ICODA
International COVID-19 Data Alliance

Session 1: Treatments of COVID19

Understanding treatments of COVID19 is of paramount importance. ICODA's first driver project (DP1) focusses on summary level data from key trials and publicly available data sources. We will first present the data assets and tools available in the workbench. Second, we'll gather several experts in the community to discuss key challenges we face and how to solve for them.

SPEAKERS

- **Névine Zariffa**
  Member of Executive Leadership Team ICODA & scientific lead of DP1
  Founder NMD Group LLC
- **Jonas Häggström**
  Chair ICODA Statistical Expert Group
  VP Global Health Cytel
- **Jaap Mandema**
  Core member of DP Project Team
  Chief Innovation Officer Certara

PANEL MEMBERS

- **Phil Ambery**
  Member DP1 Community Advisory Group (CAP)
  Global Clinical Leader AstraZeneca
- **Ben Kramer**
  Member DP1 Community Advisory Group (CAP)
  VP Medical Affairs Genentech
- **Peter Mesenbrink**
  Member ICODA Statistical Expert Group & of R&D Alliance Data Sharing SteerCo & DP1 CAP
  Executive Director Biostatistics Novartis

Agenda

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How is the Data Research Lab being constructed?

What data assets and tools are available now and soon?

Example of what can be done now:

- **High Dose Steroid**

Panel discussion

Please capture your questions and comments in the Q&A box

The International COVID-19 Data Alliance

ICODA
International COVID-19 Data Alliance

Vision 

To unite data from international clinical trials, biomedical and health research to enable discoveries that benefit all people, everywhere, by reducing the harm of the COVID-19 pandemic

Mission 

To build a trustworthy international partnership and enduring analysis infrastructure to support a rapid response to the current COVID-19 and future pandemics across the world

A Data Research Lab

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Discover data	Search relevant data sources from around the world
Request access	Request data from multiple datasets through a single mechanism
Analyse data	The Workbench provides a secure environment for analysis with a range of tools available
Federated access	If data cannot travel, federated analysis and re-combination of results can be facilitated
Collaborate	Teams of authorised researchers can work together in dedicated workspaces

Making the Data Research Lab Trustworthy

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A neutral cloud environment for scientific collaboration

- Secure, multi-tenanted project Workspaces
- Encouraging a project-based data commons model

Tools and workflow for Open Science

- Emphasis on FAIR data curation, standards and re-use
- Bringing existing code and tools – integrate and extend

Governance and security

- GDPR as the governance and security model
- Access and traceability of results and methods
- Project lead has audit on all transactions and use of data

Flexibility in data access allows more data contributors to participate

We enable data contributors to select from a menu of options to choose the approach that best aligns with their governance rules:

Level 0	Data is hosted and accessed through the Workbench. ← commitment from Pharma contributors for treatment RCTs Summary Level Data (DP1)
Level 1	Data is hosted locally by data custodian. If approved, the data extract is de-identified and transferred to the Workbench for analysis.
Level 2	Data is hosted locally by data custodian. Data stays in the local environment. If approved, federated compute launched from Workbench and analysis executed locally. Authorised results are transferred to the Workbench.

How we deliver our mission

GLOBAL REPRESENTATION	• Partners from around the world, including from low- and middle-income countries (LMICs) • Supporting reciprocity between data contributors and analysts
COLLABORATION	• Learn from and bring together existing initiatives • Work in partnership with data stewards, data contributors and data users
FACILITATE OPEN RESEARCH	• Develop interoperable technology infrastructure and tools • Focus on globally applicable data & model standards, and enable high quality reproducible research
BUILD A TRUSTWORTHY ECOSYSTEM	• Embedding public involvement and community engagement • Robust Information Governance model based on the '5 safes' framework
DRIVER PROJECT DELIVERY MODEL	• Led by research questions, demonstrating value through use cases • Scaling over time, building the number of partners, projects and available datasets

Possible research areas

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Disease and Population	Vaccines and Prophylaxis	Diagnostics	Treatments	Outcomes and residual unmet need	Other?
Transmission patterns	How to measure immunity?	How well do the tests perform?	When should I administer treatment?	What are the risk factors linked to severe outcomes?	Host virus genome interactions?
Can we predict local outbreaks	Speeding up vaccine development		How quickly to treatments work?	Long term health consequences of COVID infection	
What are the risk factors associated with severe outcomes?	Do some vaccines work better than others in patient segments?		Which treatments work best in the elderly? Renally impaired?...		
Evolution of the disease population segments?	Do some vaccines work better than others in patient segments?		Which patients benefit best from a particular treatment		
			RCT results: What is the safety and efficacy of each treatment studied?		
			How well do RCT trials translate to real-world setting?		

Summary-level Data from RCTs allow numerous investigations quickly

Randomised Controlled Trials (RCTs) offer a key source of definitive evidence for medical practice.

- Start with the highest grade trials (regulatory application or wide-scale medical practice)
- Data from graduated arms of platform trials.

Enriched Summary-level data

- Vivli and other data repositories are best for individual patient-level data (IPLD)
- Summary-level data (SLD) is not as entangled with privacy concerns, are readily useable, and can be of value to many research questions
- Beyond the text fields of ClinicalTrial.gov, press-releases and publications, we augment & enrich SDL by deploying a Data Dictionary Strategy to enable aggregation and tooling.

Data is available now and more to come soon

Data Commitment:

- Publicly available summary-level data is updated weekly by Certara in curated digitised form so it's readily useable
- A dozen pharmaceutical companies of the R&D Alliance have committed enriched summaries of the data from their randomised controlled trials (RCTs). We expect 5-8 trials by the end of 2020.
- Platform trial study teams are being approached and are receptive

Tools:

- Researchers can use ICODA supplied tools, or create their own.

COVID-19 Enriched Summary Level Data Dictionary In- hospital Setting Enables Aggregated Data Research

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Study Information

- Study name
- Study design
- Treatment arms (inc duration and dosing)
- Countries
- Inclusion/exclusion criteria
- Dates of First/last patient, first public release of information, link to any publications

Baseline Variables

- Age (by fixed intervals),
- Sex
- Race
- Ethnicity
- Duration of symptoms prior to enrollment
- Comorbidities at the time of entry to the trial
- Supplemental oxygen at time of randomization
- Oxygen saturation level
- Respiratory rate
- Smoking history
- Meds at entry
- COVID19 disease severity at presentation
- …

Efficacy Endpoints*

Number of patients and/or time to and/or duration

- 8-point scale
- NEWS and NEWS2 score
- Improvement based on 8-point scale and NEWS and NEWS2 Score
- Mechanical ventilation
- Oxygen use
- Non-invasive Ventilation/High-Flow Oxygen Use
- Mechanical Ventilation/ECMO
- Hospitalization
- Fever
- Viral clearance
- CRP
- D-dimer
- Serum ferritin
- Discharge/Ready for Discharge

Safety Endpoints*

Number of patients with

- Aes Overall
- Specifically overall
  - Cardiac
  - Gastrointestinal
  - infections and infestations
  - Metabolism
  - Renal
  - respiratory
- CTC Grade 4 AEs
- SAEs

Time to

- CTC Grade 4 AE
- Death

Exposure and Retention*

- Number of patients remaining in the trial
- Number of patients remaining on study drug

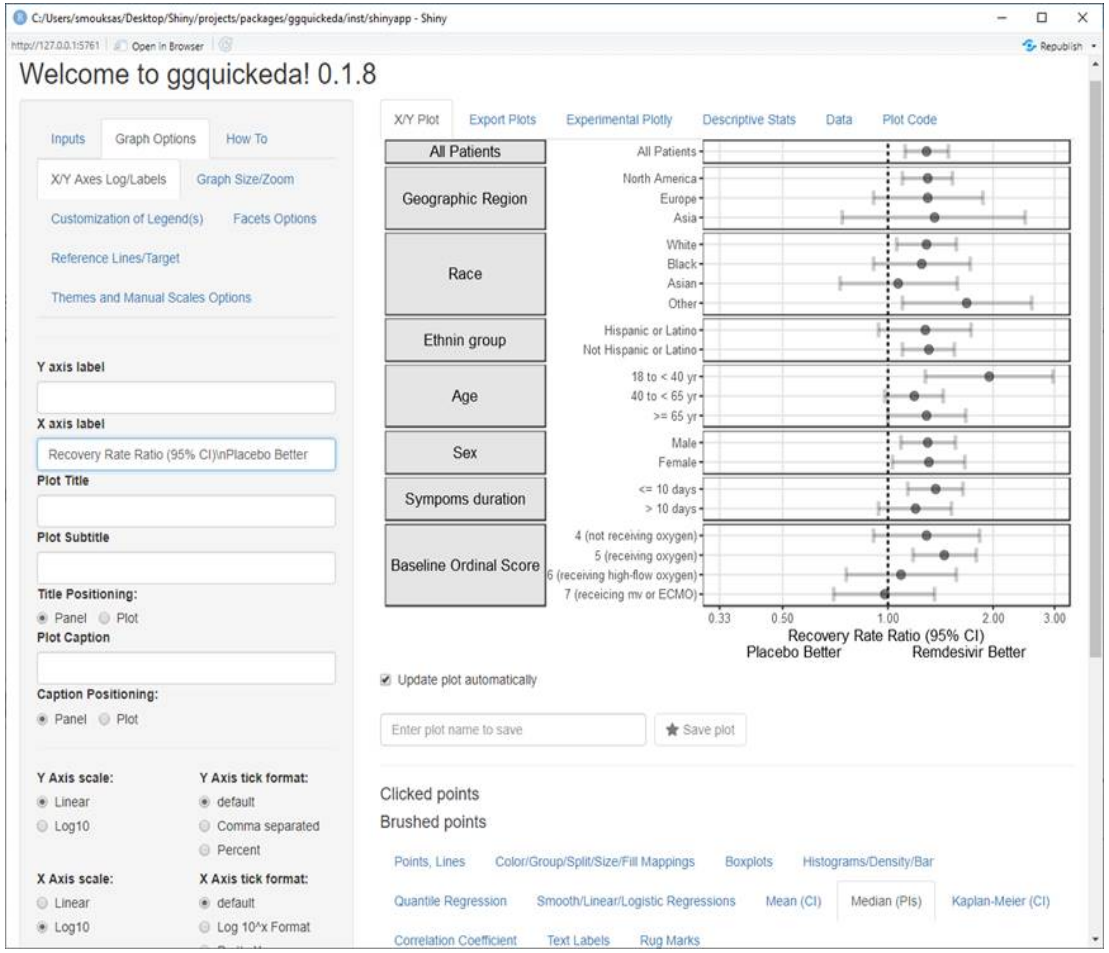
DATA DICTIONARY

Microsoft Excel Worksheet

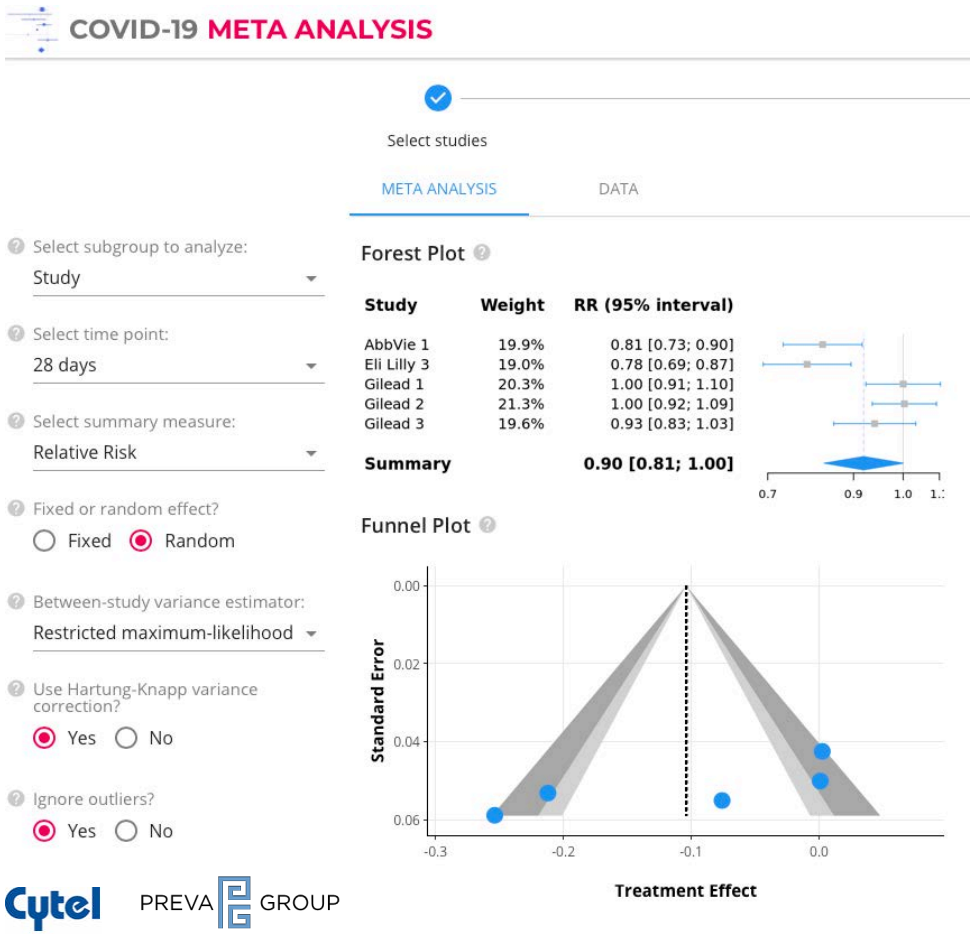
Efficacy, safety and exposure endpoints

- Baseline, Day 3, 7, 14/15, 28/29 and latest follow up time of the trial.
- By subgroups such as demog, lab based, and comorbidities

Tools to enable a quick understanding of the data: Visualization App



Tools to enable analysis of data across trials: Meta-Analysis App



CODEx

- Curated and Augmented Publicly Available Data Sources
  - publications, pre-pub, press releases, clintrial.gov, regulatory documents and others
  - patient population characteristics, concomitant treatments, statistical analyses and results (efficacy/safety/biomarkers/vital signs)
- Currently 59 RCTs (>40 K patients) and 136 Cohort studies (>147 K patients)
- Tools for Descriptive visual analytics, meta-analysis and network meta-analysis

We provide researchers with a useable snapshot of available data from which they can form full research proposals.

CODEx provides web-based access, exploration and analysis of data

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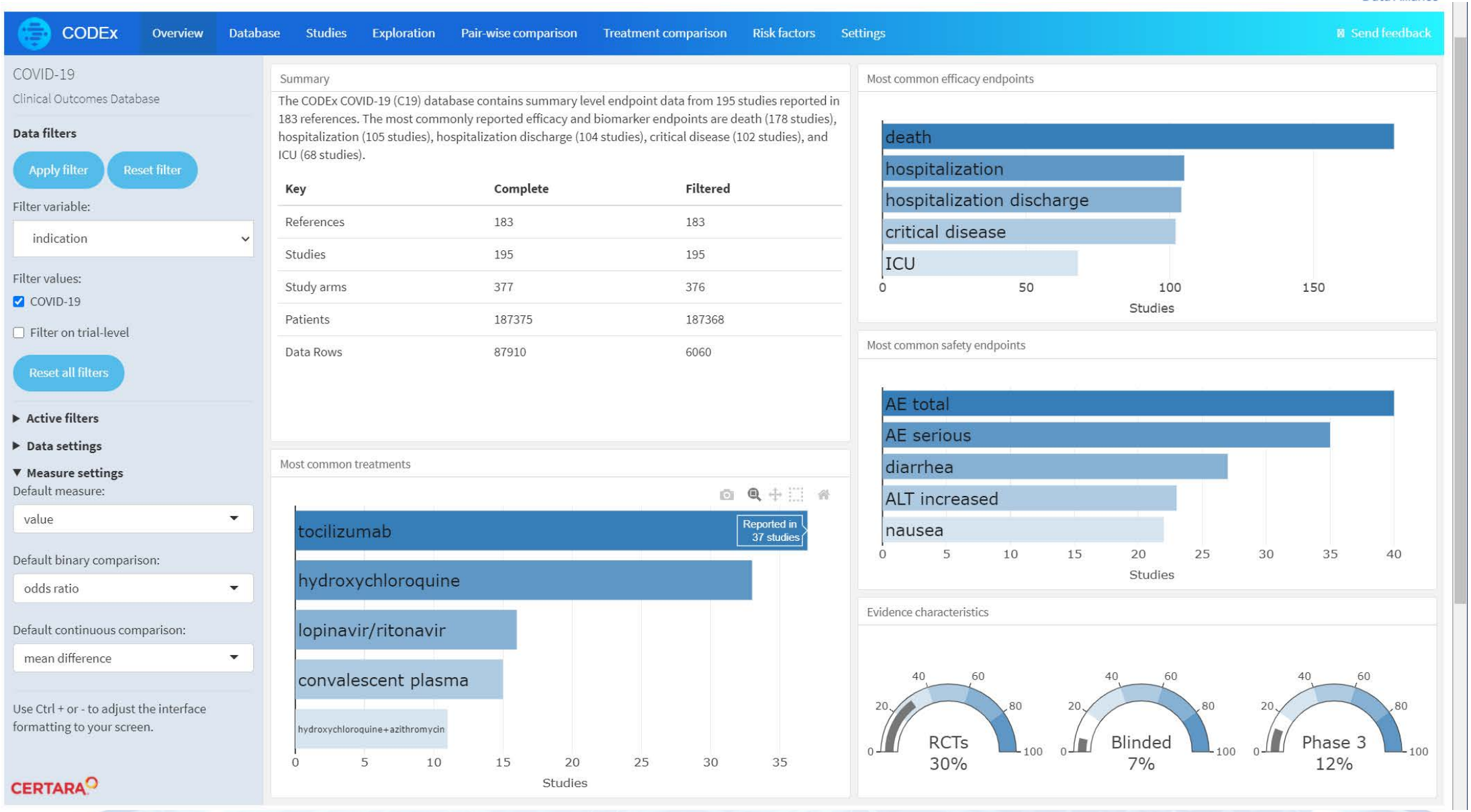

Cohort and RCT studies that evaluate a certain treatment (for example corticosteroids) can be quickly identified and reviewed

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CODEx | Overview | Database | Studies | Exploration | Pair-wise comparison | Treatment comparison | Risk factors | Settings | Send feedback

COVID-19
Clinical Outcomes Database

Data filters

Apply filter | Reset filter

Filter variable: treatment.class

Filter values: glucocorticoid

Filter on trial-level

Reset all filters

- Active filters
- Data settings
- Measure settings

Use Ctrl + or - to adjust the interface formatting to your screen.

Study details | Study summary tables | Covariate overview | Covariate correlation | Protocols

Summary columns (Select 12 columns max.):

registry.study.id | primary.drug | study.type | control.drug | arms | patients | age | males | disease.severity.group | disease.duration

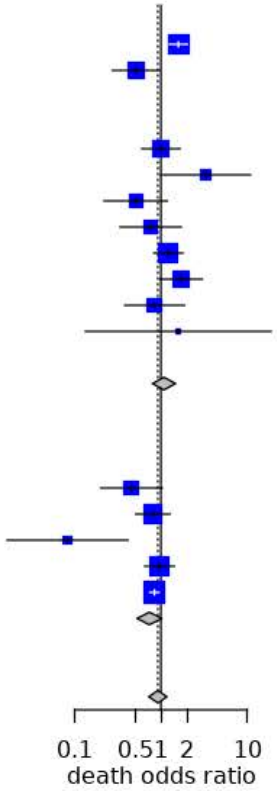
	study	registry.study.id	primary.drug	study.type	control.drug	arms	patients	age	males	disease.severity.group	disease.duration
	All	All	All	All	All	All	All	All	All	All	All
2	CAPE COVID	NCT02517489	hydrocortisone	clinical trial	control	2	149	62.2	69.8	critical	9.49
3	CoDEX	NCT04327401	dexamethasone	clinical trial	control	2	299	61.4	62.5	critical	9.49
4	Edalatifard M 2020	IRCT20200404046947N1	methylprednisolone	clinical trial	control	2	68	58.8	62.1	moderate	8.8
11	Metcovid	NCT04343729	methylprednisolone	clinical trial	placebo	2	416	55	65.3	severe	13
15	RECOVERY_dexamethasone	NCT04381936, EudraCT2020-001113-21	dexamethasone	clinical trial	control	2	6425	66.2	63.6	moderate	8.67
1	Albani F 2020	NA	corticosteroid	observational	control	2	1403	68.6	65.9	unknown	NA
5	Fernandez Cruz A 2020	EUPAS34753	corticosteroid	observational	control	2	463	65.8	68.5	moderate	10.5
6	Gong Y 2020	NA	methylprednisolone	observational	control	2	34	36.1	64.7	moderate	NA
7	Hu Y 2020	NA	corticosteroid	observational	control	2	308	52.2	47.1	mild	7
8	Liu Z 2020	NA	corticosteroid	observational	control	2	646	59.1	55.8	severe	11.7
9	Lu X 2020	NA	hydrocortisone	observational	control	2	244	57.4	51.6	moderate	NA
10	Majmundar M 2020	NA	corticosteroid	observational	control	2	205	57.6	74.6	moderate	NA
12	Mikulska M 2020	NA	tocilizumab	observational	control	4	196	67.4	67.3	severe	NA
13	Monreal E 2020	NA	methylprednisolone	observational	methylprednisolone	2	573	64.9	74.7	severe	10.3
14	PREDICO	NA	corticosteroid	observational	control	2	513	70.7	65.7	severe	6
16	SAM-COVID	NCT04355871	tocilizumab	observational	control	5	778	68.4	69.6	moderate	8.91

Showing 1 to 19 of 19 entries

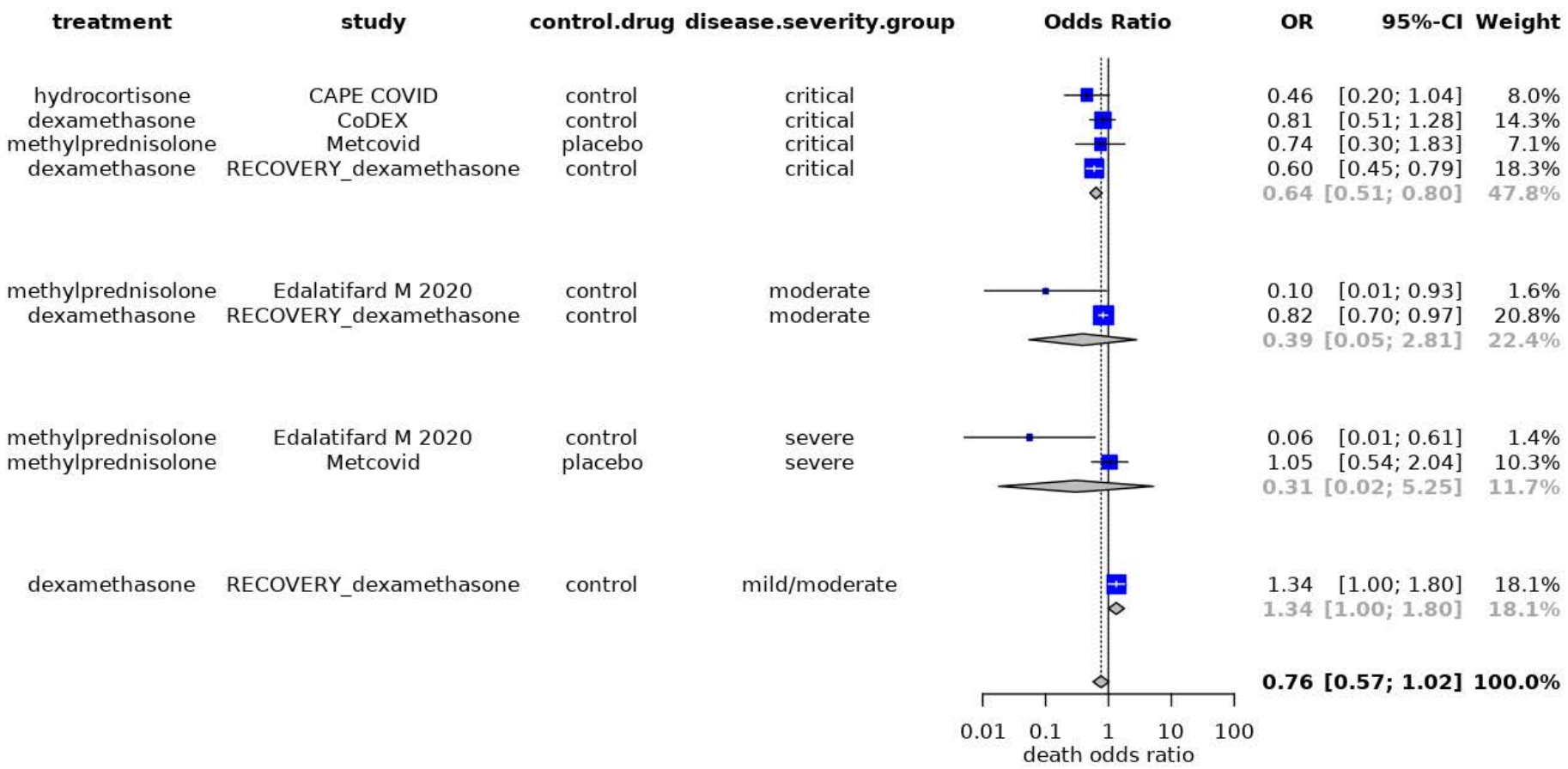
CERTARA

Endpoint data from studies (for example steroids) can be summarized with a pair-wise meta-analysis

treatment	study	disease.severity.group	control.drug	randomization	OR	95%-CI	Weight
corticosteroid	Albani F 2020	unknown	control	no	1.59	[1.25; 2.03]	11.2%
glucocorticoid	Fernandez Cruz A 2020	moderate	control	no	0.51	[0.27; 0.97]	6.8%
methylprednisolone	Gong Y 2020	severe	control	no			0.0%
glucocorticoid	Hu Y 2020	mild	control	no			0.0%
glucocorticoid	Liu Z 2020	severe	control	no	1.00	[0.60; 1.67]	8.1%
hydrocortisone	Lu X 2020	severe	control	no	3.28	[0.99; 10.90]	3.1%
glucocorticoid	Majmundar M 2020	moderate	control	no	0.51	[0.22; 1.19]	5.0%
methylprednisolone	Mikulska M 2020	severe	control	no	0.76	[0.33; 1.72]	5.2%
corticosteroid	PREDICO	severe	control	no	1.22	[0.83; 1.80]	9.5%
glucocorticoid	SAM-COVID	moderate	control	no	1.71	[0.97; 3.02]	7.5%
glucocorticoid	SAM-COVID	moderate	control	no	0.84	[0.38; 1.88]	5.3%
methylprednisolone	Wang Y 2020	severe	control	no	1.58	[0.13; 18.81]	0.9%
methylprednisolone	Zha L 2020	mild/moderate	control	no			0.0%
					1.08	[0.80; 1.47]	62.6%
hydrocortisone	CAPE COVID	critical	control	yes	0.46	[0.20; 1.04]	5.2%
dexamethasone	CoDEX	critical	control	yes	0.81	[0.51; 1.28]	8.7%
methylprednisolone	Edalatifard M 2020	moderate	control	yes	0.08	[0.02; 0.42]	1.9%
methylprednisolone	Metcovid	severe	placebo	yes	0.96	[0.65; 1.43]	9.5%
dexamethasone	RECOVERY_dexamethasone	moderate	control	yes	0.84	[0.74; 0.95]	12.2%
					0.74	[0.53; 1.03]	37.4%
					0.92	**[0.72; 1.17]**	**100.0%**

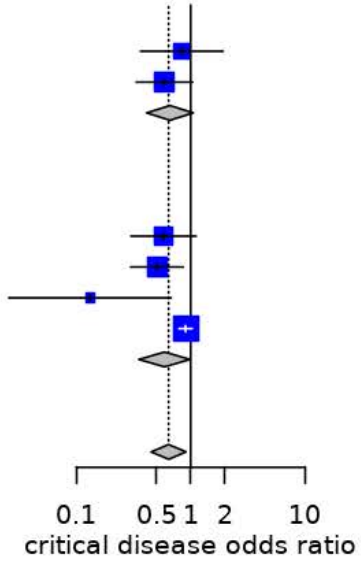


Result can be summarized by baseline patient characteristics (for example disease severity) if reported

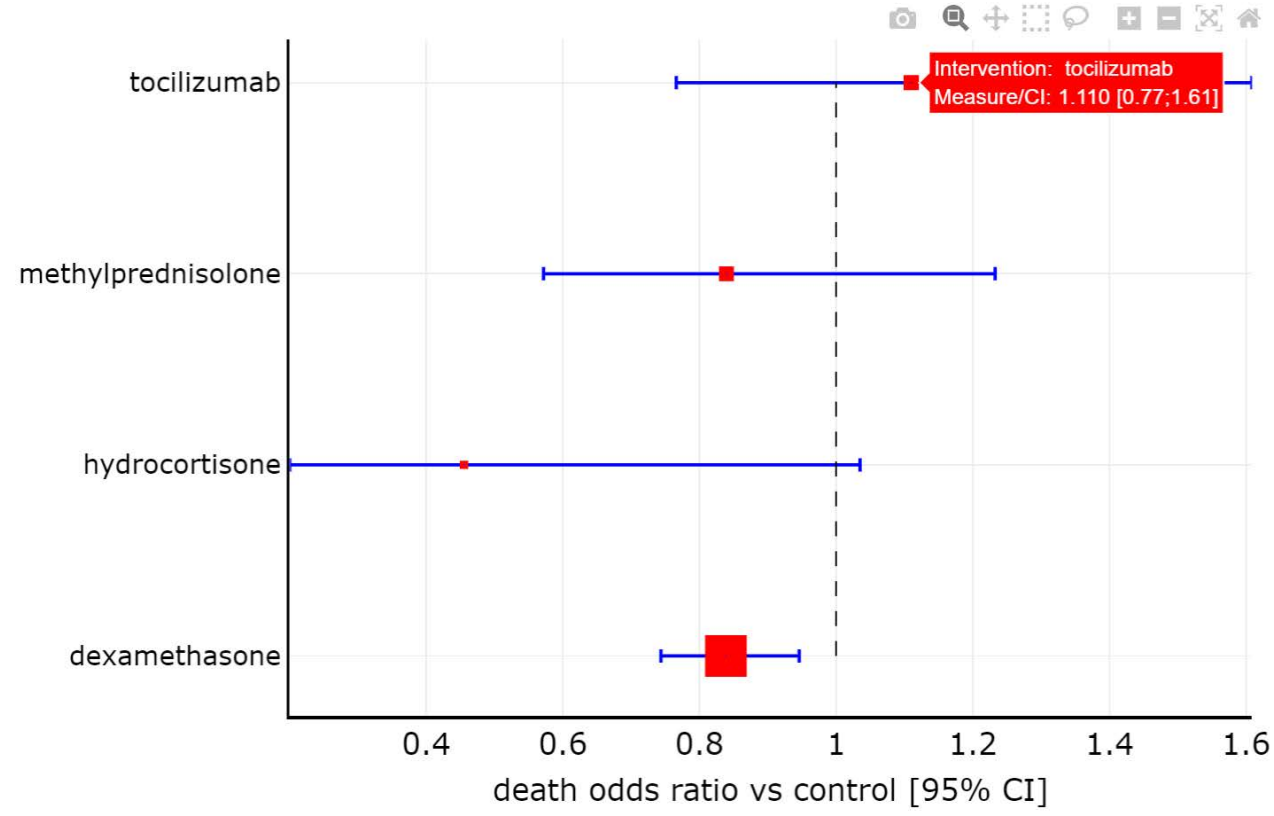


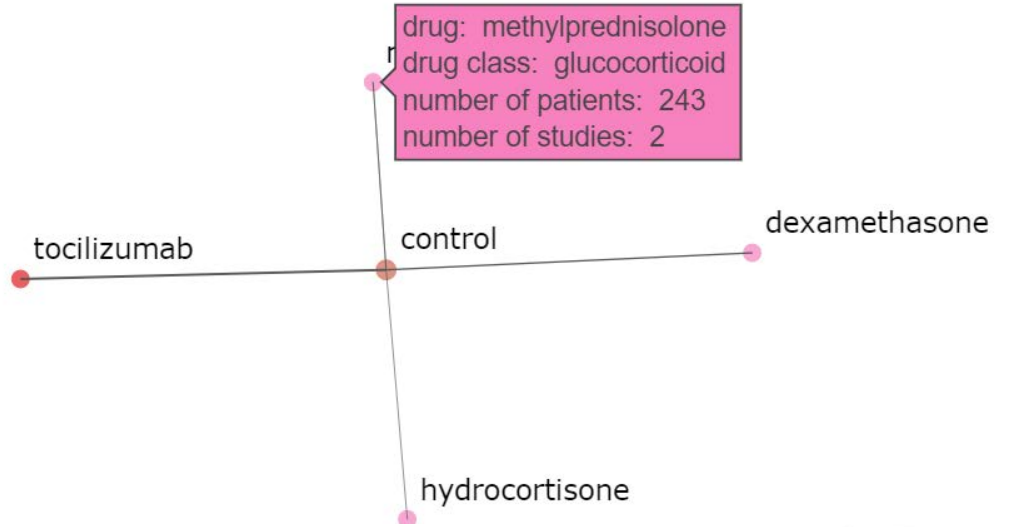
Any endpoint that is reported (for example patients with critical disease) can be evaluated

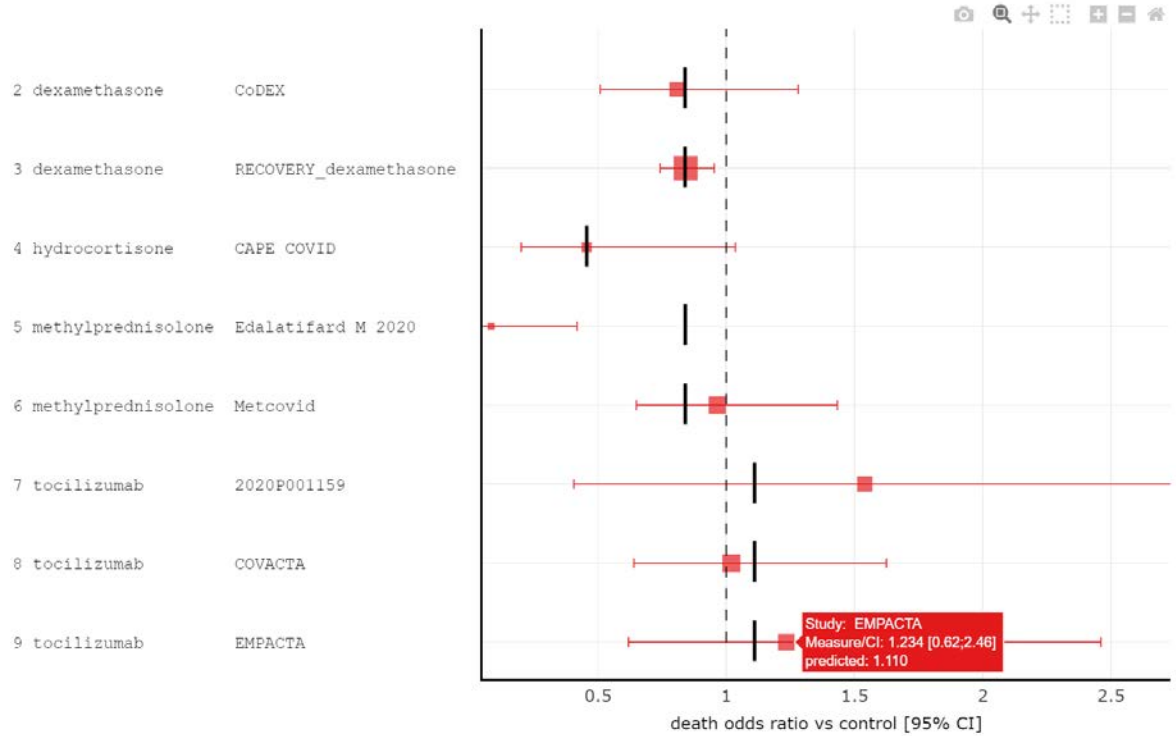
treatment	study	baseline time	control.drug	treatment.class	OR	95%-CI	Weight
tocilizumab	2020P001159	0.00 28	placebo	anti-IL-6	0.84	[0.37; 1.92]	11.7%
tocilizumab	EMPACTA	0.00 28	placebo	anti-IL-6	0.59	[0.33; 1.04]	17.9%
					0.66	[0.41; 1.05]	29.6%
hydrocortisone	CAPE COVID	81.58 21	control	glucocorticoid	0.58	[0.30; 1.12]	15.5%
dexamethasone	CoDEX	100.00 15	control	glucocorticoid	0.51	[0.30; 0.86]	19.0%
methylprednisolone	Edalatifard M 2020	0.00 3	control	glucocorticoid	0.13	[0.03; 0.68]	4.1%
dexamethasone	RECOVERY_dexamethasone	0.00 28	control	glucocorticoid	0.90	[0.79; 1.03]	31.9%
					0.59	[0.35; 0.99]	70.4%
					0.64	**[0.45; 0.91]**	**100.0%**



Treatments evaluated in RCTs can be compared in a Network Meta-Analysis







Creating a Research Community: Bright Minds Together

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The Alliance also deploys:

- Analytic toolkits, developed by experts, with training and documentation
- Proportionate reviews of research proposals and outputs
- Regular workshops with examples of best practice, including feedback to and from data researchers
- Community feedback and support.

Visit our website to become a data contributor or request access to the data

Panel Discussion

Phil Ambery
Member DP1 Community Advisory Group (CAP)
Global Clinical Leader AstraZeneca

Ben Kramer
Member DP1 Community Advisory Group (CAP)
VP Medical Affairs Genentech

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Member ICODA Statistical Expert Group & of R&D Alliance Data Sharing SteerCo & DP1 CAP
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Topics

What made you want to be a part of this initiative?

How did you convince your colleagues to contribute data?

What can we do in this sort of data research lab that we couldn't do before?

What are the key challenges we face? What do you think we can do about these?