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:

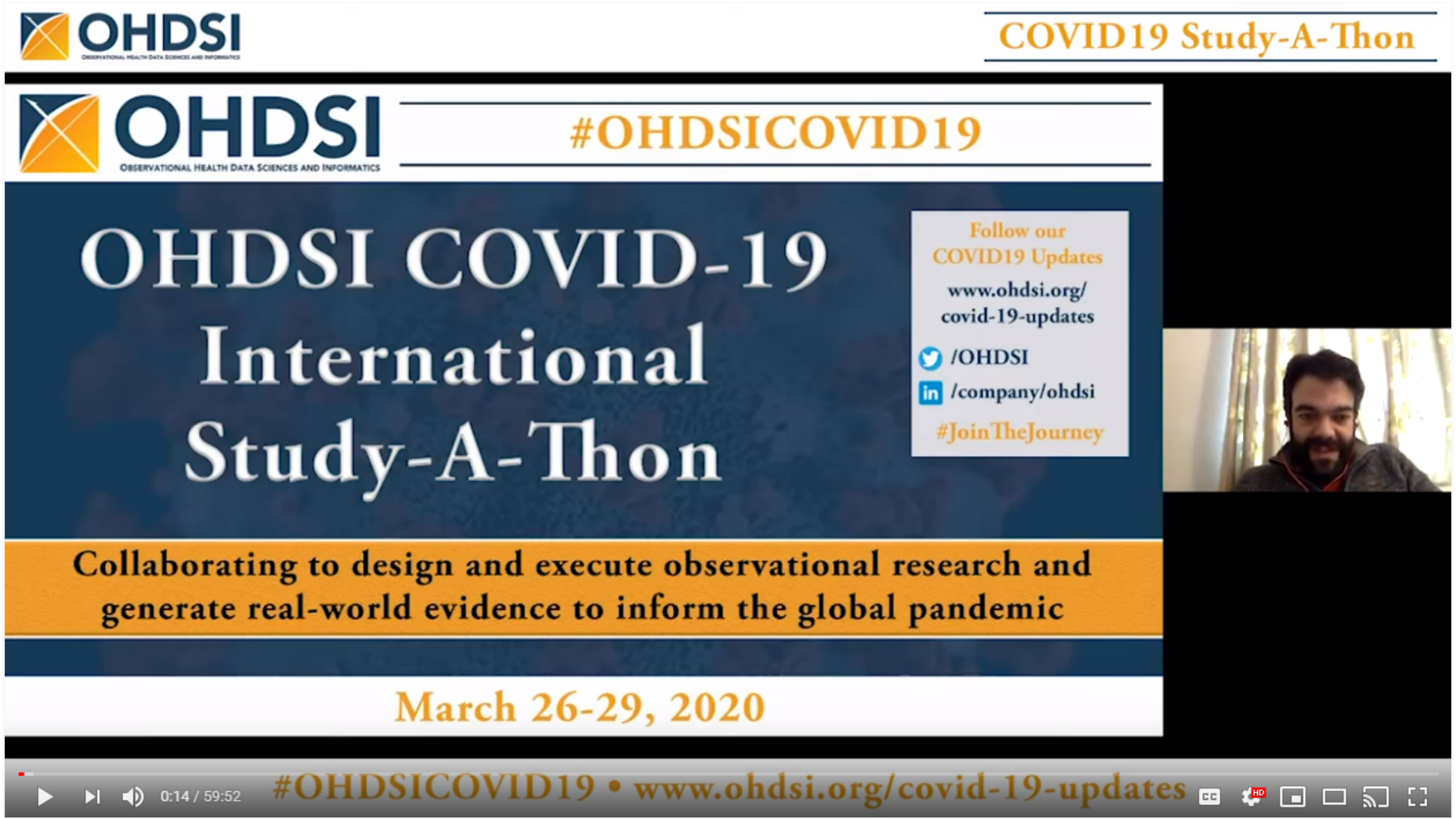
- 2,770 users
- 25 workgroups
- 18,700 posts on 3,250 topics

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/

Tracking our collaboration 26Mar2020 3amET

OHDSI COVID-19 Study-a-thon Study Tracker

Analytic use case	Study	Lit Review and protocol development	Phenotype development and evaluation	Study package development	Study execution across network	Clinical review and dissemination
Characterization						
	COVID-19 positive patients					
	COVID-19 +ve subgroup analyses					
	Influenza, symptoms, and complications					
	Invasive treatments for respiratory distress					
	other questions?					
Prediction						
	1) Who presenting with flu, symptoms, or complications will be admitted to hospital?					
	2) Who sent home with symptoms will progress to require hospitalizaton?					
	3) Who admitted to hospital will require intensive care services or die?					
	other questions?					
Estimation						
	Effects of hydroxychloroquine					
	Effects of IL6 and JAK inhibitors					
	Effects of HIV protease inhibitors					
	Effects of HepC protease inhibitors					
	Effects of ACE inhibitors					
	other questions?					

To be done
Completed

Where did we end up by 29Mar2020 7pmET?

OHDSI COVID-19 Study-a-thon Study Tracker

Analytic use case	Study	Lit Review and protocol development	Phenotype development and evaluation	Study package development	Study execution across network	Clinical review and dissemination
Characterization						
	COVID-19 positive patients					
	COVID-19 +ve subgroup analyses					
	Influenza, symptoms, and complications					
	Invasive treatments for respiratory distress					
	other questions?					
Prediction						
	1) Who presenting with flu, symptoms, or complications will be admitted to hospital?					
	2) Who sent home with symptoms will progress to require hospitalizaton?					
	3) Who admitted to hospital will require intensive care services or die?					
	other questions?					
Estimation						
	Effects of hydroxychloroquine					
	Effects of IL6 and JAK inhibitors					
	Effects of HIV protease inhibitors					
	Effects of HepC protease inhibitors					
	Effects of ACE inhibitors					
	other questions?					

To be done
In progress
Results in, more to come
Completed

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

https://www.ohdsi.org/covid-19-updates/

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

Jennifer C.E Lane, James Weaver, Kristin Kostka, Talita Duarte-Salles, Maria Tereza F. Abrahao, Heba Alghoul, Osaid Alser, Thamir M Alshammari, Patricia Biedermann, Edward Burn, Paula Casajust, Mitch Conover, Aedin C. Culhane, Alexander Davydov, Scott L. DuVall, Dmitry Dymshyts, Sergio Fernández Bertolín, Kristina Fišter, Jill Hardin, Laura Hester, George Hripcsak, Seamus Kent, Sajan Khosla, Spyros Kolovos, Christophe G. Lambert, Johan ver der Lei, Ajit A. Londhe, Kristine E. Lynch, Rupa Makadia, Andrea V. Margulis, Michael E. Matheny, Paras Mehta, Daniel R. Morales, Henry Morgan-Stewart, Mees Mosseveld, Danielle Newby, Fredrik Nyberg, Anna Ostropolets, Rae Woong Park, Albert Prats-Uribe, Gowtham A. Rao, Christian Reich, Jenna Reps, Peter Rijnbeek, Selva Muthu Kumaran Sathappan, Martijn Schuemie, Sarah Seager, Anthony Sena, Azza Shoaibi, Matthew Spotnitz, Marc A. Suchard, Joel Swerdel, Carmen Olga Torre, David Vizcaya, Haini Wen, Marcel de Wilde, Seng Chan You, Lin Zhang, Oleg Zhuk, Patrick Ryan, Daniel Prieto-Alhambra

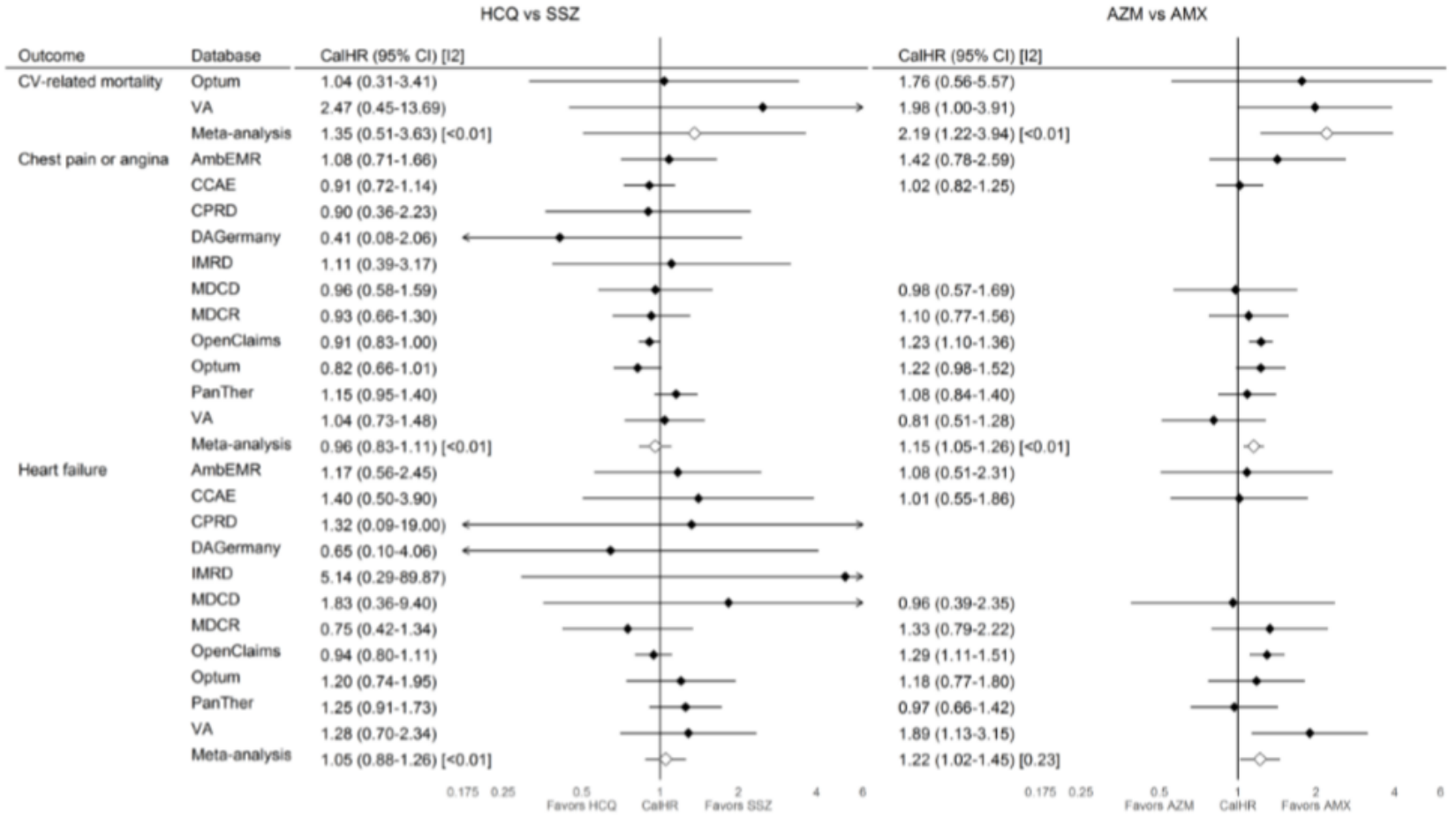
doi: https://doi.org/10.1101/2020.04.08.20054551

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

Figure 1. Source-specific and meta-analytic cardiovascular risk estimates for hydroxychloroquine vs sulfasalazine and azithromycin vs amoxicillin 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 Clinformatics Datamart; PanTher=Optum PanTherapeutic Electronic Health Record; VA=Veteran's Health Administration Database

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

*under peer review

OHDSI

OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

COVID-19 Study-A-Thon

ohdsi.org/covid-19-updates






Shabbir Syed Abdul
Aaron Abend
Tereza Abrahao
Amanda Alberga
Heba Alghoul
Muath Alser
Osaid Alser
Thamir Alshammari
Min Ho An
Alan Andryc
Miguel Angel Mayer
Katherine (Linda) Arapa
Carlos Areia
George Argyrious
Alex Asiimwe
Oliver Baclic
Charles Bailey
Juan Banda
Julio Barbour
Dave Barman
Sarah Bauermeister
Patricia Biedermann
Belay Birlie Yimer
Adam Black
Clair Blacketer
Rebecca Brown
Kate Bryan
Theresa Burkard
Wynn Burke
Edward Burn
Geert Byttebier
Martin Campodonico
Jose Manuel Cancio Trujillo
Paula Casajust
Wang Changran
Vivek Charu
Ray Chen
Ricky Chen
Jaehyeong Cho
Sylvia Cho
Young June Choe
Youn Choi
YunChang Choi
Eric Chung
Christopher Chute

Paul Coplan
Aedin Culhane
Raghava Danwada
Kourtney Davis
Alex Davydov
Maria de Ridder
Ellen de Waal
Marcel de Wilde
Rodrigo DeAntonio
Frank DeFalco
Paul-Oliver Dehaye
Sara Dempster
Freija Descamps
Nafeesa Dhalwani
Rachael DiSantostefano
Hung Do
S Dong
Iannis Drakos
Joseph Drozda
Talita Duarte Salles
Jon Duke
Scott Duvall
Dmitry Dymshyts
Noemie Elhadad
Noah Engel
John Esposito
Lee Evans
Thomas Falconer
Margarita Fernandez-Chas
Brian Fisher
Kristina Fišter
Stephen Fortin
Luca Foschini
Frank Fox
Darwin Fu
Gang Fu
Weihua Gao
Xavier Garcia Cusco
Maria Teresa Garcia Morales
Zeshan Ghory
Undina Gisladottir
Mikail Gogenur
Jose Felipe Golib Dzib
Asieh Golozar
Lisa Gonzales

Asieh Golozar
Lisa Gonzales
Artem Gorbachev
David Gotz
Anna Graber
Denis Granados
Birgitta Grundmark
Melissa Haendel
Lars Halvorsen
Jill Hardin
Rune Petring Hasselager
Oscar Hayes
Weili He
Ying (Helen) He
Yongqun Oliver He
Karin Hedenmalm
Boris Hejblum
Louis Hendriks
Ronald Herrera
Laura Hester
Na Hong
Stephanie Hong
Ji Hongxuan
Michelle Hribar
George Hripcsak
Marc Hsu
Hao Hu
Choo Hua
Nigel Hughes
(unknown) Huilin
Vojtech Huser
(unknown) Hyeong
Solomon Ioannou
Usman Iqbal
William Jang
Devasudan Jebadurai
Yuxi Jia
Yuxi Jia
Yonghua Jing
Henrik John
Beverly Johns
Kim Joohyun
Kim Jung Ae
Tae Hyun Jung
Denys Kaduk

Linda Kalilani
Michael Kallfelz
Rajesh Kamalakar
Akilah Kamaria
Prasanna Lakshmi Kandukuri
Seamus Kent
Sajan Khosla
Eanna Kiely
Chungsoo Kim
Jenny Yeon Hee Kim
Seok Kim
Yeesuk Kim
Greg Klebanov
Julianna Kohler
Spyros Kolovos
Edik Korchmar
Jan Kors
Tess Korthout
Kristin Kostka
Norbert Kremer
Steve Kundrot
Rintu Kutum
Sanggyu Kwak
K Lakshmi
Christophe Lambert
Chris Lane
Jennifer Lane
Geunhae Lee
Seongwon Lee
Alan Burton Lenarcic
Bennett Levitan
Michael Li
Asiyah Lin
George Linderman
Ying Liu
Ajit Londhe
Esteban Londono
Jim Long
Kristine Lynch
Gerardo Machnicki
R Maheswari
Rupa Makadia
Susant Mallick
Shivaji Manthena

Aniek Markus
Michael Matheny
Andrew McKinnon
James McMorran
Paras Mehta
Gong Mengchun
Swapna Menon
Evan Minty
Shazia Mitha
Maxim Moinat
Zach Moldwin
Daniel Morales
Ester Morales
Henry Morgan Stewart
Mees Mosseveld
Rajeev Nagpal
Surbhi Nagpal
Karthik Natarajan
Danielle Newby
Ryan Nguyen
Akihiko Nishimura
Fredrik Nyberg
Keith O'Rourke
Richard Ofori-Asenso
Iredia Olaye
Carmen Olga-Torres
Dr. Olwi
Anna Ostropolets
Sassan Ostvar
Helen Pai
Matvey Palchuk
Miao Panpan
Miriam Pappas
Jimyung Park
Kyoung Sik Park
Rae Woong Park
Youjin Park
S Parthiban
Pasquale Cacciatore
Alun Passey
Dony Patel
Nataly Patino
Patrick J Ryan
Eugene Paulenkovich
Melanie Philofsky

Robin Pierce
Luis Pinheiro
Tamara Polus
Jose Posada
Jelle Praet
Albert Prats-Uribe
Nicole Pratt
Daniel Prieto-Alhambra
Sanjay Purushotham
Ye Qing
Motiur Rahman
Gowtham Rao
Shilpa Ratwani
Hanieh Razzaghi
Martina Recalde
Christian Reich
Ines Reinecke
Jenna Reps
Josie Reynolds
Sang Youl Rhee
Sandy Rhie
Peter Rijnbeek
Marcela Rivera
Amy Roach
Mitra Rocca
M Rubel
Samuel Rubinstein
Stacy Russ
Patrick Ryan
Craig Sachson
Paola Saroufim
Selva Sathappan
Lisa Schilling
Judsen Schneider
Andreu Schoenenberger López
Martijn Schuemie
Sarah Seager
Tom Seinen
Anthony Sena
Alexis Sentis
unkown Seojeong
Seko Setoguchi
Michael Shamberger
Yong Shang
Jianlin Shi

Azza Shoaibi
Siddhartha Shrivastava
Anastasious Siapos
Alexander Sivura
Benjamin Skov Kaas-Hansen
Kathleen Smith
Robert Snijder
Yi Soyoung
Matthew Spotnitz
Sesh Srinivasan
Jennifer Stacey
Ty Stanford
Paul Stang
Ewout Steyerberg
Marc Suchard
Cynthia Sung
Sunkey
Marshall Sutton
Joel Swerdel
J Swetha
Ana Szarfman
Zsol Szekeres
Polina Talapova
Nick Tatonetti
Cristian Tebe Cordomi
Phyllis Thangaraj
Siva Thotapalli
Yahui Tian
Annalisa Trama
Guy Tsafnat
Adamantia Tsouchnika
Mark Samuel Tutlie
Neus Valveny
David Van Brunt
Johan van der Lei
Mui Van Zandt
Jesus Vasquez
David Vizcaya
Joshua Vogelstein
Sai Volpe
Kees von Bochove
Emma Vos
Bridget Wang
Siting Wang
Yiting Wang

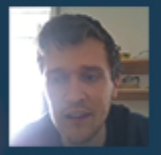
Jamie Weaver
Wu Wei
Rachel Weinstein
Haini Wen
Chunhua Weng
Thomas White
Marsha Wilcox
Andrew Williams
Ross Williams
Jennifer Wilson
Traci Wolbert
Hyunki Woo
Kristin Wrobleski
Wendi Wu
Wang Xialin
Hui Xing
Hua Xu
Cynthia Yang
Chen Yanover
Konstantin Yaroshovets
Robert Yerex
Sooyoung Yoo
Yeo Uk Yoon
Seng Chan You
Chuan Jack Li Yu
Philip Zachariah
Jakob Zeitler
Atinkut Zeleke
Dongmu Zhang
Lin Zhang
Zhenzhen Zhang
Zhihui
Lili Zhou
Yiliang Zhu
Oleg Zhuk
Jason Zucker

(other names not fully entered in registration)

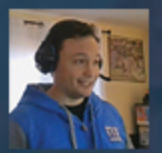
/OHDSI
/company/ohdsi

#JoinTheJourney



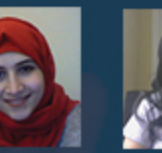
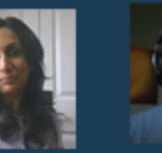



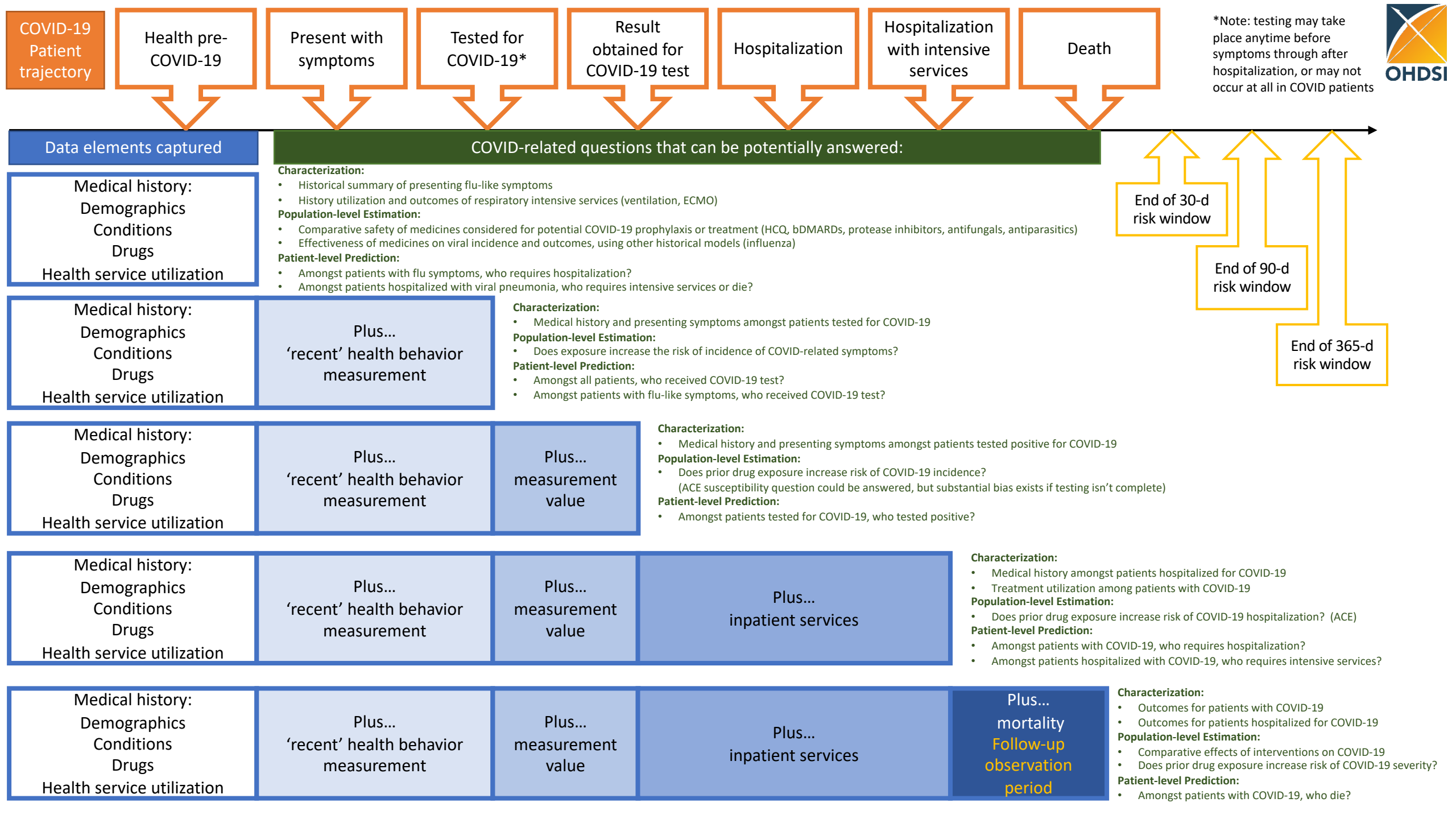








COVID-19 Patient trajectory
Health pre-COVID-19
Present with symptoms
Tested for COVID-19*
Result obtained for COVID-19 test
Hospitalization
Hospitalization with intensive services
Death
*Note: testing may take place anytime before symptoms through after hospitalization, or may not occur at all in COVID patients
OHDSI
Data elements captured
COVID-related questions that can be potentially answered:
End of 30-d risk window
End of 90-d risk window
End of 365-d risk window
Medical history:
Demographics
Conditions
Drugs
Health service utilization
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
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?
Plus…
measurement value
Characterization:
• Medical history and presenting symptoms amongst patients tested positive for COVID-19
Population-level Estimation:
• Does prior drug exposure increase risk of COVID-19 incidence?
(ACE susceptibility question could be answered, but substantial bias exists if testing isn't complete)
Patient-level Prediction:
• Amongst patients tested for COVID-19, who tested positive?
Plus…
inpatient services
Characterization:
• Medical history amongst patients hospitalized for COVID-19
• Treatment utilization among patients with 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?
• Amongst patients hospitalized with COVID-19, who requires intensive services?
Plus…
mortality
Follow-up observation period
Characterization:
• Outcomes for patients with COVID-19
• Outcomes for patients hospitalized for COVID-19
Population-level Estimation:
• Comparative effects of interventions on COVID-19
• Does prior drug exposure increase risk of COVID-19 severity?
Patient-level Prediction:
• Amongst patients with COVID-19, who die?