Building and maintaining open-access platforms for living synthesis projects

Automation analysis tools

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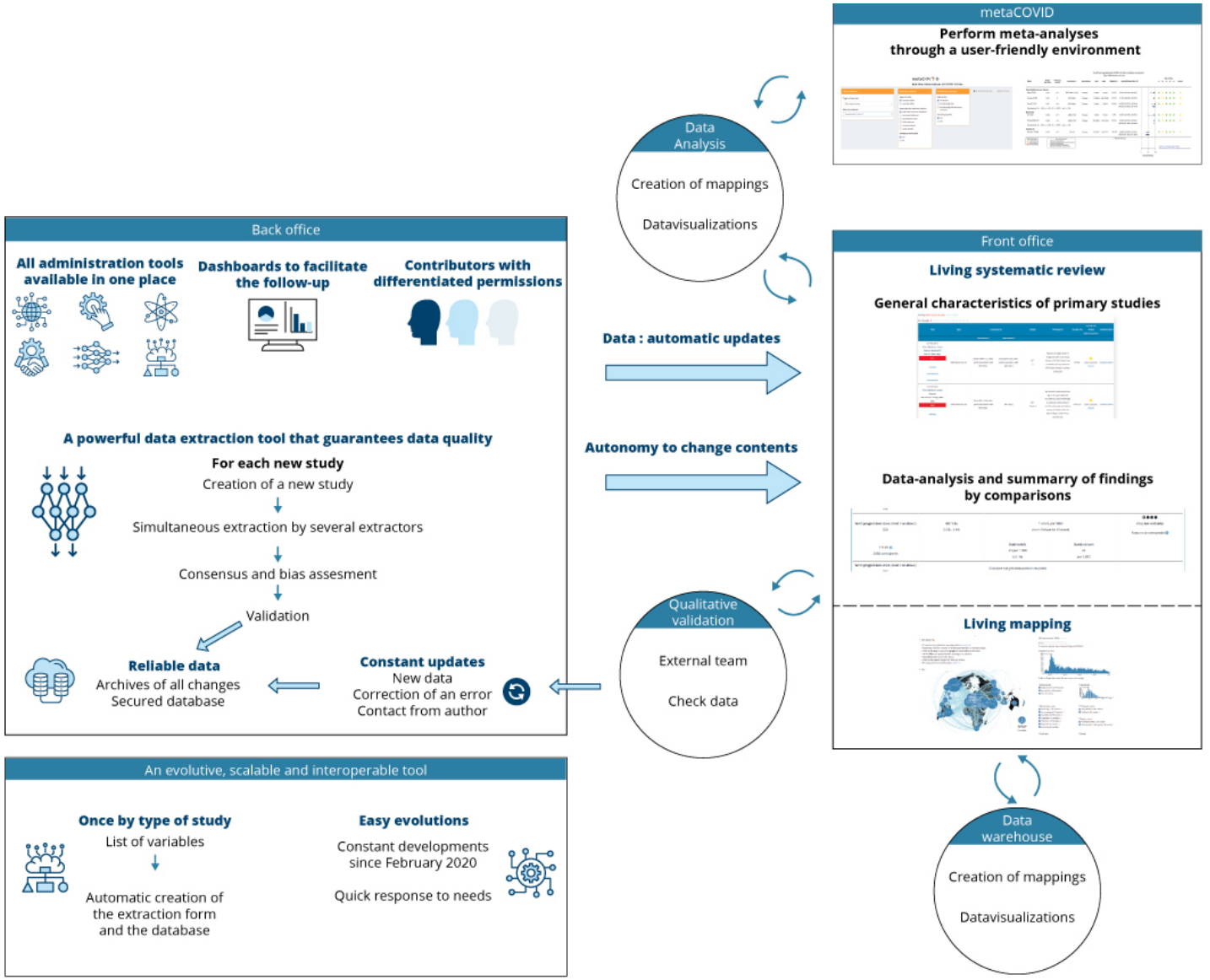
Acknowledgements: T. Yu and the COVID-NMA consortium

COVID-NMA platform



Automated tools for:

1) Mapping
2) Data Extraction
3) Pairwise meta-analysis
4) Network meta-analysis

Living Mapping of COVID-19 trials

▼ Map

▼ Table

Download the data

☐ Show full table

Treatment (per arm)	Sample size	Severity at enrollment	Sponsor/Funder	Reg. number
(1) Colchicine vs (2) Probiotics vs (3) Standard of care	150	Mild	Ain Shams University	NCT05911022
(1) Antioxidant therapy vs (2) Standard of care	85	Mild/moderate	Universitas Padjadjaran	NCT04627519
(1) Covend24 vs (2) Placebo	155	Moderate/severe	Eli Sprecher, MD	NCT04989172
(1) Bnt162b2 vs (2) Bnt162b2 vs (3) Bnt162b2 vs (4) Bnt162b2 vs (5) Mrna-1273 vs (6) Mrna-1273 vs (7) Mrna-1273 vs (8) Mrna-1273	66	Patients recovered from covid	International Network for Strategic Initiatives in Global HIV Trials (INSIGHT)	NCT04989250
(1) Flu vaccine + mrna-1273 vs (2) Flu vaccine vs (3) Mrna-1273	306	Healthy volunteers	Sanofi Pasteur, a Sanofi Company	NCT04989276
(1) Varespladib vs (2) Varespladib vs (3) Varespladib vs (4) Placebo vs (5) Varespladib vs (6) Placebo	18	Severe	Ophirex, Inc.	NCT04989991
(1) Baricitinib + remdesivir vs (2) Dexamethasone + remdesivir	382	Moderate/severe	Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders	NCT04970719
(1) Rd-x19 vs (2) Rd-x19 vs (3) Placebo	216	Mild/moderate	EmitBio Inc.	NCT04986013
(1) Pegylated interferon lambda vs (2) Placebo	763	Mild/moderate	University Health Network, Toronto	NCT04967430
(1) Olfactory training vs (2) Budesonide + olfactory training	60	Patients recovered from covid	Amanda Stapleton	NCT04984414
(1) Azithromycin + hydroxychloroquine vs (2) Hydroxychloroquine vs (3) Placebo	105	Mild	Coordinación de Investigación en Salud, Mexico	NCT04984583
(1) Bromhexine + hydroxychloroquine vs (2) Placebo	214	Health workers	Instituto Nacional de Rehabilitacion	NCT04340349
(1) Sars-cov-2 vlp vaccine-wuhan vs (2) Sars-cov-2 vlp vaccine-alpha (british) variant vs (3) Sars-cov-2 vlp vaccine-alpha variant	349	Healthy volunteers	Ihsan GURSEL, PhD, Prof.	NCT04982893
(1) Chadox1 ncov-19 + gam-covid-vac vs (2) Bbibp-corv + gam-covid-vac vs (3) Gam-covid-vac	192	Healthy volunteers	Ministerio de Salud de Ciudad Autónoma de Buenos Aires	NCT04982908
(1) Multidisciplinary rehabilitation vs (2) Standard of care	200	Patients recovered from covid	Danderyd Hospital	NCT04981333
(1) Sars-cov-2 recombinant spike protein nanoparticle vaccine (sars-cov-2 rs) vs (2) Qniv2/matrix-m1 adjuvant vs (3) Sars-cov-2 rs/matrix-m1 adjuvant	642	Healthy volunteers	Novavax	NCT04961541
(1) Hyperbaric oxygen therapy (hbo) vs (2) Standard of care	24	Patients recovered from covid	Peter Lindholm	NCT04905888
(1) Bevacizumab vs (2) Standard of care	21	Severe/critical	Maimónides Biomedical Research Institute of Córdoba	NCT04954014

VISUALISATIONS: Romain Vuillemot - LIRIS, École Centrale de Lyon; Philippe Rivière - LIRIS, VisionsCarto; Pierre Ripoll - LIRIS, INSA Lyon; Julien Barnier - Centre Max Weber, CNRS.

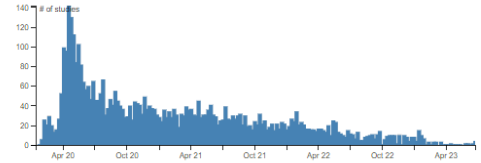
Filters

4611 selected out of 4616 trials | Reset all

Search...

Ex: Interferon, antiviral, Spain, Assistance Publique, EUCTR2020…

▼ Registration date

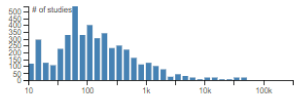


To filter by Registration dates, click and drag to create a range.

▼ Inclusion age

- ☑ minimum 18 yo (4,234 studies)
- ☑ less than 18 yo (377 studies)
- ☑ N/A (0 studies)

▼ Sample size



▼ Recruitment status

- ☑ Completed (1,634 studies)
- ☑ Not recruiting (1,028 studies)
- ☑ Recruiting (931 studies)
- ☑ Terminated (405 studies)
- ☑ Unknown (350 studies)
- ☑ Withdrawn (200 studies)
- ☑ Not reported (35 studies)
- ☑ Suspended (28 studies)

▼ Publication status

- ☑ Not published (3,697 studies)
- ☑ Published (914 studies)

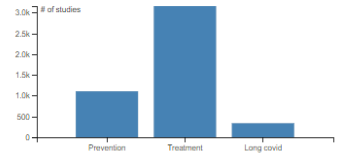
✓ Non-Published

✓ Published

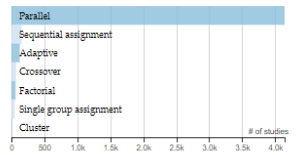
▼ Registry status

- ☑ No results posted (4,202 studies)
- ☑ Results posted in the registry (409 studies)

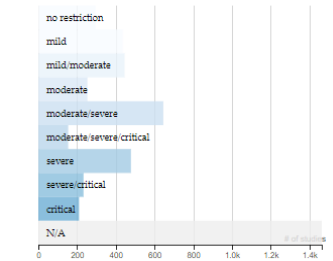
▼ Study aim



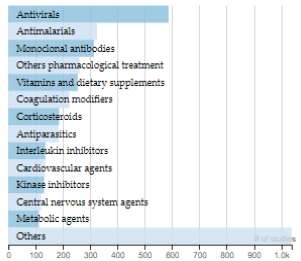
▼ Design



▼ Disease severity



▼ Type of pharmacological treatment



▼ Options

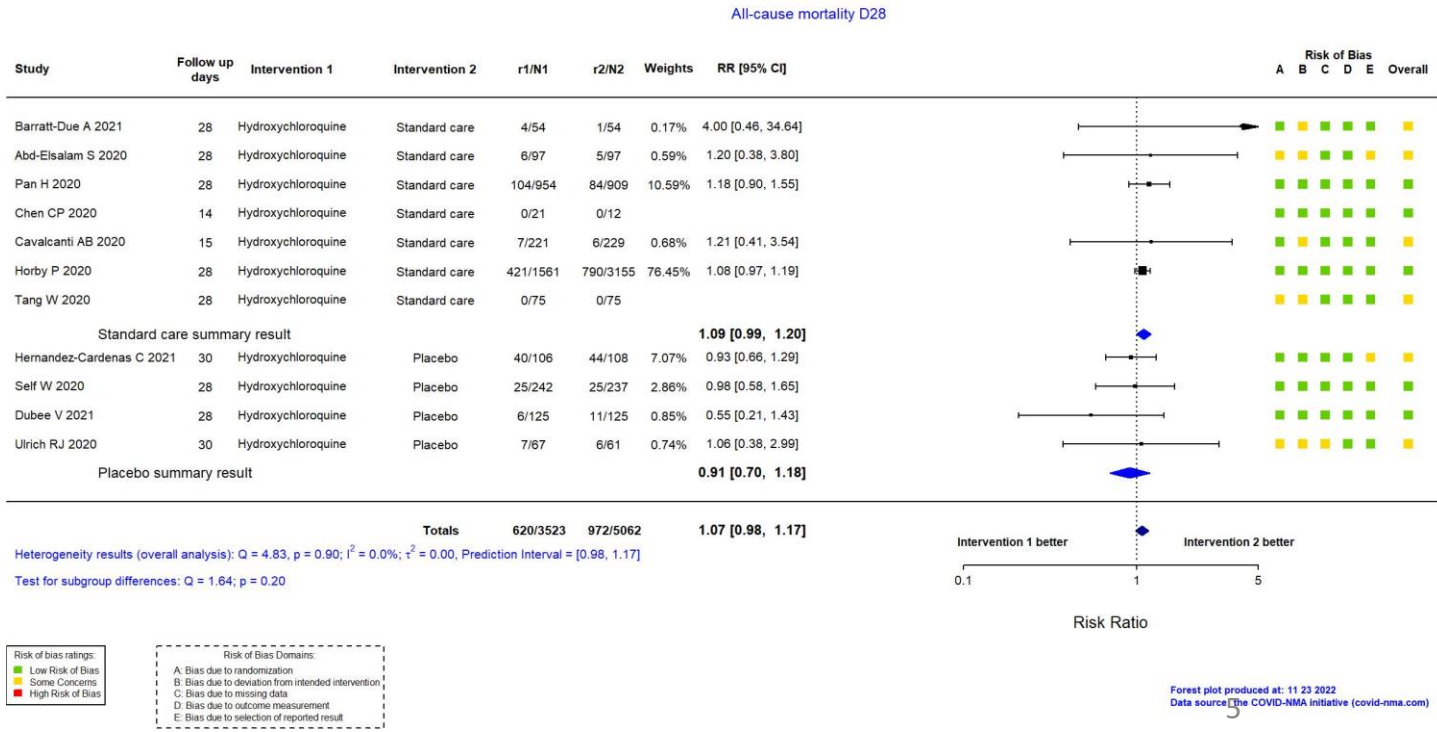
- ☐ Zoom & pan the map
- ☐ Show number of patients

Data extraction

- A semi-automated process was continuously taking place every day
  - for each new study 2 extractors had to extract the data independently by filling a pre-specified form
  - a tool was checking the entries and was returning as an output the existence or not of a consensus
  - once consensus was reached a third person was validating the extraction

- Post-validation checks
  - the generated forest plots at the analysis step were also used for checking the data
  - regular quality controls

- Due to the emergent situation small mistakes were inevitable
  - feedback from the users was also used to deal with such mistakes



Pairwise meta-analysis

Operational challenges

- During the core pandemic period we had to analyse approximately 20 studies per week
  - ~ 70 forest plots were uploaded into our platform on a weekly basis
  - workload can be very high
- Tight deadlines
  - all analyses should be posted online within the two day working framework
- The chance for either methodological or human made mistakes should be minimised
  - stakeholders and end-users will loose their trust on the platform
- Overall, the feasibility of such a project can be threatened if tasks are fulfilled manually
  - handling all the information and remaining up-to-date is very challenging
  - avoiding mistakes is almost impossible

Methodological challenges

- The results posted in the platform are non-amendable
- Stakeholders and guideline developers want to interact with the data
  - investigate the impact of trial characteristics in the results
  - produce their preferred evidence summaries
- Special analysis topics like rare events will inevitably arise with such an amount of data
  - e.g. across all trials with hospitalized patients the risk for serious adverse events is only 8%
  - in such cases the IV model is known to be problematic
  - sub-analyses should be conducted in such cases
- Accommodating such preferences through the platform is challenging

The metaCOVID application

- An R-Shiny application based on R packages metafor and meta
  - allows for a real-time analysis of COVID-19 trials based on the COVID-NMA data
  - analysis can be performed in a fast and automated way
  - allows for the flexibility to modify primary analysis

- The application follows the COVID-NMA's protocol
  - the pre-defined options are exactly the same with those used for the platform
  - special emphasis was given to the risk of bias presentation
  - findings coming from metaCOVID are based on high quality data which were validated by experts

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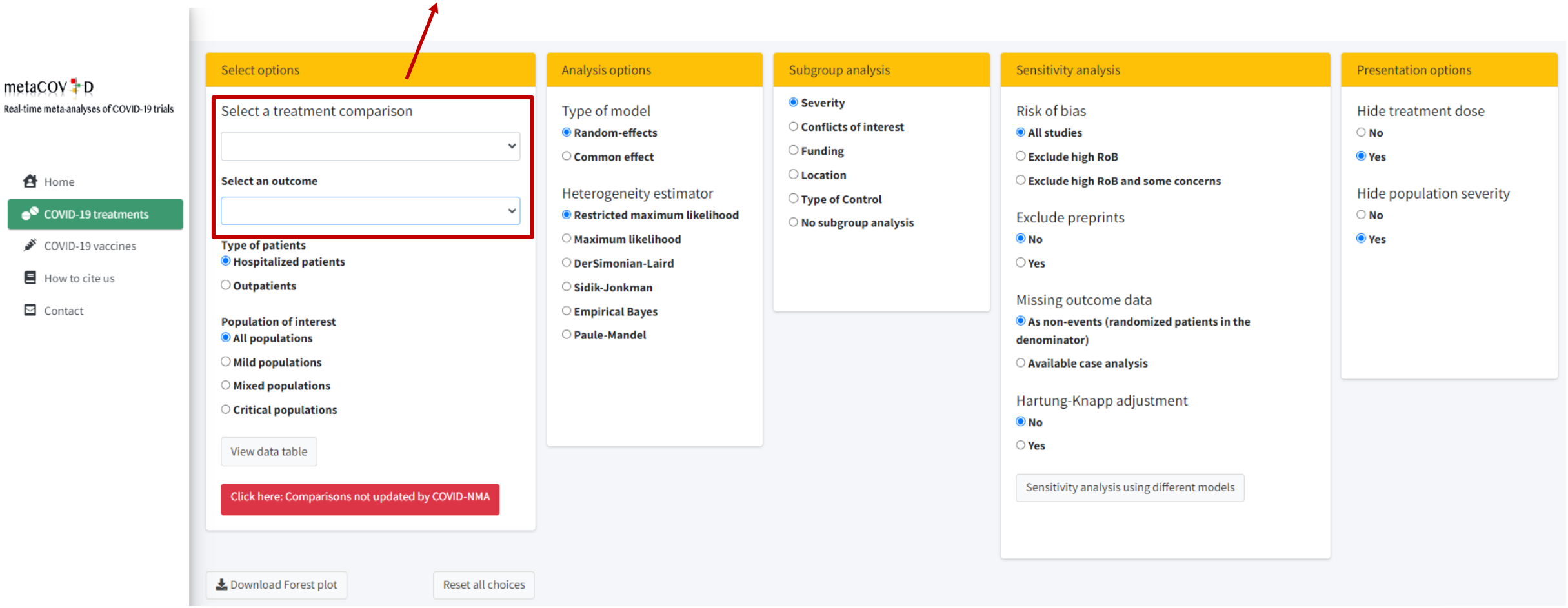
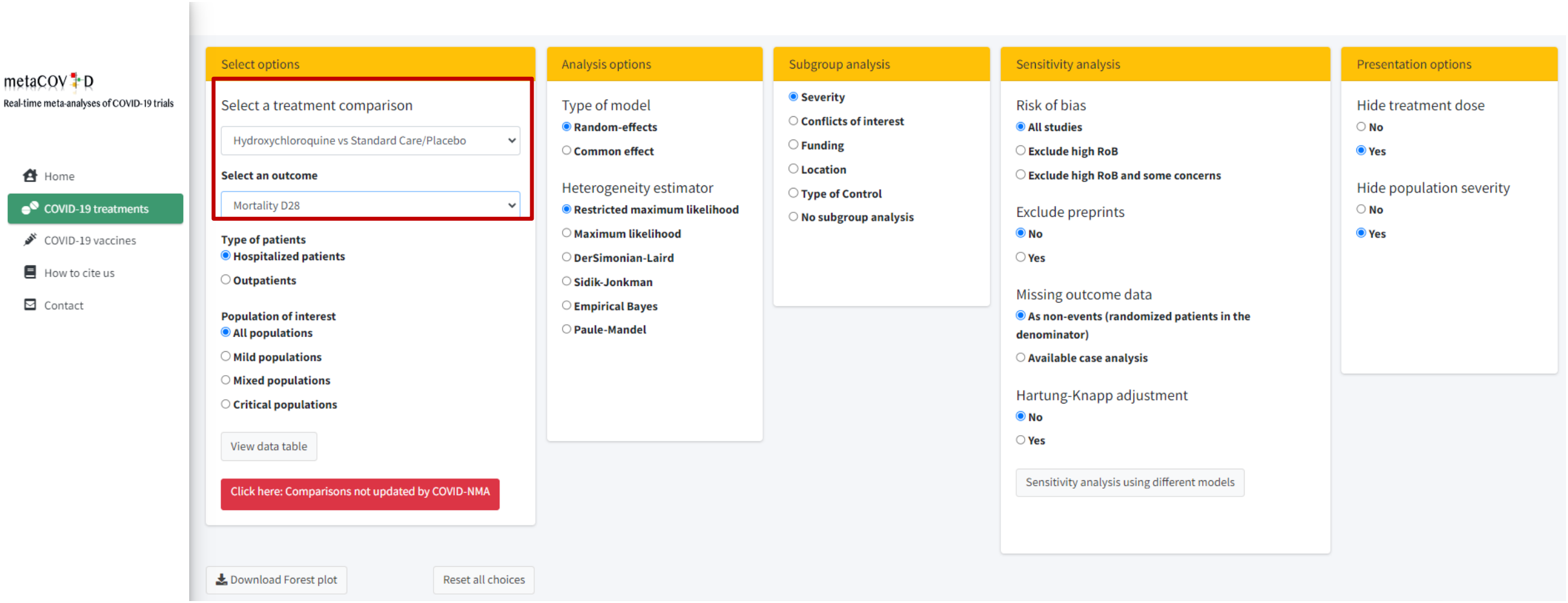
Evrenoglou, T, Boutron, I, Seitidis, G, Ghosn, L, Chaimani, A. metaCOVID: A web-application for living meta-analyses of COVID-19 trials. Res Syn Meth. 2023; 14(3): 479- 488. doi:10.1002/jrsm.1627

More than 200 comparisons are available

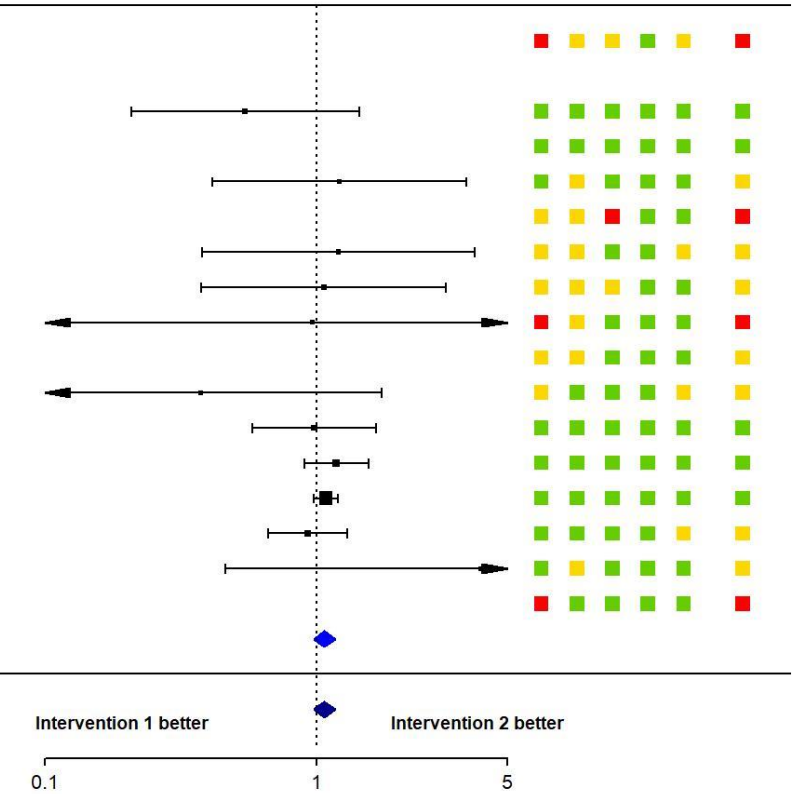



metaCOVID
Real-time meta-analyses of COVID-19 trials
Home
COVID-19 treatments
COVID-19 vaccines
How to cite us
Contact
Select options
Select a treatment comparison
Hydroxychloroquine vs Standard Care/Placebo
Select an outcome
Mortality D28
Type of patients
Hospitalized patients
Outpatients
Population of interest
All populations
Mild populations
Mixed populations
Critical populations
View data table
Click here: Comparisons not updated by COVID-NMA
Analysis options
Type of model
Random-effects
Common effect
Heterogeneity estimator
Restricted maximum likelihood
Maximum likelihood
DerSimonian-Laird
Sidik-Jonkman
Empirical Bayes
Paule-Mandel
Subgroup analysis
Severity
Conflicts of interest
Funding
Location
Type of Control
No subgroup analysis
Sensitivity analysis
Risk of bias
All studies
Exclude high RoB
Exclude high RoB and some concerns
Exclude preprints
No
Yes
Missing outcome data
As non-events (randomized patients in the denominator)
Available case analysis
Hartung-Knapp adjustment
No
Yes
Sensitivity analysis using different models
Presentation options
Hide treatment dose
No
Yes
Hide population severity
No
Yes
Download Forest plot
Reset all choices

All-cause mortality D28

Study	Follow up days	Intervention 1	Intervention 2	r1/N1	r2/N2	Weights	RR [95% CI]	Risk of Bias A	B	C	D	E	Overall
Kamran SM 2021	14	Hydroxychloroquine	Standard care	0/360	0/180								
Mild population													
Dubee V 2021	28	Hydroxychloroquine	Placebo	6/125	11/125	0.85%	0.55 [0.21, 1.43]						
Chen CP 2020	14	Hydroxychloroquine	Standard care	0/21	0/12								
Cavalcanti AB 2020	15	Hydroxychloroquine	Standard care	7/221	6/229	0.68%	1.21 [0.41, 3.54]						
Chen L 2020	28	Hydroxychloroquine	Standard care	0/28	0/14								
Abd-Elsalam S 2020	28	Hydroxychloroquine	Standard care	6/97	5/97	0.59%	1.20 [0.38, 3.80]						
Ulrich RJ 2020	30	Hydroxychloroquine	Placebo	7/67	6/61	0.73%	1.06 [0.38, 2.99]						
Lyngbakken MN 2020	30	Hydroxychloroquine	Standard care	1/27	1/26	0.11%	0.96 [0.06, 14.60]						
Tang W 2020	28	Hydroxychloroquine	Standard care	0/75	0/75								
Beltran-Gonzalez J 2021	30	Hydroxychloroquine	Placebo	2/33	6/37	0.34%	0.37 [0.08, 1.73]						
Self W 2020	28	Hydroxychloroquine	Placebo	25/242	25/237	2.85%	0.98 [0.58, 1.65]						
Pan H 2020	28	Hydroxychloroquine	Standard care	104/954	84/909	10.54%	1.18 [0.90, 1.55]						
Horby P 2020	28	Hydroxychloroquine	Standard care	421/1561	790/3155	76.11%	1.08 [0.97, 1.19]						
Hernandez-Cardenas C 2021	30	Hydroxychloroquine	Placebo	40/106	44/108	7.03%	0.93 [0.66, 1.29]						
Barratt-Due A 2021	28	Hydroxychloroquine	Standard care	4/54	1/54	0.17%	4.00 [0.46, 34.64]						
Chen J 2020	14	Hydroxychloroquine	Standard care	0/15	0/15								
Mixed population							**1.07 [0.98, 1.17]**						
			Totals	**623/3986**	**979/5334**		**1.07 [0.98, 1.17]**						

Heterogeneity results (overall analysis): Q = 6.92, p = 0.96; I^2 = 0.0%; τ^2 = 0.00, Prediction Interval = [0.98, 1.16]



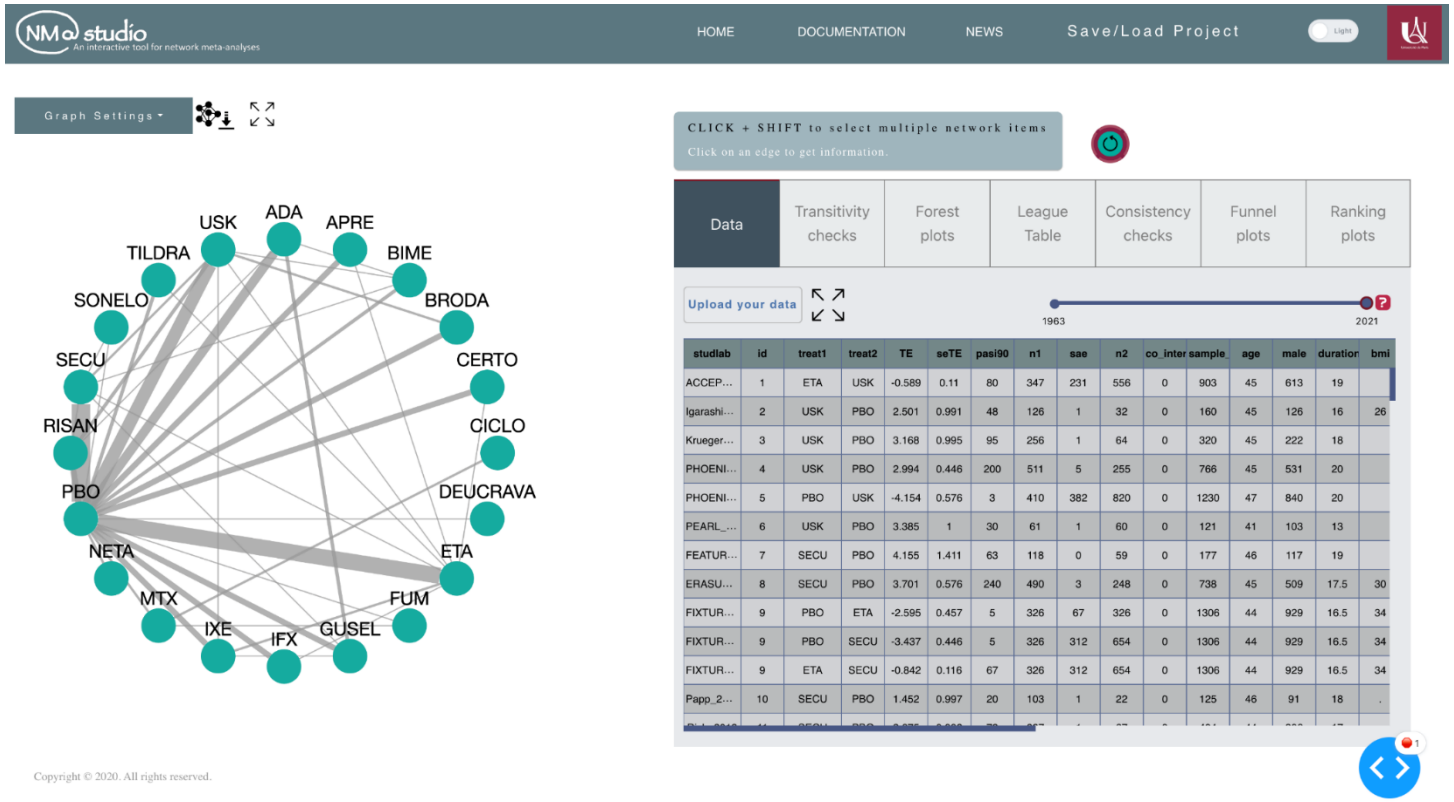
Risk of bias ratings:
- Low Risk of Bias
- Some Concerns
- High Risk of Bias

Risk of Bias Domains:
- A: Bias due to randomization
- B: Bias due to deviation from intended intervention
- C: Bias due to missing data
- D: Bias due to outcome measurement
- E: Bias due to selection of reported result

Forest plot produced at: 11 23 2022
Data source: the COVID-NMA initiative (covid-nma.com)

NMA-studio for network meta-analysis

- A fully interactive tool with a broader scope (https://www.nmastudioapp.com/)
- Users can upload their own data and perform a network meta-analysis
- Other capabilities
  - consistency checks
  - ranking
  - assessment of small-study effects
  - transitivity checks



Metelli S, Chaimani A. NMAstudio: a fully interactive web-application for producing and visualising network meta-analyses. *SRSM Annual Meeting 2021, Bern, Switzerland.*

Lessons learned

- Future living evidence synthesis projects should rely on automation tools in order to update their findings
  - ensures transparency, validity and feasibility
- For long-lasting living evidence synthesis projects such tools need to be built in a clear way
  - enables the takeover process as research teams in academia are often ephemeral
  - facilitates the creation of similar tools in other projects
- User-friendly environments do not guarantee proper interpretation of the findings
  - interpretation should always be done by researchers with expertise on meta-analysis