The Charybdis project – use of real-world data from multiple countries and opportunities for regulatory purpose

Talita Duarte-Salles
Real World Epidemiology Research Group
IDIAPJGol, Barcelona-Spain
tduarte@idiapjgol.org

AGENDA

- Why CHARYBDIS?
- Aims & Methods
- Data sources and main outputs
- Final remarks and opportunities for regulatory purpose

AGENDA

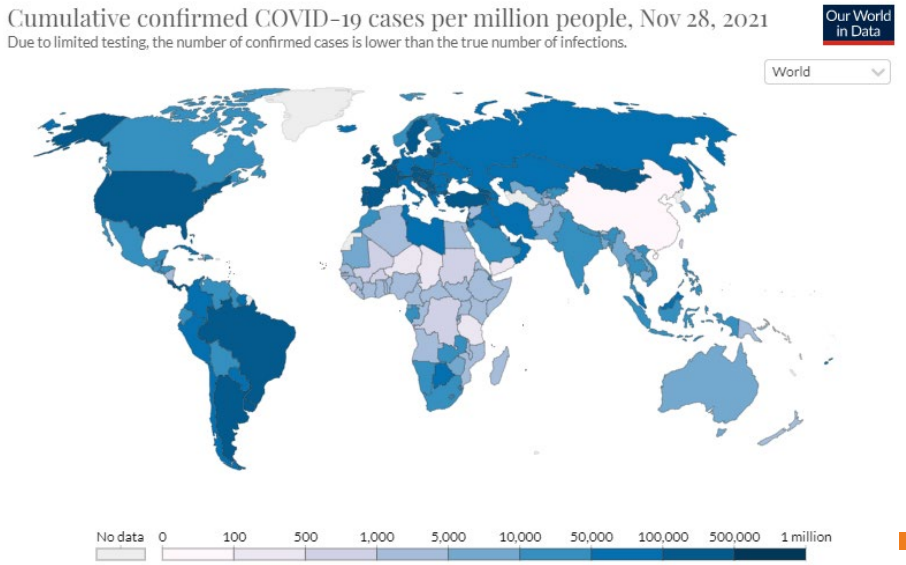
- Why CHARYBDIS?
- Aims & Methods
- Data sources and main outputs
- Final remarks and opportunities for regulatory purpose

Why CHARYBDIS?

COVID-19 -> new disease -> need to understand its natural history

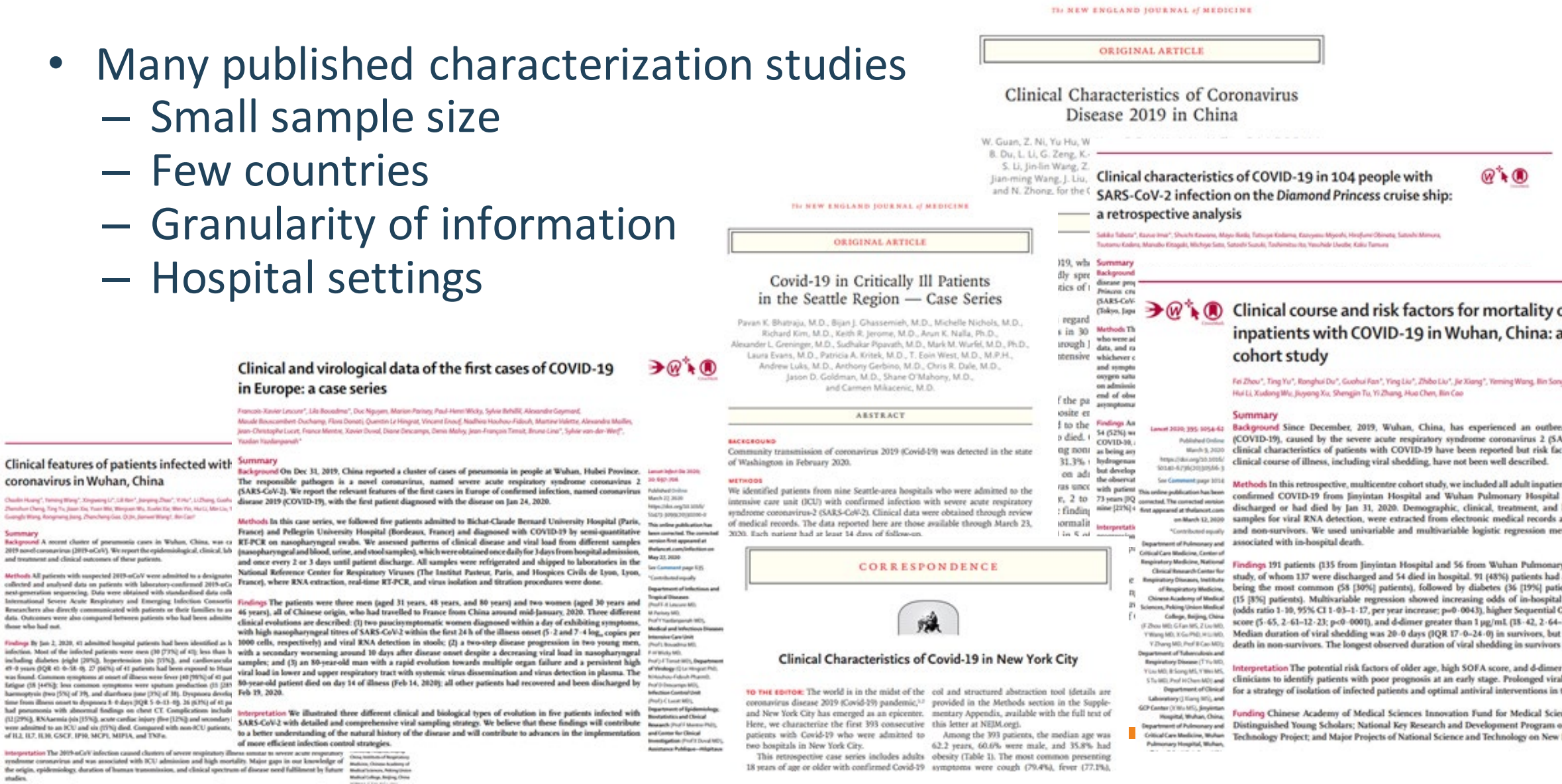
COVID-19 Patient trajectory

Presentation of symptoms	Tested for COVID-19	Tested positive or diagnosed with COVID-19	Hospitalization	Hospitalization requiring intensive services	Death



Why CHARYBDIS?

- Many published characterization studies
  - Small sample size
  - Few countries
  - Granularity of information
  - Hospital settings



Clinical and virological data of the first cases of COVID-19 in Europe: a case series

Clinical features of patients infected with coronavirus in Wuhan, China

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

Clinical characteristics of COVID-19 in 104 people with SARS-CoV-2 infection on the *Diamond Princess* cruise ship: a retrospective analysis

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Covid-19 in Critically Ill Patients in the Seattle Region — Case Series

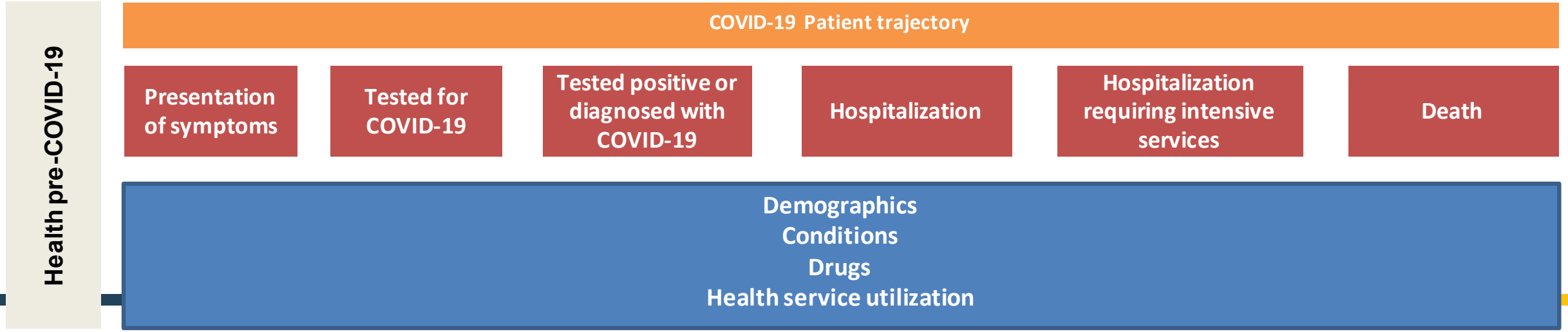
CORRESPONDENCE

Clinical Characteristics of Covid-19 in New York City

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Why CHARYBDIS?

- But many unanswered questions:
  - Who gets tested, infected and hospitalized?
    - Age and gender
    - Most frequent comorbidities
    - Treatment history
  - What are their symptoms and outcomes?
  - How different is COVID-19 from influenza?



OHDSI: a global pandemic requires a global response

OHDSI's Mission: To improve health by empowering a community to collaboratively generate the evidence that promotes better health decisions and better care

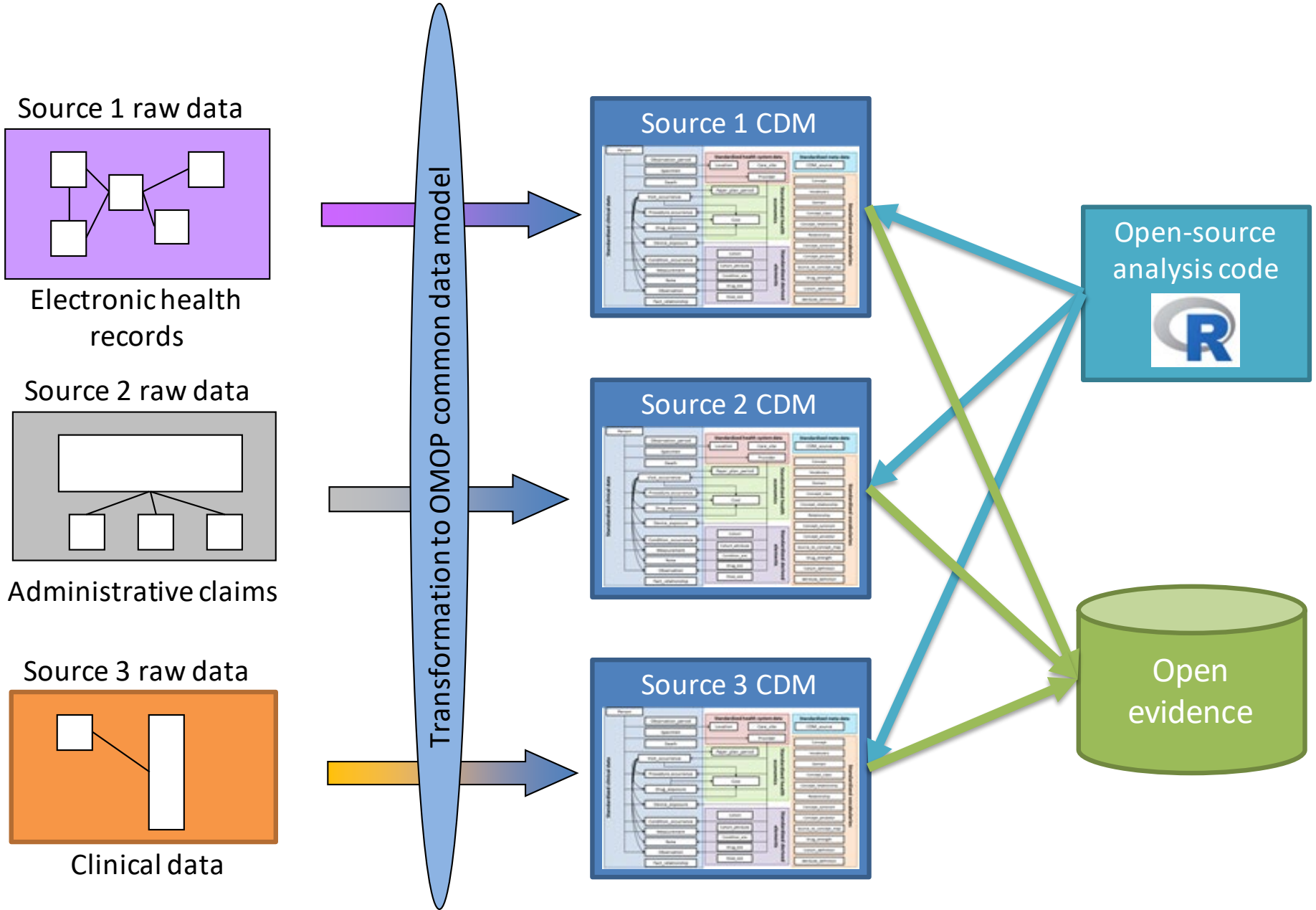
OHDSI Collaborators:

- 3,800 users
- 25 workgroups
- 152 databases
- 18 countries
- approx. 600M patient records

Stakeholders: academia, medical product industry, regulators, government, payers, technology providers, health systems, clinicians, patients

Disciplines: computer science, epidemiology, statistics, biomedical informatics, health policy, clinical sciences

Common data model to enable standardized analytics



AGENDA

- Why CHARYBDIS?
- Aims & Methods
- Data sources and main outputs
- Final remarks and opportunities for regulatory purpose

Characterizing Health Associated Risks, and Your Baseline Disease In SARS-COV-2 (CHARYBDIS)

1) Describe the baseline demographic, clinical characteristics, treatments, symptoms and outcomes of interest among individuals with COVID-19 overall and stratified by sex, age and specific comorbidities

2) Describe characteristics and outcomes of influenza patients between September 2017 and April 2018 compared to the COVID-19 population

FULL STUDY PROTOCOL AVAILABLE AT https://github.com/ohdsi-studies/Covid19CharacterizationCharybdis

CHARYBDIS – Target cohorts

COVID-19

Persons **tested** for SARS-CoV-2
Persons **tested positive** for SARS-CoV-2
Persons with a **COVID-19 diagnosis** or a SARS-CoV-2 **positive test**
Persons **hospitalized** with a COVID-19 diagnosis record or a SARS-CoV-2 positive test
Persons hospitalized and requiring **intensive services** with a COVID-19 diagnosis record or a SARS-CoV-2 positive test

Influenza

Persons with **Influenza** diagnosis or positive test 2017-2018
Persons **hospitalized with influenza** diagnosis or positive test 2017-2018
Persons hospitalized with influenza diagnosis or positive test and **requiring intensive services** 2017-2018

COHORT DEFINITIONS AVAILABLE AT:
https://atlas.ohdsi.org/

CHARYBDIS – Stratification factors

COVID-19 and…

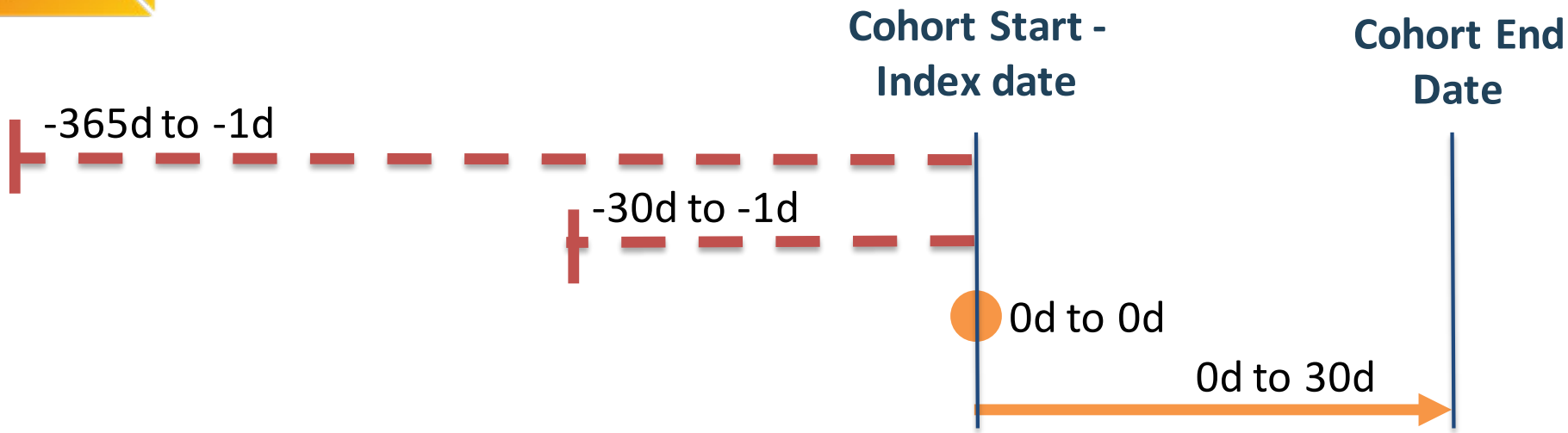
- Asthma
- Cancer
- Cardiac Outcomes
- Chronic Kidney Disease
- COPD
- Elderly
- End-Stage Renal Disease
- Gender Differences
- Heart Disease
- Hepatitis C
- HIV infection
- Hypertension
- Immune Disorders
- Obesity
- Pediatrics
- Pregnant Women
- Tuberculosis
- Type 2 Diabetes
- Dementia
- Gender

… And more!

OHDSI
Observational Health Data Sciences and Informatics

PHENOTYPE DEFINITIONS AVAILABLE AT:
https://atlas.ohdsi.org/

CHARYBDIS – Characterization framework



Pre-index characteristics:

- Sex
- Age group (5-year strata)
- Condition groups (SNOMED + descendants)
- Drug groups (ATC/RxNorm + descendants)

Index and post-index characteristics:

- Condition groups (SNOMED + descendants)
- Drug start groups (ATC/RxNorm + descendants)
- Symptoms
- Outcomes
- Procedural treatments

R package to run available at:
https://github.com/ohdsi-studies/Covid19CharacterizationCharybdis

AGENDA

- Why CHARYBDIS?
- Aims & Methods
- Data sources and main outputs
- Final remarks and opportunities for regulatory purpose

Snapshot of the CHARYBDIS Data Network

USA (13)	EUROPE (9, 6 countries)	ASIA-PACIFIC (3, 2 countries)
Columbia University (NY – EHR)	CPRD (UK – EHR)	HIRA (South Korea – Administrative Claims)
Department of Veterans Affairs (National – EHR)	IQVIA DA Germany (Germany – EHR)	DCMC (South Korea – EHR)
HealthVerity (Claims linked to diagnostic testing)	HM Hospitales (Spain – Hospital Billing)	Nanfang Hospital (China – EMR)
IQVIA Open Claims (National – Administrative Claims)	Hospital del Mar (Spain – EHR)	
IQVIA Hospital Charge Data (Hospital Billing)	IPCI (Netherlands – EHR)	
Optum EHR (National – EHR)	IQVIA LPD France (France – EHR)	
Optum SES (National – EHR linked to Socio-economic data)	IQVIA LPD Italy (Italy – EHR)	
Oregon Health 2 Sciences University (EHR)	SIDIAP (Spain – EHR)	
Premier (National – Hospital Billing)	SIDIAP-H (Spain – EHR Hospital linkage)	
Stanford University (CA – EHR)		
Tufts University (MA – EHR)		
University of Colorado Anschutz Medical Campus (CO – EHR)		
University of Washington Medicine COVID Research Dataset (WA – EHR)		

EHR = Electronic Health Records, EMR = Electronic Medical Records

As of 31Jan2021

Snapshot of the CHARYBDIS Data Network

USA (13)	EUROPE (9, 6 countries)	ASIA-PACIFIC (3, 2 countries)
Columbia University (NY – EHR)	CPRD (UK – EHR)	HIRA (South Korea – Administrative Claims)
Department of Veterans Affairs (National – EHR)	IQVIA DA Germany (Germany – EHR)	DCMC (South Korea – EHR)
HealthVerity (Claims linked to diagnostic testing)	HM Hospitales (Spain – Hospital Billing)	Nanfang Hospital (China – EMR)
IQVIA Open Claims (National – Administrative Claims)	Hospital del Mar (Spain – EHR)	
IQVIA Hospital Charge Data (Hospital Billing)	IPCI (Netherlands – EHR)	
Optum EHR (National – EHR)	IQVIA LPD France (France – EHR)	
Optum SES (National – EHR linked to Socio-economic data)	IQVIA LPD Italy (Italy – EHR)	
Oregon Health 2 Sciences University (EHR)	SIDIAP (Spain – EHR)	
Premier (National – Hospital Billing)	SIDIAP-H (Spain – EHR Hospital linkage)	
Stanford University (CA – EHR)		
Tufts University (MA – EHR)		
University of Colorado Anschutz Medical Campus (CO – EHR)		
University of Washington Medicine COVID Research Dataset (WA – EHR)		

Together, OHDSI has studied:

- **>17.2m** persons tested for SAR-COV-2
- **>4.5m** persons diagnosed or tested positive for COVID-19
- **>890k** persons hospitalized with COVID-19

EHR = Electronic Health Records, EMR = Electronic Medical Records

As of 31Jan2021

CHARYBDIS – Outputs

- >2,000 papers reviewed - literature review team
- 107 definitions of COVID-19 and conditions - phenotypes team
  - https://atlas.ohdsi.org/#/cohortdefinitions
- >100,000 variables x cohort x strata x database:
  - https://data.ohdsi.org/Covid19CharacterizationCharybdis/
- 16 scientific manuscripts
  - 7 papers published
  - 5 pre-prints to be published
  - 4 papers in preparation or recently submitted

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

CHARYBDIS – Example of findings

medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES
CSH Cold Spring Harbor Laboratory BMJ Yale

Comments (1)

Deep phenotyping of 34,128 patients hospitalised with COVID-19 and a comparison with 81,596 influenza patients in America, Europe and Asia: an international network study

Edward Burn, Seng Chan You, Anthony G. Sena, Kristin Kostka, Hamed Abedtash, Maria Tereza F. Abrahão, Amanda Alberga, Heba Alghoul, Osaid Alser, Thamir M Alshammari, Maria Aragon, Carlos Areia, Juan M. Banda, Jaehyeong Cho, Aedin C Culhane, Alexander Davydov, Frank J DeFalco, Talita Duarte-Salles, Scott DuVall, Thomas Falconer, Sergio Fernandez-Bertolin, Weihua Gao, Asieh Golozar, Jill Hardin, George Hripcsak, Vojtech Huser, Hokyun Jeon, Yonghua Jing, Chi Young Jung, Benjamin Skov Kaas-Hansen, Denys Kaduk, Seamus Kent, Yeesuk Kim, Spyros Kolovos, Jennifer C.E. Lane, Hyejin Lee, Kristine E Lynch, Rupa Makadia, Michael E. Matheny, Paras P. Mehta, Daniel R Morales, Karthik Natarajan, Fredrik Nyberg, Anna Ostropolets, Rae Woong Park, Jimyung Park, Jose D. Posada, Albert Prats-Uribe, Gowtham Rao, Christian Reich, Yeunsook Rho, Peter Rijnbeek, Lisa M. Schilling, Martijn Schuemie, Nigam H. Shah, Azza Shoaibi, Seokyoung Song, Matthew Spotnitz, Marc A. Suchard, Joel N. Swerdel, David Vizcaya, Salvatore Volpe, Haini Wen, Andrew E. Williams, Belay B. Yimer, Lin Zhang, Oleg Zhuk, Daniel Prieto-Alhambra, Patrick Ryan

doi: https://doi.org/10.1101/2020.04.22.20074336

Posted on June 28, 2020

Article | Open Access | Published: 06 October 2020

Deep phenotyping of 34,128 adult patients hospitalised with COVID-19 in an international network study

Edward Burn, Seng Chan You, [...]Patrick Ryan

Nature Communications **11**, Article number: 5009 (2020) | Cite this article

- COVID-19 is no flu
  - Healthier
  - Younger
  - Less history of medicines
  - Worse outcomes

CHARYBDIS – Example of findings

medRxiv
THE PREPRINT SERVER FOR HEALTH SCIENCES

CSH Cold Spring Harbor Laboratory BMJ Yale

Comment on this paper

Heterogeneity and temporal variation in the management of COVID-19: a multinational drug utilization study including 71,921 hospitalized patients from China, South Korea, Spain, and the United States of America

Albert Prats-Uribe, Anthony G. Sena, Lana Yin Hui Lai, Waheed-Ul-Rahman Ahmed, Heba Alghoul, Osaid Alser, Thamir M Alshammari, Carlos Areia, William Carter, Paula Casajust, Dalia Dawoud, Asieh Golozar, Jitendra Jonnagaddala, Paras P. Mehta, Mengchun Gong, Daniel R. Morales, Fredrik Nyberg, Jose D. Posada, Martina Recalde, Elena Roel, Karishma Shah, Nigam H. Shah, Lisa M. Schilling, Vignesh Subbian, David Vizcaya, Andrew Williams, Lin Zhang, Ying Zhang, Hong Zhu, Li Liu, Peter Rijnbeek, George Hripcsak, Jennifer CE Lane, Edward Burn, Christian Reich, Marc A. Suchard, Talita Duarte-Salles, Kristin Kostka, Patrick Ryan, Daniel Prieto-Alhambra

doi: https://doi.org/10.1101/2020.09.15.20195545

Posted on September 28, 2020

thebmj covid-19 Research Education News & Views Campaigr

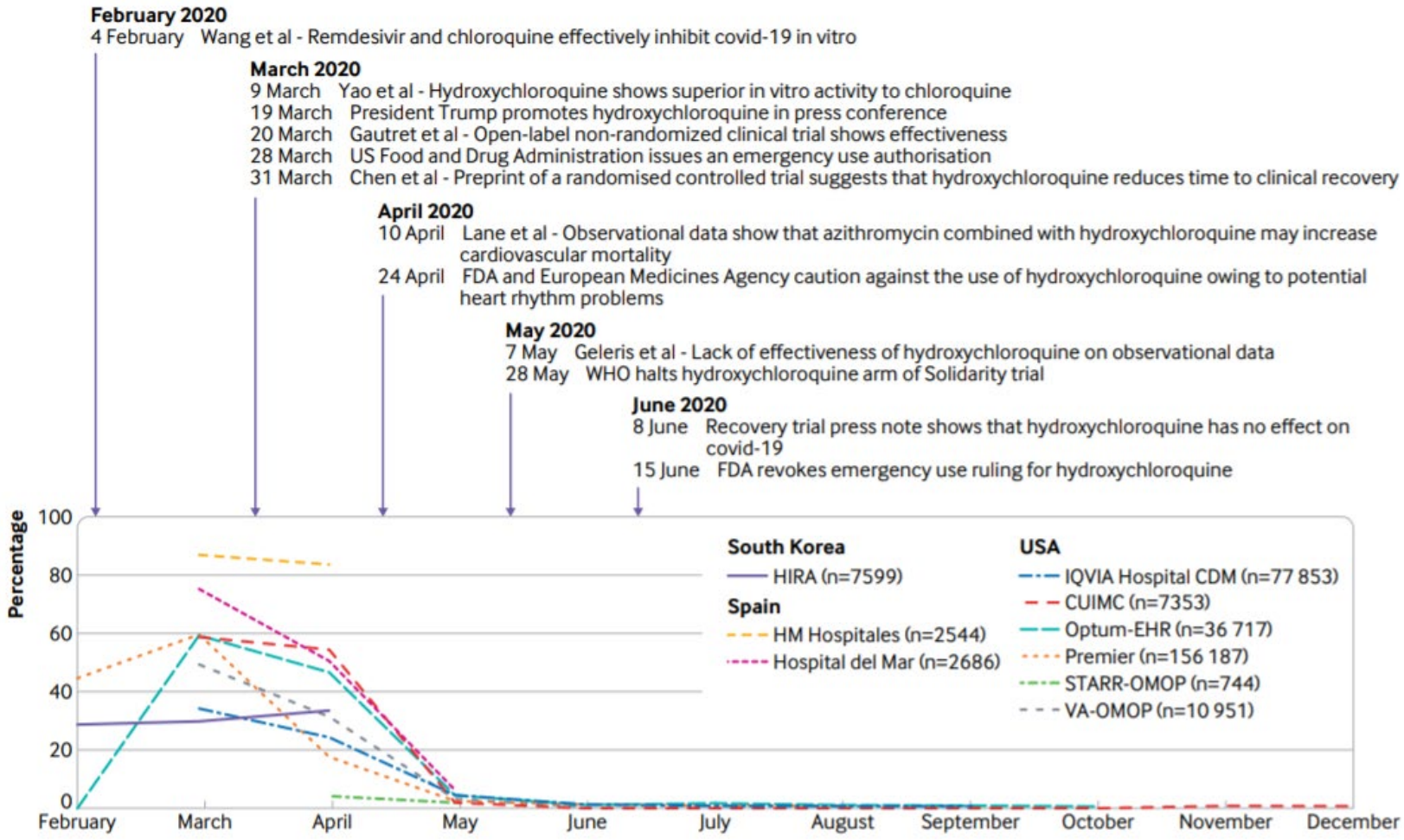
Research

Use of repurposed and adjuvant drugs in hospital patients with covid-19: multinational network cohort study

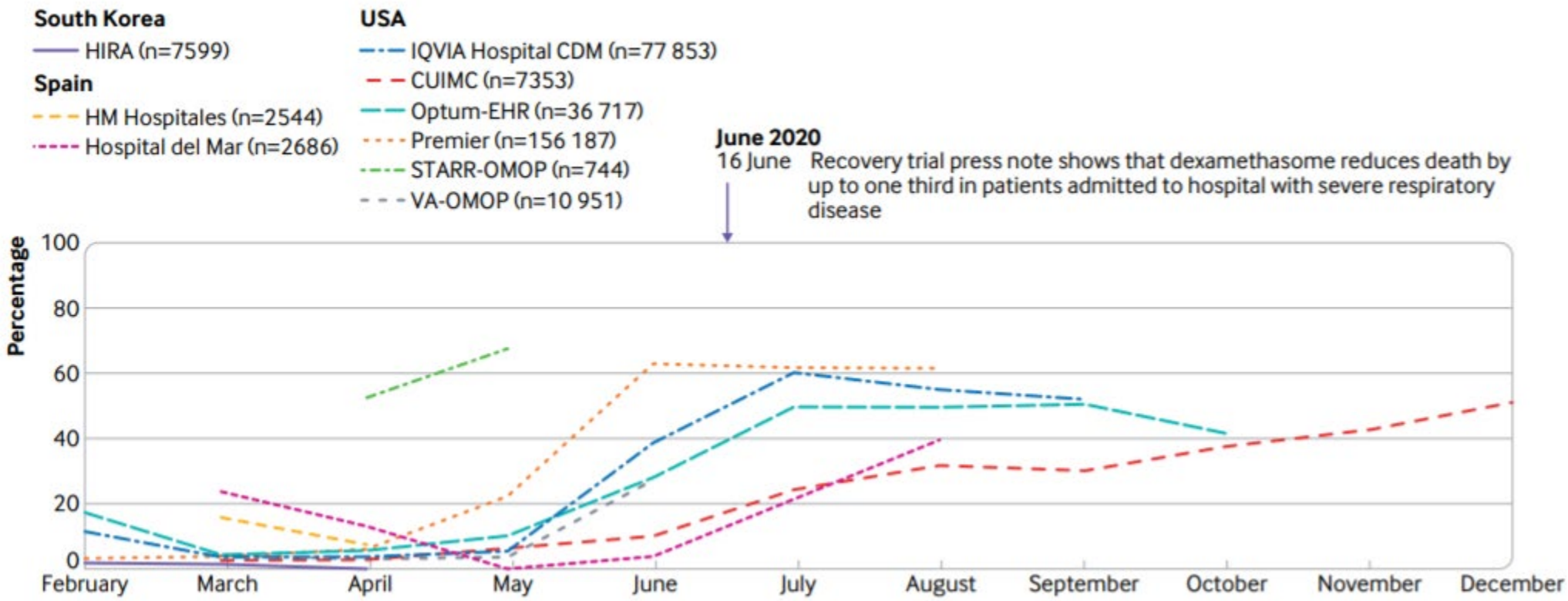
BMJ 2021 ; 373 doi: https://doi.org/10.1136/bmj.n1038 (Published 11 May 2021)
Cite this as: *BMJ* 2021;373:n1038

- Geographical and temporal variation
- Hydroxychloroquine, azithromycin, lopinavir-ritonavir, and umifenovir -> most prescribed repurposed drugs
- Antithrombotics, antibiotics, H2 receptor antagonists, and corticosteroids -> most used adjunctive treatments.

The rise and fall of drugs for COVID-19 treatment - hydroxychloroquine



The rise and fall of drugs for COVID-19 treatment - dexamethasone



AGENDA

- Why CHARYBDIS?
- Aims & Methods
- Data sources and main outputs
- Final remarks and opportunities for regulatory purpose

CHARYBDIS – Final remarks and opportunities for regulatory purpose

- Need of a global community to face a global problem
  - We were able to create the biggest COVID-19 Data Network in the world, and
  - to provide reliable and timely evidence to inform the pandemic
- Importance of leadership and international collaboration in science
  - 11 study leads, 130 co-authors, 25 data partners, hundreds of calls
- Value of the use of a common data model in RWD to provide comprehensive, valid and reliable evidence
  - Large sample size
  - Speed and quality
  - Heterogeneity of settings and data

CHARYBDIS – Final remarks and opportunities for regulatory purpose

- Open collaboration requires full transparency
  - The project was approved by local ethics committees
  - Protocol and analysis code: https://github.com/ohdsi-studies/Covid19CharacterizationCharybdis
  - Phenotype definitions: https://atlas.ohdsi.org/
  - Results (interactive R shiny application): http://data.ohdsi.org/Covid19CharacterizationCHARYBDIS/
  - Manuscripts published as pre-prints while awaiting peer-review

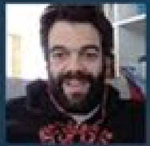
➡ Generation of reliable and reproducible evidence

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 Mayor
Katherine (Linda) Arapa
Carlos Areia
George Argyrious
Alex Asiimwe
Oliver Baclic
Charles Bailey
Juan Banda
Julie 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 Fister
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 Patring 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
Chao Hua
Nigel Hughes
(unknown) Huilin
Vojtech Huser
(unknown) Hyeong
Solomon Ioannou
Usman Iqbal
William Jang
Devasadan 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
Emma 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 Kramer
Steve Kundrot
Rintu Kutum
Sanggyu Kwak
K Lakshmi
Christophe Lambert
Chris Lane
Jennifer Lane
Geunhee 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
Mioo Panpan
Miriam Pappas
Jimyung Park
Kyoung Sik Park
Rae Woong Park
Youjin Park
S Parthiban
Pasquale Gacciatore
Alun Passey
Dony Patel
Nataly Patino
Patrick J Ryan
Eugene Pavlenkovich
Melanie Philofsky

Robin Pierce
Luis Pinheiro
Tamara Polas
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
Judson Schneider
Andreu Schoenenberger Lopez
Martijn Schuemie
Sarah Seager
Tom Seinen
Anthony Sena
Alexis Sentis
unkown Seojeong
Soko 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 Tuttle
Neus Valveny
David Van Brunt
Johan van der Lei
Mui Van Zandt
Jesus Vasquez
David Vizcaya
Joshua Vogelstein
Sal Volpe
Kees van 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
Hyeaki Woo
Kristin Wrobleski
Wendi Wu
Wang Xialin
Hui Xing
Hua Xu
Cynthia Yang
Chen Yanover
Konstantin Yaroshovets
Robert Yerex
Seoyoung Yoo
Yoo 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