Table S1: Searching strategy of the randomized controlled trials (RCTs) for the treatment of COVID-19 in each database

Database	**Search strategy**
Web of Science	("coronavirus disease 2019" OR COVID-19 OR “2019 novel coronavirus" OR 2019-nCoV OR “severe acute respiratory syndrome-related coronavirus-2" OR SARS-CoV-2 OR “novel coronavirus pneumonia (NCP)”) AND (“randomized controlled trial (RCT)”)
PubMed	((((coronavirus disease 2019 (COVID-19)) OR (2019 novel coronavirus (2019-nCoV))) OR (severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2))) OR (novel coronavirus pneumonia (NCP))) AND (randomized controlled trial (RCT))
ProQuest	‘‘coronavirus disease 2019 (COVID-19),” OR “2019 novel coronavirus (2019-nCoV),” OR “severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2),” OR “novel coronavirus pneumonia (NCP),” AND “randomized controlled trial (RCT)”

Table S2: PICO information of the randomized controlled trials (RCTs) included in the analysis for the treatment of COVID-19

Title and authors	Patient	Intervention	Control	Finding
Remdesivir for the treatment of patients in hospital with COVID-19 in Canada: a randomized controlled trial/ Karim Ali et al.[51]	Patients in hospital with COVID-19	Remdesivir 200 mg on day 0 and 100 mg on days 1 through 9 + standard care	Standard care: All care decisions were left to the discretion of the treating clinicians, including the use of co-interventions such as dexamethasone or tocilizumab, depending on factors like time period, hospital setting, and participation in other RCTs	**Primary:** in-hospital mortality, **secondary:** changes in clinical severity, oxygen- and ventilator-free days (at 28 d), incidence of new oxygen or mechanical ventilation use, duration of hospital stay, and adverse event rates
Favipiravir in Patients with Early Mild-to-moderate Coronavirus Disease 2019 (COVID-19): A Randomized Controlled Trial/ Yoav Golan et al.[50]	Patients with mild or moderate SARS-CoV-2 infection	Favipiravir 1800 mg BID daily on Day 1, followed by 800 mg BID daily on Days 2–10	Matching placebo: a placebo pill of 1800 mg BID on Day 1 and 800 mg BID from Days 2 to 10"	**Primary:** time to sustained clinical recovery, **secondary:** proportion of patients with COVID-19 progression, including emergency department visits, hospitalizations, or death and time (in days) to undetectable SARS-CoV-2 load in saliva assays.
Effect of Arbidol (Umifenovir) on COVID-19: a randomized controlled trial/ Marzieh Nojomi et al.[47]	Patients with definite diagnosis of SARS-CoV-2 infection	Hydroxychloroquine 400 mg BID on first day followed by Umifenovir 200mg TID 7 to 14 days based on the severity of disease	Hydroxychloroquine 400mg on first day followed by 400 mg KALETRA (Lopinavir/ritonavir) BID	**Primary:** duration of hospitalization and clinical improvement 7 days after admission, **secondary:** death during the 30 days of treatment, duration of hospitalization, changing laboratory tests during 7 days, changing of CT findings after 30 days, and the need for invasive mechanical ventilation.

Title and authors	Patient	Intervention	Control	Finding
A multicenter, randomized, open-label, controlled trial to evaluate the efficacy and tolerability of hydroxychloroquine and a retrospective study in adult patients with mild to moderate coronavirus disease 2019 (COVID-19)/ Cheng-Pin Chen et al.[46]	Patients with mild or moderate SARS-CoV-2 infection	Hydroxychloroquine 400 mg BID on day 1 and 200 mg BID for 6 days on days 2–7 + standard care	Standard care: supportive treatment without antibiotics for subjects with mild clinical COVID-19 symptoms and with antimicrobial therapy for subjects presenting with moderate clinical COVID-19 symptoms	**Primary:** the time to negative rRT-PCR assessments from randomization, up to 14 days, by arm, **secondary:** the proportion of negative viral rRT-PCR on hospital day 14, the resolution of clinical symptoms (time to clinical recovery), the proportion of discharges by day 14, the mortality rate and Hydroxychloroquine safety and tolerability.
Hydroxychloroquine versus placebo in the treatment of non-hospitalised patients with COVID-19 (COPE − Coalition V): A double-blind, multicentre, randomised, controlled trial/ Álvaro Avezum et al.[52]	Patients with mild or moderate SARS-CoV-2 infection	Hydroxychloroquine 400 mg BID in the first day, 400 mg once daily for a total of seven days	Matching placebo: a placebo pill of 400 mg BID on the first day and then 400 mg once daily for a total of seven days	**Primary:** hospitalisation due to COVID-19 at 30 days from randomization, **secondary:** uncontrolled asthma after ≥5 days of starting study medication, pneumonia, otitis media, fever resolution time; time to improve respiratory symptoms (cough, runny nose), hospitalisation in the intensive care unit; need for orotracheal intubation, mechanical ventilation time, and all-cause mortality
Clearing the Fog: Is Hydroxychloroquine Effective in Reducing Coronavirus Disease-2019 Progression? A Randomized Controlled Trial/ Sultan M. Kamran et al.[48]	Patients with mild SARS-CoV-2 infection	Hydroxychloroquine 400 mg BID for day 1 followed by 200 mg 12 hourly for the next five days + standard care	Standard care: oral vitamin C 2 g, oral zinc 50 mg, oral vitamin D (alfacalcidol 1 μg), and oral acetaminophen for body aches and fever	**Primary:** progression of disease within five days of start of treatment, **secondary:** PCR negativity on days 7 and 14.

Title and authors	Patient	Intervention	Control	Finding
Hydroxychloroquine plus azithromycin early treatment of mild COVID-19 in an outpatient setting: a randomized, double-blinded, placebo-controlled clinical trial evaluating viral clearance/ Cristhieni Rodrigues et al.[42]	Patients with mild SARS-CoV-2 infection	Two 200 mg Hydroxychloroquine capsules BID for a total course of 7 days and one 500 mg Azithromycin capsule taken on day 1, followed by one 250 mg Azithromycin capsule daily for the next 4 days	Matching placebo: two placebo capsules of 200 mg BID for 7 days, and a placebo capsule of 500 mg on day 1, followed by a placebo capsule of 250 mg daily for the next 4 days	**Primary:** the time (days) to viral clearance within a 9-day evaluation period following enrolment after the on- set of symptoms and the study enrolment dates, **secondary:** viral load reduction, improvement of symptoms, hospitalisation rates, and adverse effects to the trial medications.
A Comparative Study on Ivermectin-Doxycycline and Hydroxychloroquine-Azithromycin Therapy on COVID-19 Patients/ Abu Taiub Mohammed Mohiuddin Chowdhury et al.[40]	Patients with mild or moderate SARS-CoV-2 infection	Ivermectin 200µgm/kg single dose + Doxycycline 100mg BID for ten days	Hydroxychloroquine 400mg for the first day, then 200mg BID for nine days + Azithromycin 500mg daily for five days	Recovery to negative PCR and the duration of recovery to negative PCR‡
The Efficacy of Ivermectin and Metronidazole vs. Standard Treatment Protocols on Outcomes of COVID-19 in Hospitalized Patients: A Triple-Blinded Randomized Controlled Trial/ Mohammad Reza Heydari et al.[44]	Patients infected with SARS-CoV-2 and positive results for SARS-CoV-2	Ivermectin 0.2 mg/kg of body weight (max. 12 mg) as a single dose, Metronidazole 8 mg/kg q6hr for five days + standard treatment protocols	Standard treatment protocols: Oxygen therapy, water and electrolyte modification, antiviral treatment, corticosteroids and anticoagulant therapy	**Primary:** the time of disappearance of shortness of breath, the need for oxygen, the reduction of CRP and the normalization of lymphopenia

Title and authors	Patient	Intervention	Control	Finding
Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: a triple-blinded randomized controlled trial/ Keivan Ranjbar et al.[43]	Hospitalized COVID-19 patients	Methylprednisolone 2 mg/kg/day over 60 min, and tapered to half dosage every five days + standard care	Dexamethasone (6 mg/kg/day) for 10 days + standard care " WHO and Iranian COVID-19 treatment guidelines"	**Primary:** all-cause mortality in 28 days and clinical status after 5 as well as 10 days after enrollment with 9-point WHO ordinal scale, **secondary:** need for invasive mechanical ventilation, admission to ICU, duration of hospital stay and hospital death during the 28 days after enrollment
Methylprednisolone versus intravenous immunoglobulins in children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS): an open-label, multicentre, randomised trial/ Tatjana Welzel et al.[41]	Children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2	Intravenous methylprednisolone 10 mg/kg per dose once daily for 3 days, maximum dose 1000 mg per day	Intravenous immunoglobulins 2 g/kg per dose, as a single dose given as a slow infusion in line with the institutional standard operating procedures (infusion duration 12 h ± 4 h), maximum dose 100 g	**Primary:** the length of hospital stay with censoring at 28 days, **secondary:** all-cause mortality; proportion of patients needing organ support operationalised as respiratory support, inotropes, renal replacement, extracorporeal membrane oxygenation and proportion of patients with cardiac pathologies
Clinical Consequences for Individuals Treated with Tocilizumab for Serious COVID-19 Infection/ Al Shaimaa Ibrahim Rabie et al.[30]	Patients with severe SARS-CoV-2 infection	Intravenous infusion of tocilizumab 8 mg/Kg of body weight, with a starting dosage of 400 mg and a maximum dose of 800 mg, followed by a second dose 12–24 h later + conventional treatment	Conventional treatment: hydroxychloroquine, remdesivir, azithromycin, ceftriaxone, cefotaxim, meropnam, hydrocortisone, dexamesazone, methylprednisolone, vitamin C, vitamin D, zinc, naproxen and paracetamol	**Primary:** clinical deterioration within seven days of randomization, **secondary:** how long a patient would need to be on a mechanical ventilator, the length of stay, and the time to event, death, or mechanical ventilator

Title and authors	Patient	Intervention	Control	Finding
Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 Pneumonia A Randomized Clinical Trial/ Carlo Salvarani et al.[38]	Patients with COVID-19 pneumonia	Intravenous Tocilizumab within 8 hours from randomization at a dose of 8mg/kg up to a maximum of 800 mg, followed by a second dose after 12 hours.	Supportive care following the treatment protocols of each center. All drugs were allowed but IL-1 blockers, Jak inhibitors, and tumor necrosis factor inhibitors. Steroids were allowed if already taken before hospitalization	**Primary:** clinical worsening within 14 days since randomization, **secondary:** admission to ICU with mechanical ventilation, mortality, and tocilizumab toxic effects
Effect of convalescent plasma as complementary treatment in patients with moderate COVID-19 infection/ Manuel E. Baldeón et al.[31]	Patients with moderate SARS-CoV-2 infection	Convalescent plasma + standard treatment	Standard treatment: Symptomatic control and supportive care for COVID-19, mostly based on Ecuadorian COVID-19 treatment guidelines for hospital practice	**Primary:** survival, **secondary:** length of hospitalisation, days from treatment to discharge, time to clinical improvement or death within a 28-day period, and adverse reactions to treatment
High-dose versus standard-dose vitamin D supplementation in older adults with COVID-19 (COVIT TRIAL): A multicenter, open-label, randomized controlled superiority trial/ Ce´dric Annweiler et al.[49]	Patients admitted to the hospital units or living in nursing homes adjacent to the investigator centers with COVID-19	High doseVitamin D 400,000 IU	Standard dose Vitamin D 50,000 IU	**Primary:** mortality within 14 days, **secondary:** mortality within 28 days" after randomization
The Role of Vitamin C as Adjuvant Therapy in COVID-19/ Poona Kumari et al.[39]	Patients with severe SARS-CoV-2 infection	Intravenous Vitamin C 50 mg/kg/day+ standard therapy	Standard therapy: antipyretics, dexamethasone, and prophylactic antibiotics	The number of days required for the disappearance of symptoms, number of days spent in the hospital, need for ventilation, and mortality‡

Title and authors	Patient	Intervention	Control	Finding
The effect of L-arginine supplementation on amelioration of oxygen support in severe COVID-19 pneumonia/ Jananee Muralidharan et al.[32]	Patients admitted with severe COVID-19 pneumonia	100 mL solution containing 5 g powdered formulation, 3 grams of L-Arginine, followed by a 100 mL water rinse, 10 days or until the patients were off O2 support	Placebo 100 mL solution containing 5 g of flavored glucose (Glucon-D Orange)	**Primary:** complete cessation in O2 support, **secondary:** the number of days to the cessation of O2 support, length of hospital stay post-enrollment, reduction in the frequency of thrombotic events, and in-hospital mortality.
Efficacy of the Sentinox Spray in Reducing Viral Load in Mild COVID-19 and Its Virucidal Activity against Other Respiratory Viruses: Results of a Randomized Controlled Trial and an In Vitro Study/ Donatella Panatto et al.[35]	Patients with mild SARS-CoV-2 infection	Sentinox 3 times/day for arm I and Sentinox 5 times/day for arm II, for 5 days + standard therapy	Standard physician prescribed symptomatic therapy	**Primary:** the efficacy of Sentinox in reducing viral load at any time during days one to five, **secondary:** the time length to negativization between the study arms, the tolerability measured on Visual Analogue Scale, the frequency of adverse events and patient satisfaction
Nigella sativa for the treatment of COVID-19: An open-label randomized controlled clinical trial/ Abdulrahman E. Koshak et al.[37]	Patients with mild SARS-CoV-2 infection	Oral Nigella sativa oil 500 mg twice daily postprandial for 10 days + standard care	Standard care: decided by the treating physicians and included antipyretics, antihistamines, and other drugs as per the Saudi Ministry of Health and the KAUH protocol	**Primary:** the percentage of participants with clinical recovery within 14 days after randomization, **secondary:** the number of days for recovery, duration of each symptom, adverse drug reactions, and hospital admission due to disease complications.

Title and authors	Patient	Intervention	Control	Finding
Efficacy of two siddha polyherbal decoctions, Nilavembu Kudineer and Kaba Sura Kudineer, along with standard allopathy treatment in the management of mild to moderate symptomatic COVID-19 patients—a double-blind, placebocontrolled, clinical trial/ Anurag Srivastava et al.[34]	Patients with mild or moderate SARS-CoV-2 infection	60 ml of Nilavembu Kudineer for Arm I and 60 ml of Kaba Sura Kudineer for Arm II, twice a day post morning and evening meals + standard allopathy treatment, for a maximum of 10 days	Matching placebo+ standard treatment: as per ICMR guidelines, which included doxycycline/ hydroxychloroquine and Ivermectin/ Fabiparavir. Additionally, the patients with a moderate disease also received steroids (methylprednisolone or dexamethasone, if required) and low molecular weight heparin.	**Primary:** reduction in viral load, time taken by the patient to become asymptomatic from symptomatic, effect of drugs inflammatory markers (IL6,) at the end of treatment (10 days), and reduction in the hospital stay
Effectiveness of Lianhua Qingwen Capsule in Treatment of Asymptomatic COVID-19 Patients: A Randomized, Controlled Multicenter Trial/ Ling Zhang et al.[36]	Asymptomatic patients with SARS-CoV-2 infection	Oral Lianhua Qingwen capsule (0.35 g per capsule), 4 capsules TID for 14 days	Isolation according to the Diagnosis and Treatment Program for Novel Coronavirus Infection Pneumonia (Trial Eighth Edition) released by the National Health Commission of China	**Primary:** the time and rate of nucleic acid turning negative during the isolation observation period according to PCR test, **secondary:** the clinical symptoms and severity, clinical symptoms appearance time and proportion, proportion of mild and common cases of novel coronavirus pneumonia diagnosed during the isolation observation period, routine blood test, and biochemical indicators.
Effect of qigong exercise and acupressure rehabilitation program on pulmonary function and respiratory symptoms in patients hospitalized with severe COVID-19: A randomized controlled trial/ Shu-ting Liu et al.[33]	Patients with SARS-CoV-2 infection	Qigong exercise and acupressure rehabilitation program + standard therapies	Standard therapies: Rest time, laboratory and non-laboratory tests, oxygen therapy, antiviral drugs combined with antibiotics if necessary, supportive treatment and early Chinese medicine	**Primary:** the improvement in mMRC from pretreatment to discharge, **secondary:** modified Borg dyspnea scale , fatigue Scale-14, patient health questionnaire-9 scale, duration of respiratory symptoms, length of hospital stay and vital signs.

Figure S1: Risk of bias summary of included randomized controlled trials (RCTs) for treating coronavirus disease 2019 (COVID-19).