

May 4th update

COVID-NMA

- Summary of Main Results -

Introduction

This is the 2nd Summary of Main Results report from the [COVID-NMA initiative](#). It provides an overview of the results as of **May 4th, 2022** and any notable changes since the previous report are highlighted in a new section below. As before, the most up to date results are available on [covid-nma.com](#), and any studies pending data extraction are available [here](#). Feel free to get in touch with us using our [contact form](#) and to disseminate this document on twitter ([@Covid-NMA](#)).

We also want to use this occasion to share some of the decisions recently made by the steering committee and that will impact the interventions considered by the [COVID-NMA initiative](#) in the future: As of March 1, 2022, the COVID-NMA revised its protocol to **reduce the scope of the project to vaccines, immunomodulators, and antivirals**. Therefore, in the future we will not continue updating results for non-pharmacologic treatments or other pharmacological interventions.

Finally, an updated version of the [metaCOVID](#) app is now available on our site, which allows all the end-users of the COVID-NMA platform to perform their own meta-analyses for COVID-19 pharmacological treatments and vaccines through a user-friendly environment using the latest database. Among other options, the user will be able to specify the population of interest, subgroup and sensitivity analyses and the type of model to be performed (i.e. random-effects or fixed effect).

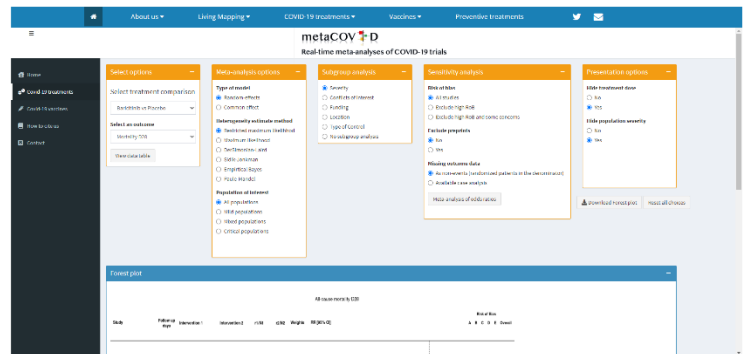


Figure 1: Screenshot of the new metaCOVID app

Updates since the previous report

Since the previous report (updated on April 4th) there have been the following changes:

- There are two new comparisons, **Ruxolitinib** vs placebo, and **Umbilical cord mesenchymal stem cell infusion** vs standard care/placebo, for which the certainty of evidence for adverse events is moderate. Both interventions probably result in little to no difference in the risk of adverse events.
- After adding two new studies comparing **Corticosteroids** vs standard care/placebo, the certainty of evidence regarding **clinical improvement** (around 28 days) is now high. It probably increases clinical improvement (around 28 days) slightly (RR 1.05, 95% CI 1.02 – 1.09).
- There is now moderate certainty regarding the effect of **Lopinavir + Ritonavir** on **viral negative conversion** and **clinical improvement** (around 28 days), indicating that this intervention probably results in little to no difference.
- The certainty of the results of **Therapeutic vs Prophylactic anticoagulant** on **clinical improvement** (around 28 days) has been downgraded from moderate to low. As no other outcome had moderate or high certainty, this comparison has been removed from our summary, but it can of course still be found [online](#).

- Additional studies have resulted in minimal changes in results for clinical improvement in the comparisons involving [Colchicine](#), [Convalescent plasma](#), [Hydroxychloroquine](#) and [Tocilizumab](#). The certainty and interpretation of these results did not change.

What is the current evidence regarding treatment of hospitalized Covid-19 patients?

Updated on May 4th, 2022

Pharmacologic treatments in hospitalized patients

Critical outcomes of interest: [Clinical improvement](#) (around day 28 or day 60), [WHO Clinical Progression Score \$\geq 7\$](#) (around day 28 or day 60), [all-cause mortality](#) (around day 28 or day 60), [viral negative conversion](#) (around day 7), [adverse events](#) and [serious adverse events](#).

For most pharmacological treatments in hospitalized patients, the certainty of the evidence is still low or very low. Below is a summary of pharmacological interventions that have **results in favor of a beneficial effect** so far compared with placebo or standard care. We only highlight outcomes of moderate and high certainty; other outcomes are of low or very low certainty.

- **Anakinra** (a monoclonal antibody) probably reduces the risk of WHO score ≥ 7 (i.e. mechanical ventilation or death, around 28 days) in hospitalized patients, as well as slightly increases the likelihood of clinical improvement around 28 days. The risk of adverse events probably does not increase. It is one of the interventions that have been authorized in the EU to treat Covid-19.
- **Baricitinib** (a kinase inhibitor) reduces the risk of WHO score ≥ 7 (i.e. mechanical ventilation or death, around 28 days) in hospitalized patients, although it results in little to no difference in clinical improvement around 28 days. It is likely to reduce the risk of all-cause mortality (around 28 days and around 60 days). It probably does not increase the risk of adverse events but probably decreases the risk of serious adverse events.
- **Casirivimab + Imdevimab (REGN-COV2)** (Monoclonal antibody combination) probably reduces the risk of all-cause mortality (around 28 days), although the likelihood of clinical improvement around 28 days and around 60 days probably is not improved. It is one of the interventions that have been authorized in the EU to treat Covid-19.
- **Corticosteroids** probably increase clinical improvement (around 28 days) slightly and reduce the risk of all-cause mortality (around 28 days) in hospitalized patients. We pooled together oral and intravenous corticosteroids of participants with various disease severity. Of note, the largest study (the RECOVERY trial) found in subgroup analysis that “differences in mortality varied considerably according to the level of respiratory support that the patients were receiving at the time of randomization”, and that “the use dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support.”
- **Tocilizumab** (a monoclonal antibody) is likely to reduce the risk of all-cause mortality (around 28 days) in hospitalized patients, although it probably results in little to no difference on clinical improvement around 28 days. It is one of the interventions that have been authorized in the EU to treat Covid-19.

For the treatments below there are outcomes with moderate or high certainty indicating **uncertainty of benefit or harm**

- **Remdesivir** (an anti-viral), which is one of the interventions recommended by the NIH and which has been authorized in the EU to treat COVID-19, we found that the risk estimate for all-cause mortality (around 28 days) and its wide confidence interval (RR 0.91, 95% CI 0.74 to 1.11) point to uncertainty of benefit or harm.

For the treatments below there are outcomes with moderate or high certainty indicating **no evidence of beneficial effects** (e.g. clinical improvement or reduction in mortality) or an increase in the risks of negative effects (e.g. serious adverse events) compared with placebo or standard care:

- **Aspirin** (acetylsalicylic acid), **Azithromycin** (an antimicrobial), **Hydroxychloroquine** (an antimalarial) and **Colchicine** (an anti-inflammatory) probably do not reduce the risk of all-cause mortality (around 28 days) and probably do not increase the likelihood of clinical improvement (around 28 days).
- **Bamlanivimab** (a monoclonal antibody) probably results in little to no difference on clinical improvement around day 60.
- **Canakinumab** (a monoclonal antibody) probably results in little to no difference on clinical improvement around 28 days and in little to no difference in the risk of adverse events.
- **Convalescent plasma** probably results in little to no difference on clinical improvement around 28 days or all-cause mortality (around 28 days).
- **Lopinavir + Ritonavir** (an anti-viral) probably results in little to no difference on viral negative conversion (around day 7), clinical improvement (around 28 days) or all-cause mortality (around 28 days).
- **Ruxolitinib** (a kinase inhibitor) probably results in little to no difference in the risk of adverse events.
- **Sotrovimab** (a monoclonal antibody) probably results in little to no difference in clinical improvement around day 60. Furthermore, it probably increases the risk of serious adverse events. While the NIH recommends this intervention for outpatients, it has not been recommended for hospitalized patients. Similarly, this intervention has been authorized in the EU to treat COVID-19, but only in patients who do not require supplemental oxygen and are at increased risk of the disease becoming severe.
- The use of **Umbilical cord mesenchymal stem cell infusion** probably results in little to no difference in the risk of adverse events.

For another intervention authorized by the European Medicines Association (Ritonavir alone) we have not yet identified randomized controlled trials reporting its effectiveness.

Summary table on next page...

Summary Table: Pharmacologic treatments in hospitalized patients
(Updated on May 4th, 2022)

Moderate/High certainty of benefit
Moderate/High certainty of little or no difference
Moderate/High certainty of harm

Legend:

Treatment (vs standard care or placebo unless stated otherwise)	Treatment effectiveness							Adverse events	
	Improvement			Covid-19 events				Adverse events	Serious adverse events
	Viral negative conversion (D7)	Clinical improvement (D28)	Clinical improvement (D60)	WHO progression score (level ≥7) (D28)	WHO progression score (level ≥7) (D60)	All-cause mortality (D28)	All-cause mortality (D60)		
Anakinra	low certainty	1.10 (1.00-1.20)	very low certainty	0.64 (0.42 - 0.98)		low certainty	very low certainty	1.02 (0.94-1.10)	low certainty
Aspirin		1.02 (1.00 - 1.04)				0.97 (0.90 - 1.04)			
Azithromycin		1.02 (0.99-1.05)		very low certainty		0.97 (0.89-1.06)			
Bamlanivimab (LY-CoV555)			0.98 (0.90 - 1.07)	low certainty		low certainty	low certainty		low certainty
Baricitinib		1.02 (1.00 - 1.05)		0.87 (0.78 - 0.97)		0.75 (0.58 - 0.98)	0.69 (0.56 - 0.86)	0.96 (0.88 - 1.05)	0.77 (0.64 - 0.94)
Canakinumab		1.05 (0.96-1.14)		low certainty		low certainty	very low certainty	1.02 (0.86-1.21)	low certainty
Casirivimab + Imdevimab (REGN-COV2)		1.02 (0.99 - 1.04)	1.04 (0.97 - 1.12)	low certainty		0.93 (0.86 - 1.01)	low certainty		
Colchicine		1.02 (0.97 - 1.07)		low certainty		0.99 (0.93 - 1.06)	very low certainty	low certainty	very low certainty
Convalescent plasma	very low certainty	0.99 (0.97-1.02)		low certainty	very low certainty	0.97 (0.92 - 1.03)	very low certainty	low certainty	low certainty
Corticosteroids	very low certainty	1.05 (1.02 - 1.09)		very low certainty		0.91 (0.85-0.98)	very low certainty	very low certainty	very low certainty
Hydroxychloroquine	very low certainty	0.97 (0.94 - 1.00)		low certainty	very low certainty	1.07 (0.98 - 1.17)	low certainty	low certainty	very low certainty
Lopinavir + Ritonavir	1.05 (0.88 - 1.25)	0.99 (0.90 - 1.09)		low certainty	very low certainty	1.02 (0.92-1.12)	low certainty	low certainty	very low certainty
Remdesivir	low certainty	low certainty		low certainty		0.91 (0.74-1.11)	very low certainty	low certainty	very low certainty
Ruxolitinib		low certainty		low certainty		low certainty		1.02 (0.84 - 1.24)	low certainty
Sotrovimab			1.05 (0.97 - 1.15)	low certainty		low certainty	low certainty	low certainty	2.03 (1.32 - 3.13)
Tocilizumab		1.04 (1.00-1.09)	very low certainty	low certainty		0.88 (0.82-0.95)	low certainty	low certainty	very low certainty
Umbilical cord mesenchymal stem cell infusion		very low certainty	very low certainty	very low certainty		low certainty	very low certainty	1.04 (0.86 - 1.25)	low certainty

All values are RR (95% CI). Bolded results have a high level of certainty, while non-bolded results have a moderate level of certainty. Last updated: May 4th 2021. Click on the treatment to access the corresponding site at covid-nma.com.

Continues with non-pharmacologic treatments on next page...

Non-pharmacologic treatments in hospitalized patients

For most of the non-pharmacological treatments, the certainty of the evidence is still low or very low. We have moderate certainty that:

Prone position vs Standard care probably slightly reduces the risk of requiring mechanical ventilation or death (WHO progression score level 7 or above) around 28 days in hospitalized patients. There are currently nine registered trials assessing this comparison that have finished recruitment, so we soon might have more data on this intervention.

Summary Table: Non- pharmacologic treatments in hospitalized patients (Updated on May 4th, 2022)

Legend:

Moderate/ High certainty of benefit
Moderate/ High certainty of little or no difference
Moderate/ High certainty of harm

Treatment (vs standard care or placebo unless stated otherwise)	Treatment effectiveness							Adverse events	
	Improvement			Covid-19 events				Adverse events	Serious adverse events
	Viral negative conversion (D7)	Clinical improvement (D28)	Clinical improvement (D60)	WHO progression score (level ≥ 7) (D28)	WHO progression score (level ≥ 7) (D60)	All-cause mortality (D28)	All-cause mortality (D60)		
Prone position vs Standard care		low certainty		0.86 (0.76 - 0.99)		low certainty		very low certainty	very low certainty

All values are RR (95% CI). Bolded results have a high level of certainty, while non-bolded results have a moderate level of certainty. Last updated: May 4th 2021. Click on the treatment to access the corresponding site at covid-nma.com.

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