OHDSI COVID-19 study-a-thon and evaluation of safety of hydroxychloroquine in RA patients

Patrick Ryan, PhD
Janssen Research and Development
Columbia University Irving Medical Center

on behalf of OHDSI community
OHDSI: a global open science community

OHDSI Collaborators:
- 2,770 users
- 25 workgroups
- 18,700 posts on 3,250 topics

OHDSI Network:
- 152 databases
- 18 countries
- approx. 600M patient records

OHDSI's Mission: To improve health by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care
OHDSI COVID-19 Study-a-thon kickoff
26Mar2020 3amEST

https://www.ohdsi.org/covid-19-updates/
<table>
<thead>
<tr>
<th>Characterization</th>
<th>Lit Review and protocol development</th>
<th>Phenotype development and evaluation</th>
<th>Study package development</th>
<th>Study execution across network</th>
<th>Clinical review and dissemination</th>
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<tbody>
<tr>
<td>COVID-19 positive patients</td>
<td>Yes</td>
<td>Yes</td>
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<td>No</td>
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<tr>
<td>COVID-19 +ve subgroup analyses</td>
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<td>Influenza, symptoms, and complications</td>
<td>Yes</td>
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<td>No</td>
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<td>Invasive treatments for respiratory distress</td>
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<td>No</td>
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<td>No</td>
<td>Yes</td>
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<tr>
<td>Prediction</td>
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<tr>
<td>1) Who presenting with flu, symptoms, or complications will be admitted to hospital?</td>
<td>Yes</td>
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<td>2) Who sent home with symptoms will progress to require hospitalization?</td>
<td>Yes</td>
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<td>Yes</td>
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## Where did we end up by 29Mar2020 7pmET?

### OHDSI COVID-19 Study-a-thon Study Tracker

<table>
<thead>
<tr>
<th>Analytic use case</th>
<th>Study</th>
<th>Lit Review and protocol development</th>
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What have we done?

In only **88** hours, we have:

- Convened **351** participants brought together from **30** countries
- Held **12** Global Huddles, **>100** collaborator calls, **>13,000** chat messages
- Engaged **15** concurrent channels
- Reviewed **>10,000** publications
- Drafted **9** protocols
- Released **13** study packages
- Designed **355** cohort definitions
- Assembled a distributed data network with **37** partners signed on to execute studies

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3 things that we did in 4 days together that nobody has ever done before

• First large-scale characterization of COVID patients in US and Asia
• First prediction model externally validated on COVID patients to support triage to ‘flatten the curve’
• Largest study ever conducted on the safety of hydroxychloroquine
Open collaboration requires FULL transparency in every step of the research process

- Study registered in ENCEPP with full protocol posted: http://www.encepp.eu/encepp/viewResource.htm?id=34498

- Phenotype definitions and analysis specifications are both human-readable and computer-executable using ATLAS against any OMOP CDM: https://atlas.ohdsi.org/#/estimation/cca/6

- Analysis source code freely available and directly downloadable: https://github.com/ohdsi-studies/Covid19EstimationHydroxychloroquine

- Manuscript posted on Medrxiv while awaiting peer-review: https://www.medrxiv.org/content/10.1101/2020.04.08.20054551v1

- All analysis results available for public exploration through interactive R shiny application: http://evidence.ohdsi.org/Covid19EstimationHydroxychloroquine
Safety of hydroxychloroquine, alone and in combination with azithromycin, in light of rapid wide-spread use for COVID-19: a multinational, network cohort and self-controlled case series study


doi: https://doi.org/10.1101/2020.04.08.20054551

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should not be used to guide clinical practice.
Methods

• New user cohort studies were conducted including 16 severe adverse events (SAEs).
• Rheumatoid arthritis patients aged 18+ and initiating hydroxychloroquine were compared to those initiating sulfasalazine and followed up over 30 days.
• Self-controlled case series (SCCS) were conducted to further establish safety in wider populations.
• Separately, SAEs associated with hydroxychloroquine - azithromycin (compared to hydroxychloroquine-amoxicillin) were studied.
• Data comprised 14 sources of claims data or electronic medical records from Germany, Japan, Netherlands, Spain, UK, and USA.
• Propensity score stratification and calibration using negative control outcomes were used to address confounding. Cox models were fitted to estimate calibrated hazard ratios (CalHRs) according to drug use.
• Estimates were pooled where $I^2 < 40\%$. 

https://www.medrxiv.org/content/10.1101/2020.04.08.20054551v1
**Key findings**

- **HCQ** appears safe in short term in RA, but long-term use may be associated with increased CV mortality.
- **HCQ+azithromycin** increases 30-day risk of heart failure and cardiovascular mortality.

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**Figure 1.** Source-specific and meta-analytic cardiovascular risk estimates for hydroxychloroquine vs sulfasalazine and azithromycin vs amoxicillin in new users during 30-day follow-up

HCQ=hydroxychloroquine; SSZ=sulfasalazine; AZM=azithromycin (plus concurrent hydroxychloroquine exposure); AMX=amoxicillin (plus concurrent hydroxychloroquine exposure); CalHR=calibrated hazard ratio; CI=confidence interval; I2=estimate heterogeneity statistic. Meta-analytic estimates reported where I2<0.4. All database-specific estimates are reported in Appendix Table S7. AmbEMR=IQVIA Ambulatory EMR; CCAE=IBM Commercial Database; CPRD=Clinical Practice Research Datalink, DAGermany=IQVIA Disease Analyzer Germany; IMRD=IQVIA UK Integrated Medical Record Data; MDCD=IBM IBM Multi-state Medicaid; MDCR=IBM Medicare Supplemental Database; OpenClaims=IQVIA Open Claims; Optum=Optum Clininformatics Datamart; PanTher=Optum PanTherapeutic Electronic Health Record; VA=Veteran’s Health Administration Database. [https://www.medrxiv.org/content/10.1101/2020.04.08.20054551v1](https://www.medrxiv.org/content/10.1101/2020.04.08.20054551v1)
**COVID-19 Patient trajectory**

- **Health pre-COVID-19**
- **Present with symptoms**
- **Tested for COVID-19**
- **Result obtained for COVID-19 test**
- **Hospitalization**
- **Hospitalization with intensive services**
- **Death**

**Data elements captured**

- **Medical history:**
  - Demographics
  - Conditions
  - Drugs
  - Health service utilization

**COVID-related questions that can be potentially answered:**

**Characterization:**
- Historical summary of presenting flu-like symptoms
- History utilization and outcomes of respiratory intensive services (ventilation, ECMO)

**Population-level Estimation:**
- Comparative safety of medicines considered for potential COVID-19 prophylaxis or treatment (HCQ, bDMARDs, protease inhibitors, antifungals, antiparasitics)
- Effectiveness of medicines on viral incidence and outcomes, using other historical models (influenza)

**Patient-level Prediction:**
- Amongst patients with flu symptoms, who requires hospitalization?
- Amongst patients hospitalized with viral pneumonia, who requires intensive services or die?

**Plus…**

- ‘recent’ health behavior measurement

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**Medical history:**
- Demographics
- Conditions
- Drugs
- Health service utilization

**Characterization:**
- Medical history and presenting symptoms amongst patients tested for COVID-19

**Population-level Estimation:**
- Does exposure increase the risk of incidence of COVID-related symptoms?

**Patient-level Prediction:**
- Amongst all patients, who received COVID-19 test?
- Amongst patients with flu-like symptoms, who received COVID-19 test?

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**Medical history:**
- Demographics
- Conditions
- Drugs
- Health service utilization

**Characterization:**
- Medical history amongst patients hospitalized for COVID-19

**Population-level Estimation:**
- Treatment utilization among patients with COVID-19

**Patient-level Prediction:**
- Amongst patients with COVID-19, who requires hospitalization?

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**Medical history:**
- Demographics
- Conditions
- Drugs
- Health service utilization

**Characterization:**
- Medical history amongst patients hospitalized for COVID-19

**Population-level Estimation:**
- Does prior drug exposure increase risk of COVID-19 hospitalization? (ACE)

**Patient-level Prediction:**
- Amongst patients with COVID-19, who requires hospitalization?

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**Medical history:**
- Demographics
- Conditions
- Drugs
- Health service utilization

**Characterization:**
- Outcomes for patients hospitalized for COVID-19

**Population-level Estimation:**
- Comparative effects of interventions on COVID-19

**Patient-level Prediction:**
- Amongst patients with COVID-19, who die?

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*Note: testing may take place anytime before symptoms through after hospitalization, or may not occur at all in COVID patients*