

# **Angiotensin-converting-enzyme inhibitors and angiotensin II receptor blockers for COVID-19: A living systematic review of randomized clinical trials**

doi:10.5867/medwave.2021.02.8105

## **Appendix 1: Included, excluded and ongoing studies**

### **Included studies**

No studies were found.

### **Excluded studies**

| Epistemonikos ID                          | Title  | Reason for exclusion |
|---|--|----------------------|
| 51dafa-fcd8246676aac8b2a1f8e1d976a38270c5 | [2019 novel coronavirus, angiotensin converting enzyme 2 and cardiovascular drugs].  | Wrong study design   |
| b7e9371d6765ab581b77b6b3bc3a940b8ff1df42  | [2019 Novel coronavirus, renin-angiotension system imbalance and coronavirus disease 2019].                                | Wrong study design   |
| d14efca0145d6dde74a9b8b8161ea17ecfafb7e   | [ACE-inhibitors, angiotensin receptor blockers and severe acute respiratory syndrome caused by coronavirus].               | Wrong study design   |
| c840e055144059aecb4b338a406f056372f6189   | [Controversy regarding ACE inhibitors / ARBs in Covid-19].   | Wrong study design   |
| a0549f86c092b382f111efe8a59efec0a120471c  | [COVID-19 and its relationship with hypertension and cardiovascular disease].  | Wrong study design   |
| b6acf950f739ec3faf9b25b346d58c467ec30053  | [COVID-19 and kidney disease].   | Wrong study design   |
| 19698ee0054a0f9a32b87a6db6570ba3d8506bc2  | [COVID-19, THE KIDNEY AND HYPERTENSION].   | Wrong study design   |
| 9aee3e707665589001ecea644fc977e0099e5c5   | [Drugs that aggravate the course of COVID-19: really ?]  | Wrong study design   |
| 658e355faa7b6157ec55e25e5bb95355af0b80f2  | [Hypertension and RAAS inhibition in times of COVID-19 - current recommendations of the European Society of Hypertension.] | Wrong study design   |
| 99f6f0c3e9ba4b6d6cbf5398c89926e0ff34e0e6  | [Hypertension, RAAS blockade and risk in COVID-19 patients].   | Wrong study design   |

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|  |  |                    |
|--|--|--------------------|
| 7692736b67ae68202b994149c06585<br>1c73c31846 | [Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia].  | Wrong study design |
| fd766d3ddc4567e108b25af6b45f3e5<br>36799993a | [Inhibitors of RAS Might Be a Good Choice for the Therapy of COVID-19 Pneumonia].  | Wrong study design |
| 74248fbc8cc48debd57ef4363fe350b<br>7492ab6c3 | [Lessons from SARS: a new potential therapy for acute respiratory distress syndrome (ARDS) with angiotensin converting enzyme 2 (ACE2)].       | Wrong study design |
| 4c2d3603ac2d937be4533bc2d2876b<br>85684af99d | [Medication and comedication in COVID-19 patients].  | Wrong study design |
| 8e69fc05b56fb31a59f8f69298d401<br>cae6daab7  | [Preliminary clinical study of direct renin inhibitor aliskiren in the treatment of severe COVID-19 patients with hypertension].               | Wrong intervention |
| 117af5230854d53176761c68700866<br>91b3d80f08 | [Renin-angiotensin system blockers and COVID-19 infection].  | Wrong study design |
| b50de2996a763848ae1990b8332ad1<br>33d6581330 | [Renin-angiotensin-aldosterone blockers and Covic-19 infection: friends or enemies ?]  | Wrong study design |
| 1144e35665d1862a724bbcff76978e<br>4b6cc022e  | [Renin-Angiotensin-System (RAS) and COVID-19 - On The Prescription of RAS Blockers].   | Wrong study design |
| 77a9cd2d725be49c9405fbacc6aa375<br>8879554ac | [Role of age, comorbidity and renin- angiotensin-aldosterone system in COVID-19. Effects of ACE inhibitors and angiotensin receptor blockers]. | Wrong study design |
| 173f5aebc7fc65f946e05227e3ffd248<br>7e2ddcd1 | [Scientific statement on using of renin angiotensin system blockers in patients with cardiovascular disease and COVID-19].                     | Wrong study design |
| 88d8742e776d0e8ec344b09fe699d6<br>22880f1979 | [The RAAS and SARS-CoV-2: A riddle to solve].  | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| 1aca-bcf2b1fc43861779e311d8724505207878f | 2019 novel coronavirus: what is currently known, cardiovascular implications and management.  | Wrong study design |
| 894305b677389471088095786a9d6ca1229b8130 | 2019 novel-coronavirus: Cardiovascular insights about risk factors, myocardial injury, therapy and clinical implications  | Wrong study design |
| dd3e0e8b4f21c9b67a00a2e49256b7976a187ded | A Comprehensive Literature Review on the Clinical Presentation, and Management of the Pandemic Coronavirus Disease 2019 (COVID-19).                                 | Wrong study design |
| 4ff53cc143ef31d9df8884d9544d91bc4fc1159a | A consensus statement on the use of angiotensin receptor blockers and angiotensin converting enzyme inhibitors in relation to COVID-19 (corona virus disease 2019). | Wrong study design |
| 2cecb2777e82bff611494ef649c943ae9e7b2218 | A global treatments for coronaviruses including COVID-19.   | Wrong study design |
| 92bd255acb9a6f07582773c661d90695e661ff4f | A human neutralizing antibody targets the receptor binding site of SARS-CoV-2.  | Wrong study design |
| e267d737ffee9e65f58496090c59e2d2fd26657c | A hypothesis for pathobiology and treatment of COVID-19: the centrality of ACE1/ACE2 imbalance.   | Wrong study design |
| 6acef577c6a0963c7e71425950b1add0c0033d54 | A Meta-analysis of the Relationship Between Renin-Angiotensin-Aldosterone System Inhibitors and COVID-19.   | Wrong study design |
| deb4dfa407710411a686de1b82ce426da170d7d9 | A Network Medicine Approach to Investigation and Population-based Validation of Disease Manifestations and Drug Repurposing for COVID-19.                           | Wrong study design |

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|  |  |                    |
|--|--|--------------------|
| a5456750f7cd9f9c441fa511fafb2cd4<br>e51956a8 | A potential protective role of losartan against coronavirus-induced lung damage.   | Wrong study design |
| 4d2a030ef947c41ae9e28abf9bac484<br>b5021b2f6 | A systematic review and meta-analysis to evaluate the clinical outcomes in COVID-19 patients on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. | Wrong study design |
| 311ef551e8a4faef99df4daccf74391c<br>abf2bf0b | A systematic review to evaluate the clinical outcomes in COVID-19 patients on angiotensin converting enzyme inhibitors or angiotensin receptor blockers                    | Wrong study design |
| 7172f457ead3953cf6a4c329f8ebf73<br>5f2afeb3  | A Viewpoint on Angiotensin-Converting Enzyme 2, Anti-Hypertensives and Coronavirus Disease 2019 (COVID-19).  | Wrong study design |
| 8f9801ae2d2ec320176db6443ba952<br>5eb1a0b32b | ACE inhibition and cardiometabolic risk factors, lung ACE2 and TMPRSS2 gene expression, and plasma ACE2 levels: a Mendelian randomization study                            | Wrong study design |
| 69c2278b9c24f939bf7f503c017fa6ef<br>b54baa67 | ACE Inhibitors and ARBs in Patients with COVID-19: Friend or Foe?  | Wrong study design |
| 99ba3e575c1a14527e5528f4db782ae<br>9180b1d4f | ACE inhibitors and COVID-19: We don't know yet.  | Wrong study design |
| d13dc3e6a8e970b972e69959c41b7d<br>82fe34115a | ACE inhibitors/ARB use and COVID-19. Time to change practice or keep gathering data?   | Wrong study design |
| 065e8a81c3651fef0868a2e2051e023<br>4bae22d67 | ACE2 and COVID-19 and the resulting ARDS.  | Wrong study design |
| 4067c593205ae932b07312f86d4d38<br>9cc4f832e8 | ACE2 and prognosis of COVID-19. Insights from Bartter's and Gitelman's syndromes patients.   | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| 42552661b2e7566cb82d704b8a98d957bae6ba02 | ACE2 as a Therapeutic Target for COVID-19; its Role in Infectious Processes and Regulation by Modulators of the RAAS System.  | Wrong study design |
| ef52203b12a48fa4b1e9097b394d258262048a76 | ACE2 the Janus-faced protein - from cardiovascular protection to severe acute respiratory syndrome-coronavirus and COVID-19.  | Wrong study design |
| ba2c1dd9ea9db292fa1d8aa41ff82d79b08db63c | ACE2, COVID-19, and ACE Inhibitor and ARB Use during the Pandemic: The Pediatric Perspective.   | Wrong study design |
| 5fc48a6a252404f4bda3264d55eac7db60c6b54e | ACE2, Much More Than Just a Receptor for SARS-COV-2.  | Wrong study design |
| 691adf55311463a5a256958a55f62202d21b593e | ACE2, the Receptor that Enables the Infection by SARS-CoV-2: Biochemistry, Structure, Allostery and Evaluation of the Potential Development of ACE2 Modulators.                     | Wrong study design |
| 85b40529a8142d110930f435b9868c6822ba7170 | ACEi and ARB with COVID-19.   | Wrong study design |
| b633c5428f7d2ac8f0c511bb384538703136bdf3 | ACEI/ARB Use and Risk of Infection or Severity or Mortality of COVID-19: A Systematic Review and Meta-analysis.   | Wrong study design |
| b9901d9447300bbf9a0146d8850567afca9270a2 | ACUTE AORTIC DISSECTION SURGERY IN PATIENT WITH COVID-19.   | Wrong study design |
| fded3f936fe3bfca32880839736aac40b72ef0ba | Acute Kidney Injury in a Case Series of Patients with Confirmed COVID-19 (Coronavirus Disease 2019): Role of Angiotensin-Converting Enzyme 2 and Renin-Angiotensin System Blockade. | Wrong study design |

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|---|---|--------------------|
| 1d5fbab274a55d13cf42d8ed5bd0d5f<br>830fe23b8  | Advanced bioinformatics rapidly identifies existing therapeutics for patients with coronavirus disease-2019 (COVID-19).                   | Wrong study design |
| 0b84e0055a22045ceeb0721e4938358<br>a2d9499590 | An immunotherapeutic method for COVID-19 patients: a soluble ACE2-Anti-CD16 VHH to block SARS-CoV-2 Spike protein.                        | Wrong study design |
| 2613b7005f82e69b56f057c57020ce7<br>7074727a1  | An update on ACE2 amplification and its therapeutic potential.  | Wrong study design |
| 62dff4325b29b345c984808c6d2414<br>95129c8180  | Angiotensin converting enzyme 2 (ACE2) and COVID-19: using antihypertensive medications, pharmacogenetic considerations.                  | Wrong study design |
| d1038e2aed5d247156fb6a62fa0d336<br>9157edd13  | Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System.                                       | Wrong study design |
| 6ed81e30d3f149c69764482901edeb<br>c0477c56b7  | Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers and Outcome of COVID-19: A Systematic Review and Meta-analysis | Wrong study design |
| f79d5fb95afbadf13c39e362f83ff31c<br>cd1543e5  | Angiotensin II Receptors - Impact for COVID-19 Severity.  | Wrong study design |
| 4d698ca49bd01138e25de674a17ccf2<br>8980531a4  | Angiotensin Receptor Blockers and 2019-nCoV.  | Wrong study design |
| fea7e4d4dc4a92a56fd038222901109<br>8608c082c  | Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics.   | Wrong study design |
| 5748b36b6bc9b0cbb4a1d900a51078<br>690be01891  | Angiotensin receptor blockers for the treatment of covid-19 and its comorbidities.  | Wrong study design |
| 5ee2331f7622a991216c359b9bf6a79<br>98bc7d033  | Angiotensin-(1-7) and Obesity: Role on cardiopulmonary fitness and COVID-19 implications.   | Wrong study design |

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|---|---|--------------------|
| 3844300acf19aa5ddad6c247dea2a99<br>220e5a801  | Angiotensin-(3-4) modulates angiotensin converting enzyme 2 (ACE2) downregulation in proximal tubule cells due to overweight and undernutrition: implications regarding the severity of renal lesions in Covid-19 infection | Wrong study design |
| 68950fe4430d0bea1cb2442dd22efff<br>5d6283cb2  | Angiotensin-converting enzyme 2 (ACE2) expression increases with age in patients requiring mechanical ventilation.  | Wrong study design |
| 6dcc74fc29876dde219d3f4de10cab6<br>383b78442  | Angiotensin-Converting Enzyme 2 and Antihypertensives (Angiotensin Receptor Blockers and Angiotensin-Converting Enzyme Inhibitors) in Coronavirus Disease 2019  | Wrong study design |
| 48b49a3754f38985f5250b62947404<br>69efffb4389 | Angiotensin-converting enzyme inhibitors and angiotensin receptor blocker in coronavirus disease 2019: Safe and possibly beneficial.  | Wrong study design |
| 063e367728e0b05f187219f09c7a253<br>af5df1b1c  | Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers in Patients With Coronavirus Disease 2019: Friend or Foe?  | Wrong study design |
| ebe9f3f072a32530c1d3e192af94fc09<br>6a1ab6cf  | Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic.   | Wrong study design |
| 4ef2eada8790fd1f8a1c21e7ae731c98<br>3516295a  | Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers and coronavirus.   | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| fa344fed20dfbe055037d7599bb4830<br>da3114e29 | Angiotensin-converting enzyme inhibitors, angiotensin II type 1 receptor blockers and risk of COVID 19: information from Bartter's and Gitelman's syndromes patients. | Wrong study design |
| cd982381ad41325ea326a756f0fbf9b<br>a553a89fc | Angiotensin-converting enzyme-2 (ACE2), SARS-CoV-2 and pathophysiology of coronavirus disease 2019 (COVID-19).  | Wrong study design |
| 950e3e9ce3fd4ee08e1d216629f5ee4<br>8d22ee00d | Angiotensin-converting-enzyme inhibitors (ACE inhibitors) and Angiotensin II receptor blocker (ARB) Use in COVID-19 prevention or treatment: A Paradox.               | Wrong study design |
| 7938e4c5a6faa3ab7ed13de1a9fcf3e1<br>42e5a565 | Angiotension-converting enzyme inhibitors and angiotensin-receptor blockers are not associated with increased risk of SARS-CoV-2 infection.                           | Wrong population   |
| 79a50b9c070149a8dd8cdaca9780dae<br>a60017005 | ANNALS EXPRESS: Coronavirus disease 2019 (COVID-19) and the renin-angiotensin system: a closer look at angiotensin-converting enzyme 2 (ACE2).                        | Wrong study design |
| da7357f035546f4824995f76cae8e41<br>8394db74e | Antagonizing the renin-angiotensin-aldosterone system in the era of COVID-19.   | Wrong study design |
| 1f2b8ca30bee7becda1f1c31c636230<br>67d7b3e4e | Anti-RAS drugs and SARS-CoV-2 infection.  | Wrong study design |
| bb8c6dfe0d6a089673dd928ffb0858f<br>491e87695 | Antihypertensive medication uses and serum ACE2 levels  | Wrong population   |
| ba5907bc7cbe727dd15547f5937df0f<br>639bda86a | Antihypertensive treatment with ACEI/ARB of patients with COVID-19 complicated by hypertension.   | Wrong study design |

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|--|--|--------------------|
| 673faf23a6e89c3189703816439a8b2<br>f7bed3d01 | Association Between ACEIs or ARBs Use and Clinical Outcomes in COVID-19 Patients: A Systematic Review and Meta-analysis  | Wrong study design |
| 96244b03e261fbb7b90083dd97244a<br>1f652976a9 | Association between angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers use and the risk of infection and clinical outcome of COVID-19: a comprehensive systematic review and meta-analysis. | Wrong study design |
| c2e188a058275ef5ace13342e768d25<br>9f8eb1930 | Association of previous medications with the risk of COVID-19: a nationwide claims-based study from South Korea  | Wrong population   |
| 1a8cd76be7b604ca38833b16a40af20<br>7bf63aea0 | Association of Renin Angiotensin System Blockers with Outcomes in Patients with Covid-19: A Systematic Review and Meta-analysis  | Wrong study design |
| 1047aef98486b613b61a0a19695418<br>2d6d73c803 | Blocking mineralocorticoid receptor with spironolactone may have a wide range of therapeutic actions in severe COVID-19 disease.   | Wrong study design |
| 45d405de02b71f1068a6f981170d54<br>11db864088 | Blood Targets of Adjuvant Drugs Against COVID19.   | Wrong study design |
| 493b8ecd3fb3de383897f41a0472fd2<br>a6f6d01c2 | Calcium channel blocker amlodipine besylate is associated with reduced case fatality rate of COVID-19 patients with hypertension   | Wrong study design |
| b0624da2fe91087e0c971ff0643edfe<br>d0896a11d | Cardiac patients and COVID-19: What the general practitioner should know   | Wrong study design |
| d61382f494423cc752214e3c879a273<br>34c2738d5 | Cardiovascular Disease and Use of Renin-Angiotensin System Inhibitors in COVID-19.   | Wrong study design |

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|--|---|--------------------|
| 0ad463be494a2dec27857959941e28f<br>e65c73816 | Cardiovascular disease management during the coronavirus disease 2019 pandemic.   | Wrong study design |
| f69e401f727af8308dc8b2dd8970e6<br>497ea9f25  | Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19.  | Retracted article  |
| a5d8b968b6740e8f8d107148983435<br>17957af9fa | Cardiovascular manifestations and treatment considerations in covid-19.   | Wrong study design |
| 75e0efdc91cbd7ad28ace4fac8ee8f0b<br>7737bd21 | Cardiovascular medications and regulation of COVID-19 receptors expression  | Wrong study design |
| ef130f490189dac71510e6c5d65591d<br>8ce74942c | Clinical and Genetic Characteristics of Covid-19 Patients from UK Biobank   | Wrong population   |
| bf11bbc97cd3bfee26a86a4e9caa8ce<br>1bf9dea4f | Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.                                     | Wrong intervention |
| 385ae60eccb4453950e90a8ed94fc13<br>04cd233ba | Clinical experience with therapeutic dose of Low-Molecular-Weight Heparin.  | Wrong study design |
| 017d802e28534e2dbea34128e56f3c9<br>1b335706b | Clinical impact of renin-angiotensin system inhibitors on in-hospital mortality of patients with hypertension hospitalized for COVID-19.                            | Wrong study design |
| 8ecee8540fdb75aa0564894494a9638<br>41842cb54 | Clinical Implications of SARS-CoV2 Interaction with Renin Angiotensin System.   | Wrong study design |
| db5209e69b36410082efd2c349db34<br>d6a488dc25 | Clinical presentation and initial management critically ill patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Brescia, Italy. | Wrong intervention |

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|  |   |                    |
|--|---|--------------------|
| e401deb8cfb020f53c3a2953ee326d41fe1ef8ab | Combination of Recombinant Bacterial ACE2 Receptors -Like Enzyme of B38-CAP and Isotretinoin Could be Promising COVID-19 Infection- and Lung Injury Preventing Drug Better Than Recombinant Human ACE2                        | wrong intervention |
| 78c34849b299aed2e1ccdcf8e528a5f42ba83efe | Comment on "ACE inhibitors and COVID-19: We don't know yet".  | Wrong study design |
| b9559084fc514d3cb85bf8dd6aab158e51288e26 | Comparison of renin-angiotensin-aldosterone system inhibitors with other antihypertensives in association with coronavirus disease-19 clinical outcomes: systematic review and meta-analysis                                  | Wrong study design |
| b91eba75b18bae2b43401a2fa3e56a40d2b0fb0  | Comparisons of <i>Staphylococcus aureus</i> infection and other outcomes between users of angiotensin-converting-enzyme inhibitors and angiotensin II receptor blockers: lessons for COVID-19 from a nationwide cohort study. | Wrong population   |
| c30377b9fae543271eb008057af6e16f67ea1b6  | Compliance of Antihypertensive Medication and Risk of Coronavirus Disease 2019: A Cohort Study Using Big Data from the Korean National Health Insurance Service.  | Wrong population   |
| 040406b6e4f42274b3c6e759a14e1459df8f0272 | Computational Design of Peptides to Block Binding of the SARS-CoV-2 Spike Protein to Human ACE2   | Wrong study design |
| 70a8b0894ebcfaa4f66e3804f1907a74304baf16 | Considerations about the relationship between hypertension and the prognosis of COVID-19  | Wrong study design |

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|   |   |                    |
|---|---|--------------------|
| 67a3d10ada304275894b9962290ba6b56693b351  | Contentious Issues and Evolving Concepts in the Clinical Presentation and Management of Patients with COVID-19 Infectionwith Reference to Use of Therapeutic and Other Drugs used in Co-morbid Diseases (Hypertension, Diabetes etc)                                | Wrong study design |
| d5a38bd406dd63ea09027302cf75c3a00cb171e9  | Continue ACE inhibitors/ ARB'S till further evidence in Coronavirus disease 2019 (COVID-19).  | Wrong study design |
| a5489c9736d126ee30a581b4f689869ade4aec61  | Controversial Relationship between Renin-Angiotensin System Inhibitors and Severity of COVID-19: Announcing a Large Multicentre Case-Control Study in Italy.  | Wrong study design |
| af971cbc013ca89bed585f848143b112018aac94  | Controversies of renin-angiotensin system inhibition during the COVID-19 pandemic.  | Wrong study design |
| 65850e914a9a0987fdbd71506ed6036e4a1766518 | Controversy regarding ACE inhibitors / ARBs in COVID-19.  | Wrong study design |
| 8c3f6b5a4c8b7258e90092e1306406311bc307b2  | Coronavirus Disease 2019 (COVID-19) and Cardiovascular Disease: A Viewpoint on the Potential Influence of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers on Onset and Severity of Severe Acute Respiratory Syndrome Coronavirus 2 Infection | Wrong study design |
| bf538797d1960243999b1b71cf271b68698bf952  | Coronavirus Disease 2019 (COVID-19) Infection and Renin Angiotensin System Blockers.  | Wrong study design |
| 18c126ca7c24f795aabf6e2b0fc7a405762811e6  | Coronavirus disease 2019 (COVID-19): angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers and cardiovascular disease.   | Wrong study design |

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|--|--|--------------------|
| b4c1c73e336b0e437c623cae55b9b471b9de7cb3 | Coronavirus Disease 2019 (COVID-19): Do Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers Have a Bi-phasic Effect?                                  | Wrong study design |
| a15a4eb7f7b604eab32bb56794d0a35a7bb080a9 | Coronavirus Pandemic-Therapy and Vaccines.   | Wrong study design |
| f9ec570dca94dbca767b047bcab619fd058b9a13 | Coronavirus: a clinical update of Covid-19.  | Wrong study design |
| 3a0f0f34f6a2149af3c10c8644fb5a83c08b0ba5 | Correlation between renin-angiotensin system and Severe Acute Respiratory Syndrome Coronavirus 2 infection: What do we know?   | Wrong study design |
| 839137b0b86cf17776a72c6dc73d19bc959f1297 | Could renin-angiotensin-aldosterone system inhibitors be used for hypertensive patients with coronavirus disease 2019?   | Wrong study design |
| e5e1d99ee2573ce2302c5eb9bee5ac97fe5553ef | Counter-regulatory 'Renin-Angiotensin' System-based Candidate Drugs to Treat COVID-19 Diseases in SARS-CoV-2-infected patients.  | Wrong study design |
| 6b360f18fa6fd994bd855b069752fd2cc6b3217  | COVID 19 and heart failure: from infection to inflammation and angiotensin II stimulation. Searching for evidence from a new disease.                                    | Wrong study design |
| 0c2e36bd98058c9f904d8af0984eacd3eda5b83  | COVID-19 - Does This Disease Kill Due to Imbalance of the Renin Angiotensin System (RAS) Caused by Genetic and Gender Differences in the Response to Viral ACE 2 Attack? | Wrong study design |
| 68d4190c2d00204d4adbb75641daa4e42f5b09ee | COVID-19 and Angiotensin-Converting Enzyme Inhibitor/Angiotensin-Receptor Blocker Therapy.   | Wrong study design |

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|   |  |                    |
|---|--|--------------------|
| 3c5c19906477755db2391b0f98bb4b<br>fd783d851c  | COVID-19 and Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers: What Is the Evidence?   | Wrong study design |
| d58a2dacb5ae8b7a40e0d04fb47345<br>6273e1a73c  | COVID-19 and arterial hypertension: Hypothesis or evidence?  | Wrong study design |
| 58041be97e2fec1884f3ee5a0c9e6ce7<br>8db84d18  | COVID-19 and cardiovascular diseases: viewpoint for older patients.  | Wrong study design |
| bd7a5c79624f7da70c1d71c7417202<br>483908756f  | Covid-19 and cardiovascular risk: Susceptibility to infection to SARS-CoV-2, severity and prognosis of Covid-19 and blockade of the renin-angiotensin-aldosterone system. An evidence-based viewpoint. | Wrong study design |
| b715bf7cd2e68d6a73d2ee72fdf1f34<br>105c24d20  | COVID-19 and Diabetes: Knowledge in Progress.  | Wrong study design |
| 9c36e2a3c46228bfcc20ea-<br>caf54c30d52d529262 | COVID-19 and hypertension-evidence and practical management: Guidance from the HOPE Asia Network.  | Wrong study design |
| 420b15f92526d232917f55bca701d1<br>c7c0cf1a18  | COVID-19 And Older Adults: What We Know.   | Wrong study design |
| 7b0085a7a1f333ae7641b884df1d651<br>e570dda63  | COVID-19 and RAS: Unravelling an Unclear Relationship.   | Wrong study design |
| a7252cb693ed8d60dedb1b2c6a600b<br>53b68e2507  | COVID-19 and Renin Angiotensin Blockers: Current Evidence and Recommendations.   | Wrong study design |
| 10566eea559cbab56f1d78231fe7224<br>ae9d939ed  | COVID-19 and Renin-Angiotensin system inhibition - role of angiotensin converting enzyme 2 (ACE2) - Is there any scientific evidence for controversy?  | Wrong study design |

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|   |  |                    |
|---|--|--------------------|
| 5b09398bf82991f686b30a0ab90d53<br>6ae829b1c1  | COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options.  | Wrong study design |
| 3bc3c5c3815e46c3819026c2a65a316<br>8d68550d2  | COVID-19 and the heart: An update for clinicians.  | Wrong study design |
| c17150b1070026102327d63a92fb38<br>8bdb8a8c3e3 | COVID-19 and the RAAS-a potential role for angiotensin II?   | Wrong study design |
| 08e435700e12d063f57632a06fcc44f<br>abb760724  | COVID-19 and the RAAS.   | Wrong study design |
| fd23e82ad-<br>dfe0c5850700f3d2f4b0448eb7d71c5 | COVID-19 and the role of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers  | Wrong study design |
| d5f7d241561fda7beb538c7eff1f1cc8<br>703e92cf  | COVID-19 Blood Pressure Endothelium Interaction Study (OBELIX)   | Wrong intervention |
| 90fefc9b4b83d4adb0143453cba744<br>b8f78e5ae3  | COVID-19 in diabetic patients: related risks and specifics of management.  | Wrong study design |
| 1bac43fdb9cedd84acdec3bd4ba-<br>bfd8addf98d3a | COVID-19 pandemic and therapy with ibuprofen or renin-angiotensin system blockers: no need for interruptions or changes in ongoing chronic treatments. | Wrong study design |
| b3c3059a42fdec05f355f02e32492b5<br>dff796fc1  | COVID-19 Related Lockdown Effects On Chronic Diseases  | Wrong population   |
| e53bc6b85af83129b18c9333022d88<br>465cf5c368  | COVID-19, ACE -inhibitors and angiotensin receptor blockers-: The need to differentiate between early infection and acute lung injury                  | Wrong study design |
| e57d022ef1dbe3ef0a33be0bffbdbb3<br>8362c9041  | COVID-19, ACE2 and the Cardiovascular Consequences.  | Wrong study design |
| 291c9c6f0558c6f74bb6c084f5a4ef59<br>d24e3f08  | COVID-19, ACEI/ARBs and gastrointestinal symptoms: the jury is still out on the association.   | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| 836ee91300cdf749add0a48fe43b028<br>ee89dcc83 | COVID-19, Angiotensin Receptor Blockers, and the Brain.   | Wrong study design |
| af301fe046fded59990ef-faf07c7a3af458352d3    | COVID-19, hypertension and cardiovascular diseases: Should we change the therapy?   | Wrong study design |
| e94cf111213a5729e02940d383b601<br>7097dab461 | COVID-19, Renin-Angiotensin System and Endothelial Dysfunction.   | Wrong study design |
| b3d1663237fd001bcaa6dd61d28ab0<br>ac39d63bd4 | COVID-19: ACE2centric infective disease?  | Wrong study design |
| 8b779937b66a55ae210a5aaab643f32<br>6d68b5f75 | COVID-19: is there a link between the course of infection and pharmacological agents in diabetes?   | Wrong study design |
| 3642c8f60705e87e6f091f1a1cd7d13<br>030306f61 | Covid-19: the renin-angiotensin system imbalance hypothesis.  | Wrong study design |
| a0ea531c7578997dd1984d4fcf88720<br>3bd411f06 | COVID-19: Updated Data and its Relation to the Cardiovascular System.   | Wrong study design |
| c39472fb55da1dd1f3926c45533a791<br>330c1b978 | COVID19 inhibitors: A prospective therapeutics.   | Wrong study design |
| 8f3f74b1dc65ce23ab66ac832a69fcf8<br>9456b8d4 | Curative anticoagulation prevents endothelial lesion in COVID-19 patients.  | Wrong comparison   |
| 0f4872434fe8a9d1056377acedfb8a5<br>06bfd7759 | Dangers of ACE inhibitor and ARB usage in COVID-19: evaluating the evidence   | Wrong study design |
| 06f3f62de34852f0ef65a5ced6a1a4d6<br>0f0ca8d1 | Decreased Mortality of COVID-19 with Renin-Angiotensin-Aldosterone System Inhibitors Therapy in Patients with Hypertension:A Meta-Analysis. | Wrong study design |
| e1b3d7d1044254f1779c050ea2a753<br>175962a165 | Diabetes and COVID-19: evidence, current status and unanswered research questions.  | Wrong study design |

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|  |  |                    |
|--|--|--------------------|
| 5c83e27ff92804153694dd7ebd7c7ab<br>a55b37c6e | Discovery of Drug-like Ligands for the Mac1 Domain of SARS-CoV-2 Nsp3  | Wrong study design |
| 3621d4c49614f500b5d1927fd45879<br>c4795f3568 | DISEQUILIBRIUM BETWEEN THE CLASSIC RENIN-ANGIOTENSIN SYSTEM AND ITS OPPOSING ARM IN SARS-COV-2 RELATED LUNG INJURY.                          | Wrong study design |
| a1b2f5d0fa74f0821f958eb20d24588<br>50b834de9 | Do ACE inhibitors and angiotensin receptor antagonists increase the risk of severe COVID-19?   | Wrong study design |
| 0cfac32ea5e9344e2994b1725cd14f2<br>2883eae49 | Do not discontinue ACE inhibitors and sartans!: RAS inhibitors could even protect hypertensive patients against severe COVID-19 progressions | Wrong study design |
| f61f14fdc6aa6497268b662f2f98949a<br>ba4bf476 | Does the direct renin inhibitor have a role to play in attenuating severity of the outbreak coronavirus disease 2019 (COVID-19)?             | Wrong study design |
| d3212b7510f7bd1684a1b5d8205796<br>8e16bb1b7a | Downregulation of ACE2 induces overstimulation of the renin-angiotensin system in COVID-19: should we block the renin-angiotensin system?    | Wrong study design |
| 0670c92b515844c19ab8ef04707d32<br>c204c923f7 | Drug treatments affecting ACE2 in COVID-19 infection: a systematic review protocol.  | Wrong study design |
| 1b547a4b3dff9abc750fc200c46179<br>972d4b5a3  | Drugs acting on renin angiotensin system and use in ill patients with COVID-19.  | Wrong study design |
| 25b67a1daa80988d198ff2cea697d43<br>000ba6432 | Effect of angiotensin II blockers on the prognosis of COVID-19: a toxicological view.  | Wrong study design |
| 81e87c07b4e5dfc3cbefa9f0323d301<br>b55271ce0 | Effects of ACEIs and ARBs on Clinical Outcomes in COVID-19 Patients: A Meta-Analysis   | Wrong study design |

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|  |  |                    |
|--|--|--------------------|
| 8b6da29dc6dc642ba4ecc301fbb234<br>a158256812 | Effects of Renin-Angiotensin Inhibition on ACE2 and TMPRSS2 Expression: Insights into COVID-19.  | Wrong study design |
| c49fe85113cf4b445af3a65b459ce21<br>d8bdeb613 | Effects of Renin-Angiotensin Inhibition on ACE2 and TMPRSS2 Expression: Insights into COVID-19.  | Wrong study design |
| a9837db5841b850ebd7429cc2d9913<br>110bb7ae9c | Estimation of RAAS-Inhibitor effect on the COVID-19 outcome: A Meta-analysis.  | Wrong study design |
| 6da1935915462498ba26fef69ee2c5<br>cf9653cd   | Evidence for Use or Disuse of Renin-Angiotensin System Modulators in Patients Having COVID-19 With an Underlying Cardiorenal Disorder. | Wrong study design |
| 1d5b6c6f08077dce4fd05860e3aa58<br>01c614b35  | Facts and reflections on COVID-19 and anti-hypertensives drugs.  | Wrong study design |
| e0f2906a4dd1166569aa3f37cdca2f1<br>4c7264005 | Further developments in the literature on RAAS inhibitors and COVID-19.  | Wrong study design |
| 80dc2fd169dd18e43455c61dc6c31<br>1f5e148673  | Good or bad: Application of RAAS inhibitors in COVID-19 patients with cardiovascular comorbidities.                                    | Wrong study design |
| 837b7fe496920cb76e3e87df9ab3ce0<br>09735a03d | Good things come in threes (and sometimes fours): Update on renin-angiotensin-aldosterone system inhibitors and COVID-19               | Wrong study design |
| a5701119efa49dac8f2249f91471944<br>cf3a4e6e7 | Headache medication and the COVID-19 pandemic.   | Wrong study design |
| db40f143d5de1b37f72c1078fb383a4<br>66a19166b | Hiding in Plain Sight: an Approach to Treating Patients with Severe COVID-19 Infection.  | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| b888e8db8089b1c0b5ea09e245bff5<br>4fafaf060a | Hypertension and renin-angiotensin system blockers are not associated with expression of Angiotensin Converting Enzyme 2 (ACE2) in the kidney | Wrong study design |
| 78ef663fe2417633e26a209f5017954<br>c092c9abc | Hypertension prevalence in human Coronavirus: The role of ACE system in infection spread and severity.  | Wrong study design |
| 594dc673eaefcbc19f051775862da08<br>b3040f8f2 | Hypertension, renin-angiotensin-aldosterone system inhibition, and COVID-19.  | Wrong study design |
| dd28c837c4c2fa2da818a81bb22062<br>0559174f8d | Hypertension, the renin-angiotensin system, and the risk of lower respiratory tract infections and lung injury: implications for COVID-19.    | Wrong study design |
| 81988e84a51fe51c9f9bbded742e6ee<br>cc9b3126d | Hypothesis: angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may increase the risk of severe COVID-19.              | Wrong study design |
| dbc047620dd88ca6d2b36be4fd85dc<br>b9a7033075 | Immunomodulatory therapy for the management of severe COVID-19. Beyond the anti-viral therapy: A comprehensive review.                        | Wrong study design |
| f4c96704c8ed6ba660e53deb8ce1984<br>f05e1c71c | Impact of Angiotensin II Type 2 Receptor Agonists Treatment in Patients With COVID 19 (COVID-ARA2)  | Wrong comparison   |
| 00aafea16571e9355a00ec97b65d6be<br>761bd7fb0 | Impact of hospitalised patients with COVID-19 taking Renin-Angiotensin-Aldosterone System inhibitors: a systematic review and meta-analysis   | Wrong study design |
| b6ce3b2319fb183b36c3d362b118b9<br>4730216093 | Important Steps to Control COVID-19/SARS-CoV-2 Infection.   | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| 273b1d3531a2b4183264f28b82aac6<br>5480a3b01e   | Influenza Vaccination, ACEI and ARB in the Evolution of SARS-Covid19 Infection  | Wrong comparison   |
| 8b48056fcdbc21b726f7f4b3140fcdf9f<br>1d1fee1a8 | Inhibitors of the renin-angiotensin system and SARS-CoV-2 infection.  | Wrong study design |
| cd976a29604c5c1e013dbb99830b73<br>bafe87dcf9   | Inhibitors of the renin-angiotensin system: The potential role in the pathogenesis of COVID-19.   | Wrong study design |
| 830a23a877bca790e88751ccaeb6651<br>889494098   | Inhibitors of the Renin-Angiotensin-Aldosterone System and Covid-19.  | Wrong study design |
| 770090b8e01a88046b2418556b2bca<br>45a4f6f97a   | Interaction between RAAS inhibitors and ACE2 in the context of COVID-19.  | Wrong study design |
| 4c1d3bd5219c748bf4b81dd5b99b3f<br>a1f1556d68   | Interactions of coronaviruses with ACE2, angiotensin II, and RAS inhibitors-lessons from available evidence and insights into COVID-19. | Wrong study design |
| 3bd4349a6ba5b62cb7a2a25d87b0a7<br>b7d8bb3fb5   | Intoxication With Endogenous Angiotensin II: A COVID-19 Hypothesis.   | Wrong study design |
| e84cf3d6db5de0929e861db76e84fa6<br>267186cf9   | Is Hypertension a Real Risk Factor for Poor Prognosis in the COVID-19 Pandemic?   | Wrong study design |
| 5c21f92e87e6c621f54b1b3f5fd38bc<br>bb134a54b   | Is the use of RAS inhibitors safe in the current era of COVID-19 pandemic?  | Wrong study design |
| ace012922a457250c87c011e7bdda<br>7a118157da    | Is There an Association Between COVID-19 Mortality and the Renin-Angiotensin System-a Call for Epidemiologic Investigations.            | Wrong study design |
| e3fc094e2fe02b2408eba87e1275dce<br>ea86647f1   | Is there enough evidence to discontinue the renin-angiotensin system inhibitors in patients with COVID-19?                              | Wrong study design |

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|---|---|--------------------|
| 203e6e50c331e2a436ec950f6940b5b<br>a6d8140a5  | Issues of Cardiovascular Risk Management in People With Diabetes in the COVID-19 Era.   | Wrong study design |
| 5c26507ce73a1f3c6293f654637dd7a<br>1a0772c56  | JAK Inhibition as a New Treatment Strategy for Patients with COVID-19.  | Wrong study design |
| 708e113c1197347f81fc7842d9ae610<br>80f5c578a  | Keep Taking Your ACE Inhibitors and ARBs During the COVID 19 Pandemic.  | Wrong study design |
| 6a8e607c53267856cfdae290216d66d<br>82adf669f  | Kidney and Lung ACE2 expression after an ACE inhibitor or an Ang II receptor blocker: implications for COVID-19   | Wrong study design |
| 67402cef6570f8a6f031247d5c92fa04<br>b717afdf7 | Kidney and Lung ACE2 Expression after an ACE Inhibitor or an Ang II Receptor Blocker: Implications for COVID-19.  | Wrong study design |
| 76cd330ab69d13a5de57f0758a54e6<br>edc588b17   | Lack of Association Between Genetic Variants at ACE2 and TMPRSS2 Genes Involved in SARS-CoV-2 Infection and Human Quantitative Phenotypes.                                  | Wrong study design |
| 4b79fd1ec8af22edf238a46ae6dc02<br>ae464b151   | Lessons Learned to Date on COVID-19 Hyper-inflammatory Syndrome: Considerations for Interventions to Mitigate SARS-CoV-2 Viral Infection and Detrimental Hyperinflammation. | Wrong study design |
| 188906d3137590062c8a9dbc9876df<br>1ea9e7c9a4  | Letter in response to the article: Comorbidities in COVID-19: Outcomes in hypertensive cohort and controversies with renin angiotensin system blockers (Singh et al.).      | Wrong study design |

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|  |   |                    |
|--|---|--------------------|
| 3ece3e51acd5f94fd2767ee66c1b486<br>699f390c5 | Letter to the editor: The role of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in developing a COVID-19 comorbidity-based host risk score.                          | Wrong study design |
| a7cc4acbafdce851699d849026b454e<br>112798161 | Letter to the editors in response to: Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic (Cure et al.). | Wrong study design |
| c203479f7803e7edff6805c8d9e22cb<br>c35030ff3 | Lipid-lowering therapy and renin-angiotensin-aldosterone system inhibitors in the era of the COVID-19 pandemic.   | Wrong study design |
| ac3a25c0d62069c89085f4d6d5a070b<br>9301ad253 | Management of hypertension in COVID-19.   | Wrong study design |
| e43e430f8672ecbe8646f11c20ef7cb<br>954867e9c | Mechanism of inflammatory response in associated comorbidities in COVID-19.   | Wrong study design |
| dd9da8f7c52fd41c9aab9757de859fb<br>f91638fa1 | Might renin-angiotensin system blockers play a role in the COVID-19 pandemic?   | Wrong study design |
| aa9448f35c03db1da660bb369f17b7e<br>5583b19f1 | Modulation of the acute defence reaction by eplerenone prevents cardiac disease progression in viral myocarditis.   | Wrong study design |
| 6c68f0383c72cdbd3823a9d5ebefb<br>bbb22a5b29  | Molecular Insights Into SARS COV-2 Interaction With Cardiovascular Disease: Role of RAAS and MAPK Signaling.  | Wrong study design |
| 495e1b48958f3b707c147d59d4b304<br>bc077926c4 | More evidence is urgently needed to confirm the relation between angiotensin-converting enzyme inhibitors and COVID-19.   | Wrong study design |

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|   |  |                    |
|---|--|--------------------|
| 1319a5c3694420043b362d36a781d7<br>6b8bd1a2aa  | Mortality and use of angiotensin converting enzyme inhibitors in Covid 19 disease - a systematic review.   | Wrong study design |
| d4d73c87773b1dd0fa8eb4c6393301<br>acdf9d5ab8  | Mortality in COVID-19 patients treated with ACEIs/ARBs: re-estimated meta-analysis results following the Mehra et al. retraction.  | Wrong study design |
| 10101152479158301e1f5ec-<br>deab1bcbd9138b332 | Multiple functions of angiotensin-converting enzyme 2 and its relevance in cardiovascular diseases.  | Wrong study design |
| e614840211d94c0293c7f33972979f6<br>572f0cef4  | Neprilysin inhibitor-angiotensin II receptor blocker combination (sacubitril/valsartan): rationale for adoption in SARS-CoV-2 patients.  | Wrong study design |
| f11c31cb2bcb82ee64189f15d352349<br>bb61d883c  | NON-WHITE ETHNICITY, MALE SEX, AND HIGHER BODY MASS INDEX, BUT NOT MEDICATIONS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM ARE ASSOCIATED WITH CORONAVIRUS DISEASE 2019 (COVID-19) HOSPITALISATION: REVIEW OF THE FIRST 669 CASES FROM THE UK BIOBANK | Wrong population   |
| 4d00816caa9e1f50313d981f297dbe3<br>36eb67bf3  | Organ-protective Effect of Angiotensin-converting Enzyme 2 and its Effect on the Prognosis of COVID-19.  | Wrong study design |
| b948d10e4a82e27d8d38336e91e347<br>cecec32dc6  | Outcomes in Patients with COVID-19 Infection Taking ACEI/ARB.  | Wrong study design |
| 526c902da8da5c0beb54fccfa4f9333<br>efa57e0d3  | Outcomes of renin-angiotensin-aldosterone system blockers in patients with COVID-19: a systematic review and meta-analysis.  | Wrong study design |

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|  |  |                    |
|--|--|--------------------|
| 64c41b28b3e1ca71212875ef5ff849<br>75d567692  | Overview of Covid-19 regarding the cardiovascular situation in the light of current reports.   | Wrong study design |
| f67992687855414ca5e088d0de1d12<br>63ae12e7b5 | Pathological Role of Angiotensin II in Severe COVID-19.  | Wrong study design |
| 1dc4b723c28aea7ad467aea0e245d8f<br>1e26e55cb | Pharmaco-Immunomodulatory Therapy in COVID-19.   | Wrong study design |
| 7b330b086c0d870b75fc3c38f0fc91a<br>bf22fc3a8 | Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review.  | Wrong study design |
| 4d8f8e409d9de9cb7498aeda87ebb8<br>b50a832323 | Pharmacotherapy in COVID-19 patients: A review of ACE2-raising drugs and their clinical safety.  | Wrong study design |
| 9a841c7cc78b03b88965c2cb7ee31<br>bb72c3bc3   | Pharmacotherapy in COVID-19; A narrative review for emergency providers  | Wrong study design |
| 4d952fe73268f522b00680e001c5af3<br>9ad2a25ad | Pharmacovigilance in patients with diabetes: A data-driven analysis identifying specific RAS antagonists with adverse pulmonary safety profiles that have implications for COVID-19 morbidity and mortality. | Wrong population   |
| 23de999173b2f554a31762e34ed38f5<br>7fe967cee | Possible effects of coronavirus infection (COVID-19) on the cardiovascular system  | Wrong study design |
| 6b24db98e83fac1f6f8dead48506978<br>fc76f1013 | Possible Protective Effect of Renin-Angiotensin System Inhibitors in COVID-19 Induced Acute Kidney Injury.   | Wrong study design |
| 3d3a40cea88551b4c0cd667a6c230fc<br>187043f26 | Potential differential effects of renin-angiotensin system inhibitors on SARS-CoV-2 infection and lung injury in COVID-19.   | Wrong study design |
| 40155b1385d628856b996a072873ce<br>f14d02c379 | Potential harmful effects of discontinuing ACE-inhibitors and ARBs in COVID-19 patients.   | Wrong study design |

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|   |  |                    |
|---|--|--------------------|
| 02427695c27e2a4393afcf63a6b531fe7d92a69   | Potential inhibitors of the interaction between ACE2 and SARS-CoV-2 (RBD), to develop a drug.  | Wrong study design |
| 05ef2381c1e009e6b8f4bd530639a0552b924fb6  | Potential Role of ACE2 in Coronavirus Disease 2019 (COVID-19) Prevention and Management.   | Wrong study design |
| 35980bc57fc9b227cbe86ca028f26ee0957e2e5a  | Prognostic factors in patients with diabetes hospitalized for COVID-19: Findings from the CORONADO study and other recent reports.   | Wrong study design |
| 6c2e183ef5a16440d06cf44ad5d3cee a4786d76b | Proper Management of People with Obesity during the COVID-19 Pandemic.   | Wrong study design |
| eaae35a050e5f265b682439b68d9938a4f89eee6  | RAAS blockade, kidney disease, and expression of ACE2, the entry receptor for SARS-CoV-2, in kidney epithelial and endothelial cells | Wrong study design |
| 5c1a0b010f2f8f1672744aaa0bd8e8083a2a3225  | RAAS blockers in hypertension posing a higher risk towards the COVID-19.   | Wrong study design |
| 52e53f748e44fc403f89ad69870bf59866392c86  | RAAS inhibitors do not increase the risk of COVID-19.  | Wrong study design |
| 2b180207d4013791f17b390bd4b8c38cbdb02426  | Ramipril in High Risk Patients with COVID-19.  | Wrong study design |
| c3d4f6ebf077d8a2ab4b10b71155b516bfe28f77  | Recombinant Human Angiotensin-converting Enzyme 2 (rhACE2) as a Treatment for Patients With COVID-19                                 | Retracted article  |
| c860c61ca2eae77d815bb03824104cf02e74ef6a  | Recombinant Human Angiotensin-converting Enzyme 2 (rhACE2) as a Treatment for Patients With COVID-19                                 | Wrong intervention |

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|  |   |                    |
|--|---|--------------------|
| 2a86b2d7c45df4a9fa827ed1a6d0ca4<br>59b022bb8 | Relationship between ACE-inhibitors, ARBs and SARS-CoV-2 infection: where are we?   | Wrong study design |
| d7f18e35eae4590ed6345c2d7b0189<br>7915a05e63 | Relationship Between ACE2 and Other Components of the Renin-Angiotensin System.   | Wrong study design |
| be2f5fbf8891d442f1708053a28c78ef<br>ae0e91bc | Renin-angiotensin system and SARS-CoV-2 interaction: underlying mechanisms and potential clinical implications.   | Wrong study design |
| dd5f891f54786fadb096f1f3dd3f890<br>0b89e7e57 | Renin-Angiotensin System Blockade in COVID-19: Good, Bad, or Indifferent?   | Wrong study design |
| 96a705f8f5883bff8637dc9ddc1bd66<br>bd1c5d44c | Renin-Angiotensin System Blockers and the COVID-19 Pandemic: At Present There Is No Evidence to Abandon Renin-Angiotensin System Blockers.  | Wrong study design |
| 6f3270c493a8ba2022586ea136aab16<br>a15047785 | Renin-Angiotensin System Inhibition in Cardiovascular Patients at the Time of COVID19: Much Ado for Nothing? A Statement of Activity from the Directors of the Board and the Scientific Directors of the Italian Society of Hypertension. | Wrong study design |
| cee6e2d1685e4bfb049347fe395f63c<br>8391ecd3a | Renin-angiotensin system inhibition in COVID-19 patients: Friend or foe?  | Wrong study design |
| c9343ae34bb436139fae21b97fc8083<br>c48707d91 | Renin-angiotensin system inhibition in COVID-19 patients.   | Wrong study design |
| 18f84f198d6985bc89e1d5bc6166bcc<br>e055ce185 | Renin-Angiotensin System Inhibitors and COVID-19: Potential Therapeutics Rather Than Perpetrators.  | Wrong study design |
| 179437c7124d84d152fc590420d853<br>d62bf582df | Renin-angiotensin system inhibitors in COVID-19.  | Wrong study design |

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|   |  |                    |
|---|--|--------------------|
| 794bd721af940f2108a77dbc71c62bc5cdba340f  | Renin-angiotensin system inhibitors in management of hypertension during the COVID-19 pandemic.  | Wrong study design |
| b7eabfdbf330a0c6112af1bd1e147e03cc9e5c10  | Renin-angiotensin system inhibitors in the COVID-19 pandemic: consequences of antihypertensive drugs.  | Wrong study design |
| cf32779fb6199aebfdca543a3726bf d024ab8d3  | Renin-Angiotensin-Aldosterone Inhibitors and Susceptibility to and Severity of COVID-19.   | Wrong study design |
| 396cff89b2d736eb2f2a05f23991361 73e146f48 | Renin-angiotensin-aldosterone system and COVID-19 infection.   | Wrong study design |
| 74e0936b4de9638520d5661b809d5b 4e2be86e25 | Renin-Angiotensin-Aldosterone System Blockers and the Risk of Covid-19.  | Wrong population   |
| 4b475488c289949a4e03e9ed9a79ffa 55fedb471 | Renin-angiotensin-aldosterone system in new coronavirus infection 2019   | Wrong study design |
| 5eae5c4dc8155d7e80789a45df56958 3e87cb929 | Renin-angiotensin-aldosterone system inhibitors and COVID-19.  | Wrong study design |
| c133f6202425c851bfe312cbdf47ef7f 42f40f4b | Renin-angiotensin-aldosterone system inhibitors and mortality in patients with hypertension hospitalized for COVID-19: a systematic review and meta-analysis | Wrong study design |
| b35d1d2ea2dbe1b3b1294f4df77286 9d065b236c | Renin-angiotensin-aldosterone system inhibitors impact on COVID-19 mortality: What's next for ACE2?  | Wrong study design |
| bd4afc7b43a3fa4fc5a36b6460357a3 c1880484a | Renin-Angiotensin-Aldosterone System Inhibitors in Covid-19.   | Wrong study design |
| 84dae6cbf9191269f26e463986d992a 4ec9d2092 | Renin-Angiotensin-Aldosterone System Inhibitors in Covid-19. Reply.  | Wrong study design |

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|---|--|--------------------|
| 2cfe0df2b84629cb6086c8df6d11d6d<br>aaabc9a87  | Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19.   | Wrong study design |
| 94e71bf36e2f500c9301cf3b24468f2f<br>dac5fdb7  | Renin-angiotensin-aldosterone system inhibitors to treat COVID-19?   | Wrong study design |
| af774b2f6607e3eec6a70164191e560<br>2dff038a0  | Reply to the letter of Mahajan and Gaur in response to the article: Comorbidities in COVID-19: Outcomes in hypertensive cohort and controversies with renin angiotensin system blockers (Singh et al.).  | Wrong study design |
| deb324f67f1d74bfb70783d45360e6<br>46d7904d94  | Repurposing of FDA-approved antivirals, antibiotics, anthelmintics, antioxidants, and cell protectives against SARS-CoV-2 papain-like protease.  | Wrong study design |
| ceaf41cd61e7fb74ee673dec7dcc805f<br>39779664  | Response by Cohen et al to Letter Regarding Article, "Association of Inpatient Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Mortality Among Patients With Hypertension Hospitalized With COVID-19". | Wrong study design |
| 2c0e7b71379032d52cd2c95d6b0509<br>311df6549e  | Response by Zhang et al to Letter Regarding Article, "Association of Inpatient Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Mortality Among Patients With Hypertension Hospitalized With COVID-19". | Wrong study design |
| 77d2818029028177064e7f9ccc9771<br>5caeef7e756 | Response to COVID-19 and ACEI/ARB: NOT ASSOCIATED?   | Wrong study design |

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| 16b2fb02ae24049ea8b97b7a467982ae17ab3e4f | Response to recent commentaries regarding the involvement of angiotensin-converting enzyme 2 (ACE2) and renin-angiotensin system blockers in SARS-CoV-2 infections.     | Wrong study design |
| 486c16ee8553728338086860620acb8686a0e1b6 | Review of evidence on using ACEi and ARBs in patients with hypertension and COVID-19  | Wrong study design |
| 9920f31200647f91f60f431f42020ebff633616  | Rheumatologists' perspective on coronavirus disease 19 (COVID-19) and potential therapeutic targets.  | Wrong study design |
| 937cc0a462189d293f53eb85845f78718995562b | Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults.  | Wrong study design |
| 7542fac1b992e2b2f622eed04ff85d94aa5b941  | Risks of ACE inhibitor and ARB usage in COVID-19: evaluating the evidence.  | Wrong study design |
| 9b5785ac6d261f7a732dadb26094173eb427c6a7 | Robust ACE2 protein expression localizes to the motile cilia of the respiratory tract epithelia and is not increased by ACE inhibitors or angiotensin receptor blockers | Wrong study design |
| 2b341d6809027ec6f8e052a484c537a96cb9f4fd | Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19.   | Wrong study design |
| 36624f4b9575179121819b537ead442c1dcbe51b | Role of Dipeptidyl Peptidase 4 Inhibitors in Diabetic Patients with Coronavirus-19 Infection.   | Wrong study design |
| f577135c14405a9ef40ab5df6b47e1a67ba34bc5 | Role of the Backbenchers of the Renin-Angiotensin System ACE2 and AT2 Receptors in COVID-19: Lessons From SARS.   | Wrong study design |
| ca60c373f91643125891b79d9274162b5026b372 | Sacubitril/valsartan in COVID-19 patients: the need for trials.   | Wrong study design |

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|--|--|--------------------|
| 77327e0a4bd82ac188bcad48de31d6<br>177d29d170 | SARS-CoV-2 (COVID 19) Infection in Hypertensive Patients and in Patients With Cardiac Disease.   | Wrong study design |
| 5e29bfd5af6fc8577df41ef64c6ea26c<br>db186b22 | SARS-CoV-2 comorbidity network and outcome in hospitalized patients in Crema, Italy  | Wrong study design |
| 04e8d81dcea80380217dafcf1ab1b9b<br>18ceda082 | SARS-CoV-2 downregulation of ACE2 and pleiotropic effects of ACEIs/ARBs.   | Wrong study design |
| 96069323dd15769ad80f970d6bb098<br>382e4d7494 | SARS-CoV-2 pandemic and research gaps: Understanding SARS-CoV-2 interaction with the ACE2 receptor and implications for therapy.   | Wrong study design |
| b7e950af3e0634328154046635c0a5a<br>32f4988b7 | SARS-CoV-2 receptor ACE2 gene expression and RAAS inhibitors.  | Wrong study design |
| 5d60531273e591242ce7053609dc45<br>eaef98d8   | SARS-CoV2: should inhibitors of the renin-angiotensin system be withdrawn in patients with COVID-19?   | Wrong study design |
| 2c02542b1083340b347e57822df9bf<br>a11c372ccf | Scientific statement of the Chinese Society of Cardiology (CSC) on using of renin angiotensin system blockers in patients with cardiovascular disease and COVID-19.                                | Wrong study design |
| 337afd2739902e11a60c0a70abfe-faf9ece03342    | Searching therapeutic strategy of new coronavirus pneumonia from angiotensin-converting enzyme 2: the target of COVID-19 and SARS-CoV.   | Wrong study design |
| 59bf5c0ecb806004c3f294efa9d81bf<br>3877f7601 | Severe acute respiratory syndrome coronavirus 2 infection, angiotensin-converting enzyme 2 and treatment with angiotensin-converting enzyme inhibitors or angiotensin II type 1 receptor blockers. | Wrong study design |

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|---|---|--------------------|
| 8b679e4fa0bb8de8fd448f95e56cf6f<br>486ab079d  | Severe respiratory SARS-CoV2 infection: Does ACE2 receptor matter?  | Wrong study design |
| c19e21c52814ad10c8fab489d63b2b<br>ea73edb7dd  | Should COVID-19 Concern Nephrologists? Why and to What Extent? The Emerging Impasse of Angiotensin Blockade.  | Wrong study design |
| 8c84ca74af680ae176cee0b11eaafdf59<br>909fd95f | Should Patients Receiving ACE Inhibitors or Angiotensin Receptor Blockers be Switched to Other Antihypertensive Drugs to Prevent or Improve Prognosis of Novel Coronavirus Disease 2019 (COVID-19)? | Wrong study design |
| e1d9bef595454ef512126c095efefd7<br>636aebaa7  | Soluble angiotensin-converting enzyme 2: a potential approach for coronavirus infection therapy?  | Wrong study design |
| b9e5a48fca2803e5d442957cb97dc6<br>b53298acf0  | Spironolactone in Covid-19 Induced ARDS   | Wrong intervention |
| e8d9b09dc174c0a22881cfa528e9f1c<br>d06d900c9  | Substituting Angiotensin-(1-7) to Prevent Lung Damage in SARS-CoV-2 Infection?  | Wrong study design |
| dff1324350e1006661a37f4c0060f22<br>c6754d3d1  | Susceptibility of the Elderly to SARS-CoV-2 Infection: ACE-2 Overexpression, Shedding, and Antibody-dependent Enhancement (ADE).  | Wrong study design |
| 369176494abc9be0ad8e3535e6d21c<br>c3b8527bcb  | Switching to another antihypertensive effective drug when using ACEIs/ARBs to treat arterial hypertension during COVID-19.  | Wrong study design |
| 55fc44a93fe768b14f9bd64d6ccebd7<br>10347b7c9  | Targeting of renin-angiotensin system in COVID-19 patients affected by stroke: Emerging concerns about detrimental vs. benefit effect   | Wrong study design |

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|---|---|--------------------|
| ce03a13247ed8c00d3d9e450e84258<br>44f5c50c3e  | Telmisartan as tentative angiotensin receptor blocker therapeutic for COVID-19.   | Wrong study design |
| 28dd7d78672b7e49aeb24436cf9427<br>3dc4d96e60  | The ACE-2 in COVID-19: Foe or Friend?   | Wrong study design |
| 1a6db1432f0d5980fde8f21c251bb5c<br>2bf0c8c97  | The angiotensin-converting enzyme 2 (ACE2) receptor in the prevention and treatment of COVID-19 are distinctly different paradigms.   | Wrong study design |
| 5d68fa532fb28231faebe8b98093fc9<br>368fa0334  | The Association Between Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers and the Number of Covid-19 Confirmed Cases and Deaths in the United States: Geospatial Study | Wrong study design |
| 4cc67cfef3bc19dba3256b55bfce633<br>6e0a31249  | The Dilemma of Renin Angiotensin System Blockers in Coronavirus Disease (Covid-19): Insights on the Lung Fluid Handling and Gas Exchange in Heart Failure Patients.                             | Wrong study design |
| 9e0f957fc3798454989ea58bb6f26f9<br>b241a8888  | The dual impact of ACE2 in COVID-19 and ironical actions in geriatrics and pediatrics with possible therapeutic solutions.  | Wrong study design |
| f293ba221bcbed82feec5b1be8a62fd4<br>4f5fc67d5 | The effect of angiotensin converting enzyme inhibitors and angiotensin receptor blockers on death and severity of disease in patients with coronavirus disease 2019 (COVID-19): A meta-analysis | Wrong study design |
| 794c2ca95bea4ca2301a7c194140f66<br>2a5a354ac  | The Effect of Coronavirus Disease 2019 on Cardiovascular Diseases.  | Wrong study design |
| fe6e10d26aa54dc41d03ecb55a9fdb6<br>c4d6f929c  | The emerging role of ACE2 in physiology and disease.  | Wrong study design |

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|---|--|--------------------|
| fcdefe13ec1e339b9b0aa0456692232<br>8fb2f5331  | The impact of SARS-CoV-2 transmission fear and COVID-19 pandemic on the mental health of patients with primary immunodeficiency disorders, severe asthma, and other high-risk groups   | Wrong population   |
| a37dae78ab3712567851f60c3ebbe10<br>d994f2001  | The Impact of the COVID-19 "Infodemic" on Drug-Utilization Behaviors: Implications for Pharmacovigilance.  | Wrong study design |
| 3a1464d54158b967934431b2936db<br>4ffd6e27299  | The Lung, the Heart, the Novel Coronavirus, and the Renin-Angiotensin System; The Need for Clinical Trials   | Wrong study design |
| f63c88e5fa9ea70d9942016e807d679<br>45ed6ad0f  | The mechanistic overview of SARS-CoV-2 using angiotensin-converting enzyme 2 to enter the cell for replication: possible treatment options related to the renin-angiotensin system.    | Wrong study design |
| 25f7a2afe-<br>afa506ec764660e880a322c08c68d0a | The Network of Angiotensin Receptors in Breast Cancer.   | Wrong study design |
| b2e1c527060a74373fca3af7154beaf<br>1fb6d634f  | The potential benefit of telmisartan to protect overweight COPD patients from the acquisition of COVID-19.   | Wrong study design |
| 2cb0007ea1feb8e2ec19ea08ca136ec<br>d88f6592b  | The renin-angiotensin system - a therapeutic target in COVID-19?   | Wrong study design |
| dfb17237a6ceae3825a9904a0d1bd5e<br>8d3864e52  | The role of ACEIs/ARBs in COVID-19: Friend or foe?   | Wrong study design |
| 4f9ac0937c6cb2ec511d8ae8d5e142d<br>2eb601137  | The SARS-CoV-2 receptor, ACE-2, is expressed on many different cell types: implications for ACE-inhibitor- and angiotensin II receptor blocker-based antihypertensive therapies-reply. | Wrong study design |

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|---|---|--------------------|
| 4d34457daa50d905eb-dcd5c25839ea8ad39c34cc | The SARS-CoV-2 receptor, ACE-2, is expressed on many different cell types: implications for ACE-inhibitor- and angiotensin II receptor blocker-based cardiovascular therapies: comment. | Wrong study design |
| 8ae28e0c9f91530ddb8f74ff8f384cf95e0ef68c  | The SARS-CoV-2 receptor, ACE-2, is expressed on many different cell types: implications for ACE-inhibitor- and angiotensin II receptor blocker-based cardiovascular therapies.          | Wrong study design |
| 4dc2bc229ba483e5fb89870fd75918bf9e02ee4b  | The Two Faces of ACE2: The Role of ACE2 Receptor and Its Polymorphisms in Hypertension and COVID-19.  | Wrong study design |
| a88e3aaa0450394fad7b1c0a13db315e9db7ffd1  | The use of Captopril - angiotensin converting enzyme (ACE) inhibitor for cystinuria during COVID-19 pandemic.   | Wrong study design |
| 465868adbd310d3aaa8a286465f0bdf e069831df | The use of renin angiotensin system inhibitor on mortality in patients with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis.                                 | Wrong study design |
| 103b568435e98745695608d413518029d7918c53  | The vascular endothelium: the cornerstone of organ dysfunction in severe SARS-CoV-2 infection.  | Wrong study design |
| 7aa4beca4b0bc99dc8a0766a6441b32afeddaec6  | Therapeutic strategies in an outbreak scenario to treat the novel coronavirus originating in Wuhan, China.  | Wrong study design |
| 2d265dfc0e8015c005391dab15e9bc656353fd7a  | Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad.   | Wrong study design |
| 8e10a92ec2a05e471b22c6a3e438bacbf8f9f0a8  | Treatment options for COVID-19: The reality and challenges.   | Wrong study design |

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|   |   |                    |
|---|---|--------------------|
| 07a7892268796010dcbbba154b7dc53<br>07bcc402be | Treatment with ACE inhibitors or ARBs and risk of severe/lethal COVID-19: a meta-analysis.  | Wrong study design |
| 2caf1ca3ef45f245ca0168846ed3a556<br>d7ccb7bf  | TWIRLS, a knowledge-mining technology, suggests a possible mechanism for the pathological changes in the human host after coronavirus infection via ACE2. | Wrong study design |
| 1502a156c6c94e3f4f876b40b3616db<br>a71d67f6e  | Two hits to the renin-angiotensin system may play a key role in severe COVID-19.  | Wrong study design |
| 638c84e8b20e4c50664dbd9cc08aa0<br>8c49d5d2a5  | Understanding the Renin-Angiotensin-Aldosterone-SARS-CoV-Axis: A Comprehensive Review.  | Wrong study design |
| cb7013eac07486b6d8425fd3985b29<br>ba861cf21b  | Update Alert 2: Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults.          | Wrong study design |
| b09395365a7e38747ea9df31232465c<br>7428bba4e  | Update Alert: Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults.            | Wrong study design |
| e0f49fcf18976873b759131a32ff7599<br>c54f3614  | Use of inhibitors of the renin angiotensin system and COVID-19 prognosis: a systematic review and meta-analysis   | Wrong study design |
| 9178615c384265ddcaf43801ec5d34<br>30628b5fd0  | Use of Renin-Angiotensin System Blockers During the COVID-19 Pandemic: Early Guidance and Evolving Evidence.  | Wrong study design |
| c58911138d975cc047a5c8bbde3699<br>479a55540f  | Use of Spironolactone in SARS-CoV-2 ARDS Patients.  | Wrong intervention |
| cfa228a08c0a397945716c27cb9e67c<br>3aeba4824  | Vasculopathy and Coagulopathy Associated with SARS-CoV-2 Infection.   | Wrong study design |

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|---|---|--------------------|
| 811e459a6b8d82bfde1bbcc931bb52<br>3b5fbdbd3e      | Virtual Screening of Natural Products against Type II Transmembrane Serine Protease (TMPRSS2), the Priming Agent of Coronavirus 2 (SARS-CoV-2). | Wrong study design |
| 9313872720b46cf96a6790ab099a4ca<br>cb6dcbb63      | What could be the better choice between ACE inhibitors and AT1R antagonists in coronavirus disease 2019 (COVID-19) patients?                    | Wrong study design |
| e4ae2e5be006752584ca328e1b5a872<br>1e58721f1      | What Solid Organ Transplant Healthcare Providers should know about Renin-Angiotensin-Aldosterone System Inhibitors and COVID-19.                | Wrong study design |
| 6a22754d249e6fde40c39f8e9d07c89<br>e799fc97b      | What We Learned about COVID-19 So Far? Notes from Underground.  | Wrong study design |
| 9eb-<br>bef238024294127c0d0753dc55e03f4<br>70e24c | What would Sérgio Ferreira say to your physician in this war against COVID-19: How about kallikrein/kinin system?                               | Wrong study design |
| 4a702e5e97cd8218e4c302a26852d2f<br>a2f018e62      | Would ACEIs/ARBs be beneficial for COVID-19 patients without hypertension?  | Wrong study design |

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## **Appendix 2: Included, excluded and ongoing studies**

### **Excluded studies references**

1. Shi HZ, Ma P, Gao FY, Chen GL, Yu YH, Wang XD, et al. [2019 novel coronavirus, angiotensin converting enzyme 2 and cardiovascular drugs]. Zhonghua xin xue guan bing za zhi. 2020;48(0):E010.
2. Fang Y, Guo Z, Chai Y, Zhang H, Wang Z. [2019 Novel coronavirus, renin-angiotension system imbalance and coronavirus disease 2019]. Zhonghua wei zhong bing ji jiu yi xue. 2020;32(5):613-7.

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10. Usman MS, Siddiqi TJ, Khan MS, Ahmed A, Ali SS, Michos ED, et al. A Meta-analysis of the Relationship Between Renin-Angiotensin-Aldosterone System Inhibitors and COVID-19. The

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