Supplementary Online Content

Baral R, Tsampasian V, Debski M, et al. Association between renin-angiotensin-aldosterone system inhibitors and clinical outcomes in patients with COVID-19: a systematic review and meta-analysis. *JAMA Netw Open*. 2021;4(3):e213594. doi:10.1001/jamanetworkopen.2021.3594

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Search Strategy in PubMed

1. Angiotensin converting enzyme [All Fields]
2. Angiotensin receptor blocker* [All Fields]
3. Renin angiotensin aldosterone system [All Fields]
4. ACEi [All Fields]
5. ARB [All Fields]
6. RAAS [All Fields]
7. perindopril [mesh] OR Lisinopril [mesh] OR enalapril [mesh] OR captopril [mesh]
8. olmesartan [mesh] OR candesartan [mesh] OR losartan [mesh] OR telmisartan [mesh]
9. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8
10. Coronavirus [All Fields]
11. covid-19 [All Fields]
12. 2019-n-COV [All Fields]
13. SARS-CoV-2 [All Fields]
14. 2019-nCOV [All Fields]
15. 10 OR 11 OR 12 OR 13 OR 14
16. 9 AND 15

eTable. Quality Assessment of Included Clinical Trials: Newcastle Ottawa Scale for Nonrandomized Clinical Trials and Cochrane Collaboration Tool for Assessing Risk of Bias in Randomized Clinical Trials

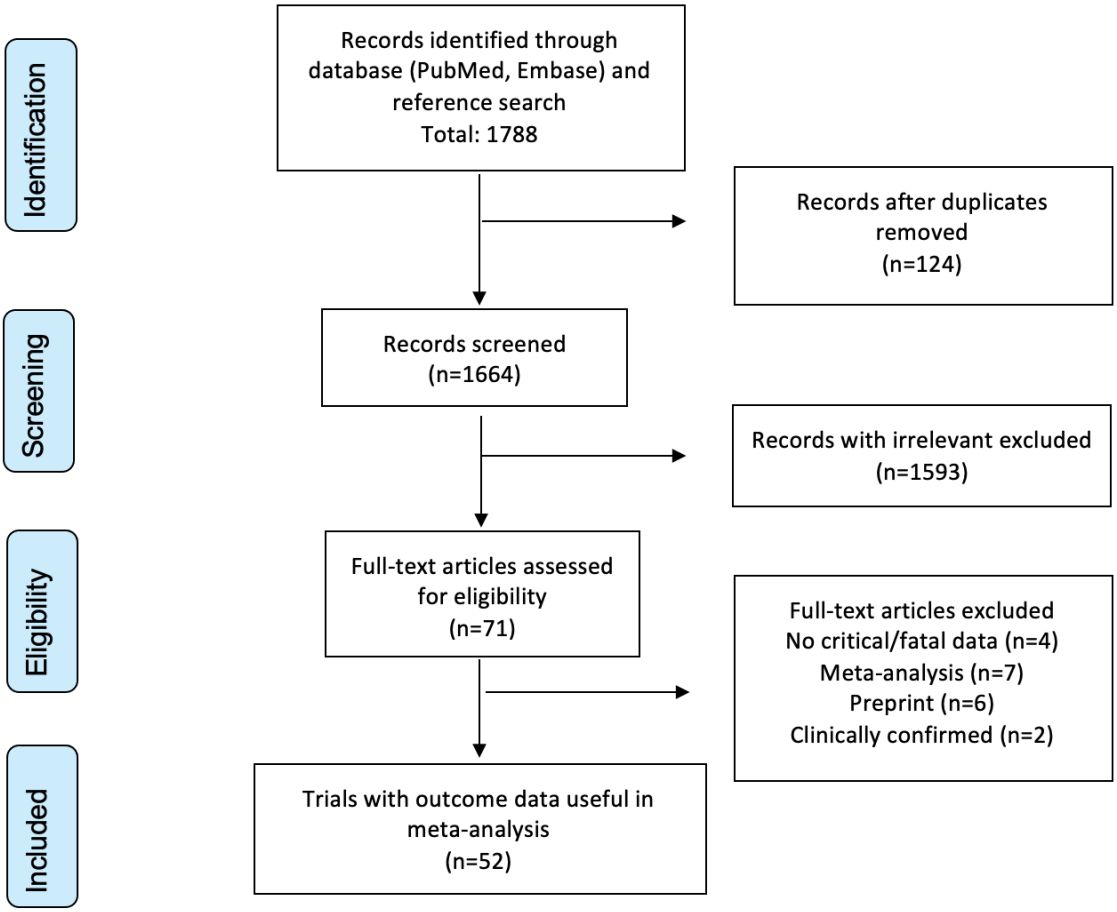
Non-RCT					
Authors	Selection	Comparability	Outcome/Exposures	Total	Quality of study
Andrea	***	*	**	6	Moderate
Bae	***	**	**	7	High
Bean	****	**	**	8	High
Bravi	****	**	***	9	High
Cannata	***	**	**	7	High
Chen C	***	**	**	7	High
Chen F	**	**	**	6	Moderate
Chen Y	****	**	**	8	High
Cox	****	**	***	9	High
Felice	***	**	**	7	High
Feng	****	**	**	8	High
Fosbol	***	**	**	7	High
Gao	***	**	**	7	High
Gormez	***	**	**	7	High
Grasseli	***	**	**	7	High
Guo	***	*	**	6	Moderate
Hu	***	**	**	7	High
Huang	***	**	**	7	High
Hwang	***	**	**	7	High
Iaccarino	****	**	**	8	High

Jung C	***	**	**	7	High
Jung S	***	**	**	7	High
Khan	***	**	**	7	High
Lam	***	*	**	6	Moderate
Li	***	*	**	6	Moderate
Liabeuf	***	**	**	7	High
Liu	****	**	*	7	High
Lopez-Otero	***	*	**	6	Moderate
Mancia	****	**	**	8	High
Matsuzawa	***	**	**	7	High
Mehta	****	*	**	7	High
Meng	***	**	**	7	High
Mostaza	***	**	**	7	High
Oussalah	***	**	**	7	High
Pan	***	**	**	7	High
Reynolds	****	**	**	8	High
Richardson	***	*	**	6	Moderate
Rossi	****	**	***	9	High
Sardu	***	**	**	7	High
Selcuk	***	**	**	7	High
Senkal	***	**	**	7	High
Shah	***	**	**	7	High
Tan	***	*	**	6	Moderate
Tedeschi	***	**	**	7	High

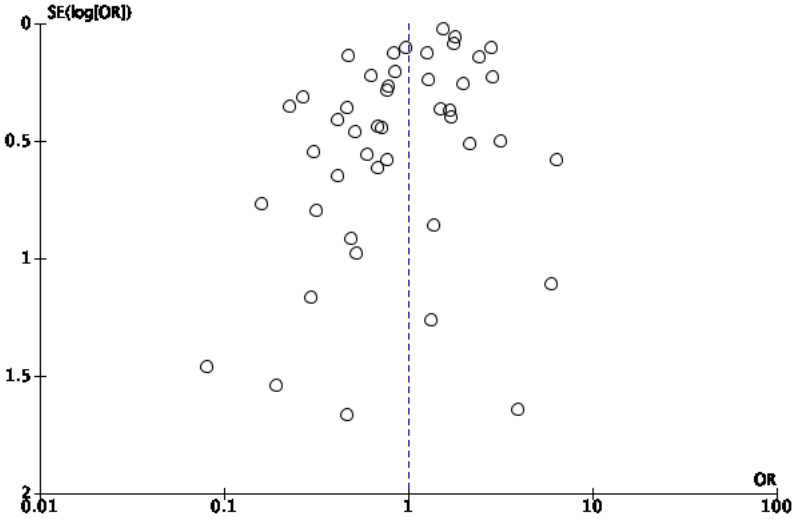
Trifiro	***	**	**	7	High
Xu	***	**	**	7	High
Yang	****	**	**	8	High
Yuan	***	**	**	7	High
Zhang	***	**	**	7	High
Zhou F	**	**	**	6	Moderate
Zhou X	***	**	*	6	Moderate
RCT					
Amat-Santos[#]	Domain 1 Domain 2 Domain 3 Domain 4 Domain 5 Overall			Some concerns Some concerns Low Low Low Some concerns	

*Each star indicates a point for each component. Any study can obtain a maximum of four, two and three stars for each component (selection, comparability, outcomes) respectively. Trials with a total score of 7 or higher are considered to be high-quality studies, and those lower than 5 are considered as low-quality studies. These scores indicate at least moderate quality of the included trials.
[#]Cochrane risk of bias 2 tool was used to assess the risk of bias in the randomised trial.

eFigure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Diagram of the Clinical Trial Selection Process

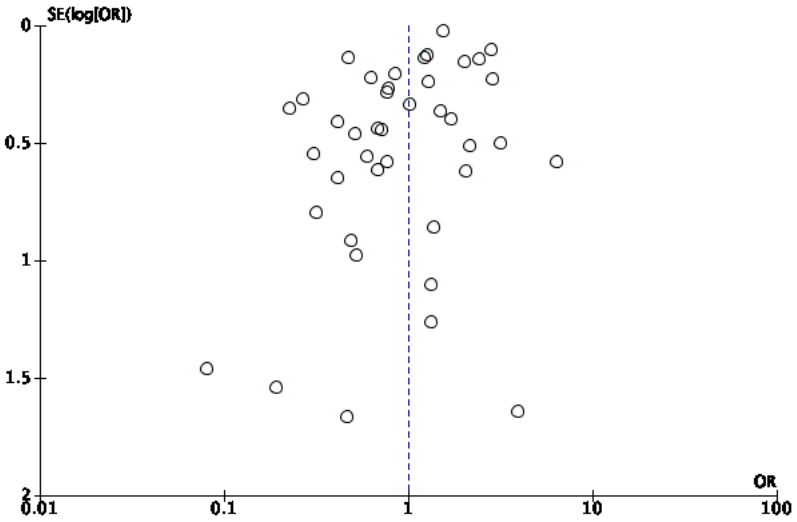


eFigure 2. Funnel Plot for Unadjusted Critical or Fatal Outcomes for Patients With COVID-19 Receiving ACEIs or ARBs



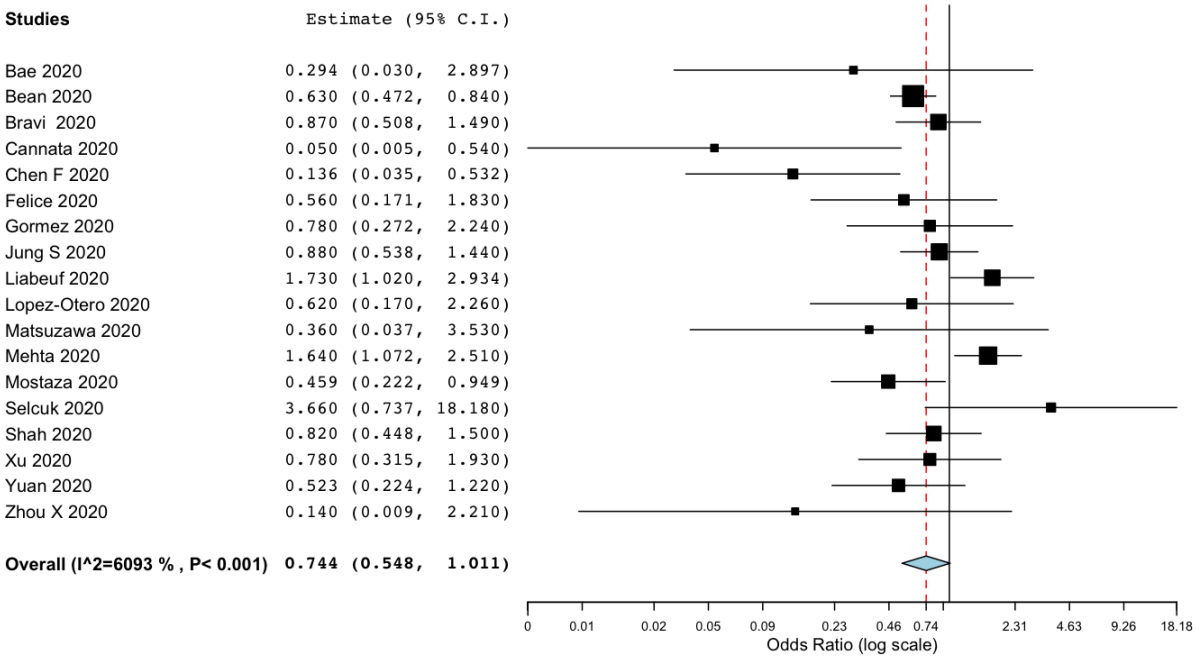
Funnel plot for unadjusted critical or fatal outcomes for patients with COVID-19 receiving ACEIs or ARBs indicating no substantial publication bias.

eFigure 3. Funnel Plot for Unadjusted Death for Patients With COVID-19 Receiving ACEIs or ARBs



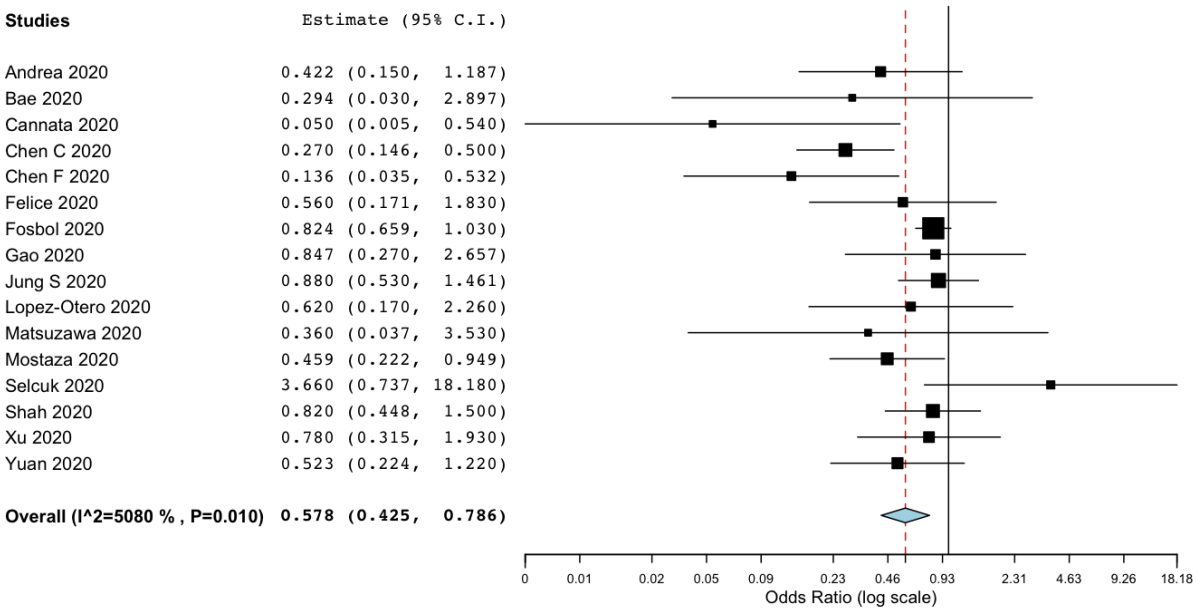
Funnel plot for unadjusted mortality outcome for patients with COVID-19 receiving ACEIs or ARBs indicating no substantial publication bias.

eFigure 4. Sensitivity Analysis Excluding Studies Reporting Hazard Ratios for Critical or Fatal Outcomes



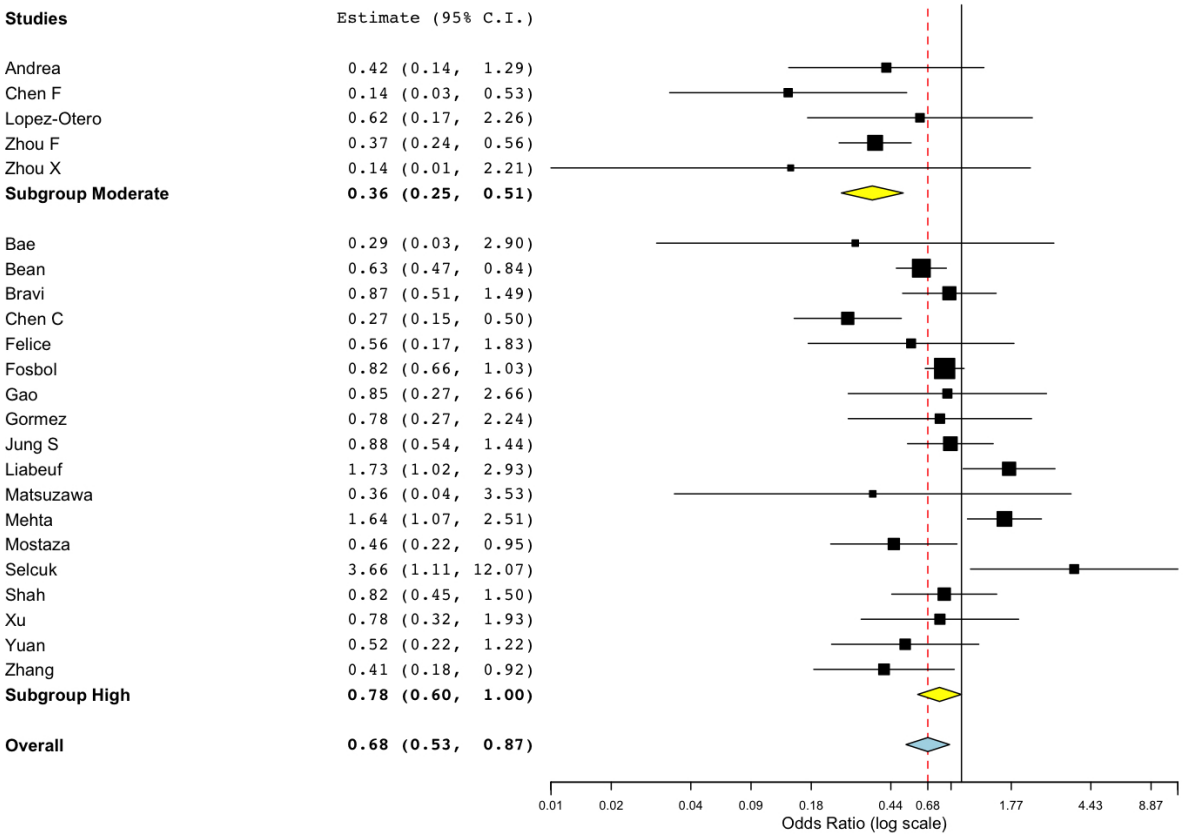
Sensitivity analysis excluding studies reporting hazard ratios for critical or fatal outcomes (OR, 0.744; 95% CI, 0.548-1.011; *P* = .059).

eFigure 5. Sensitivity Analysis Excluding Studies Reporting Hazard Ratios for Mortality Outcomes



Sensitivity analysis excluding studies reporting hazard ratios for mortality outcomes (OR, 0.578; 95% CI, 0.425-0.786; *P* < .001).

eFigure 6. Subgroup Analysis of Studies With Moderate or High Quality for Adjusted Critical or Fatal Outcomes



Subgroup analysis of studies with moderate (OR, 0.36; 95% CI, 0.25-0.51; *P* < .01) and high quality (OR, 0.78; 95% CI, 0.60-1.00; *P* = .05) indicated reduced association for adjusted critical or fatal outcomes in both groups.