# Effects of corticosteroids in patients with sickle cell disease and acute complications: a systematic review and meta-analysis

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Received: September 28, 2021.
Accepted: January 4, 2022.
Prepublished: January 13, 2022.

https://doi.org/10.3324/haematol.2021.280105

©2022 Ferrata Storti Foundation Haematologica material is published under a CC-BY-NC license © ①⑤ Supplemental data: Effects of corticosteroids in patients with sickle cell disease and acute complications: a systematic review and meta-analysis

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\* equal contribution

#### **METHOD**

#### Data extraction

Two authors (JL and EB) independently checked titles and abstracts identified from the searches. We obtained the full text of all potentially relevant studies and the authors decided which trials fitted the inclusion criteria. If the two authors did not agree, the authors achieved consensus by discussion or adjudication by a third reviewer (AMD). Two authors (JL, EB) independently extracted data. The following data were recorded from each selected study: year of publication, study design, details on corticosteroids therapy, population characteristics (age, comorbidities, and diseases), rate of readmission, mean time to readmission, length of hospital stay, transfusion requirement, duration of analgesic therapy, number of opioids doses, incidence rate of oxygen therapy, duration of oxygen therapy. Missing data were requested from authors of identified studies when necessary

## Supplemental table S1: Rate of severe ACS in retrospective trials

	Standard treatment group	Corticosteroids group	P value		
Strouse 2008 <sup>22</sup> , n (%)	8 (9)	11 (29)	0.01 a		
Sobota 2009 <sup>24</sup> , n (%)	755 (17)	276 (32)	< 0.001 <sup>a</sup>		
Kumar 2010 <sup>23</sup> , n (%)	1 (4)	21 (40)	0.001 b		

Results are reported as number (percentage). Between-group comparisons were performed using Chi 2 test <sup>a</sup> and Fisher's exact test <sup>b</sup> when appropriate.

Abbreviations: ACS: Acute Chest syndrome

# Supplemental table S2: Reasons for readmission in included studies

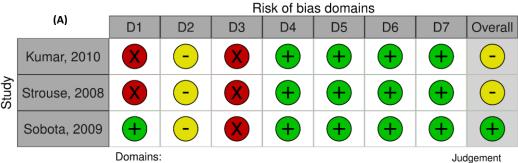
Trial, year	Reasons for readmission
Bernini, 1998 <sup>20</sup>	Painful crisis n=4 Stroke n=1* ACS n=1 Aplastic crisis n=1
Griffin, 1994 <sup>19</sup>	Painful crisis n=5
Quinn, 2011 <sup>21</sup>	Painful crisis n=1
Strouse, 2008 <sup>22</sup>	Painful crisis n=13 Painful crisis and fever n=3 ACS n=2 Hemorrhagic stroke n=2 ** NI n=2
Sobota, 2009 <sup>24</sup>	NI
Kumar, 2010 <sup>23</sup>	Painful crisis n=8 Hemolytic reaction n=1 Worsening ACS n=1

<sup>\*</sup> Patient had received dexamethasone

**Abbreviations: NI:** no information; **ACS:** acute chest syndrome

<sup>\*\*</sup> Both had received dexamethasone and transfusion

## Supplementary figure S1: Risk of bias analysis for retrospective (A) and prospective (B) studies.



Domains:

D1: Bias due to confounding.

D2: Bias due to selection of participants.
D3: Bias in classification of interventions.

D4: Bias due to deviations from intended interventions.

D5: Bias due to missing data.

D6: Bias in measurement of outcomes. D7: Bias in selection of the reported result.

(p)	Risk of bias domains									
(B)	D1	D2	D3	D4	D5	Overall				
Bernini, 1998	+	-	-	+	+	+				
Quinn, 2011	-	+	+	-	-	-				
Griffin, 1994	-	-	-	-	-	(-)				

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.

Judgement

Some concerns

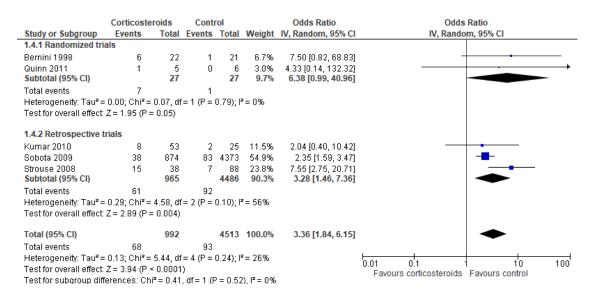
Serious Moderate

Low

Low

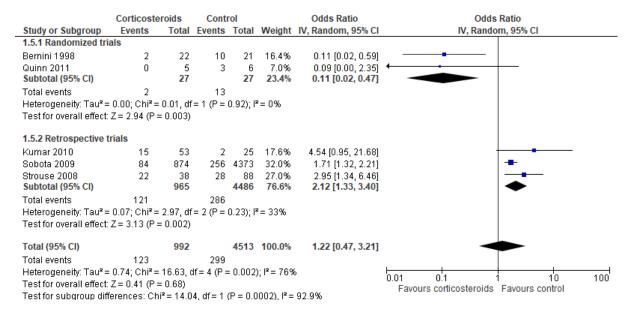
**Supplementary figure S2:** Sensitivity analysis of the effect of corticosteroids on readmission rate (A), length of stay (B) and transfusion requirement (C) in studies on acute chest syndrome

(A)



(B)

	Cortico	ostero	ids	Co	ntro	I		Mean Difference	Me	ean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV,	Random, 95% CI		
Bernini 1998	47	16	22	80	50	21	27.2%	-33.00 [-55.41, -10.59]		_		
Quinn 2011	42	9	5	62	14	6	72.8%	-20.00 [-33.70, -6.30]	-	-		
Total (95% CI)			27			27	100.0%	-23.54 [-35.23, -11.85]	<	▶		
Heterogeneity: $Tau^2 = 0.00$ ; $Chi^2 = 0.94$ , $df = 1$ ( $P = 0.33$ ); $I^2 = 0\%$ Test for overall effect: $Z = 3.95$ ( $P < 0.0001$ )							-100 -50	0	50	100		
restior overall ellect	Z = 3.90 i	(F ~ U.	.0001)						Favours corticoste	roids Favours co	ontrol	



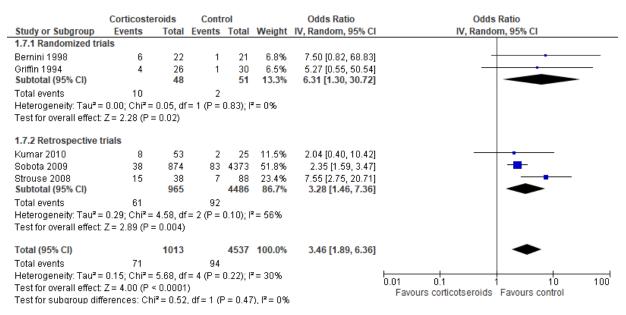
# **Supplementary Table S3:** Effect estimate for complete and sensitivity analysis in studies on acute chest syndrome.

	Complete analysis (6 studies)	Sensitivity analysis (5 studies on ACS)		
Readmission rate (OR)	3.21 [1.97, 5.24]	3.36 [1.84, 6.15]		
Length of stay (MD)	-24.44 [-35.28, -13.60]	-23.54 [-35.23, -11.85]		
Transfusion requirement (OR)	0.98 [0.38, 2.53]	1.22 [0.47, 3.21]		

OR: Odds ratio; MD: mean difference

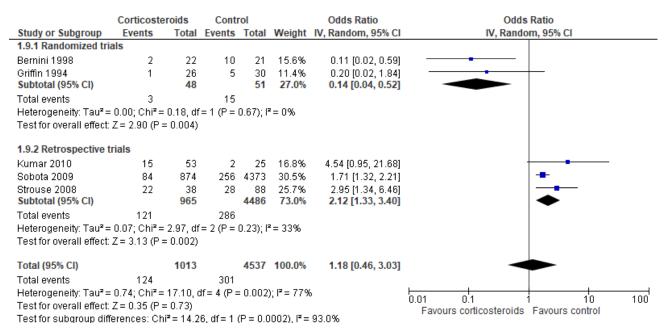
**Supplementary figure S3:** Sensitivity analysis of the effect of corticosteroids on readmission rate (A), length of stay (B) and transfusion requirement (C) in studies involving pediatric population

### (A)



(B)

	Cortico	ostero	ids	Co	ntro	I		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Bernini 1998	47	16	22	80	50	21	62.6%	-33.00 [-55.41, -10.59]	<del></del>
Griffin 1994	92	45	26	122	65	30	37.4%	-30.00 [-58.99, -1.01]	
Total (95% CI)			48			51	100.0%	-31.88 [-49.61, -14.15]	•
Heterogeneity: Tau²: Test for overall effect				1 (P = 0	).87);	<b>=</b> 0%	5		-100 -50 0 50 100 Favours corticosteroids Favours control



# **Supplementary Table S4:** Effect estimate for complete and sensitivity analysis in studies involving pediatric population.

	Complete analysis (6 studies)	Sensitivity analysis (5 studies on pediatric population )			
Readmission rate (OR)	3.21 [1.97, 5.24]	3.46 [1.89, 6.36]			
Length of stay (MD)	-24.44 [-35.28, -13.60]	-31.88 [-49.61, -14.15]			
Transfusion requirement (OR)	0.98 [0.38, 2.53]	1.18 [0.46, 3.03]			

OR: Odds ratio; MD: mean difference