# **Supplementary file 4 Data and synthesis script**

2023-09-26

Dataset

id	ee	ne	ec	nc	factor	corticosteroid	outcome	RoB	zero
Van Runnard 2006	1	15	1	16	antepartum	prednisolone	Abruptio placenta	low	F
Magann 1994	3	12	3	13	antepartum	dexa	Apgar score at 5 minutes < 7	some concerns	F
Van Runnard 2006	1	16	2	17	antepartum	prednisolone	Apgar score at 5 minutes < 7	low	F
Ozer 2009	23	30	26	30	antepartum	beta	Cesarean section	low	F
Van Runnard 2006	15	15	14	16	antepartum	prednisolone	Cesarean section	low	F
Fonseca 2019	6	35	8	38	mixed	dexa	Composite morbidity	low	F
Van Runnard 2006	1	15	4	16	antepartum	prednisolone	Composite morbidity	low	F
Ozer 2009	1	30	0	30	antepartum	beta	Dialysis	low	F
Fonseca 2005	8	66	10	66	mixed	dexa	Eclampsia	low	F
Fonseca 2019	2	40	1	41	mixed	dexa	Eclampsia	low	F
Magann 1994	1	12	0	13	antepartum	dexa	ICH	some concerns	F
Van Runnard 2006	4	16	2	17	antepartum	prednisolone	ICH	low	F
Fonseca 2005	3	66	1	66	mixed	dexa	Maternal death	low	F
Fonseca 2019	0	42	2	45	mixed	dexa	Maternal death	low	F
Katz 2008	2	56	2	49	postpartum	dexa	Maternal death	low	F
Ozer 2009	0	30	0	30	antepartum	beta	Maternal death	low	Т
Van Runnard 2006	0	15	1	16	antepartum	prednisolone	Maternal death	low	F
Vigil-De Gracia 1997	0	17	1	17	postpartum	dexa	Maternal death	high	F
Ozer 2009	0	30	1	30	antepartum	beta	Maternal liver morbidity	low	F
Van Runnard 2006	0	15	3	16	antepartum	prednisolone	Maternal liver morbidity	low	F
Fonseca 2005	3	66	1	66	mixed	dexa	Maternal pulmonary edema	low	F
Fonseca 2019	0	41	1	43	mixed	dexa	Maternal pulmonary edema	low	F
Katz 2008	2	56	5	49	postpartum	dexa	Maternal pulmonary edema	low	F

Ozer 2009	1	30	1	30	antepartum	beta	Maternal pulmonary edema	low	F
Fonseca 2005	6	66	8	66	mixed	dexa	Maternal renal failure	low	F
Fonseca 2019	1	37	6	42	mixed	dexa	Maternal renal failure	low	F
Katz 2008	9	56	12	49	postpartum	dexa	Maternal renal failure	low	F
Ozer 2009	2	30	3	30	antepartum	beta	Maternal renal failure	low	F
Yalcin 1998	3	15	3	15	postpartum	dexa	Maternal renal failure	some concerns	F
Van Runnard 2006	0	16	2	17	antepartum	prednisolone	Necrotizing enterocolitis	low	F
Magann 1994	3	12	1	13	antepartum	dexa	Neonatal RDS	some concerns	F
Van Runnard 2006	6	16	8	17	antepartum	prednisolone	Neonatal RDS	low	F
Magann 1994	1	12	3	13	antepartum	dexa	Perinatal death	some concerns	F
Van Runnard 2006	3	16	4	17	antepartum	prednisolone	Perinatal death	low	F
Fonseca 2005	12	66	10	66	mixed	dexa	Platelet transfusion	low	F
Fonseca 2019	12	42	15	45	mixed	dexa	Platelet transfusion	low	F

# **Synthesis**

# **Pre-specified outcomes**

- 1. Maternal Death
- 2. Liver morbidity (hematoma, rupture, failure)
- 3. Acute pulmonary edema
- 4. Acute renal failure
- 5. Dialysis
- 6. Platelet transfusion
- 7. Perinatal death

#### Maternal Death

### Pairwise meta-analysis

Study	RR	95%-CI %	W(common)	
Fonseca 2005	3.0000	[0.3202; 28.1042]	25.4	
Fonseca 2019	0.2141	[0.0106; 4.3328]	14.1	
Katz 2008	0.8750	[0.1280; 5.9809]	34.5	
Ozer 2009	NA		0.0	
Van Runnard 2006	0.3548	[0.0156; 8.0730]	13.0	
Vigil-De Gracia 1997	0.3333	[0.0146; 7.6344]	13.0	

Number of studies: k = 5

Number of observations: o = 449

Number of events: e = 12

	RR	95%-CI	Z	p-value
Common effect model	0.7700	[0.2492; 2.3799]	-0.45	0.6499

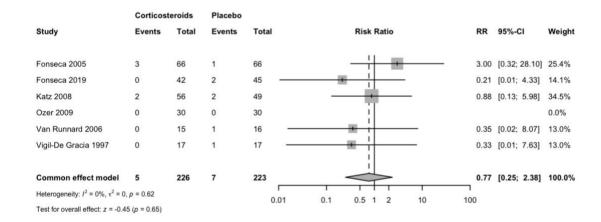
## Quantifying heterogeneity:

tau^2 = 0 [0.0000; 7.4236]; tau = 0 [0.0000; 2.7246]

I^2 = 0.0% [0.0%; 79.2%]; H = 1.00 [1.00; 2.19]

Test of heterogeneity: Q = 2.64; d.f. = 4; p-value 0.6192

- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Continuity correction of 0.5 in studies with zero cell frequencies

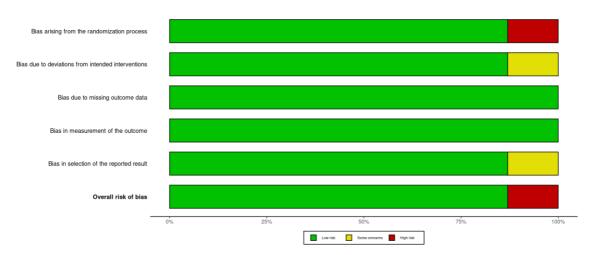


Risk of bias

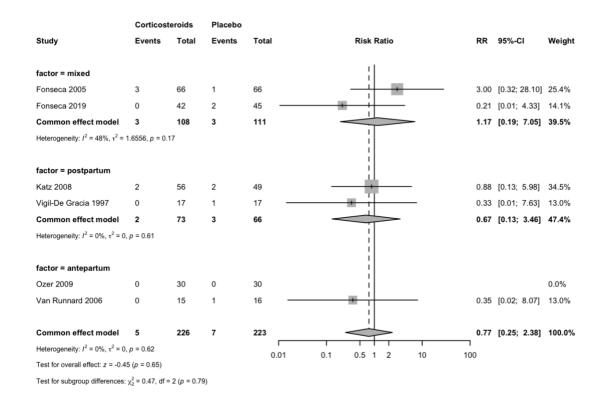
# Summary traffic-light plot of risk-of-bias assessments

				Risk of bia	s domains						
		D1	D2	D3	D4	D5	Overall				
	Fonseca 2005	•	•	•	•	•	•				
Study	Fonseca 2019	•	•	•	•	•	•				
	Katz 2008	•	•	•	•	•	•				
Str	Ozer 2009	•	•	•	•	•	•				
	Van Runnard 2006	•	•	•	•	•	•				
	Vigil de Garcia 1997	8	-	•	•	-	8				
	Domains: D1: Bias arising from the randomization process. D2: Bias due to deviations from intended intervention. D3: Bias due to missing outcome data. D4: Bias in measurement of the outcome. D5: Bias in selection of the reported result.										

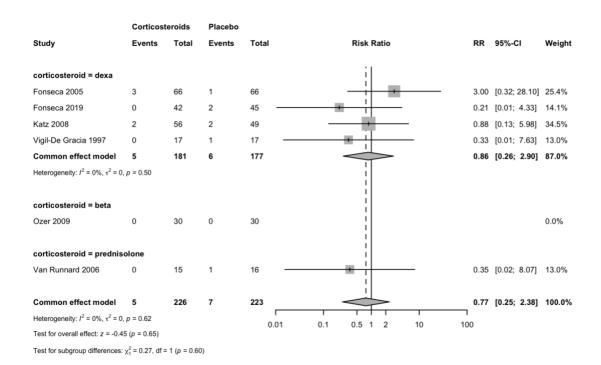
# Summary weighted barplot of risk-of-bias assessments



Subgroup analysis: Antepartum vs postpartum vs mixed



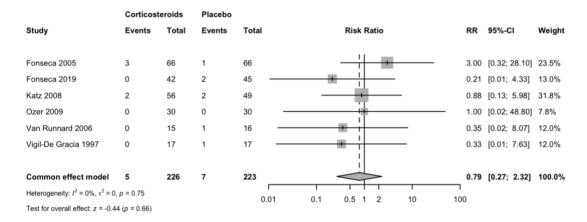
Subgroup analysis: Dexa vs Beta vs Prednisolone



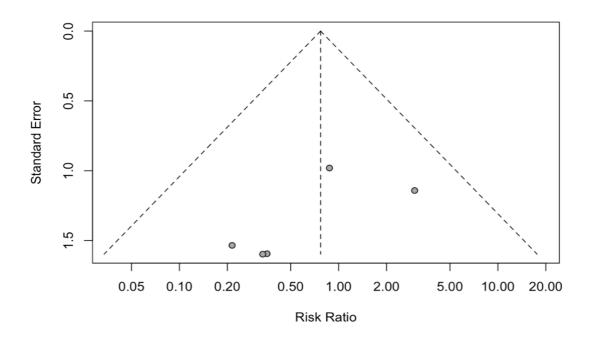
# Sensitivity analysis: Low RoB

	Corticosteroids		Placebo	Placebo					
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight	
Fonseca 2005	3	66	1	66	<del>    •</del>	3.00	[0.32; 28.10]	29.2%	
Fonseca 2019	0	42	2	45 —		0.21	[0.01; 4.33]	16.2%	
Katz 2008	2	56	2	49		0.88	[0.13; 5.98]	39.6%	
Ozer 2009	0	30	0	30	i			0.0%	
Van Runnard 2006	0	15	1	16 -		0.35	[0.02; 8.07]	15.0%	
					1				
Common effect model	5	209	6	206		0.87	[0.26; 2.92]	100.0%	
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $\mu$	= 0.51			0.01	0.1 0.5 1 2 10 100	1			
Test for overall effect: z = -0.22	(p = 0.83)			0.01	0.1 0.5 1 2 10 100	,			

Sensitivity analysis: Studies with zero events included



# Funnel plot



# Acute pulmonary edema

RR 95%-CI %W(common)

Fonseca 2005 3.0000 [0.3202; 28.1042] 24.2

Fonseca 2019 0.3494 [0.0146; 8.3368] 12.0

Katz 2008 0.3500 [0.0711; 1.7238] 47.6

Ozer 2009 1.0000 [0.0655; 15.2598] 16.3

Number of studies: k = 4

Number of observations: o = 381

Number of events: e = 14

RR 95%-CI z p-value

Common effect model 0.6975 [0.2323; 2.0944] -0.64 0.5207

Quantifying heterogeneity:

tau^2 = 0.1164 [0.0000; 13.2337]; tau = 0.3412 [0.0000; 3.6378]

I^2 = 0.0% [0.0%; 84.7%]; H = 1.00 [1.00; 2.56]

Test of heterogeneity:

Q d.f. p-value

2.60 3 0.4572

- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Continuity correction of 0.5 in studies with zero cell frequencies

Corticosteroids		Placebo					
Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
3	66	1	66	<del>- ;   •</del>	3.00	[0.32; 28.10]	24.2%
0	41	1	43 —		0.35	[0.01; 8.34]	12.0%
2	56	5	49	<del> </del>	0.35	[0.07; 1.72]	47.6%
1	30	1	30	<del></del>	1.00	[0.07; 15.26]	16.3%
6	193	8	188		0.70	[0.23; 2.09]	100.0%
1164, p = 0.46			0.01	01 05 1 2 10 10	l no		
4(p = 0.52)			0.01	0.1 0.0 1 2 10 10	,,		
	3 0 2 1 6 1164, p = 0.46	3 66 0 41 2 56 1 30 6 193 1164, $\rho = 0.46$	Events         Total         Events           3         66         1           0         41         1           2         56         5           1         30         1           6         193         8           1164, ρ = 0.46	Events         Total         Events         Total           3         66         1         66           0         41         1         43           2         56         5         49           1         30         1         30           6         193         8         188           1164, p = 0.46         0.01         0.01	Events Total Events Total Risk Ratio  3 66 1 66 0 41 1 43 2 56 5 49 1 30 1 30 6 193 8 188 0.01 0.1 0.5 1 2 10 10	Events         Total         Events         Total         Risk Ratio         RR           3         66         1         66         3.00           0         41         1         43         3.00           2         56         5         49         4.00           1         30         1         30         1.00           6         193         8         188         0.70           1164, p = 0.46         0.01         0.1         0.5         1         2         10         100	Events Total Events Total Risk Ratio RR 95%-CI  3 66 1 66

#### Acute renal failure

Study	RR	95%-CI %	W(common)
Fonseca 2005	0.7500	[0.2754; 2.0428]	26.7
Fonseca 2019	0.1892	[0.0239; 1.4998]	6.3
Katz 2008	0.6563	[0.3025; 1.4238]	44.8
Ozer 2009	0.6667	[0.1198; 3.7087]	9.1
Yalcin 1998	1.0000	[0.2390; 4.1844]	13.1

Number of studies: k = 5 Number of observations: o = 406 Number of events: e = 53

	RR	95%-CI	Z	p-value
Common effect model	0.6658	[0.3965; 1.1179]	-1.54	0.1239

# Quantifying heterogeneity:

tau^2 = 0 [0.0000; 2.4607]; tau = 0 [0.0000; 1.5687] I^2 = 0.0% [0.0%; 79.2%]; H = 1.00 [1.00; 2.19]

Test of heterogeneity: Q = 1.78; d.f. = 4; p-value = 0.7753

### Details on meta-analytical method:

- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau

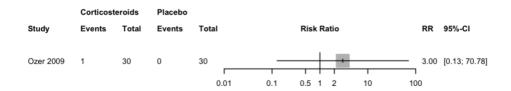
	Corticoste	eroids	Placebo					
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
Fonseca 2005	6	66	8	66	<del>-  </del>	0.75	[0.28; 2.04]	26.7%
Fonseca 2019	1	37	6	42		0.19	[0.02; 1.50]	6.3%
Katz 2008	9	56	12	49		0.66	[0.30; 1.42]	44.8%
Ozer 2009	2	30	3	30	<del></del>	0.67	[0.12; 3.71]	9.1%
Yalcin 1998	3	15	3	15	<del>- ¦ +</del>	1.00	[0.24; 4.18]	13.1%
Common effect model	21	204	32	202		0.67	[0.40; 1.12]	100.0%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ ,	p = 0.78			0.01	0.1 0.5 1 2 10 10	0		
Test for overall effect: $z = -1.54$	(p = 0.12)			0.01	5.1 5.5 1 2 10 10	•		

# Dialysis

Number of observations: o = 60 Number of events: e = 1

Study	RR	95%-CI	Z	p-value
Ozer 2009	3.0000	[0.1271; 70.7833]	0.68	0.4958

Details: Continuity correction of 0.5



## Liver morbidity

RR 95%-CI %W(common)

Ozer 2009 0.3333 [0.0141; 7.8648] 45.4

Van Runnard 2006 0.1521 [0.0085; 2.7116] 54.6

Number of studies: k = 2

Number of observations: o = 91

Number of events: e = 4

RR 95%-Cl z p-value

Common effect model 0.2171 [0.0258; 1.8257] -1.41 0.1598

Quantifying heterogeneity:

tau^2 = 0; tau = 0; I^2 = 0.0%; H = 1.00

Test of heterogeneity:

Q d.f. p-value

0.13 1 0.7191

- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Continuity correction of 0.5 in studies with zero cell frequencies

	Corticost	eroids	Placebo					
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
Ozer 2009	0	30	1	30 —	<del> </del>	0.33	[0.01; 7.86]	45.4%
Van Runnard 2006	0	15	3	16 ←		0.15	[0.01; 2.71]	54.6%
Common effect model	0	45	4	46		0.22	[0.03; 1.83]	100.0%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ ,	p = 0.72			0.01	0.1 0.5 1 2 10	コ 100		
Test for overall effect: $z = -1.41$	1 (p = 0.16)			0.01	0.1 0.5 1 2 10	100		

### Platelet transfusion

RR 95%-CI %W(common)

Fonseca 2005 1.2000 [0.5574; 2.5832] 40.5

Fonseca 2019 0.8571 [0.4556; 1.6126] 59.5

Number of studies: k = 2

Number of observations: o = 219

Number of events: e = 49

RR 95%-Cl z p-value

Common effect model 0.9821 [0.6031; 1.5994] -0.07 0.9422

Quantifying heterogeneity:

tau^2 = 0; tau = 0; I^2 = 0.0%; H = 1.00

Test of heterogeneity:

Q d.f. p-value

0.44 1 0.5069

- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2

	Corticosteroids		Placebo						
	Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
						1			
	Fonseca 2005	12	66	10	66	-	1.20	[0.56; 2.58]	40.5%
	Fonseca 2019	12	42	15	45	-	0.86	[0.46; 1.61]	59.5%
						T			
	Common effect model	24	108	25	111	<b>♦</b>	0.98	[0.60; 1.60]	100.0%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $\rho = 0.51$			0.04	1 05 1 0 10	100				
	Test for overall effect: $z = -0.07$	(p = 0.94)			0.01 0.	.1 0.5 1 2 10	100		

### Perinatal death

RR 95%-CI %W(common)

Magann 1994 0.3611 [0.0432; 3.0169] 28.3

Van Runnard 2006 0.7969 [0.2103; 3.0197] 71.7

Number of studies: k = 2

Number of observations: o = 58

Number of events: e = 11

RR 95%-Cl z p-value

Common effect model 0.6372 [0.2062; 1.9693] -0.78 0.4337

Quantifying heterogeneity:

tau^2 = 0; tau = 0; I^2 = 0.0%; H = 1.00

Test of heterogeneity:

Q d.f. p-value

0.38 1 0.5359

- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2

		Corticosteroids		Placebo					
	Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
	Magann 1994	1	12	3	13		0.36	[0.04; 3.02]	28.3%
	Van Runnard 2006	3	16	4	17	<del></del>	0.80	[0.21; 3.02]	71.7%
						丁			
	Common effect model	4	28	7	30		0.64	[0.21; 1.97]	100.0%
		-		•			7 0.04	[0.21, 1.07]	100.070
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $\rho = 0.54$			0.01	0.1 0.5 1 2 10	100				
	Test for overall effect: $z = -0.78$	(p = 0.43)			0.01	0.1 0.5 1 2 10	100		