HCQ cocktail against early Covid-19 infection

n ≪ *p* logistic regression: deep learning solution?

Richard D. Gill - Mathematical Institute, Leiden University

Contributed paper at Bernoulli-IMS One World Symposium 2020
Session on high dimensional data

This version: 17/10/21

https://www.math.leidenuniv.nl/~gill/Presentation.pdf

Preprint, links to data sets, ..., at my homepage, soon
https://www.math.leidenuniv.nl/~gill

Thuan

Collaborators

and Acknowledgments

Dipro

- Leila Schneps (Paris)
- Dipro Mondal (Leiden)
- Hoang Van Thuan (Vietnam and Marseilles)
- Philippe Gautret, Didier Raoult & others in Marseilles
- Rob Elens and others in Meijel
- Also thanks to many friends and colleagues for help with R, JASP, AgenaRisk, lasso, splines, Bayesian Cox regression, ...

Leila

HCQ + AZM + Zn as preventive treatment

(HCQ cocktail as prophylaxis)

- Corona: many are exposed; some become infected, some become infectious, some have symptoms
- Not many get very sick; but many of those who do get sick die or suffer permanent harm
- Tests are very unreliable
- Symptoms are very unspecific
- Hydroxychloroquine, with azithromycine and Zinc, might be a useful prophylactic
- There exists a plausible biochemical explanation

Back of envelope power calculation

Why we still don't know

- Suppose 50% who go to their doctor because fear they are exposed and have some symptoms don't actually have Covid-19
- Suppose 75% of remainder will have mild episode of sickness & completely recover in few weeks
- So, only 1 in 8 is going to get seriously ill
- Suppose HCQ+ prophylactic treatment could halve that to 1 in 16
- Then question is: $p_1 = p_2 = 1/8$; or $p_1 = 1/8$, $p_2 = 1/16$?

- Suppose n = 2^11 = 2048
- Then in *control group* expect 2^7 = 128 –ve outcomes, in *treatment group* either 2^7 = 128 or 2^6 = 64
- Square roots of observed numbers approx $N(11.3, 1/4)$ and $N(11.3, 1/4)$, or $N(11.3, 1/4)$ and $N(8, 1/4)$
- Difference of square roots very approx $N(0, 1/2)$, or $N(3.3, 1/2)$
- Root 2 times difference of square roots very approx $N(0, 1)$ or $N(4.7, 1)$
- Have a very good chance of observing right answer, whatever it is!
- 4x smaller sample (n = 512) is some use, but not conclusive: $N(0, 1)$ or $N(2.34, 1)$.
- 4x smaller sample still (n = 128) is pretty useless: $N(0, 1)$ or $N(1.17, 1)$.

Two early publicised observational studies

Marseilles; Meijel

- First **publicised** "trials" had $n \approx 40$
- Spectacular positive results
- Politics: Macron, Trump, the alt-right (Corona deniers and anti-vaxers)
- Fish pond cleaning fluid and a witch doctor from the Cameroons, conspiracy theorists and the interests of Big Pharma, distrust of models and science, ...

Marseilles

https://rpubs.com/gill1109/raoult

- **Philippe Gautret**, Jean-Christophe Lagier, Philippe Parola, **Hoang Van Thuan**, Line Meddeb, Morgane Mailhe, Barbara Doudier, Johan Courjone, Valérie Giordanengo, Vera Esteves Vieira, Hervé Tissot Dupont, Stéphane Honoré, Philippe Colson, Eric Chabrière, Bernard La Scola, Jean-Marc Rolain, Philippe Brouqui, **Didier Raoult**
- *International Journal of Antimicrobial Agents* **56** (1) 2020, 105949 (6pp.)
- Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial
- https://doi.org/10.1016/j.ijantimicag.2020.105949

Gautret et al.(2000)
https://doi.org/10.1016/j.ijantimicag.2020.105949

Table 2
Proportion of patients with virological cure (negative nasopharyngeal PCR) by day, in COVID-19 patients treated with hydroxychloroquine and in COVID-19 control patients.

$n = 36$

	Day6 post inclusion		
	Number of negative patients/total number of patients	%	p-value
Hydroxychloroquine treated patients (N=20)	14/20	70.0	0.001
Control patients (N=16)	2/16	12.5	

[a]control patients from centers other than Marseille did not undergo daily sampling, but were sampled every other day in most cases, they were considered positive for PCR when actually positive the day(s) before and the day(s) after the day(s) with missing data.

p-value: one pro mille

https://rpubs.com/gill1109/raoult

Marseilles

ITT analysis, endpoint = disease free after 6 days

$n = 42$

	good outcome	bad outcome
treatment	15	11
control	2	14

```
##  Fisher's Exact Test for Count Data
##
## data:  numbers
## p-value = 0.004491
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##   1.575364 98.091226
## sample estimates:
## odds ratio
##   9.031585
```

p-value: one half of 1 percent

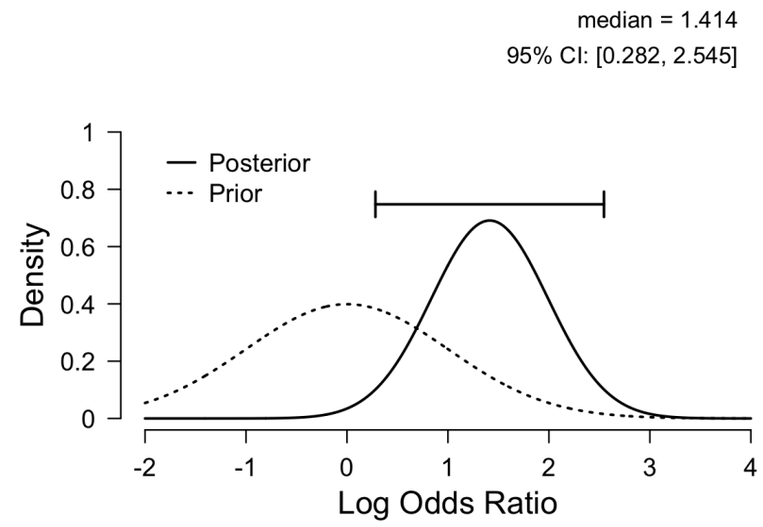
Barnard's unconditional test: almost the same

https://www.math.leidenuniv.nl/~gill/raoultJASP.html

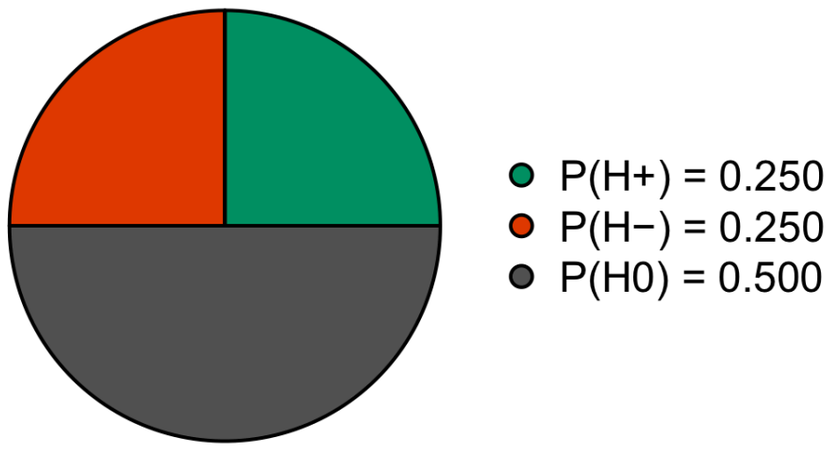
Bayesian analysis ("slab and slice prior"; JASP package)

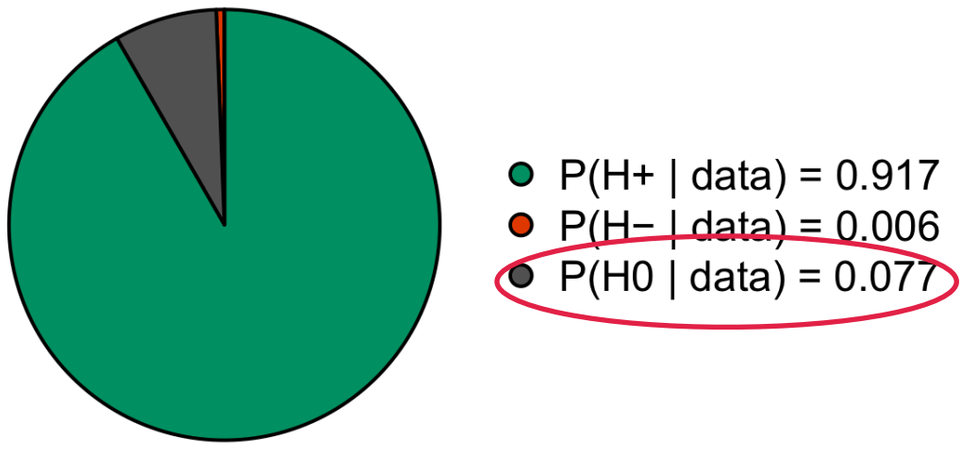
$n = 42$

```
## Bayesian A/B Test Results:
##
##  Bayes Factors:
##
##  BF10: 11.61384
##  BF+0: 23.77204
##  BF-0: 0.1589173
##
##  Prior Probabilities Hypotheses:
##
##  H+: 0.25
##  H-: 0.25
##  H0: 0.5
##
##  Posterior Probabilities Hypotheses:
##
##  H+: 0.9167
##  H-: 0.0061
##  H0: 0.0771
```



Prior and posterior,
both **conditional on inequality**





Left: prior; right: posterior

A posteriori, still 8% chance of no group *difference* at all!

NB: A *difference* is not necessarily a *treatment effect*

Meijel

https://rpubs.com/gill1109/elens

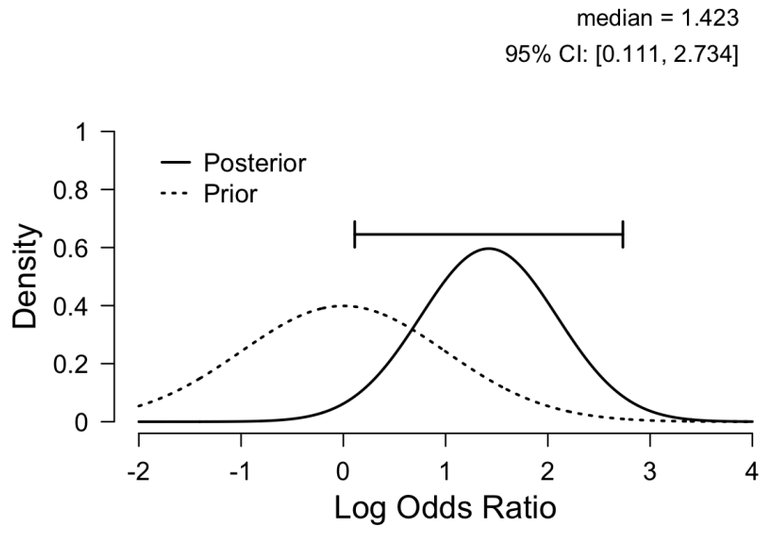
- Dutch family doctor Elens first had 25 patients whom he gave the then standard treatment: 12 of 25 died.
- He gave the next 10 chloroquine: all 10 recovered.
- He was then ordered to stop that treatment.
- His next patient (no chloroquine) … died.
- And so his story was reported in the media
- Internet petition, demonstrations, …

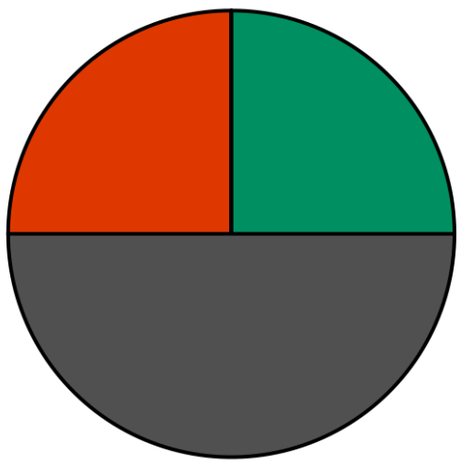
$n = 40$

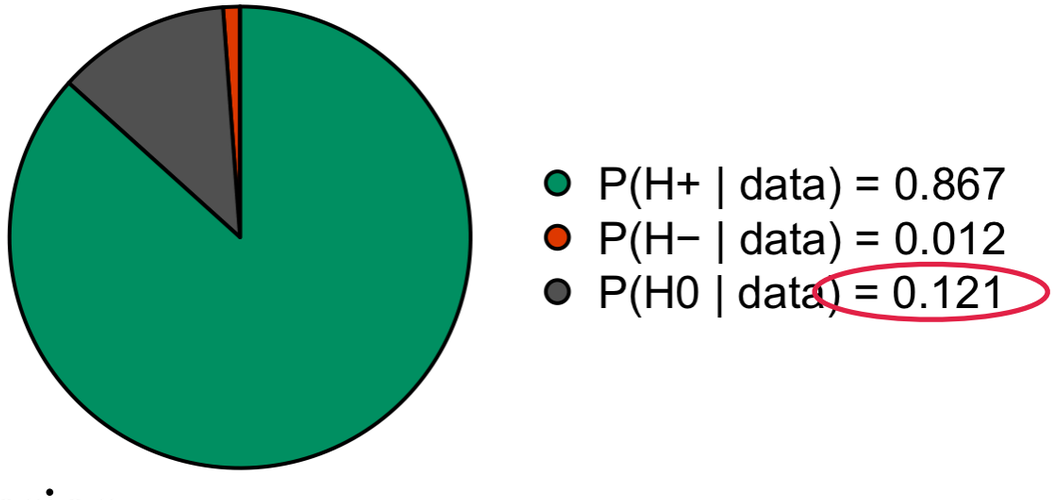
```
##  Fisher's Exact Test for Count Data
##
## data:  numbers
## p-value = 0.005848
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  1.720653      Inf
## sample estimates:
## odds ratio
##        Inf
```

https://rpubs.com/gill1109/elens

```
## Bayesian A/B Test Results:
##
##  Bayes Factors:
##
##  BF10: 6.997186
##  BF+0: 14.27489
##  BF-0: 0.1953377
##
##  Prior Probabilities Hypotheses:
##
##  H+: 0.25
##  H-: 0.25
##  H0: 0.5
##
##  Posterior Probabilities Hypotheses:
##
##  H+: 0.8667
##  H-: 0.0119
##  H0: 0.1214
```







Left: prior; right: posterior

A posteriori, still 12% chance of no group difference at all!

Confounders

Known confounders

- Age [effect is very nonlinear]
- Sex [certainly has interaction with most other variables]
- Various *comorbidities* (“existing conditions”)
- Severity and duration of various *symptoms*

- Ethnicity?
- Air pollution?
- Bloodgroup!
- Earlier exposure to similar virus infections?

Marseilles; Meijel

Two much too small but very influential early studies

- $n \approx 40$, $p \approx 40$++
- Age, sex, comorbidities, symptoms
- What we now know: your chance of death from Covid-19 **this year** is very similar to your chance of death from natural causes
- Risk groups: the old, the sick, obese, diabetics, Alzheimer patients, poor, financially insecure, … , some ethnic minorities, …
- [Those who come in close contact with many sick people]

Marseilles (and Nice)

Gautret … Hoang … Raoult (2020)

- Marseilles and Nice: observational study of patients at two different clinics
- "Treatment" confounded with "clinic"
- Noncompliance (6 patients "dropped out")
- Published analysis (Fisher exact test; some comparison of some covariates — sex, age [t-test], …) — did **not** control for covariates and did **not** use ITT (intention to treat) principle

Meijel

A small town between Eindhoven and Venlo in the South of the Netherlands

- GP and “orthomolecular doctor” Rob Elens was early adopter of HCQ. But forbidden from giving it at some point. So treatment was determined exogenously!
- Still, his groups are unbalanced regarding age and sex, and anyway, “time” may also be a confounder

Why controlling for confounders can help

Perfect matching

- With perfect matching we could have “identical twins” with **either** both the same outcome [usually good], **or** a small number with HCQ has good outcome, without HCQ has bad outcome.
- If HCQ works then: 1 in 16 twins could be like that. 7 in 8 twins, both have a good outcome. 1 in 16 twins, both have a bad outcome.
- If HCQ doesn’t work, then: 7 in 8 twins both good outcome, 1 in 8 both have bad outcome.
- 20 twins would not be enough but 200 twins would start to provide pretty convincing evidence.

Results with Marseilles, Meijel data

Two studies with n ≈ 40

- Fisher exact test gives highly significant **group difference**, p= 0.005 [NB: I deliberately do not say "**treatment effect**"]
- Odds ratio is estimated to be about 10 in favour of HCQ
- Bayesian analysis with slab and spike prior gives much milder conclusion
- With prior of 50% "no difference", 50% uninformative prior on log odds ratio, the posterior probability of "no difference" is still about 5%. The remaining posterior probability says "HCQ group does better", but size of improvement could well be much less than m.l.e.

Logistic regression with end-point "Covid-19 free" after 7 days

Covariates: age (linear), sex, #comorbidities, #symptoms

- Crazy coefficients with huge standard errors or even breakdown because "perfect fit", ie log odds ratios diverging
- *Lasso* (model selection) throws away all covariates except either sex or treatment!
- Not enough data to validate model selection by sample splitting
- Spline curve for effect of age gives nice looking results - from age 20 to 55 about flat, sharply rising from 55 to 95; but cannot fit age and sex and treatment, let alone age/sex interaction ...
- Some other end-points (e.g. Cox regression for duration of hospitalisation) gave even worse/crazier results.
- Nicely, however, leaving out some extremely young and extremely old patients did not alter Meijel results
- ITT analysis did not alter Marseilles results
- Meijel and Marseilles results **are** very similar

Idea

Cf: deep learning: a neural net shouldn't have to be taught the laws of physics every time anew. Once is enough.

- Use e.g. standard life-insurance tables to combine age, sex and comorbidities to one "Corona effective age"
- Use results of other studies aimed at different treatments to give one index of severity/progression of Corona infection
- Now we have $n \approx 40$, one treatment variable, and two continuous covariates. Discretise or, better, use splines. We can bring p down to ca. 10 **before** testing the effect of treatment

Dipro Mondal's results

To be written

- To be written: work in progress, very promising!!!

Conclusions

Summary

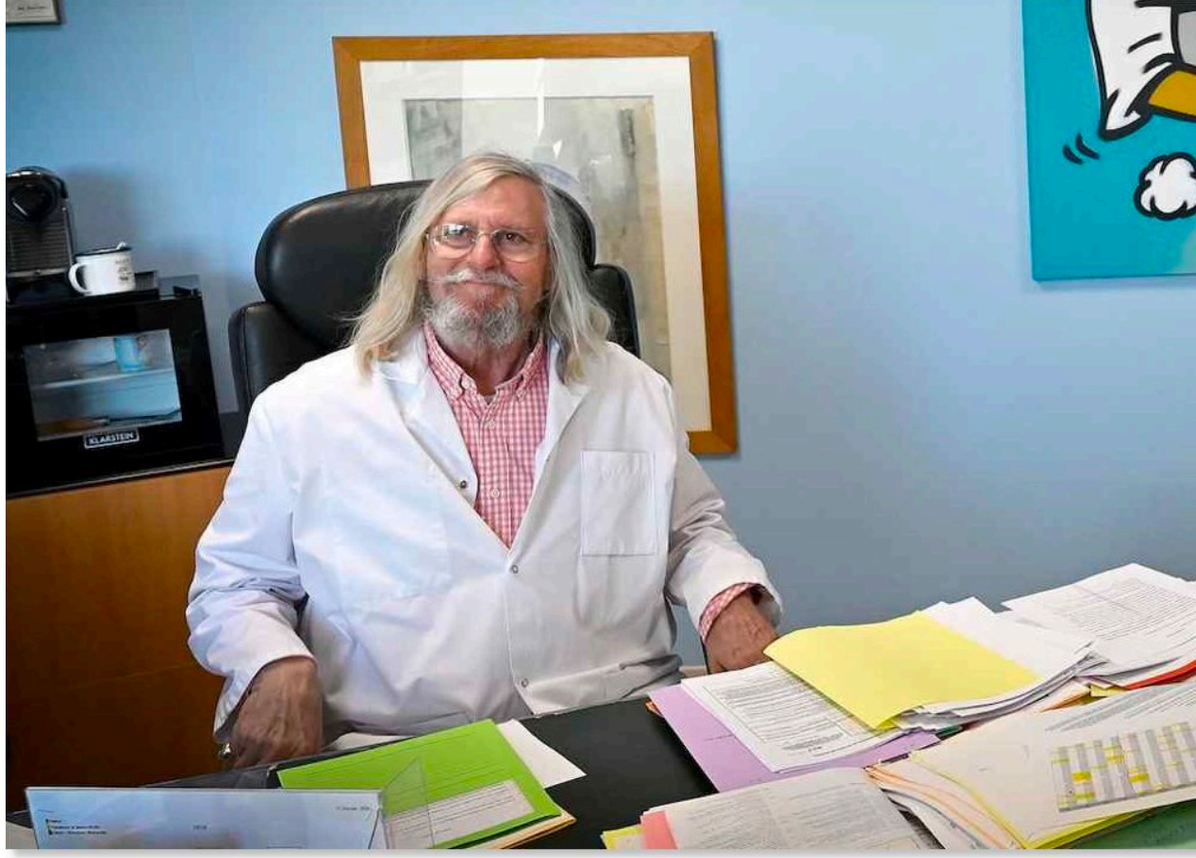
- We badly need a big RCT with *n* at least 1000
- We have by now learnt a great deal: we have decent measure of "general health status" (taking account of age, sex, comorbidities); and we have decent measures of severity of Covid-19 symptoms
- Lesson from "deep learning": we don't *have* to learn the separate effects of each of those separate components again; we only need two (continuous) covariates, and treatment indicator
- Medical doctors must learn not to fear statisticians – both sides need to get their act together!

Epilogue

and gallery...

- Latest research
- An RCT and an analysis of Zelenko's data
- Dr Fauci, Trump, ...
- The latest news (infection rate, hospitalisation rate, death rate, long term Covid...; HCQ findings from Isala hospital, Zwolle

Stella Immanuel



Didier Raoult

Vladimir Zelenko

Rob Elens

NIH U.S. National Library of Medicine

ClinicalTrials.gov

A failed trial

Evaluating the Efficacy of Hydroxychloroquine and Azithromycin to Prevent Hospitalization or Death in Persons With COVID-19

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04358068

Recruitment Status : Completed
First Posted : April 22, 2020
Last Update Posted : July 20, 2020

Sponsor:
National Institute of Allergy and Infectious Diseases (NIAID)

Collaborator:
Teva Pharmaceuticals Industries LTD

Information provided by (Responsible Party):
National Institute of Allergy and Infectious Diseases (NIAID)

https://clinicaltrials.gov/ct2/show/NCT04358068

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

Go to

Brief Summary:
The purpose of this study is to evaluate the efficacy of hydroxychloroquine (HCQ) and azithromycin (Azithro) to prevent hospitalization or death in symptomatic adult outpatients with COVID-19 caused by SARS-CoV-2 infection.

Condition or disease	Intervention/treatment	Phase
COVID-19 SARS-CoV 2	Drug: Hydroxychloroquine (HCQ) Drug: Azithromycin (Azithro) Drug: Placebo for Hydroxychloroquine Drug: Placebo for Azithromycin	Phase 2

Detailed Description:

A failed trial

News Releases

NIAID Now Blog

Media Contacts

Dr. Fauci in the News

NIAID-Funded Research News

Congressional Testimony

BULLETIN—NIH Clinical Trial Evaluating Hydroxychloroquine and Azithromycin for COVID-19 Closes Early

June 20, 2020

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has stopped enrollment in its clinical trial evaluating whether hydroxychloroquine and azithromycin can prevent hospitalization and death from coronavirus disease 2019 (COVID-19). This action was taken because NIAID, the study leadership and the independent data and safety monitoring board (DSMB) overseeing the trial determined that the rate of participant enrollment has been inadequate for the trial to meet its objectives in a timely manner. No safety concerns were associated with the trial.

Launched in May 2020, the NIAID-sponsored Phase 2b trial aimed to determine whether a short course of hydroxychloroquine and azithromycin could safely and effectively prevent disease progression among adults with mild-to-moderate COVID-19. Hydroxychloroquine is approved by the Food and Drug Administration to treat autoimmune diseases and to prevent and treat malaria. Preliminary evidence had suggested that the drug, alone or in combination with the FDA-approved antibiotic azithromycin, might benefit people with COVID-19.

Although recent research suggests that hydroxychloroquine may not be an effective treatment for patients hospitalized with COVID-19, the question of whether it offers benefit when given early in the course of the disease remains unanswered. The NIAID study, conducted by the AIDS Clinical Trials Group (ACTG), sought to fill this knowledge gap by testing it in a randomized, placebo-controlled trial—considered the gold standard for determining whether an intervention

https://www.niaid.nih.gov/news-events/bulletin-nih-clinical-trial-evaluating-hydroxychloroquine-and-azithromycin-covid-19

had laboratory-confirmed infection with SARS-CoV-2, the virus that causes COVID-19, and were experiencing symptoms consistent with COVID-19. Participants were randomly assigned to receive either hydroxychloroquine and azithromycin or matching placebo pills to take at home for seven days.

Since its launch in May, however, the study had enrolled only 20 participants, despite efforts by the study sites to enhance recruitment, raising concerns that it would not be feasible to continue the trial to full enrollment. On June 15,

Dr Fauci chooses his words carefully (but not completely honestly):

On Wednesday [29 July] Dr Anthony Fauci, a leading member of the White House coronavirus task force, told the **BBC** that hydroxychloroquine was not effective against the virus.

"We know that every single good study – and by good study I mean randomised control study in which the data are firm and believable – has shown that hydroxychloroquine is not effective in the treatment of Covid-19," he said.

Last month, the US Food and Drug Administration (FDA) cautioned against using the drug to treat coronavirus patients, following reports of "serious heart rhythm problems" and other health issues.

The FDA also revoked its emergency-use authorisation for the drug to treat Covid-19. The World Health Organization (WHO) says "there is currently no proof" that it is effective as a treatment or prevents Covid-19.

ACCEPTED MANUSCRIPT

Early Outpatient Treatment of Symptomatic, High-Risk Covid-19 Patients that Should be Ramped-Up Immediately as Key to the Pandemic Crisis FREE

Harvey A Risch

American Journal of Epidemiology, kwaa093, https://doi.org/10.1093/aje/kwaa093

Published: 27 May 2020 **Article history** ▼

Abstract

More than 1.6 million Americans have been infected with SARS-CoV-2 and >10 times that number carry antibodies to it. High-risk patients presenting with progressing symptomatic disease have only hospitalization treatment with its high mortality. An outpatient treatment that prevents hospitalization is desperately needed. Two candidate medications have been widely discussed: remdesivir, and hydroxychloroquine+azithromycin. Remdesivir has shown mild effectiveness in hospitalized inpatients, but no trials have been registered in outpatients. Hydroxychloroquine+azithromycin has been widely misrepresented in both clinical reports and public media, and outpatient trials results are not expected until September. Early outpatient illness is very different than later hospitalized florid disease and the treatments differ. Evidence about use of hydroxychloroquine alone, or of hydroxychloroquine+azithromycin in inpatients, is irrelevant concerning efficacy of the pair in early high-risk outpatient disease. Five studies, including two controlled clinical trials, have demonstrated significant major outpatient treatment efficacy. Hydroxychloroquine+azithromycin has been used as standard-of-care in more than 300,000 older adults with multicomorbidities, with estimated proportion diagnosed with cardiac arrhythmias attributable to the medications 47/100,000 users, of which estimated mortality is <20%, 9/100,000 users, compared to the 10,000 Americans now dying each week. These medications need to be widely available and promoted immediately for physicians to prescribe.

– 27 –

Zelenko's data

Preprint **Article** *Version 1* **This version is not peer-reviewed**

COVID-19 Outpatients – Early Risk-Stratified Treatment with Zinc Plus Low Dose Hydroxychloroquine and Azithromycin: A Retrospective Case Series Study

https://www.preprints.org/manuscript/202007.0025/v1

Martin Scholz *, Roland Derwand, Vladimir Zelenko

Version 1 : Received: 30 June 2020 / Approved: 3 July 2020 / Online: 3 July 2020 (08:52:22 CEST)

How to cite: Scholz, M.; Derwand, R.; Zelenko, V. COVID-19 Outpatients – Early Risk-Stratified Treatment with Zinc Plus Low Dose Hydroxychloroquine and Azithromycin: A Retrospective Case Series Study. *Preprints* **2020**, 2020070025 (doi: 10.20944/preprints202007.0025.v1).

Abstract

Objective: To describe outcomes of patients with coronavirus disease 2019 (COVID-19) in the outpatient setting after early treatment with zinc, low dose hydroxychloroquine, and azithromycin (the triple therapy) dependent on risk stratification. *Design:* Retrospective case series study. *Setting:* General practice. *Participants:* 141 COVID-19 patients with laboratory confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in the year 2020. *Main Outcome Measures:* Risk-stratified treatment decision, rate of hospitalization and all-cause death. *Results:* Of 335 positively PCR-tested COVID-19 patients, 127 were treated with the triple therapy. 104 of 127 met the defined risk stratification criteria and were included in the analysis. In addition, 37 treated and eligible patients who were confirmed by IgG tests were included in the treatment group (total N=141). 208 of the 335 patients did not meet the risk stratification criteria and were not treated. After 4 days (median, IQR 3-6, available for N=66/141) of onset of symptoms, 141 patients (median age 58 years, IQR 40-67; 73% male) got a prescription for the triple therapy for 5 days. Independent public reference data from 377 confirmed COVID-19 patients of the same community were used as untreated control. 4 of 141 treated patients (2.8%) were hospitalized, which was significantly less ($p<0.001$) compared with 58 of 377 untreated patients (15.4%) (odds ratio 0.16, 95% CI 0.06-0.5). Therefore, the odds of hospitalization of treated patients were 84% less than in the untreated group. One patient (0.7%) died in the treatment group versus 13 patients (3.5%) in the untreated group (odds ratio 0.2, 95% CI 0.03-1.5; $p=0.16$). There were no cardiac side effects. *Conclusions:* Risk stratification-based treatment of COVID-19 outpatients as early as possible after symptom onset with the used triple therapy, including the combination of zinc with low dose hydroxychloroquine, was associated with significantly less hospitalizations and 5 times less all-cause deaths.

A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19

https://www.nejm.org/doi/full/10.1056/NEJMoa2016638

David R. Boulware, M.D., M.P.H., Matthew F. Pullen, M.D., Ananta S. Bangdiwala, M.S., Katelyn A. Pastick, B.Sc., Sarah M. Lofgren, M.D., Elizabeth C. Okafor, B.Sc., Caleb P. Skipper, M.D., Alanna A. Nascene, B.A., Melanie R. Nicol, Pharm.D., Ph.D., Mahsa Abassi, D.O., M.P.H., Nicole W. Engen, M.S., Matthew P. Cheng, M.D., et al.

Article   Figures/Media

An inconclusive trial

EJMoa2016638

No AZM, Zn

18 References   39 Citing Articles   Letters

Abstract

BACKGROUND

Coronavirus disease 2019 (Covid-19) occurs after exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). For persons who are exposed, the standard of care is observation and quaranti... infection after SARS-CoV...

METHODS

We conducted a randomi... and parts of Canada testi... adults who had househol... a distance of less than 6 f... eye shield (high-risk expo... exposure). Within 4 days... placebo or hydroxychloro... mg daily for 4 additional... confirmed Covid-19 or ill...

RESULTS

We enrolled 821 asymptomatic participants. Overall, 87.6% of the participants (719 of 821) reported a high-risk exposure to a confirmed Covid-19 contact. The incidence of new illness compatible with Covid-19 did not differ significantly between participants receiving hydroxychloroquine (49 of 414 [11.8%]) and those receiving placebo (58 of 407 [14.3%]); the absolute difference was −2.4 percentage points (95% confidence interval, −7.0 to 2.2; P=0.35). Side effects were more common with hydroxychloroquine than with placebo (40.1% vs. 16.8%), but no serious adverse reactions were reported.

Related Articles

EDITORIAL JUN 3, 2020

Hydroxychloroquine for the Prevention of Covid-19 — Searching for Evidence

M.S. Cohen

Family Medicine   Montoursville, Pennsylvania

Primary Care Physician

https://clinicaltrials.gov/ct2/show/NCT04370782

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources | About Site

A sensible trial

Home > Search Results > Study Record Detail

Save this study

Hydroxychloroquine and Zinc With Either A[illegible] 19 in Outpatient Setting

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04370782

Recruitment Status : Recruiting
First Posted : May 1, 2020
Last Update Posted : May 18, 2020

See Contacts and Locations

Sponsor:
St. Francis Hospital, New York

Information provided by (Responsible Party):
Avni Thakore MD, St. Francis Hospital, New York

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

Study Description

Go to

Brief Summary:
This is a randomized, open-label trial to assess the safety and efficacy of hydroxychloroquine, and zinc in combination with either azithromycin or doxycycline in a higher risk COVID-19 positive outpatient population.

– 30–

Hydroxychloroquine mogelijk wél effectief tegen corona

Gepubliceerd op: 10-10-2020

Terug naar het overzicht

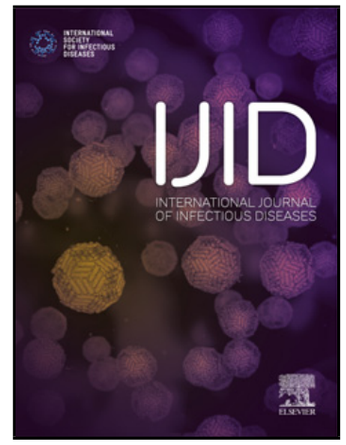
Coronavirus (COVID-19)
Hier vindt u belangrijke informatie over uw afspraak, onderzoek of behandeling.

Het antimalariamiddel hydroxychloroquine leidt bij COVID-19 patiënten op de verpleegafdeling tot significant betere resultaten dan tot dusver gedacht. De kans op overplaatsing naar de IC ligt 53 procent lager dan bij patiënten die geen behandeling kregen. Dit blijkt uit landelijk retrospectief onderzoek onder 1064 patiënten. Dr. Jolanda Lammers en dr. Paul Groeneveld, onderzoekers en internist-infectiologen in het Zwolse Isala, spreken van een verrassend resultaat.

https://www.isala.nl/nieuws/hydroxychloroquine-wel-effectief-tegen-corona/

31

Journal Pre-proof



Early Hydroxychloroquine but not Chloroquine use reduces ICU admission in COVID-19 patients

A.J.J. Lammers, R.M. Brohet, R.E.P. Theunissen, C. Koster, R. Rood, D.W.M. Verhagen, K. Brinkman, R.J. Hassing, A. Dofferhoff, R. el Moussaoui, G. Hermanides, J. Ellerbroek, N. Bokhizzou, H. Visser, M. van den Berge, H. Bax, D.F. Postma, P.H.P. Groeneveld

PII: S1201-9712(20)32175-5

DOI: https://doi.org/10.1016/j.ijid.2020.09.1460

Reference: IJID 4694

To appear in: *International Journal of Infectious Diseases*

Received Date: 1 August 2020

Revised Date: 23 September 2020

Accepted Date: 23 September 2020