SCYLLA: Large-scale characterization of COVID-19 treatment utilization

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AGENDA

- Why SCYLLA (if we have trials)
- Aims & Methods
- Data source/s and Ns to date
- DUS – findings to date
- A call for participation!

Are we killing trials with RWE?

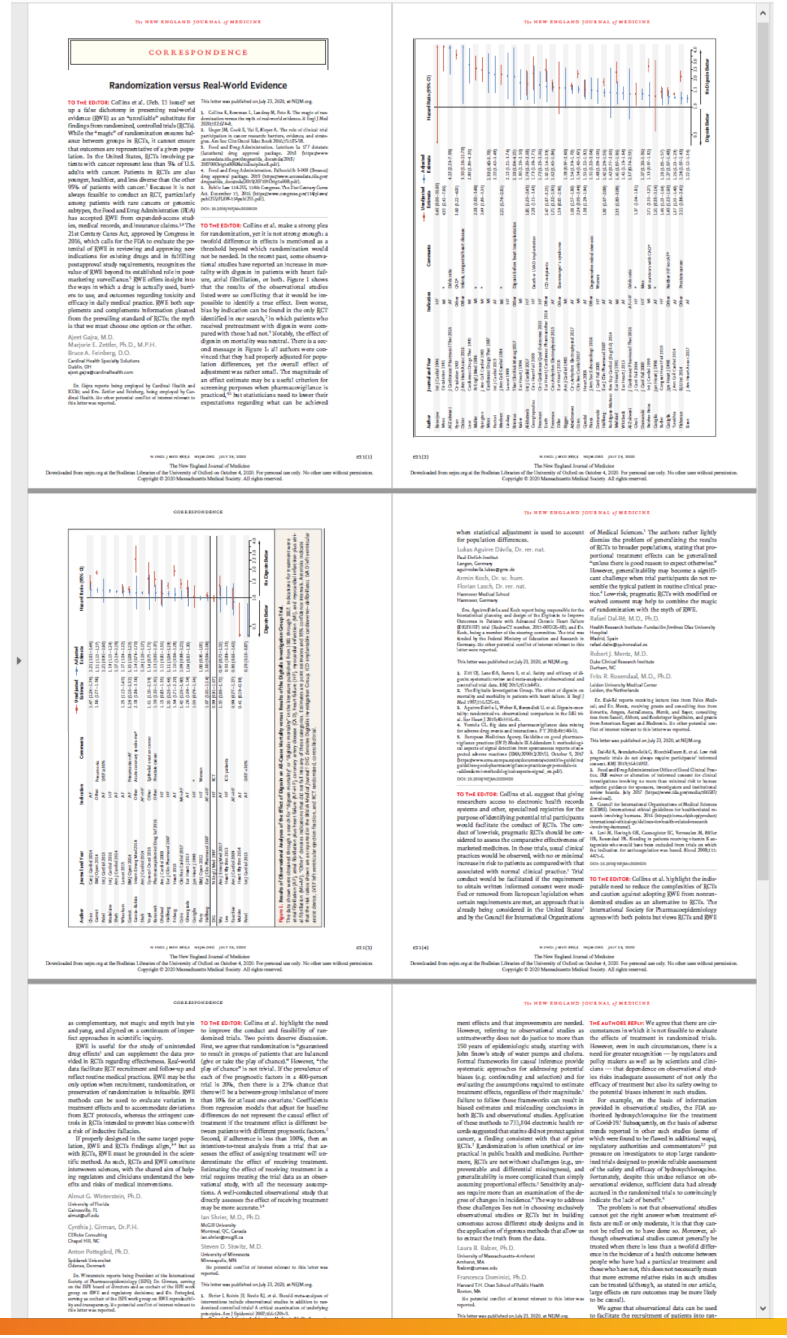
The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

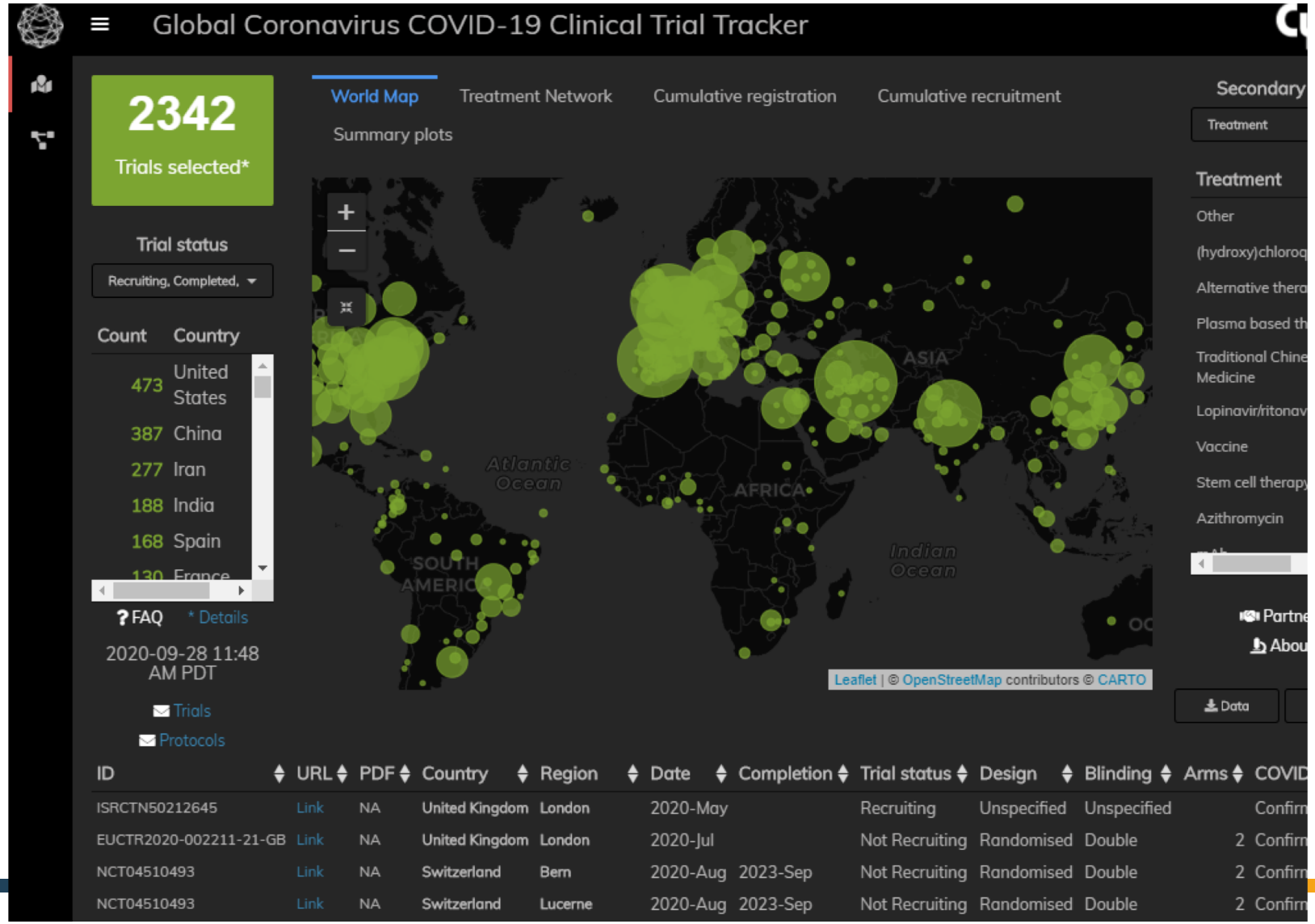
The Magic of Randomization versus the Myth of Real-World Evidence

Rory Collins, F.R.S., Louise Bowman, M.D., F.R.C.P., Martin Landray, Ph.D., F.R.C.P., and Richard Peto, F.R.S.

Nonrandomized observational analyses of large electronic patient databases are being promoted as an alternative to randomized clinical trials as a source of "real-world evidence" about the efficacy and safety of new and existing treatments.[1-3] safety and efficacy because the potential biases with respect to both can be appreciable. For example, the treatment that is being assessed may well have been provided more or less often to patients who had an increased or decreased risk



I’m afraid we are… there’s only 2,342 covid-19 trials ongoing …



So, why do we need Scylla?
2. We have tones of data available, without incurring additional risks

USA (8)	EUROPE (7)	ASIA-PACIFIC (3)
Premier (National – Hospital Billing)	CPRD (UK – Electronic Health Records)	HIRA (South Korea – Administrative Claims)
HealthVerity (Claims linked to diagnostic testing)	SIDIAP (Spain – Electronic Health Records)	DCMC (South Korea – Electronic Health Records)
Optum EHR (National – Electronic Health Records)	SIDIAP-H (Spain – EHR hospital linkage	Nanfang Hospital (China – Electronic Medical Records)
IQVIA Open Claims (National – Administrative Claims)	HM Hospitales (Spain – Hospital Billing)	
Department of Veterans Affairs (National – Electronic Health Records)	ICPI (Netherlands – Electronic Health Records)	
Stanford University (CA – Electronic Health Records)	LPD France (France – Electronic Health Records)	
Tufts University (MA – Electronic Health Records)	Germany DA (Germany – Electronic Health Records)	
Columbia University (NY – Electronic Health Records)		

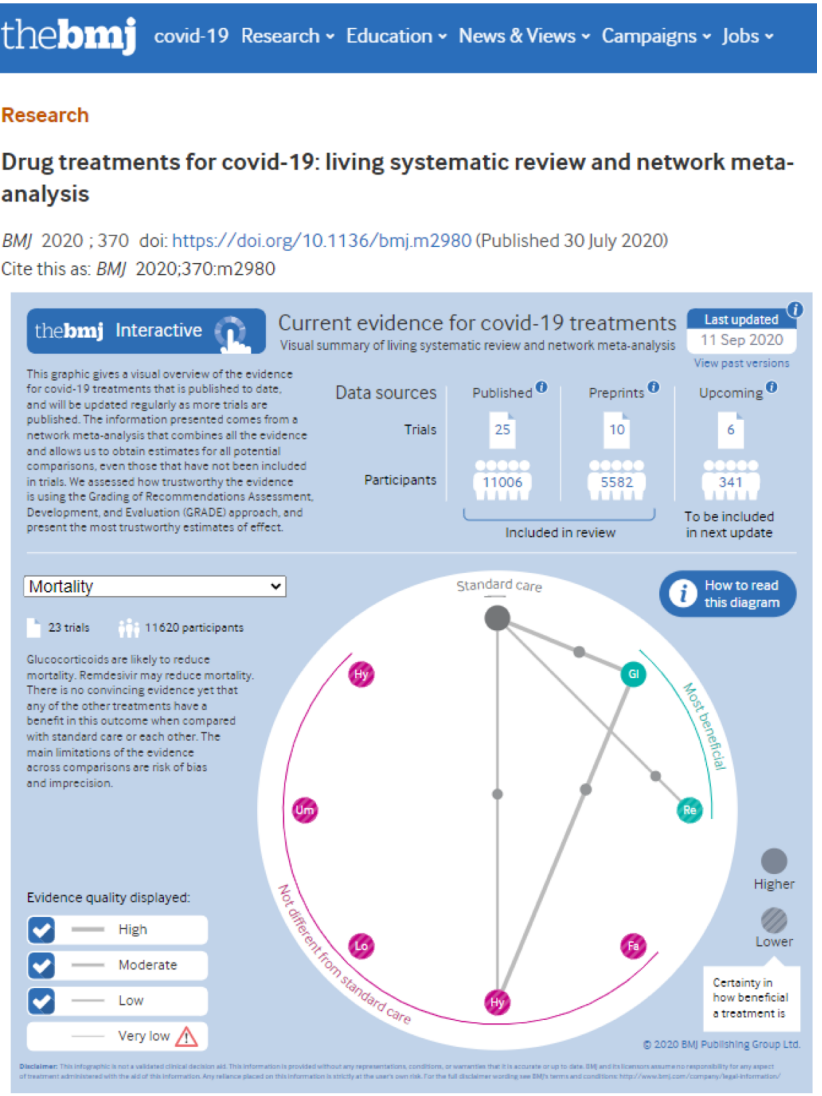
Together, OHDSI has studied (to date):

- **>7m patients tested for SAR-COV-2**
- **>1.6m patients diagnosed or tested positive for COVID-19**
- **>300k hospitalized for COVID-19**

So, why do we need Scylla?
3. Comparative effects (risks and benefits) DO matter

- Many trials ongoing
- 25 published, 10 preprints
- All study treatment/s vs placebo or 'standard care'

- But …
  - Are all corticosteroids equally safe?
  - Are all IL-inhibitors equally effective?
  - Are IL-inh safer than corticosteroids?
  - …



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Study Aims

- To assess the comparative effectiveness and safety among treatments administered **during hospitalization** and *prior to intensive services*

- To assess comparative effectiveness and safety among treatments administered after COVID-19 positive testing or diagnosis in **outpatient setting** *without prior hospitalization*

FULL STUDY PROTOCOL REGISTERED AT
http://www.encepp.eu/encepp/viewResource.htm?id=37226

METHODS

- New user, active comparator, cohort designs
- Large-scale propensity scores - observed confounding
- Negative control outcomes and empirical calibration – unobserved confounding

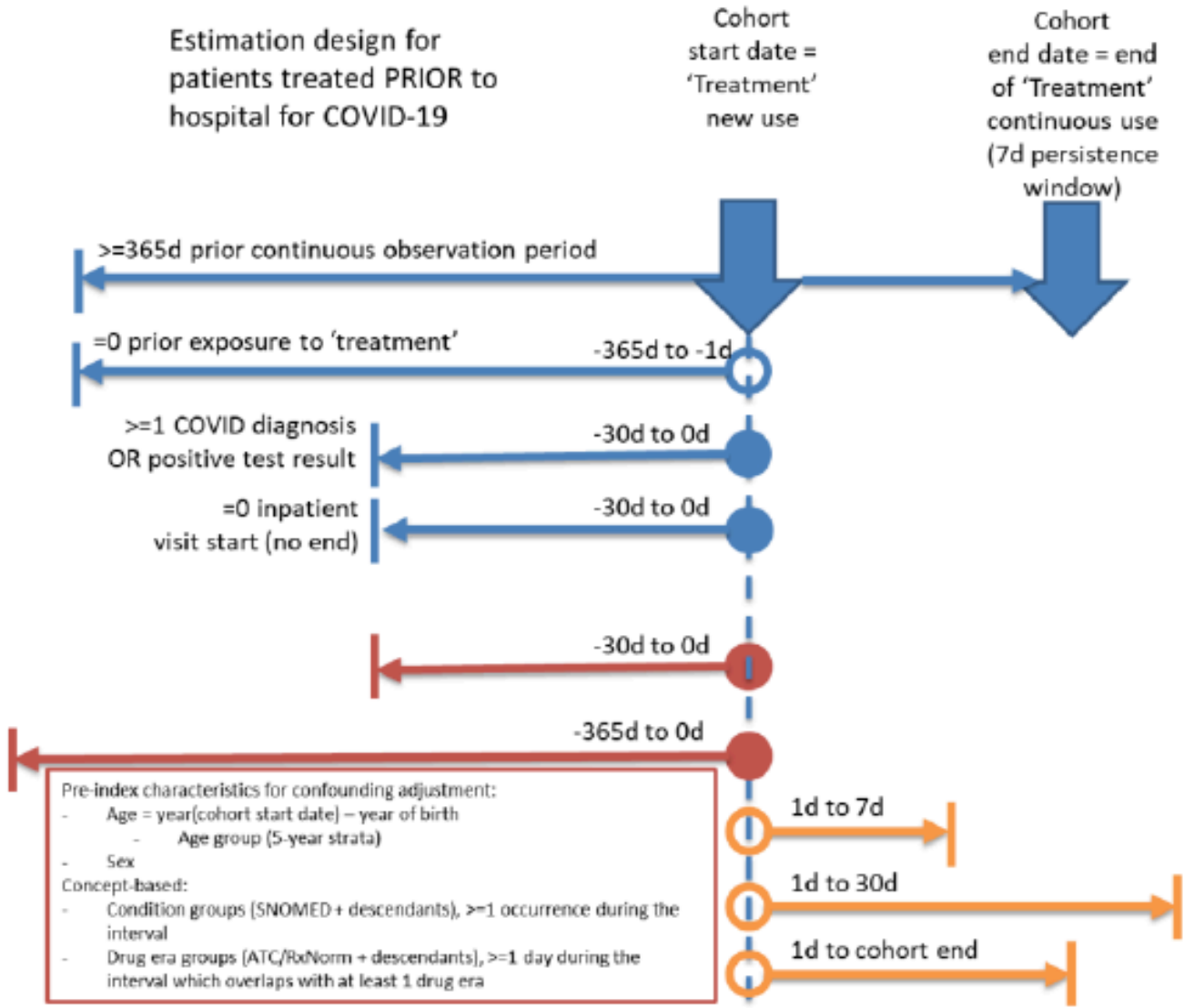
HADES
HEALTH ANALYTICS DATA-TO-EVIDENCE SUITE

Population-level estimation
CohortMethod package

Study drugs/exposures

- Antivirals/repurposed therapies
- Immune-based therapies (GCs, biologic rx, etc)
- Antithrombotic therapies (heparin, oral anticoagulants, etc)
- Concomitant
  - Antibiotic therapy
  - CV prevention therapy (statins, ACEi, etc)
  - Other concomitant therapies

New user cohorts in Scylla - OUTPATIENT



'Treatment' Cohorts: (can be used as target AND comparator)

- Antivirals
- Immune-based therapies
- Antithrombotics
- Antibiotics
- Anti-hypertensives
- Anti-diabetics
- Statins
- Concomitant therapies

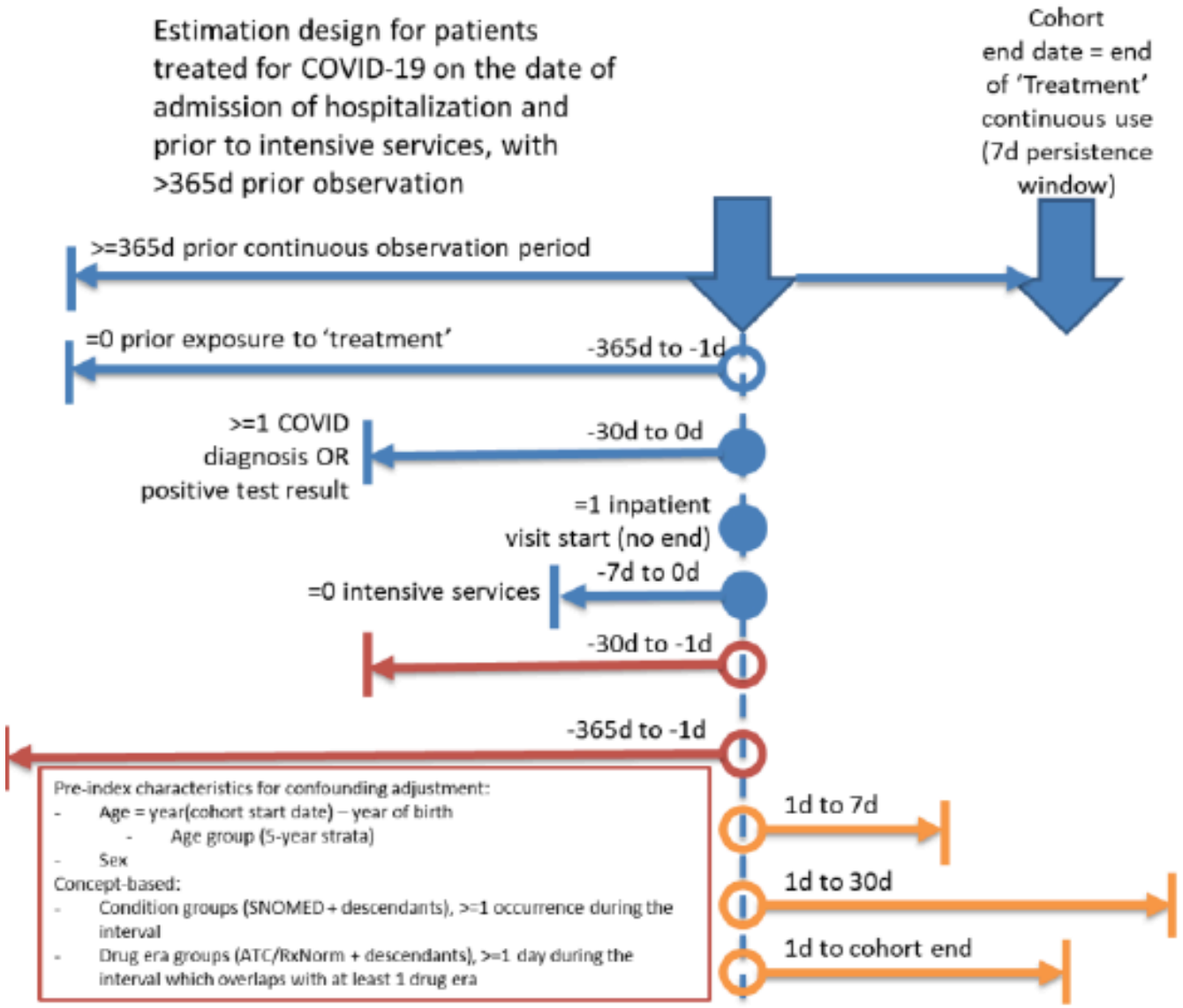
Outcomes:

- Admission to Hospitalization
- Initiation of hospitalization intensive services (ventilation, tracheostomy, ECMO)
- Haemodialysis
- Death (all-cause mortality, cardiovascular-related mortality)
- Pneumonia
- Acute kidney injury
- Sepsis
- Venous thromboembolism (Pulmonary embolism, Deep Vein Thrombosis)
- Arrhythmia
- Haemorrhage
- Angina
- Asthma/COPD exacerbation
- Hepatic failure
- Acute pancreatitis
- Cardiovascular disease events (stroke, heart failure, acute myocardial infarction, sudden cardiac death)
- Transient ischemic attack
- Gastrointestinal bleeding

Analysis:

- Logistic regression (odds ratio on proportion having event in TAR)
- Cox PH (hazards ratio for time-to-event analysis)

New user cohorts in Scylla – INPATIENT (pre-ICU)



'Treatment' Cohorts: (can be used as target AND comparator)

- Antivirals
- Immune-based therapies
- Antithrombotics
- Antibiotics
- Anti-hypertensives
- Anti-diabetics
- Statins
- Concomitant therapies

Outcomes:

- Initiation of hospitalization intensive services (ventilation, tracheostomy, ECMO)
- Haemodialysis
- Discharge from Hospitalization (or Death)
- Death (all-cause mortality, cardiovascular-related mortality)
- Pneumonia
- Acute kidney injury
- Sepsis
- Venous thromboembolism (Pulmonary embolism, Deep Vein Thrombosis)
- Arrhythmia
- Haemorrhage
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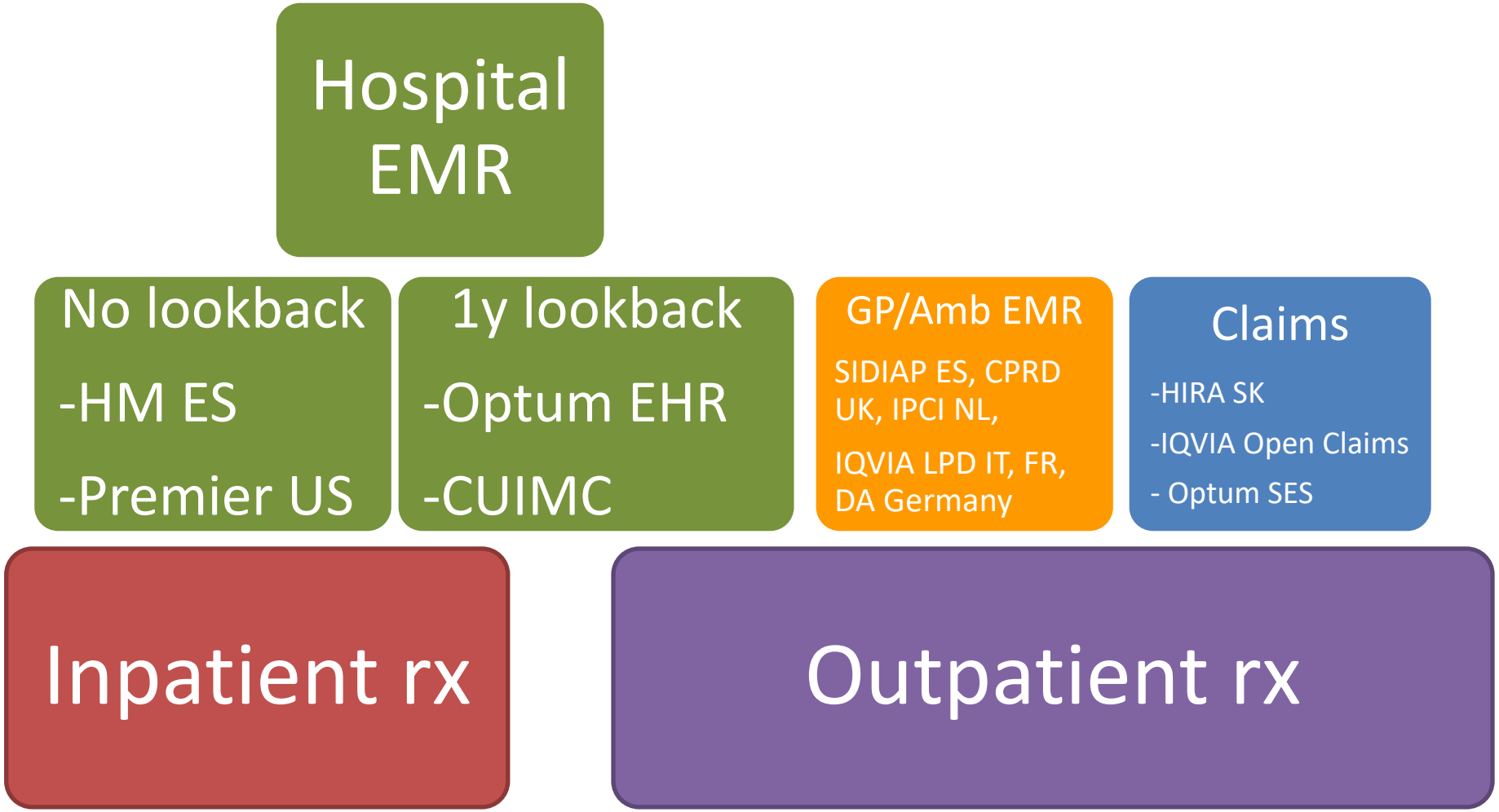
DATA SOURCES to date



N to date – Outpatient new user cohorts

DRUG	OPTUM SES	OPTUM-EHR	SIDIAP	LPD-IT	CPRD	Health Verity	LPD Fr	TOTAL
antivirals	272	5872	8208	754	5	2247	1326	18,692
immune-based therapies	60	5403	1797	135	48	744	435	8,627
antithrombotics	37	3878	1341	209	37	242	125	5,864
antibiotics	221	6486	8784	682	127	1906	1567	19,778
concomitant cv prevention	6	2231	952	16	11	222	115	3,558
Antidiabetics	<5	809	215	14	6	97	28	1,164
Other concomitants	<5	657	197	12	11	68	46	986

N to date …

DRUG	SETTING	OPTUM SES	OPTUM-EHR	SIDIAP	HVERITY	PREMIER	HM-ES	TOTAL
antivirals	INPATIENT - SAME DAY	204	7778	398	187	29289	1759	39,615
antivirals	INPATIENT	151	5696	395	74	58		6,374
immune-based therapies	INPATIENT - SAME DAY	56	6323	282	126	10808	831	18,426
immune-based therapies	INPATIENT	36	4650	276	31	26		5,019
antithrombotics	INPATIENT - SAME DAY	88	10531	1665	146	31194	1628	45,252
antithrombotics	INPATIENT	69	7492	1643	46	48		9,298
antibiotics	INPATIENT - SAME DAY	186	7963	425	186	23956	1706	34,422
antibiotics	INPATIENT	122	5729	419	70	52		6,392
concomitant cv	INPATIENT - SAME DAY	20	4127	208	64	16613	558	21,590
concomitant cv	INPATIENT	13	2829	207	11	31		3,091
antidiabetics	INPATIENT - SAME DAY	11	1574	85	19	1280	61	3,030
antidiabetics	INPATIENT	6	1051	84	6	<5		1,142
Other	INPATIENT - SAME DAY	5	1039	76	19	3491	175	4,805
Other	INPATIENT	<5	784	76	<5	10		860

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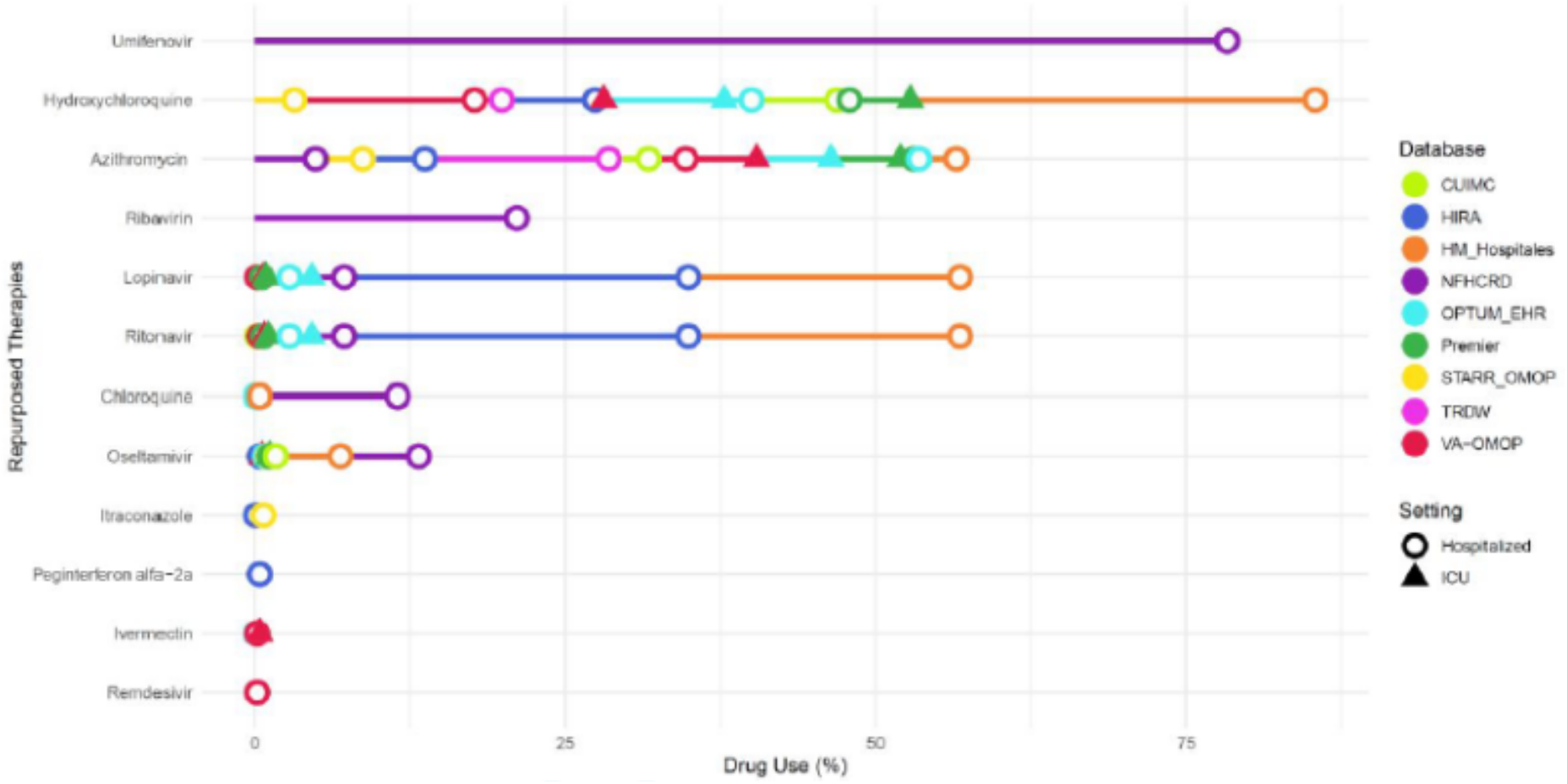
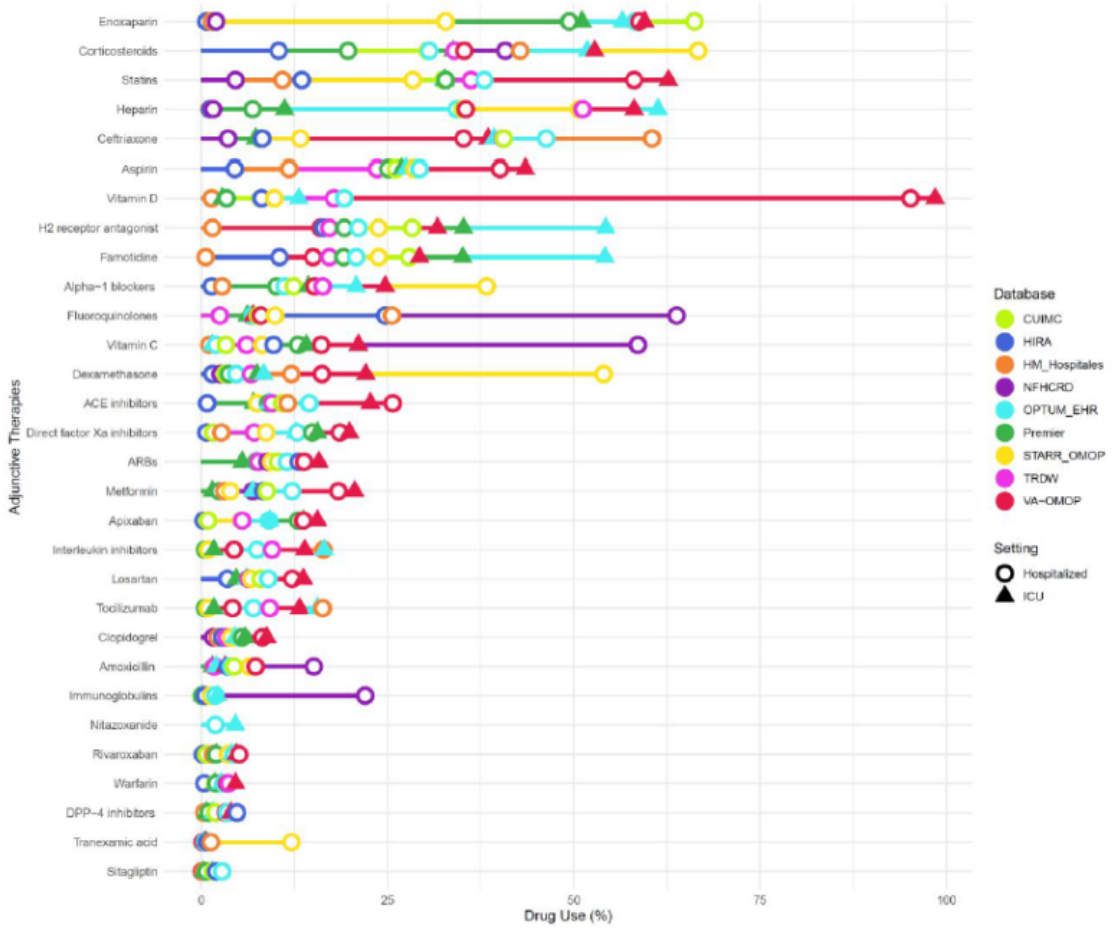
Pop-level Drug Utilisation – inpatient data
Antivirals/repurposed therapies



Pop-level Drug Utilisation – inpatient data
Adjunctive/concomitant therapies



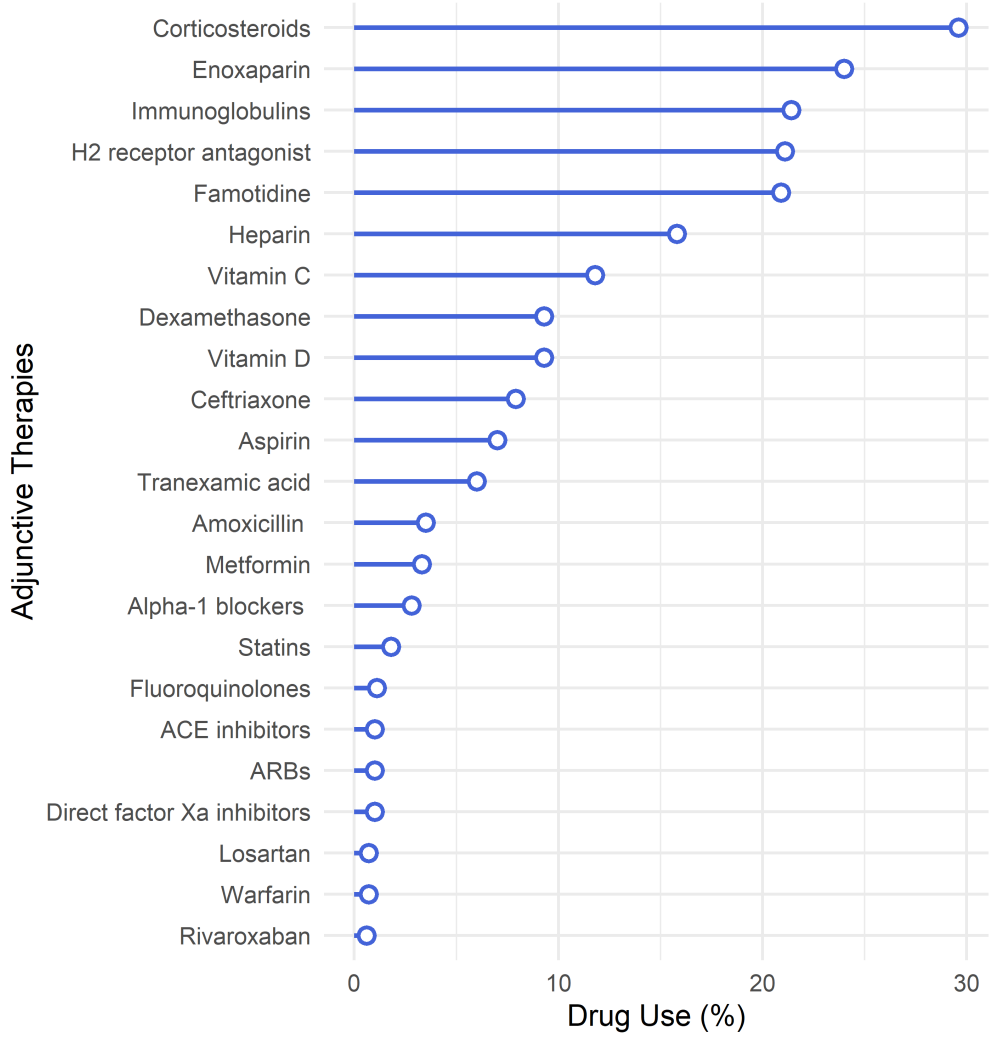
- Great heterogeneity in the use of concomitant therapies

- Very common:
  - Antithrombotics/anticoagulants
  - Antibiotics
  - Immune-based rx (mostly corticosteroids)

DUS in Pregnant women hospitalized with COVID19

- Charybdis - drug utilization in 2,031 pregnant women hospitalized with COVID19

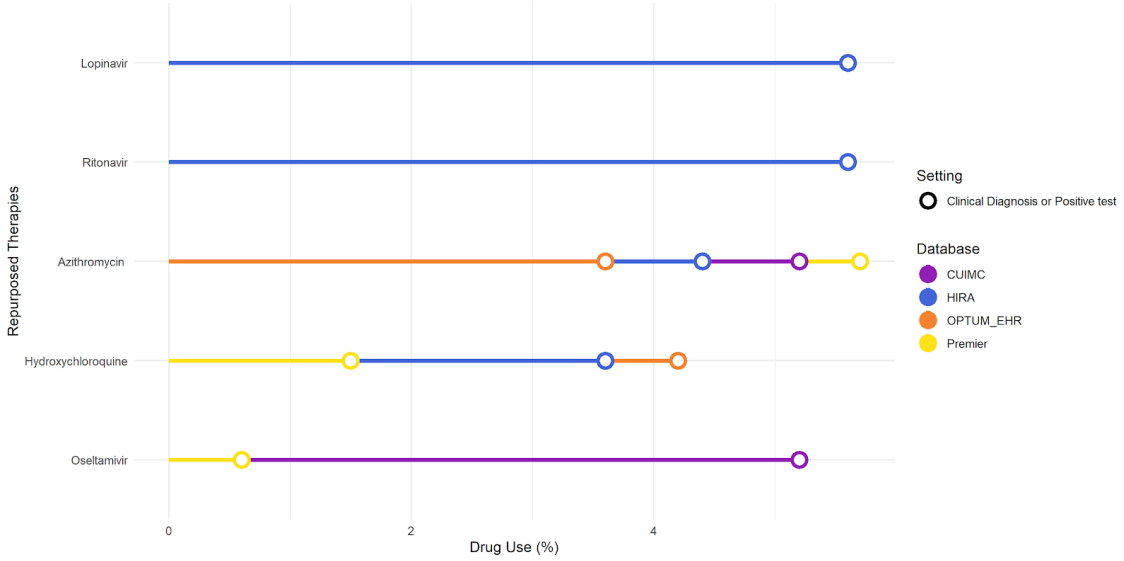
- Substantial use of corticosteroids, antithrombotics, antibiotics, vitamins …

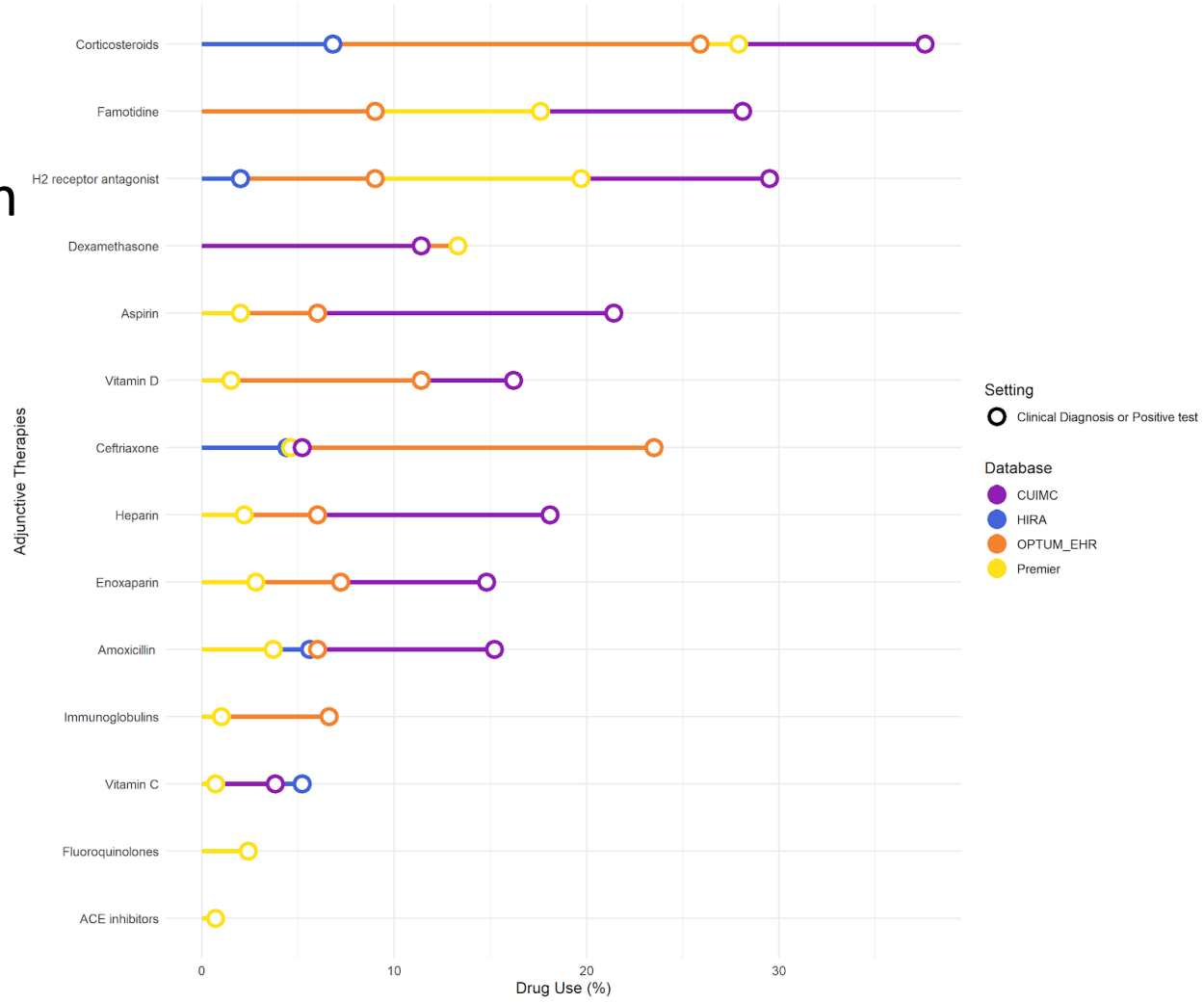


DUS in children/adolescents hospitalized with COVID19

- Antivirals (<10%), systemic steroids (6.8% to 37.6%), famotidine (9.0% to 28.1%), and antithrombotics eg heparin (2.2% to 18.1%)

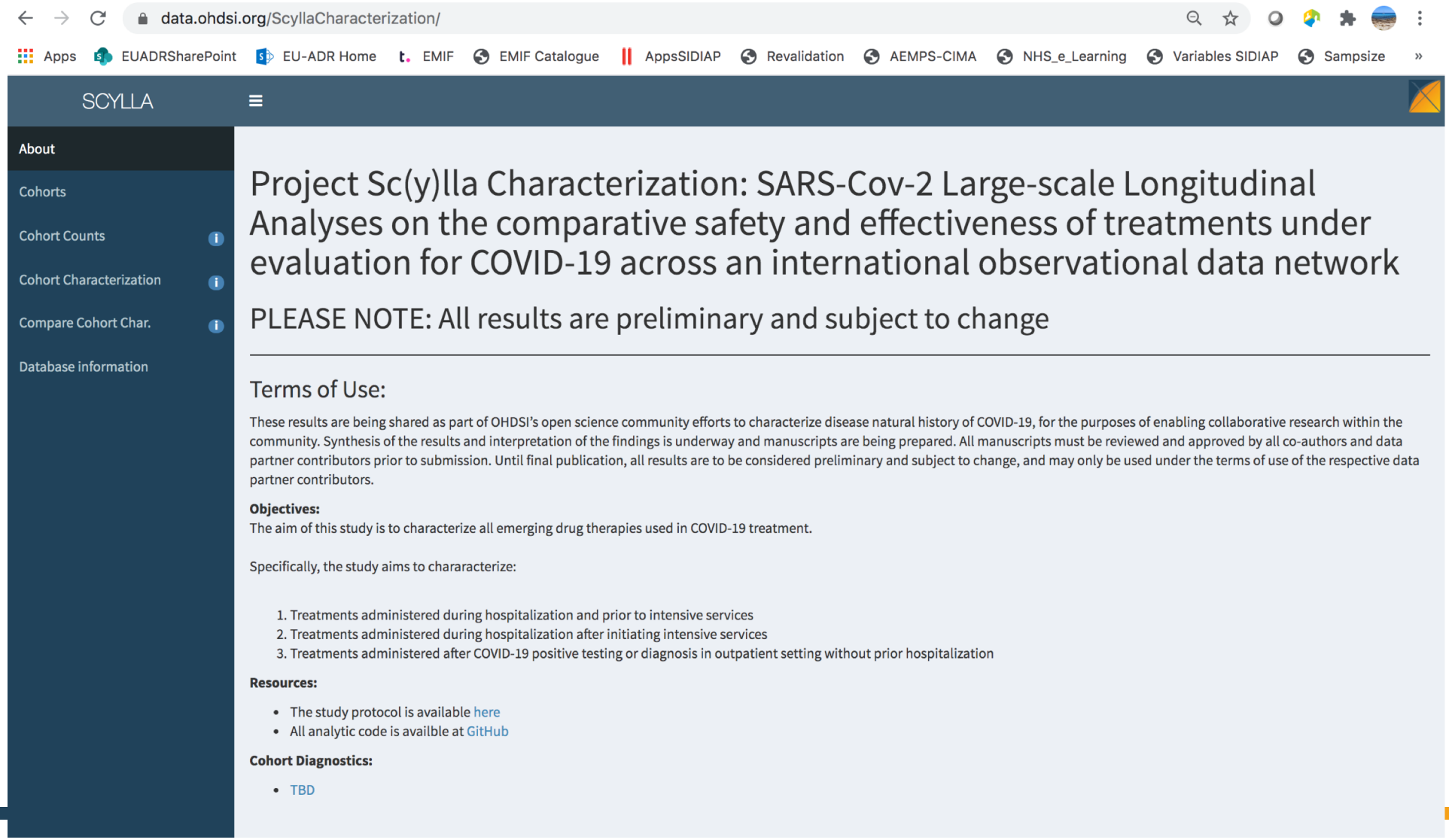
- Antibiotics, vitamin supplements and immunoglobulins were also used.



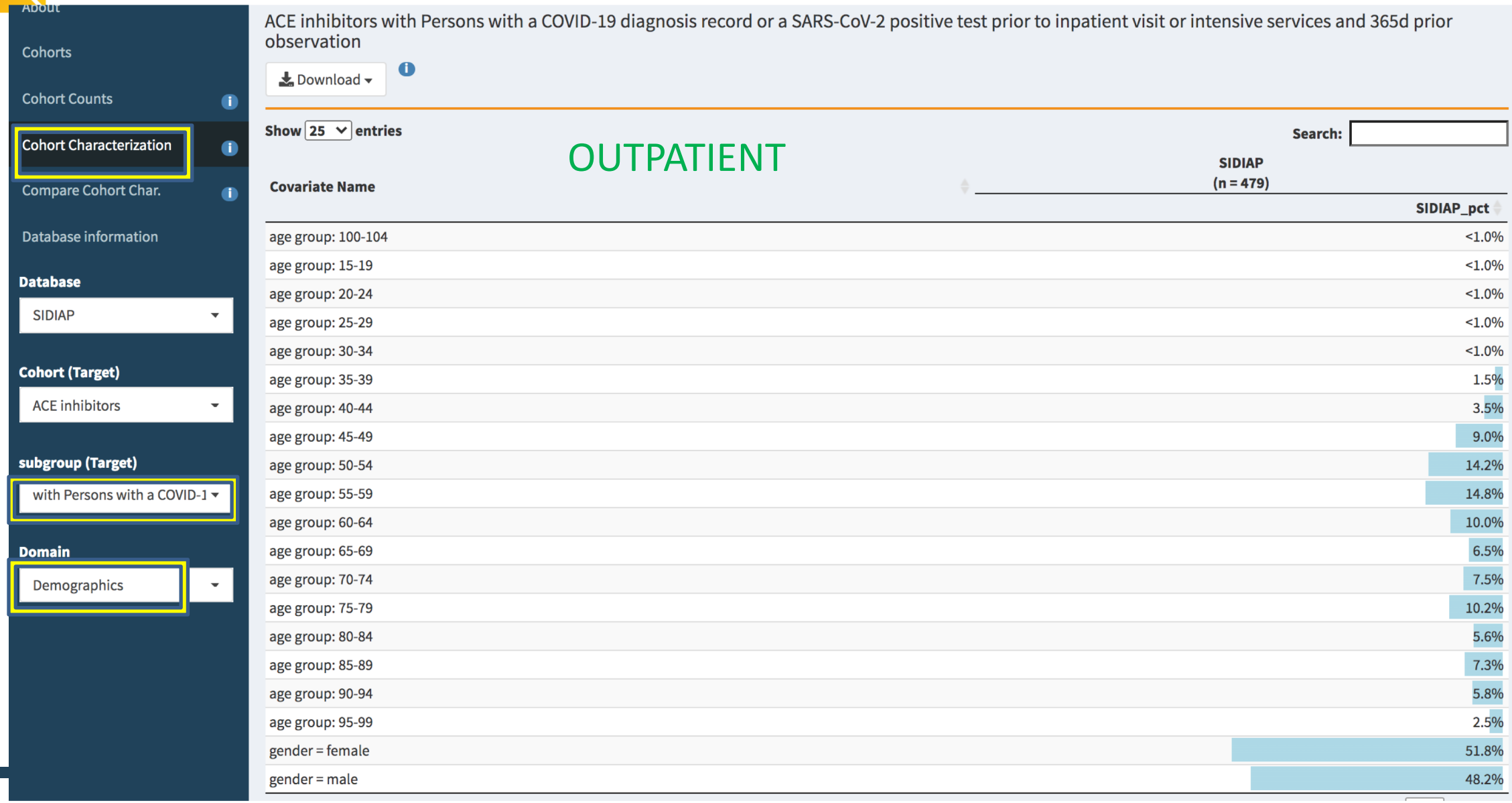


Patient-level DUS – web app

data.ohdsi.org/ScyllaCharacterization/



Setting-specific characterization -demographics

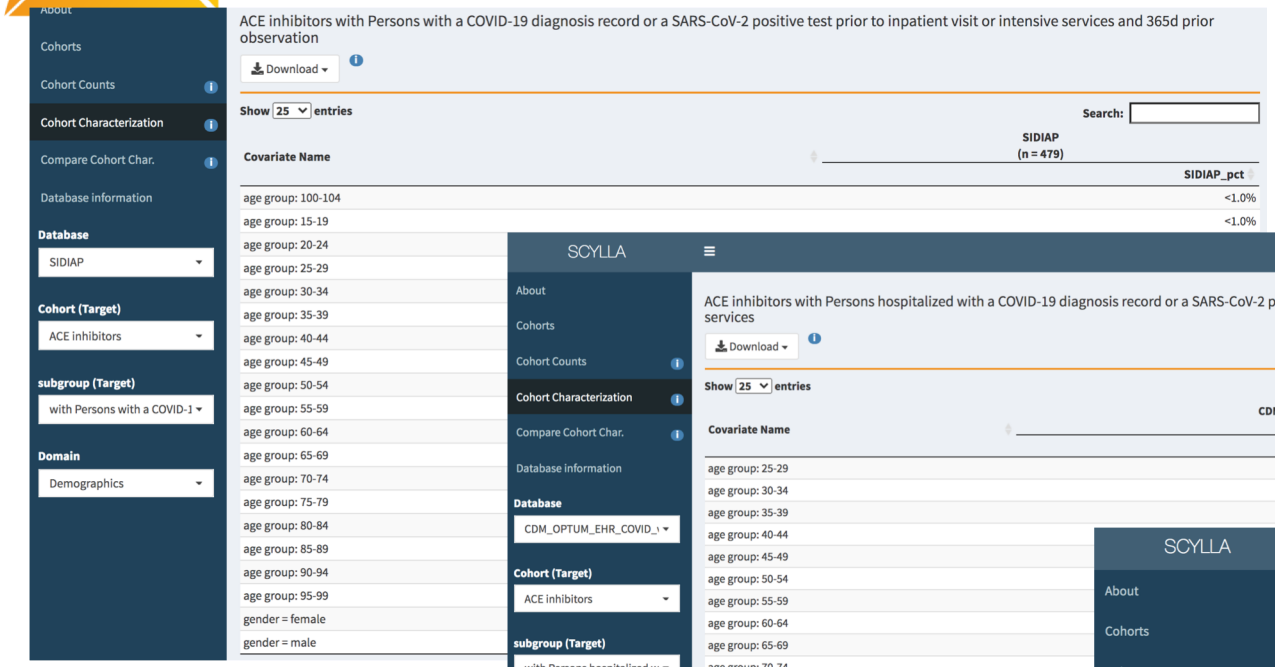


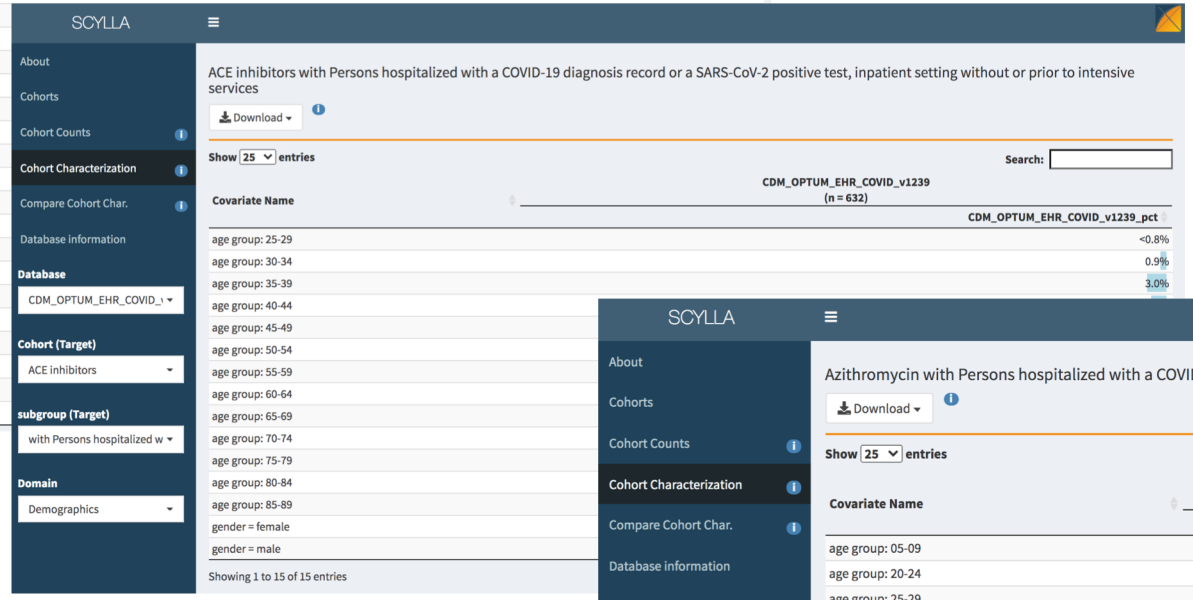
Setting-specific characterization – BY SETTING

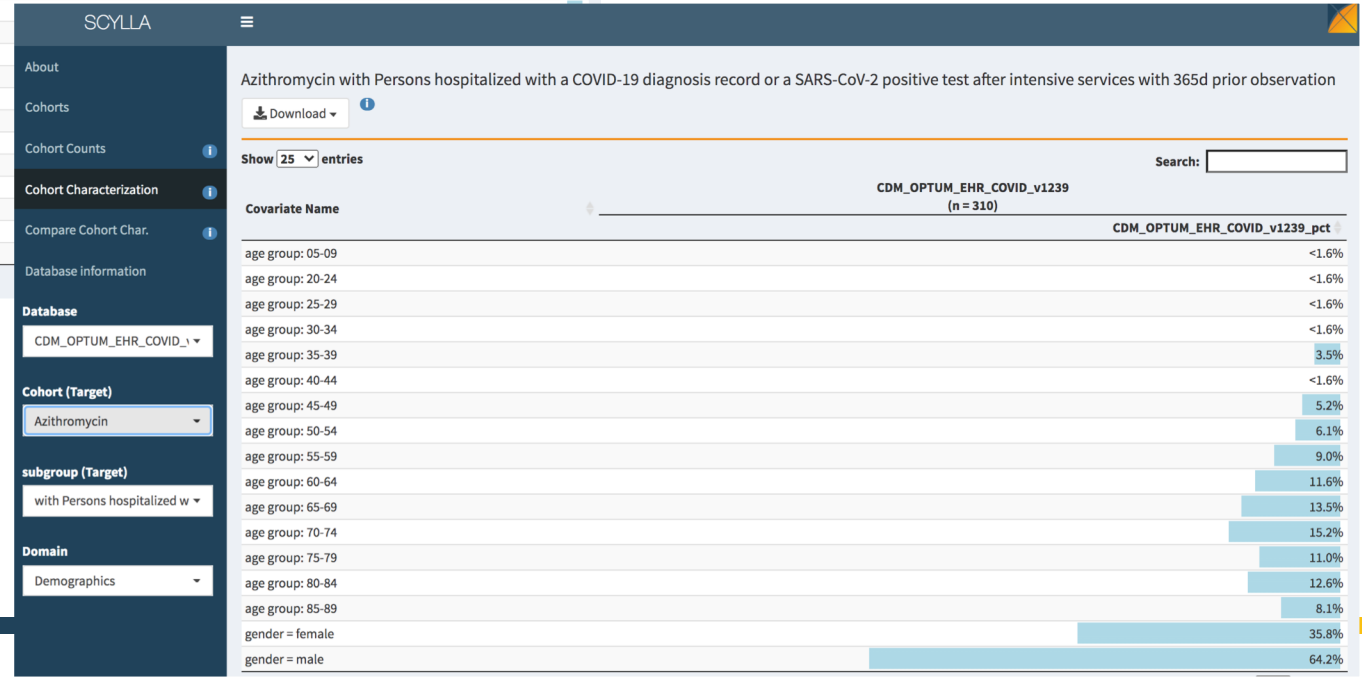
OUTPATIENT

INPATIENT

INTENSIVE SERVICES







Drug and setting-specific, across data source characterisation

Cohort Characterization

Compare Cohort Char.

Database information

Database

HM, IPCI, cdm_health_verity

Cohort (Target)

dexamethasone

subgroup (Target)

with Persons hospitalized w

Domain

Demographics

INPATIENT, DEXAMTH

Show 25 entries

Search:

Covariate Name	CDM_OPTUM_EHR_COVID_v1239 (n = 222)	cdm_premier_covid_v1260 (n = 1,020)	HM (n = 216)
	CDM_OPTUM_EHR_COVID_v1239_pct	cdm_premier_covid_v1260_pct	HM_pct
age group: 00-04	<2.3%	2.6%	
age group: 05-09	<2.3%	<0.5%	
age group: 10-14	<2.3%	<0.5%	
age group: 15-19	<2.3%	0.8%	
age group: 20-24	2.7%	2.0%	
age group: 25-29	3.2%	4.2%	
age group: 30-34	5.0%	4.1%	
age group: 35-39	5.4%	4.7%	<2.3%
age group: 40-44	5.0%	5.4%	<2.3%
age group: 45-49	5.4%	6.9%	5.6%
age group: 50-54	6.8%	7.2%	5.1%
age group: 55-59	12.2%	9.4%	9.7%
age group: 60-64	9.0%	9.7%	8.8%
age group: 65-69	9.0%	9.9%	14.8%
age group: 70-74	12.2%	8.1%	13.9%
age group: 75-79	8.1%	8.0%	13.4%
age group: 80-84	4.5%	7.4%	9.7%
age group: 85-89	7.7%	6.6%	6.5%
age group: 90-94		2.3%	9.7%
age group: 95-99			<2.3%
gender = female	59.5%	49.5%	31.0%
gender = male	40.5%	50.5%	69.0%

DB and drug-specific, across setting …
Premier, DEXA, inpatient pre vs post-ICU initiators

Compare Cohort Char.

Database information

Database

cdm_premier_covid_v126(

Cohort (Target)

dexamethasone

subgroup (Target)

with Persons hospitalized w

Cohort (Comparator)

dexamethasone

subgroup (Comparator)

with Persons hospitalized w

Domain

Demographics

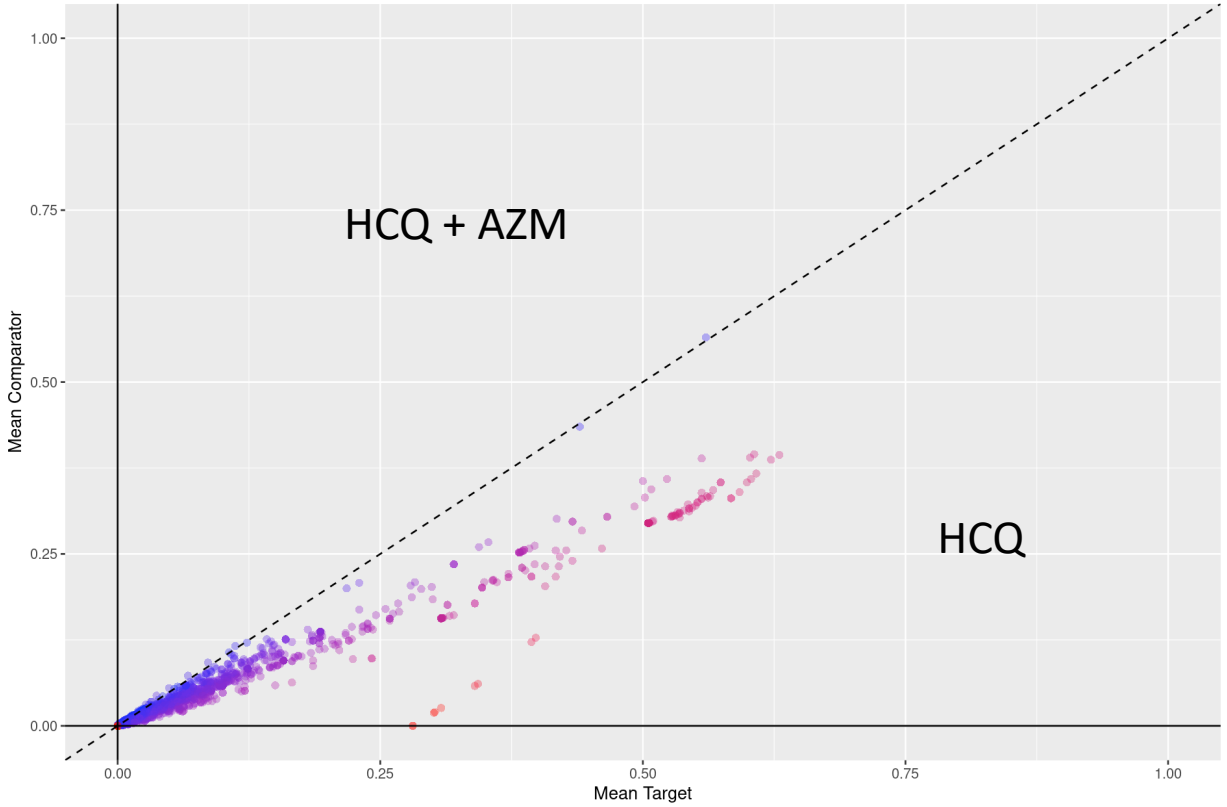
Table Plot

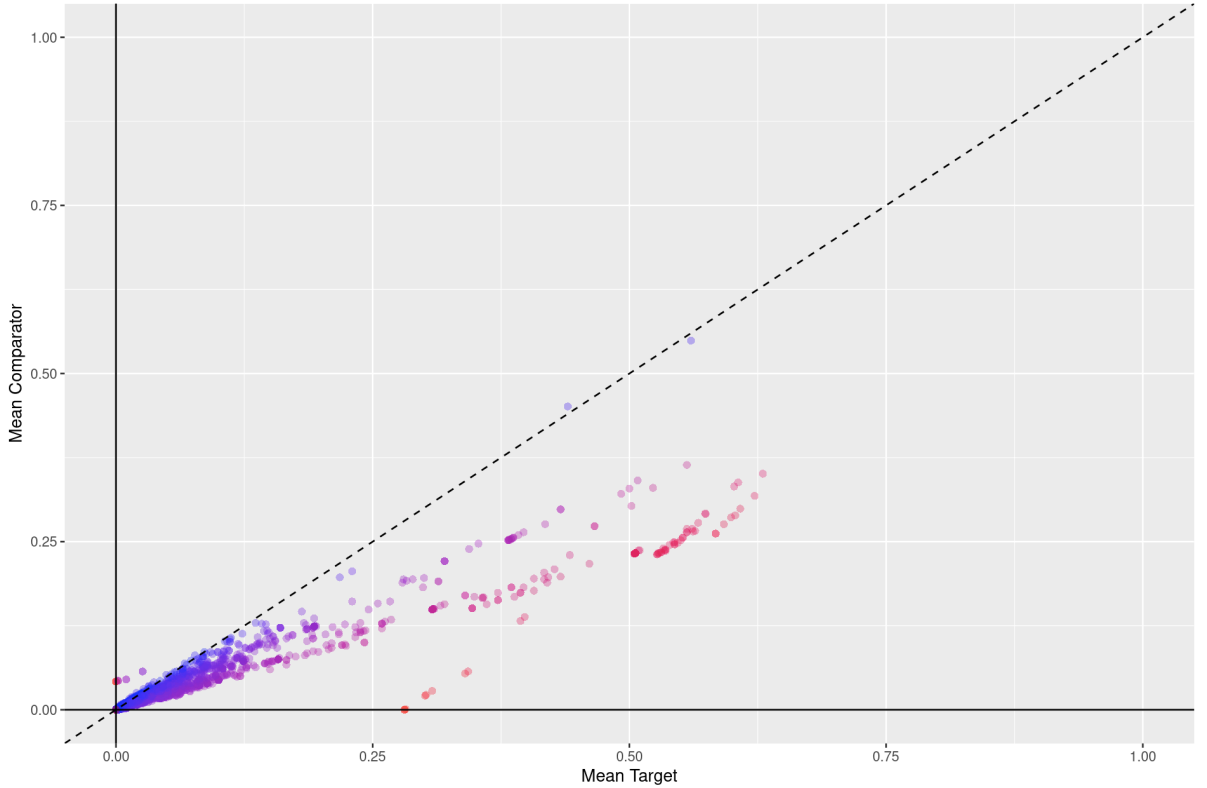
Show 25 entries

Search:

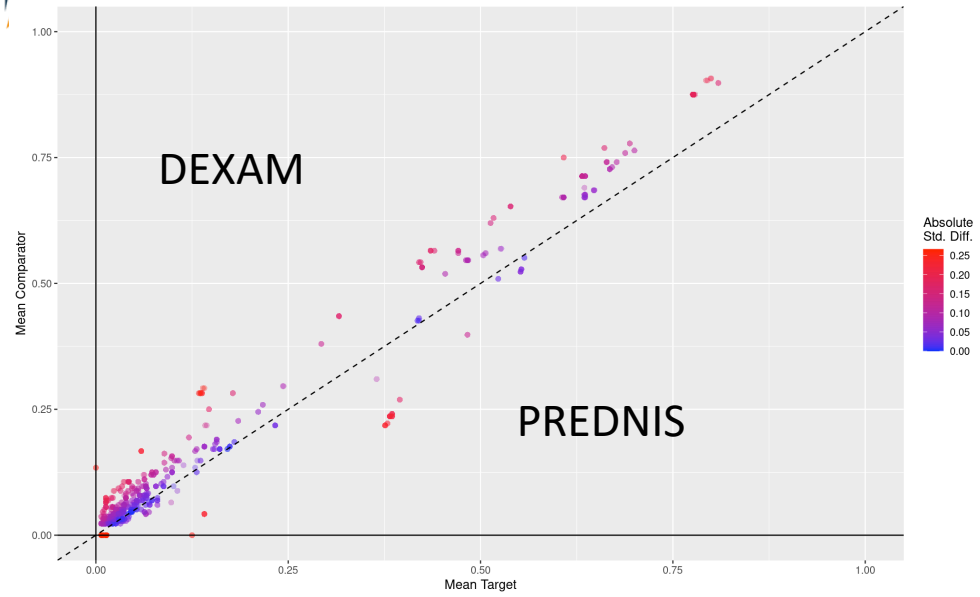
Covariate name	Mean Target	SD Target	Mean Comparator	SD Comparator	StdDiff
age group: 00-04	2.6%	0.16	3.8%	0.19	0.05
age group: 05-09	<0.5%		<0.6%		
age group: 10-14	<0.5%		<0.6%		
age group: 15-19	0.8%	0.09	<0.6%		
age group: 20-24	2.0%	0.14	1.4%	0.12	-0.03
age group: 25-29	4.2%	0.20	1.0%	0.10	-0.14
age group: 30-34	4.1%	0.20	1.5%	0.12	-0.11
age group: 35-39	4.7%	0.21	4.2%	0.20	-0.02
age group: 40-44	5.4%	0.23	4.3%	0.20	-0.04
age group: 45-49	6.9%	0.25	5.1%	0.22	-0.05
age group: 50-54	7.2%	0.26	7.8%	0.27	0.02
age group: 55-59	9.4%	0.29	11.7%	0.32	0.05
age group: 60-64	9.7%	0.30	12.5%	0.33	0.06
age group: 65-69	9.9%	0.30	15.1%	0.36	0.11
age group: 70-74	8.1%	0.27	11.8%	0.32	0.09
age group: 75-79	8.0%	0.27	7.9%	0.27	-0.00
age group: 80-84	7.4%	0.26	6.3%	0.24	-0.03
age group: 85-89	6.6%	0.25	3.7%	0.19	-0.09
age group: 90-94	2.3%	0.15	0.9%	0.09	-0.08
gender = female	49.5%	0.50	43.8%	0.50	-0.08
gender = male	50.5%	0.50	56.2%	0.50	0.08

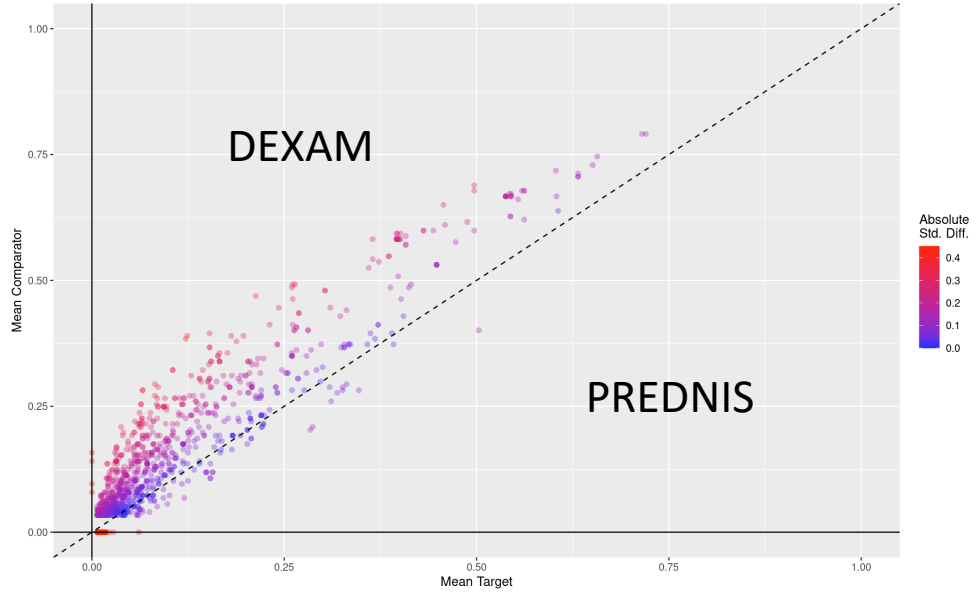
Antivirals – Premier

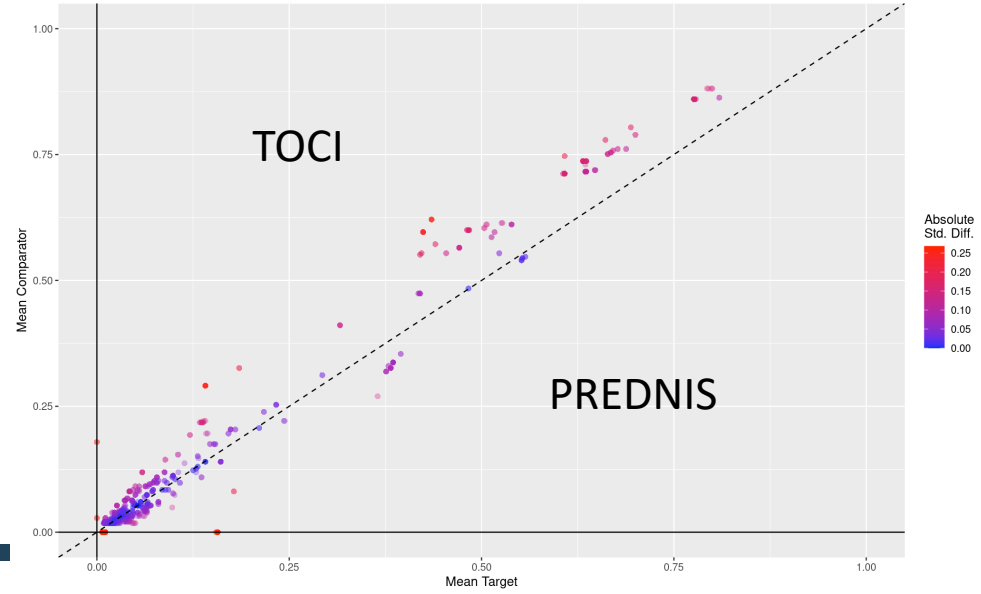


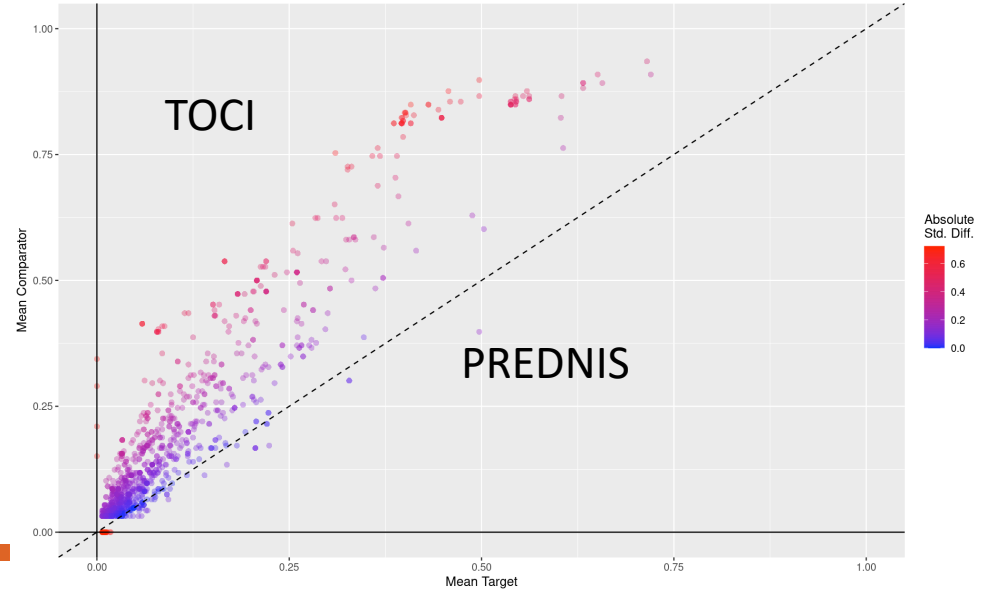


Immune-based therapies in HM (L) and Optum HER (R)









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JOIN the SCYLLA team

"She has twelve feet, all dangling in the air, and six long scrawny necks, each ending in a grisly head with triple row of fangs, set thick and close, and darkly menacing death…"

(*Odyssey*, 12:87-95)

We can't fight this monster without you!

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