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Letter to the Editor

Reply to Letter to Editor

We sincerely thank Dr Au for the interest in our article, "Stroke as a Neurological Complication of COVID-19: A Systematic Review and Meta Analysis of Incidence, Outcomes and Predictors" and her concern regarding possible overlap between some of the studies included in our analysis. This has been a significant issue for researchers conducting systematic reviews during the COVID-19 pandemic as the urgent need for data can result in datasets being included in multiple manuscripts but their providence not clearly reported.

While conducting the systematic review we excluded studies where there was clear evidence of overlap. However, we agree that it is important to readdress this for the studies in question, namely: (i) Nalleballe et al.¹ and all 29 other studies included in this analysis; (ii) Jain et al.² & Yaghi et al.³; (iii) Varatharaj et al.⁴, Beyrouiti et al.⁵ & Bengener et al.⁶; (iv) Belani et al.⁷ & Kihira et al.⁸ To clarify whether there was truly an overlap, we contacted each of the above authors individually. We determined that there

was no overlap between patients in the studies by Varatharaj et al. and Bengener et al. through direct correspondence with Dr Bengener. There was likely an overlap between the studies by Varatharaj et al. and Beyrouiti et al. However, due to the nature of some databases, we were unable to determine if there was overlap between patients in the remaining studies in question. To exclude this possibility and to address Dr Au's concern, we have performed further sensitivity analyses.

Subsequent sensitivity analyses yielded minimal changes between the pooled results originally published in our study and after including the above-mentioned studies. Patient demographics including age (Mean age: 65.5 years in original article vs 65.7 years in revised analysis), percentage of males (70.5% vs 73.2%) and admission NIHSS score (Mean: 17.9 vs 15.2) were similar in both analyses. The comorbidity profiles were also similar. The proportion of patients with ischaemic stroke (compared to haemorrhagic stroke) was similar between original and revised analyses (82.8% vs 81.3%). Incidence of stroke as a complication for COVID-19 was slightly lower in our

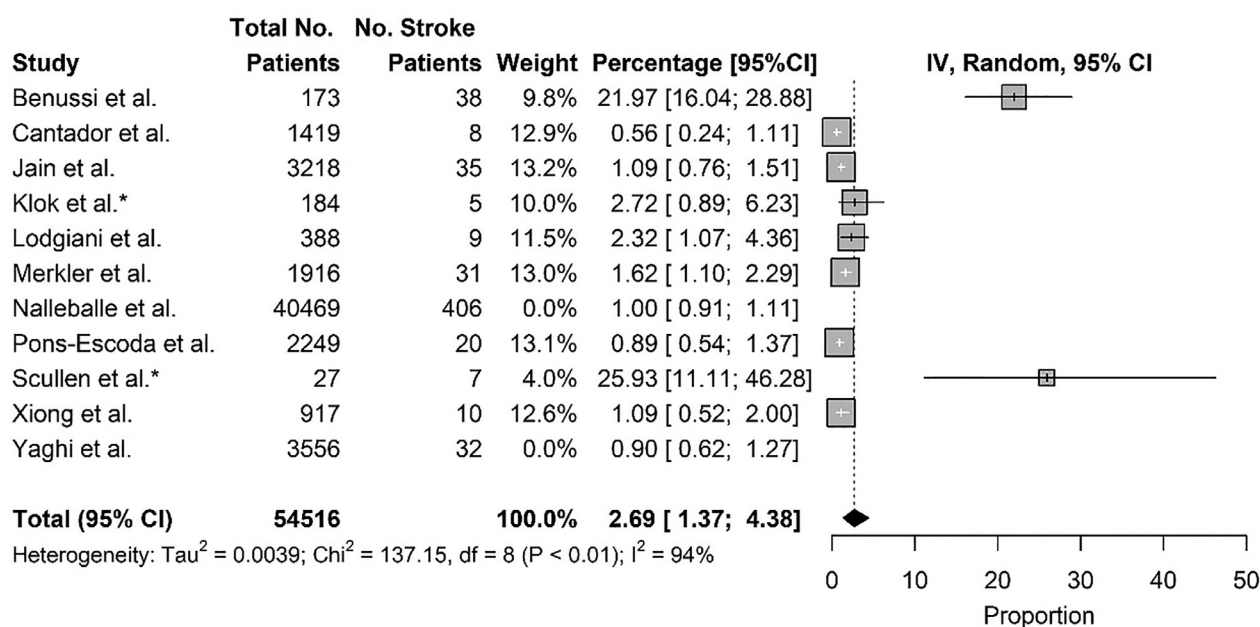


Fig. 1. Incidence of stroke.

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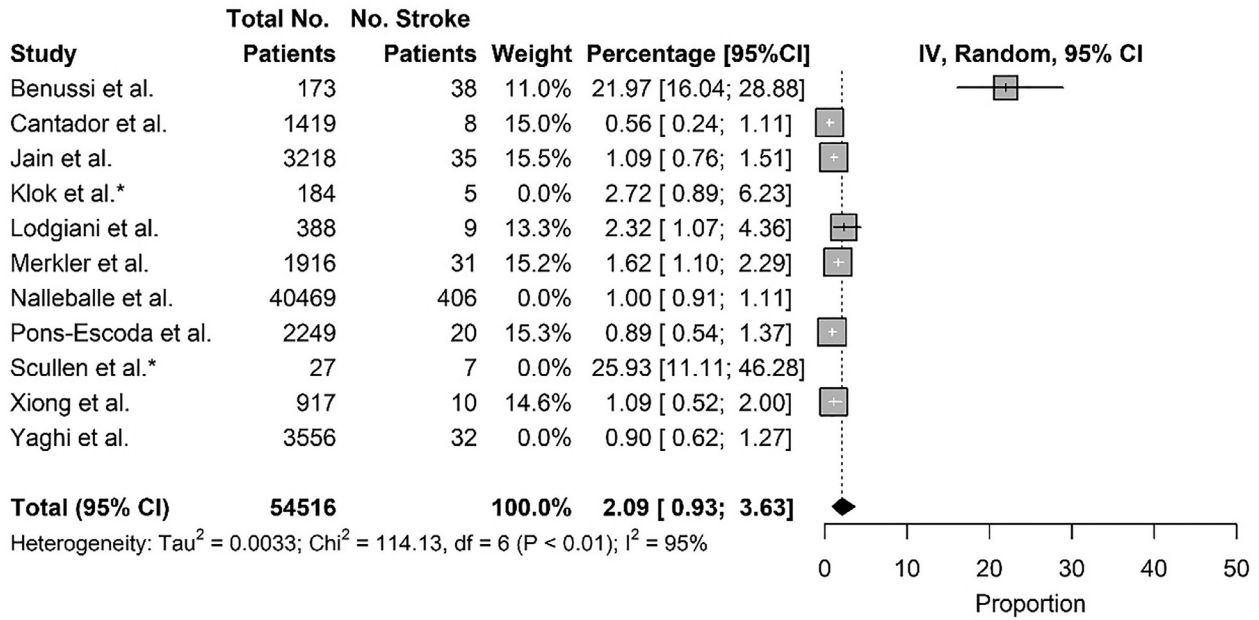


Fig. 2. Incidence of stroke excluding critically-ill studies.

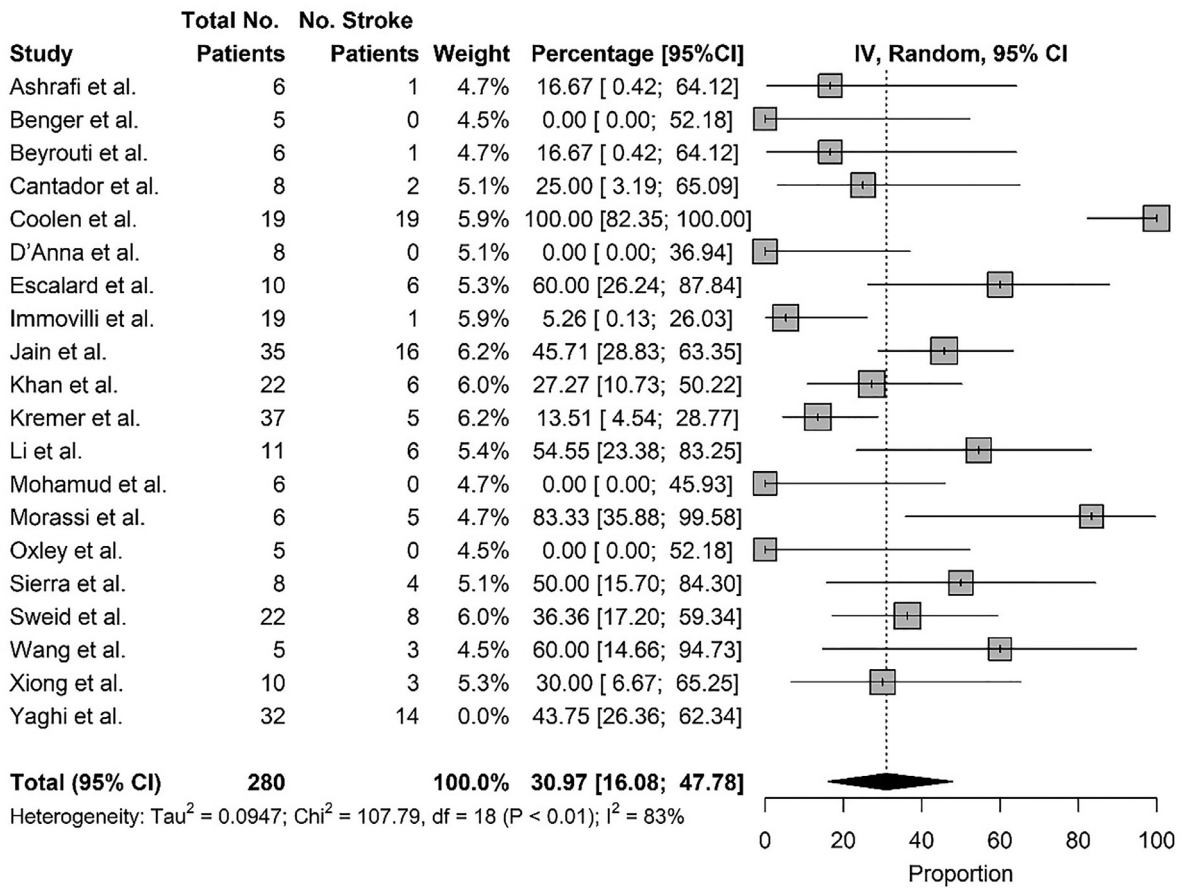


Fig. 3. Outcomes, mortality.

Table 1. Summary of studies.

Study	Country	Study design	No. stroke patients	Age, Mean	Male, N (%)	NIHSS, Mean
Ashrafi et al.	Iran	Case series	6	43.5	3 (50.0)	10.2
Belani et al.	United States	Cross-sectional	19	65.6		
Benger et al.	United States	Case series	5	52.5	3 (60.0)	
Benussi et al.	United States	Cross-sectional	38			
Cantador et al.	Spain	Cross-sectional	8	76.4	7 (87.5)	
Coolen et al.	United States	Cross-sectional	19	77	14 (73.7)	
D'Anna et al.	United Kingdom	Case series	8	64.4	7 (87.5)	9.1
Escalard et al.	United States	Cross-sectional	10	59.5*	8 (80.0)	22.0*
Immovilli et al.	Italy	Case series	19			9.8
Jain et al.	Netherlands	Cross-sectional	35	66*		
Khan et al.	United Kingdom	Case series	22	46.3	20 (90.9)	
Klok et al.	United States	Cross-sectional	5			
Kremer et al.	United States	Case series	37	61	30 (81.1)	
Li et al.	China	Case series	11	75.5	5 (45.5)	14.4
Lodgiani et al.	United States	Cross-sectional	9	68.4	6 (66.7)	
Merkler et al.	United States	Cross-sectional	31	69*	18 (58.1)	16.0*
Mohamud et al.	United States	Case series	6	65.8	5 (83.3)	13.3
Morassi et al.	Italy	Case series	6	68.5	5 (83.3)	
Oxley et al.	United States	Case series	5	40.4	4 (80.0)	16.8
Pons-Escoda et al.	Spain	Cross-sectional	20	71*	13 (65.0)	
Scullen et al.	United States	Cross-sectional	7			
Sierra et al.	Germany	Case series	8	68.5*	7 (87.5)	27.0*
Sweid et al.	United Kingdom	Case series	22	59.5	10 (45.5)	13.8
Varatharaj et al.	United Kingdom	Cross-sectional	66	73.5*	44 (66.7)	
Wang et al.	United Kingdom	Case series	5	52.8	4 (80.0)	22.8
Xiong et al.	United States	Cross-sectional	10			
Overall			437	65.7 [†]	213 (73.2)	15.2 [†]

*Data originally reported as median

[†]Weighted average

Table 2. *Comorbidities.*

Study	No. stroke Patients	Diabetes Mellitus, N (%)	Hypertension, N (%)	Hyperlipidaemia, N (%)	Chronic Kidney Disease, N (%)	Ischaemic heart disease, N (%)	Malignancy, N (%)	Smoking, N (%)
Ashrafi et al.	6	1 (16.7)	3 (50.0)	0 (0.0)				
Benger et al.	5	2 (40.0)	4 (80.0)	1 (20.0)		1 (20.0)		
Beyrouti et al.	6	1 (16.7)	2 (33.3)					1 (16.7)
Cantador et al.	8	4 (50.0)	8 (100.0)	7 (87.5)			5 (62.5)	6 (75.0)
Coolen et al.	29	6 (20.7)	16 (55.2)			7 (24.1)	5 (17.2)	5 (17.2)
D'Anna et al.	8	2 (25.0)	5 (62.5)	1 (12.5)		2 (25.0)	2 (25.0)	2 (25.0)
Escalard et al.	20	4 (20.0)	5 (25.0)	3 (15.0)				1 (5.0)
Immovilli et al.	19	2 (10.5)	16 (84.2)					
Jain et al.	35		14 (40.0)					
Khan et al.	22	8 (36.4)	7 (31.8)	2 (9.1)		2 (9.1)		
Li et al.	11	6 (54.5)	9 (81.8)			3 (27.3)	1 (9.1)	1 (36.4)
Lodgiani et al.	9						2 (22.2)	
Merkler et al.	31	23 (74.2)	30 (96.8)	17 (54.8)	8 (25.8)	16 (51.6)		
Mohamud et al.	6	5 (83.3)		6 (100.0)	1 (16.7)			
Morassi et al.	6	3 (50.0)	4 (66.7)			2 (33.3)		1 (16.7)
Oxley et al.	5	2 (33.3)	1 (16.7)	1 (16.7)				
Pons-Escoda et al.	20	5 (25.0)	13 (65.0)	9 (45.0)				1 (5.0)
Sierra et al.	8	3 (37.5)	5 (62.5)	4 (50.0)				0 (0.0)
Sweid et al.	22	2 (9.1)	10 (45.5)		1 (4.5)	3 (13.6)		
Wang et al.	5	1 (20.0)	2 (40.0)			2 (40.0)		
Overall	281	80 (33.8)	154 (57.9)	51 (38.3)	10 (16.9)	38 (27.3)	15 (23.1)	18 (16.7)

Table 3. Type of stroke (Ischaemic VS Haemorrhagic).

Study	No. stroke patients	Ischaemic stroke, N (%)	Haemorrhagic stroke, N (%)
Ashrafi et al.	6	6 (100.0)	0
Belani et al.	19	19 (100.0)	0
Benger et al.	5	0 (0.0)	5
Benussi et al.	38	35 (92.1)	3
Cantador et al.	8	8 (100.0)	0
Coolen et al.	19	4 (21.1)	15
D'Anna et al.	8	7 (87.5)	1
Escalard et al.	10	10 (100.0)	0
Immovilli et al.	19	17 (89.5)	2
Jain et al.	35	26 (74.3)	9
Khan et al.	22	22 (100.0)	0
Klok et al.	5	5 (100.0)	0
Kremer et al.	37	17 (45.9)	20
Li et al.	11	10 (90.9)	1
Lodgiani et al.	9	9 (100.0)	0
Merkler et al.	31	31 (100.0)	0
Mohamud et al.	6	6 (100.0)	0
Morassi et al.	6	4 (66.7)	2
Oxley et al.	5	5 (100.0)	0
Pons-Escoda et al.	20	13 (65.0)	7
Scullen et al.	7	4 (57.1)	3
Sierra et al.	8	8 (100.0)	0
Sweid et al.	22	19 (86.4)	3
Varatharaj et al.	66	57 (86.4)	9
Wang et al.	5	5 (100.0)	0
Overall	427	347 (81.3)	80 (17.2)

original analysis than in our revised analyses (1.74% vs 2.69%). The mortality rate of COVID-19 patient who developed stroke was similar between original and revised analyses (31.8% vs 31.0%) (Figs. 1–3, Tables 1–3).

In conclusion, despite the possible overlap in patients between a few of the studies, the pooled results in our original analysis did not defer greatly from the revised analyses after removing the studies in question, indicating that the results in our original analysis were robust and accurate.

Declaration of Competing Interest

None.

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