

### Supplementary Material\*

Hernandez AV, Roman YM, Pasupuleti V, et al. Update alert 2: hydroxychloroquine or chloroquine for the treatment or prophylaxis of COVID-19. *Ann Intern Med.* 21 August 2020. [Epub ahead of print]. doi:10.7326/L20-1054

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\* This supplementary material was provided by the authors to give readers further details on their article. The material was reviewed but not copyedited.

Supplement Table 1. Effect of Hydroxychloroquine Reported in Controlled Studies

Name	Type	RoB	Unadjusted Absolute effect of HCQ vs. Control (95% CI)	SOE
<b>All-Cause Mortality</b>				
Cavalcanti <sup>3</sup>	RCT	H	HCQ: 5/159 vs. 5/173; RD 0.3% (-3.4% to 3.9%)	L
Cavalcanti <sup>3</sup>		H	HCQ+AZ: 3/172 vs. 5/173; RD -1.2% (-4.3% to 2.0%)	
Mitjà <sup>4</sup>		SC	HCQ: 0/136 vs. 0/157; RD 0% (NA)	
Skipper <sup>5</sup>		H	HCQ: 1/201 vs. 1/194; RD -0.02% (-1.4% to 1.4%)	
Horby <sup>6</sup>		SC	HCQ: 418/1561 vs. 788/3155; RD 1.8% (-0.9% to 4.5%)	
C-P Chen <sup>7</sup>		SC	HCQ: 0/21 vs. 0/12; RD 0% (NA)	
J Chen <sup>11</sup>		SC	HCQ: 0/15 vs. 0/15; RD 0% (NA)	
L Chen <sup>12</sup>		H	HCQ: 0/15 vs. 0/12; RD 0% (NA)	
Paccoud <sup>8</sup>	Cohort	S	HCQ: 3/38 vs. 6/46; RD -5.2% (-18.1% to 7.8%)	L
Lecronier <sup>9</sup>		C	HCQ: 9/38 vs. 9/22; RD -17.2% (-41.8% to 7.4%)	
Barbosa <sup>13</sup>		C	HCQ: 4/31 vs. 1/32; RD 9.8% (-3.5% to 23.3%)	
Magagnoli <sup>14</sup>		S	HCQ±AZ: 27/97 vs. 18/158; RD 16.4% (6.2% to 26.6%) †	
Mallat <sup>15</sup>		S	HCQ: 0/23 vs. 0/11 [0%]; RD 0% (NA)	
Membrillo <sup>16</sup>		C	HCQ: 27/123 vs. 21/43; RD -26.9% (-43.5% to -10.3%) †	
Geleris <sup>17</sup>		M	HCQ±AZ: 157/811 vs. 75/565; RD 6.1% (2.2% to 10%) †	
Rosenberg <sup>18</sup>		S	HCQ±AZ: 54/271 vs. 28/221; RD 7.3% (0.8% to 13.7%) †	
Mahévas <sup>19</sup>		S	HCQ: 9/84 vs. 8/97; RD 2.5% (-6.1% to 11.1%)	
Ip <sup>20</sup>		S	HCQ: 383/1914 vs. 120/598; RD -0.1% (-3.7% to 3.6%)	
Sbidian <sup>21</sup>		M	HCQ: 111/623 vs. 830/3792; RD -4.1% (-7.4% to 0.8%)	
Singh <sup>22</sup>		S	HCQ: 104/910 vs. 109/910; RD -0.6% (-3.5% to 2.4%)	
Yu <sup>23</sup>		S	HCQ: 9/48 vs. 238/502; RD -29.7% (-40.5% to -16.8%) †	
Arshad <sup>24</sup>		S	HCQ±AZ: 162/1202 vs. 108/409; RD -12.9% (-17.6% to -8.2%) †	
<b>Composite of Intubation or Death</b>				
Horby <sup>6</sup>	RCT	SC	HCQ: 388/1300 vs. 696/2623; RD 3.3% (0.3% to 6.3%) †	L
Geleris <sup>17</sup>	Cohort	M	HCQ±AZ: 262/811 vs. 84/565; RD 17.4% (13.1% to 21.8%) †	I
<b>Composite of ICU Admission Within 7-Days or Death</b>				
Paccoud <sup>8</sup>	Cohort	S	HCQ: [By 12 days] 13/38 vs. 16/46; RD -0.6% (-21.0% to 19.9%)	I
Mahévas <sup>25</sup>		S	HCQ: 16/84 vs. 21/97; RD -2.6% (-14.3% to 9.1%)	
<b>ICU Admission</b>				
Rosenberg <sup>18</sup>	Cohort	S	HCQ±AZ: 52/271 vs. 27/221; RD 7% (0.6% to 13.3%) †	I
<b>Survival without ICU Admission</b>				
Mahévas <sup>19</sup>	Cohort	S	HCQ: 17/84 vs. 22/89; RD -4.5% (-16.9% to 7.9%)	I
<b>Need of Mechanical Ventilation</b>				
Cavalcanti <sup>3</sup>	RCT	H	HCQ: 12/159 vs. 12/173; RD 0.6% (-5.0% to 6.2%)	L
Cavalcanti <sup>3</sup>		H	HCQ+AZ: 19/172 vs. 12/173; RD 4.1% (-1.9% to 10.1%)	
Mitjà <sup>4</sup>		SC	HCQ: 0/136 vs. 0/157; RD 0% (NA)	
Horby <sup>6</sup>		SC	HCQ: 118/1300 vs. 215/2623; RD 0.9% (-1.0% to 2.8%)	
Lecronier <sup>9</sup>	Cohort	C	HCQ: 5/38 vs. 2/22; RD 4.1% (-12.1% to 20.2%)	L
Magagnoli <sup>14</sup>		S	HCQ±AZ: 12/90 vs. 25/177; RD -0.8% (-9.5% to 7.9%)	

Mallat <sup>15</sup>		S	HCQ: 0/23 vs. 0/11; RD 0% (NA)	
Geleris <sup>17</sup>		M	HCQ±AZ: 154/811 vs. 26/565; RD 14.4% (11.2% to 17.6%) †	
Rosenberg <sup>18</sup>		S	HCQ±AZ: 51/271 vs. 18/221; RD 10.7% (4.8% to 16.6%) †	
Singh <sup>22</sup>		S	HCQ: 46/910 vs. 57/910; RD -1.2% (-3.3% to 0.9%)	
<b>Severe Disease Progression</b>				
J Chen <sup>11</sup>	RCT	SC	HCQ: 1/15 vs. 0/15; RD 6.7% (-6.0% to 19.3%)	I
L Chen <sup>12</sup>		H	HCQ: 0/15 vs. 0/12; RD 0% (NA)	
Z Chen <sup>26</sup>		SC	HCQ: 0/31 vs. 4/31; RD -12.9% (-24.7% to -1.1%) †	
Barbosa <sup>13</sup>	Cohort	C	HCQ: [Respiratory support level] +0.63±0.79 vs. +0.16±0.64 points; MD 0.47 (0.11 to 0.83) †	I
Mallat <sup>15</sup>		S	HCQ: [High flow oxygen therapy] 0/23 vs. 0/11; RD 0% (NA)	
Mahévas <sup>25</sup>		S	HCQ: [ARDS] 24/84 vs. 23/95; RD 4.4% (-8.6% to 17.3%)	
<b>Hospitalization</b>				
Mitjà <sup>4</sup>	RCT	SC	HCQ: 8/136 vs. 11/157; RD -1.1% (-6.7% to 4.5%)	I
Komissarov <sup>10</sup>	Cohort	C	HCQ: 7/33 vs 0/10; RD 21.2% (7.3% to 35.2%) †	I
<b>Discharge from Hospital</b>				
Horby <sup>6</sup>	RCT	SC	HCQ: 941/1561 vs. 1982/3155; RD -2.5% (-5.5% to 0.4%)	L
Paccoud <sup>8</sup>	Cohort	S	HCQ: 21/38 vs. 26/46; RD -1.3% (-22.6% to 20.1%)	I
Mahévas <sup>19</sup>		S	HCQ: 67/84 vs. 71/89; RD 0% (-12% to 12%)	
Sbidian <sup>21</sup>		M	HCQ: 351/623 vs. 1507/3792; RD 16.6% (12.4% to 20.8%)	
<b>Symptom Resolution</b>				
Skipper <sup>5</sup>	RCT	H	HCQ: [At 14 days:] 152/201 vs. 135/194; RD 6.0% (-2.7% to 14.8%)	I
J Chen <sup>11</sup>		SC	HCQ: [Fever] 1 vs. 1 day; MD 0 days (NA)	
L Chen <sup>12</sup>		H	HCQ: [Days to recovery [Median(IQR)]: 6 (3-8) vs. 7.5 (5-16.3)	
Z Chen <sup>26</sup>		SC	HCQ: [Fever] 2.2±0.4 vs. 3.2±1.3 days; MD -1 day (-1.5 to -0.5) † [Cough] 2.0±0.2 vs. 3.1±1.5 days; MD -1.1 days (-1.6 to -0.6) †	
Tang <sup>27</sup>		H	HCQ: [Composite symptom resolution] 32/64 vs. 24/55; RD 6.4% (-11.6% to 24.3%)	
<b>Progression of Pulmonary Lesions on CT Scan</b>				
J Chen <sup>11</sup>	RCT	SC	HCQ: 5/15 vs. 7/15; RD -13.3% (-48.1% to 21.4%)	L
Z Chen <sup>26</sup>		SC	HCQ: 2/31 vs. 9/31; RD -22.6% (-40.8% to -4.4%) †	
<b>Improvement in Pulmonary Lesions on CT Scan</b>				
Z Chen <sup>26</sup>	RCT	SC	HCQ: 25/31 vs. 17/31; RD 25.8% (3.4% to 48.2%) †	I
<b>Upper Respiratory Virological Clearance</b>				
C-P Chen <sup>7</sup>	RCT	SC	HCQ: [Day 14] 17/21 vs. 9/12; RD 6.0% (-23.8% to 35.7%)	I
J Chen <sup>11</sup>		SC	HCQ: [Day 7] 13/15 vs. 14/15; RD -6.7% (-28% to 14.7%) [Day 14] 15/15 vs. 15/15; RD 0% (NA)	
L Chen <sup>12</sup>		H	HCQ: [Day 10] 15/15 vs/ 12/12; RD 0% (NA)	
Tang <sup>27</sup>		H	HCQ: [Day 23] 53/75 vs. 56.75; RD -4% (-18.3% to 10.3%)	
C-P Chen <sup>7</sup>	Cohort	C	HCQ: [Day 14] 12/28 vs. 5/9; RD -12.7% (-50.0% to 24.6%)	I
Lecronier <sup>9</sup>		C	HCQ: [Day 7] 7/26 vs. 2/14; RD 12.6% (-12.4% to 37.7%)	
Mallat <sup>15</sup>		S	HCQ: [Day 14] 11/23 vs. 10/11; RD -43.1% (-69.6% to -16.5%) †	
Gautret <sup>28</sup>		C	HCQ±AZ: [Day 6] 14/20 vs. 2/16; RD 57.6% (31.8% to 83.3%) †	

ARDS = acute respiratory distress syndrome; HCQ = hydroxychloroquine; MD = mean difference; RCT = randomized controlled trial; RD = absolute risk difference; RoB = risk of bias; SOE = strength of evidence.

† Denotes a statistically significant finding.

Risk of bias codes: SC – some concerns, H– high, M – moderate, S –serious, C – critical, NI – no information.

Strength of evidence codes: I – insufficient, L- low.