

UPDATE ALERT

Update Alert 6: Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults

We searched MEDLINE (Ovid) weekly from 29 September to 26 October 2020 using the same search strategy as described in the original review (1). We did not limit the search by language. This search update yielded 64 results (de-duplicated), and after an independent dual-review process, we identified 15 new studies meeting our inclusion criteria—12 observational studies and 3 systematic reviews with meta-analyses.

NEW EVIDENCE

Findings from 1 new observational study found no evidence of an association with angiotensin-converting enzyme inhibitor (ACEI) or angiotensin-receptor blocker (ARB) use and risk for coronavirus disease 2019 (COVID-19) (2). Findings from an additional 11 new observational studies did not demonstrate an association between use of ACEIs or ARBs and worse outcomes in COVID-19 (3–13). These findings are supported by 3 new systematic reviews with meta-analyses (14–16).

Overall, inclusion of 15 studies from this search update does not change the certainty of evidence rating we reported in the original manuscript for key questions 1 or 2. Studies have not examined the benefits and harms of initiating ACEIs or ARBs (that is, new users) in COVID-19 treatment; therefore, evidence for key question 3 remains unclear.

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References

1. Mackey K, King VJ, Gurley S, et al. Risks and impact of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers on SARS-CoV-

2 infection in adults: a living systematic review. *Ann Intern Med.* 2020; 173:195-203. doi:10.7326/M20-1515

2. Dublin S, Walker R, Floyd JS, et al. Renin-angiotensin-aldosterone system inhibitors and COVID-19 infection or hospitalization: a cohort study. *Am J Hypertens.* 2020. [PMID: 33048112] doi:10.1093/ajh/hpaa168

3. Braude P, Carter B, Short R, et al. The influence of ACE inhibitors and ARBs on hospital length of stay and survival in people with COVID-19. *Int J Cardiol Heart Vasc.* 2020;31:100660. [PMID: 33083516] doi:10.1016/j.ijcha.2020.100660

4. Covino M, De Matteis G, Burzo ML, et al; GEMELLI AGAINST COVID-19 Group. Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers and prognosis of hypertensive patients hospitalized with Covid-19. *Intern Med J.* 2020. [PMID: 33022124] doi:10.1111/imj.15078

5. Cui H, Wu F, Fan Z, et al. The effects of renin-angiotensin system inhibitors (RASi) in coronavirus disease (COVID-19) with hypertension: a retrospective, single-center trial. *Med Clin (Engl Ed).* 2020;155:295-298. [PMID: 33043142] doi:10.1016/j.medcle.2020.06.007

6. Desai A, Voza G, Paiardi S, et al; Humanitas COVID-19 task force. The role of anti-hypertensive treatment, comorbidities and early introduction of LMWH in the setting of COVID-19: a retrospective, observational study in Northern Italy. *Int J Cardiol.* 2020. [PMID: 32980434] doi:10.1016/j.ijcard.2020.09.062

7. COVID-19 RISK and Treatments (CORIST) Collaboration. RAAS inhibitors are not associated with mortality in COVID-19 patients: findings from an observational multicenter study in Italy and a meta-analysis of 19 studies. *Vascul Pharmacol.* 2020;135:106805. [PMID: 32992048] doi:10.1016/j.vph.2020.106805

8. Georges JL, Cochet H, Roger G, et al. Association of hypertension and antihypertensive agents and the severity of COVID-19 pneumonia: a monocentric French prospective study. *Ann Cardiol Angeiol (Paris).* 2020;69:247-254. [PMID: 33039120] doi:10.1016/j.ancard.2020.09.030

9. Feng Z, Li J, Yao S, et al. Clinical factors associated with progression and prolonged viral shedding in COVID-19 patients: a multicenter study. *Aging Dis.* 2020;11:1069-1081. [PMID: 33014523] doi:10.14336/AD.2020.0630

10. Hu J, Zhang X, Zhang X, et al. COVID-19 is more severe in patients with hypertension; ACEI/ARB treatment does not influence clinical severity and outcome [Letter]. *J Infect.* 2020. [PMID: 32474032] doi:10.1016/j.jinf.2020.05.056

11. Palazzuoli A, Mancone M, De Ferrari GM, et al. Antecedent administration of angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists and survival after hospitalization for COVID-19 syndrome. *J Am Heart Assoc.* 2020;9:e017364. [PMID: 33023356] doi:10.1161/JAHA.120.017364

12. Rodilla E, Saura A, Jiménez I, et al. Association of hypertension with all-cause mortality among hospitalized patients with COVID-19. *J Clin Med.* 2020;9. [PMID: 32998337] doi:10.3390/jcm9103136

13. Yahyavi A, Hemmati N, Derakhshan P, et al. Angiotensin enzyme inhibitors and angiotensin receptor blockers as protective factors in COVID-19 mortality: a retrospective cohort study. *Intern Emerg Med.* 2020. [PMID: 33085063] doi:10.1007/s11739-020-02523-9

14. Kurdi A, Abutheraa N, Akil L, et al. A systematic review and meta-analysis of the use of renin-angiotensin system drugs and COVID-19 clinical outcomes: what is the evidence so far. *Pharmacol Res Perspect.* 2020;8:e00666. [PMID: 33084232] doi:10.1002/prp2.666

15. Wang Y, Chen B, Li Y, et al. The use of renin-angiotensin-aldosterone system (RAAS) inhibitors is associated with a lower risk of mortality in hypertensive COVID-19 patients: a systematic review and meta-analysis. *J Med Virol.* 2020. [PMID: 33095513] doi:10.1002/jmv.26625

16. Xu J, Teng Y, Shang L, et al. The effect of prior ACEI/ARB treatment on COVID-19 susceptibility and outcome: a systematic review and meta-analysis. *Clin Infect Dis.* 2020. [PMID: 33079200] doi:10.1093/cid/ciaa1592