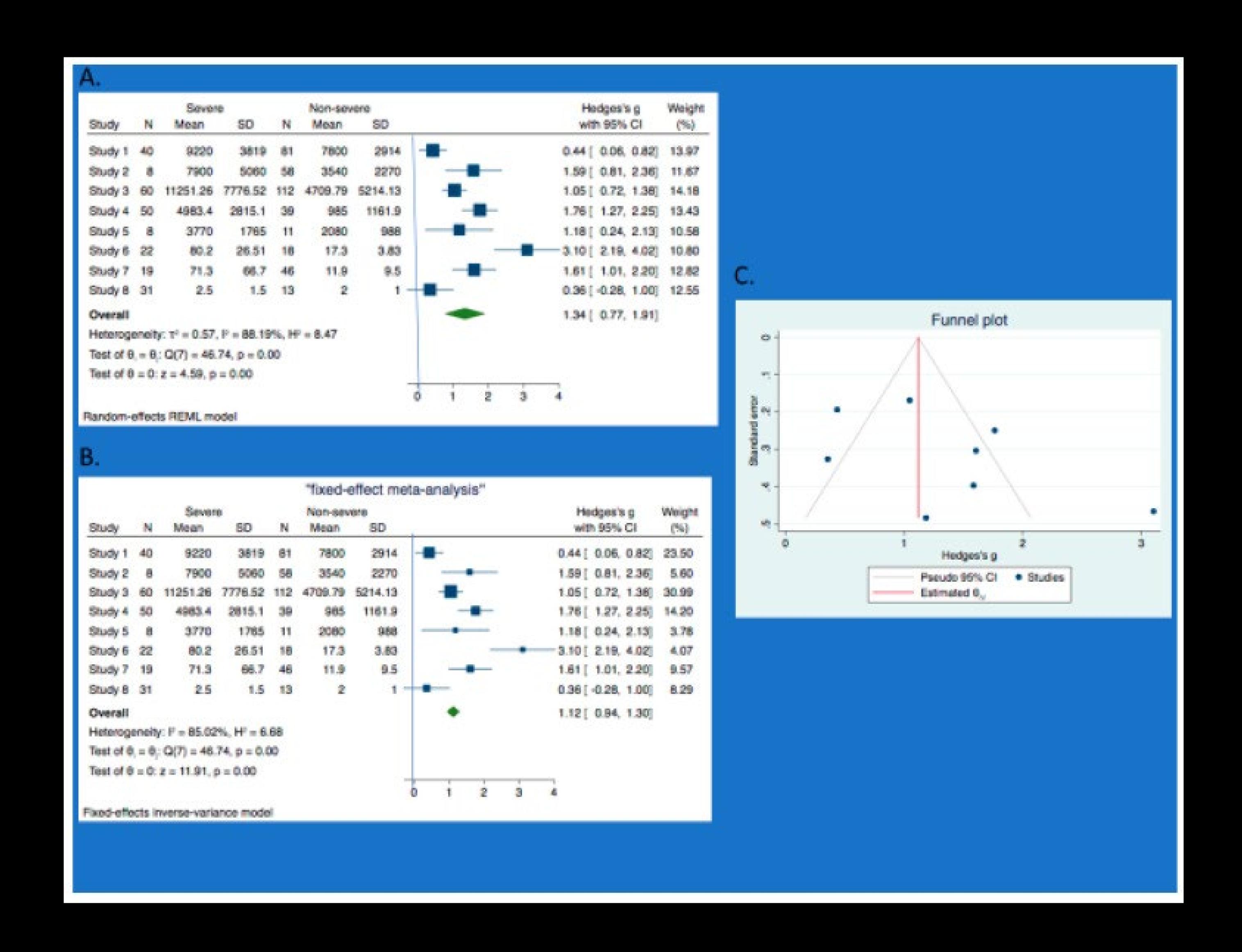
Calprotectin Metadata in COVID-19



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- * Circulating calprotectin is elevated in COVID-19
- * Higher levels in severe cases of COVID-19 offer opportunity for risk stratification and outcome prediction
 - * Potential therapeutic strategy as a druggable target for TASQUINIMOD

Calprotectin, an Emerging Biomarker of Interest in COVID-19: A Systematic Review and Meta-Analysis

Raphael Udeh, Shailesh Advani, Luis García de Guadiana Romualdo and Xenia Dolja-Gore **RESULTS**

INTRODUCTION

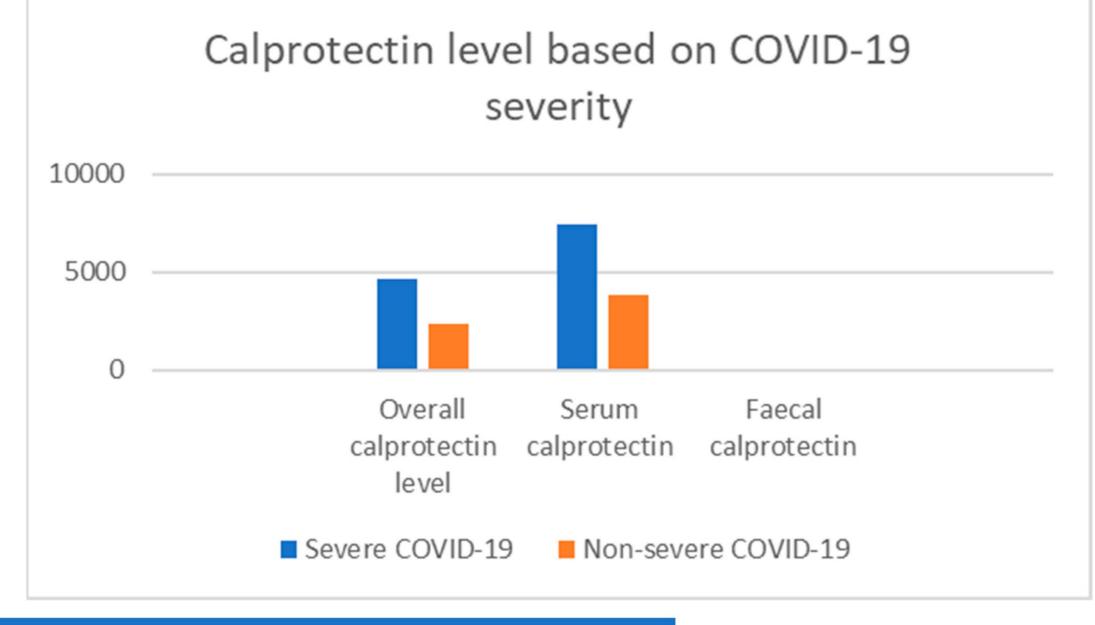
- 19?
- RQ 2: What is the role of calprotectin as a marker of
- Background: Varied clinical course described for COVID-19 – such that mild/moderate cases often recover while severe cases could end up in the intensive care unit [ICU] or die
- Recent evidence had earlier shown that calprotectin has an expanded potential role as a diagnostic and stratifying tool in COVID-19 patients [Silvin et al, 2020].
- Hence, our systematic review aimed at evaluating calprotectin levels in severe and non-severe cases of COVID-19.

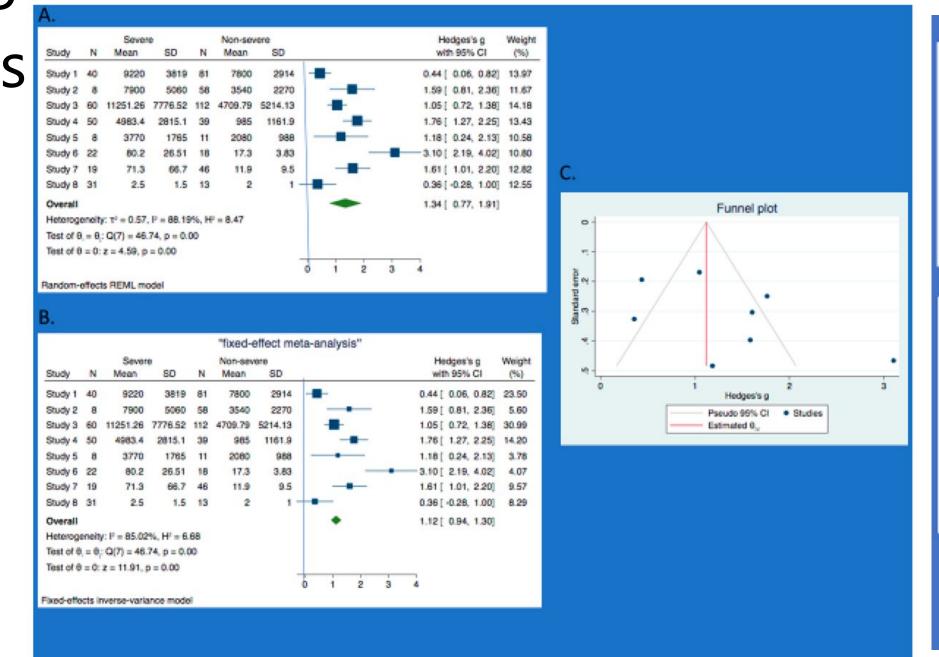
METHODS

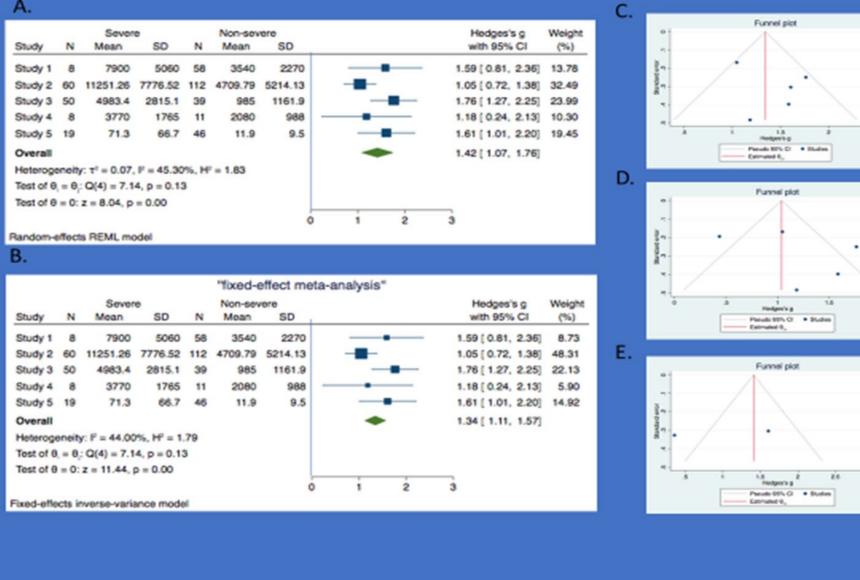
Databases searched include MEDLINE, EMBASE, the Cochrane Library, Web of Science, and MedRxiv.

• RQ 1: What is the difference in calprotectin level • A pooled analysis of data in the 8 quantitative studies from between patients with and without severe COVID- 613 patients who were RT-PCR positive for COVID-19 (average age = 55 years; 52% males) showed an overall estimate as 1.34 (95%CI: 0.77, 1.91).

disease progression and as an outcome predictor? Stata was further employed to carry out an in-depth investigation of the in-between study heterogeneity. All the other correlations in the ammo bar.







CONCLUSION

Stata was employed in meta-analysis to compare "Calprotectin is significantly elevated in COVID-19 patients who develop the severe form of the disease, and it also has the serum/faecal levels of calprotectin between severe and non-severe COVID-19 infections. prognostic importance.

REFERENCES

*Silvin et al. Cell. 2020 Sep 17;182(6):1401-18.

Calprotectin Metadata in COVID-19 | Recent Evidence

Cell

Elsevier

Elevated Calprotectin and Abnormal Myeloid Cell Subsets Discriminate Severe from Mild COVID-19

Aymeric Silvin, Nicolas Chapuis, [...], and Eric Solary Additional article information

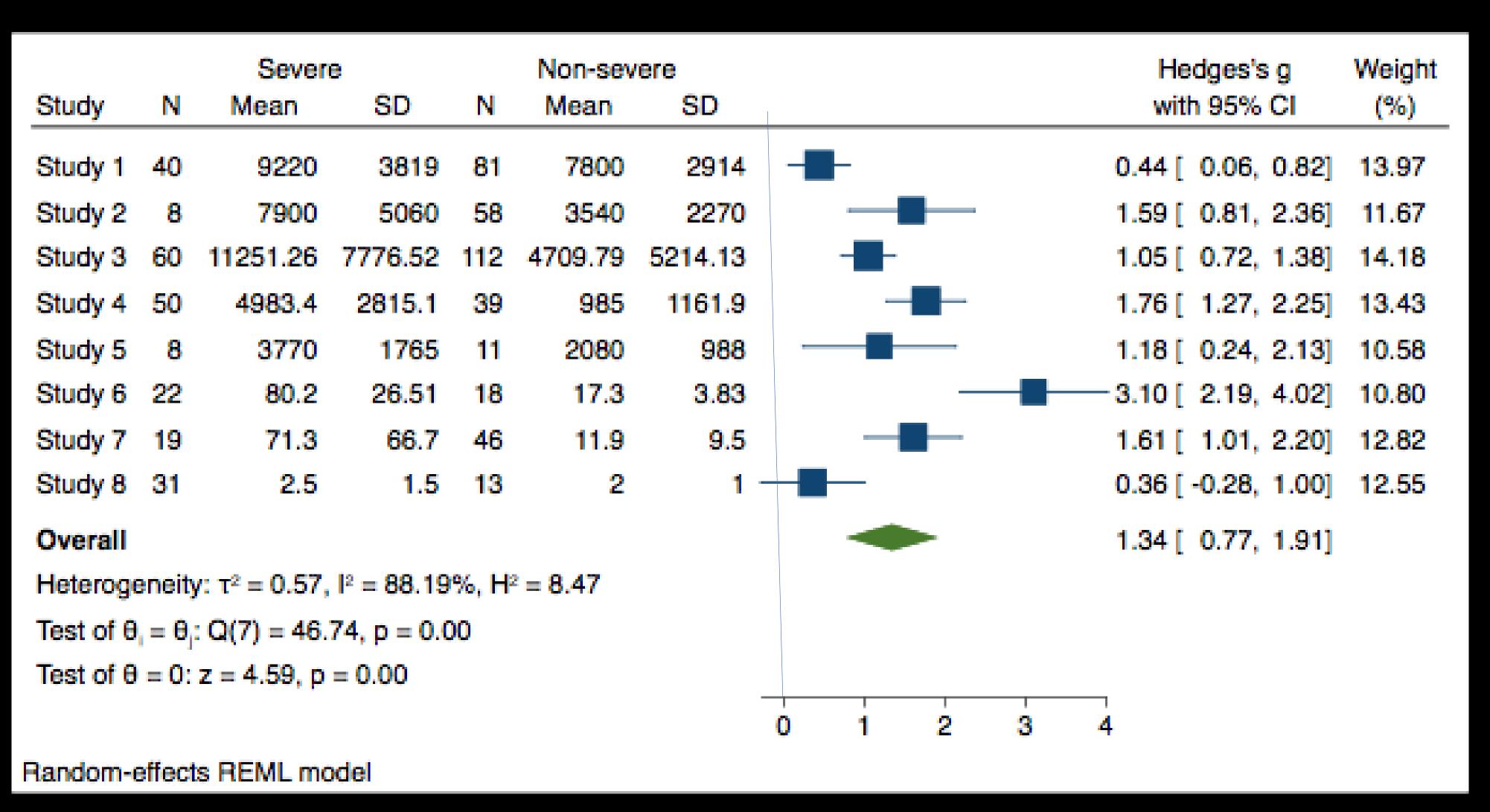
Associated Data

Supplementary Materials

Data Availability Statement

Abstract

• Blood myeloid cells are known to be dysregulated in coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2. It is unknown whether the innate myeloid response differs with disease severity and whether markers of innate immunity discriminate high-risk patients. Thus, we <u>performed high-dimensional flow cytometry and single-cell RNA sequencing of COVID-19 patient peripheral blood cells and detected disappearance of non-classical CD14^{Low}CD16^{High} monocytes, accumulation of HLA-DR^{Low} classical monocytes (Human Leukocyte Antigen - DR isotype), and <u>release of massive amounts of calprotectin (S100A8/S100A9) in severe cases</u>.</u>



					"fixed-	effect me	eta-analysis"				
	Severe			Non-severe				Hedges's g	Weight		
Study	N	Mean	SD	N	Mean	SD		with 95% CI	(%)		
Study 1	40	9220	3819	81	7800	2914		0.44 [0.06, 0.82]	23.50		
Study 2	8	7900	5060	58	3540	2270		1.59 [0.81, 2.36]	5.60		
Study 3	60	11251.26	7776.52	112	4709.79	5214.13	-	1.05 [0.72, 1.38]	30.99		
Study 4	50	4983.4	2815.1	39	985	1161.9		1.76 [1.27, 2.25]	14.20		
Study 5	8	3770	1765	11	2080	988		1.18 [0.24, 2.13]	3.78		
Study 6	22	80.2	26.51	18	17.3	3.83		3.10 [2.19, 4.02]	4.07		
Study 7	19	71.3	66.7	46	11.9	9.5		1.61 [1.01, 2.20]	9.57		
Study 8	31	2.5	1.5	13	2	1		0.36 [-0.28, 1.00]	8.29		
Overall							•	1.12 [0.94, 1.30]			
Heteroge	eneity	/: I ² = 85.02	%, H ² = 6.	68							
Test of θ	= θ	Q(7) = 46.	74, p = 0.0	00							
Test of $\theta = 0$: $z = 11.91$, $p = 0.00$											
							0 1 2 3	3 4			
Fixed-effe	Fixed-effects inverse-variance model										

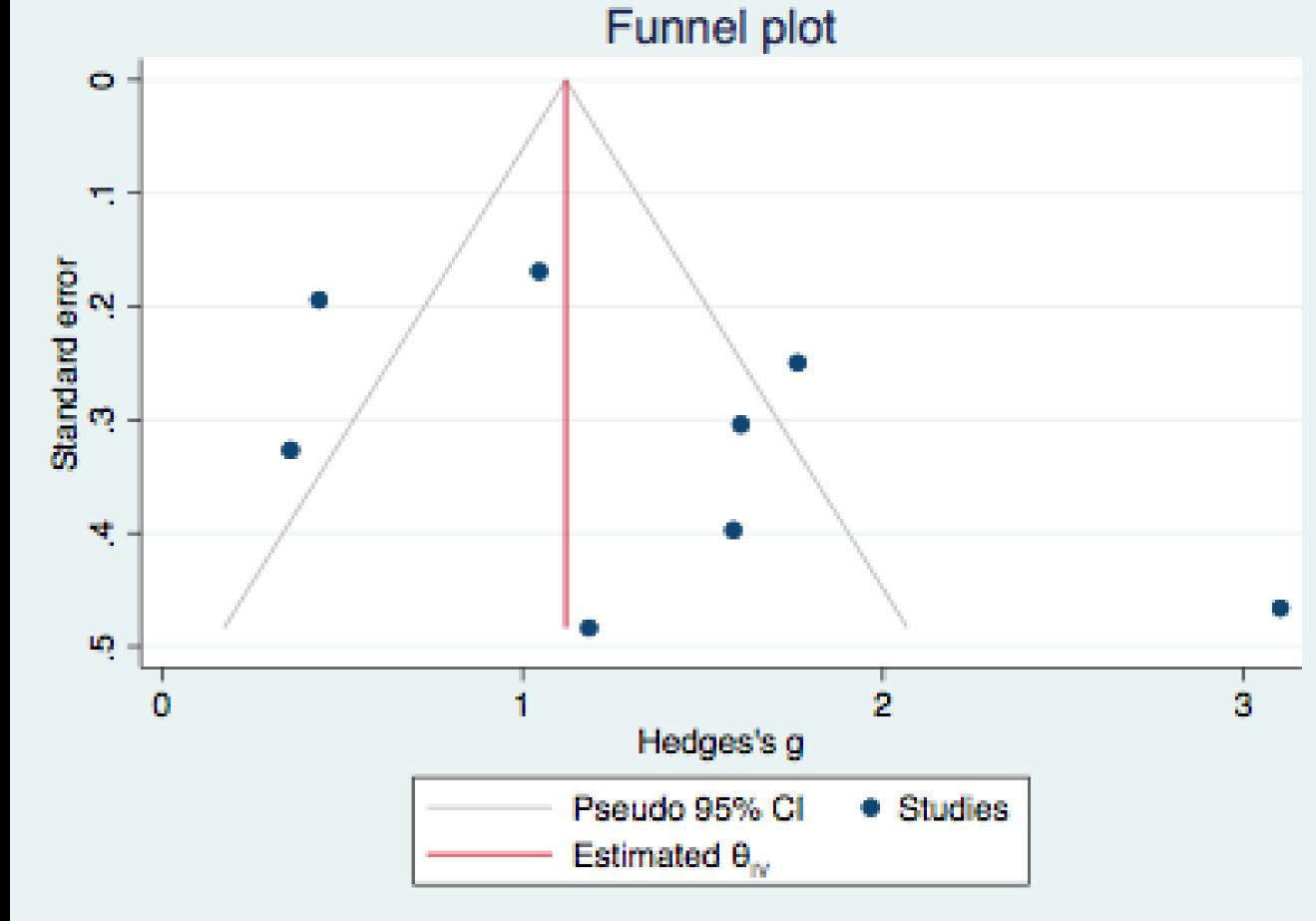


Figure 3: Meta-analysis (Total cohort).

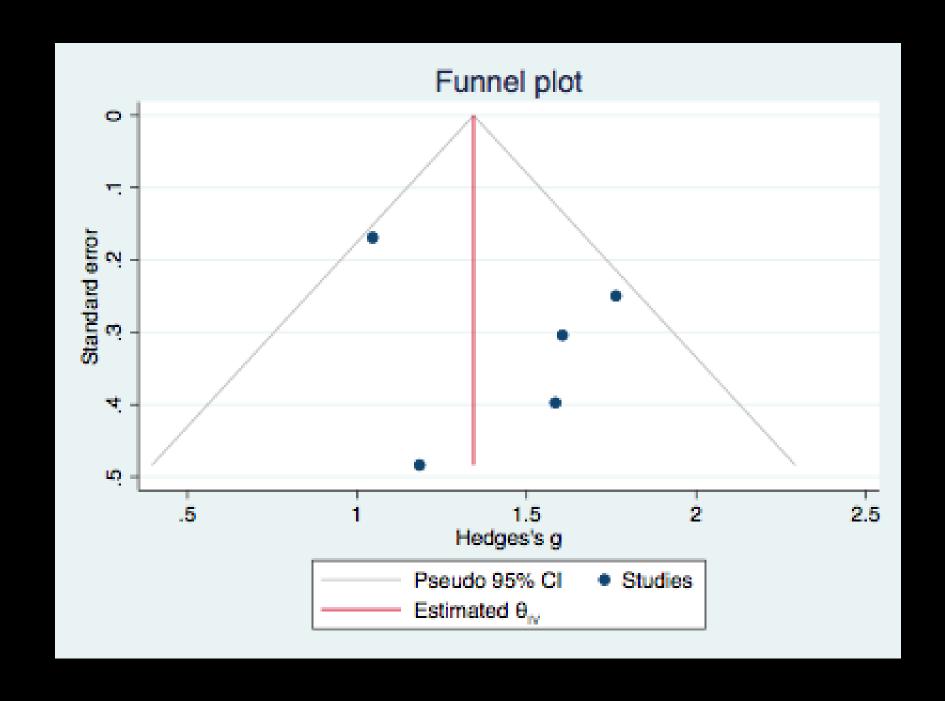
A. Forest plot (REM) and

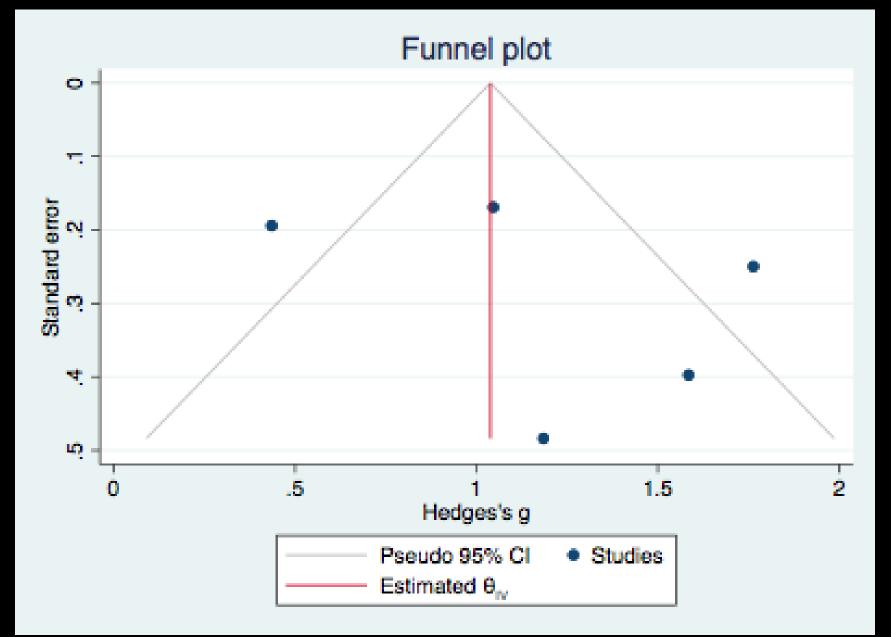
B. Forest plot (FEM) comparing the mean differences in calprotectin level between severe and non-severe COVID-19. Studies 1-8 are respectively: Chen et al14; De Guadiana et al25; Shi et al23; Silvin et al12; Bauer et al24; Effenberger et al16; Ojetti et al26; Britton et al27.

C. Funnel plot showing some publication bias.

		Severe			Non-sev	ere		Hedges's g	Weight		
Study	N	Mean	SD	N	Mean	SD		with 95% CI	(%)		
Study 1	8	7900	5060	58	3540	2270		1.59 [0.81, 2.36]	13.78		
Study 2	60	11251.26	7776.52	112	4709.79	5214.13		1.05 [0.72, 1.38]	32.49		
Study 3	50	4983.4	2815.1	39	985	1161.9		1.76 [1.27, 2.25]	23.99		
Study 4	8	3770	1765	11	2080	988		1.18 [0.24, 2.13]	10.30		
Study 5	19	71.3	66.7	46	11.9	9.5		1.61 [1.01, 2.20]	19.45		
Overall								1.42 [1.07, 1.76]			
Heterogeneity: $\tau^2 = 0.07$, $I^2 = 45.30\%$, $H^2 = 1.83$											
Test of $\theta_i = \theta_i$: Q(4) = 7.14, p = 0.13											
Test of θ	= 0:	z = 8.04, p	= 0.00								
						(1 2	3			
Random-effects REML model											

"fixed-effect meta-analysis"										
	Severe			Non-severe				Hedges's g	Weight	
Study	N	Mean	SD	N	Mean	SD		with 95% CI	(%)	
Study 1	8	7900	5060	58	3540	2270		1.59 [0.81, 2.36]	8.73	
Study 2	60	11251.26	7776.52	112	4709.79	5214.13		1.05 [0.72, 1.38]	48.31	
Study 3	50	4983.4	2815.1	39	985	1161.9		1.76 [1.27, 2.25]	22.13	
Study 4	8	3770	1765	11	2080	988		1.18 [0.24, 2.13]	5.90	
Study 5	19	71.3	66.7	46	11.9	9.5		1.61 [1.01, 2.20]	14.92	
Overall								1.34 [1.11, 1.57]		
Heterogeneity: $I^2 = 44.00\%$, $H^2 = 1.79$										
Test of $\theta_i = \theta_j$: Q(4) = 7.14, p = 0.13										
Test of $\theta = 0$: $z = 11.44$, $p = 0.00$										
						(1 2	3		
Fixed-effects inverse-variance model										





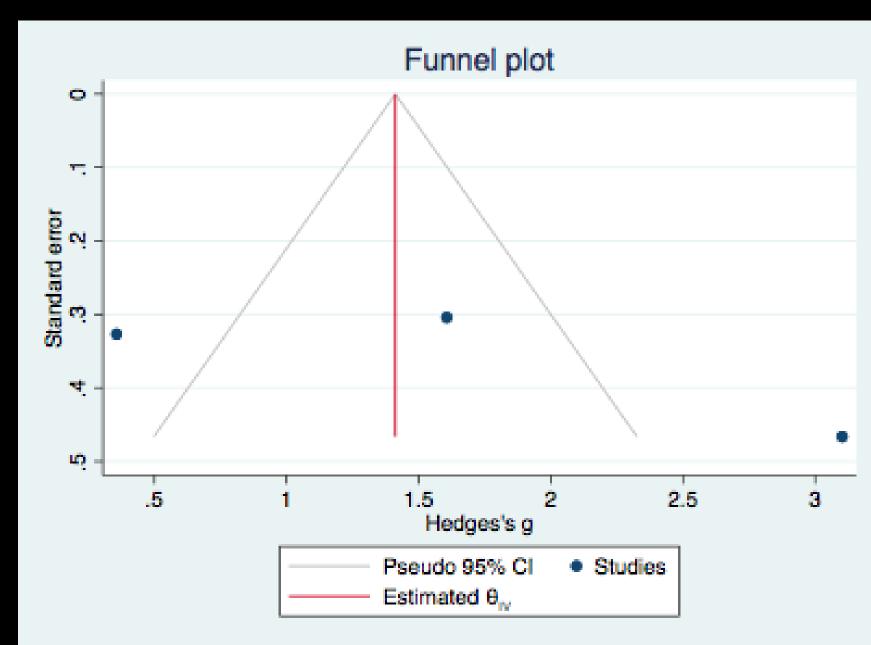


Figure 4: Meta-analysis (sensitivity analysis excluding three studies). A. Forest plot (REM) and B. Forest plot (FEM) comparing the mean differences in calprotectin level between severe and non-severe COVID-19. Studies 1-5 are respectively: De Guadiana et al²⁵; Shi et al²³; Silvin et al¹²; Bauer et al²⁴; Ojetti et al²⁶. C. Funnel plot (for the sensitivity analysis excluding three studies) shows no publication bias, an improvement from the total cohort funnel plot shown in figure 3c. D. Funnel plot (Subgroup analysis - Serum group) shows no publication bias. E. Funnel plot (Subgroup analysis - faecal group) shows some evidence of publication bias with much asymmetry.

