

# Demo Walkthrough: COVID-19 Antivirals

Welcome to the walkthrough of the *COVID-19: Antivirals* demo Nest (open in your original tab). In this walkthrough, we'll explain the core functionalities of Nested Knowledge through this Nest. We encourage you to work through the Nest as you follow the walkthrough. The Nest available to you is a copy of the original and may be freely modified, so roll up your sleeves and get your hands dirty!

This Nest is a copy of a previously-completed review presenting the evidence regarding the safety and efficacy of anti-virals that had randomized controlled trial (RCT) evidence reported in the treatment of COVID-19 as of January 2022.

## Nest Home

The screenshot shows the 'COVID-19: Antivirals (Demo)' Nest Home page. The interface includes a top navigation bar with 'Our Team', 'Our Vision', 'Enterprise', 'AutoLit', and a user profile 'Karl'. A left sidebar menu lists modules: 'Nest Home', 'Literature Search', 'Screening', 'Tagging', 'Extraction', 'Synthesis', and 'Settings'. The main content area is titled 'COVID-19: Antivirals (Demo)' and contains sections for 'About', 'Title', 'Study Coordinator/Corresponding Author', and 'Team Members and Their Organizational Affiliations'. The 'About' section states: 'This Nest is a copy of a previously-completed review presenting the evidence regarding the safety and efficacy of anti-virals that had randomized controlled trial (RCT) evidence reported regarding the treatment of COVID-19 as of January 2022.' The 'Title' section is 'Efficacy of antiviral therapies for COVID-19: A systematic review of randomized controlled trials'. The 'Study Coordinator/Corresponding Author' is 'Erin Sheffield'. The 'Team Members and Their Organizational Affiliations' section lists several authors and their affiliations. A right sidebar shows 'Comments' with two entries from 'Karl Holub' and 'Kathryn Cowie'. At the bottom, there is a 'Comment' input field.

You've landed on your demo Nest in AutoLit, and you're looking at the Nest Home page. This page includes a menu on the left of the page, the protocol in the center, and discussion about the Nest on the right. The menu includes links to all modules & configurations available to you in AutoLit. We'll now walk through these modules one by one. (click the title in the menu to navigate to the the corresponding module).

## Literature Search

The Literature Search page allows import of studies to a nest and shows where studies were sourced. This review includes two searches - an API-based (automatic integration) search of PubMed and a file-based import from Embase. Hover and click the "History and Details" column to see greater detail about the searches, including when they were run and any query structuring available. The PubMed

search is API-based and may be run on demand. Hover the Pubmed row and click the “Run” button to update this search- you may import some new records!

The screenshot displays the NESTED KNOWLEDGE web application. The top navigation bar includes links for 'Our Team', 'Our Vision', 'Enterprise', 'AutoLit', and a user profile for 'Karl'. The main header shows the current search: 'Literature Search: COVID-19: Antivirals' with a progress indicator '2/2'. A left sidebar contains a 'Nest Home' dashboard and several tool categories: 'Literature Search' (2/2), 'Screening' (91/100), 'Tagging' (11/16), 'Extraction' (16/16), 'Synthesis', and 'Settings'. The central 'Searches' table lists two searches. The first search, 'Jupivir OR Ritonavir OR Remdesivir OR Ribavirin OR Arbidol OR Favipir...', is associated with the 'Embase' engine and has a 'Never' schedule. The second search, '["Therapeutics" OR "antiviral therapies"] AND (RCT OR "randomized contr...', is associated with 'PubMed' and has a 'Never' schedule. Both searches show a 'Last Run' of '2022-02-09' and 'Results: 59'. The interface also includes buttons for 'Add Search', 'Search Now', 'Full History', and 'Interactions'.

Term	Search Engine	Schedule	Search Now	History and Details	Delete
Jupivir OR Ritonavir OR Remdesivir OR Ribavirin OR Arbidol OR Favipir...	Embase	Never	File	Full History	
["Therapeutics" OR "antiviral therapies"] AND (RCT OR "randomized contr...	PubMed	Never	Last Run: 2022-02-09	Method: api Results: 59	

## Other Sources

Records may be imported through other means. Click the “Other Sources” menu item under “Literature Search” to view records that were individually added as expert recommendations. 19 such studies were imported into this Nest. Try importing the DOI or PMID of your favorite study using the “Add by Identifier” form on the right of the page

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Other Sources: COVID-19: Antivirals

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Add Individual References

Bibliome

Title	Author	Source	Date Added	Added By	
Efficacy and safety of favipiravir, an oral RNA-dependent RNA pol...	Zari F Ullahda	International journal of infectio...	9/7/2021	Ranita Tarchand	X
Clinical outcomes of using remdesivir in patients with moderate to ...	Lakshmi Mahajan	Indian J Anaesth	9/7/2021	Ranita Tarchand	X
Efficacy of favipiravir in COVID-19 treatment: a multi-center rando...	Hany M Dabbous	Archives of virology	9/6/2021	Ranita Tarchand	X
Clinical Outcomes and Plasma Concentrations of Remdesivir Marboxi...	Yue Lou	European journal of pharmaceut...	9/6/2021	Ranita Tarchand	X
AVIFAVIR for Treatment of Patients with Moderate COVID-19: Inter...	Andrey A Ivashchen...	Clinical infectious diseases: an o...	9/6/2021	Ranita Tarchand	X
Lopinavir-ritonavir in patients admitted to hospital with COVID-19 ...	Horby Peter W	Lancet (London, England)	9/6/2021	Ranita Tarchand	X
Remdesivir for the Treatment of Covid-19 - Final Report.	John H Beigel	The New England journal of me...	9/6/2021	Ranita Tarchand	X
A Novel Protein Drug, Nisofexone, as the Potential Antiviral Drug fo...	Fang Zheng		1/5/2021	Jorge Polanco	X
Triple combination of interferon beta-1b, lopinavir-ritonavir, and rib...	Icon Fan-Hai Hung	Lancet (London, England)	1/5/2021	Jorge Polanco	X
No Statistically Apparent Difference in Antiviral Effectiveness Obs...	Yie-Qu Huang	Frontiers in pharmacology	1/5/2021	Jorge Polanco	X
Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial	Chong Chen		1/5/2021	Jorge Polanco	X
Interferon-α2b Treatment for COVID-19	Zhou Qing	Frontiers in immunology	1/5/2021	Jorge Polanco	X
Arbidol monotherapy is superior to lopinavir/ritonavir in treating C...	Zhen Zhi	The Journal of infection	1/5/2021	Jorge Polanco	X
Efficacy and Safety of Lopinavir/Ritonavir or Arbidol in Adult Patie...	Huaying Li	Med (New York, NYC)	1/5/2021	Jorge Polanco	X
Repurposed Antiviral Drugs for Covid-19 - Interim WHO Solidarity ...		The New England journal of me...	1/4/2021	Jorge Polanco	X
A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Co...	Bin Cao	The New England journal of me...	10/26/2020	Kevin Kallines	X
Effect of Remdesivir in Standard Care on Clinical Status at 10 Days L...	Christoph D Spinner	JAMA	10/26/2020	Kevin Kallines	X
Remdesivir in adults with severe COVID-19: a randomised, double-...	Yeming Wang	Lancet (London, England)	10/26/2020	Kevin Kallines	X
Experimental Treatment with Favipiravir for COVID-19: An Open-L...	Qingxian Gai	Engineering (Beijing, China)	10/26/2020	Kevin Kallines	X

Add by Identifier

Add by Article ID

Published ID

DOI

Enter a single or comma separated list of identifiers. Bibliographic data will be automatically imported from PubMed or Crossref

Add Manually

Title

Author Format

First (Last, Full)

First Name

Last Name

Publication Date

mm / dd / yyyy

Journal/Source

Publisher

Volume

Issue

Corporate Author

Organization

Link

URL

DOI

10.000000000

Abstract / Summary

Placeholder

Add Reference

# Screening

Once studies are imported into a nest, they are “Screened” for relevance to the review in the Screening Module. Click the Screening menu header to visit this module.

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Screening: COVID-19: Antivirals

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Effect of anti-interleukin drugs in patients with COVID-19 and signs of cytokine release syndrome (COV-AID): a factorial, randomised, controlled trial.

Abstract

Full Text

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Navigation

Each

Stop

Screening

Full Text Review

Upload Full Text

Search

Not an RCT of a drug of interest

Protocol or Methods article

Systematic Review or Meta-analysis

Editorial, comment, or opinion article

Not an antiviral

Not related to COVID-19

Qualitative review of existing research

Update or guideline article

Published before 2019-11-01

In vitro, in silico, or in vivo study

Basic Information

Prophylaxis Not Treatment

Retracted

Technical note

Correspondence or Letter to the Editor

Case Study

Full Text Unavailable

secondary analysis

Suspected COVID

Not Published in English

BACKGROUND Infections with SARS-CoV-2 continue to cause significant morbidity and mortality. Interleukin (IL)-1 and IL-6 blockade have been proposed as therapeutic strategies in COVID-19, but study outcomes have been conflicting. We sought to study whether blockade of the IL-6 or IL-1 pathway shortened the time to clinical improvement in patients with COVID-19, hypoxic respiratory failure, and signs of systemic cytokine release syndrome. METHODS We did a prospective, multicentre, open-label, randomised, controlled trial in hospitalised patients with COVID-19, hypoxia, and signs of a cytokine release syndrome across 16 hospitals in Belgium. Eligible patients had a proven diagnosis of COVID-19 with symptoms between 6 and 16 days, a ratio of the partial pressure of oxygen to the fraction of inspired oxygen (PaO2/FiO2) of less than 350 mm Hg on room air or less than 280 mm Hg on supplemental oxygen, and signs of a cytokine release syndrome in their serum (either a single ferritin measurement of more than 2000 µg/L and immediately requiring high flow oxygen or mechanical ventilation, or a ferritin concentration of more than 1000 µg/L, which had been increasing over the previous 24 h, or lymphopenia below 800/mL, with two of the following criteria: an increasing fibrinogen concentration of more than 700 µg/L, an increasing lactate dehydrogenase concentration of more than 300 international units per L, an increasing C-reactive protein concentration of more than 70 mg/L, or an increasing D-dimers concentration of more than 1000 ng/mL). The COV-AID trial has a 2 × 2 factorial design to evaluate IL-6 blockade versus no IL-1 blockade and IL-6 blockade versus no IL-6 blockade. Patients were randomly assigned by means of permuted block randomisation with varying block size and stratification by centre. In a first randomisation step, patients were allocated to receive a single dose of siltuximab (11 mg/kg) intravenously, or a single dose of tocilizumab (8 mg/kg) intravenously, or to receive no IL-6 blockade (1:1). The primary outcome was the time to clinical improvement, defined as time from randomisation to an increase of at least two points on a 6-category ordinal scale or to discharge from hospital alive. The primary and supportive efficacy endpoints were assessed in the intention-to-treat population. Safety was assessed in the safety population. This study is registered online with ClinicalTrials.gov (NCT04330438) and [BioRxiv](#) (2020-07500-40) and is complete. FINDINGS Between April 4, and Dec 8, 2020, 342 patients were randomly assigned to IL-6 blockade (n=172) or no IL-6 blockade (n=170) and simultaneously randomly assigned to IL-6 blockade (n=227, 114 for tocilizumab and 113 for siltuximab) or no IL-6 blockade (n=115). Most patients were male (265 [77%] of 342), median age was 65 years (IQR 54-73), and median Systemic Organ Failure Assessment (SOFA) score at randomisation was 3 (2-4). All 342 patients were included in the primary intention-to-treat analysis. The estimated median time to clinical improvement was 12 days (95% CI 10-16) in the IL-1 blockade group versus 12 days (10-15) in the no IL-1 blockade group (hazard ratio [HR] 0.94 [95% CI 0.73-1.21]). For the IL-6 blockade group, the estimated median time to clinical improvement was 11 days (95% CI 10-16) versus 12 days (11-16) in the no IL-6 blockade group (HR 1.00 [0.78-1.29]). 55 patients died during the study, but no evidence for differences in mortality between treatment groups was found. The incidence of serious adverse events and serious infections was similar across study groups. INTERPRETATION Drugs targeting IL-1 or IL-6 did not shorten the time to clinical improvement in this sample of patients with COVID-19, hypoxic respiratory failure, low SOFA score, and low baseline mortality risk. FUNDING Belgian Health Care Knowledge Center and VIB Grand Challenges program.

Population/Problem

Intervention

Outcome

User Keywords

Keywords

Bibliographic fields

6/8

This screening module displays studies that have yet to be screened, allowing you to decide to include or exclude from the rest of your review and analysis. So far in our review, 91 studies have been screened and 16 included. Try including a reference by clicking the include button. Exclude a reference by selecting an exclusion reason from the drop-down menu and then clicking the exclude button. You may also skip studies you aren't yet sure about, or jump to a prior study, using the

buttons under the Navigation menu.

## Abstract Highlighting

Why are study abstracts so colorful? We perform ML-based PICO annotation of abstracts using a model derived from [RobotReviewer](#). To turn off PICO highlighting, toggle off the slide button in the legend just beneath the abstract text.

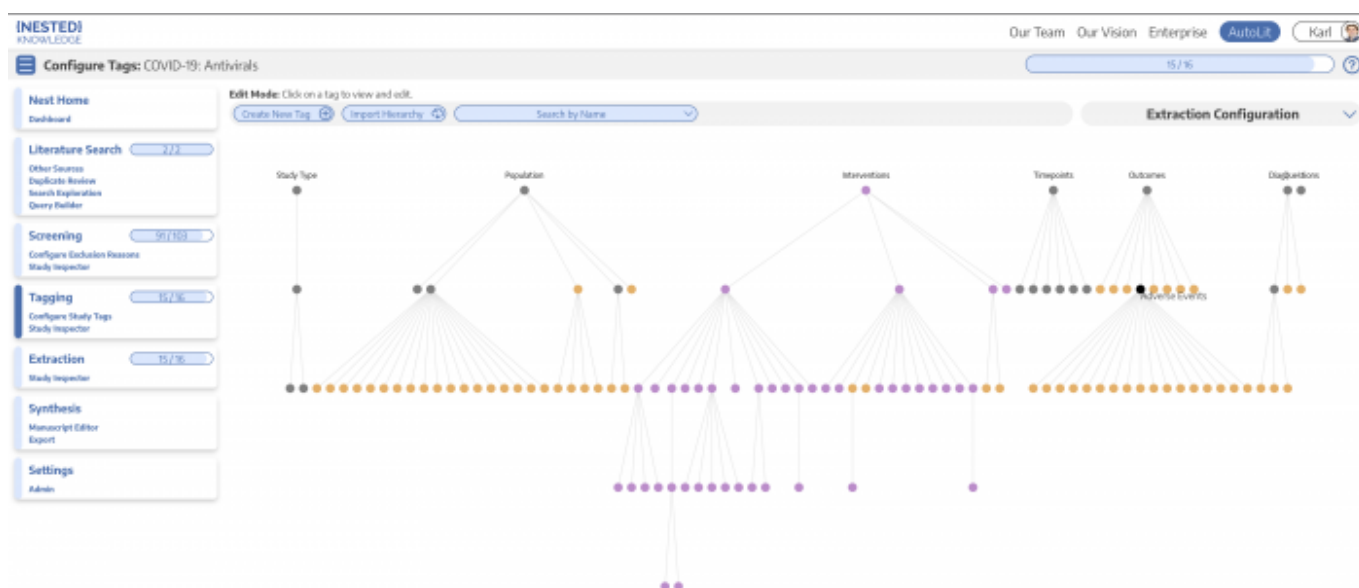
Abstract text may also be underlined with User Keywords, which are configured under the Settings menu item.

## Tagging

The Tagging module allows included studies to be categorized according to their characteristics, such as design, population, outcomes, etc. Nested Knowledge uses hierarchical tags to describe characteristics.

### Tag Hierarchy

Click the “Configure Study Tags” menu item to get started. Tag hierarchies consist of tags (visualized as points) and relationships between them (visualized as connecting lines). The tag hierarchy in this review includes 7 “root” tags - the highest level categories we’re considering in the review. Hierarchies should be created and read as a series of “is a” relationships. For example, “Adverse Event” is a “Outcome”, “Septic Shock” is a “Adverse Event”. Hover around the hierarchy to explore tags and read off the “is a” relationships as you go.



# Tagging Module

Inside the Tagging module, tags may be applied to studies, indicating that a concept is relevant to a study.

Nested Knowledge

Tagging: COVID-19: Antivirals

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Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial.

Abstract

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Supplements

PMC

Research

AMA | Original Investigation

Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial

Chen et al. JAMA. 2020;323(18):1783-1792. doi:10.1001/jama.2020.10491

Abstract

Full Text

Supplements

PMC

Background

Remdesivir demonstrated clinical benefit in a placebo-controlled trial in patients with severe coronavirus disease 2019 (COVID-19), but its effect in patients with moderate disease is unknown.

Objective

To determine the efficacy of 5 or 10 days of remdesivir treatment compared with standard care in patients with moderate COVID-19.

Design, Setting, and Participants

Randomized, open-label trial of hospitalized patients with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and moderate COVID-19 pneumonia (pulmonary infiltrates and oxygen saturation <90%) enrolled from March 15 through April 16, 2020, at 105 hospitals in the United States, Europe, and Asia. The study ended follow-up was May 20, 2020.

Results

Patients were randomized to a 10-day course of remdesivir (n = 191), a 5-day course of remdesivir (n = 196), or standard care (n = 300). Remdesivir was dosed intravenously at 200 mg on day 1 followed by 100 mg/d.

Conclusions and Relevance

The primary end point was clinical status on day 11 on a 3-point ordinal scale ranging from death/categorization 1 to discharged/categorization 3. Differences between remdesivir treatment groups and standard care were calculated using proportional odds models and expressed as odds ratios. An odds ratio greater than 1 indicates a higher clinical status distribution toward category 1 for the remdesivir group vs the standard care group.

Limitations

Among 596 patients who were randomized, 504 began the study and received remdesivir or continued standard care (median age, 57 [interquartile range, 46-68] years; 227 [38%] women; 54% had cardiovascular disease, 42% hypertension, and 40% diabetes), and 553 (93%) completed the trial. Median length of treatment was 5 days for patients in the 10-day remdesivir group and 4 days for patients in the 5-day remdesivir group. On day 11, patients in the 5-day remdesivir group had statistically significantly higher odds of a better clinical status distribution than those receiving standard care (odds ratio, 1.65; 95% CI, 1.09-2.48; P = .02). The clinical status distribution on day 11 between the 10-day remdesivir and standard care groups was not significantly different (P = .18 by Wilcoxon rank-sum test). By day 28, 26 patients had died (2.2%) in the 5-day remdesivir group, 3 (2%) in the 10-day remdesivir group, and 4 (2%) in the standard care group. However (10% vs 3%), hypokalemia (0% vs 2%), and headache (3% vs 2%) were more frequent among remdesivir-treated patients compared with standard care.

Conclusions and Relevance

Among patients with moderate COVID-19, those randomized to a 10-day course of remdesivir had a higher clinical status on day 11 than those randomized to standard care.

Navigation

Tagging

Tag	Text
10-day course of Remdesivir	10-day course of remdesivir (n = 191).
Open label	Randomized, open-label trial of hospitalized patients with confirmed COVID-19.
Cardiovascular Disease	Patients in the 3 groups were balanced in demographic and disease characteristics (Table 1). Overall, 54% of patients had cardiovascular disease, 42% had hypertension, 40% had diabetes, and 14% had asthma.
Diabetes	Table 3
Diabetes Mellitus	Patients in the 3 groups were balanced in demographic and disease characteristics (Table 1). Overall, 54% of patients had cardiovascular disease, 42% had hypertension, 40% had diabetes, and 14% had asthma.
5-day course of Remdesivir	5-day course of remdesivir (n = 196).
Control/Standard of Care	200 Randomized to continue standard care 200 Continued standard care.
11 Days	The primary end point was clinical status on day 11 on a 3-point ordinal scale ranging from death/categorization 1 to discharged/categorization 3.
Remdesivir	To determine the efficacy of 5 or 10 days of remdesivir treatment compared with standard care.
Asthma	Patients in the 3 groups were balanced in demographic and disease characteristics (Table 1). Overall, 54% of patients had cardiovascular disease, 42% had hypertension, 40% had diabetes, and 14% had asthma.
Nausea	Table 3
Hypertension	Patients in the 3 groups were balanced in demographic and disease characteristics (Table 1). Overall, 54% of patients had cardiovascular disease, 42% had hypertension, 40% had diabetes, and 14% had asthma.
Mortality	Table 3

Cardiovascular Disease

Patients in the 3 groups were balanced in demographic and disease characteristics (Table 1). Overall, 54% of patients had cardiovascular disease, 42% had hypertension, 40% had diabetes, and 14% had asthma.

Comments (0)

History

In the Tagging form, select any tag from the dropdown menu, then click Apply Tag; it should now appear in the Tagging Table.

Click a row in the Tagging table that has a non-empty excerpt column to view past applied tags and their “excerpts”, which user-entered pieces of text, typically extracted from the manuscript, supporting the tag.

# Study Inspector

Study Inspector is the tool in AutoLit for reviewing and searching your past extracted data. Each row in Study Inspector is a study, and columns may be user-selected in the upper left dropdown menu. Studies may be searched into the table by creating Filters. Filters may be created using the Add Filter dropdown menu, but oftentimes the typeahead search bar is fastest. In the below example, we are filtering to studies with a full text uploaded and using the typeahead menu to find all studies tagged with Mortality. Try out the title/abstract (TIAB) filter by typing “Lopinavir” into the search bar.

Nested Knowledge - <https://wiki.nested-knowledge.com/>

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Study Inspector: COVID-19: Antivirals

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Full Text

Uploaded X

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TIAB search Mart

Author search Mart

Filter by Tagged With Mortality

Study Inspector

Save

Filter Sets

Bulk Actions

Download

Clear Filters

Title	TI	Publication Year	%	Screening Status
A Trial of Lopinavir-Ritonavir in Adults Hospitalized...		2020		Included
A Novel Protein Drug, Novafosin, as the Potential Antiviral Dr...	Zheng, Fang	2020		Excluded: Not an antiviral
Sofosbuvir and daclatasvir for the treatment of COVID-19 outp...	Rasouli, Fatemeh	2020		Included
Efficacy and Safety of Lopinavir/Ritonavir or Arbidol in Adult P...	Li, Yaping	2020		Included
Remdesivir in adults with severe COVID-19: a randomised, dou...	Wang, Yeming	2020		Included
Sofosbuvir and daclatasvir compared with standard of care in t...	Sadeghi, Anahita	2020		Included
Effect of Remdesivir vs Standard Care on Clinical Status at 11 D...	Spinner, Christoph D	2020		Included
Treatment of COVID-19 pneumonia with glucocorticoids [CORT...	Lee Rajanda, Vilgo	2021		Excluded: Protocol or Methods article
Favipiravir and Hydroxychloroquine Combination Therapy in P...	Bosseel, Mohammad	2021		Included
Hydroxychloroquine with or without azithromycin for treatme...	Johnstone, Christine	2021		Excluded: Not an RCT of a drug of interest
Clinical outcomes of using remdesivir in patients with moderat...	Mahajan, Lakshmi	2021		Included
Efficacy and Safety of Triazolin Therapy for Coronavirus Disea...	Xiao, Wu	2020		Excluded: Not an RCT of a drug of interest
Antibiral Combination Clinically Better Than Standard Therapy ...	Pandya, Prasan Kumar	2021		Excluded: Biased Subpopulation
Evaluation of the effectiveness and safety of adding isemmed...	Olumuyi, Nurullah	2021		Excluded: Not an antiviral
Remdesivir for the Treatment of Covid-19 - Final Report	Beigel, John H	2020		Included
Efficacy and safety of favipiravir, an oral RNA-dependent RNA...	Ukeshima, Zarif F	2021		Included
Efficacy and safety of sofosbuvir plus daclatasvir or remdesivir L...	Abbasi, Sherif	2021		Included
Favipiravir versus Arbidol for COVID-19: A Randomized Clinical ...	Chen, Chang	2020		Included
Efficacy of Favipiravir in COVID-19 treatment: a multi-center r...	Dabbeas, Hany M	2021		Included
Efficacy and Safety of Favipiravir in Moderate COVID-19 Patie...	Shinkai, Masaharu	2021		Included
Clinical Outcomes and Plasma Concentrations of Baloxavir Mar...	Lee, Yan	2020		Included
Triple combination of interferon beta-1b, lopinavir-ritonavir, an...	Hang, Ikon Fan-Ngai	2020		Excluded: Not an antiviral
Lopinavir-ritonavir in patients admitted to hospital with COVI...	Peter W. Horby	2020		Included

Displaying 23 matching records Load All

# Extraction

Please see our [Extraction Documentation](#) page to review how Extraction was configured for this Nest. Click the Extraction menu item to view and perform Extraction for this review.

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Data Extraction: COVID-19: Antivirals

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Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial

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Navigation

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Complete

Study Design

Arms

Status	Intervention	Arm Size
✓	Control(Standard of Care)	280
✓	5-day course of Remdesivir	199
✓	10-day course of Remdesivir	197

Measurement Points

Status	Timepoint	Value	Units
✓	Baseline	D	(days)
✓	Outcome	T1	(days)

Filter Data Elements

Hypertension

Status	Arm	Events	Total
✓	Control(St...	81	280
✓	5-day cou...	82	199
✓	10-day cou...	85	197

Mortality

Status	Arm	Events	Total
✓	Control(St...	4	280
✓	5-day cou...	2	199
✓	10-day cou...	8	197

Nausea

Status	Arm	Events	Total
✓	Control(St...	6	280
✓	5-day cou...	19	199
✓	10-day cou...	16	197

Length of hospital stay

Status	Arm	Median	IQR Lower	IQR Upper	N
✓	Control(St...				280
✓	5-day cou...				199
✓	10-day cou...				197

Age Mean

Status	Arm	Mean	SD	N
✓	Control(St...			280
✓	5-day cou...			199

The Study Design form specifies intervention arms in the study (Standard of care and 2 different Remdesivir dosages, in this case) as well as outcome measurement timepoints in the study (0 and 11 days).



## Synthesis

Our Team

Our Vision

Enterprise

AutoLit

Karl

Contributors

Karl Heibach

COVID-19: Antivirals

This nest displays a network meta-analysis of all studies reporting patient outcomes from randomized controlled trials (RCTs) for antivirals used to treat COVID-19. We report over 8,000 patients treated in 16 RCTs of 6 anti-virals compared against each other or against standard of care (SOC). Though variation in study size meant there is insufficient evidence for some therapies, we found a wide range in reported rates of ventilation at follow-up (from 1.8% to 18.4% compared to 9.5% for SOC) and mortality (from 1.2% to 10.7%), though SOC had the highest mortality rate at 13.5%. The dataset had high heterogeneity of data reported and also in patient populations; most notably, rate of severe COVID-19 infection at baseline ranged from 9.8% to 86.5%. Our findings indicate a pressing need for improved data harmonization in COVID-19 research to enable more effective cross-trial comparisons of therapies.

AutoLit

Construct or edit your living systematic review. You can also invite collaborators, share your work, or write a report.

Qualitative Synthesis

Browse common concepts discussed in studies of interest. You can interact with the tag diagram to find studies that address your research goals.

Most Frequent Tags

Tag	Frequency
Control/Standard of Care	17
Mortality	17
Diabetes Mellitus	16
Total Patient Population/Number of Patients	14

Quantitative Synthesis

Examine summary data and statistical analysis. You can compare therapies across outcomes of interest or review evidence from the underlying studies.

Meta-Analysis

Outcomes	Interventions
Mechanical Ventilation	Control/Standard of Care
Supplemental Oxygen	Favipiravir
Mortality	Lopinavir/Ritonavir
Diarhea	Sofosbuvir/Vedolizumab

Manuscript

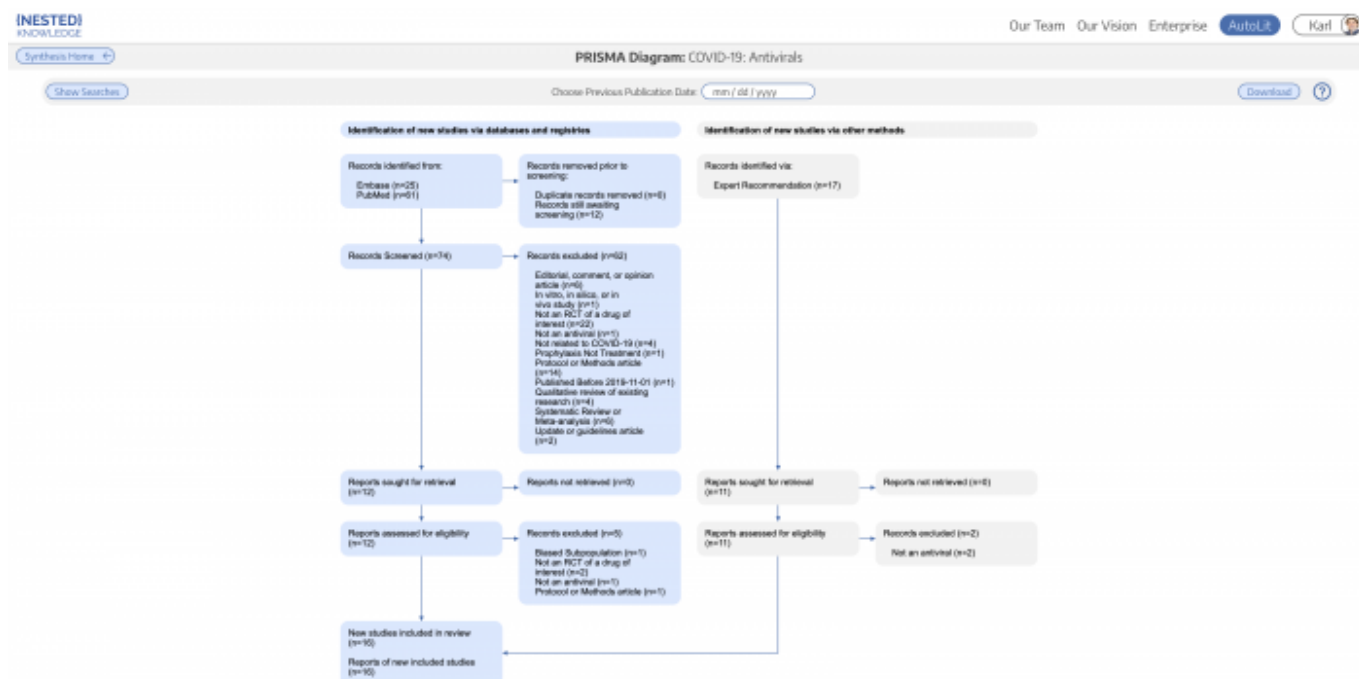
Read the authors' report of key findings and conclusions. You can also view updated methods, figures, and sources for this review.

PREPARE

Risk of Bias

## PRISMA

Click the PRISMA button in the bottom left of the page to view a PRISMA 2020 flow diagram. The diagram is auto-populated based on searches imported and studies screened in AutoLit.

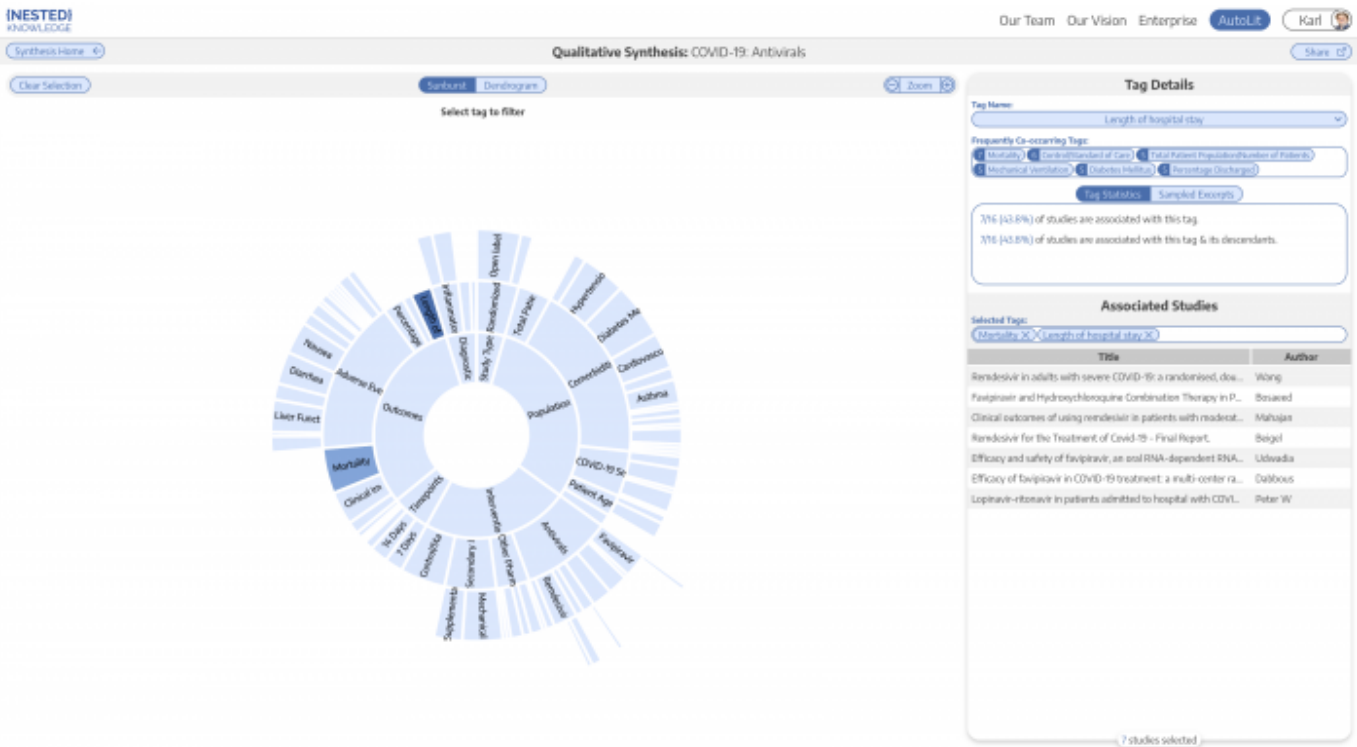


We can see that the 2 searches and 17 (19 - 2 duplicated records already imported in search) expert recommendations are displayed in the diagram. The diagram may be right clicked and saved as an arbitrary resolution SVG or exported in a variety of formats.

## Qualitative Synthesis

Navigate back to Synthesis Home and click the Qualitative Synthesis box. Qualitative Synthesis (QLS) displays data gathered in the Tagging Module. Each slice in the sunburst diagram is a tag. Its width corresponds to how frequently it was applied. Its distance from the center corresponds to its depth in the hierarchy (how many "is a" relationships are between it and its root tag). Click a slice to filter studies displayed to those where the tag was applied. Clicking multiple slices filters to studies with all the selected tags applied. The rightmost bar shows relevant studies (bottom) and some data about the tag (top), like its frequency, excerpts, and tags that were commonly applied with the selected tag.





In this tag selection, we see that Mortality and Length of Stay were reported as outcomes in 7 of 16 included studies. Click the rows of the study table to take a deep dive into the extracted data.

Quantitative Synthesis

Navigate back to Synthesis Home and click the Quantitative Synthesis box. Quantitative Synthesis (QNS) displays data gathered in the Extraction Module. QNS contains 3 different analyses automatically computed from extracted data.

The Summary tab contains pooled estimates of outcomes, broken out by interventions. Interventions may be expanded to different levels of precision, while outcomes analyzed may be selected from the dropdown menus. In the below example, we find a 7.3% mortality rate among all antivirals, against an 11.6% mortality rate for control/standard of care; Arbidol suggests a lower rate but is only supported by a single study.

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Synthesis Home

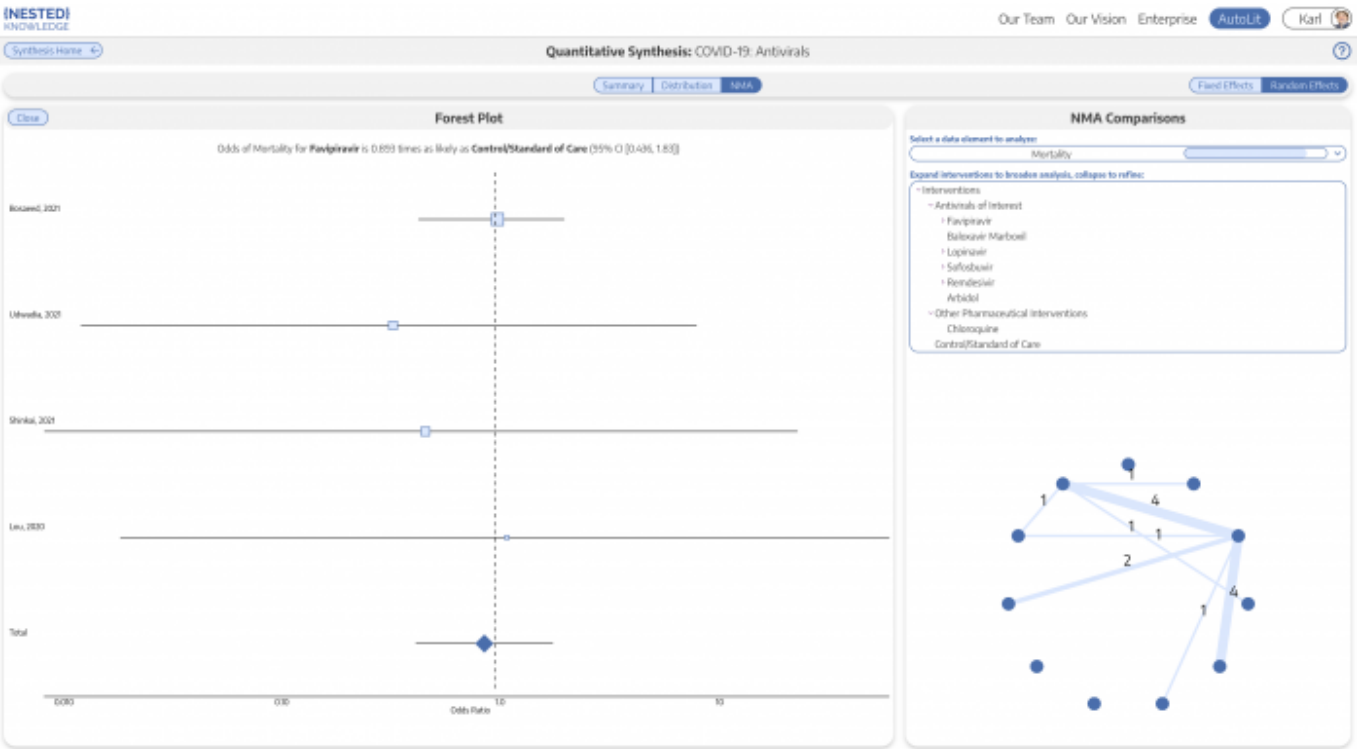
Quantitative Synthesis: COVID-19: Antivirals

Summary Distribution NMA

Fixed Effects Random Effects

Intervention	Outcome: Mortality			Outcome: Diarrhea			Outcome: Mechanical Ventilation		
	(n/N)	%	[CI]	(n/N)	%	[CI]	(n/N)	%	[CI]
Interventions	14238297	9.8%	[7.7%, 12.3%]	1051725	6.7%	[4.4%, 10.1%]	8527991	8.4%	[5.0%, 11.7%]
Antivirals of Interest	58415595	7.3%	[4.8%, 11.0%]	8611143	8.5%	[5.2%, 13.4%]	3703443	7.7%	[4.3%, 11.8%]
Favipiravir	161476	2.3%	[0.5%, 8.0%]	21234	9.0%	[3.7%, 26.0%]	42294	15.3%	[9.4%, 23.8%]
Baloxavir Marboxil	0/10	4.5%	[0.3%, 44.8%]	1/10	10.0%	[1.4%, 46.7%]	1/10	10.0%	[1.4%, 46.7%]
Lopinavir	3931715	22.9%	[21.0%, 25.0%]	13133	11.2%	[5.5%, 50.8%]	1601975	9.3%	[8.0%, 10.8%]
Rilastavir									
Atazanavir									
Sofosbuvir	16163	10.4%	[6.4%, 16.0%]				6763	5.3%	[2.5%, 10.9%]
Dactaravir									
Remdesivir	581921	6.6%	[3.2%, 13.1%]	2159	5.0%	[3.5%, 7.2%]	1347021	1.7%	[0.2%, 15.4%]
Ribavirin									
Arbital	0/100	0.4%	[0.0%, 6.3%]	18185	11.7%	[7.5%, 17.8%]	23700	22.5%	[15.9%, 30.8%]
Li et al.				305	8.8%	[2.8%, 23.4%]			
Chen et al.	0/100	0.4%	[0.0%, 6.3%]	15120	12.5%	[7.7%, 19.7%]	23700	22.5%	[15.9%, 30.8%]
Noxafeiron									
Arvidine									
Other Pharmaceutical Interventions	3148	4.2%	[1.0%, 15.2%]	2348	4.2%	[1.0%, 15.2%]	448	8.3%	[3.2%, 20.2%]
Secondary Interventions									
Control/Standard of Care	9014654	11.8%	[7.9%, 16.8%]	11534	3.3%	[1.3%, 8.2%]	4784530	9.2%	[4.7%, 17.5%]

The NMA tab computes a Network Meta-Analysis, which estimates effect sizes between pairwise comparisons of interventions on an outcome. The NMA comes with a network diagram (showing how commonly interventions were compared with one another), an effect size matrix, and forest plots (accessed by clicking on a cell in the effects matrix). Use the intervention expansion menu on the right of the page to refine interventions analyzed.



## Closing Remarks

You've now seen how a review may be completed & shared with the Nested Knowledge platform. We encourage you to head back to AutoLit and explore the variety of configuration options, and ever-

growing feature set we didn't get to cover here. If you're feeling ambitious, start your own Nest from scratch!

Use this documentation to guide you through more complex topics, and as always, please reach out to our support team via email and make requests on [Nolt](#).

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Last update: **2022/02/14 07:57**