# Effect of Tocilizumab in Patients with COVID-19 Regarding Oxygen Therapy and Days Since Symptom Onset: Data Extraction Protocol*

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### Protocol question

What is the effect of tocilizumab in patients with COVID-19 regarding oxygen therapy and days since symptom onset?

### Searches

We will manually search the bibliography of Cochrane's systematic living review on tocilizumab and COVID-19 (Ghosn et al. 2021). We will extract data from the studies that attend to the inclusion criteria described in this document.

### Condition or domain being studied

COVID-19

### Participants/population

Adults ($\geq$ 18 years of age) with a clinical and/or laboratory diagnosis of COVID-19, regardless of other medications use.

### Intervention(s), exposure(s)

Tocilizumab

### Comparator(s)/control

Placebo or usual care

### Types of study to be included

Randomized clinical trials

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**Context**

*Inclusion criteria*

Randomized controlled trials; tocilizumab; adults hospitalized with COVID-19; available data sub-grouped by the type of oxygen therapy (no oxygen, simple oxygen, non-invasive ventilation or invasive mechanical ventilation) and/or days since symptom onset (cutoffs of 7 +- 2 days)

*Exclusion criteria*

Preclinical studies; case reports; observational studies; data on mortality or use of oxygen therapy not available; full-text not available.

**Main outcome(s)**

Mortality (regardless of end-point)

**Additional outcome(s)**

Discharge from hospital within 28 days.

**Data extraction (selection and coding).**

We will screen the title and abstract from the randomized controlled trials included in the systematic living review (Ghosn et al. 2021) independently and in duplicate. Reviewers will attempt to reach a consensus on their choice of studies. If this is not possible, a third reviewer will be used as an adjudicator. The selected studies' full text will be reviewed independently and duplicated for final inclusion in the review.

Data extraction will be conducted independently and in duplicate using a prefabricated and pilot-tested Excel-based digital extraction form. There will be two separate forms: one for subgroup data and one for overall trial characteristics. Extractors will attempt to reach a consensus. If this is not possible, a third reviewer will act as an adjudicator.

Because this living review gets updated weekly, we will screen it two times: before analyzing and extracting the data and at the end of the analyses, to check if any new trials were published. In case a new study gets published, we will extract its data if the study fits our inclusion criteria mentioned above.

**The domains for the subgroup extraction form will include:**

1. Trial name
2. Type of oxygen therapy
3. Days since symptom onset subgroup
4. Outcome
5. Events in the tocilizumab group
6. Sample size in the tocilizumab group

7. Events in the control group
8. Events in the control group
9. Sample size in the control group

**The domains for the overall trial extraction form will include:**

1. Trial name
2. Year
3. Blind status
4. Length of follow-up for the mortality outcome
5. Length of follow-up for the hospital discharge outcome
6. The cutoff used for days since symptom onset subgroups
7. Type of treatment in the control group (placebo or standard of care)
8. The proportion of patients on corticosteroids in the tocilizumab group
9. The proportion of patients on corticosteroids in the control group
10. The proportion of patients with a negative PCR in the tocilizumab group
11. The proportion of patients with a negative PCR in the control group

**Strategy for data synthesis**

We will use the data gathered from this living systematic review to create evidence-based priors for a Bayesian analysis. We will pre-register the protocol for this analysis along with this document on OpenScienceFramework, in which we will explain all the details underlying our analyses.

**Analysis of subgroups or subsets**

We will also explain this topic in the pre-registered protocol on OpenScienceFramework.

**Stage at time of this submission**

The data extraction has not yet started.

**Conflicts of interest**

Dr. Tramujas participated as a co-principal investigator on the TOCIBRAS trial (Veiga et al. 2021).

**References**

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