



OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

#OHDSICOVID19

OHDSI COVID-19 International Study-A-Thon

Follow our
COVID19 Updates

[www.ohdsi.org/
covid-19-updates](http://www.ohdsi.org/covid-19-updates)

 /OHDSI

 /company/ohdsi

#JoinTheJourney

The meeting will begin shortly.

**Collaborating to design and execute observational research and
generate real-world evidence to inform the global pandemic**

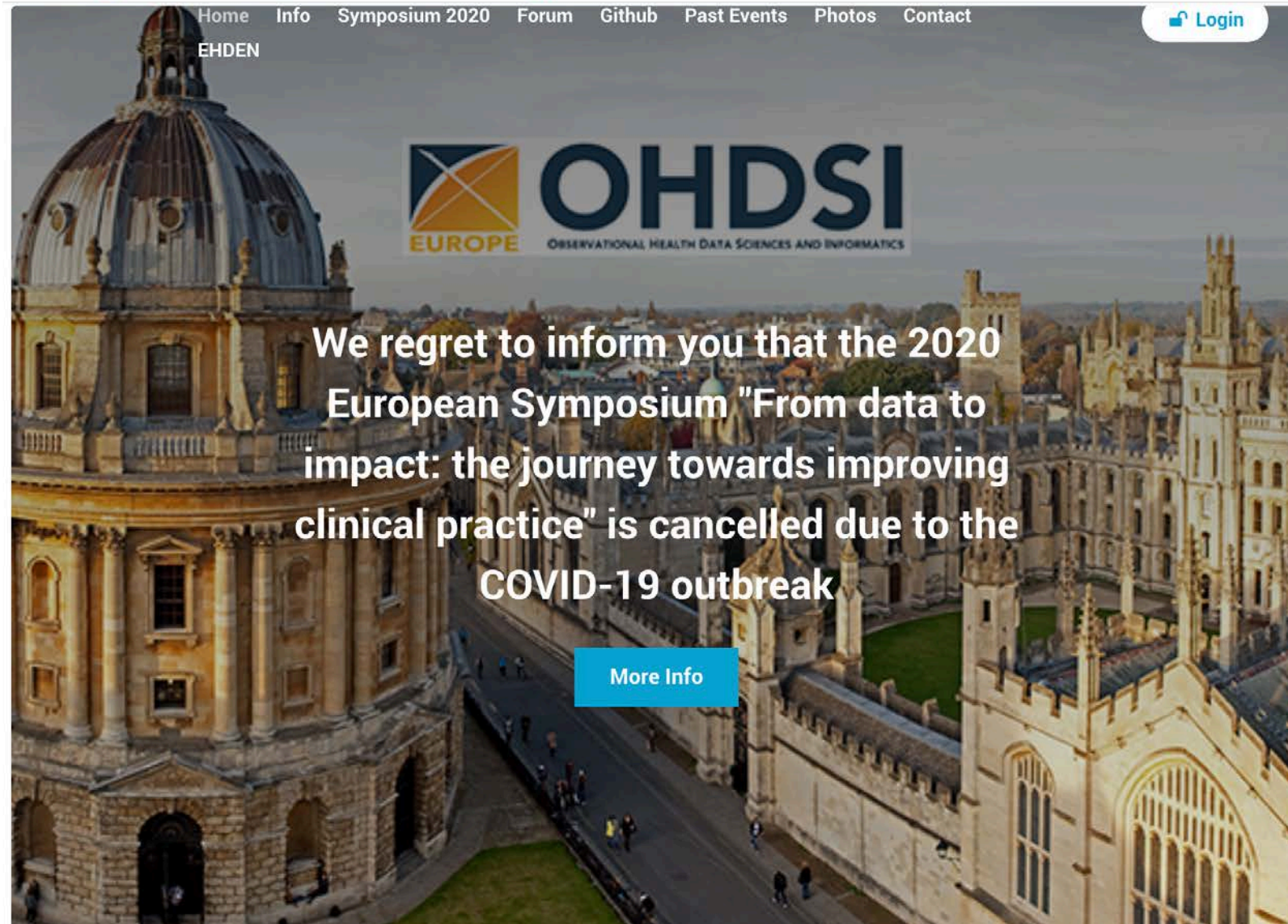
March 26-29, 2020



To improve health by
empowering a community to
collaboratively generate the
evidence that promotes better
health decisions and better care




... #flattenthecurve

The image is a screenshot of the OHDSI Europe website. The background is a photograph of a historic European city with a large domed building in the foreground and a street with people. The website's navigation bar at the top includes links for Home, Info, Symposium 2020, Forum, Github, Past Events, Photos, and Contact. A 'Login' button is in the top right corner. The OHDSI Europe logo is centered, with the text 'OHDSI' in large blue letters and 'EUROPE' in smaller yellow letters below it. A large white text block in the center of the page reads: 'We regret to inform you that the 2020 European Symposium "From data to impact: the journey towards improving clinical practice" is cancelled due to the COVID-19 outbreak'. Below this text is a blue button with the text 'More Info'.



OHDSI COVID-19 Study-a-thon kickoff

26Mar2020 3amEST

**OHDSI**
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

COVID19 Study-A-Thon

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#OHDSICovid19

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#JoinTheJourney

Collaborating to design and execute observational research and
generate real-world evidence to inform the global pandemic

March 26-29, 2020



▶ ⏮ 🔊 0:14 / 59:52 #OHDSICovid19 • www.ohdsi.org/covid-19-updates CC HD [] [] [] []



When we started on 26 March 2020



29th March 6:00pmEST



JOHNS HOPKINS
UNIVERSITY & MEDICINE

Coronavirus
Resource Center

Map Information

Map FAQ



Coronavirus COVID-19 Global Cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

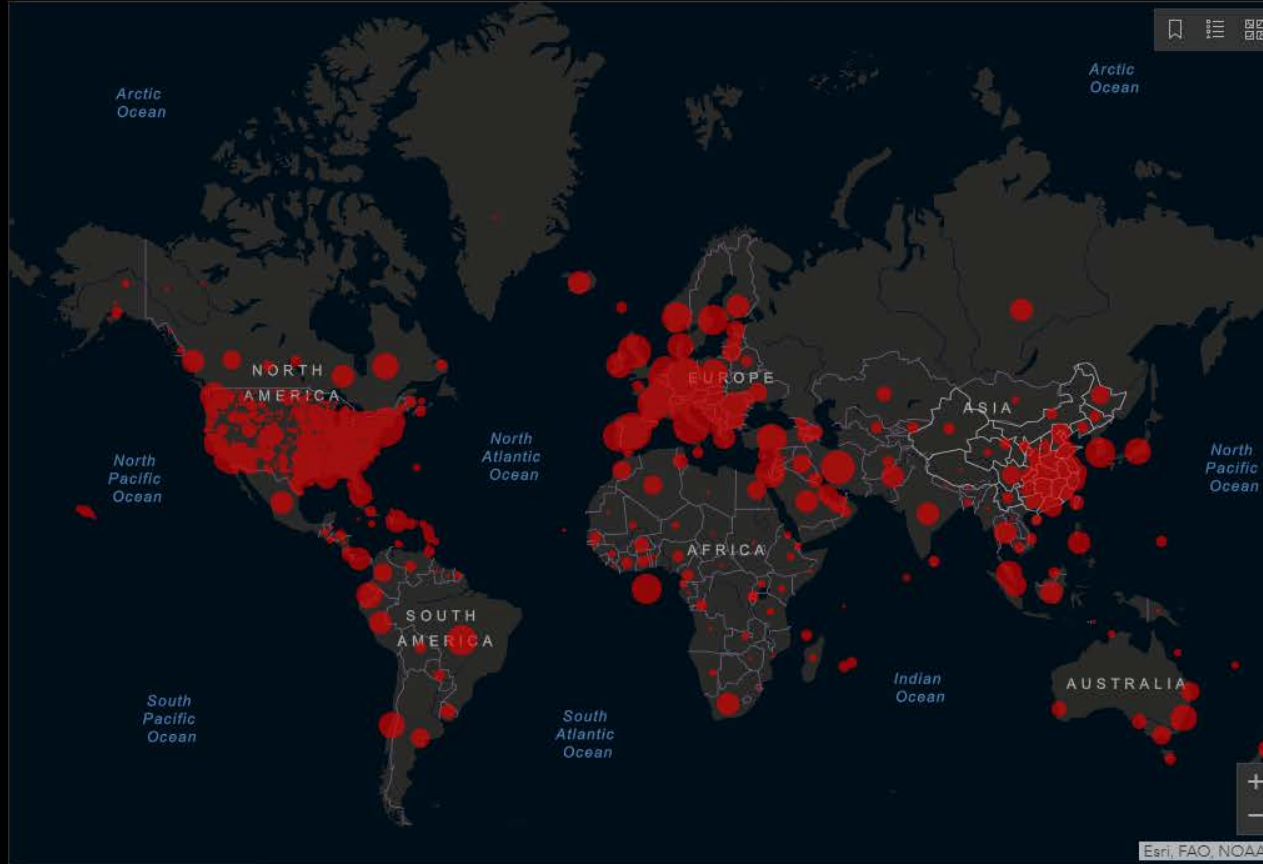


Total Confirmed

716,101

Confirmed Cases by
Country/Region/Sovereignty

137,294 US
97,689 Italy
82,122 China
80,031 Spain
62,095 Germany
40,704 France
38,309 Iran
19,772 United Kingdom
14,829 Switzerland
10,930 Netherlands
10,836 Belgium
9,583 Korea, South
9,217 Turkey
8,743 Austria
6,243 Canada
5,962 Portugal
4,268 Norway



Cumulative Confirmed Cases

Active Cases

177

countries/regions

Lancet Inf Dis Article: [Here](#). Mobile Version: [Here](#). Visualization: JHU CSSE. Automation Support: [Esri Living Atlas team](#) and JHU APL. Contact US, FAQ.
Data sources: WHO, CDC, ECDC, NHC, DXY, 1point3acres, Worldometers.info, BNO, state and national government health departments, and local media reports. Read more in this [blog](#).
Downloadable database: GitHub: [Here](#). Feature layer: [Here](#).

Total Deaths

33,854

10,779 deaths
Italy

6,802 deaths
Spain

3,182 deaths
Hubei China

2,640 deaths
Iran

2,606 deaths
France

1,228 deaths
United Kingdom

771 deaths
Netherlands

678 deaths
New York City New York US

525 deaths
Germany

Total Recovered

149,071

75,582 recovered
China

14,709 recovered
Spain

13,030 recovered
Italy

12,391 recovered
Iran

9,211 recovered
Germany

7,226 recovered
France

5,033 recovered
Korea, South

2,660 recovered
US

1,595 recovered
Switzerland



Confirmed

Logarithmic

Daily Increase

Last Updated at (M/D/YYYY)

3/29/2020, 4:56:20 PM



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 hospitalization?					
	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 are we now?

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 hospitalization?					
	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



OHDSI

OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Who We Are ▾ Latest News Standards Software Tools Methods Book of OHDSI ▾ Research Resources ▾ Join the Journey

The Journey Newsletter ▾ Past Events Upcoming Events

[Home](#) ▸ [COVID-19 Updates Page](#)

COVID-19 Updates Page

The Observational Health Data Sciences and Informatics (OHDSI) international community will host a COVID-19 virtual study-a-thon this week (March 26-29) to inform healthcare decision-making in response to the current global pandemic.

Day 4

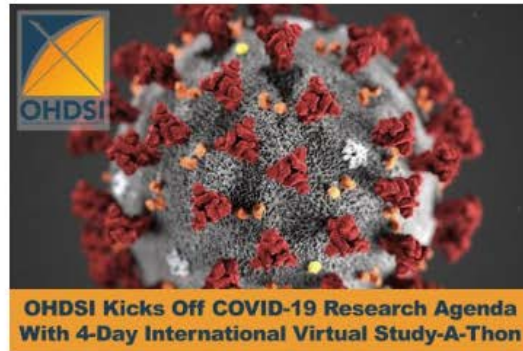
Early Call: [Video](#)

Global Call: [Video](#)

FINAL CALL: [Use This Link To Watch Live](#) (regardless of whether you registered)

Please take a look at the early calls, but we're going to save the exciting study-a-thon updates for our final call tonight! [This link will work for anybody](#), regardless of whether you registered for the study-a-thon. We are so excited to share our studies and early results with the world. Please share this link with people in your networks, so they can see the power of global collaboration in the OHDSI community.

Day 3 Updates



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 (Ed)
- First prediction model externally validated on COVID patients to support triage to 'flatten the curve' (Jenna)
- Largest study ever conducted on the safety of hydroxychloroquine (Dani)



3 things we're about to do that nobody has ever done before

- Designed self-controlled case series to examine safety of IL6 and JAK inhibitors....package is running
- Designed and implemented international study to evaluate protease inhibitors....package is running (Albert)
- Designed and implemented a study to evaluate impact of ACE inhibitor amongst Covid....need more COVID data (Daniel)



Ground rules for presentation

- We will be sharing the journey we've been on through all our studies
 - Celebrate the tremendous progress
 - Highlight the rigorous analytical methods and scientific best practices applied through the week
 - Share ***preliminary*** results, which should not be over-interpreted but provide an exciting view of the journey ahead



Collaborative literature review

Jenny Lane

University of Oxford



Pre Study-a-thon...



AIM TO SUPPORT STUDY TEAMS,
ESPECIALLY IN ESTIMATION



DMARDs



ANTIVIRALS



Systematic approach



PubMed
Embase (1974)
Clinicaltrials.gov
ICTRP
BioRxiv & medRxiv



5458 DMARD Articles
(Hydroxychloroquine/ csDMARDs
Biologics- IL6 & JAK inhibitors)

4800 Antiviral Articles
Protease Inhibitors (Lopinavir/ ritonavir)
Hep C/ H1N1 / Ebola/ Influenza



Results

Rayyan (<https://rayyan.qcri.org>) to collaboratively screen
Data extraction files (efficacy, safety, mechanism of action)
Written summaries for protocols & manuscripts
Updated searches
Chinese clinical trial registry
Clinical guidelines



bioRxiv
beta
THE PREPRINT SERVER FOR BIOLOGY

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COVID-19 SARS-CoV-2 preprints from [medRxiv](#) and [bioRxiv](#)

 **中国临床试验注册中心**
Chinese Clinical Trial Registry
世界卫生组织国际临床试验注册平台一级注册机构

Today is 2020-03-30

[Home](#) | [About ChiCTR](#) | [Trial Search](#) | [Document](#) | [Guideline of registration](#) | [Frequently Asked Questions](#) | [简体中文](#) | [English](#)



The Team & Final Products



5 continents; core team 15, 25 in total



Data scientists to clinicians



Teams -> files -> Competency Literature Review -> HCQ / IL6 / HepC Study Channel



BIG thanks to everyone!!



OHDSI Data Network in Action

Kristin Kostka

IQVIA



United Nations of OMOP (Our Global Network)

- 37 databases participating
 - Insurance claims, EHRs, Administrative data, Registries
 - 10 countries on 3 continents
- 8 databases with COVID+ patients (and growing)
- Everyone adopted OMOP CDMv5+





Executing 9 OHDSI network studies concurrently...



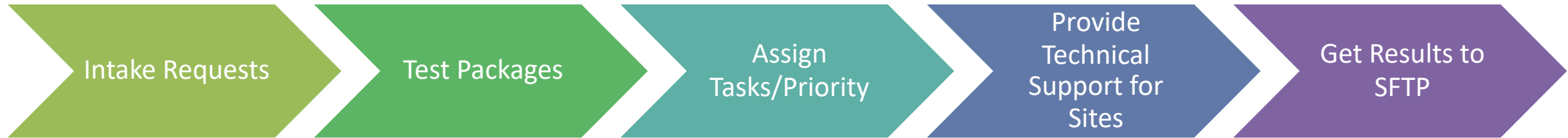
Expectation



Reality



Process for managing 9 OHDSI network studies concurrently





Mobilizing our action plan

Activity	Shiny App	Data Owners																												
		HIRA	FEEDER-NET COVID Cases (2)	Tufts CLAF	CUM	Daegu Catholic University Medical Center--	STARR-OMC	Maine Medical Center	AUSOM	KNUH	WKUH	Seoul National CDM	CCAIE (Janssen)	CCAIE (UNM)	MDCR (Janssen)	MDCR (UNM)	IPCI	IMRD	France	IGVIA DA	IGVIA DA Belgium	IGVIA DA Germany	IGVIA Hospital CDM	IGVIA US Open Claims	CPRD	JMDC	Optum DOD	Optum PANTHER	SIDIAF	Vanderbilt Synthetic Derivative
Pre Work: File Protocol with Local IRB / Go																														
Pre Work: Phenotype Evaluation																														
Cohort Diagnostics of Exposures: Covid19CohortEvalu	https://data.hirol.org/Covid19CohortEvaluationExposures/																													
Characterization Runs	TBC																													
COVID-19 positive patients	TBC																													
Run Package																														
Share Results																														
COVID-19 +ve subgroup	TBC																													
Run Package																														
Share Results																														
Influenza, symptoms and complications	TBC																													
Run Package																														
Share Results																														
Invasive treatments for respiratory distress	TBC																													
Run Package																														
Share Results																														
COVID-19 testing	TBC																													
Run Package																														
Share Results																														
Prediction Studies	-																													
Hospitalization In Sent Home Patients (Internal Validation)	-																													
Hospitalization In Sent Home Patients (External Validation)	-																													
Installing library into Rstudio																														
Check Cohort Counts																														
Run Package																														
Share Results in OHDSI SFTP																														
Results Published in Shiny App																														
Hospitalization In Symptomatic Patients (External Validation)	-																													
Installing library into Rstudio																														
Check Cohort Counts																														
Run Package																														
Share Results in OHDSI SFTP																														
Results Published in Shiny App																														
Severe In Hospitalized Patients (Internal Validation)	-																													
Severe In Hospitalized Patients (External Validation)	-																													
Installing library into Rstudio																														
Check Cohort Counts																														
Run Package																														

Thank you HIRA, AUSOM, Tufts, CUMC, Stanford, UC Denver, Vanderbilt, SIDIAP and Veteran's Affairs/VINCI!



A snapshot of our journey...

Teams

OH

OHDSI-COVID-19

General

Collaborator Introductions

Competency-Literature review

Competency-Phenotype dev...

Competency-Study execu...

Competency-Study package de...

Study-Estimation-ACE inhibi...

Study-Estimation-HepC prot...

Study-Estimation-Hydroxych...

Study-Prediction

Support-Analytics

Support-Data

Competency-Study execu...

Board

Charts

Schedule

Pre-work

Add task

Yellow

Covid19CohortEvaluation

5/6

Sergio Fernández Bertolin (G...

Red

Phenotype Evaluation

Characterization study

Add task

Red

Package that needs to be executed

0/1

Yellow

CohortDiagnostics: OHDSI-COVID-19-HospitalisationsCharacterisation

New CohortDiagnostic COVID19-Hospitalisations package available for testing (see instructions from Ed below): <https://github.com/edward-burns/OHDSI-COVID19-HospitalisationsCharacterisation>

03/29

3/16

Prediction study

Add task

Red

Q1: HospitalizationInSymptomatic

The objective of this study is to inf...

03/29

4/5

Red

Q2: Predicting which patients...

The objective of this study is to...

tduarte (Guest) 3:56 PM

IMPORTANT!

Announcement #2: Prediction validation packages for Q2 and Q3 ready

Hi again TEAM, 😊

We are very excited to announce that the packages for prediction validation of questions 2 and 3 are ready and available for you to run here:

Q2: [HospitalizationInSentiHomePatientsValidation](#)

Q3: [SevereInHospitalizedPatientsValidation](#)

If you think you can run it in your data, please assign yourself to this following task in the planner:

Q2: Predicting which patients sent home after being seen at outpatient for flu or flu-like symptoms end up in hospital 2-30 days later en Planner

Q3: [Predicting which patients admitted to hospital for pneumonia will be more severe \(e.g. require ventilator or ICU\) en Planner](#)

If you need help running this in your data, please let us know!

Please remember to share the results using the OHDSI SFTP. See instructions here: [OHDSI SFTP Guide](#)

Results for Question 2 should go in this folder: [Prediction/ValidationQ2](#)

And results for question 3 here: [Prediction/ValidationQ3](#)

Can't wait to see your results!

Search: CCAE

Entries

Subjects

983

983

7,222

7,222

26,509

26,509

26,509

26,509

97,814

97,814

97,814

97,814

69,881

69,881

69,881

69,881

186

186

9,838

9,838

9,838

9,838

12,145

12,145

12,145

12,145

12,145

12,145

New users of tocilizumab with prior rheumatoid arthritis

New users of sulfasalazine with prior rheumatoid arthritis

New users of sulfasalazine with prior rheumatoid arthritis

New users of methotrexate with prior rheumatoid arthritis

New users of methotrexate with prior rheumatoid arthritis

New users of Hydroxychloroquine with prior rheumatoid arthritis

New users of Hydroxychloroquine with prior rheumatoid arthritis

New users of Baricitinib with prior rheumatoid arthritis

New users of Baricitinib with prior rheumatoid arthritis

New users of Baricitinib with prior rheumatoid arthritis

New users of ribavirin monotherapy with prior HIV

New users of ribavirin monotherapy with prior HIV

New users of ribavirin monotherapy with prior HIV

New users of -nucleoside inhibitors with prior HIV

New users of -nucleoside inhibitors with prior HIV

New users of lopinavir monotherapy with prior HIV

New users of lopinavir monotherapy with prior HIV

Not secure | 34.207.230.121:8787/s/54bcf95944cbc851703f0/

File Edit Code View Plots Session Build Debug Profile Tools

Go to file/function

Addins

library(Covid19EstimationI16Jakinhibitors)

Optional: specify where the temporary files (used by the ff package) will be stored. If not specified, the files will be stored in the temporary directory.

dir.create(file.path(getwd(), "/tmp"), showWarnings = FALSE)

options(fftempdir = str_c(getwd(), "/tmp"))

Maximum number of cores to be used:

maxCores <- parallel::detectCores()

The folder where the study intermediate and result files will be stored.

outputFolder <- paste0(getwd(), "/Results/OpenClaims")

Details for connecting to the server:

connectionDetails <- createConnectionDetails(dbms = "redshift", server = "rwes-e360-and...")

19:49 (Top Level)

Console Terminal

~/COVID19-Estimation/COVID19EstimationI16Jakinhibitors-master/

Executing SQL took 49.8 secs

Creating negative control outcome cohorts

Executing SQL took 9.72 secs

Counting cohorts

Running CohortMethod analyses

*** Creating cohortMethodData objects ***

*** Creating study populations ***

*** Fitting shared propensity score models ***

100%

100%

100%

78%

Covid19EstimationI16

ATLAS: Concept Sets

-0.7718

0.7147

0.6315

Series: Procedure Occurrence Short Term

Covariate: procedure_occurrence during day -30 through 0 days relative to index

Chemotherapy administration, intravenous infusion technique: up to 1 hour, single or initial substance/drug

X: 1.46%

Y: 39.30%

40

20

0

0

10

20

30

40

50

60

70

80

90

100

[OHDSI] Covid19 New users of tocilizumab with prior rheumatoid arthritis

[OHDSI] Covid19 New users of sulfasalazine with prior rheumatoid arthritis

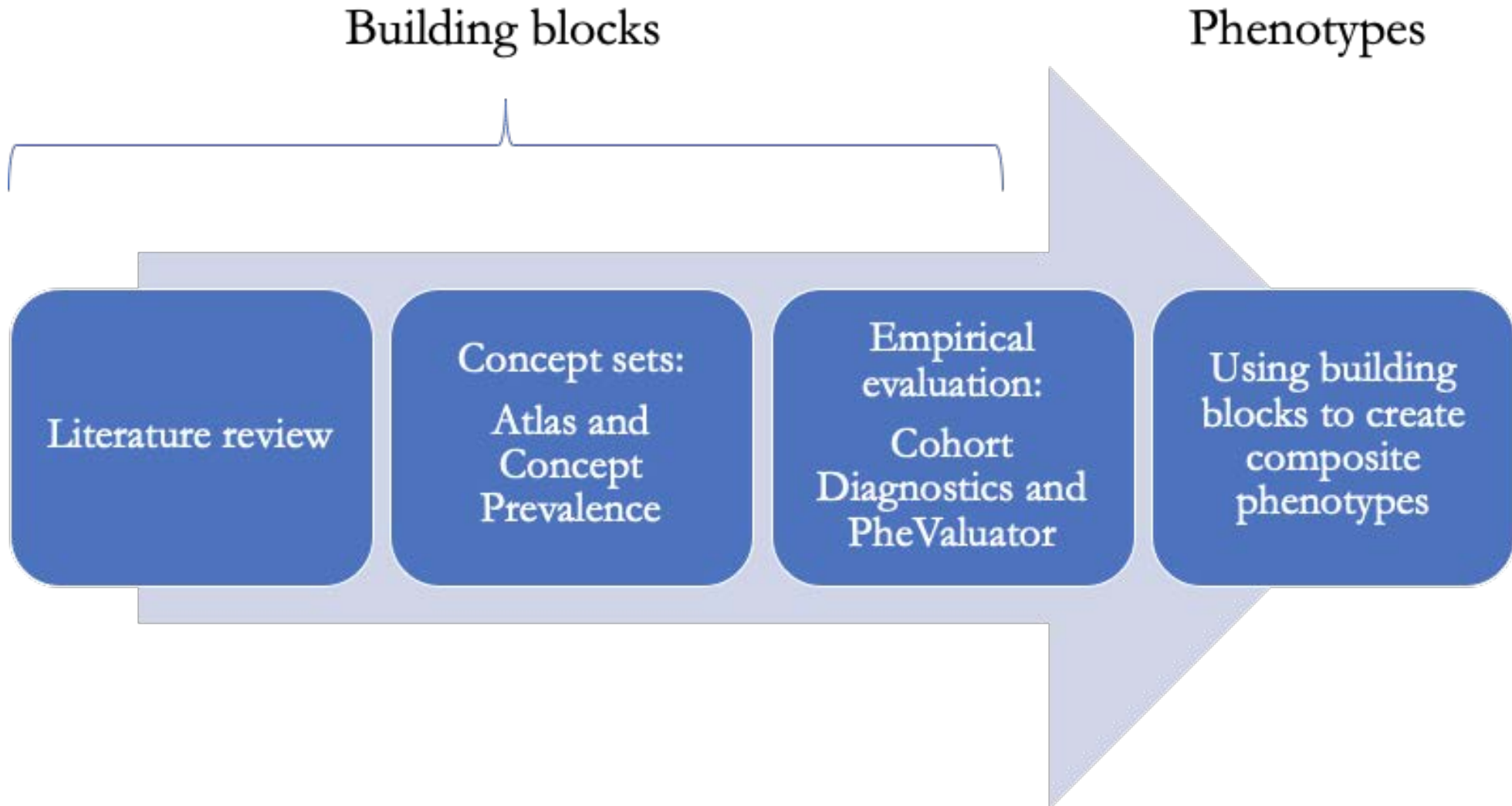


Phenotype development and evaluation

Anna Ostropolets
Columbia University



Systematic process we followed





Three lesson we learned

1. To create composite phenotypes we first have to create and validate building blocks.

Example: pneumonia is used in 29 different phenotypes.

2. Phenotypes are driven by their intended use.

Example: how to find influenza?

- Narrow: diagnosis of influenza or test result
- Broad: suspected, confirmed, symptoms (fever AND (cough OR dyspnea OR malaise OR fatigue OR myalgia))

3. Phenotypes require knowledge of the data: data exploration is a must!



Exploring the data: creating comprehensive concept sets

Sepsis

Concept Set Expression Included Concepts 208 Included Source Codes Explore Evidence Export Compare

Show 25 entries Search:

Showing 1 to 15 of 15 entries

Concept Id	Concept Code	Concept Name	Domain	Standard Concept Caption	Exclude	Descendants
37395517	1048491000000106	Acute kidney injury due to acute tubular necrosis due to sepsis	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
36716312	722278006	Acute kidney injury due to sepsis	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
132736	5758002	Bacteremia	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
40487101	447931005	Clinical sepsis	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4205449	55528005	Menosepsis	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4085627	18613002	Miscarriage with septic shock	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4204036	308887002	Postprocedural intra-abdominal sepsis	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4066124	200195002	Puerperal septicemia - delivered with postnatal complication	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
132797	91302008	Sepsis	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4029281	238150007	Sepsis syndrome	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4046106	230361008	Sepsis-associated encephalopathy	Condition	Standard	<input type="checkbox"/>	<input checked="" type="checkbox"/>

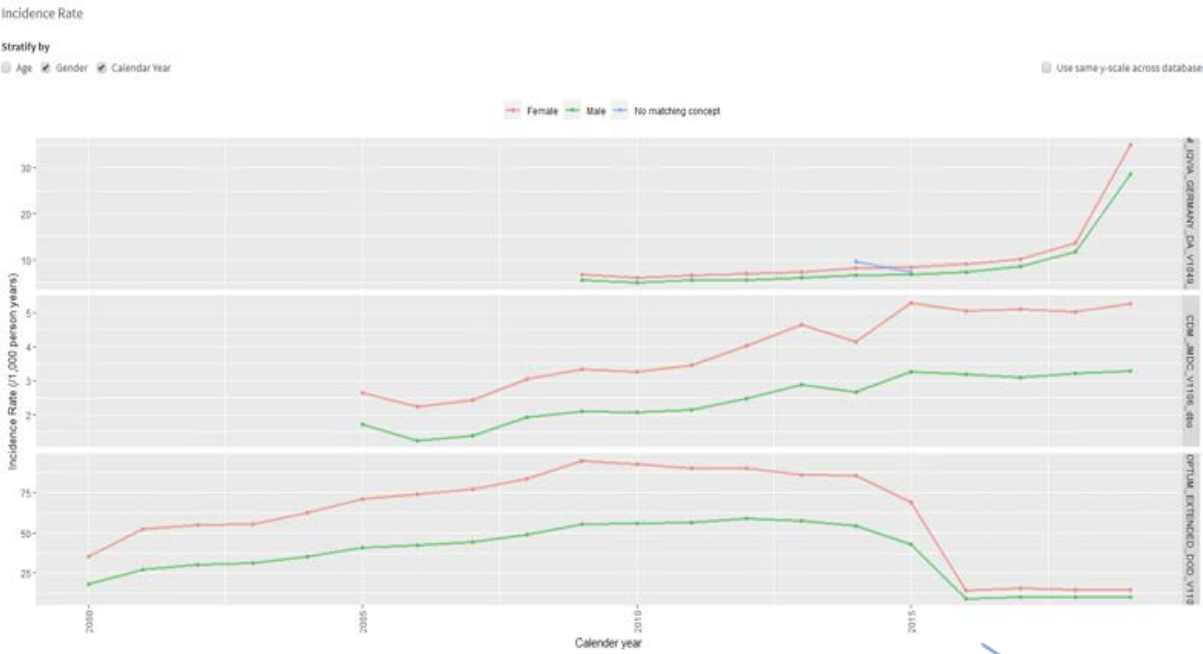
Show 25 entries

Count	Concept ID	Standard	Vocabulary	Code	Name
160,614	36712860	S	SNOMED	139201000119107	Non-infectious systemic inflammatory response syndrome without acute organ failure
160,614	45539355		ICD10CM	R65.10	Systemic inflammatory response syndrome (SIRS) of non-infectious origin without acute organ dysfunction
131,540	434821	S	SNOMED	238149007	Systemic inflammatory response syndrome
110,914	44826026		ICD9CM	995.90	Systemic inflammatory response syndrome, unspecified

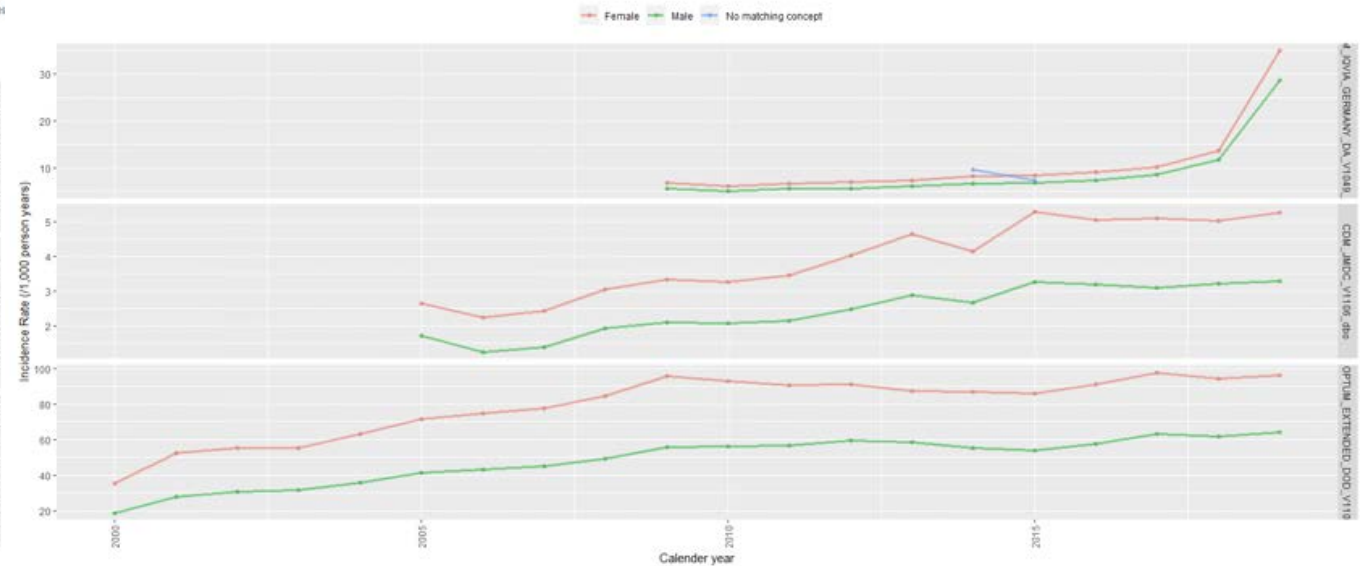


Exploring the data: capturing coding practices

Malaise



Malaise OR (malaise and fatigue)



Incidence rate dropped,
need to add fatigue



Final Results

- Literature reviews done for 36 phenotypes
- 355 cohorts created in atlas-covid19.ohdsi.org
- 114 validated and reviewed cohorts for prediction, estimation and characterization on atlas.ohdsi.org
- Results of Covid19CohortEvaluation are posted on data.ohdsi.org

Cohort #294

[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d

Definition **Concept Sets** Generation Reporting Export Messages 29

Patients with GP/OP/ER visits presenting with Covid flu or flu-like symptoms (fever AND (cough OR myalgia OR dyspnea OR malaise OR fatigue) AND no di

Cohort Entry Events

Events having any of the following criteria:

a visit occurrence of COVID19 v1 Out...

with continuous observation of at least 0 days before and 0 days after event index date
Limit initial events to: all events per person.

Restrict initial events to:
having any of the following criteria:

with at least 1 using all occurrences of:
a condition occurrence of COVID-19 (includ...

where event starts between 0 days Before and All days After index start date
✗ and event starts between All days Before and 0 days After index end date
- restrict to the same visit occurrence
- allow events from outside observation period

or with at least 1 using all occurrences of:
a condition occurrence of Any Condition

✗ Condition Source Concept is COVID-19 source...

where event starts between 0 days Before and All days After index start date
✗ and event starts between All days Before and 0 days After index end date
- restrict to the same visit occurrence
- allow events from outside observation period

or with at least 1 using all occurrences of:
a measurement of COVID-19 specifi...

where event starts between 0 days Before and All days After index start date
✗ and event starts between All days Before and 0 days After index end date
- restrict to the same visit occurrence
- allow events from outside observation period

or with at least 1 using all occurrences of:
a measurement of COVID-19 specifi...

✗ Value as Concept is: ✗ Detected ✗ Detected ✗ Positive ✗ Present ✗ Present ✗ Positive Add Import

where event starts between 0 days Before and All days After index start date
✗ and event starts between All days Before and 0 days After index end date
- restrict to the same visit occurrence
- allow events from outside observation period

or with at least 1 using all occurrences of:
an observation of COVID-19 specifi...

✗ with Value as Concept: ✗ Detected ✗ Detected ✗ Positive ✗ Positive ✗ Present ✗ Present Add Import

where event starts between 0 days Before and All days After index start date
✗ and event starts between All days Before and 0 days After index end date
- restrict to the same visit occurrence
- allow events from outside observation period

or with at least 1 using all occurrences of:
an observation of Any Observation



Next Steps

- Complete the remaining cohorts for characterization
- Finalize the CohortEvaluation package for all cohorts and run across the OHDSI network
- Write a paper about our phenotyping experience



Clinical characterization of COVID-19

Ed Burn



Background

Characterisation in OHDSI: Defining Cohorts

- A cohort is a set of persons who satisfy one or more inclusion criteria for a duration of time

[COVID ID4 v1] Persons hospitalized with COVID-19, broad, no prior observation required

Definition ⓘ Concept Sets Generation Reporting Export Messages 12

Persons hospitalized with COVID-19, age >= 18, no prior observation required, broad defined = (confirmed OR suspected associated hospitalization in prior 6 mo, and after 1Dec2019)

Cohort Entry Events

Events having any of the following criteria:

a visit occurrence of [OHDSI Covid19 v1] Inpatient...

✖ occurrence start is: After 2019-12-01



Background

Characterisation in OHDSI: Cohort characterisation

- OHDSI approaches characterization through descriptive statistics of all conditions, drug and device exposures, procedures and other clinical observations that are present in the person's history.

Using FeatureExtraction

Martijn J. Schuemie

2019-08-28

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3	Constructing covariates for a cohort of interest	5
3.1	Configuring the connection to the server	5
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Background

Characterisation in OHDSI: Incidence

Incidence rates and proportions are statistics that are used in public health to assess the occurrence of a new outcome in a population during a time-at-risk (TAR)



Figure 11.2: Person-level view of incidence calculation components. In this example, time-at-risk is defined to start one day after cohort start, and end at cohort end.



Our to do list

- Elucidating research questions
 - Writing protocols
 - Develop study packages
 - Review results
 - Disseminate results



Research questions

1. Characterizing adults hospitalized with influenza in 2009-2010 and 2014-2019, and COVID-19 in 2019-2020
2. Characterization of individuals tested for COVID-19
3. Characteristics and outcomes of COVID-19 in children



Research questions

1. Characterizing adults hospitalized with influenza in 2009-2010 and 2014-2019, and COVID-19 in 2019-2020
2. Characterization of individuals tested for COVID-19
3. Characteristics and outcomes of COVID-19 in children



Research questions

1. Characterizing adults hospitalized with influenza in 2009-2010 and 2014-2019, and COVID-19 in 2019-2020
2. Characterization of individuals tested for COVID-19
3. Characteristics and outcomes of COVID-19 in children



Protocols

Research questions



D Protocol template

1. Table of contents
2. List of abbreviations
3. Abstract
4. Amendments and Updates
5. Milestones
6. Rationale and Background
7. Study Objectives
 - Primary Hypotheses
 - Secondary Hypotheses
 - Primary Objectives
 - Secondary Objectives
8. Research methods
 - Study Design
 - Data Source(s)
 - Study population
 - Exposures
 - Outcomes
 - Covariates
9. Data Analysis Plan



Protocols

Characterization and outcomes of individuals tested for COVID-19: evidence from the OHDSI network

Characterizing adults hospitalized with influenza in 2009-2010 and 2014-2019, and COVID-19 in 2019-2020: protocol for an OHDSI network study

Protocol

Characteristics and outcomes of COVID-19 in Children in 2019-2020: evidence from the OHDSI network



Preparing study packages

edward-burn / OHDSI-COVID19-HopitalisationsCharacterisation

generated from `ohdsi-studies/emptyStudyRepository`

Unwatch 1 Star 0 Fork 3

Code Issues 3 Pull requests 0 Actions Projects 0 Wiki Security Insights Settings

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27 commits 3 branches 0 packages 1 release 3 contributors

Branch: master • [New pull request](#) [Create new file](#) [Upload files](#) [Find file](#) [Clone or download](#)

edward-burn Merge pull request #6 from edward-burn/test Latest commit 71066a7 1 hour ago

COVID Cohort Diagnostics	Update CreateCohorts.R	5 hours ago
Influenza Cohort Diagnostics	minor edits	14 hours ago
.gitignore	COVID 19 cohort diagnostics	yesterday
OHDSI-COVID19-HopitalisationsCharacterisation.Rproj	project	2 days ago
README.md	Update README.md	16 hours ago



Characteristics of adults hospitalized with influenza

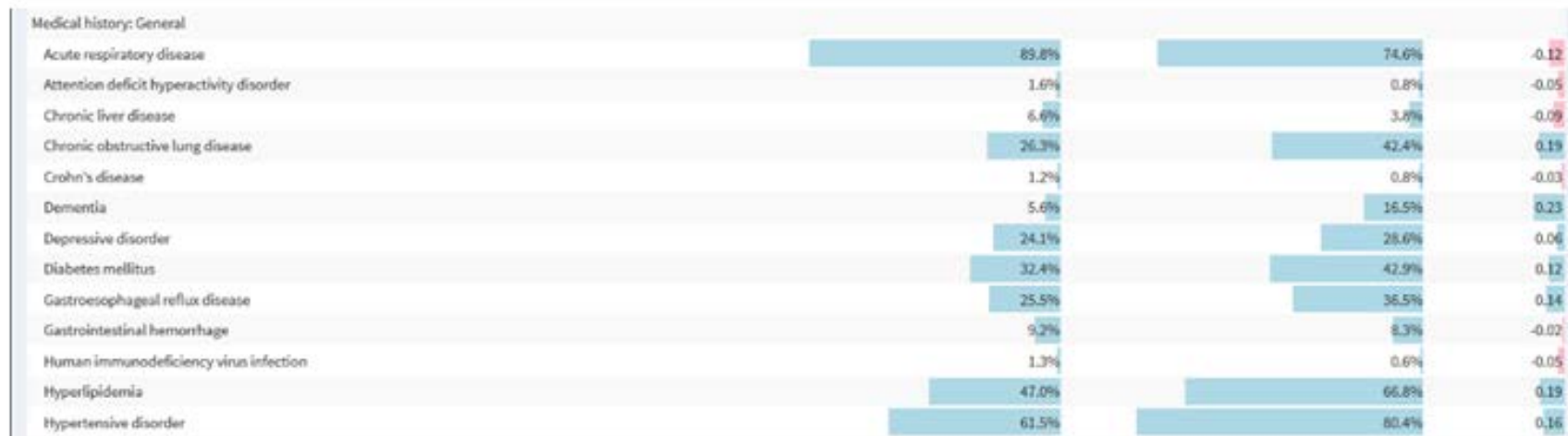
- 2009 vs 2014-2019

Characteristic	Proportion Target	Proportion Comparator	StdDiff
Age group			
15-19	1.8%	0.3%	-0.10
20-24	3.2%	0.9%	-0.11
25-29	5.0%	1.2%	-0.15
30-34	6.3%	1.6%	-0.17
35-39	6.4%	1.7%	-0.17
40-44	7.2%	1.8%	-0.18
45-49	8.5%	2.5%	-0.18
50-54	10.8%	3.7%	-0.19
55-59	9.4%	5.6%	-0.10
60-64	8.5%	7.2%	-0.03
65-69	7.3%	10.9%	0.06
70-74	6.1%	13.7%	0.17
75-79	6.3%	13.7%	0.17
80-84	10.4%	13.0%	0.05
85-89	2.7%	21.0%	0.38
90-94		1.2%	



Characteristics of adults hospitalized with influenza

- 2009 vs 2014-2019





Characteristics of adults who have tested positive for COVID-19

Characteristic	Columbia University Irving Medical Center
N	1,076
Age (median [IQR])	67
Gender: female (%)	51.2
Charlson score (median [IQR])	6
Medical history: General	
Acute respiratory disease (%)	29.6
Chronic obstructive lung disease (%)	19.7
Gastroesophageal reflux disease (%)	24.2
Hyperlipidemia (%)	41.8
Hypertensive disorder (%)	60.4
Pneumonia (%)	32.2
Renal impairment (%)	39.7
Urinary tract infectious disease (%)	15.7
Atrial fibrillation (%)	20.4
Heart disease (%)	60.7
Heart failure (%)	30.1
Malignant neoplastic disease (%)	22.2



Characteristics of adults who have tested positive for COVID-19

Characteristic	Columbia University Irving Medical Center
N	1,076
Medication use	
Anti-inflammatory and antirheumatic products (%)	33.2
Antithrombotic agents (%)	77.3
Beta blocking agents (%)	41.1
Calcium channel blockers (%)	36.3
Immunosuppressants (%)	16.1
Lipid modifying agents (%)	46.5



Our to do list

- Elucidating research questions
 - Writing protocols
 - Develop study packages
 - Review results
 - Disseminate results

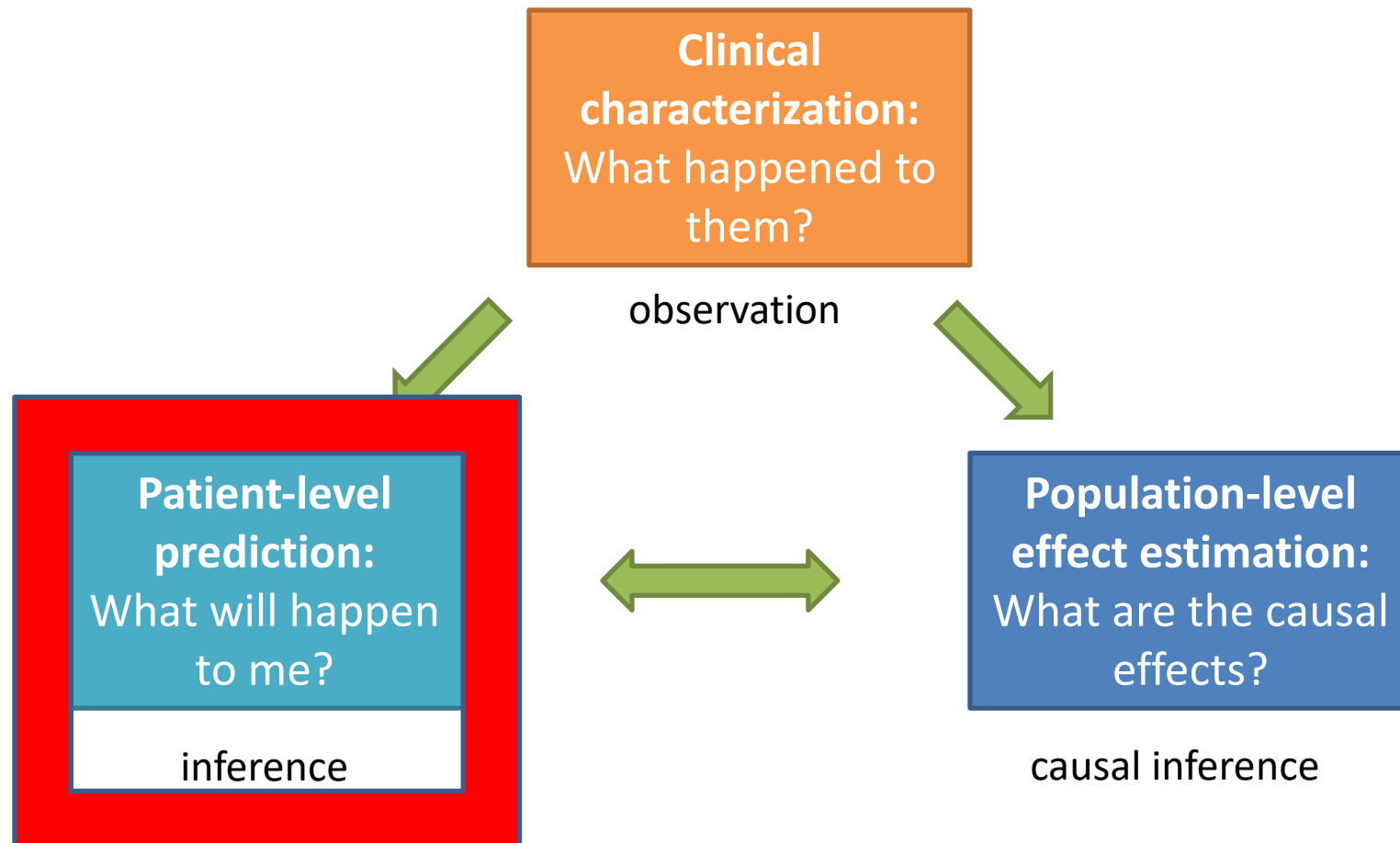


The journey through patient-level prediction

Peter Rijnbeek
Erasmus MC

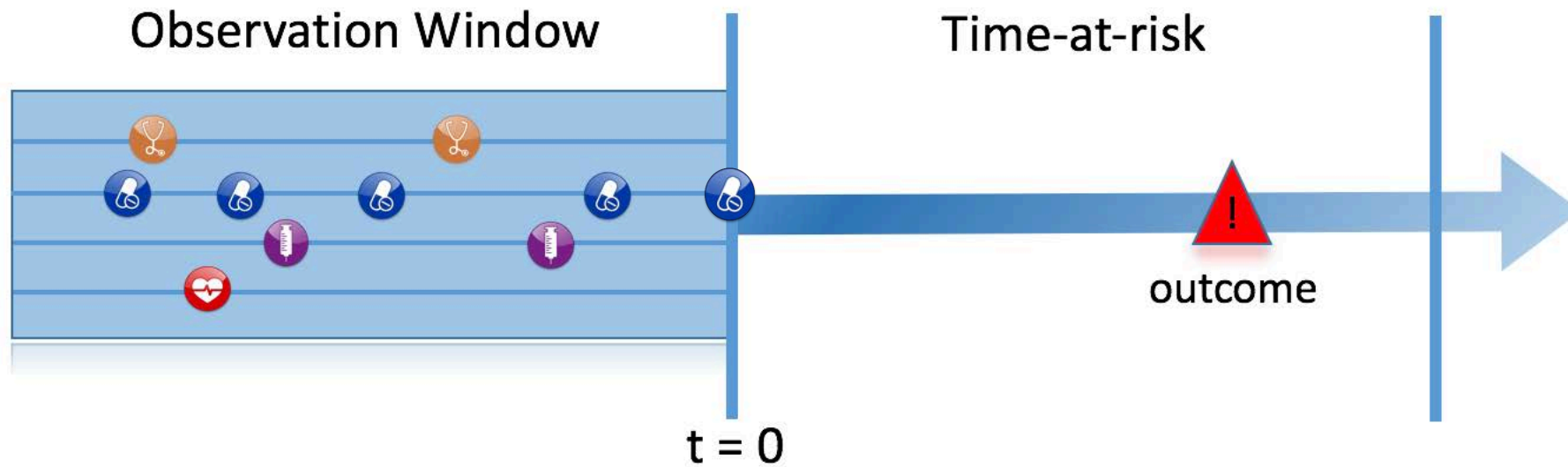


Complementary evidence to inform the patient journey





Prediction Problem Definition



Among a target population (T), we aim to predict which patients at a defined moment in time ($t=0$) will experience some outcome (O) during a time-at-risk. Prediction is done using only information about the patients in an observation window prior to that moment in time.



Important questions to ask!

- What decision is the prediction model intended to inform?
- When is the decision made in the context of the patient's health experience and interaction with the healthcare system?
- Who is the decision-maker, and from which stakeholder vantage point are we evaluating the decision?
- What is the trade-off between True Positive, False Positive, True Negative, False Negative?
- Etc.



OHDSI Mission for Patient-Level Prediction

OHDSI aims to develop a systematic process to learn and evaluate large-scale patient-level prediction models using observational health data in a data network





OHDSI's Patient-Level Prediction Framework



Design and implementation of a standardized framework to generate and evaluate patient-level prediction models using observational healthcare data

Jenna M Reps , Martijn J Schuemie, Marc A Suchard, Patrick B Ryan, Peter R Rijnbeek

Journal of the American Medical Informatics Association, Volume 25, Issue 8, August 2018, Pages 969–975, <https://doi.org/10.1093/jamia/ocy032>

Published: 27 April 2018 **Article history** ▼

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Abstract

Objective

To develop a conceptual prediction model framework containing standardized steps and describe the corresponding open-source software developed to consistently implement the framework across computational environments and observational healthcare databases to enable model sharing and reproducibility.

R-package

www.github.com/OHDSI/PatientLevelPrediction

- Vignettes
- Videos
- Online training material

Book-of-OHDSI

<https://ohdsi.github.io/TheBookOfOhdsi/>

Study Results

www.data.ohdsi.org

The prediction chapter and the publication are added on top of our channel in Teams



The Journey: Problem Definition



Problem pre-specification. A study protocol should unambiguously pre-specify the planned analyses.

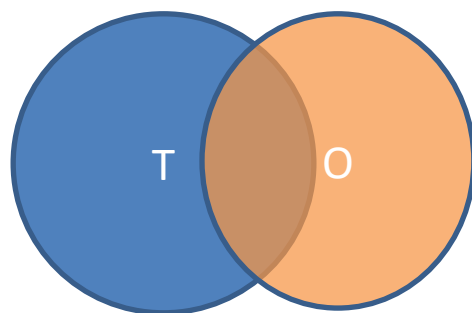
Transparency. Others should be able to reproduce a study in every detail using the provided information. All analysis code should be made available as open source on the OHDSI Github.

Team Effort:

- Problem Definition + Questions
- Literature Research -> Prior work, Rationale
- Study Protocol Development



The Journey: Data Extraction



We extract data for the patients in the Target Cohort (T) and we select all patients that experience the outcome (O)

The Target Cohort (T) and Outcome Cohort (O) can be defined using ATLAS or custom code (see later today).

For model development all outcomes (O) of patients in the Target Cohort (T) are used.

Team Effort:

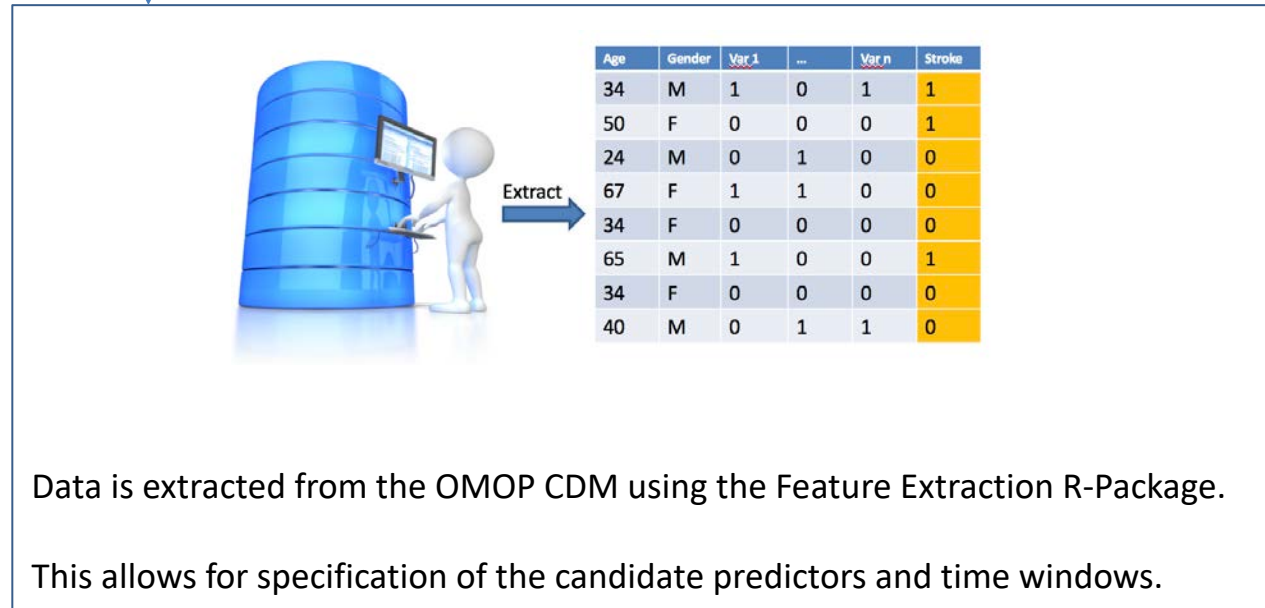
- Literature Review
- Cohort Definition



Work done with the phenotype group



The Journey: Model Development



Team effort:
Cohort Diagnostics
Package



Work done with
other channels



The Journey: Model Development



Model training and **Internal validation** is done using a train test split:

1. Person split: examples are assigned randomly to the train or test set, or
2. Time split: a split is made at a moment in time (temporal validation)



2014-01-15

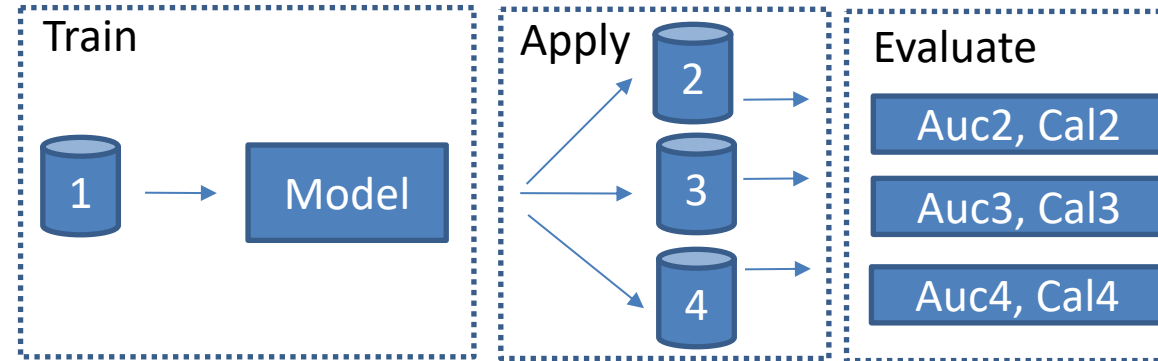
- Study Package Development
- Study Execution



The Journey: External Validation



External validation is performed using data from multiple populations not used for training.



- Data Partners



The Journey: Dissemination



Dissemination of study results should follow the minimum requirements as stated in the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement ¹.

- Internal and external validation
- Sharing of full model details
- Sharing of all analyses code to allow full reproducibility



Website to share protocol, code, models and results for all databases



PLP Aims Study-A-Thon

Build and evaluate models developed on Flu patients to:

- 1) Test them on COVID patients if data becomes available
- 2) Have tools ready to learn on COVID patients

And,

Replicate some of the models found in literature



Team Effort

51 Participants in our channel and literature study



Thank you all for the great collaboration in the PLP team



Patient-level prediction #1:
Amongst patients presenting with COVID-19, influenza, or associated symptoms, who are most likely to be admitted to hospital in next 30d?

Jenna Reps
Janssen Research and Development



Background

- Can we predict who is going to be hospitalized at the point they have their first outpatient visit with flu/covid19 or flu-like symptoms?
- This could be used to aid the '**do I hospitalize or send this patient home?**' decision that doctors will need to make
- Simple model could potentially be used for phone screen (patient calls medical staff and model answers questions)



Methods

T1: GP/OP/ER visits of patients presenting with Covid-19, flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d

O1: Hospitalizations with pneumonia (**narrow**)

O2: Hospitalizations with pneumonia or ARDS or sepsis or AKI (**broad**)

O3: Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services or resulting in death in 30d (**severe**)

O4: Death (**severe**)

TAR: 0-30d



Preliminary results

Analysis	Dev	Val	T	O	Model	TAR start	TAR end	AUC	AUPRC	T Size	O Count	O Incidence (%)
Analysis_2	optumDod	optumDod	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.8721	0.3542	37500	2617	6.9787
Analysis_6	optumDod	optumDod	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.8387	0.2625	37499	2616	6.9762
Analysis_2	optumDod	ccae	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.7876	0.1358	3146729	53842	1.711
Analysis_2	optumDod	HIRA	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.74	0.082	6011	165	2.745
Analysis_2	optumDod	ipci	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.76241	0.00585	27610	36	0.13039
Analysis_2	optumDod	jmdc	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.679683	0.006628	1276478	1011	0.079202
Analysis_2	optumDod	mdcd	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.819	0.307	536410	53319	9.94
Analysis_2	optumDod	mdcr	[COVID ID13 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms AND no symptoms or pneumonia in prior 60d	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	0	30	0.709	0.351	248964	48170	19.348



Discussion and next steps

- Made a simple score model: 7 variables + age + gender model - shiny: <https://data.ohdsi.org/Covid19PredictionSimpleHospitalizationModel/>
 - External validation of OHDSI score model
 - External validation existing risk models
-



Patient-level prediction #2:
Amongst patients at GP presenting with
virus or associated symptoms
with/without pneumonia who are sent
home, who are most likely to require
hospitalization in next 30d?

Ross D. Williams
Erasmus MC



Background

A large proportion of patients presenting with symptoms will be sent home

Some of these patients will go on to experience disease progression

This model can act as a safety net for a clinician and reassurance for patient.



Methods

T1: Visit with COVID or Influenza or flu-like symptoms and with NO pneumonia and NO admission

T2: same as T1 except WITH pneumonia

O1: Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services

O2: Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services or resulting in death in 30d

TAR: 2-30d



Preliminary results

Analysis	Dev	Val	T	O	Model	TAR start	TAR end	AUC	AUPRC	T Size	O Count	O Incidence (%)
Analysis_1	optumDod	optumDod	[COVID ID14 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms with pneumonia and no admission	[COVID19 ID27 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services or resulting in death in 30d	Lasso Logistic Regression	2	30	0.75216	0.03286	25282	115	0.45487
Analysis_2	optumDod	optumDod	[COVID ID15 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms with no pneumonia and no admission	[COVID19 ID27 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services or resulting in death in 30d	Lasso Logistic Regression	2	30	0.8643	0.03104	74826	109	0.14567
Analysis_3	optumDod	optumDod	[COVID ID14 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms with pneumonia and no admission	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	2	30	0.72116	0.08942	25283	827	3.27097
Analysis_4	optumDod	optumDod	[COVID ID15 v1] GP/OP/ER visits of patients presenting with Covid flu or flu-like symptoms with no pneumonia and no admission	[COVID19 ID26 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI	Lasso Logistic Regression	2	30	0.8374	0.1153	74826	788	1.0531
			[COVID ID14 v1] GP/OP/ER visits of	[COVID19 ID27 V1] Hospitalizations with	Lasso							



Discussion and next steps

COVID-19 validation and external validation

Model parsimonisation

Tool creation

- how can we best present the model for application?

Model dissemination



Patient-level prediction #3:
Amongst patients hospitalized with
pneumonia, who are most likely to require
intensive services or die?

Aniek Markus
Erasmus MC



Background

- Lack of evidence of factors associated with disease severity
- Enables close monitoring of high risk patients
- Indicator for short-term demand of intensive services



Methods

- T [IV]: Hospitalization with pneumonia
- T [EV]: Hospitalization with COVID-19
- O1: Patients requiring intensive services* or death
- O2: Death

* Includes ventilation, intubation, tracheotomy, or ECMO.



Preliminary results

Analysis	Dev	Val	T	O	Model	TAR start	TAR end	AUC	AUPRC	T Size	O Count	O Incidence (%)
Analysis_1	optumDod	optumDod	[COVID19 ID29 V1] Hospitalizations with pneumonia, age>=18	[COVID19 ID27 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services or resulting in death in 30d	Lasso Logistic Regression	0	30	0.642	0.322	37499	8062	21.499
Analysis_2	optumDod	optumDod	[COVID19 ID29 V1] Hospitalizations with pneumonia, age>=18	[COVID19 ID28 v1] persons who die	Lasso Logistic Regression	0	30	0.72077	0.1743	37500	2783	7.42133
Analysis_3	optumDod	optumDod	[COVID19 ID29 V1] Hospitalizations with pneumonia, age>=18	[COVID19 ID27 V1] Hospitalizations with pneumonia or ARDS or sepsis or AKI requiring intensive services or resulting in death in 30d	Lasso Logistic Regression	0	30	0.538	0.236	37499	8062	21.499
Analysis_4	optumDod	optumDod	[COVID19 ID29 V1] Hospitalizations with pneumonia, age>=18	[COVID19 ID28 v1] persons who die	Lasso Logistic Regression	0	30	0.6305	0.1106	37499	2782	7.4189



Discussion and next steps

- Developing more parsimonious models
 - easier to use and understand in practice
- External validation in COVID-19 data
- In the future: also train models in COVID-19 data



Population-level Estimation #1: Hydroxychloroquine

Dani Prieto-Alhambra
University of Oxford



BACKGROUND

What have we achieved?

TWO RQs

1. What is the safety profile of hydroxychloroquine?
 2. What is its potential anti-viral efficacy?
-



METHODS

DESIGN

1. Comparative cohort HCQ (t) vs SSZ (o) in RA patients
2. SCCS (regardless of indication)

PARTICIPANTS

1. RA diagnosis + new use of HCQ or SSZ
 2. HCQ use (on/off) + outcome of interest (“case”)
-



METHODS (2)

OUTCOMES

1. Serious adverse events, including: arrhythmia, cv disease, vte, liver failure, kidney failure, GI bleeds, mortality
2. Flu/viral infections, hospitalized pneumonia (not in SCCS)

ANALYSES

1. PS stratification + negative control outcome calibration
 - On treatment and ITT (up to 5y)
 2. Age and season-adjusted SCCS
-



RESULTS (VTE)

Power

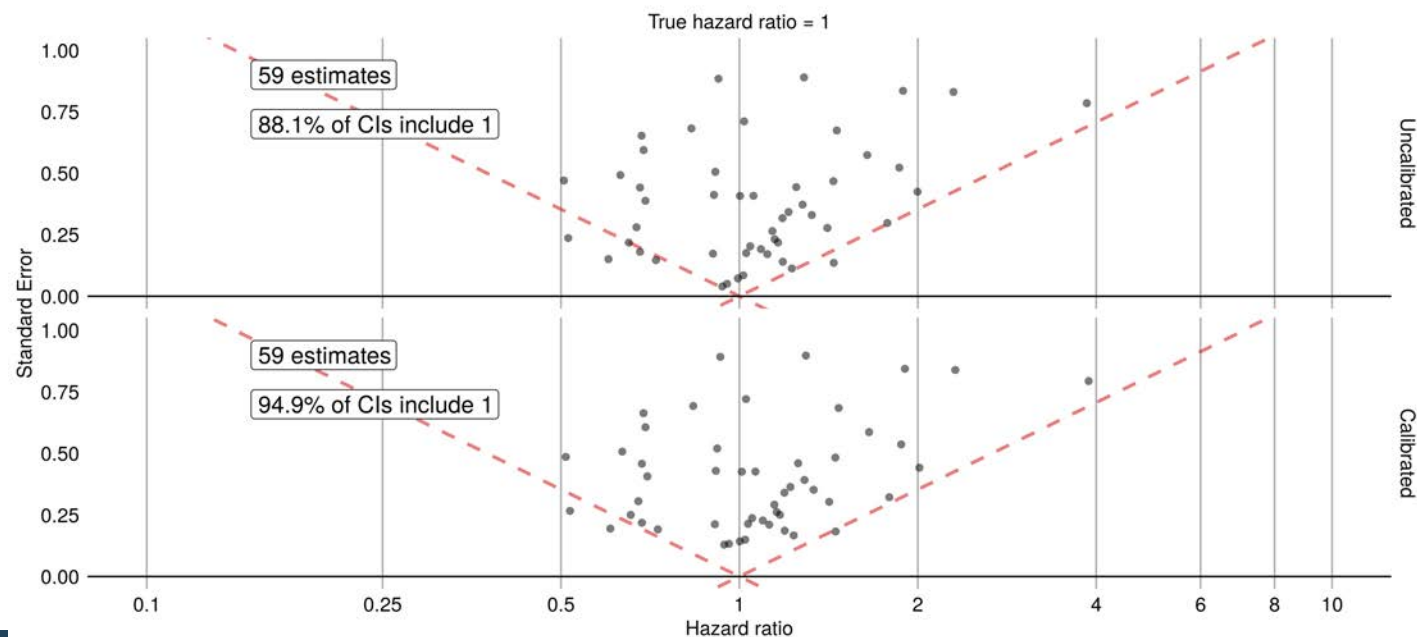
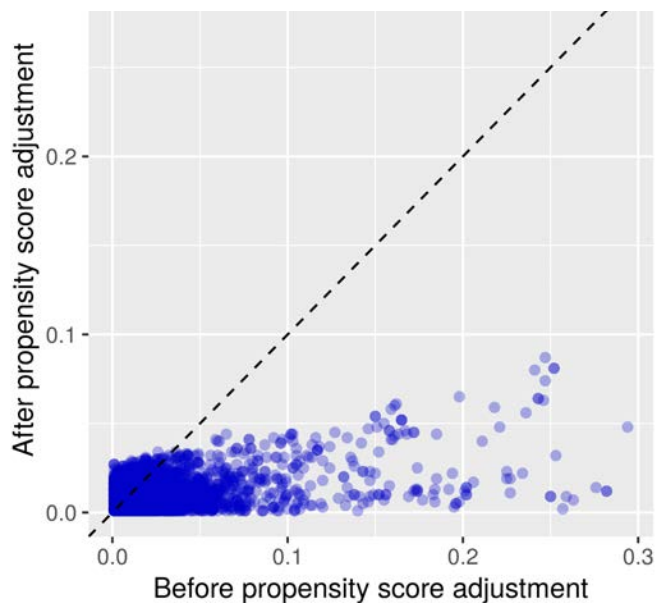
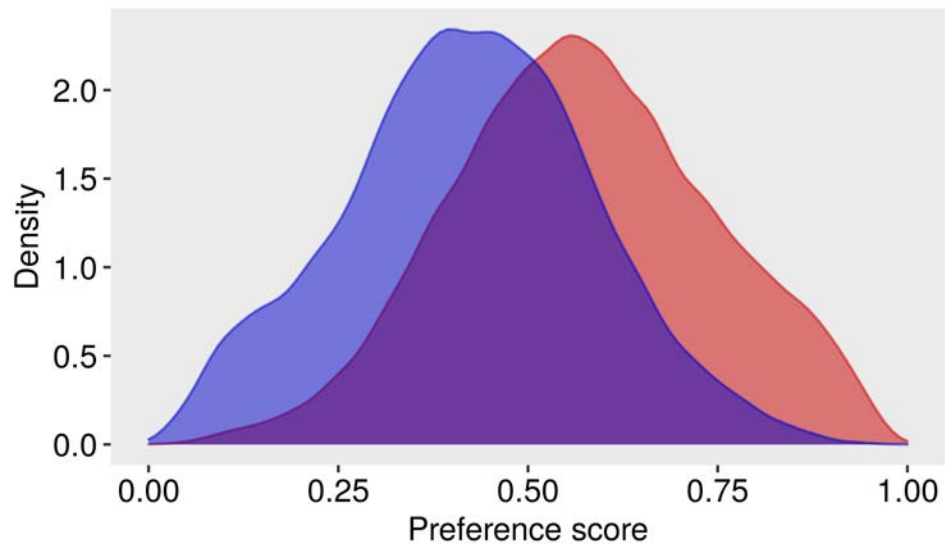
DATA SOURCE	N HCQ	N SSZ	T events HCQ	C events SSZ
CCAE	66,162	23,319	641	159
CPRD	9,134	11,401	131	176
IQVIA-DE	3,898	5,052	34	47
OPTUM	51,288	17,464	946	209
TOTAL	130,482	57,236	1,752	591



RESULTS (VTE)

Diagnostics (CCA-E)

- ✓ PS overlap
- ✓ Covariate balance
- ✓ Negative control outcomes





RESULTS (3)

Risk estimates

OHDSI COVID-19 Studyathon: Hydroxychloroquine population-level effect estimation

About Explore results

Target

[OHDSI Cov19] New users of Hydroxychloroquine with prior rheumatoid arthritis

Comparator

[OHDSI Cov19] New users of sulfasazine with prior rheumatoid arthritis

Outcome

[LEGEND HTN] Venous thromboembolic (pulmonary embolism and deep vein thrombosis) events

Data source

- ☒ CCAE
- ☒ CPRD
- ☒ IQVIA_GERMANY
- ☒ OptumDOD

Show 15 entries

Analysis	Data source	HR	LB	UB	P	Cal.HR	Cal.LB	Cal.UB
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	CCAE	0.99	0.82	1.20	0.92	1.00	0.74	1.35
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	CPRD	1.06	0.81	1.38	0.66	1.01	0.52	1.98
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	IQVIA_GERMANY	0.98	0.58	1.63	0.94	0.72	0.42	1.23
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	OptumDOD	1.04	0.89	1.22	0.64	1.06	0.84	1.32
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	CCAE	0.97	0.87	1.07	0.51	0.98	0.88	1.10
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	CPRD	0.99	0.83	1.19	0.94	1.01	0.83	1.23
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	IQVIA_GERMANY	0.86	0.65	1.14	0.30	0.76	0.57	1.02
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	OptumDOD	0.95	0.87	1.04	0.24	0.97	0.88	1.07

Showing 1 to 8 of 8 entries

Previous



RESULTS (3)

Risk estimates

Analysis	Data source	HR	LB	UB	P	Cal.HR	Cal.LB	Cal.UB	Cal.P
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	CCAE	0.99	0.82	1.20	0.92	1.00	0.74	1.35	0.88
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	CPRD	1.06	0.81	1.38	0.66	1.01	0.52	1.98	0.83
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	IQVIA_GERMANY	0.98	0.58	1.63	0.94	0.72	0.42	1.23	0.28
No prior outcome in last 30d, 5 PS strata, TAR on-treatment+14d	OptumDOD	1.04	0.89	1.22	0.64	1.06	0.84	1.32	0.69
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	CCAE	0.97	0.87	1.07	0.51	0.98	0.88	1.10	0.77
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	CPRD	0.99	0.83	1.19	0.94	1.01	0.83	1.23	0.73
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	IQVIA_GERMANY	0.86	0.65	1.14	0.30	0.76	0.57	1.02	0.09
No prior outcome in last 30d, 5 PS strata, TAR intent-to-treat 5yr	OptumDOD	0.95	0.87	1.04	0.24	0.97	0.88	1.07	0.56



DISCUSSION

COMPLETED

- ✓ The biggest study to date on the safety of HCQ
- ✓ Reassuringly, no consistent signals found

WORK IN PROGRESS

- Running across the whole network (where possible)
- SCCS

OUTSTANDING

- Anti-viral efficacy (new user design in COVID19 infectees)



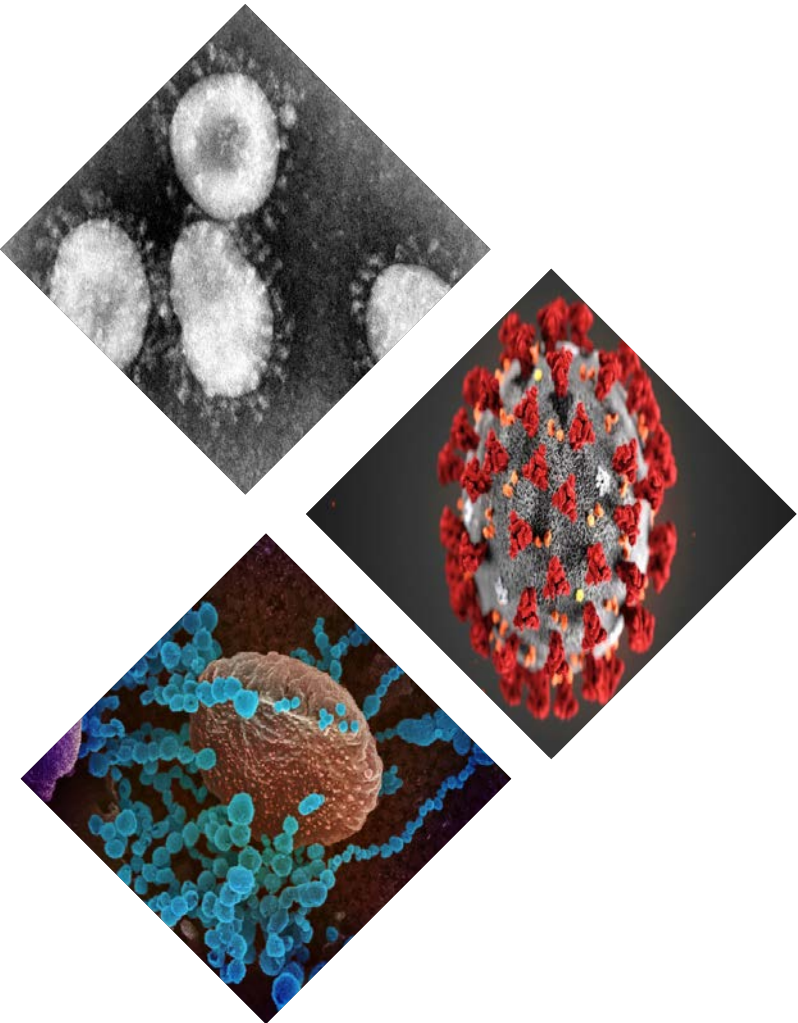
Population-level Estimation #1: Safety of HIV/HepC protease inhibitors

Albert Prats
University of Oxford

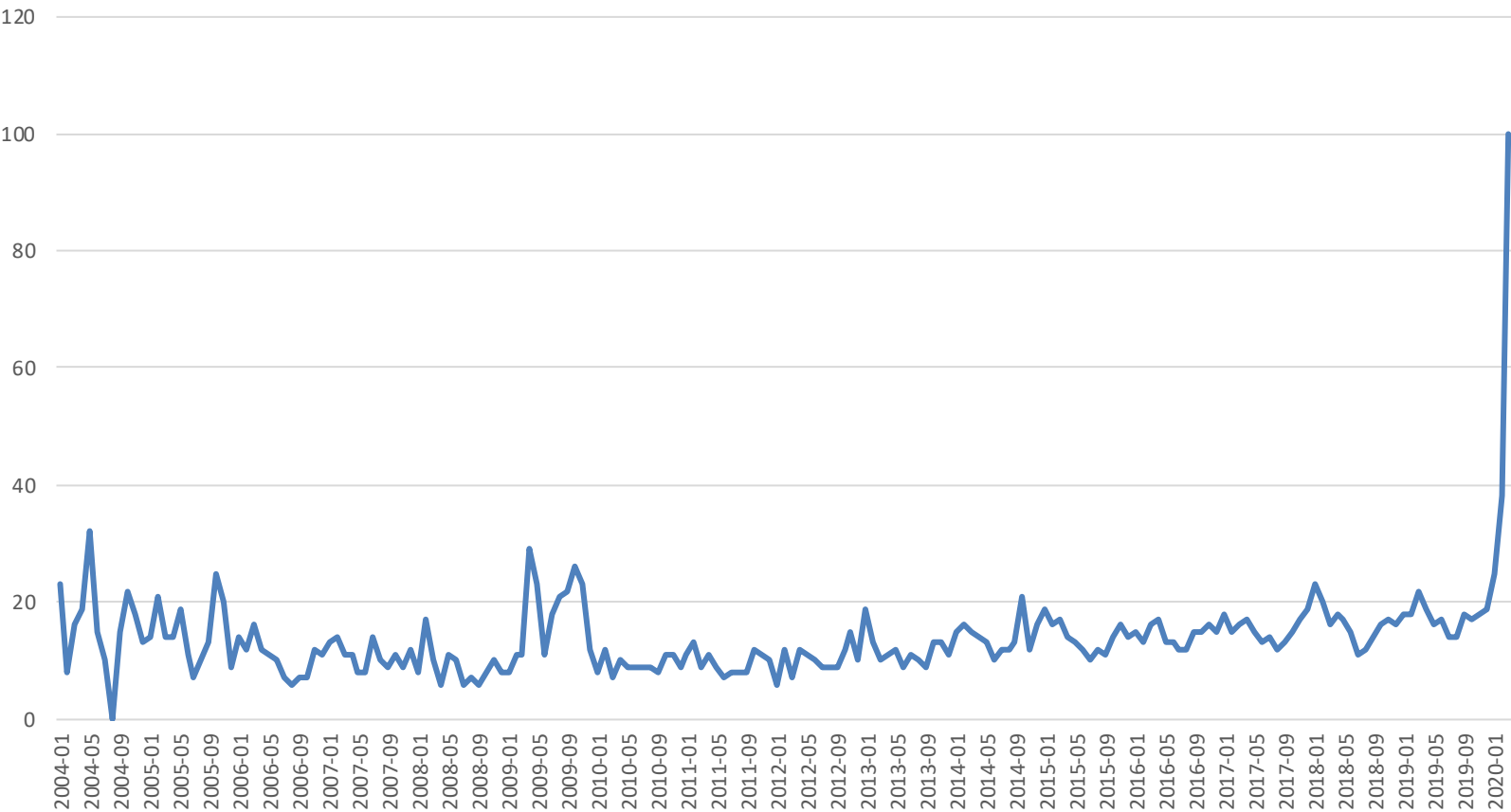


SARS-CoronaVirus-2

A little piece of enveloped RNA!



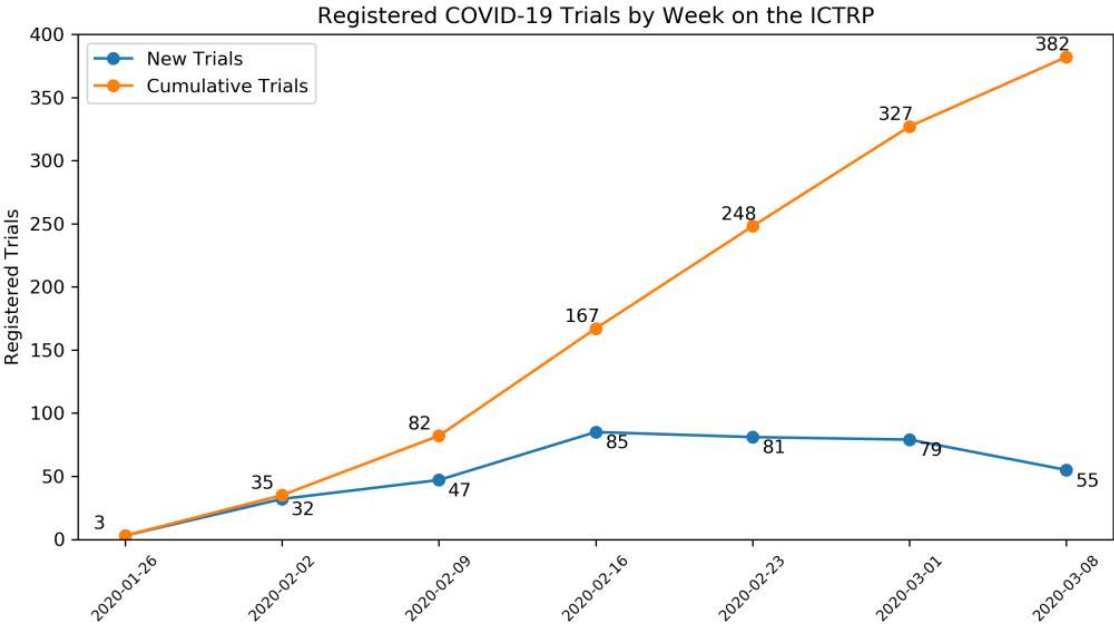
Antiviral
searches globally





SARS-CoV-2 Antiviral Trials

COVID Treatments being tested!



Antiviral drugs, non-specific		
Interferons	Activate cytoplasmic enzymes affecting viral messenger RNA translation and protein synthesis; evidence of minor efficacy in MERS-CoV in combination with ribavirin	4
Antiviral drugs, antiretrovirals		
ASC09	HIV protease inhibitor; to be used in combination with ritonavir	4
Azvudine	Azidocytidine nucleoside analogue; HIV reverse transcriptase inhibitor	4
Danoprevir	Hepatitis C virus NS3 protease inhibitor; to be used in combination with ritonavir	1
Darunavir	HIV protease inhibitor; used in combination with cobicistat, a CYP3A inhibitor	2
Lopinavir + ritonavir	Both HIV reverse transcriptase inhibitors; ritonavir is mainly used to enhance the action of other drugs by inhibition of CYP3A4; in vitro and possible clinical efficacy in SARS-CoV	2
Remdesivir	Nucleotide analogue; inhibitor of RNA-dependent RNA polymerase; used to treat Ebola and Marburg viruses; effective in vitro against SARS-CoV-1 and MERS and blocks infection with 2019-nCoV in vitro	2



Antivirals Background

HIV antivirals

Hepatitis C antivirals



Effectiveness
Does it work?



Safety
Does it harm
patients?

SARS

? COVID

in-vitro

X SARS

? COVID

Gastrointestinal events

Liver Injury

Pancreatitis

etc ...

Arrhythmia

Liver Injury

Hematologic

etc ...



Safety
Does it harm
patients?

HIV Antivirals Estimation

Ritonavir/lopinavir

SCCS

All HIV protease inhibitors

VS

NNRTIs

Cohort study

Integrase inhibitors

of HIV treatment naïve patients

(PS stratification)



Effectiveness
Does it work?

HIV Antivirals Estimation

Cohort study

of SARS-CoV-2 Patients

(PS stratification)

Ritonavir/lopinavir

All HIV protease inhibitors

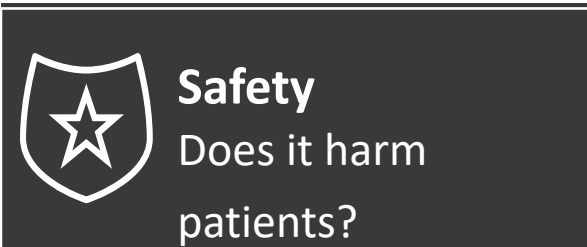
VS

Hydroxychloroquine

Hospital treated

pneumonia

Poor outcomes



Hep C Antivirals Estimation

**Hepatitis C
protease inhibitors**

Peginterferon alfa-2b

Ribavirin

SCCS

Cohort study

Pairwise Comparisons

(PS stratification)



Effectiveness
Does it work?

Hep C Antivirals Estimation

**Hepatitis C
protease inhibitors**

Peginterferon alfa-2b

Ribavirin

Hydroxychloroquine

Cohort study pairwise

comparisons

of SARS-CoV-2 Patients

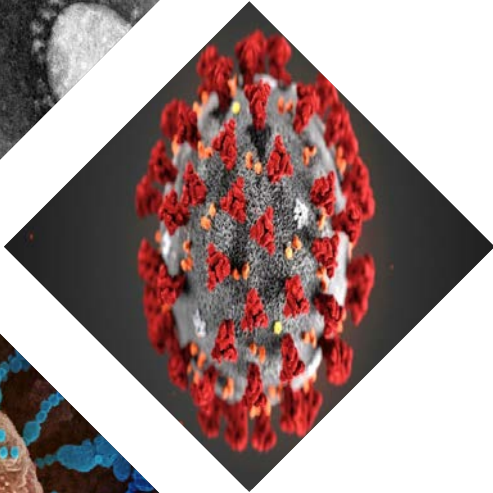
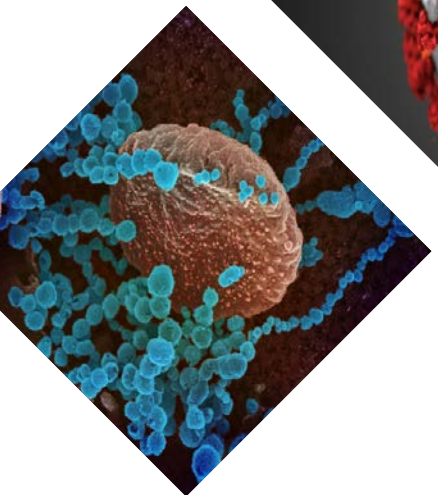
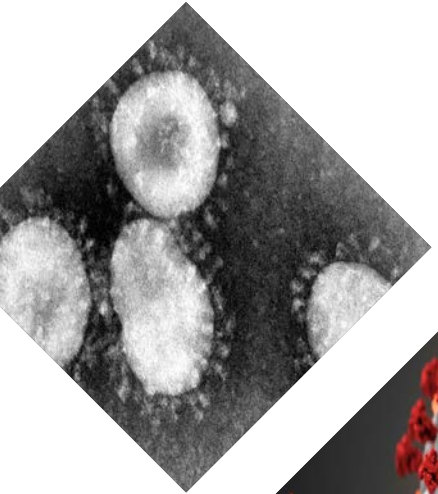
(PS stratification)

Hospital treated pneumonia

Poor pneumonia outcomes



Progress



Protocol

Done!

Safety Analyses

**SCCS
Cohorts**

Effectiveness Analyses

Cohorts

Paper writing

**Background
and methods**



Population-level Estimation #3: Association of angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) on COVID incidence and complications

Daniel Morales
University of Dundee



Background

Authors	COVID Patients	Location	Key Content
Guan et al	1099	China	24% HTN in severe disease (vs 13%)
Zhou	191	China	HTN Univariate OR 3.1 (1.6-6.0) for death
Wang et al	138	China	HTN admissions 31%, HTN ICU 58%
Wu et al	201	China	HTN admissions 19%, HTN ARDS 27%

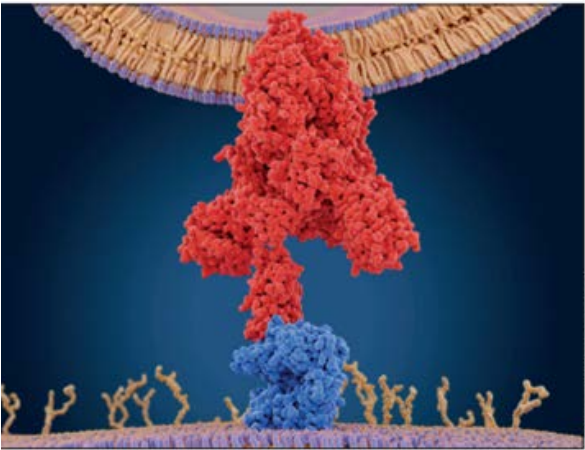
- People with hypertension (HTN) have worse COVID-19 outcomes
- Speculation that ACE/ARBs taken for HTN may be detrimental
 - Coronaviruses interact with RAS ACE-2 receptor, allowing them to enter the cell
 - ACE & ARBs upregulate ACE-2 receptors (limited data)
 - RAS ACE-2 expressed in lung, kidney, heart, GI tract
- Speculation that ARBs may be protective
 - Prevent the angiotensin I receptor from being stimulated
 - Regulate ACE-2 and reduce angiotensin production by ACE and increase production of the vasodilator angiotensin(1-7)



Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?

The most distinctive comorbidities of 32 non-survivors from a group of 52 intensive care unit patients with novel coronavirus disease

inhibitors and ARBs, which results in an upregulation of ACE2.⁵ ACE2 can also be increased by thiazolidinediones and ibuprofen. These data suggest that ACE2 expression is increased in diabetes and treatment with ACE inhibitors and ARBs increases ACE2 expression. Consequently, the increased expression of ACE2 would facilitate infection with COVID-19. We therefore hypothesise that diabetes and hypertension treatment with



Juan Carlos Gomez-Solano/Photo Library

Fang et. Al. Lancet Resp Medicine 11 March 2020



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EMA advises continued use of medicines for hypertension, heart or kidney disease during COVID-19 pandemic

Share

Press release 27/03/2020

EMA is aware of recent [media reports and publications](#) which question whether some medicines, for instance angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs, or sartan medicines), could worsen [coronavirus disease \(COVID-19\)](#). ACE inhibitors and ARBs are most commonly used for treating patients with high blood pressure, heart failure or kidney disease.

<https://www.ema.europa.eu/en/news/ema-advises-continued-use-medicines-hypertension-heart-kidney-disease-during-covid-19-pandemic>

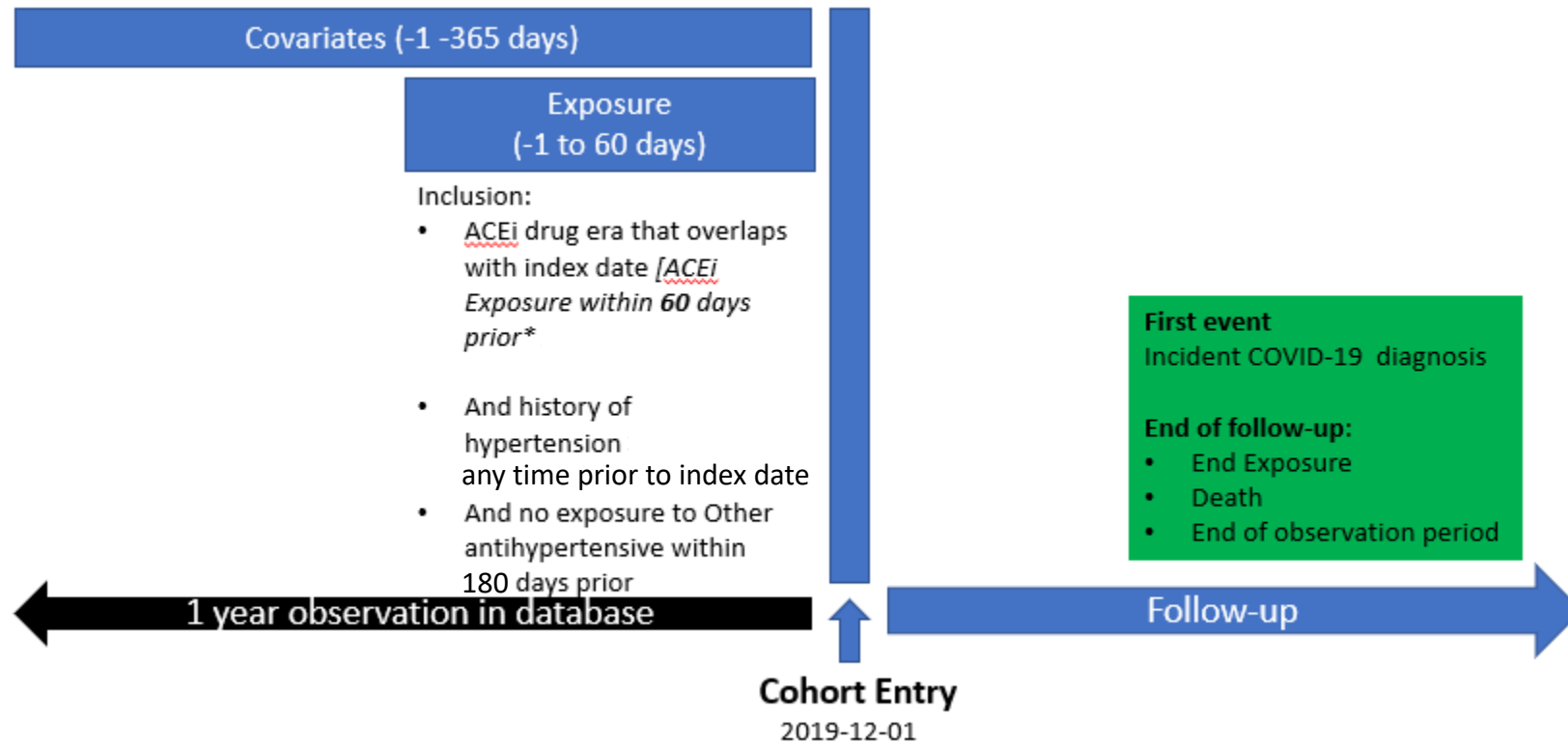


Clinical Hypotheses

1. Prevalent ACE or ARB use is associated with a difference in risk of COVID-19 infection relative to an active comparator in hypertensive patients
2. Prevalent ACE or ARB use in COVID-19+ patients is associated with a difference in risk of intensive outcomes relative to an active comparator in hypertensive patients

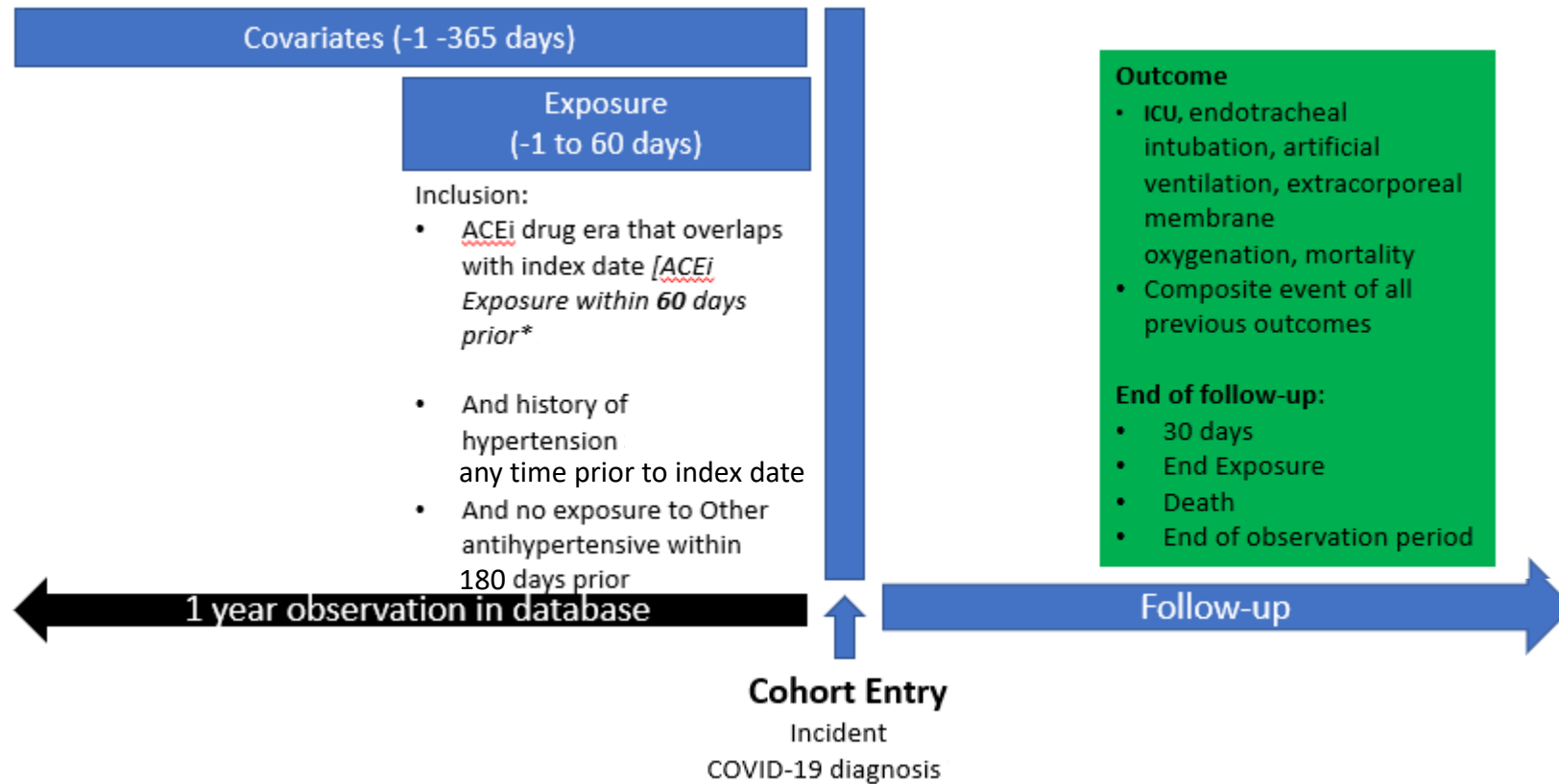


Protocol for Hypothesis 1





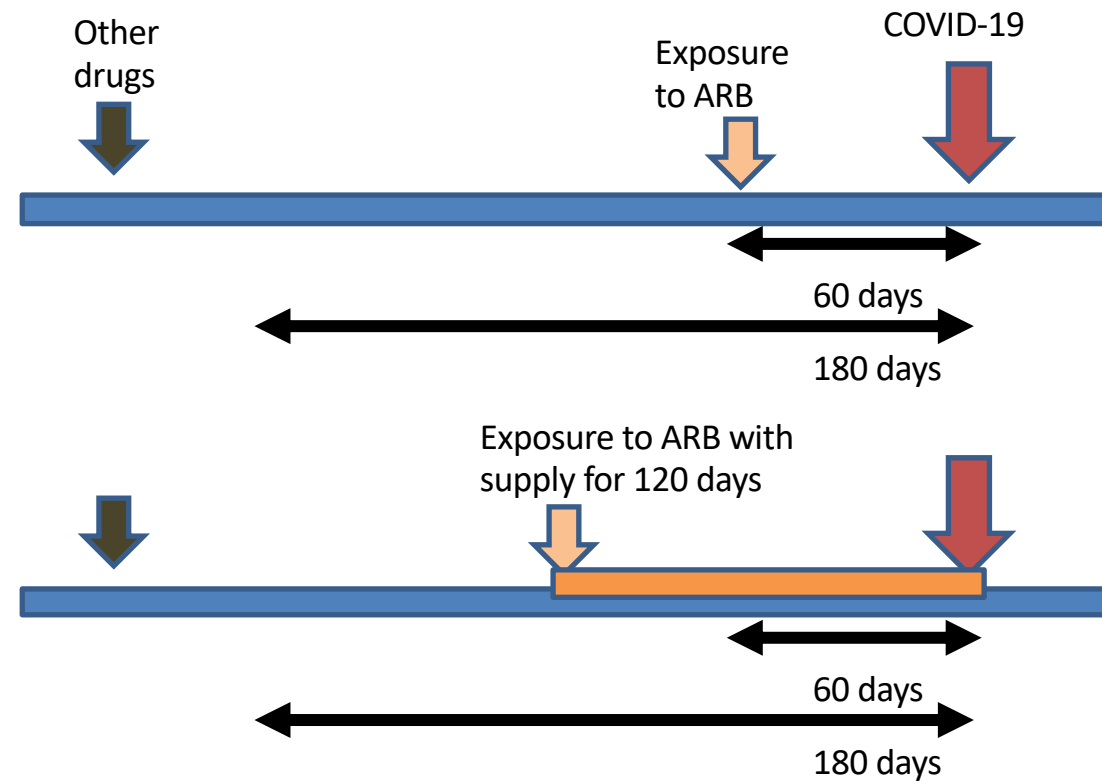
Protocol for Hypothesis 2





Drug Exposure Specification

Prevalent users of ARBs, with COVID-19, history of hypertension





Specification

ATLAS

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Data Sources

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Concept Sets

Cohort Definitions

Characterizations

Cohort Pathways

Incidence Rates

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Estimation

Prediction

Jobs

Configuration

Feedback

Population Level Effect Estimation - Comparative Cohort Analysis #14

Association between use of RAS inhibitors and clinical outcomes of COVID-19

Specification Utilities

Association between use of RAS inhibitors and clinical outcomes of COVID-19

VIEW: Full Specification Comparisons Analysis Settings Evaluation Settings

Comparative Cohort Settings

Comparisons

+ Add Comparison

Show 10 entries Filter:

Remove	Target	Comparator	Outcomes	NC Outcomes	Copy
	[Hypothesis 2] Prevalent users of ACE inhibitors or ARBs with COVID-19, history of hypertension	[Hypothesis 2] Prevalent users of dCCBs with COVID-19, history of hypertension	[LEGEND-HTN]Total cardiovascular disease events (12+ more outcomes)	LEGEND-Negative Concept Sets (1)	
	[Hypothesis 2] Prevalent users of ACE inhibitors or ARBs with COVID-19, history of hypertension	[Hypothesis 2] Prevalent users of thiazide/thiazide-like diuretics with COVID-19, history of hypertension	[LEGEND-HTN]Total cardiovascular disease events (12+ more outcomes)	LEGEND-Negative Concept Sets (1)	
	[Hypothesis 2] Prevalent users of ACE inhibitors or ARBs with COVID-19, history of hypertension	[Hypothesis 2] Discontinuers of ACE inhibitors or ARBs with COVID-19, history of hypertension	[LEGEND-HTN]Total cardiovascular disease events (12+ more outcomes)	LEGEND-Negative Concept Sets (1)	

Apache 2.0 open source software provided by OHDSI

Comparisons:

- ACE vs CCB
- ACE vs ARB
- ACE vs THZ
- RAS vs CCB
- ARB vs CCB
- RAS vs THZ
- ARB vs THZ
- RAS vs Discontinued RAS

Outcomes:

- ICU Care
- Ventilation
- ECMO
- All-cause mortality
- MI, HF, Stroke, CV death
- AKI
- LEGEND negative controls

Design:

- Logistic regression outcome (30/60/90 days) (cohort 2)
- PS matched / stratified (including age, gender, month)
- Potential for large-scale PS with larger cohorts



Results

- HIRA: study executes and preliminary results (coming in next presentation)
- Columbia University Medical Center/NYP
 - Successfully ran the main cohort of HTN, recent ACE, no other anti-HTN drugs, sufficient lookback => about 20 patients
 - Analysis using SQL showed we can increase patient numbers using less recent ACE (note we have 30d prescriptions with 5 refills = 180d)
 - Do not have hospital disposition yet, but have inferred ICU, for example, via medications given
 - (Do have a subpopulation on hydroxychloroquine)



Acknowledgments

Key participants:

- Kees van Bochove
- Mitchell Conover
- George Hripcsak
- Christophe Lambert
- Michael Matheny
- Daniel Morales
- Fredrik Nyberg
- Nicole Pratt
- Daniel Prieto Alhambra
- Marc Suchard
- Cynthia Sung
- Seng Chan You

Apologies if your name is not here; let Marc know – he haphazardly compiled this list



Partial funding provided
through NIH U19 AI135995
and R01 LM006910





#OpenData4COVID

Seng Chan You, Ajou University
Yeunsook Rho, HIRA

Summary of COVID-19 Study w/ HIRA Data

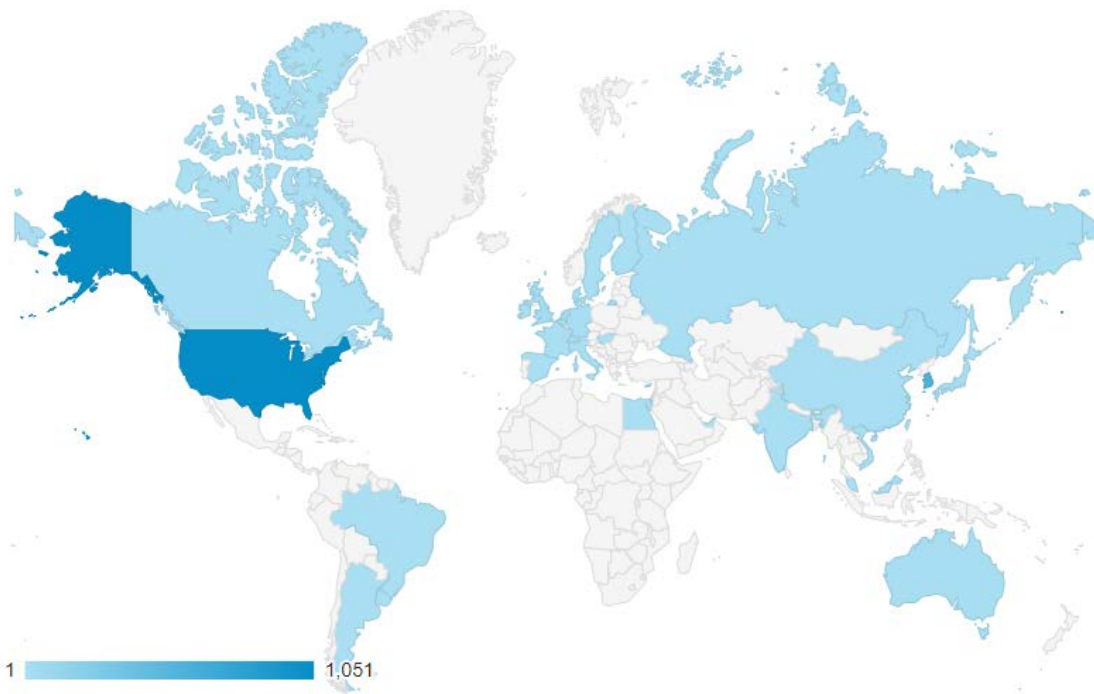
March 29/30, 2020



SUMMARY OF "OPENDATA4COVID19" PROJECT W/ HIRA DATA

WE'VE GOT 1,772 VISITORS FROM 32 COUNTRIES FOR 3 DAYS

- More than 160 individual researchers have registered from 15 countries
- Nearly, 30 research projects are submitted for analysis
(disease characterization, relationship b/w baseline condition and death, relationship baseline drug intake and death, patient-level prediction using machine learning program, etc.)
- Ongoing project



국가	획득		
	사용자	신규 방문자	세션
	1,772 전체 대비 비율 (%): 100.00% (1,772)	1,772 전체 대비 비율 (%): 100.00% (1,772)	1,988 전체 대비 비율 (%): 100.00% (1,988)
1. United States	1,051 (59.31%)	1,051 (59.31%)	1,083 (54.48%)
2. South Korea	575 (32.45%)	575 (32.45%)	734 (36.92%)
3. United Kingdom	24 (1.35%)	24 (1.35%)	27 (1.36%)



SUMMARY OF “OPENDATA4COVID19” PROJECT W/ HIRA DATA

FUTURE CONSIDERATIONS

- Wonderful experience
 - Data update issues
 - Further opportunities
- 
- 

CHARACTERIZATION OF PATIENTS WITH COVID-19

Covariate Name	HIRA
	Proportion
Age group	
15-19	1.9%
20-24	10.9%
25-29	13.9%
30-34	10.5%
35-39	11.6%
40-44	9.4%
45-49	7.2%
50-54	5.7%
55-59	6.5%
60-64	5.7%
65-69	3.9%
70-74	3.3%
75-79	4.1%
80-84	3.2%
85-89	1.8%
90-94	0.5%
Gender: female	51.9%
Race	
race = Korean	100.0%

Cohort	HIRA	
	Entries	Subjects
COVID ID1 v1	4,123	4,123

Medical history: General		
Chronic liver disease	5.5%	
Chronic obstructive lung disease	3.8%	
Crohn's disease	<0.2%	
Dementia	4.5%	
Depressive disorder	11.7%	
Diabetes mellitus	16.0%	
Gastroesophageal reflux disease	29.8%	
Gastrointestinal hemorrhage	2.7%	
Human immunodeficiency virus infection	<0.2%	
Hyperlipidemia	29.9%	
Hypertensive disorder	21.7%	
Lesion of liver	4.7%	
Obesity	0.3%	
Osteoarthritis	13.6%	
Pneumonia	13.8%	
Psoriasis	1.4%	
Renal impairment	3.9%	
Rheumatoid arthritis	3.3%	
Schizophrenia	1.4%	

Medication use	
Agents acting on the renin-angiotensin system	13.8%
Antibacterials for systemic use	74.4%
Antidepressants	12.5%
Antiepileptics	11.8%
Antiinflammatory and antirheumatic products	63.2%
Antineoplastic agents	3.2%
Antipsoriatics	0.8%
Antithrombotic agents	36.7%
Beta blocking agents	10.6%
Calcium channel blockers	14.0%
Diuretics	10.4%
Drugs for acid related disorders	66.5%
Drugs for obstructive airway diseases	24.9%
Drugs used in diabetes	9.7%
Immunosuppressants	2.9%
Lipid modifying agents	16.8%
Opioids	65.8%
Psycholeptics	29.7%
Psychostimulants, agents used for adhd and nootropics	8.2%

Led by Edward Burn (Oxford University, UK)

COMPARISON OF CLINICAL OUTCOME BETWEEN ANTI-HYPERTENSIVE MEDICATIONS

Evidence Explorer

Target

Prevalent ARB user as monotherapy for HTN within 30 days before COVID-19 diagnosis

Comparator

Prevalent dCCB user as monotherapy for HTN within 30 days before COVID-19 diagnosis

Outcome

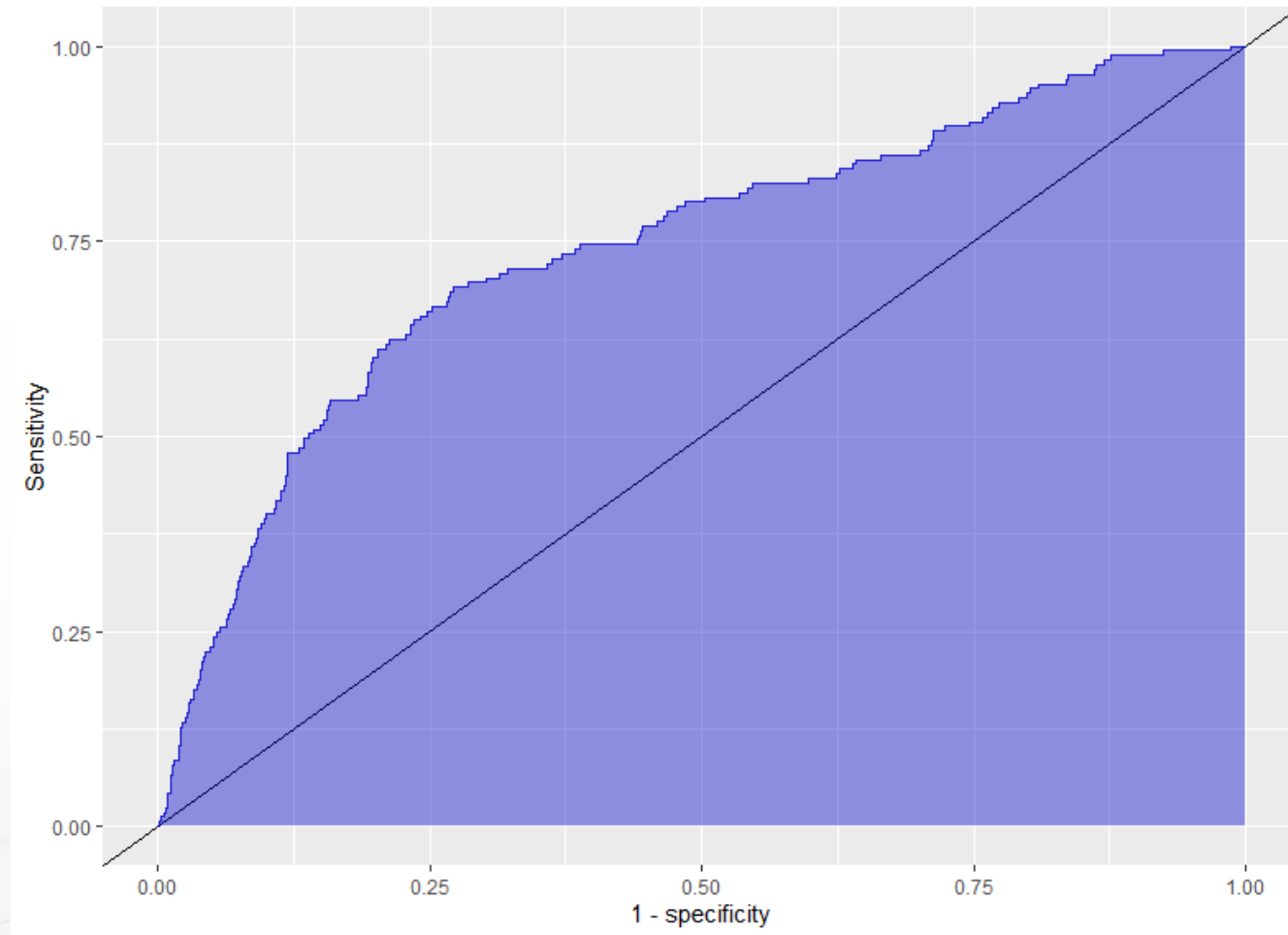
All-cause mortality

Show 15 entries

Analysis	Data source	HR	LB	UB	P
Without PS adjustment-Logistic (age/gender/year/month)	HIRA	1.21	0.14	10.32	0.86
Without PS adjustment-Cox (age/gender/year/month)	HIRA	1.21	0.15	10.07	0.86
Minimum PS stratification -Cox	HIRA	1.21	0.15	10.07	0.86
Minimum PS stratification -Logistic	HIRA	1.21	0.14	10.05	0.86
Full PS stratification -Cox	HIRA	1.21	0.15	10.07	0.86
Full PS stratification -Logistic	HIRA	1.21	0.14	10.05	0.86
Unadjusted with all demographic covariates (+14 / logistic)	HIRA	2.42	0.23	52.80	0.52

Showing 1 to 7 of 7 entries

PREDICTION OF HOSPITALIZATION AMONG PATIENTS SYMPTOMS RELATED WITH VIRAL INFECTION OR DIAGNOSIS OF COVID-19



Led by Peter Rijnbeek (Erasmus University, Netherland)



Thank you!



The journey ahead

Patrick Ryan

Janssen Research and Development

Columbia University

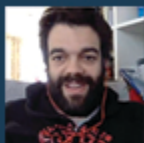


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OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

COVID-19 Study-A-Thon

ohdsi.org/covid-19-updates



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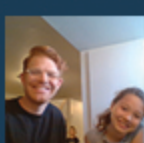
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Oleg Zhuk
Jason Zucker

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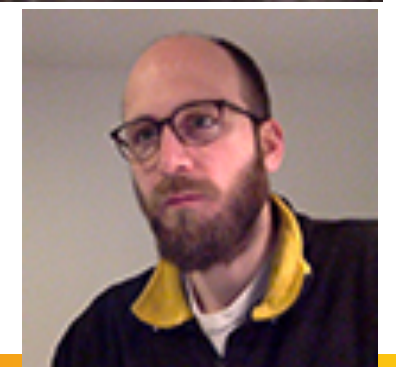
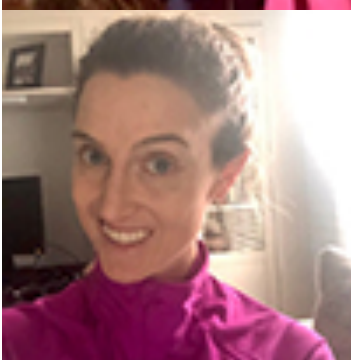
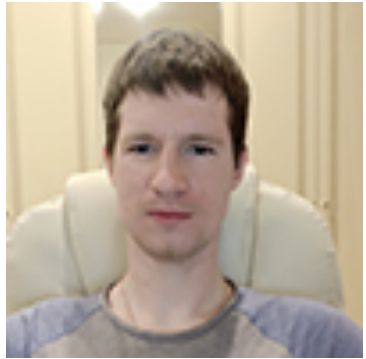
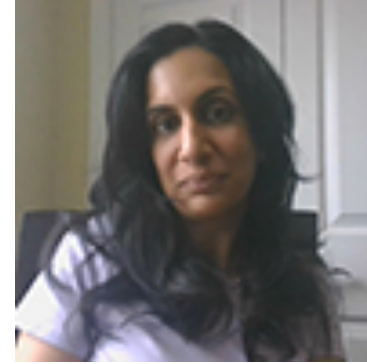
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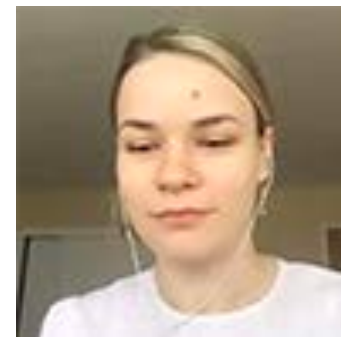


Thank you literature review team!



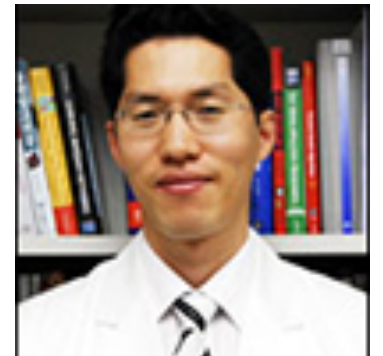
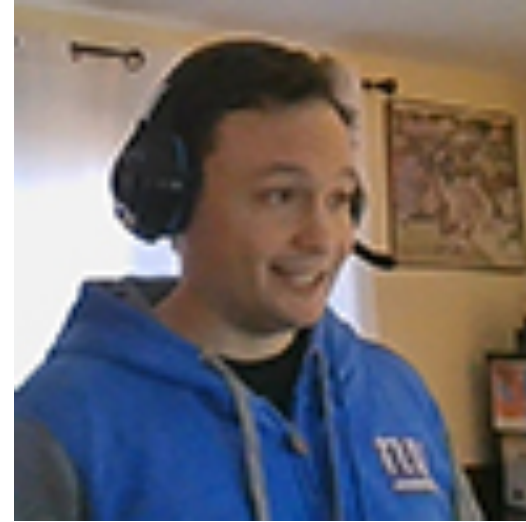


Thank you phenotype team!



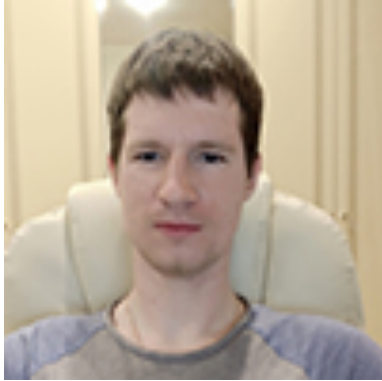


Thank you network execution team!



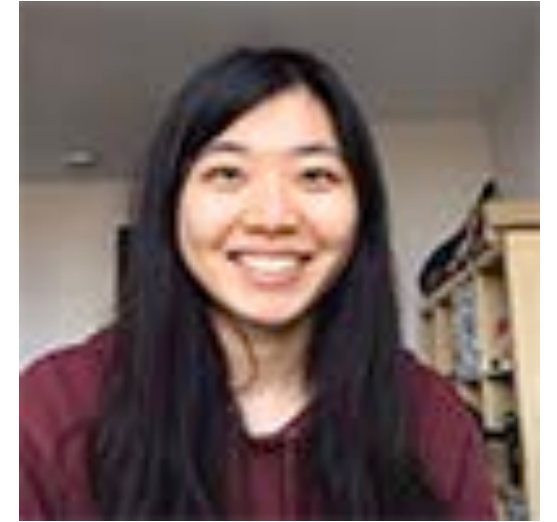
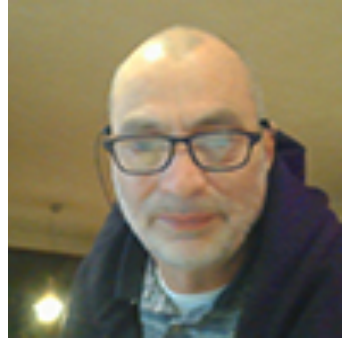


Thank you characterization team!



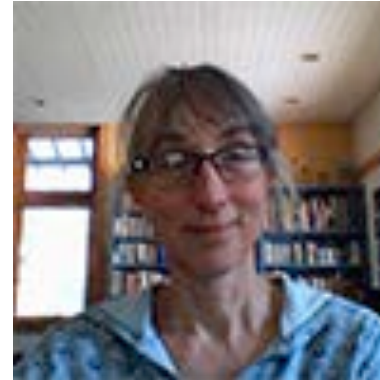


Thank you prediction team!





Thank you estimation teams!





Thank you infrastructure support teams!





The journey ahead

- Study-a-thon may be finishing today, but this is only the START of our journey today
 - Thanks to Erasmus MC, The MSTeams collaboration platform will continue to be available to support OHDSI collaborations
 - ATLAS-COVID19.ohdsi.org will remain available for collaborative development of analyses
 - Each study team needs to determine their own strategy for dissemination
 - Data.ohdsi.org to make results publicly available as soon as possible
 - Publications to be drafted by the community will be open access



Many more important questions need answering...

Name	Question
Alan Goldhammer	Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19
Jeff Hammerbacher	Blood groups of stratified subpopulations of interest
Geert Byttebier	Potential impact of statin use
Rimma Belenkaya	Specific patterns in the lungs as markers of the disease as it develops over the course of a week and a half
Michael_Shamberger	Does evidence support that taking anti inflammatories can cause adverse outcome?
Sajan Khosla	Length of Stay or 30 Day mortality in patients hospitalized with viral pneumonia to understand patterns of antiviral use and potential differences in endpoints?
Chiara Attanasio	Clinical use cases on cancer patients in relation with COVID-19
Annalisa Trama	Treatment choices for cancer patients planned for surgery and those on cytotoxic chemotherapy or immunotherapy?
Jenny Lane	Compare epidemiological characteristics of the Chinese infections to other countries
Evan Minty	Risk of cardiac injuries (e.g. myocarditis) in COVID-19
Vojtech_Huser	Chronic medication stockpiling (preparing for pandemic) by patients
Jason 10033	The role of steroids in COVID-19 ARDS and ventilation management for patients
Sara Dempster	COVID-19 mortality in different countries
Ru Cheng	Studying pregnancy and lactation: rate of infection in pregnancy, complication rates for pregnant infected women, transmission to newborn (especially c-section vs vaginal) and through milk, premature birth rates, fetal loss
Michael Kallfelz	Role of coinfection with Varicella Zoster or Epstein Barr

Our ask of all of you:

- Keep asking good questions....
 - post your thoughts on the OHDSI forums
-and continue to collaborate with each other to help:
 - translate those questions into analysis designs...
 - implement those designs into study packages....
 - execute those packages to generate results....
 - share results across the community to synthesis reliable real-world evidence



OHDSI

OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

THANK YOU

We like to thank the large group of community members that worked extremely hard to make these four days possible.

We like to thank the Data Partners that have participated in this effort, and those who will join the journey shortly.

We like to thank you for your active participation in these four days.



Questions & Answers





Start of a Journey

- This disease isn't stopping yet, and neither will we
- We will remain committed to generating reliable real-world evidence to meet the needs of public health
- Thank you for continuing on the journey with us

