

Appendix 2: Included, excluded and ongoing studies - Macrolides for the treatment of COVID-19: A living systematic review - VERSION 1.0, 6 AUGUST, 2020.

INCLUDED STUDY

Cavalcanti et al, 2020	Details or comments
Study design	Multicenter, randomized three arms controlled trial, open-label, involving hospitalized patients with suspected or confirmed COVID-19. Groups: standard care (Control); standard care plus hydroxychloroquine; or standard care plus azithromycin and plus hydroxychloroquine
Population (inclusion criteria)	Adults hospitalised with suspected or confirmed mild or moderate COVID-19 and fewer than 14 days since symptoms onset. Patients were excluded if they needed oxygen supplementation > 4 L/min via nasal cannula or ≥ 40% via Venturi mask, oxygen supplementation via high-flow nasal cannula, non-invasive ventilation, invasive mechanical ventilation.
Intervention	Standard care plus hydroxychloroquine at a dose of 400 mg twice daily plus azithromycin at a dose of 500 mg once a day for 7 days
Comparison	Standard care plus hydroxychloroquine at a dose of 400 mg twice daily for 7 days (hydroxychloroquine-alone group)

<p>Outcomes</p>	<p>Quote:</p> <p>The primary outcome was clinical status at 15 days, evaluated with the use of a seven-level ordinal scale. Scores on the scale were defined as follows: a score of 1 indicated not hospitalized with no limitations on activities; 2, not hospitalized but with limitations on activities; 3, hospitalized and not receiving supplemental oxygen; 4, hospitalized and receiving supplemental oxygen; 5, hospitalized and receiving oxygen supplementation administered by a high-flow nasal cannula or noninvasive ventilation; 6, hospitalized and receiving mechanical ventilation; and 7, death.</p> <p>Secondary outcomes included: clinical status at 7 days, evaluated with the use of a six-level ordinal scale (see below and the Supplementary Appendix); indication for intubation within 15 days; the receipt of supplemental oxygen administered by a high-flow nasal cannula or noninvasive ventilation since randomization to 15 days; duration of hospital stay; in-hospital death; thromboembolic complications; acute kidney injury; and the number of days alive and free from respiratory support up to 15 days. A day alive and free from respiratory support was defined as any day in which the patient did not receive supplemental oxygen or invasive or noninvasive mechanical ventilation, from randomization to day 15. Patients who died during the 15-day window were assigned a value of 0 days alive and free from respiratory support in this assessment. Safety outcomes are listed in the Supplementary Appendix. All the trial outcomes were assessed by the site investigators, who were aware of the trial-group assignments (except as noted above for patients who had been discharged before day 15 and who were assessed for the primary outcome by means of a blinded telephone interview). No formal adjudication of trial outcomes was performed.</p>
<p>Risk of bias assessment (RoB 2.0)</p>	
<p>Risk of bias arising from the randomization process</p>	<p>Low risk of bias</p> <p>"The trial statistician, not involved with patient enrollment or care, generated the randomization table in R software (R Core Team, 2019) and implemented in the RedCap. The study treatment was revealed to investigators only after patients were registered in the RedCap,</p>

	ensuring proper concealment of the allocation sequence."
Risk of bias due to deviations from intended intervention	High risk of bias "Second, the trial was not blinded" 20,7% excluded from azithromycin group, 28% from control group
Risk of bias due to missing outcome data	Low risk of bias "The 15-day follow-up was completed for all the remaining 665 patients"
Risk of bias in measurement of outcomes	Low risk of bias "All the trial outcomes were assessed by the site investigators, who were aware of the trial-group assignments (except as noted above for patients who had been discharged before day 15 and who were assessed for the primary outcome by means of a blinded telephone interview). "
Risk of bias in selection of reported results	Low risk of bias Outcomes prespecified in protocol reported in published study

Included study references

1. Cavalcanti et al., 2020

- a. Cavalcanti AB, Zampieri FG, Rosa RG, Azevedo LCP, Veiga VC, Avezum A, et al. Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19. *New England Journal of Medicine* [Internet]. 2020; Disponible en: <http://www.epistemonikos.org/documents/79704ea40a0f18569c3315ad29cc32ad3a8c63f9>
- b. Alexandre B Cavalcanti, Fernando G Zampieri, Luciani CP Azevedo, Regis G Rosa, Alvaro Avezum, Viviane C Veiga, et al. Hydroxychloroquine alone or in combination with azithromycin to prevent major clinical events in hospitalised patients with coronavirus infection (COVID-19): rationale and design of a randomised, controlled clinical trial. *medRxiv* [Internet]. 2020; Disponible en: <http://www.epistemonikos.org/documents/96503f28453df78a82f39ff139ed120961da5495>

- c. Hospital do C. Safety and Efficacy of Hydroxychloroquine Associated With Azithromycin in SARS-Cov-2 Virus. clinicaltrials.gov. [Internet]. 2020; Disponible en: <https://www.epistemonikos.org/en/documents/642d2e56c7e5b1477fafce586e12ae9af718117d>

EXCLUDED STUDIES

Epistemonikos ID	Title	Reason for exclusion
988af4d6445cdbbdec6a15099c66759c74e2cce9	[Clinical features and therapy of 106 cases of severe acute respiratory syndrome].	Wrong study design
f22a9cd1c7a13503743936700a99b3f5208eb88e	[Clinical features of 77 patients with severe acute respiratory syndrome].	Wrong study design
8f5fd6731a967cf75b7c13b8c2acc418d0057c3c	[Hydroxychloroquine. Cardiology's viewpoint in times of coronavirus pandemic].	Wrong study design
8e425d333bf3a91feda0b57037b53e5a6840a0e7	A clinical, randomized study to evaluate the efficacy and safety of Naproxen compared to placebo in combination with Azithromycin or Levofloxacin in patients with Severe Acute Respiratory Syndrome during the Covid-19 pandemic	Wrong comparison
af57c2e336258fab95941088157dc6f86f40950d	A cohort of 1061 COVID-19 patients, treated for at least 3 days with the HCQ-AZ combination and a follow-up of at least 9 days	Wrong study design
4971cbebec8215708f9b5ecdc0dc754b3ae25fe5	A Comparative Study on Ivermectin and Hydroxychloroquine on the COVID19 Patients in Bangladesh	Wrong comparison
569d06159235a365450c12305df4297b9a54ad79	A randomized multicenter clinical trial to evaluate the efficacy of melatonin in the prophylaxis of SARS-CoV-2 infection in high-risk contacts (MeCOVID Trial): A structured summary of a study protocol for a randomised controlled trial.	Wrong comparison
de0efc16dde3e6070d336dcb02b7c3be9801b24b	A Real-life Experience on Treatment of Patients With COVID 19	Wrong comparison
a5fd6a4738f1081ebf2b75d521812dd1903b825a	A short therapeutic regimen based on hydroxychloroquine plus azithromycin for the treatment of COVID-19 in patients with non-severe disease. A strategy associated with a reduction in hospital admissions and complications.	Wrong study design

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cc316192aef67df464dd65fb75f3e92ebfb43755	A SINGLE-BLINDED RANDOMIZED, PLACEBO-CONTROLLED PHASE II TRIAL OF PROPHYLACTIC TREATMENT WITH ORAL AZITHROMYCIN VERSUS PLACEBO IN CANCER PATIENTS UNDERGOING ANTINEOPLASTIC TREATMENT DURING THE CORONA VIRUS DISEASE 19 (COVID-19) PANDEMIC	Wrong population
6d1d1827c22dc866c650e86e8cb7e0a642fa6ba4	ACUTE QT INTERVAL MODIFICATIONS DURING HYDROXYCHLOROQUINE-AZITHROMYCIN TREATMENT IN THE CONTEXT OF COVID-19 INFECTION	Wrong study design
75a9736626a1da5ea1fbc85d1003be83ec63fdcd	Acute Respiratory Failure Secondary to COVID-19 Viral Pneumonia Managed With Hydroxychloroquine/Azithromycin Treatment.	Wrong study design
dc53a11df1a9317496e00d88ca4e00b0a9449424	Additional safety consideration for azithromycin in the management of SARS-CoV-2 infection.	Wrong study design
7a3be14021257bec2411bc2cc4ee1009cfd3abdd	ADL-dependency, D-Dimers, LDH and absence of anticoagulation are independently associated with one-month mortality in older inpatients with Covid-19.	Wrong study design
193585215bac31de3033be1c158a1481e4053ebd	Adverse Events Related to Treatments Used Against Coronavirus Disease 2019	Wrong study design
fcd36368ca9d56f6476b23868f001e2717025dd8	An Observational Cohort Study of Hydroxychloroquine and Azithromycin for COVID-19: (Can't Get No) Satisfaction.	Wrong study design
c7b982903c02645f7a77c38ac85a78bd4a71df16	An Observational Study to Assess the Protocol for the COVID-19 Treatment in Burkina Faso	Wrong comparison
bc6aedc01b74a22f6637876890c86dfbddd39c06	An overview of coronaviruses including the SARS-2 coronavirus - Molecular biology, epidemiology and clinical implications.	Wrong study design
c3d19da69f556d94682ccc55214bec704b9983b	An overview of safety assessment of the medicines currently used in the treatment of COVID-19 disease.	Wrong study design
c52566c69eee662c48c8f74ed1f31de662ecdda7	An Update on Current Therapeutic Drugs Treating COVID-19.	Wrong study design
1a4c51c24b5254ddf96cd93de681e2d8a2785b42	An update on therapeutic repurposing strategies for COVID-19	Wrong study design

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18be58024e1f775ca925575ca51d4f8ac072d8e6	Anti-inflammatory Clarithromycin for Improving COVID-19 Infection Early	Wrong study design
f374df5fdb319b85261693623ed58df269fc2e6	Antimalarial and cytotoxic drugs on COVID-19 and the cardiovascular burden: Literature review and lessons to be learned.	Wrong study design
3b5e78ec676a8a7ef497f7a03ef80e740c86be3e	Apparent inefficacy of hydroxychloroquine combined with azithromycin on SARS-CoV-2 clearance in an incident cohort of geriatric patients with COVID-19.	Wrong study design
cc58de275ec31ca4df9992b1b5a5a0f79c74d86c	Arrhythmic profile and 24-hour QT interval variability in COVID-19 patients treated with Hydroxychloroquine and azithromycin.	Wrong population
ac07ea05f283c2b966b82c86075aadb1e855efe0	Assessment of Efficacy and Safety of HCQ and Antibiotics Administered to Patients COVID19(+)	Wrong study design
7dfea8fe43e12aa85d9a649ae5a133b3e6e5f288	Atovaquone and Azithromycin Combination for Confirmed COVID-19 Infection	Wrong study design
2fe4ac09beaed6b83234779dc2d9d57dd1d409cb	Azithromycin and ciprofloxacin have a chloroquine-like effect on respiratory epithelial cells	Wrong study design
a6ffd787097daaa36e13c3c618928248703bc4ff	Azithromycin and COVID-19 Prompt Early Use at First Signs of this Infection in Adults and Children An Approach Worthy of Consideration.	Wrong study design
97f29d57de511164f4480b3207bcc7737daf3c98	Azithromycin and SARS-CoV-2 infection: where we are now and where we are going.	Wrong study design
f40cb8090516435cb4d9f11b11b51a91295d73a3	Azithromycin for COVID-19: More Than Just an Antimicrobial?	Wrong study design
da51c0e3a1851999dffdf8e8c7d977f798e7c2f9	AZITHROMYCIN FOR CRITICALLY ILL PATIENTS WITH MIDDLE EAST RESPIRATORY SYNDROME	Wrong study design
e9d6a591817a7521db3178fdbc32e12ca5d0a20a	Azithromycin in COVID-19 Patients: Pharmacological Mechanism, Clinical Evidence and Prescribing Guidelines.	Wrong study design
bca63b13ab723253799e12c39433c600a7ccdd40	Azithromycin Should Not Be Used to Treat COVID-19.	Wrong study design

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5ceb31989365c792e414fd48661dcad011e37302	Beneficial effect of the hydroxychloroquine/azithromycin combination in elderly patients with COVID-19: Results of an observational study	Wrong study design
e61218e099523ab70e643e2dbddb662ab5080b48	Cardiac safety of off-label COVID-19 drug therapy: a review and proposed monitoring protocol.	Wrong study design
397b4e5fb7d2570430714666d57586ed9f87dcaf	Cardiovascular Safety of Potential Drugs for the Treatment of Coronavirus Disease 2019.	Wrong study design
9bbf3006fbf6b1883e0f78f941df8dd9ea932076	CD147 as a Target for COVID-19 Treatment: Suggested Effects of Azithromycin and Stem Cell Engagement.	Wrong study design
4417d78813548ef83b89c27a7e1d88da8103030e	Characteristics and Outcomes of Hospitalized Young Adults with Mild Covid -19.	Wrong study design
eb1f05c35ffcd888a10aba6eb66a7cd09bd1ef3	Characteristics and Outcomes of Hospitalized Young Adults with Mild to Moderate Covid-19 at a University Hospital in India	Wrong study design
36fae73d5c1ce3cc9ce783fd2e4ed0c87f104c3e	Chloroquine diphosphate in two different dosages as adjunctive therapy of hospitalized patients with severe respiratory syndrome in the context of coronavirus (SARS-CoV-2) infection: Preliminary safety results of a randomized, double-blinded, phase IIb clinical trial (CloroCovid-19 Study)	Wrong comparison
fcc55ce426e369bdc2ed308ceea340729c5b5498	Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study.	Wrong study design
ad06aebf9c98157631fa41efd596dc9c97983694	Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: an observational study	Wrong study design
898a295498b6cb14cd38a6a2990a8b7d5c979015	Clinical management of COVID-19	Wrong study design
47fb72e5e035e0355cc0547972059c7f1b6f47a5	Clinical Pharmacology Perspectives on the Antiviral Activity of Azithromycin and Use in COVID-19.	Wrong study design

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fe555acd94d416237a0d1b093a1cac6c32dfe8a8	Clinical Trial of Combined Use of Hydroxychloroquine, Azithromycin, and Tocilizumab for the Treatment of COVID-19	Wrong comparison
c31459e956bac5e5b0583952f24da3892769a3f8	Combination treatments with hydroxychloroquine and azithromycin are compatible with the therapeutic induction of anticancer immune responses	Wrong study design
c140265ba485ecfc46e38a7fd8e27cb92fe52b2c	Commentary on "Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open label non-randomized clinical trial" by Gautret et al.	Wrong study design
fdbd5a90045c8e3e9a8ef2f15a62887be1f607ee	Comorbidity and Sociodemographic determinants in COVID-19 Mortality in an US Urban Healthcare System	Wrong study design
b9b683ca97bc5708dead6882ae169fc1c12c487b	Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: A systematic review and network meta-analysis of confounder-adjusted 20212 hospitalized patients	Wrong study design
bacde88237ff62c23cf467ff6d4cfabccec72732	Comparative Efficacy and Safety of Pharmacological Interventions for the Treatment of COVID-19: A Systematic Review and Network Meta-Analysis of Confounder-Adjusted 36813 Hospitalized Patients	Wrong study design
c3720f963743adf1350ce9821516fed49c2ff897	Containment of pertussis in the regional pediatric hospital during the Greater Cincinnati epidemic of 1993.	Wrong population
94b86d575425134da949870c833b742122273d7c	Convalescent Plasma for Patients With COVID-19: A Randomized, Open Label, Parallel, Controlled Clinical Study	Wrong comparison
f9ec570dca94dbca767b047bcab619fd058b9a13	Coronavirus: a clinical update of Covid-19.	Wrong study design
e3b17b2547daae6a58cb8574223b1fc1afc7aa30	Correction: Safety considerations with chloroquine, hydroxychloroquine and azithromycin in the management of SARS-CoV-2 infection (CMAJ (2020) 192 (E450-E453) DOI: 10.1503/cmaj.200528)	Wrong study design
499f0cb1fd25b1cba5c77fb2358449814d7	Correction: Should Clinicians Use Chloroquine or Hydroxychloroquine Alone or in Combination With Azithromycin for the Prophylaxis or Treatment of COVID-19?	Wrong study design
df8baed66f3ed6da1d2ccf95606b2d75d8fb775e	COVID-19 and cardiac arrhythmias: a global perspective on arrhythmia characteristics and management strategies.	Wrong study design

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e17e7de526ceb45ba963373b77588f6048de4dec	COVID-19 and chronological aging: senolytics and other anti-aging drugs for the treatment or prevention of corona virus infection?	Wrong study design
48e47708801879ad0e75b351888795968c35c230	Covid-19 and lung cancer: A greater fatality rate?	Wrong study design
2b2f4f6d3d799b77e88701a2767d91ee1f32e816	Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid.	Wrong study design
8688967268e9eb34e337c1d58d0d209462c89a8d	COVID-19: A case report from Bangladesh perspective.	Wrong study design
87ee3ccac8cd34fb06d8297ba2edc6c78b46597d	Description and clinical treatment of an early outbreak of severe acute respiratory syndrome (SARS) in Guangzhou, PR China.	Wrong population
9eec298d77eea7a2882f89269655e2d82f835c7b	Does Adding of Hydroxychloroquine to the Standard Care Provide any Benefit in Reducing the Mortality among COVID-19 Patients?: a Systematic Review.	Wrong study design
f957aa50f2e0ce807b36cd990e5ee4f1985f3938	Early Impact of COVID-19 on Transplant Center Practices and Policies in the United States.	Wrong population
7de9d4a907fa3619c9ca2fee2a0a7e45d6350dac	Early Outpatient Treatment of Symptomatic, High-Risk Covid-19 Patients that Should be Ramped-Up Immediately as Key to the Pandemic Crisis.	Wrong population
a2d832e8e0bd1ee1670e72f672dae1abc54567f5	Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France.	Wrong study design
53780645a340530ef8ad08310d4abeca20127fdf	Effectiveness and Safety of Chloroquine or Hydroxychloroquine as a mono-therapy or in combination with Azithromycin in the treatment of COVID-19 patients: Systematic Review and Meta-Analysis	Wrong study design
c57f2bca6e1bc03b4c177f1979f2bf9d1088df0f	Effectiveness and toxicity of chloroquine and hydroxychloroquine associated (or not) with azithromycin for the treatment of COVID-19. What do we know so far?	Wrong study design
4431ea25b9b651b5598a441559a65a9e26852afe	Effectiveness of the combined treatment with hydroxycloquine and azithromycin vs lopinavir/ritonavir + hydroxycloquine in hospitalized patients with confirmed COVID-19 infection	Wrong comparison

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19eaddea9a12aa61a42fd3a34be98be4eb4b22f7	Effects on QT interval of hydroxychloroquine associated with ritonavir/darunavir or azithromycin in patients with SARS-CoV-2 infection.	Wrong comparison
f076eea19db68e03641ea5ffc569a259b5690ed1	Efficacy and Safety of Antibiotic Agents in Children with COVID-19: A Rapid Review	Wrong study design
10c85bb47e2b5ec883efd7277ed23df250784fd8	Efficacy and safety of antibiotic agents in children with COVID-19: A rapid review	Wrong study design
3f43be729d7a5a303ac04b4e70e8e69636868025	Efficacy and Safety of Hydroxychloroquine and Azithromycin for the Treatment of Ambulatory Patients With Mild COVID-19	Wrong study design
a1fad9e7de28f9a8039b367e319ccbea72586cfb	Efficacy and Safety of Hydroxychloroquine and Azithromycin for the Treatment of Hospitalized Patients With Moderate to Severe COVID-19	Wrong study design
de6730a0a569ef551429627e3e4198c3213ce21e	Efficacy of Chloroquine or Hydroxychloroquine in COVID-19 Patients: A Systematic Review and Meta-Analysis	Wrong study design
91e19a2cf9d8baa03222771a3f807d637ce668c3	Electrocardiographic safety of daily Hydroxychloroquine 400mg plus Azithromycin 250mg as an ambulatory treatment for COVID-19 patients in Cameroon.	Wrong study design
54a3690b9c75ea43a363f6f3093ac4008e6d323	Empirical treatment with hydroxychloroquine and azithromycin for suspected cases of COVID-19 followed-up by telemedicine	Wrong population
34212245d317cd906d27864f2b3943c3705fc29c	Encephalopathy and seizure activity in a COVID-19 well controlled HIV patient.	Wrong study design
d238c489daf7b9d8e08afb59c93585828b875755	Evaluate the Efficacy and Safety of Oral Hydroxychloroquine, Indomethacin and Zithromax in Subjects With Mild Symptoms of COVID-19	Wrong study design
1328553b15a98fbf0c09973c8e5e6b6e6f31088b	Evaluating the effects of different treatments on severe acute respiratory syndrome	Wrong comparison
b800908a3dbba72e95adedb9fbc5009fdb0a2900	Experience of short-term hydroxychloroquine and azithromycin in COVID-19 patients and effect on QTc trend.	Wrong study design
57e55cb61024355af4ebc4766c032506cdb3d69a	Experience with Hydroxychloroquine and Azithromycin in the COVID-19 Pandemic: Implications for QT Interval Monitoring.	Wrong study design

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76e20e0f7c6e24b0dfe1b924f7684cd98d158179	Expression of concern: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis.	Wrong study design
fa4ead4c7296315ebcefa91bef9d80faf3cc0611	Guidance On Minimizing Risk of Drug-Induced Ventricular Arrhythmia During Treatment of COVID-19: A Statement from the Canadian Heart Rhythm Society.	Wrong study design
f990ae5aae829a76450910b2326a33d861eeca39	Guidelines for the pharmacological treatment of COVID-19. The task-force/consensus guideline of the Brazilian Association of Intensive Care Medicine, the Brazilian Society of Infectious Diseases and the Brazilian Society of Pulmonology and Tisiology.	Wrong study design
6a3d7c6477ee82bfce4acbc14f2e477d061c0179	Hydroxychloroquine / chloroquine and azithromycin association for COVID-19: rapid systematic review	Wrong study design
6a3d922261c7ca7de362ecfd523e851e5626285a	Hydroxychloroquine and Azithromycin as a treatment of COVID-19: preliminary results of an open-label non-randomized clinical trial	Wrong study design
0d9f5f4a26df49e055fe8609c30e1943c25406e1	Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial	Wrong study design
678ec4156db27122671549fbec353da2379e43b8	Hydroxychloroquine and azithromycin as a treatment of COVID-19.	Wrong study design
1c24ee7478f94f44b46fbcda39385f0b9f6f1c4	Hydroxychloroquine and azithromycin as potential treatments for COVID-19; clinical status impacts the outcome.	Wrong study design
9b9e2f6cbc566a3ac0066f6ceabd322b08fe7f2	Hydroxychloroquine and Azithromycin as Prophylaxis for Healthcare Workers Dealing With COVID19 Patients	Wrong population
2d9eb9ce6c9c2f8c21325d62cbb4c5e6c948cb72	Hydroxychloroquine and Azithromycin to Treat Patients With COVID-19: Both Friends and Foes?	Wrong study design
36f1b9ce610c3e4a930e3908e6b5b3505c425095	Hydroxychloroquine and mortality risk of patients with COVID-19: a systematic review and meta-analysis of human comparative studies	Wrong study design
5194a3b7bd083bcea521248c3138fa897611e5a0	Hydroxychloroquine and Tocilizumab Therapy in COVID-19 Patients - An Observational Study	Wrong comparison

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abd5af0ac6ab929b402efba7d0ab8dbf444fd5eb	Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis.	Wrong study design
8e2bb4bcc11b4db4e3c56354c5162071e9a49e88	Hydroxychloroquine plus azithromycin: a potential interest in reducing in-hospital morbidity due to COVID-19 pneumonia (HI-ZY-COVID)?	Wrong study design
903bf49b8c01bc2394d5d62af9b9790c89813ea0	Hydroxychloroquine/ chloroquine as a treatment choice or prophylaxis for Covid-19 at the primary care level in developing countries: A Primum non Nocere dilemma.	Wrong study design
5f15a37631f5bf47260e539462a333ec0a60594d	Impact of disease on plasma and lung exposure of chloroquine, hydroxy-chloroquine and azithromycin: application of PBPK modelling.	Wrong study design
dcd4d5b689c7067ab936e3328628e794acc6ab31	In vitro testing of combined hydroxychloroquine and azithromycin on SARS-CoV-2 shows synergistic effect.	Wrong study design
b3428c1b91d331ff7f537c83c8bd24e75ccef420	Incidence and Determinants of QT Interval Prolongation in COVID-19 Patients Treated with Hydroxychloroquine and Azithromycin.	Wrong study design
2d9386d1c557a41c1dc9cb571081e88733fc88e8	Inpatient Use of Ambulatory Telemetry Monitors for COVID-19 Patients Treated with Hydroxychloroquine and/or Azithromycin.	Wrong comparison
b2d73ff88d3de39801ed73f4686a90fc5c0ca1bd	Intracellular ABCB1 as a Possible Mechanism to Explain the Synergistic Effect of Hydroxychloroquine-Azithromycin Combination in COVID-19 Therapy.	Wrong study design
91191506a64f70a66734c0adeebb53e423d490b4	Investigational Treatments for COVID-19 in Tertiary Care Hospital of Pakistan	Wrong comparison
bd59e73f964f03b5a1d782c45e7e7008558ba666	Investigational treatments for COVID-19 may increase ventricular arrhythmia risk through drug interactions	Wrong study design
d759d66db67ee42995f3ca7adb52b015434db363	Lack of viral clearance by the combination of hydroxychloroquine and azithromycin or lopinavir and ritonavir in SARS-CoV-2-related acute respiratory distress syndrome.	Wrong comparison
264daa7860828ebe6af02fa6f33d6006ed03bd8c	Levamisole and Isoprinosine in the Treatment of COVID19: A Proposed Therapeutic Trial	Wrong comparison

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a75f85819f3cfa6a982a46a71aaaa4672d9b2d97	Macrolide treatment for COVID-19: Will this be the way forward?	Wrong study design
871bd5039257096e9bdc10d1ccc28579d71215e7	Macrolides and viral infections: focus on azithromycin in COVID-19 pathology.	Wrong study design
dab849fe461bf656b47ffc85d8c65f4d26cebef0	Macrolides in critically ill patients with Middle East Respiratory Syndrome.	Wrong study design
0c6ef6394a490a6d1dce82b665de42e050358b0e	Mechanistic insights into ventricular arrhythmogenesis of hydroxychloroquine and azithromycin for the treatment of COVID-19	Wrong study design
669514a07cb20f6e3c3dcfda1336edbb6fef1448	Medications in COVID-19 patients: summarizing the current literature from an orthopaedic perspective.	Wrong study design
f95ee64457a6975eb29793152d8fe0cb9008f86c	Natural history of COVID-19 and current knowledge on treatment therapeutic options	Wrong study design
b937f2fb415aef18ccad31b4856439084f1914ac	Nitazoxanide/Azithromycin combination for COVID-19: A suggested new protocol for COVID-19 early management.	Wrong study design
333a30b1d9fbde1527d3ae1ddd5dc22df5161c42	Nitazoxanide/azithromycin combination for COVID-19: A suggested new protocol for early management	Wrong study design
2709f76166f6ca49a4364854e17a1f095512a74e	No evidence of clinical benefits of early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: Comment on "Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France".	Wrong study design
ea3ca720cb17dca7b6eefe3bbc61fc2dd2f369ac	No Evidence of Rapid Antiviral Clearance or Clinical Benefit with the Combination of Hydroxychloroquine and Azithromycin in Patients with Severe COVID-19 Infection	Wrong study design
d508690cf8ff3382213e4a8459bac9a63086d7e1	Off-label use of hydroxychloroquine, azithromycin, lopinavir-ritonavir and chloroquine in COVID-19: A survey of cardiac adverse drug reactions by the French Network of Pharmacovigilance Centers.	Wrong study design
e45980d738b56c89ca832e622290a9e9f74c7679	Old and re-purposed drugs for the treatment of COVID-19.	Wrong study design

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8fa0b5a56e73b48aebc65a7ad19dc28b0f14c3cb	Patient Preference Trial for COVID-19 (PPT-COVID)	Wrong study design
9a841c7cc78b03b88965c2cbcdcee31bb72c3bc3	Pharmacotherapy in COVID-19; A narrative review for emergency providers	Wrong study design
93f02027e308b09b1f701e3621fe06a6e1e59f98	Pneumonia in pregnancy.	Wrong study design
9ddb381558b5eee41a2f892225269dd4d2b3fea1	Potential use of hydroxychloroquine, ivermectin and azithromycin drugs in fighting COVID-19: trends, scope and relevance.	Wrong study design
5505c961632c7dc86acd7572d31affec0c3b1050	Predictions of Systemic, Intracellular, and Lung Concentrations of Azithromycin with Different Dosing Regimens used in COVID-19 Clinical Trials.	Wrong study design
f553f9304a1f435f725429d7f48a24bcf86260a8	Prevention of SARS-CoV-2 in Hospital Workers s Exposed to the Virus	Wrong population
d7e75ead5eba40b0955d1c17758953c561f54586	Problems with the analysis in "Treatment with Hydroxychloroquine, Azithromycin and Combination in Patients Hospitalized with COVID-19".	Wrong study design
d25a4533fb1153a5fbb0119e6b979c3736a0b04b	QT Interval Control to Prevent Torsades de Pointes during Use of Hydroxychloroquine and/or Azithromycin in Patients with COVID-19.	Wrong study design
12fe38349a710a0952b925751d9ed087cc72a276	QT Interval Prolongation and Torsade De Pointes in Patients with COVID-19 treated with Hydroxychloroquine/Azithromycin	Wrong study design
87965b8c5161e906c33443ae03d5d85c18f7289d	QT Interval Prolongation and Torsade De Pointes in Patients with COVID-19 treated with Hydroxychloroquine/Azithromycin.	Wrong study design
7cb60c0e9414706cd2cc1e517ce46f6065e98051	QT interval prolongation under hydroxychloroquine/ azithromycin association for inpatients with SARS-CoV-2 lower respiratory tract infection.	Wrong study design
c50a2b1c2bd8dc0e1ee6583c82a6869348281e54	QT Prolongation and Torsade De Pointes Related to Antimalarial Drugs and Azithromycin: A Pharmacovigilance Study in the Context of the COVID-19 Crisis	Wrong study design
5ebcee87bce4f8cb116a2dc10c2068afac45f0a3	QT prolongation in a diverse, urban population of COVID-19 patients treated with hydroxychloroquine, chloroquine, or azithromycin.	Wrong study design

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b5945896a2879eb55f0bb186ca4a2f08528a7be1	Quantifying treatment effects of hydroxychloroquine and azithromycin for COVID-19: a secondary analysis of an open label non-randomized clinical trial (Gautret et al, 2020)	Wrong study design
421bd3d968d0cff2348bd85bb2d3ab1d1eddd2b6	Reduction of coronavirus burden with mass azithromycin distribution.	Wrong population
fbaf9b39fe3435cf341fe3106f78827cfe2d9be8	Reply to Gautret et al: hydroxychloroquine sulfate and azithromycin for COVID-19: what is the evidence and what are the risks?	Wrong study design
a146c9a8e322d85da7a7ce1caa884a68e419f963	Reply to Gautret et al. 2020: A Bayesian reanalysis of the effects of hydroxychloroquine and azithromycin on viral carriage in patients with COVID-19	Wrong study design
96a4cc40315effa457e2b2f127f7195bae41229d	Response to the editorial "COVID-19 in patients with cardiovascular diseases": Covid-19 treatment with hydroxychloroquine or chloroquine and azithromycin: A potential risk of Torsades de Pointes.	Wrong study design
13576d7efe7c74c3fe0d9504486dbff742421bf3	Retraction-Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis.	Wrong study design
e1bbb0f02f615f513f3ea3cc47a200b8ef8ae45b	Review of: "Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial Gautret et al 2010, DOI:10.1016/j.ijantimicag.2020.105949.	Wrong study design
382368ee353e75db7cda2297106a9605576fcd9f	Risk of drug-induced Long QT Syndrome associated with the use of repurposed COVID-19 drugs: a systematic review	Wrong study design
6e93ece0886ec79de03d9a536ea4ca9a3412cf71	Safety considerations with chloroquine, hydroxychloroquine and azithromycin in the management of SARS-CoV-2 infection.	Wrong study design
694893ec631e43de9c4a8d4bd20d7fba06a2b2e7	Safety considerations with chloroquine, hydroxychloroquine and azithromycin in the management of SARS-CoV-2 infection.	Wrong study design
b219270dd74fd722cd3c1396e9652d5c716569a3	Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study	Wrong population

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f5e53b31747fdb4429edcbb40313263be1694f21	Safety of Short-term Hydroxychloroquine Plus Azithromycin Treatment in Critically Ill Patients With Severe COVID-19	Wrong study design
5e91efa52aa5dab49739841db9e3c23eb7d514f3	Safety use of hydroxychloroquine and its combination with azithromycin in the context of Sars-CoV-2 outbreak: Clinical experience in a Belgian tertiary center.	Wrong study design
7b49402f34319f0dfe784aa52baa62895a294393	Should azithromycin be used to treat COVID-19? A rapid review.	Wrong study design
2f07bcb3c93f403e0bc975553308194f90827fa7	Should Clinicians Use Chloroquine or Hydroxychloroquine Alone or in Combination With Azithromycin for the Prophylaxis or Treatment of COVID-19?	Wrong study design
b40f721029a251de15c3b3c5b4cdb48bb839d087	Study of Immune Modulatory Drugs and Other Treatments in COVID-19 Patients: Sarilumab, Azithromycin, Hydroxychloroquine Trial - CORIMUNO-19 - VIRO	Wrong study design
2231d24b3e8dae8f7367af84f63280b0b72d5150	Successful recovery of COVID-19 pneumonia in a patient from Colombia after receiving chloroquine and clarithromycin.	Wrong study design
1d95b384de9f97755a9fe4bf71317052e0fcd45b	Surviving the surge: Evaluation of early impact of COVID-19 on inpatient pharmacy services at a community teaching hospital.	Wrong outcomes
375ebb45c0e60ee59f2df2598f83870b367a1ad3	Systematic literature review on novel corona virus SARS-CoV-2: a threat to human era.	Wrong study design
6f2e824fef00dc9baf9baf49d23d4d4c54b426b9e6	Systematic Review and Meta-analysis of the Effectiveness and Safety of Hydroxychloroquine in COVID-19.	Wrong study design
709f80913b98d91edc88c47dbf29192f6a420b2d	The Cardiac Toxicity of Chloroquine or Hydroxychloroquine in COVID-19 Patients: A Systematic Review and Meta-regression Analysis	Wrong comparison
7383fdd3845c33b601fa829ab9f3cc4dddc59457	The cardiovascular effects of treatment with hydroxychloroquine and azithromycin.	Wrong study design
aa016af932d81686762d588c3d37137cef59b1bb	The clinical value of two combination regimens in the Management of Patients Suffering from Covid-19 pneumonia: a single centered, retrospective, observational study.	Wrong comparison

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8edaabd7dde3884c8023c90d3517c8073e7a90a7	The comparison of the effectiveness of lincocin® and azitro® in the treatment of covid-19-associated pneumonia: A prospective study.	Wrong comparison
910250b1ca032e7f9626ca3a78ff5b66bccb7bae	The potential of drug repositioning as a short-term strategy for the control and treatment of COVID-19 (SARS-CoV-2): a systematic review.	Wrong study design
34e9c1fd15fc47fb329e4ca97607eee48ec259ed	The QT interval in patients with COVID-19 treated with hydroxychloroquine and azithromycin	Wrong study design
624afc48cf058afd56e09a9d37b024cb6381ca69	The QT Interval in Patients with SARS-CoV-2 Infection Treated with Hydroxychloroquine/Azithromycin	Wrong study design
7c9512c1ac13d6a35c5a95234db1242426e0b634	The use of hydroxychloroquine plus azithromycin and early hospital admission are beneficial in Covid-19 patients: Turkey experience with real-life data.	Wrong comparison
563881e3a99da14694f66e887de1c9096a70df87	Tocilizumab for Treatment of Severe COVID-19 Patients: Preliminary Results from SMAteo COvid19 Registry (SMACORE).	Wrong comparison
d2c6730a0c2ca7b5a6679b89a9f95fea0fbc8433	Treatment and preliminary outcomes of 150 acute care patients with COVID-19 in a rural health system in the Dakotas.	Wrong study design
8e10a92ec2a05e471b22c6a3e438bacbf8f9f0a8	Treatment options for COVID-19: The reality and challenges.	Wrong study design
c110d03abb1150b102248f32ecda7b59f03013af	Update Alert 2: Should Clinicians Use Chloroquine or Hydroxychloroquine Alone or in Combination With Azithromycin for the Prophylaxis or Treatment of COVID-19? Living Practice Points From the American College of Physicians.	Wrong study design
f511ca672e575a7652f38f6942ae0a09a1325550	Update Alert: Should Clinicians Use Chloroquine or Hydroxychloroquine Alone or in Combination With Azithromycin for the Prophylaxis or Treatment of COVID-19? Living Practice Points From the American College of Physicians.	Wrong study design
08e9d62b665519455103552ca2fdc6f727f280cd	Viral Dynamics Matter in COVID-19 Pneumonia: the success of early treatment with hydroxychloroquine and azithromycin in Lebanon.	Wrong study design

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COMPARATIVE OBSERVATIONAL STUDIES ASSESSING THE INTERVENTION

Epistemonikos ID	Title
f11fe296e18fa3833560da64daea562834904cb9	Assessment of QT Intervals in a Case Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated With Hydroxychloroquine Alone or in Combination With Azithromycin in an Intensive Care Unit.
9037117bee99ccf5fcb26feb1e55702d0ceb62b4	Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State.
8e3d3bfb45338ef8990a2b46777338d95aaf230c	Clinical outcomes and adverse events in patients hospitalised with COVID -19, treated with off- label hydroxychloroquine and azithromycin.
e0f6ba80ac639df5b8212ff2e6b43d5b1fc51071	Experience with Hydroxychloroquine and Azithromycin in the COVID-19 Pandemic: Implications for QT Interval Monitoring
f997b35e908b62c416aedab831a6dd849b078504	Hydroxychloroquine with or without azithromycin and in-hospital mortality or discharge in patients hospitalized for COVID-19 infection: a cohort study of 4,642 in-patients in France
722c27d9aa21991f667371bded0e628dbda6728e	Negative nasopharyngeal SARS-CoV-2 PCR conversion in Response to different therapeutic interventions

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db5110c9465bc46fde463973e8eb7458b9075a36	Outcome of Non-Critical COVID-19 Patients with Early Hospitalization and Early Antiviral Treatment Outside the ICU.
8dc9d91c85cf014a71a44142fbba53483723b117	Outcomes of 3,737 COVID-19 patients treated with hydroxychloroquine/azithromycin and other regimens in Marseille, France: A retrospective analysis.
f78b2f3832f39f7cc110d9ebd49fe7868f5ec332	Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19
d36f6517423f918b2698a87ca4a107a11a99ea15	QT Interval Evaluation Associated With Use of Hydroxychloroquine with Combined Use of Azithromycin Among Hospitalized Children Positive for COVID-19.
822f55e2ca09e430f19d65a0b01a883b2f5d3ad2	Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19).
c5abc9bf53b84171b827a35ecfb0f9d124f3b08e	The Effect of Chloroquine, Hydroxychloroquine and Azithromycin on the Corrected QT Interval in Patients with SARS-CoV-2 Infection.
37edb813de4f56ee6576fd0b361909f1052a64d4	Treatment with Hydroxychloroquine, Azithromycin, and Combination in Patients Hospitalized with COVID-19.

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ONGOING STUDIES

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