In search of COVID-19 therapy: OHDSI APIS study
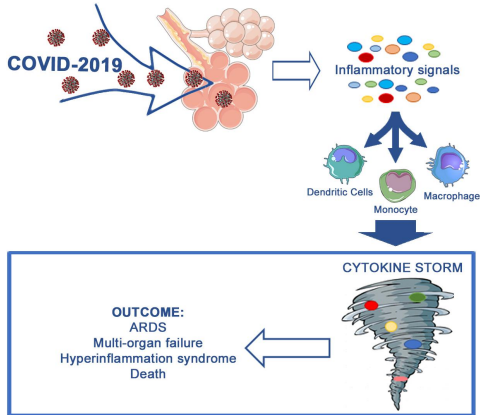
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JOHNS HOPKINS
BLOOMBERG SCHOOL
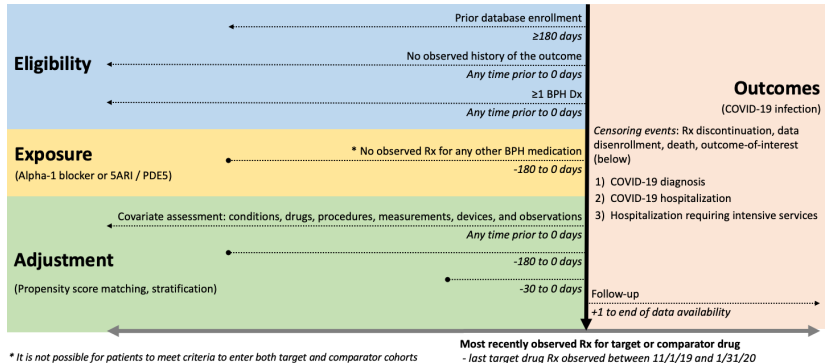of PUBLIC HEALTH

Biostatistics

Hyper-inflammation seems to account for many of severe Covid cases.

Hypothesis:
Blocking alpha-1 adrenergic receptor signaling may reduce inflammatory injury.

APIS study: risk of severe Covid symptoms among BPH patients

Among BPH patients, compare incidences of
Covid diagnosis / + Hospitalization / + Intensive services
between those on alpha-blocker and on 5ARI / PDE5.

Eligibility

Prior database enrollment
≥180 days

No observed history of the outcome
Any time prior to 0 days

≥1 BPH Dx
Any time prior to 0 days

Outcomes
(COVID-19 infection)

Censoring events: Rx discontinuation, data disenrollment, death, outcome-of-interest (below)

1) COVID-19 diagnosis
2) COVID-19 hospitalization
3) Hospitalization requiring intensive services

Exposure
(Alpha-1 blocker or 5ARI / PDE5)

* No observed Rx for any other BPH medication
-180 to 0 days

Adjustment
(Propensity score matching, stratification)

Covariate assessment: conditions, drugs, procedures, measurements, devices, and observations
Any time prior to 0 days

-180 to 0 days

-30 to 0 days

Follow-up
+1 to end of data availability

It is not possible for patients to meet criteria to enter both target and comparator cohorts

Most recently observed Rx for target or comparator drug
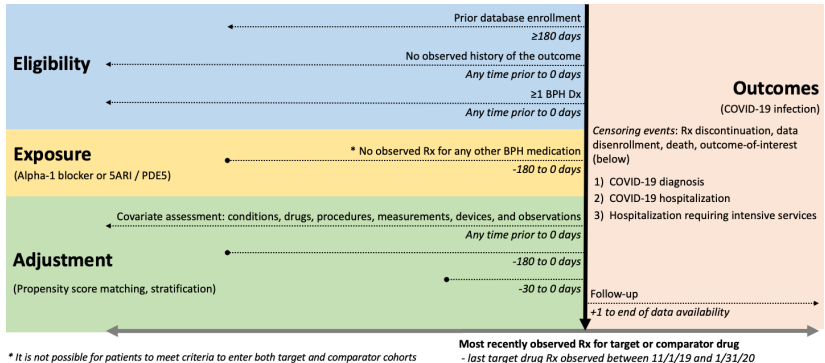- last target drug Rx observed between 11/1/19 and 1/31/20

APIS study: risk of severe Covid symptoms among BPH patients

Alpha-blocker for Palliating Inflammatory injury Severity study

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Covid diagnosis / + Hospitalization / + Intensive services

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Adjustment
(Propensity score matching, stratification)
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Most recently observed Rx for target or comparator drug
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Example cohort definition in the study protocol:

1. COVID-19 conditions

Concept Id	Concept Name	Domain	Vocabulary	Excluded	Descendants	Mapped
439676	Coronavirus infection	Condition	SNOMED	NO	YES	NO
4100065	Disease due to Coronaviridae	Condition	SNOMED	NO	YES	NO
37311060	Suspected disease caused by 2019-nCoV	Observation	SNOMED	NO	YES	NO
37311061	Disease caused by 2019-nCoV	Condition	SNOMED	NO	YES	NO

2. SARS-CoV-2 positive test measurement pre-coordinated

Concept Id	Concept Name	Domain	Vocabulary	Excluded	Descendants	Mapped
37310282	2019 novel coronavirus detected	Measurement	SNOMED	NO	YES	NO

3. SARS-CoV-2 test measurement

Concept Id	Concept Name	Domain	Vocabulary	Excluded	Descendants	Mapped
756055	Measurement of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	Measurement	OMOP Extension	NO	YES	NO
37310281	2019 novel coronavirus not detected	Measurement	SNOMED	YES	YES	NO

OHDSI study R package: deployed locally by data-holders

ohdsi-studies / **Covid19SusceptibilityAlphaBlockers**

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aki-nishimura Combine three outcome risk info into one table   c8bdad8 17 days ago   ⏱ **100 commits**

📁 Documents	Update protocol	3 months ago
📁 R	Replace OT results with IIT ones for Optum	2 months ago
📁 extras	Combine three outcome risk info into one table	17 days ago
📁 inst	Change shinyName of target and comparator	last month
📁 man	Update with Roxygen re-run	2 months ago
📄 .Rbuildignore	give better name	5 months ago
📄 .Rprofile	put files in the correct place	5 months ago
📄 .gitignore	profile the likelihood function	5 months ago
📄 Covid19SusceptibilityAlphaBlockers....	give better name	5 months ago
📄 DESCRIPTION	Update with Roxygen re-run	2 months ago
📄 HydraConfig.json	Finish replacing package name throughout repo	5 months ago
📄 NAMESPACE	Update with Roxygen re-run	2 months ago
📄 README.md	add link to protocol	5 months ago
📄 study_package_readme.md	Give more informative name to study package readme	5 months ago

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Contributors 2

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OHDSI COVID-19 Studyathon: Alpha-1 blocker for Palliating Inflammatory injury Severity (APIS) study

Multiple outcomes / databases / analyses — all at once

OHDSI-style evidence generation:

- 3 outcomes — diagnosis, hospitalization, intensive service
- 6 database — SIDIAP, VA, CUIMC, OpenClaims, Optum
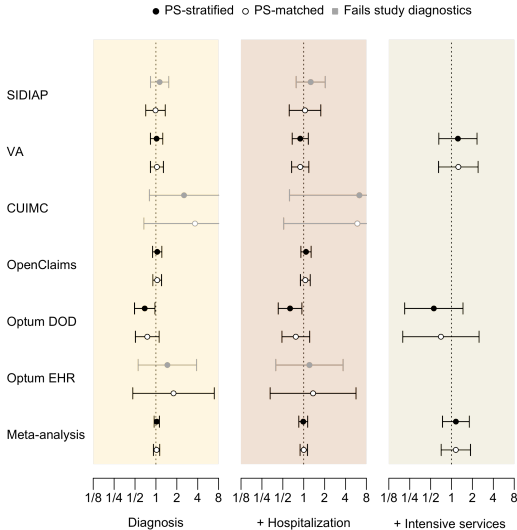- 2 analysis plans — stratified, matched

	Patients		Time (years)		Diagnosis		Hospital		Intensive		MDRR (Diagnosis)
	T	C	T	C	T	C	T	C	T	C	
Stratified analysis											
SIDIAP	11,793	1,318	4,162	471	334	51	132	20	0	0	1.61
VA	360,802	54,723	189,564	29,642	1,854	236	636	96	111	12	1.20
CUIMC	2,414	582	338	84	27	<5	16	<5	0	0	4.53
OpenClaims	1,995,594	366,734	817,994	160,225	4,809	767	2,621	407	0	0	1.11
Optum DOD	241,842	39,032	56,438	9,613	193	47	131	35	18	6	1.69
Optum EHR	15,275	2,136	1,031	149	50	7	32	5	<5	0	3.10
Matched analysis											
SIDIAP	8,994	1,315	3,211	471	275	51	115	20	0	0	1.59
VA	312,522	54,642	165,688	29,600	1,485	236	495	96	92	12	1.21
CUIMC	1,873	520	261	74	18	<5	11	<5	0	0	6.58
OpenClaims	1,873,014	365,534	774,635	159,742	4,351	764	2,361	407	0	0	1.11
Optum DOD	218,032	38,988	51,451	9,602	175	47	118	35	18	6	1.69
Optum EHR	12,303	2,114	848	148	33	7	19	5	<5	0	3.50

Emulating randomization via large-scale propensity score model

Propensity score method groups patients into strata,
within which their clinical characteristics are balanced.

Characteristic	VA					
	Before stratification $N = 360,802$ (T)		and	After stratification $54,723$ (C)		
	T (%)	C (%)	SDf	T (%)	C (%)	SDf
Medical history: General						
Chronic liver disease	2.6	1.5	0.08	2.5	2.3	0.01
Chronic obstructive lung disease	15.7	14.3	0.04	15.6	15.6	0.00
Dementia	3.9	6.0	-0.10	4.1	4.3	-0.01
Diabetes mellitus	32.8	31.0	0.04	32.5	32.8	0.00
Hyperlipidemia	48.7	48.3	0.01	48.6	48.3	0.01
Hypertensive disorder	58.6	57.0	0.03	58.4	58.1	0.01
Obesity	12.3	8.8	0.11	11.8	11.7	0.00
Renal impairment	14.2	14.5	-0.01	14.2	14.2	0.00
Medication use						
Antiinflammatory and antirheumatic products	43.6	37.2	0.13	42.7	42.8	0.00
Antineoplastic agents	4.8	4.5	0.01	4.8	4.7	0.00
Antithrombotic agents	39.6	40.1	-0.01	39.7	39.7	0.00
Drugs used in diabetes	32.3	29.7	0.06	31.9	32.1	0.00
Immunosuppressants	3.5	3.0	0.03	3.4	3.3	0.00
Race						
American Indian or Alaska Native	0.6	0.6	0.01	0.6	0.6	0.00
Asian	0.6	0.7	-0.01	0.6	0.6	0.00
Black or African American	16.1	12.2	0.11	15.5	15.4	0.00
Native Hawaiian or Other Pacific Islander	0.7	0.7	0.00	0.7	0.7	0.00
White	76.1	79.7	-0.09	76.6	76.7	0.00
Other or unknown	5.9	6.2	-0.01	6.0	6.0	0.00

Results: does alpha-blocker alleviate Covid symptoms?

Confidence intervals consistently indicates "null effects."

Meta-analysis hazard estimate is also close to the null.

Thank you!

. . . and see you at future OHDSI studies ;)