

UPDATE ALERT

Update Alert 7: 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 27 October to 23 November 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 48 results (de-duplicated), and after an independent dual-review process, we identified 14 new studies meeting our inclusion criteria (8 observational and 6 new systematic reviews with or without meta-analyses) (2-15). These studies are all relevant to key question (KQ) 2 about the association of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin-receptor blocker (ARB) use and coronavirus disease 2019 (COVID-19) severity, and they support our prior conclusion that ACEI or ARB use is not associated with a higher risk for severe COVID-19 illness. Two systematic reviews also address KQ1, adding support to our prior conclusion that ACEI or ARB use is not associated with an increased risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (11, 14).

EVIDENCE SUMMARY

In total, 9 primary studies (8 observational and 1 randomized controlled trial) have met our inclusion criteria for KQ1 to date, including those identified in the original review, previous update alerts, and the most recent search described earlier (16-24). In total, 78 primary studies (77 observational and 1 randomized controlled trial) have met our inclusion criteria for KQ2 to date, excluding 1 retracted study (2-9, 16, 22-91). We have not identified any primary studies addressing KQ3 about the benefits and harms of initiating ACEIs or ARBs during COVID-19 disease (that is, new users).

KEY QUESTION 1: DOES THE USE OF ACEIS AND ARBS BEFORE INFECTION WITH SARS-CoV-2 INCREASE THE RISK FOR COVID-19?

Evidence suggests that ACEI or ARB use is not associated with a higher likelihood of positive SARS-CoV-2 test results. Our confidence in this finding is high (rather than moderate as we previously concluded). New evidence since the publication of our original review includes results from a randomized controlled trial and 4 large database studies that included patients with a mix of disease severity (16-19, 23). These studies consistently found that ACEI or ARB use was not associated with a higher risk for SARS-CoV-2 infection, findings which are further supported by 5 systematic reviews or meta-analyses (11, 14, 92-94). Because we consider these findings to be stable (meaning that future studies are likely to have the same results), we will no longer do literature surveillance on this KQ and will retire it from our living review.

KEY QUESTION 2: IS USE OF ACEIS AND ARBS ASSOCIATED WITH MORE SEVERE COVID-19 ILLNESS?

Evidence suggests that use of ACEIs or ARBs before COVID-19 illness is not associated with increased severity. Our

confidence in this finding remains high after incorporating new evidence since the publication of our original review given the consistency of results across studies, representing adults from several geographic regions during different phases of the pandemic. Results are supported by several systematic reviews or meta-analyses (92-112).

Because we consider these findings to be stable (meaning that future studies are likely to have the same results), we will no longer do routine literature surveillance for this KQ. We have identified 3 in-progress trials that are aimed at addressing this KQ (**Supplement Table**), and we will continue to monitor these trials for updates monthly and provide a brief status update quarterly (113-115). If the results would change our conclusions or strength of evidence assessment, we will provide an updated evidence synthesis.

KEY QUESTION 3: WHAT ARE THE BENEFITS AND HARMS OF INITIATING ACEI OR ARB TREATMENT FOR PATIENTS WITH COVID-19?

We have identified 5 in-progress trials that are aimed at addressing this KQ (**Supplement Table**) (116-120). We will monitor these trials for updates monthly and provide a brief status update quarterly. When results are available, we will provide an updated evidence synthesis.

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