



**Karolinska
Institutet**

Öppna data och registerforskning

Gustav Nilsson

2020-11-26



Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis



Mandeep R Mehra, Sapan S Desai, Frank Ruschitzka, Amit N Patel

Summary

Background Hydroxychloroquine or chloroquine, often in combination with a second-generation macrolide, are broadly and widely used for treatment of COVID-19, despite no conclusive evidence of their benefit. Although generally safe when used for approved indications such as autoimmune disease or malaria, the safety and benefit of these treatment regimens are poorly evaluated in COVID-19.

Methods We did a multinational registry analysis of the use of hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19. The registry comprised data from 671 hospitals in six continents. We included patients hospitalised between Dec 20, 2019, and April 14, 2020, with a positive laboratory finding for SARS-CoV-2. Patients who received one of the treatments of interest within 48 h of diagnosis were included in one of four treatment groups (chloroquine alone, chloroquine with a macrolide, hydroxychloroquine alone, or hydroxychloroquine with a macrolide), and patients who received none of these treatments formed the control group. Patients for whom one of the treatments of interest was initiated more than 48 h after diagnosis or while they were on mechanical ventilation, as well as patients who received remdesivir, were excluded. The main outcomes of interest were in-hospital mortality and the occurrence of de-novo ventricular arrhythmias (as defined or confirmed ventricular tachycardia or ventricular fibrillation).

Findings 96 032 patients (mean age 53·8 years, 46·3% women) with COVID-19 were hospitalised during the study period and met the inclusion criteria. Of these patients, 74 117 were in the treatment groups (1868 received chloroquine, 3783 received chloroquine with a macrolide, 3016 received hydroxychloroquine, and 6221 received hydroxychloroquine with a macrolide) and 21 915 patients were in the control group. 10 698 (11·1%) patients died in hospital. After controlling for multiple confounding factors (age, sex, race or ethnicity, body-mass index, underlying cardiovascular disease and its risk factors, diabetes, underlying lung disease, smoking, immunosuppressed condition, and baseline disease severity), when compared with mortality in the control group (9·3%), hydroxychloroquine (18·0%; hazard ratio 1·335, 95% CI 1·223–1·457), hydroxychloroquine with a macrolide (23·8%; 1·447, 1·368–1·531), chloroquine (16·4%; 1·365, 1·218–1·531), and chloroquine with a macrolide (22·2%; 1·368, 1·273–1·469) were each independently associated with an increased risk of in-hospital mortality. Compared with the control group (0·3%), hydroxychloroquine (6·5%; 2·365, 1·935–2·906), hydroxychloroquine with a macrolide (8·1%; 5·106, 4·106–5·983), chloroquine (4·3%; 1·751, 1·310–4·596), and chloroquine with a macrolide (6·5%; 4·011, 3·344–4·812) were independently associated with an increased risk of de-novo ventricular arrhythmia during hospitalisation.

Interpretation We were unable to confirm a benefit of hydroxychloroquine or chloroquine, when used alone or with a macrolide, on in-hospital outcomes for COVID-19. Each of these drug regimens was associated with decreased in-hospital mortality but with an increased frequency of ventricular arrhythmias when used for treatment of COVID-19.

Funding William M Conway Distinguished Chair in Advanced Cardiovascular Medicine at Brigham and Women's Hospital.

Published Online

May 22, 2020

[https://doi.org/10.1016/S0140-6736\(20\)31180-6](https://doi.org/10.1016/S0140-6736(20)31180-6)

S0140-6736(20)31180-6

This online publication has been corrected. The corrected version first appeared at [thelancet.com](https://www.thelancet.com) on May 29, 2020

See Online/Comment

[https://doi.org/10.1016/S0140-6736\(20\)31174-0](https://doi.org/10.1016/S0140-6736(20)31174-0)

S0140-6736(20)31174-0

Brigham and Women's Hospital Heart and Vascular Center and Harvard Medical School, Boston, MA, USA

(Prof M R Mehra MD);

Surgisphere Corporation,

Chicago, IL, USA (S S Desai MD);

University Heart Center,

University Hospital Zurich,

Zurich, Switzerland

(Prof F Ruschitzka MD);

Department of Biomedical

Engineering, University

of Utah, Salt Lake City, UT, USA

(A N Patel MD); and HCA

Research Institute, Nashville,

TN, USA (A N Patel)

Correspondence to:

Prof Mandeep R Mehra, Brigham

and Women's Hospital Heart and

Vascular Center and Harvard

Medical School, Boston,

MA 02115, USA

mmehra@bwh.harvard.edu

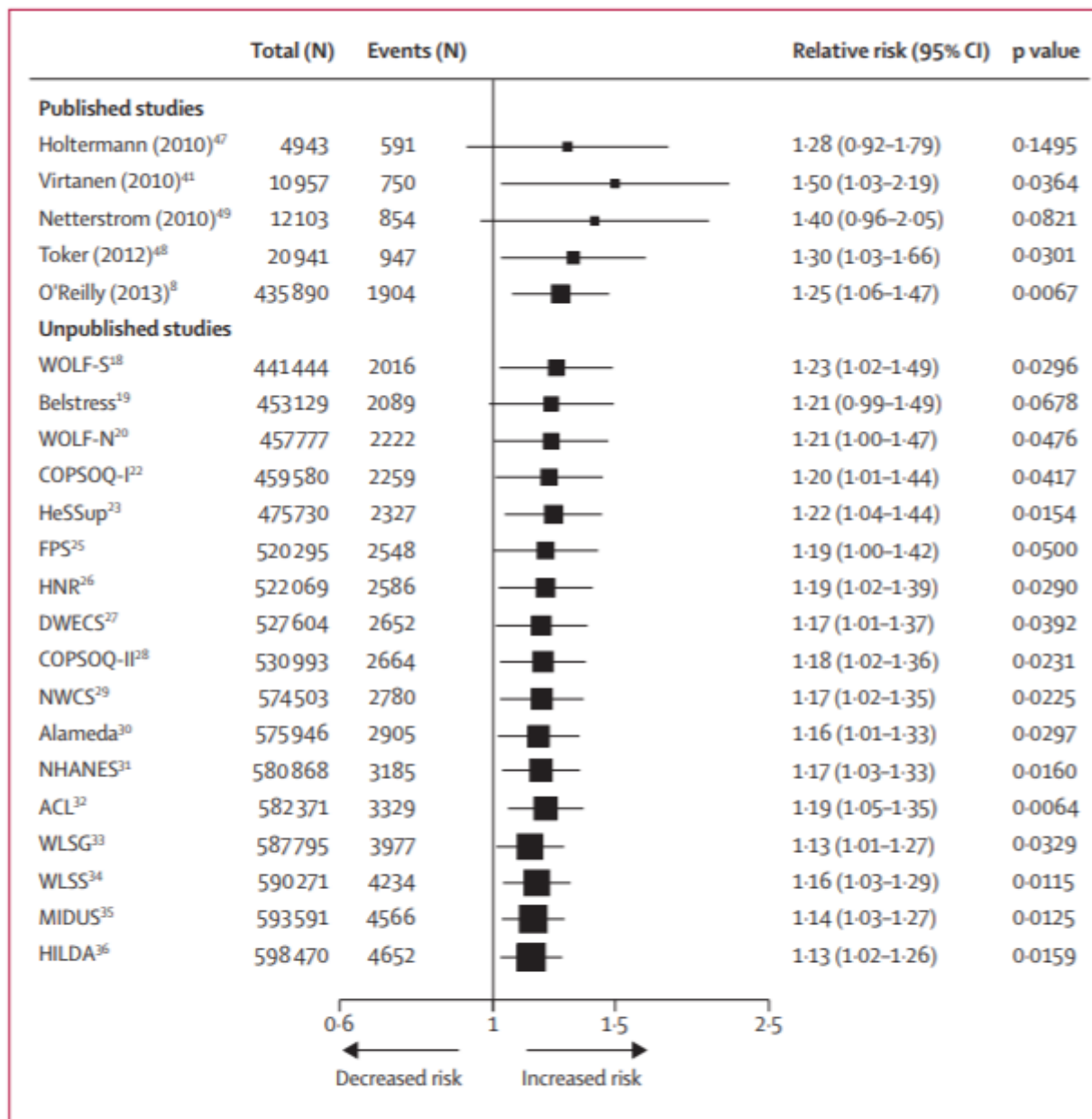
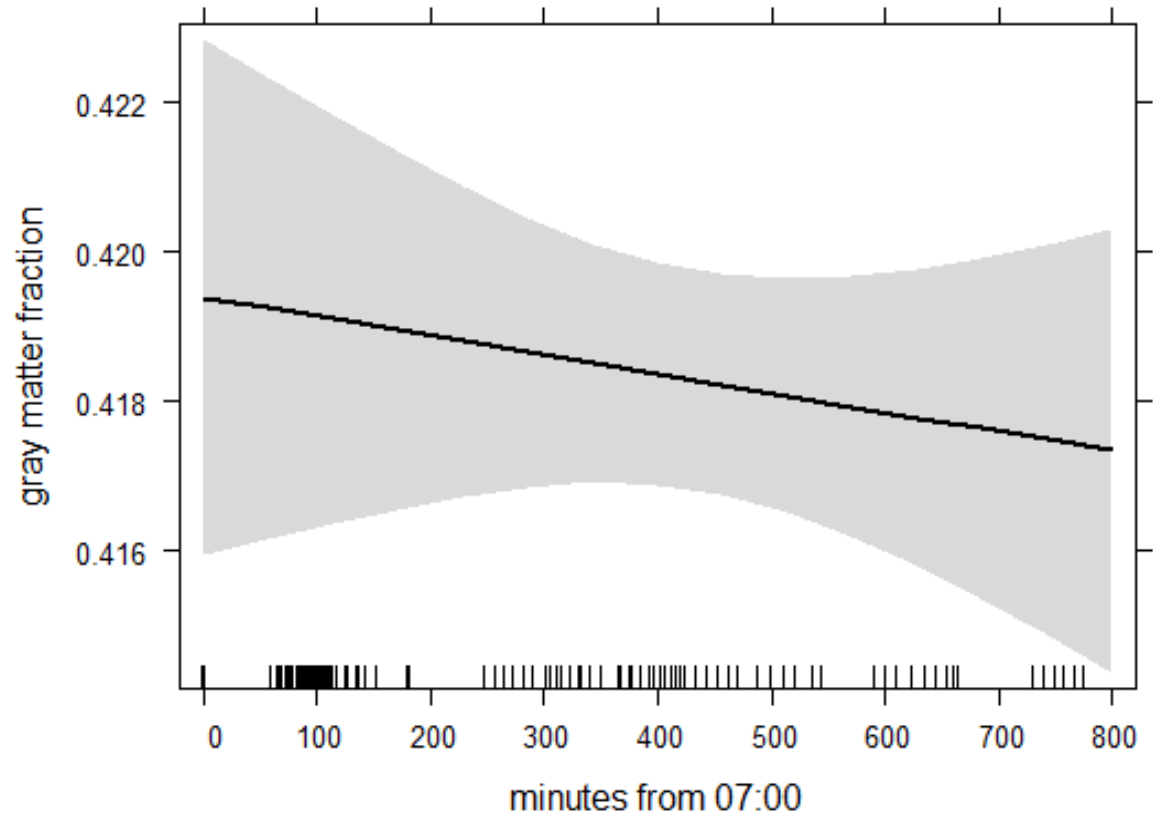


Figure 2: Cumulative meta-analysis of published and unpublished data of the association between long working hours and incident coronary heart disease

Estimates adjusted for age, sex, and socioeconomic status.

[https://doi.org/10.1016/S0140-6736\(15\)60295-1](https://doi.org/10.1016/S0140-6736(15)60295-1)

Predicted, linear model



Forskare behöver kunna:

- Verifiera att registerdata existerar
- Reproducera rapporterade resultat
- Analysera om data med olika metoder, antaganden etc
- Planera nya analyser, t.ex. antalsberäkna
- Validera nya resultat i oberoende dataset

Öppna registerforskningspraktiker

- Forskare bör rapportera exakt vilka variabler de har använt, med registrhållarens namn, så att dessa kan spåras
- Forskare bör göra egna insamlade och deriverade data tillgängliga, exempelvis genom att återföra dessa till registret
- Forskare bör använda skript till all bearbetning och analys av data, och göra koden fritt tillgänglig

Registerhållare bör

- Ansluta sitt register till ett metadataverktyg (RUT)
- Göra detaljerade metadata tillgängliga i RUT
 - Medelvärde, spridningsmått, frekvenstabeller
- Göra mikrodata på variabelnivå tillgängliga i RUT
 - Endast olänkade variabler
- Tillåta federerad analys
 - Skript in till MONA/motsvarande, resultat på gruppnivå i retur
- Lämna ut anonymiserade data utan vidare villkor
 - Efter riskbedömning

Variable Description

Name CACG1

Label Satisfied with life at present

Pre-Question Text And now a few questions about you.

Question Text At present, how satisfied are you with your LIFE? Very, somewhat, a little, or not at all?

Dataset [M3_MKE2_SURVEY_N389_20180604](#)

Value	Label	Frequency	% of valid	% of all
1	VERY	212	54.64%	54.50%
2	SOMEWHAT	141	36.34%	36.25%
3	A LITTLE	23	5.93%	5.91%
4	NOT AT ALL	12	3.09%	3.08%
7	DON'T KNOW	1		0.26%

Valid	Invalid	Min	Max
388	1	1	4

Norges nationella strategi för öppen tillgång till forskningsdata

- Brett perspektiv på behov av utveckling: beställarkompetens på lärosätena, tekniskt och administrativt stöd m.m.
- Uppdrag till Statistisk Sentralbyrå och hälsodataregister att förbättra möjligheterna att analysera data för forskning och samköra olika datakällor samt etablera och förstärka tekniska metoder och gränssnitt