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About the paper published in The Lancet: data coming from five different continents cannot be so homogeneous. There is either data manipulation (not mentionned in Material and Methodes), or incorporation of faked data.

Table S3. Summary Data by Continent

Variable	North America	South America	Europe	Africa	Asia	Australia
N	63,315	3,577	16,574	4,402	7,555	609
Age (years)	54.4 +/- 17.8	53.6 +/- 17.1	52.7 +/- 17.0	53.9 +/- 16.9	51.9 +/- 17.2	55.8 +/- 17.7
BMI (Kg/m²)	28.1 +/- 5.3	26.4 +/- 5.4	28.1 +/- 5.3	23.8 +/- 5.4	24.8 +/- 5.3	28.1 +/- 5.4
Female sex	29,288 (46.3)	1,678 (46.9)	7,730 (46.6)	1,981 (45.0)	3,486 (46.1)	263 (43.2)
Coronary artery disease	7,850 (12.4)	485 (13.6)	2,169 (13.1)	614 (13.9)	980 (13.0)	39 (6.4)
Congestive heart failure	1,639 (2.6)	73 (2.0)	366 (2.2)	105 (2.4)	179 (2.4)	6 (1.0)
History of arrhythmia	2,293 (3.6)	118 (3.3)	543 (3.3)	146 (3.3)	256 (3.4)	25 (4.1)
Diabetes mellitus	8,654 (13.7)	521 (14.6)	2,360 (14.2)	570 (12.9)	1,069 (14.1)	86 (14.1)
Hypertension	17,159 (27.1)	954 (26.7)	4,368 (26.4)	1,140 (25.9)	2,010 (26.6)	179 (29.4)
Hyperlipidemia	20,032 (31.6)	1,088 (30.4)	5,131 (31.0)	1,380 (31.3)	2,374 (31.4)	193 (31.7)
COPD	2,069 (3.3)	97 (2.7)	590 (3.6)	132 (3.0)	254 (3.4)	35 (5.7)
Current smoker	6,316 (10.0)	347 (9.7)	1,604 (9.7)	453 (10.3)	707 (9.4)	61 (10.0)
Former smoker	10,707 (16.9)	670 (18.7)	2,936 (17.7)	830 (18.9)	1,301 (17.2)	109 (17.9)
Immunocompromised	1,997 (3.2)	52 (1.5)	463 (2.8)	127 (2.9)	208 (2.8)	21 (3.4)
ACE inhibitor	5,327 (8.4)	285 (8.0)	1,341 (8.1)	325 (7.4)	605 (8.0)	66 (10.8)
Statin	6,188 (9.8)	306 (8.6)	1,552 (9.4)	436 (9.9)	674 (8.9)	89 (14.6)
ARB	3,913 (6.2)	220 (6.2)	963 (5.8)	259 (5.9)	454 (6.0)	40 (6.6)
Antiviral Therapy use	25,646 (40.5)	1,444 (40.4)	6,747 (40.7)	1,771 (40.2)	3,085 (40.8)	234 (38.4)
Chloroquine alone	1,091 (1.7)	114 (3.2)	295 (1.8)	153 (3.5)	199 (2.6)	16 (2.6)
Hydroxychloroquine alone	2,127 (3.4)	72 (2.0)	540 (3.3)	83 (1.9)	184 (2.4)	10 (1.6)
CQ + macrolide	2,324 (3.7)	217 (6.1)	562 (3.4)	256 (5.8)	391 (5.2)	33 (5.4)
HCQ + macrolide	4,335 (6.8)	150 (4.2)	1,129 (6.8)	168 (3.8)	399 (5.3)	40 (6.6)
qSOFA < 1	52,301 (82.6)	2,958 (82.7)	13,682 (82.6)	3,670 (83.4)	6,267 (83.0)	490 (80.5)
SPO_2 < 94%	6,191 (9.8)	345 (9.6)	1,576 (9.5)	439 (10.0)	701 (9.3)	65 (10.7)
Outcomes						
Ventricular arrhythmia	869 (1.4)	41 (1.1)	179 (1.1)	56 (1.3)	89 (1.2)	5 (0.8)
Hospital LOS	9.1 +/- 6.4	8.9 +/- 6.2	9.1 +/- 6.4	9.1 +/- 6.4	9.2 +/- 6.4	8.7 +/- 6.2
ICU LOS	2.9 +/- 5.5	3.0 +/- 5.9	2.9 +/- 5.6	2.8 +/- 5.1	2.8 +/- 5.4	2.9 +/- 5.7
Total LOS	12.0 +/- 8.8	11.9 +/- 9.0	12.0 +/- 8.8	11.9 +/- 8.5	11.9 +/- 8.6	11.6 +/- 8.7
Mechanical Ventilation	5,660 (8.9)	425 (11.9)	1,874 (11.3)	542 (12.3)	780 (10.3)	73 (12.0)
Mortality	7,534 (11.9)	382 (10.7)	1,537 (9.3)	437 (9.9)	735 (9.7)	73 (12.0)
Ventilator use or Mortality	10,441 (16.5)	606 (16.9)	2,577 (15.5)	710 (16.1)	1,071 (14.2)	114 (18.7)

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Signs of flaws in the Lancet paper

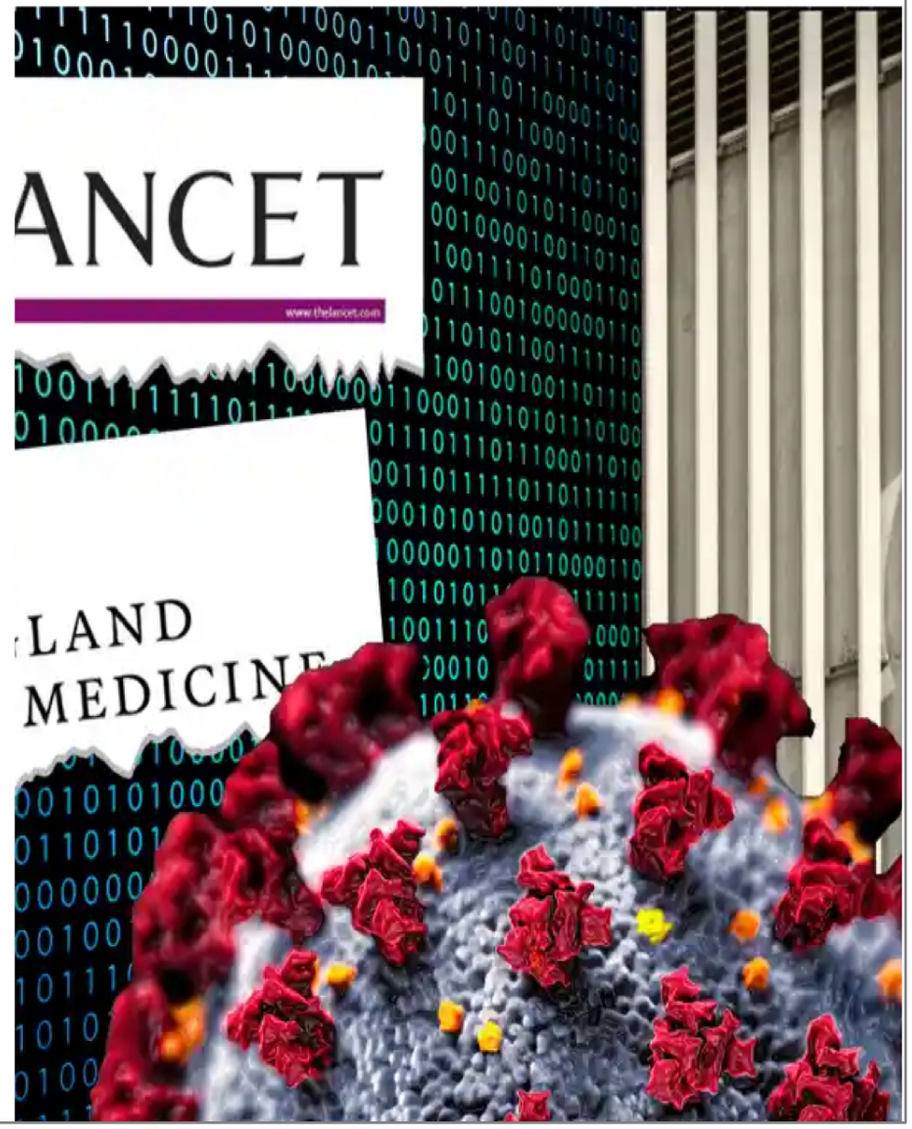
- Number of dead in Australia were much higher than in reality;
- All countries had same amount of smokers;
- In 2008 Surgisphere was a publisher of medical textbook: how could it become the owner of such powerful database?
- Only 11 employees with no scientific background and including “a science fiction writer and an adult model” (Guardian Australia)
- The company had only 170 Twitter followers, “with no posts between October 2017 and March 2020” (Guardian Australia)

Medical research

Surgisphere: governments and WHO changed Covid-19 policy based on suspect data from tiny US company

Melissa Davey *in Melbourne and* **Stephanie Kirchgaessner** *in Washington and* **Sarah Boseley** *in London*

Wed 3 Jun 2020 19.47 BST



The Lancet paper

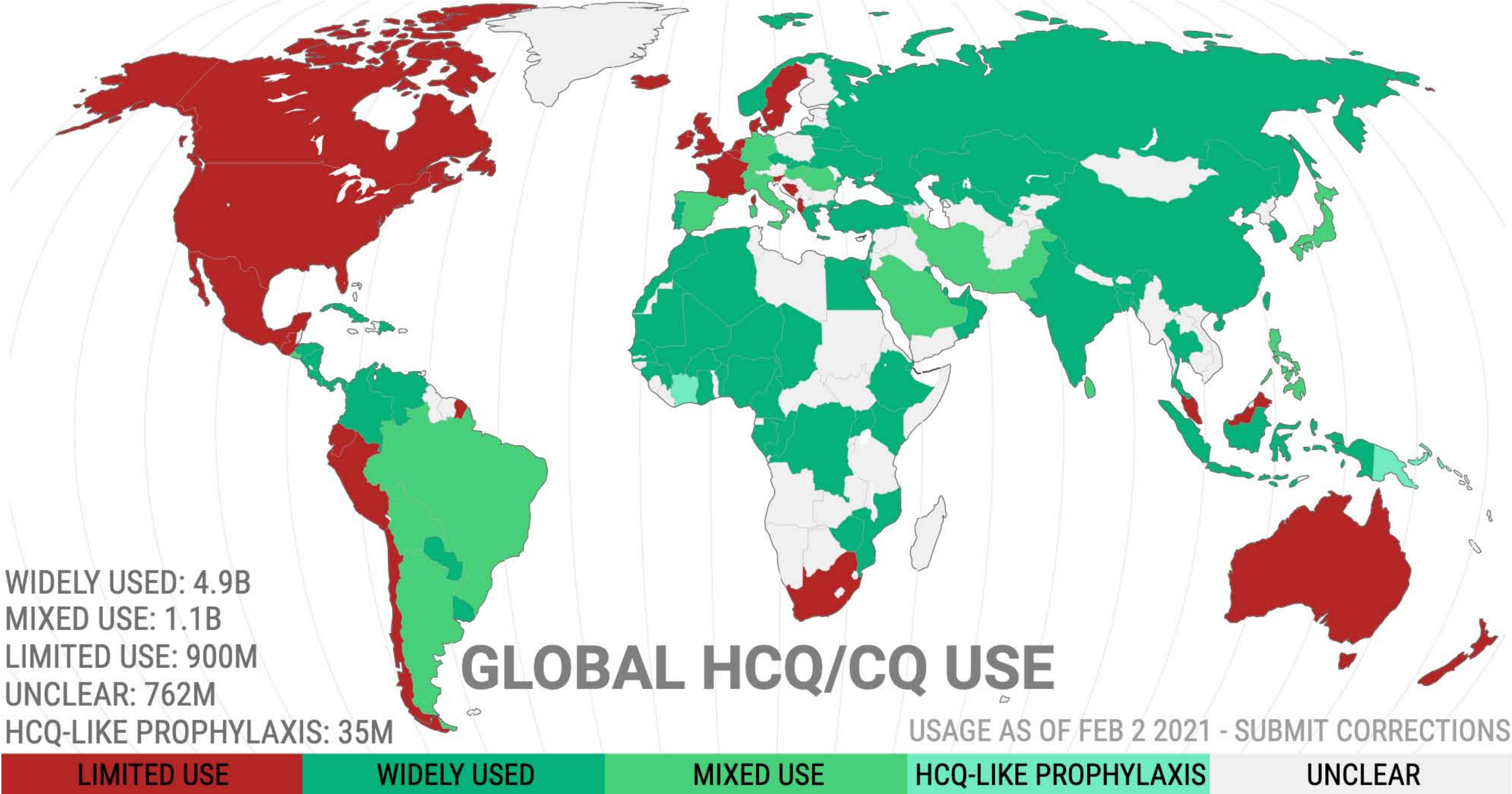
- The lead author (Dr Mandeep Mehra) was a renowned Harvard University vascular surgeon;
- Study based on a surgeon analytics company Surgisphere databases that included 96000 patients' medical files from 671 hospitals in 11 countries in the period 20/12/19-14/04/20; 14888 patients were treated with HCQ;
- The paper concluded HCQ did not work for Covid-19 and led to increase mortality rate;
- Interestingly, the paper's results did *not* come from a Random Control Trial (RCT), but it was a *meta analysis*.

Still, it had massive consequences:

- The Lancet paper was published on Friday, May 22nd 2020. Less than 24 hours later, the World Health Organization (WHO) stopped all 131 HCQ Covid-19 trials (including the European trial Discovery and Solidarity), with thousands of patients already enrolled;
- May 27th: use of HCQ to treat Covid-19 is forbidden in France;
- The use off-label of HCQ is forbidden in Italy. 150 doctors contested it. In December 2020 they won. The judges wrote: "The continuing uncertainty about the therapeutic efficacy of HCQ, admitted by the same Aifa to justify the further evaluation in RCT is not sufficient reason on the legal level to justify the unreasonable suspension of its use in the national territory".

Observations

- Arguments are not treated equally in all spaces: different communities may resort to different notions of proof (with their own hierarchy of proofs), have different expectations with respect to errors, levels of uncertainty and acceptable time frames to remove such uncertainties; different notions of acceptability (Dov's "Acceptance is declarative", cf. yesterday's discussion?);
- The HCQ debate created a collision between media and the scientific world: TV debates transformed a scientific controversy into a matter of opinion;
- Reaction vs. HCQ have not been the same in all countries


WIDELY USED: 4.9B
MIXED USE: 1.1B
LIMITED USE: 900M
UNCLEAR: 762M
HCQ-LIKE PROPHYLAXIS: 35M
GLOBAL HCQ/CQ USE
USAGE AS OF FEB 2 2021 - SUBMIT CORRECTIONS
LIMITED USE
WIDELY USED
MIXED USE
HCQ-LIKE PROPHYLAXIS
UNCLEAR

The research continues

- Since August 2020 https://c19hcq.com collects all research papers on HCQ (those who show positive results and those who show negative ones);
- For each paper, the site's authors interpret the results, clearly explain the criteria used, and detail eventual disagreements with the paper's authors;
- One can follow the international discussion in real-time;
- The authors are anonymous (to avoid death threats), but the quality of the analysis indicates real academic competences;
- Papers are still produced at high rate, sign that the dispute is not closed.

HCQ FOR COVID-19

257 TRIALS, 4,112 SCIENTISTS, 384,791 PATIENTS

66% IMPROVEMENT IN 26 EARLY TREATMENT TRIALS RR 0.34 [0.24-0.49]

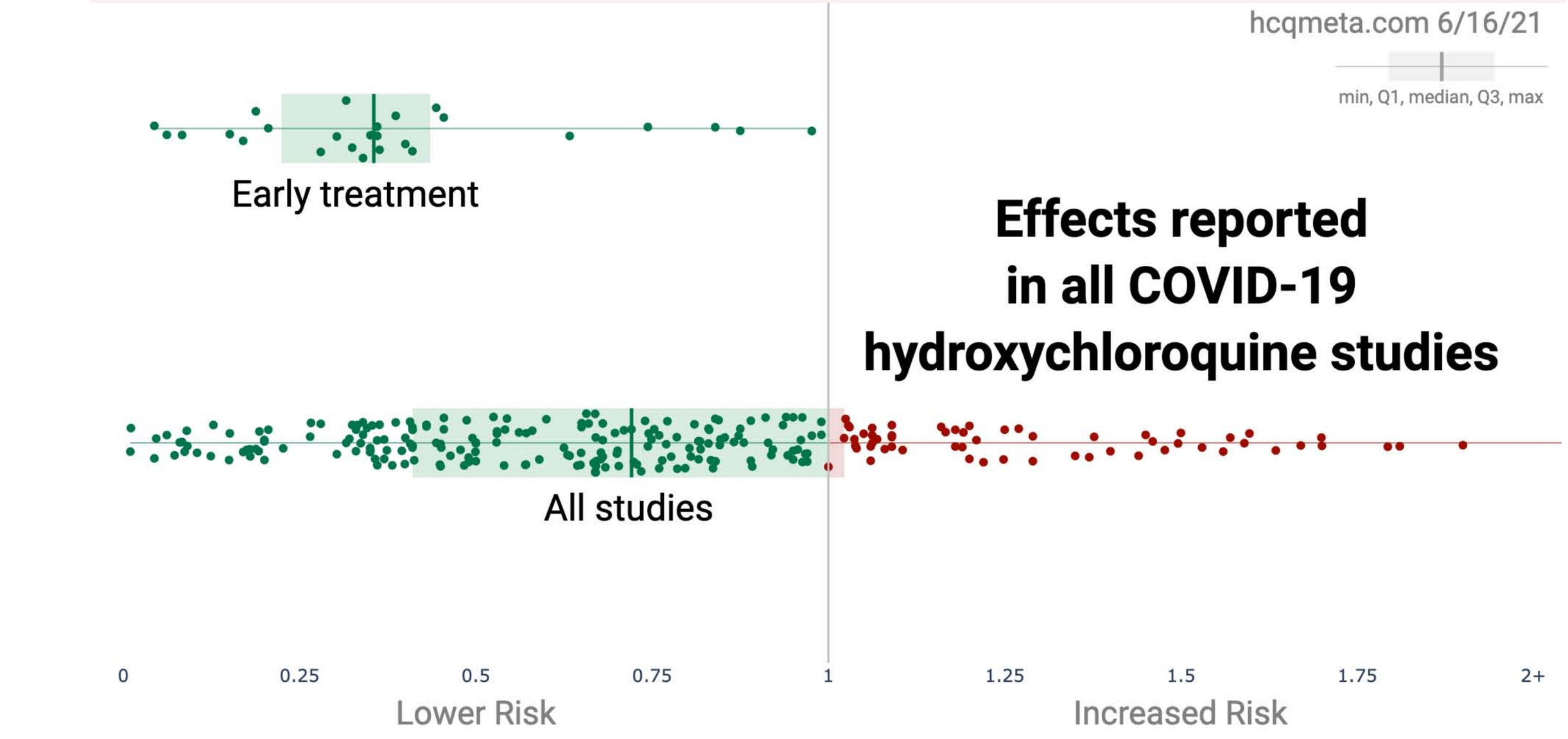
75% IMPROVEMENT IN 11 EARLY TREATMENT MORTALITY RESULTS RR 0.25 [0.16-0.40]

46% IMPROVEMENT IN 6 EARLY TREATMENT RCT RESULTS RR 0.54 [0.33-0.86]

22% IMPROVEMENT IN 175 LATE TREATMENT TRIALS RR 0.78 [0.73-0.84]

24% IMPROVEMENT IN 39 RANDOMIZED CONTROLLED TRIALS RR 0.76 [0.63-0.92]

SUMMARY OF RESULTS REPORTED IN HCQ STUDIES FOR COVID-19. 06/16/21. HCQMETA.COM



HCQ for COVID-19: real-time meta analysis of 257 studies

Covid Analysis, Oct 20, 2020 (Version 118, **Jun 16, 2021 — added Saib**)

https://hcqmeta.com/

- 100% of the 29 early treatment studies report a positive effect (13 statistically significant in isolation).
- Random effects meta-analysis with pooled effects using the most serious outcome reported shows 66% improvement for the 29 early treatment studies (RR 0.34 [0.24-0.49]). Results are similar after exclusion based sensitivity analysis: 67% (RR 0.33 [0.24-0.44]), and after restriction to 20 peer-reviewed studies: 65% (RR 0.35 [0.25-0.47]). Restricting to the 6 RCTs shows 46% improvement (RR 0.54 [0.33-0.86]). Restricting to the 13 mortality results shows 75% lower mortality (RR 0.25 [0.16-0.40]).
- Late treatment is less successful, with only 70% of the 175 studies reporting a positive effect. Very late stage treatment is not effective and may be harmful, especially when using excessive dosages.
- The probability that an ineffective treatment generated results as positive as the 257 studies to date is estimated to be 1 in 698 trillion (p = 0.0000000000000014).
- 87% of Randomized Controlled Trials (RCTs) for early, PrEP, or PEP treatment report positive effects, the probability of this happening for an ineffective treatment is 0.0037.
- There is substantial evidence of bias towards publishing negative results. 80% of prospective studies report positive effects, and only 72% of retrospective studies do. Studies from North America are 3.3 times more likely to report negative results than studies from the rest of the world combined, p = 0.0000000049.
- Negative meta analyses of HCQ generally choose a subset of trials, focusing on late treatment, especially trials with very late treatment and excessive dosages.
- While many treatments have some level of efficacy, they do not replace vaccines and other measures to avoid infection. Only 5% of HCQ studies show zero events in the treatment arm.
- Elimination of COVID-19 is a race against viral evolution. No treatment, vaccine, or intervention is 100% available and effective for all current and future variants. All practical, effective, and safe means should be used. Not doing so increases the risk of COVID-19 becoming endemic; and increases mortality, morbidity, and collateral damage.
- All data to reproduce this paper and the sources are in the appendix. See *[**Ladapo**, **Prodromos**, **Risch**, **Risch (B)**]* for other meta analyses showing efficacy when HCQ is used early.

Total	257 studies	4,112 authors	384,791 patients
Positive effects	191 studies	2,957 authors	270,418 patients

Early treatment	66% improvement	RR 0.34 [0.24-0.49]
Late treatment	22% improvement	RR 0.78 [0.73-0.84]

Conclusions

- Discussions can change of topic (*sliding arguments*): from HCQ to Raoult as a person (*ad hominem*) (Graph 1);
- The proof can change according to what suits us best: at the beginning, RCT is required to prove that HCQ works (*argument by established rule*). However, when The Lancet paper 'shows' that HCQ is dangerous using a meta-analysis, this new type of proof is accepted;
- Sometimes, some participants in a debate do not see some arguments (especially if they are of the opposing view), cf. The Lancet graph (*confirmation bias*?);
- Participants do not necessarily share the same notion of defeat. The media's view seems to be that there is a disagreement over two incompatible issues (T and T') between two parties A and B:

A wins over B = A proves T or falsifies T'

Whereas the scientific view is that:

A wins over B = A refutes B's arguments

- Underlying seems to be a non realistic view of how science works. Interestingly, the two different views above come from M. Pera "Rhetoric and Scientific Controversies", where he compares the views of science of the philosopher-scientists who gave rise to modern science (the Fathers), deeply attached to the idea that science is uncontroversial, and us (their Sons).

Thank you!