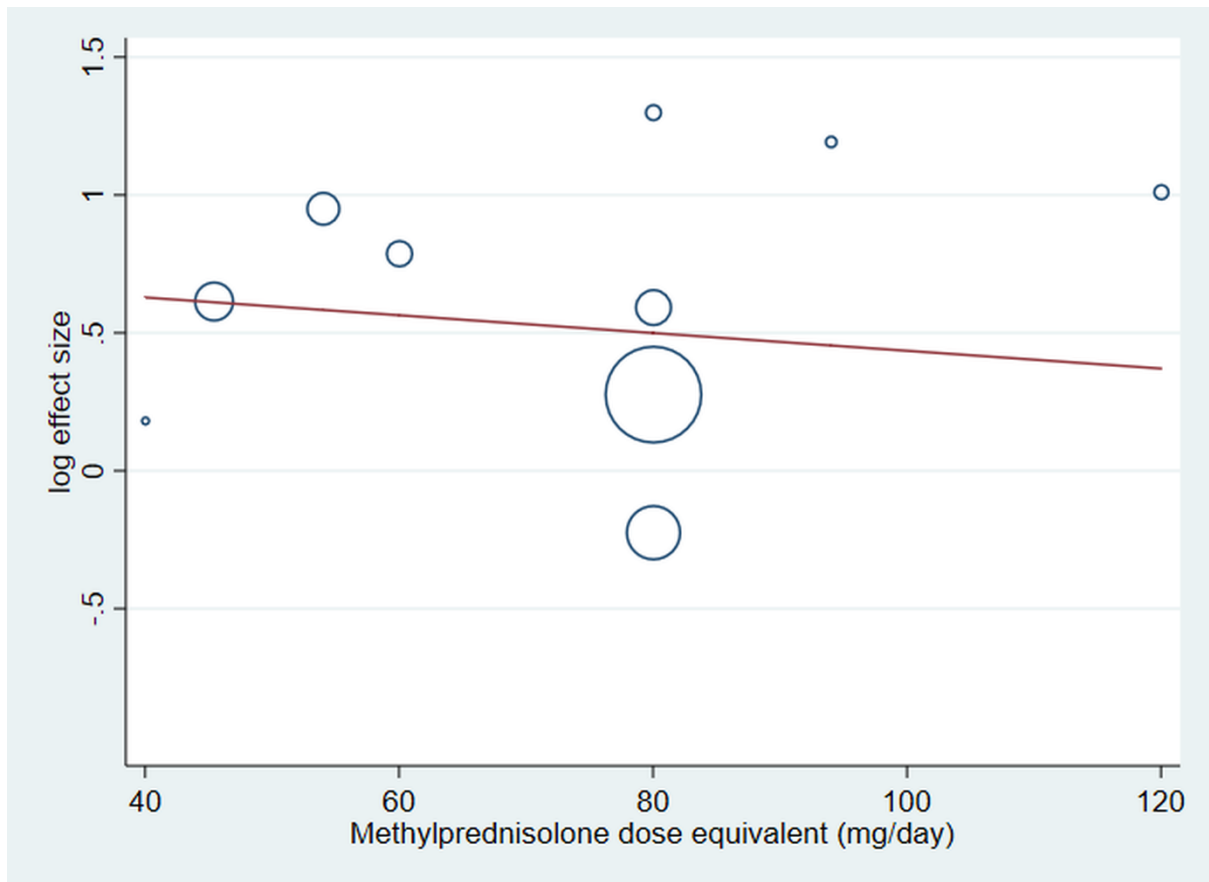
Figure 3 Random-effects meta-regression of log of mortality effect size and dose of corticosteroid expressed as methylprednisolone equivalent per day.

Footnote for figure 3: Estimates from each included study are represented as circles. The area of each circle is inversely proportional to the variance of the log effect size, with circle area representative of the weight of each study.

Table 1 Summary of studies reporting clinical outcomes other than mortality

Outcome	Study, Year (reference)	Corticosteroid Treatment	No Corticosteroid treatment (unless otherwise specified)	Unadjusted estimate of effect, 95% CI or p value
Critical disease	Han 2011 (49)	Early CS 12/17 (70.6)	Late or no CS 26/66 (39.4)	RR 1.8, 95% CI 1.2 to 2.8
Composite outcome of ICU admission/death	Jain 2009 (48)	29/86 (33.7)	27/153 (17.6)	OR 2.37, 95% CI 1.29 to 4.37
ICU admission	Li 2017 (34)	678/1055	282/1086	OR 5.13, 95% CI 4.26 to 6.17
ICU admission	Wirz 2016 (52)	1/11 (9.1)	1/13 (7.7)	OR 1.2, 95% CI 0.07 to 21.72
Rate of MV	Kim 2011 (30)	91/107 (85.0)	71/138 (51.4)	OR 5.37, 95% CI 2.87 to 10.05
Rate of MV	Linko 2011 (36)	53/72 (73.6)	14/60 (23.3)	OR 9.17, 95% CI 4.14 to 20.30
Rate of MV	Li 2017 (34)	367/1055 (34.8)	49/1086 (4.5)	OR 11.29, 95% CI 8.25 to 15.44
Rate of MV	Moreno 2018 (38)	506/604 (83.8)	921/1242 (74.2)	OR 1.78, 95% CI 1.35 to 2.35
Length of ICU stay: median days (IQR)	Brun-Buisson 2011 (15)	22 (13 to 39)	17 (11 to 30)	P = 0.11
Length of ICU stay: median days (IQR)	Moreno 2018 (38)	10 (5 to 19)	8 (5 to 18)	P = 0.50
LOS: mean days (SD)	Kim 2011 (30)	30.8 (36.9)	18.9 (20.0)	P < 0.001
LOS median days (IQR)	Kudo 2012 (51)	8.2 (5 to 14)	7.7 (3 to 14)	P = 0.607
LOS: median days (IQR)	Linko 2011 (36)	20 (12 to 34)	8 (5 to 13)	P < 0.001
LOS	Al-Busaidi 2016 (45)	Not reported	Not reported	MV coefficient 2.06, 95% CI 1.55 to 2.74 (adjusted for severity)
LOS	Lee 2015 (32)	Not reported	Not reported	Beta coefficient = 3.15 (95% CI 2.19 to 4.10); P value <.001
Time to effective hospital discharge: mean days (SD)	Wirz 2016 (52)	9.2 (9.4)	10.4 (8.0)	Unadjusted difference -1.57, 95% CI -8.78 to 5.65; adjusted difference -2.24, 95% CI -9.61 to 5.12
Hospital readmission at 30-days post discharge	Wirz 2016 (52)	1/11 (9.1)	1/13 (7.7)	OR 1.2, 95% CI 0.07 to 21.72; aOR 1.01, 95% CI 0.03 to 37.36
Time to clinical stability: median days (IQR)	Wirz 2016 (52)	4.0 (1.4 to 7.0)	5.0 (3.0 to 10.4)	Unadjusted HR 1.26, 95% CI 0.54 to 2.92; adjusted HR 4.50, 95% CI 1.17 to 17.25
Hospital-acquired infection				
ICU-acquired infection	Brun-Buisson 2011 (15)	38/83 (45.8)	44/125 (35.2)	OR 1.55, 95% CI 0.88 to 2.74

Hospital-acquired infection	Kim 2011 (30)	54/107 (50.5)	24/138 (17.4)	OR 4.84, 95% CI 2.71 to 8.65
Hospital-acquired infection	Viasus 2011 (42)	6/37 (16.2)	4/129 (3.1)	OR 6.05, 95% CI 1.61 to 22.75
Hospital-acquired infection	Cao 2016 (26)	17/65 (26.2)	18/65 (27.2)	OR 0.92, 95% CI 0.42 to 2.00
Hospital-acquired infection	Delaney 2016 (28)	92/265 (32.8)	89/310 (27.5)	OR 1.32 95% CI 0.93 to 1.88
Hospital-acquired infection	Lee 2015 (32)	58/600 (9.7)	55/2049) (2.7)	P value <0.001
Hospital-acquired infection	Li 2017 (34)	227/1055 (21.5)	46/1086 (4.2)	OR 6.20 (95% CI 4.46 to 8.62)