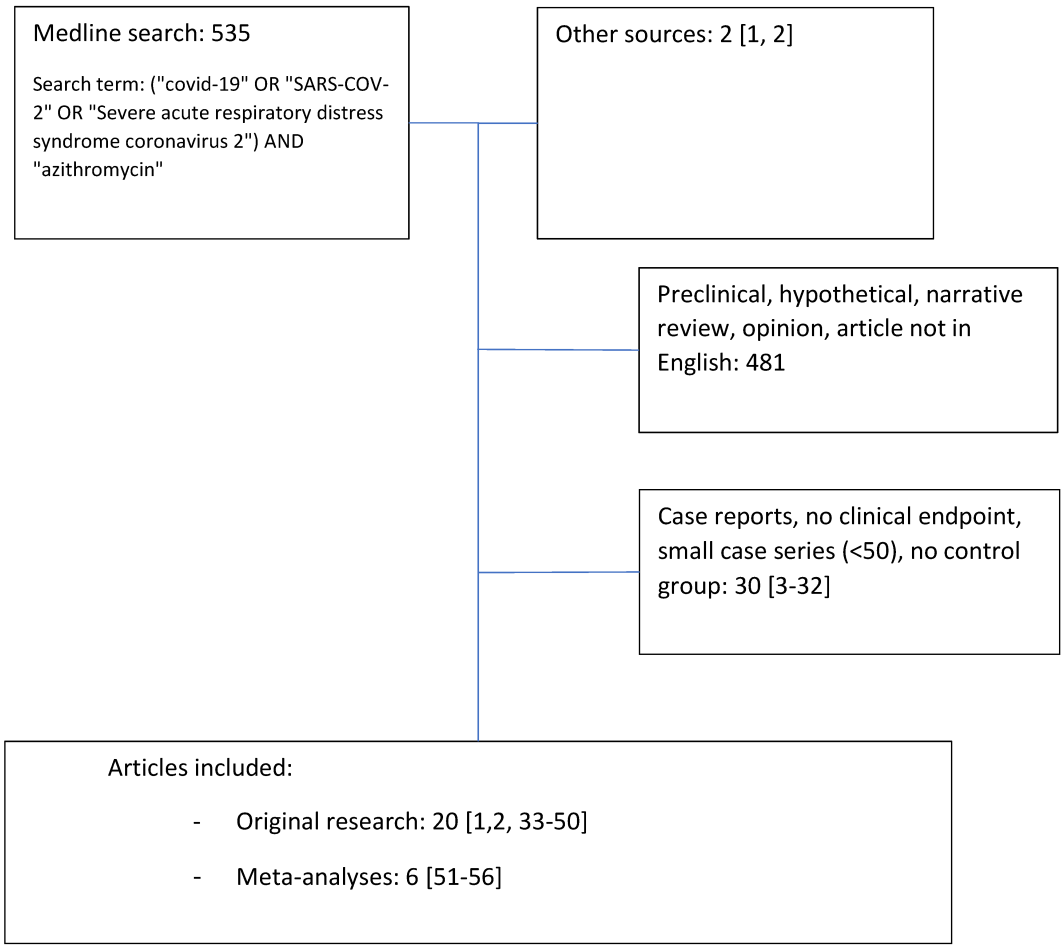
Supplementary figure A: study selection flowchart



Supplementary table A: studies assessing azithromycin (monotherapy and combination therapies)

Reference	Study type and setting	Treatment/intervention	Outcome	Results	Safety	Limitations, remarks
ORIGINAL RESEARCH						
Kuderer et al. May 2020 [33]	Multicentric, retrospective cohort study Cancer patients with confirmed or probable diagnosis, in- and outpatients	**HQ alone (n = 89)** **AZ alone (n = 93)** **HQ + AZ (n = 181)** **Neither (n = 486)** *Dosing:* *Not reported*	30-day mortality	Multivariable adjusted odds ratios for all-cause mortality: - HQ vs neither: OR, 1.06; 95% CI, 0.51 - 2.20 - AZ vs neither: OR, 1.30; 95% CI 0.65 - 2.64 - AZ + HQ vs neither: OR, 2.93; 95% CI, 1.79 – 4.79	Not reported	- Adjusted for baseline patient characteristics, but not for disease severity - Secondary endpoint of severe illness (composite of death, hospital admission, ICU admission) was associated with both AZ or HQ + AZ, for which indication bias by disease severity is a more plausible explanation than worsening with association of azithromycin
Geleris et al. June 2020 [2]	Monocentric, retrospective cohort study, USA Hospitalized patients with confirmed infection	**HQ + AZ (n = 486)** **HQ alone (n = 325)** **AZ alone (n = 127)** **Other (n = 438)** *Dosing:* *HQ: 600mg bid day 1, 400mg od day 2-5* *AZ: 500mg od day 1, 250mg od day 2-5*	Time from study baseline to intubation or death (for patients who died after intubation, the timing of the primary end point was defined as the time of intubation)	Multivariable Cox model with inverse probability weighting according to propensity score for composite endpoint: - no significant association between treatment with azithromycin and the composite end point (hazard ratio, 1.03; 95% CI, 0.81 to 1.31).	Not reported	- Data extracted from clinical data warehouse; no data were manually extracted from electronic medical records
Rosenberg et al. June 2020 [34]	Multicentric, retrospective cohort study, USA Hospitalized patients with confirmed infection	**HQ alone (n = 271)** **AZ alone (n = 211)** **HQ + AZ (n = 735)** **neither (221)** *Dosing:* *Different regimens*	In hospital mortality	Adjusted Cox regression hazard ratio for mortality - HQ + AZ vs neither: HR, 1.35; 95% CI, 0.76 - 2.40; p = 0.31 - HQ alone vs neither: HR, 1.08; 95% CI, 0.63 - 1.85; p = 0.79 - AZ alone vs neither: HR, 0.56; 95% CI, 0.27 - 1.56; p = 0.14	Cardiac arrest more likely in HQ + AZ but not in either AZ alone or HQ alone	- Adverse events recorded at any point during hospitalization, potentially before drug initiation - Some potential confounders (e.g. inflammatory markers) not available for multivariate analysis - Mortality endpoint was not adjusted for MV or CPAP

Arshad et al. July 2020 [35]	Multicentric, retrospective cohort study, USA Hospitalized patients with confirmed infection	**HQ alone (n = 1202)** **AZ alone (n = 147)** **HQ + AZ (n = 783)** **Neither** *Dosing:* *HQ: 400mg bid day 1 and 200mg bid day 2-5* *AZ: 500mg od day 1, 250 od day 2-5*	In-hospital mortality	Adjusted Cox regression hazard ratio for mortality - HQ alone vs neither: HR, 0.340; 95% CI, 0.254 - 0.455; p<0.001 - AZ alone vs neither: HR, 1.050; 95% CI 0.682 - 1.616; p = 0.825 - HQ + AZ vs neither: HR, 0.294; 95% CI, 0.218 - 0.396; p<0.001 NB: 190 propensity matched HQ patients vs 190 neither: HR, 0.487; 95% CI 0.285 - 0.832; p = 0.009	- No patient had documented torsade de pointes. - Suggests no differences between treatment arms, although specific data not provided.	- More steroid use in treated patients (although corrected for in propensity matching, however no propensity matching was done for azithromycin effect) - Immortal time bias - Discrepancy between higher mortality and lower ICU stay in not-treated group may depend on patient characteristics not accounted for in multivariate analysis (e.g. no treatment because palliative care)
Tanriverdi et al. July 2020 [36]	Monocentric, retrospective cohort study, Turkey Hospitalized patients with probable or confirmed infection	**HQ alone (n=30)** **HQ + AZ (n =26)** **HQ + favipiravir (n = 9)** **HQ + lopinavir/ritonavir (n = 18)** *Dosing:* *HQ: 400mg bid day 1, 200mg bid day 2-10* *AZ: 500mg od day 1, 250 od day 2-5*	Clinical course, duration of hospitalization, mortality, …	Duration of hospitalization: - subgroup analysis of HQ + AZ vs HQ + other antibiotic: 6.68 days vs 8.16 days; p = 0.027 No difference in other outcomes including mortality, ICU admission	No unexpected arrhythmia or cardiac event observed.	- 51% were probable cases without PCR confirmation - Small sample size - AZ patients recruited after guidance update, possible increased experience with COVID patients not accounted for
Satlin et al. July 2020 [37]	Multicentric, retrospective cohort study, USA Hospitalized patients with confirmed infection	**HQ alone (n = 132)** **HQ + AZ (n =27)** *HQ: 600mg bid day 1, 400mg od day 2-5* *AZ: 500mg bid day 1, 250mg od day 2-5*	Safety, tolerability and clinical outcomes (hypoxia, need for MV, mortality)	Multivariate adjusted odds ratio for hypoxia improvement - HQ + ≥3 days of azithromycin vs HQ alone: multivariate adjusted OR, 0.99; 95% CI, 0.38 – 2.60; p not reported Multivariate adjusted odds ratio for mortality - HQ + ≥3 days of azithromycin vs HQ alone: OR, 1.14; 95% CI, 0.37–3.50; p not reported	QTc increased above 500ms in 47 of 117 patients who had ECG follow up, of which 3 concomitantly used azithromycin. Only 1 patient developed non-sustained monomorphic VT and this was in the HQ alone group. No other ventricular tachycardia was reported.	- Small sample size with low number of AZ patients - Univariate prefiltering and small sample size may have excluded confounders from the multivariate model

Cavalcanti et al. July 2020 [38]	Multicentric, open label randomized controlled trial, Brazil Hospitalized patients with confirmed infection, mild to moderate disease	**HQ alone (n = 159)** **HQ + AZ (n = 172)** **Neither (n = 173)** *Dosing:* *HQ: 400mg bid for 7 days* *AZ: 500mg od for 7days*	Clinical status on day 15 on ordinal scale	Proportional odds of having a worse score at day 15: - HQ +AZ vs SOC: OR 0.99; 95% CI, 0.57 - 1.73; p=1.00 - HQ alone vs SOC: OR, 1.21; 95% CI, 0.69 - 2.11; p=1.00 - HQ + AZ vs HQ alone: OR, 0.82; 95% CI, 0.47 - 1.43; p=1.00	- Safety population also included AZ alone patients. - More AE reported in HQ + AZ group or HQ alone group than in AZ alone group and neither group - Prolongation of QT and elevated liver enzymes were more common in HQ alone group or HQ + AZ group than in neither group (however more serial ECG follow up in treated patients)	- Point of estimate instead of cox regression
Guerin et al. July 2020 [1]	Prospective observational study in MDs and their relatives, France Outpatients with flu-like symptoms with confirmed and suspected infection	**AZ alone (n = 34)** **AZ + HQ (n = 20)** **Neither (n = 34)** *Dosing:* *AZ: 500mg od day 1, 250mg od day 2-5* *HQ: 600mg od for 7 to 10 days*	Time to complete clinical recovery	Mean times to achieve clinical recovery - Neither: 25.8 days - AZ: 12.9 days ($p < 0.0001$ for AZ vs neither) - AZ + HQ: 9.2 days ($p < 0.0001$ for AZ + HQ vs neither; $p = 0.26$ for AZ vs AZ + HQ) Similar results with Logrank analysis. Similar results in case-control analysis (3x19 patients matched for age, sex and body mass index)	- No serious adverse event nor cardiovascular events were reported in any treatment group (ECG done before initiation of HQ in all patients) - Gastrointestinal adverse events reported in treatment group	- 42% of patients were not PCR confirmed - Some patients were not treated because of contra-indications, which may signal more comorbid untreated population - Matched controls not matched for disease severity
Monforte et al. July 2020 [39]	Monocentric, retrospective cohort study, Milan Hospitalized patients with confirmed infection	**HQ alone (n = 197)** **HQ + AZ (n = 94)** **Neither (n = 92), but 47 received other treatment (lopinavir, darunavir, steroids or other immunomodulatory drugs)** *Dosing: not reported*	In-hospital mortality	Adjusted hazard ratio for in hospital mortality: - HQ vs neither: HR, 0.66; 95% CI, 0.39 – 1.11; p = 0.118 - HQ + AZ vs neither: HR, 0.44; 95%CI, 0.24 – 0.82; p = 0.009 NB: treatment effectiveness was more substantial in less severe cases	Not reported	
Ip et al. August 2020 [40]	Multicentric, retrospective cohort study, USA Hospitalized patients with confirmed infection	**HQ alone (n = 441)** **AZ alone (n = 256)** **HQ + AZ (n = 1473)** **Neither (n = 342)** *Dosing: heterogeneous*	30-day mortality	Propensity score stratification adjusted hazard ratio for 30-day mortality - HQ alone vs no HQ: HR, 1.02; 95% CI, 0.83 – 1.27; p = 0. 83 - AZ alone vs no AZ: HR, 0.89; 95% CI, 0.72 – 1.10; p = 0.28 - HQ + AZ vs neither: HR, 0.98; 95% CI, 0.75–1.28; p = 0.89	Not reported	- Sampling bias as data was collected from convenience sample - Better to use propensity matching than stratification

Magagnoli et al. Aug 2020 [41]	Multicentric, retrospective cohort study, USA Hospitalized patients with confirmed infection	**HQ alone (n = 198)** **HQ + AZ (n = 214)** **Neither (n = 395)** Dosing: Different regimens	Mortality, use of MV	Propensity score adjusted (regression on propensity splines) hazard ratio for risk of death from any cause - HQ alone vs neither: HR, 1.83; 95% CI 1.16 - 2.89; p = 0.009 - HQ + AZ vs neither: HR, 1.31; 95% CI 0.80 - 2.15; p = 0.28 Propensity score adjusted hazard ratio for risk of mechanical ventilation - HQ alone vs neither: HR, 1.19; 95% CI, 0.78–1.82; p = 0.42 - HQ + AZ vs neither: HR, 1.09; 95% CI, 0.72–1.66; p=0.69	Not reported	- Factors that may have influenced treatment decisions (e.g. palliative care) are possibly not accounted for in propensity scoring for multivariate regression - Loss of significance for addition of AZ suggests indication bias or effect from AZ
Sekhavati et al. August 2020 [42]	Monocentric, open label RCT, Teheran Hospitalized patients with confirmed disease	**AZ + HQ + LPV/R (n = 56)** **HQ + LPV/R (n = 55)** Dosing: *AZ 500mg od 5 days* *HQ 400mg od 5 days* *Liponavir/ritonavir 400/100mg bid 5 days*	Vital signs, hypoxia, duration of hospitalisation, need for and length of intensive care unit admission, mortality rate and results of 30-day follow-up after discharge	Duration of hospitalization - AZ group 4.61 days vs non-AZ group 5.96 days; p = 0.02 Mean duration of ICU stay: - AZ-group 5 days vs non-AZ group 4.43 days; p = 0.157 NB: Also, better oxygenation at discharge for AZ-group	No adverse events while using a risk scoring system to exclude patients at high risk for QT-prolongation	- ICU admission was less for AZ-group (2) versus non-AZ group (7), which was not significant but could with this low numbers have significantly impacted length of stay - Exclusion for high risk of QT-prolongation would have better been done before study inclusion rather than after inclusion in AZ group per protocol, but no such patients occurred in study
Albani et al. Aug 2020 [43]	Monocentric, retrospective cohort study, Italy Hospitalized patients with confirmed infection	**HQ alone (n = 211)** **AZ alone (n = 421)** **HQ + AZ (n = 166)** **Neither (n = 605)** Dosing: *HQ: 200mg bid 5-7 days* *AZ: 500mg od for 5 days*	In-hospital mortality	Overlap weighted propensity score adjusted odds ratio for in hospital mortality - AZ alone vs neither: OR, 0.60; 95% CI, 0.42–0.85 - HQ alone vs neither OR, 0.76; 95% CI, 0.53–1.08 - HQ + AZ vs neither: OR, 1.13; 95% CI, 0.77–1.69	Not reported	- Factors that may have influenced treatment decisions (e.g. palliative care) or some measures for disease severity (lymphocytes, D-dimers) were not accounted for in multivariate regression

Rodriguez-Molinero et al. Sep 2020 [44]	Multicentric, retrospective cohort study, Spain Hospitalized patients with confirmed infection	**Regimen without AZ (n = 29) or with AZ (n = 29)** Matched subcohorts **Regimen without AZ (n = 63) or with AZ (n = 120)** Unmatched subcohorts Dosing: *AZ: 500mg od day 1 and 250mg od day 2-5*	O_2/FiO_2 at 48 hours after inclusion and length of hospital stay	Mean difference in O_2/FiO_2 at 48 hours of matched subcohorts - AZ vs no AZ: Δ O2/FiO2, 0.02%; 95% CI, -1.35% - 1.39%; p=0.980 Adjusted Cox regression hazard ratio for time to discharge in unmatched cohorts - AZ vs no AZ: HR, 1.45; 95% CI, 0.88-2.41; p=0.150	Insufficient events to draw conclusions	- Small sample sizes, especially after matching.
Furtado et al. Sep 2020 [45]	Multicentric open label randomized controlled trial, Brazil Hospitalized patients with confirmed infection, severe disease	**HQ alone (n = 183)** **HQ + AZ (n = 214)** Dosing: *HQ: 400mg bid 10 days* *AZ: 500mg od 10 days*	Clinical status on day 15	Proportional odds of being in worse clinical category: - AZ + HQ vs HQ: OR, 1.36; 95% CI, 0.94–1.97; p=0.11	Proportion of patients with any serious adverse event was 42% in the azithromycin group and 38% in the control group (p=0.35)	- Large estimated effect size limits power analysis
Lauriola et al. Sep 2020 [46]	Monocentric, retrospective cohort study, Italy Hospitalized patients with confirmed infection	**HQ alone (n = 17)** **HQ + AZ (n = 297)** **neither (n = 63)** Dosing: *HQ: 200mg bid 10 days* *AZ: 500mg od 10 days*	In-hospital mortality	Adjusted Cox regression hazard ratio for in hospital mortality - HQ alone vs neither: HR 1.108; 95% CI, 0.536 – 2.293; p=0.782 - HQ + AZ vs neither: HR, 0.265; 95% CI, 0.171-0.412; p<0.001	No fatal arrhythmias have been observed during treatment	- Small sample size, monocentric
Ayerbe et al. Sep [47]	Multicentric, retrospective cohort study, Spain Hospitalized patients with confirmed infection	**HQ alone (n = 670)** **HQ + AZ (n = 1187)** **neither (n = 162)** *Dosing:* *HQ: 400mg bid day 1, 200mg bid day 2-5* *AZ: not reported*	Mortality (over study window: March – April)	Multivariate logistic regression adjusted odds ratio for mortality for AZ + HQ vs HQ alone (3th of 4 tested models): - main effect of AZ on mortality: OR, 0.53; 95% CI, 0.19-1.50; p = 0.233 - No interaction effect between AZ and HQ on mortality: OR, 1.11; 95% CI, 0.38 – 3.29; p = 0.846 NB: HQ was associated with lower mortality: OR, 0.45; 95% CI, 0.30 – 0.68; p < 0.001	Not reported	

Lammers et al. Sep [48]	Multicentric, observational cohort study, The Netherlands Hospitalized patients with confirmed infection or typical disease findings on CT, mild to moderate disease	**HQ/CQ alone (n = 487)** **HQ/CQ + AZ (n = 79)** **AZ alone (n = 131)** **neither (n = 367)** *Dosing* *HQ: 400mg bid day 1, 200mg bid day 2-5* *AZ: not reported*	Death and ICU admission (composite endpoint)	Logrank test shows no difference in Kaplan-Meier curves for reaching composite endpoint of death or ICU admission with or without AZ (p = 0.071) NB: HQ but not CQ was associated with decreased propensity adjusted hazard ratio for reaching composite endpoint: HR, 0.68; 95% CI, 0.49-0.95; p = 0.24	Not reported	- Propensity matching was done for HQ and not for AZ - Factors that may have influenced treatment decisions (e.g. palliative care) or some measures for disease severity (lymphocytes, D-dimers) were not accounted for in multivariate regression
Annie et al. Oktober [49]	Multicentric, retrospective cohort study Hospitalized patients with confirmed infection	**HQ alone (n = 367) vs no HQ (n = 367)** **HQ + AZ (n = 199) vs no HQ (n = 199)** **(propensity matched sample taken from 3012 hospitalized patients)** *Dosing: not reported*	All-cause 30-days mortality	Propensity score matched odds ratio for mortality - HQ alone vs neither: OR, 0.95; 95% CI, 0.62 – 1.46; p = 0.828 - HQ + AZ vs neither: OR, 1.24; 95% CI 0.70 – 2.22; p = 0.461	Propensity matched odds ratio for composite of overall mortality and arrhythmia: - HQ + AZ vs neither: OR, 1.00; 95% CI, 0.59 – 1.69; p = 1.00	- Factors that may have influenced treatment decisions (e.g. palliative care) or some measures for disease severity (lymphocytes, D-dimers) were not accounted for in multivariate regression
Szente et al. November [50]	Prospective observational study Outpatients with confirmed infection	**HQ, AZ, prednisolone, zinc sulphate, ivermectin and oseltamivir were allowed** **AZ without HQ or prednisone (n = 106)** **AZ combined with HQ or prednisone (n = 489)** **No antiviral treatment (n = 122)** *Dosing:* *HQ: 400mg bid day 1, 400mg od day 2-5* *Predni: 1mg/kg od 5 days starting not earlier than day 6* *AZ: 500mg od 5 days*	Hospitalization risk	Multivariate logistic regression adjusted odds ratio for hospitalization - AZ vs no AZ containing regimens: OR, 0.93; 95% CI 0.72 – 1.90)	No cardiac arrhythmia events requiring medication termination for any of the medications used were observed, not deaths attributable to such arrhythmias	- Of initial sample of 25000 patients, only 717 with confirmed infection were analyzed - Indication bias may still exist despite multivariate correction

META ANALYSES						
Patel et al. June 2020 [51]	Systematic review and meta-analysis; uses data Magagnoli et al, Rosenberg et al	**HQ + AZ (n = 854) vs SOC (n = 395)** **HQ + AZ (n = 854) vs HQ alone (n = 388)**	All-cause mortality	Odds ratio for death - HQ + AZ vs neither: OR, 2.33; 95% CI, 1.63 - 3.34; p < 0.00001 - HQ + AZ vs HQ alone: OR, 1.07; 95% CI, 0.58 - 1.98); p = 0.83	Increased all-cause mortality but causes not assessed	
Das et al. July 2020 [52]	Meta-analysis using data from Magagnoli et al, Rosenberg et al for AZ assessment	**HQ alone (n = 3481)** **HQ + AZ (n = 1145)** **Neither (n = 1165)**	All-cause mortality	Odds ratio for death - HQ alone vs neither: OR, 0.87; 95% CI, 0.46 – 1.64; p 0.66 - HQ + AZ vs neither: OR, 2.84; 95% CI, 2.19–3.69; p < 0.001 - HQ vs HQ + AZ: OR, 0.7; 95% CI, 0.54 – 0.9; p = 0.006	- HQ + AZ associated with increased mortality (HQ alone vs HQ + AZ OR 0.7) - HQ +/- AZ was associated with increased occurrence of cardiac adverse events but no difference in cardiac adverse events between HQ alone and HQ + AZ	- The outcomes that favoured HQ over HQ + AZ were not cardiac adverse events but mortality rate and development of severe disease; little mechanistic rationale to expect disease worsening with association of AZ and effect may thus be due to residual indication bias
Fiolet et al. August [53]	Meta-analysis using data from Ip et al, Magagnoli et al, Rosenberg et al, Ip et al	**HQ alone (n = 11932)** **AZ + HQ (8081)** **Neither (n = 12930)**	Mortality	Relative risk for death - HQ alone vs neither: RR, 0.83; 95% CI, 0.65 - 1.06 - HQ + AZ vs neither: RR, 1.27; 95% CI, 1.04 - 1.54	- HQ + AZ associated with increased mortality	
Yang et al. September [54]	Meta-analysis using data from Magagnoli et al, Rosenberg et al	**HQ alone (n = 451)** **vs** **neither (n = 930)** **HQ + AZ (n = 854)** **vs** **neither (n = 395)**	All-cause mortality, progression to severe illness	Odds ratio for death - HQ alone vs neither: OR, 1.23; 95% CI, 0.38 – 3.97; p = 0.73 - HQ + AZ vs neither: OR, 2.34; 95% CI, 1.63–3.36; p < 0.00001	- HQ + AZ associated with increased mortality - Trend towards QT prolongation in HQ treatment did not reach significance	- Duration of follow up (< 14 days or > 14 days) reduces mortality difference (early CV side effects but long term infection reduction?) - Trend towards increased progression to severe disease in combination treatment; little mechanistic rationale to expect disease worsening with association of AZ and effect may thus be due to residual indication bias
Kashour et al. Oktober [55]	Meta-analysis using data from Rosenberg et al, Magagnoli et al, Kuderer et al,	**15938 patients to assess effect of HQ** **3430 patients to assess effect of HQ + AZ**	Short-term mortality	Adjusted OR on short term mortality: - HQ alone vs neither: effect estimate, 1.05; 95% CI, 0.96 – 1.15; p = 0.647 - HQ + AZ vs neither: effect estimate, 1.32; 95% CI, 1.00 – 1.75; p = 0.008	- HQ + AZ associated with increased short-term mortality	
Mega et al. October [56]	Meta-analysis using data from Magagnoli et al, Rosenberg et al	**HQ + AZ (n = 729)** **HQ alone (n = 1684)**	All-cause mortality, ICU admission, QT prolongation	Odds ratio for composite of death or ICU admission - HQ vs HQ + AZ: OR, 0.88; 95% CI, 0.55-1.43; p = 0.61	Odds ratio for QT prolongation: - HQ + AZ vs HQ alone: OR, 1.11; 95% CI, 0.54 – 2.28; p =0.79	

AZ: azithromycin, CI: confidence interval, CQ: chloroquine, HQ: hydroxychloroquine, HR: hazard ratio, O_2/FiO_2: ratio of oxygen saturation (%) over fraction of inspired oxygen (%), MV: mechanical ventilation, OR: odds ratio, RCT: randomized controlled trial, RR: relative risk

References:

1 Guérin V, Lévy P, Thomas J-L, *et al.* Azithromycin and Hydroxychloroquine Accelerate Recovery of Outpatients with Mild/Moderate COVID-19. *Asian J Med Heal* 2020;**18**:45–55. doi:10.9734/ajmah/2020/v18i730224

2 Geleris J, Sun Y, Platt J, *et al.* Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19. *N Engl J Med* 2020;**382**:2411–8. doi:10.1056/nejmoa2012410

3 Mori N, Katayama M, Nukaga S. Triple therapy with hydroxychloroquine, azithromycin, and ciclesonide for COVID-19 pneumonia. *J Microbiol Immunol Infect* Published Online First: 2020. doi:10.1016/j.jmii.2020.09.003

4 Calles A, Aparicio MI, Alva M, *et al.* Outcomes of COVID-19 in Patients With Lung Cancer Treated in a Tertiary Hospital in Madrid. *Front Oncol* 2020;**10**. doi:10.3389/fonc.2020.01777

5 Lubetzky M, Aull MJ, Craig-Schapiro R, *et al.* Kidney allograft recipients, immunosuppression, and coronavirus disease-2019: a report of consecutive cases from a New York City transplant center. *Nephrol Dial Transplant* 2020;**35**:1250–61. doi:10.1093/ndt/gfaa154

6 Enzmann MO, Erickson MP, Grindeland CJ, *et al.* Treatment and Preliminary Outcomes of 150 Acute Care Patients with COVID-19 in a Rural Health System in the Dakotas. *Epidemiol Infect* 2020;**148**. doi:10.1017/S0950268820001351

7 Ng KK, Ng MK, Zhyvotovska A, *et al.* Acute Respiratory Failure Secondary to COVID-19 Viral Pneumonia Managed With Hydroxychloroquine/Azithromycin Treatment. *Cureus* 2020;**12**. doi:10.7759/cureus.8268

8 Vahedi E, Ghanei M, Ghazvini A, *et al.* The clinical value of two combination regimens in the Management of Patients Suffering from Covid-19 pneumonia: a single centered, retrospective, observational study. *DARU, J Pharm Sci* Published Online First: 2020. doi:10.1007/s40199-020-00353-w

9 Takahashi N, Abe R, Hattori N, *et al.* Clinical course of a critically ill patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *J Artif Organs* Published Online First: 2020. doi:10.1007/s10047-020-01183-y

10 Guvenmez O, Keskin H, Ay B, *et al.* The comparison of the effectiveness of lincocin® and azitro® in the treatment of covid-19-associated pneumonia: A prospective study. *J Popul Ther Clin Pharmacol* 2020;**27**:5–10. doi:10.15586/jptcp.v27iSP1.684

11 Hor CP, Hussin N, Nalliah S, *et al.* Experience of short-term hydroxychloroquine and azithromycin in COVID-19 patients and effect on QTc trend. J. Infect. 2020;**81**:e117–9. doi:10.1016/j.jinf.2020.05.058

12 Das S, Bhowmick S, Tiwari S, *et al.* An Updated Systematic Review of the Therapeutic Role of Hydroxychloroquine in Coronavirus Disease-19 (COVID-19). Clin. Drug Investig. 2020;**40**:591–601. doi:10.1007/s40261-020-00927-1

13 Hraiech S, Bourenne J, Kuteifan K, *et al.* Lack of viral clearance by the combination of hydroxychloroquine and azithromycin or lopinavir and ritonavir in SARS-CoV-2-related acute respiratory distress syndrome. Ann. Intensive Care. 2020;**10**. doi:10.1186/s13613-020-00678-4

14 Gheysarzadeh A, Sadeghifard N, Safari M, *et al.* Report of five nurses infected with severe acute respiratory syndrome coronavirus 2 during patient care: case series. New Microbes New Infect. 2020;**36**. doi:10.1016/j.nmni.2020.100694

15 Aranda-Abreu GE, Aranda-Martínez JD, Araújo R, *et al.* Observational study of people infected with SARS-Cov-2, treated with amantadine. *Pharmacol Reports* Published Online First: 2020. doi:10.1007/s43440-020-00168-1

16 Louhaichi S, Allouche A, Baili H, *et al.* Features of patients with 2019 novel coronavirus admitted in a pneumology department: The first retrospective Tunisian case series. *Tunisie Medicale* 2020;**98**:261–5.

17 Wang D, Hu B, Hu C, *et al.* Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA - J Am Med Assoc* 2020;**323**:1061–9. doi:10.1001/jama.2020.1585

18 Castelnuovo A Di, Costanzo S, Antinori A, *et al.* Use of hydroxychloroquine in hospitalised COVID-19 patients

is associated with reduced mortality: Findings from the observational multicentre Italian CORIST study. *Eur J Intern Med* 2020;**0**. doi:10.1016/j.ejim.2020.08.019

19 Lopez A, Duclos G, Pastene B, *et al.* Effects of Hydroxychloroquine on Covid-19 in Intensive Care Unit Patients: Preliminary Results. *Int J Antimicrob Agents* 2020;**56**:106136. doi:10.1016/j.ijantimicag.2020.106136

20 Gautret P, Lagier JC, Parola P, *et al.* Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* 2020;**56**:105949. doi:10.1016/j.ijantimicag.2020.105949

21 Nachega JB, Ishoso DK, Otokoye JO, *et al.* Clinical Characteristics and Outcomes of Patients Hospitalized for COVID-19 in Africa: Early Insights from the Democratic Republic of the Congo. *Am J Trop Med Hyg* 2020;:3–5. doi:10.4269/ajtmh.20-1240

22 Huang HD, Jneid H, Aziz M, *et al.* Safety and Effectiveness of Hydroxychloroquine and Azithromycin Combination Therapy for Treatment of Hospitalized Patients with COVID-19: A Propensity-Matched Study. *Cardiol Ther* 2020;:523–34. doi:10.1007/s40119-020-00201-7

23 Coll E, Fernández-Ruiz M, Sánchez-Álvarez JE, *et al. Covid-19 in transplant recipients: the spanish experience.* 2020. doi:10.1111/ajt.16369

24 Derwand R, Scholz M, Zelenko V. low-dose hydroxychloroquine and azithromycin : a retrospective case series study. *Int J Antimicrob Agents* Published Online First: 2020. doi:10.1016/j.ijantimicag.2020.106214

25 Million M, Lagier J-C, Gautret P, *et al.* Early treatment of COVID-19 patients with hydroxychloroquine and azithromycin: A retrospective analysis of 1061 cases in Marseille, France. *Travel Med Infect Dis* 2020;**35**:101738. doi:10.1016/j.tmaid.2020.101738

26 Molina JM, Delaugerre C, Le Goff J, *et al.* No evidence of rapid antiviral clearance or clinical benefit with the combination of hydroxychloroquine and azithromycin in patients with severe COVID-19 infection. Med. Mal. Infect. 2020;**50**:384. doi:10.1016/j.medmal.2020.03.006

27 Gautret P, Lagier J-C, Parola P, *et al.* 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. *Travel Med Infect Dis* 2020;**34**:101663. doi:10.1016/j.tmaid.2020.101663

28 Esper RB, da Silva RS, Costa Oikawa FT, *et al.* Empirical treatment with hydroxychloroquine and azithromycin for suspected cases of COVID-19 followed-up by telemedicine. 2020;:1–25.https://pgibertie.files.wordpress.com/2020/04/2020.04.15-%0Ajournal-manuscript-final.pdf.

29 Aversa M, Benvenuto L, Anderson M, *et al.* COVID-19 in lung transplant recipients: A single center case series from New York City. *Am J Transplant* 2020;**20**:3072–80. doi:10.1111/ajt.16241

30 Ali T, Al-Ali A, Fajji L, *et al.* Coronavirus Disease-19. *Transplantation* 2020;**Publish Ah**. doi:10.1097/tp.0000000000003433

31 Kalligeros M, Shehadeh F, Atalla E, *et al.* Hydroxychloroquine use in hospitalised patients with COVID-19: An observational matched cohort study. *J Glob Antimicrob Resist* 2020;**22**:842–4. doi:10.1016/j.jgar.2020.07.018

32 Mazzitelli M, Davoli C, Scaglione V, *et al.* Apparent inefficacy of hydroxychloroquine combined with azithromycin on SARS-CoV-2 clearance in an incident cohort of geriatric patients with COVID-19. Travel Med. Infect. Dis. 2020;**37**. doi:10.1016/j.tmaid.2020.101826

33 Kuderer NM, Choueiri TK, Shah DP, *et al.* Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020;**395**:1907–18. doi:10.1016/S0140-6736(20)31187-9

34 Rosenberg ES, Dufort EM, Udo T, *et al.* Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State. *JAMA* 2020;**323**:2493–502. doi:10.1001/jama.2020.8630

35 Arshad S, Kilgore P, Chaudhry ZS, *et al.* Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19. *Int J Infect Dis* 2020;**97**:396–403. doi:10.1016/j.ijid.2020.06.099

36 Tanriverdİ E, ÇÖrtÜk M, Yildirim BiZ, *et al.* The use of hydroxychloroquine plus azithromycin and early hospital

admission are beneficial in Covid-19 patients: Turkey experience with real-life data. *Turkish J Med Sci* 2020;**Online ahe**. doi:10.3906/sag-2005-82

37 Satlin MJ, Goyal P, Magleby R, *et al.* Safety, tolerability, and clinical outcomes of hydroxychloroquine for hospitalized patients with coronavirus 2019 disease. *PLoS One* 2020;**15**:e0236778. doi:10.1371/journal.pone.0236778

38 Cavalcanti AB, Zampieri FG, Rosa RG, *et al.* Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19. *N Engl J Med* Published Online First: 23 July 2020. doi:10.1056/NEJMoa2019014

39 Monforte A d'Arminio, Tavelli A, Bai F, *et al.* Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information. *Int J Infect Dis* 2020;**99**:75–6.

40 Ip A, Berry DA, Hansen E, *et al.* Hydroxychloroquine and tocilizumab therapy in COVID-19 patients—An observational study. *PLoS One* 2020;**15**:e0237693. doi:10.1371/journal.pone.0237693

41 Magagnoli J, Narendran S, Pereira F, *et al.* Outcomes of Hydroxychloroquine Usage in United States Veterans Hospitalized with COVID-19. *Med* Published Online First: 2020. doi:https://doi.org/10.1016/j.medj.2020.06.001

42 Sekhavati E, Jafari F, SeyedAlinaghi SA, *et al.* Safety and effectiveness of azithromycin in patients with COVID-19: An open-label randomised trial. *Int J Antimicrob Agents* 2020;**56**:106143. doi:10.1016/j.ijantimicag.2020.106143

43 Albani F, Fusina F, Giovannini A, *et al.* Impact of Azithromycin and/or Hydroxychloroquine on Hospital Mortality in COVID-19. *J Clin Med* 2020;**9**. doi:10.3390/jcm9092800

44 Rodríguez-Molinero A, Pérez-López C, Gálvez-Barrón C, *et al.* Observational study of azithromycin in hospitalized patients with COVID-19. *PLoS One* 2020;**15**:1–13. doi:10.1371/journal.pone.0238681

45 Furtado RHM, Berwanger O, Fonseca HA, *et al.* Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil (COALITION II): a randomised clinical trial. *Lancet* Published Online First: 21 September 2020. doi:10.1016/S0140-6736(20)31862-6

46 Lauriola M, Pani A, Ippoliti G, *et al.* Effect of combination therapy of hydroxychloroquine and azithromycin on mortality in COVID-19 patients. *Clin Transl Sci* 2020;**n/a**. doi:10.1111/cts.12860

47 Ayerbe L, Risco-Risco C, Ayis S. The association of treatment with hydroxychloroquine and hospital mortality in COVID-19 patients. *Intern Emerg Med* 2020;**15**:1501–6. doi:10.1007/s11739-020-02505-x

48 Lammers AJJ, Brohet RM, Theunissen REP, *et al.* Early Hydroxychloroquine but not Chloroquine use reduces ICU admission in COVID-19 patients. *Int J Infect Dis* 2020;**101**:283. doi:10.1016/j.ijid.2020.09.1460

49 Annie FH, Sirbu C, Frazier KR, *et al.* Hydroxychloroquine in hospitalized COVID-19 patients: Real world experience assessing mortality. *Pharmacother J Hum Pharmacol Drug Ther* 2020;:0–2. doi:10.1002/phar.2467

50 Szente SNF, De Queiroz Sousa A, Wolkoff AG, *et al.* Risk of hospitalization for Covid-19 outpatients treated with various drug regimens in Brazil: Comparative analysis. *Travel Med Infect Dis* 2020;**38**. doi:https://doi.org/10.1016/j.tmaid.2020.101906 Received

51 Patel TK, Barvaliya M, Kevadiya BD, *et al.* Does Adding of Hydroxychloroquine to the Standard Care Provide any Benefit in Reducing the Mortality among COVID-19 Patients?: a Systematic Review. *J Neuroimmune Pharmacol* 2020;**15**:350–8. doi:10.1007/s11481-020-09930-x

52 Das RR, Jaiswal N, Dev N, *et al.* Efficacy and Safety of Anti-malarial Drugs (Chloroquine and Hydroxy-Chloroquine) in Treatment of COVID-19 Infection: A Systematic Review and Meta-Analysis. *Front Med* 2020;**7**:482. doi:10.3389/fmed.2020.00482

53 Fiolet T, Guihur A, Rebeaud ME, *et al.* Effect of hydroxychloroquine with or without azithromycin on the mortality of coronavirus disease 2019 (COVID-19) patients: a systematic review and meta-analysis. Clin. Microbiol. Infect. 2020. doi:10.1016/j.cmi.2020.08.022

54 Yang T-H, Chou C-Y, Yang Y-F, *et al. Systematic Review and Meta-analysis of the Effectiveness and Safety of Hydroxychloroquine in Treating COVID-19 Patients.* 2020. doi:10.1097/jcma.0000000000000425

55 Kashour Z, Riaz M, Garbati MA, *et al.* Efficacy of chloroquine or hydroxychloroquine in COVID-19 patients: a systematic review and meta-analysis. *J Antimicrob Chemother* 2020;:1–13. doi:10.1093/jac/dkaa403

56 Ayele Mega T, Feyissa TM, Dessalegn Bosho D, *et al.* The Outcome of Hydroxychloroquine in Patients Treated for COVID-19: Systematic Review and Meta-Analysis. *Can Respir J* 2020;**2020**:1–16. doi:10.1155/2020/4312519