

Demo Nest: COVID-19 Antivirals

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 2021.

In this walkthrough, we'll explain the core functionalities of Nested Knowledge through the *COVID-19: Antivirals* Nest. We encourage you to work through the nest as you follow this 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!

Nest Home

The screenshot shows the 'Nest Home' page for 'COVID-19: Antivirals (Demo)'. The interface includes a top navigation bar with 'Our Team', 'Our Vision', 'Enterprise', 'AutoLit', and a user profile 'Karl'. A left sidebar contains a 'Nest Home' menu and a 'Literature Search' section with options like 'Other Sources', 'Duplicate Review', 'Search Explanations', and 'Query Builder'. The main content area is titled 'COVID-19: Antivirals (Demo)' and includes sections for 'About', 'Title', 'Study Coordinator/Corresponding Author', and 'Team Members and Their Organizational Affiliations'. The 'About' section describes the nest as a copy of a previously-completed review. 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 a 'Comments' section with two comments from Karl Holub and Kathryn Cowie. The bottom of the page has a 'Comment' button.

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'. On the left sidebar, there are several menu items: 'Nest Home', 'Literature Search' (with a sub-menu '2/2'), 'Screening' (31/100), 'Tagging' (11/1%), 'Extraction' (11/1%), 'Synthesis', and 'Settings'. The main content area is titled 'Searches' and contains a table with columns: 'Term', 'Search Engine', 'Schedule', 'Search Now', 'History and Details', and 'Delete'. The table lists two searches: one for 'Lapinavir OR Ritonavir OR Remdesivir OR Ribavirin OR Arbidol OR Favipiravir' using 'Embase' with a 'Never' schedule, and another for '["Therapeutics" OR "antiviral therapies"] AND (RCT OR "randomized contr...)' using 'PubMed' with a 'Never' schedule. The last run for the PubMed search was on 2022-02-09, resulting in 59 results. The interface also includes an 'Add Search' button and an 'Interactions' link.

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 Marbo...	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, Nisofirone, 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...	Yin-Qiu 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

Supplements

PMC

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-1 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-1 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-1 blockade (n=172) or no IL-1 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.

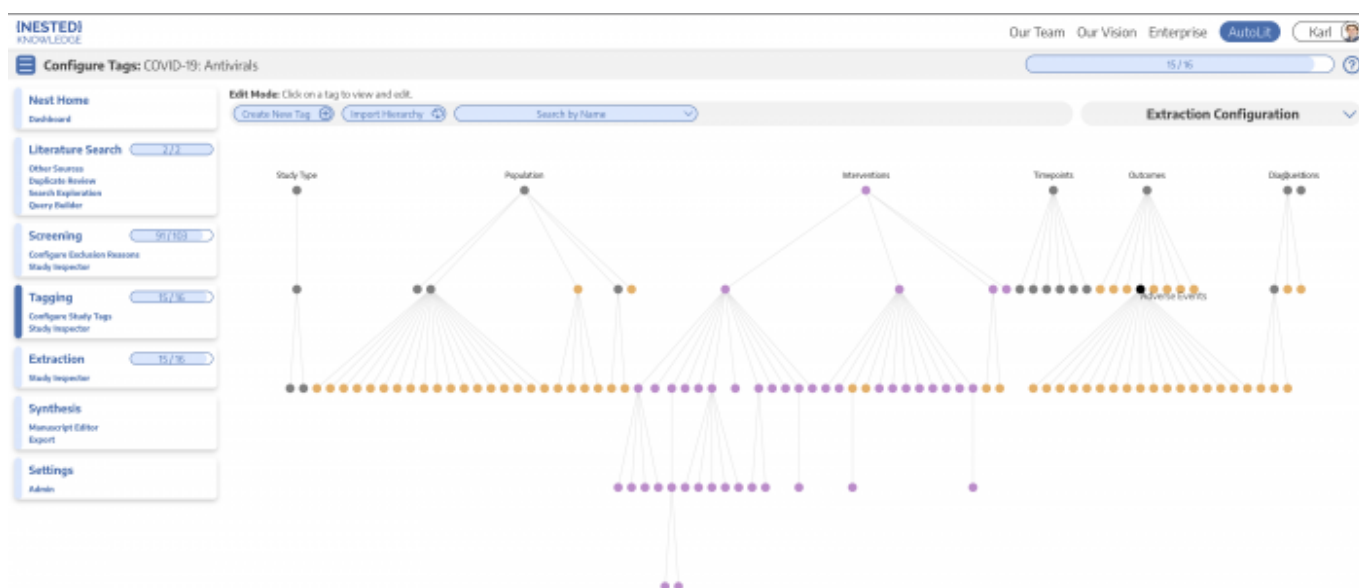
Abstract text may also be underlined with User Keywords, which are configured under the Settings menu item.

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

Full Text

Supplements

PMC

Research

1 of 10

50%

Abstract

Full Text

Supplements

PMC

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

Abstract

Full Text

Supplements

PMC

Abstract

Full Text

Supplements

PMC

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

Abstract

Full Text

Supplements

PMC

Tagging

Navigation

Tag

Text

10-day course of Remdesivir

10-day course of remdesivir (n = 137).

Open label

Randomized, open-label trial of hospitalized patients with confir...

Cardiovascular Disease

Patients in the 3 groups were balanced in demographic and disea...

Diabetes

Table 3

Diabetes Mellitus

Patients in the 3 groups were balanced in demographic and disea...

5-day course of Remdesivir

5-day course of remdesivir (n = 155)

Control/Standard of Care

250 Randomized to continue standard care 200 Continued stand...

11 Days

The primary end point was clinical status on day 11 as a T-point or...

Remdesivir

To determine the efficacy of 5 or 10 days of remdesivir treatment ...

Asthma

Patients in the 3 groups were balanced in demographic and disea...

Nausea

Table 3

Hypertension

Patients in the 3 groups were balanced in demographic and disea...

Mortality

Table 3

Cardiovascular Disease

Patients in the 3 groups were balanced in demographic and disea...

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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Columns

Add Filter

Full Text

Uploaded X

More

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 dactarasin 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 dactarasin 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, Nigo	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 Dise...	Xiao, Wu	2020		Excluded: Not an RCT of a drug of interest
Antibiotic Combination Clinically Better Than Standard Therapy ...	Pandya, Prasen 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 dactarasin 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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Abstract

Full Text

Supplements

PhD

Navigation

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Complete

Study Design

Arms

Measurement Points

Extracted Data

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

Extracted Data

Filter Data Elements

Hypertension

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

Baseline Outcome

Mortality

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

Baseline Outcome

Nausea

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

Baseline Outcome

Length of hospital stay

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


Baseline Outcome

Age Mean

Status	Arm	Mean	SD	N
✓	Control/Std...			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

Karli

Contributors



Karli Halab

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	16




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
Dyspnea	Sofosbuvir/Vedolizumab



Manuscript

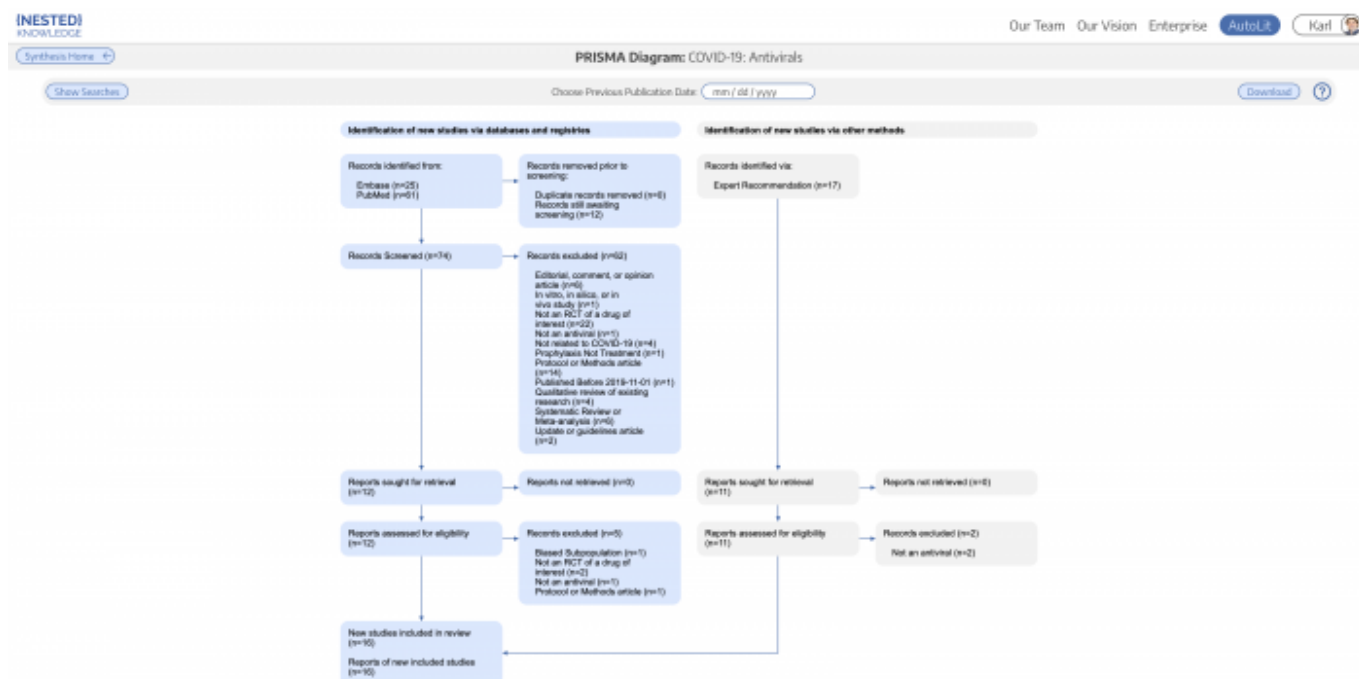
Read the authors' report of key findings and conclusions. You can also view updated methods, figures, and sources for this review.

PREVIEW

Risk of Bias

PRISMA

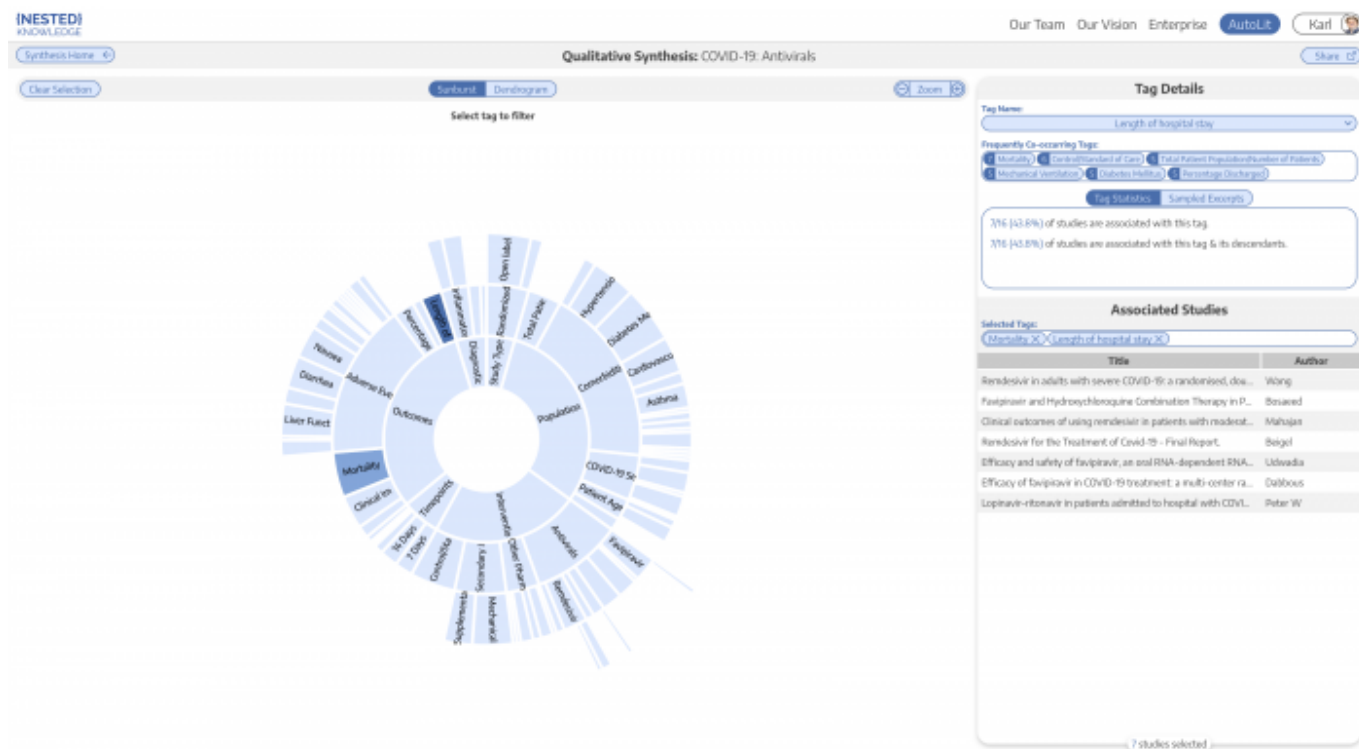
Click the PRISMA button in the bottom left of the page to view a PRISMA 2020 flow diagram. The diagram is auto-populated based on searches imported and studies screened in AutoLit.



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.

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