# **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**

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Nest Home	(Show Table of Contents) Protocol Description Materials)	Comments
Gashbaard		Nest Your Mentions All Mentions
Literature Search 2/2	COVID-19: Antivirals (Demo)	2 Karl Holub X20(23, 12:04 (
Here Sources	About	GNicole Hardy GRathryn Coule I have admin on this next, so I copied is
spilicate Review sands Exploration sany Builder	This Nest is a copy of a previously-completed review preserting the evidence regarding the safety and efficacy of anti-virals that had randomized controlled trial (PCT) evidence reported regarding the treatment of CDVID-10 as of January 2020.	the old protocol!
Screening ( <u>91/103</u> ) Certigues Exclusion Rescent	In this nest, you can examine the soardy, screening, tagging, and extraction completed in this review, as well as editing the protocol (below) and practicing adding and numming watches, including and excluding recents, editing the tagging hierarchy, and collecting tags and data based on underlying includied studies. To failway a guided well-through of the dense, places with aut colour-estation.	Kathryn Cowie 7020(27, 12-50) (Bilad Holub Thuris Karl
Ikaly inspector	If you have any questions, view our Documentation using the "7" in the upper right, or contact support. Happy next building!	
Tagging Tills	Title	
Centfigure Study Tege Study Inspector	Efficacy of antiviral therapies for CDVID-19: A systematic review of randomized controlled trials	
Extraction (15/16)	Study Coordinator/Corresponding Author	
Hady Inspector	Etin Steffels	
Synthesis	39 erinsheffels@supedit.com	
Manuscript Editor Expert	29 (763) 486-9684	
apar.	30 P0 8xx 6000545	
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ldenie	32 St Paul, MN 55106	
	Team Members and Their Organizational Affiliations	
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	<sup>b</sup> 19 Superior Nedical Experts, 1425 Minnehalia Ave E, St. Paul, MN, USA 55105 14 "Wested Knewledge, 1430 Avon Street N, Saint Paul, MN, USA 55107	
	<sup>4</sup> Ohio University Heritage College of Ostespathic Medicine, 6775 Balocat Way, Dublin, OH, 16 USA 63016	
	9Kamineni Academy of Medical Sciences and Research Center, Hyderabad - 500368, Telangana, 181ndia	
	<sup>1</sup> Department of Medicine, Lakeridge Health, 1 Hospital Crt, Cubawa, ON LLG 289 Reading Hospital, 420 South 5 20 <sup>(b)</sup> Avenue, West Reading, PA, USA 1907	
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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 filebased 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!

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#### **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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#### Demo Walkthrough: COVID-19 Antivirals

Other Sources: COVID-19: Ant	ivirals						2/2	
Nest Home		Add Individual Refere	nos Bblanire				Add by Identifier	
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Literature Search 212	Efficacy and safety of favipiravir, an oral RNA-dependent RNA pol	Zarir F Udwadia	International journal of infectiou	9/7/2021	Ranita Tarchand	×	(PutMediD	
Other Sources Duplicate Review	Clinical autoomes of using remdesivir in patients with moderate to	Ləkshmi Məhajarı	Indian   Anaesth	9/7/2021	Ranita Tarchand	×	Enter a single or comma separated list of identifiers. Bit be automatically imported from PubMed or CrossRef	lographic data
Search Exploration Duery Guilder	Difficacy of fasiginavir in COVID-19 treatment: a multi-center rando	Hany M Dabboas	Archives of virology	5/6/2021	Ranita Tarchand	×		
Screening 91/103	Clinical Outcomes and Plasma Concentrations of Balaxavir Marboxi	Yan Lou	European journal of pharmaceut	9/6/2021	Ranita Tanhand	×	Add Manually	
Configure Exclusion Research Rody Inspector	AVEAVER for Treatment of Patients with Moderate COVID-13: Inter-	Androy Alsoshche	Clinical infectious diseases : an o	9/6/2021	Ranita Tarchand	×	(Title Author Format	
Tagging (5/%)	Leginavir-ritenavir in patients admitted to hespital with COVID-19	Horby Peter W	Lancet (Landon, England)	9/6/2021	Ranita Tanhand	×	First/Last Full	
Configure Study Tage	Rendesivir for the Treatment of Cavid-19 - Final Report.	John H Beigel	The New England journal of me	9/6/2021	Ranita Tarchand	×	First Name Last Name	
Study Inspector	A Novel Protein Drug, Novaferon, as the Patential Antivinal Drug fo	Fang Zhong		1/15/2021	Jorge Polanco	×	Publication Date (mm/dd/ywy)	
Extraction (15/16) Noty Impector	Triple combination of interferon beta-fb, lopinavir-ritanavir, and rib	Ivan Fan-Nigal Hung	Lancet (Landon, England)	1/15/2021	Jorge Polanca	×	Publisher	
Synthesis	No Statistically Apparent Difference in Antiviral Effectiveness Obse	Yin-Qu Huang	Frontiers in pharmacology	1/15/2021	Jorge Polanco	×	Volume Insue	
Manascript Editor Export	Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial	Chang Chen		1/15/2021	Jorge Polanco	×	Corporate Author	
	Interferon -u2b Treatment for COVID-19	Zhou Qiong	Frontiers in Immunology	1/15/0021	Jorge Polanco	×	( Organization	
Settings Admin	Arbidol monotherapy is superior to lopinaviri/itonavir in treating C	Zhon Zha	The Journal of infection	1/15/2021	Jorge Polanco	×	CURL BOI	
	Efficacy and Safety of Lapinovic/Ritonavir or Arbidol in Adult Patie	YUeping U	Med (New York, N21)	1/15/2021	Jorge Polanca	×	(10.0000/0000 Abstract / Semmary	
	Repurposed Antiviral Drugs for Covid-13 - Interim WHD Solidarity		The New England journal of ree	1/14/2021	Jorge Polanco	×	Placeholder	
	A Trial of Lapinavir-Ritanavir in Adults Hospitalized with Severe Co	Bin Cao	The New England journal of me	12/28/2020	Kevin Kallines	×		
	Effect of Remdesivir vs Standard Care on Clinical Status at 10 Days i	Christoph D Spinner	JAMA	10/08/0200	Kevin Kalimes	×		
	Rendesivir in adults with severe COVID-19: a randomised, double	Yoming Wang	Lancet (London, England)	12/28/2020	Kevin Kallmes	×		AddRefere
	Experimental Treatment with Favipiravir for COVID-19: An Open-L	Qingxian Cai	Engineering (Beijing, China)	12/28/2020	Kevin Kallines	x		
	Experimental Trostment with Favipravir for COVID-19: An Open-L	Qingulan Cal	Engineering (Beijing, China)	12/28/2020	Kevin Kallines			

### 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.

lest Home	Effect of anti-interleukin drugs in patients with COVID-19 and si	ans of cytokine release	Abstract Pull Text Supplements PMC V	#	Navigation	
anhhoand	syndrome (COV-AID): a factorial, randomised, controlled trial.			Back		Ski
terature Search 2/2	BACKGROUND Infections with SARS-CoV-2 continue to cause significant morbid	ity and mortality. Interleukin (IL)-1 and II	-6 blockade have been proposed as therapeutic strategies	-		
her Taurees	in COVID-79, but study outcomes have been conflicting. We sought to study why with COVID-79, hypoxic respiratory failure, and signs of systemic cytokine release			Test Review	Screening	
plionte Review arch Exploration	in hospitalised patients with COVID-19, hypoxia, and signs of a cytokine release s	undrame across 16 hospitals in Belgium.	Eligible patients had a proven diagnosis of COVID-19 with	Uplead Pull Te		
sery Builder	symptoms between 6 and 16 days, a ratio of the partial pressure of oxygen to the Hig on supplemental oxygen, and signs of a cytokine release syndrome in their se			Bearch	10.	
creening (101)	flow oxygen or mechanical ventilation, or a ferritin concentration of more than %	00 µg/L, which had been increasing over	er the previous 24 h, or lymphopenia below BOQ/mL with		a drug of interest	
orficere Exclusion Dessors	two of the following criteria: an increasing ferritin concentration of more than 70 L, an increasing C-reactive protein concentration of more than 70 mg/L, or an inc			Protocol or Mi		
ady importor	design to evaluate IL-1 blockade versus no IL-1 blockade and IL-6 blockade versu	no IL-6 blockade. Patients were randor	nly assigned by means of permuted block randomisation		view or Meta-analysis nent. or goinion article	
agging (15/16)	with varying block size and stratification by centre. In a first randomisation, patis discharge, or to receive no IL-1 blockade (12). In a second randomisation step, pat	rits were assigned to receive subcutane joints were allocated to receive a single.	ous anakima once daily (100 mg) for 28 days or until foce of situationali (11 ma loc) intra-products, or a sincle doce.	Net an antivity		
infigure Study Tags	of toolizumab (8 mg/kg) intravenously, or to receive no IL-6 blockade (11:1). The	primary outcome was the time to clinica	improvement, defined as time from randomisation to an	Not related to		
ady importan	increase of at least two points on a 6-category ordinal scale or to discharge from treat population. Safety was assessed in the safety population. This study is regi				eless of existing research	j.
straction (15/36)	complete. FINDINGS Between April 4, and Dec 6, 2020, 342 patients were rando			Update or gui Published Befi		
adv inspector	assigned to IL-6 blockade (n=227, 114 for toolizumab and 113 for siltuximab) or no 54-731, and median Systematic Organ Failure Assessment (SOFA) score at rando				o, or in viva study	
and and action	estimated median time to clinical improvement was 12 days (95% CI 10-16) in the			Based Subport		
ynthesis	[95% CI 0.73-12(]). For the L-6 blockade group, the estimated median time to cli	nical improvement was 11 days (95% CI 1	0.46) versus 12 days (11.46) in the no L-6 blockade group	Prophylaxis N Retsacted	ot Treatment	
anuscript Editor gort	(HR 1-00 [078-129]). 55 patients died during the study, but no evidence for diffe and serious infections was similar across study groups. INTERPRETATION Drugs			Technical note		
9001	with COVID-19, hypexic respiratory failure, low SOFA score, and low baseline mo	itality risk. FUNDING Belgian Health Car	e Knowledge Center and VIB Grand Challenges program.		ce or Letter to the Edito	Į.
ettings	Population/Problem     Intervention     Outcome     C     User Key	aranta		Case Study Full Text Linux	alahia	
dmin .				secondary and		
	( Reywords	Obliographic fields	9 (6R)	Suspected CD		
				Not Published	lin English	

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 peform 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.

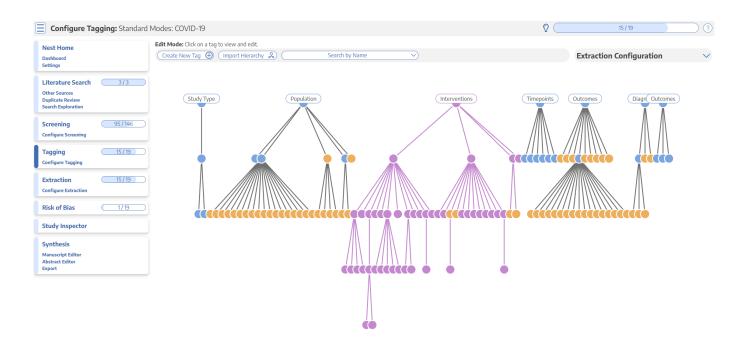
Abstract text may also be underlined with User Keywords, which are configured under the Settings menu item.

## 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 a you go.



#### **Tagging Module**

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

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Tagging: COVID-19: Antivirals				15/16				
iest Home	Effect of Remdesivir vs Standard Care on Abstract Editors Sec	olements) PMC V	2	Navigation				
ashbased	Clinical Status at 11 Days in Patients With			Havigedon	000			
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anfigure Exclusion Reasons	Effect of Remdesivir vs Standard Care on Clinical Status	s at 11 Days	Diantea	Table 3				
hady inspector	in Patients With Moderate COVID-19		Diabetes Mellitus	Patients in the 3 groups were balanced in demo	washirsand disea			
Tagging (15/15)	A Randomized Clinical Trial		5-day course of Remdesivin	5-day course of remdesivir (n = 199)				
anligure Study Tags	Ovistugh D Spinner, MO/ROBYTL, Gottled, MD /PID/Genet J Direct, MD, Josef Ramón Amber Jópez, MD, Han Alex Sonaro-Hodomiu, MD/Ovjerne Oppugg, MD, Promarchatham, MD, Rathewritt Multine, DD, Antonik		Centrol/Standard of Care	200 Randomized to continue standard care 200	Continued stand			
haly inspector	Louis Y Anno Chai, MD Mitra Reinitar/Derg, MD Owen Tar Yer Trang, MD Unon Remaccini, MD, Paul La Tarrier, N Devi Sendiagta, MD, Robert H, Hyland, DPHA, His E, Deinak, MD, Haver Do, MD, Oriettaro/Rein, MD, Hangaue	(b, Shan-Chwar Chung, IRD)	11 Days	The primary end point was clinical status on da				
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hally inspector		Vaul Meters	Asthma	Patients in the 3 groups were balanced in demo				
	Interesting Renderivit denominated clinical benefit in a placebo-controlled trial in	E Baltanial page 1041	Naurea	Table 1				
iynthesis	patients with severe constant as disease 2018 (CDVID 19), but its effect in patients with modecize diseases articloses.	C Septemental content	Hypertension	Patients in the 3 groups were balanced in demo	waanhirsand disea			
fanuszript Editor Isport	OBJOCHVE To determine the efficacy of 3 or 10 days of remdealer treatment compared with standard carries directly datas on day 11 after initiation of treatment.		Mortality	Table 3	grap was worked.			
	with standard carrow simularization on 66/11 after instances of treatment. Design, 10/1990, with HARDONARTS Randomized, open-label trial of hospitalized potents.		C	Cardiovascaliar Disease				
iettings Idmin	with confirmed servers and metaphotery purchase terminates a CARE Conf. 2 induction and metaphote CONFIP preserves calculations and preserve and these and memory and examples statistication while and black from March 15 through topil ML 2020, at 100 inception in the initial States, Europe, and black Theories of Hims Marchine are not March 2020.		Patients in the 3 groups were balanced in demographicand disease characteristics. [Table 1]. Cherall, SERs of patients had continvescular disease, 42% had hypertension;40% had diabetes, and 14% had asthma.					
	INTERVIEW DWK Patients wave-vanished in a 111 satis to resolve a 10-day counter of remotency (in = MP), a 5-day-counter of remotency (in = MK, or translated case (in = 200). Remotency was closed intervenceusly at 200 arg gran day 16 shows the job Or mat.							
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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.

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ther Sources aplicate Review	A Trial of Lopinavir-Ritonavir in Adults Hospitalized w Filter to Tagged WK	Mortality	2020	Induded
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aly inspector	Rendesivir in adults with severe COVID-19: a randomised, dou	Wang, Yeming	2020	Included
igging <u>5(16</u> )	Sofesbuvir and dadatesiir compared with standard of care in t	Sadeghi, Anahita	2020	Included
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and a company	Treatment of COVID-19 pneumonia with glucocorticaids (CORT	Les Bujanda, Migo	2021	Excluded: Protocol or Methods article
traction ( <u>TS (16</u> ) dytequator	Faviginavir and Hydroxychloroquine Combination Therapy in P	Bosawed, Mohammad	2027	Included
	Hydroxychloroquine with or without azithramycin for treatme	johnston, Christine	2021	Excluded: Not an RCT of a drug of interest
nthesis warigt Editor	Clinical outcomes of using remdesivir in patients with moderat	Mahajan, Lakshmi	2023	Included
pert	Efficacy and Safety of Triazzvinin Therapy for Coronavirus Dise	Xiaolee, Wa	2020	Excluded: Not an RCT of a drug of interest
ttings	Antininal Combination Clinically Better Than Standard Therapy	Panda, Prasan Kumar	2021	Excluded: Biased Subpopulation
ela	Evaluation of the effectiveness and safety of adding ivermecti	Okumug, Nurullah	2021	Excluded Not an antiviral
	Rendesivir for the Treatment of Covid-19 - Final Report.	Beigel, John H	2020	Induded
	Efficacy and safety of favipiravir, an oral RNA-dependent RNA	Udwadia, Zarir F	2028	Included
	Efficacy and safety of sofesbuvir plus dadatasvir or ravidasvir i	Abbass, Sherif	2023	Included
	Fastpitasir versus Arbidol for CDV/D-19: A Randomized Clinical	Chen, Chang	2020	Included
	Efficacy of favipiravir in COVID-19 treatment: a multi-center ra	Dabboes, Hany M	2028	Included
	Efficacy and Safety of Fasipirasir in Moderate COVID-19 Press.	Shinkai, Masaharu	2028	Included
	Clinical Outcomes and Plasma Concentrations of Balowavir Mar	Lou, Yan	2020	Included
	Triple combination of interferon beta-lb, lopinavir-ritonavir, an	Hung, Ixan Fan-Ngal	2020	Excluded: Not an antiviral
	Lopinavir-ritonavir in patients admitted to hospital with ODVL.	Peter W, Horby	2020	Included

### 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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inthesis	REPORTANCE Rendesive demonstrated direct benefit in a planetic controlled trial in	Editorial page 1041	Hypertension	n @				Enviro	0.8
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port	orance with reasoning the efficacy of i.or to days of remote virit reasonerst cangared	-					81		
	with standard care on clinical status on day if after initiation of treatment.				day cour		52		
rttings	MEMOR, SETTING, AND INSTICUMENTS Randomized, open-label initial frequenties		Mortality @		-349 080		60	(insing)	-
min	with confirmed severe acute requiratory syndrome carametrical.3 (3495 CaV 2) infection and moderate-COHD-19 preumonia (pulmanary inflictates and room-air oxygen saturation-VPHA)		Status		Arm	Events		Tabl	
	emplied from March 15 through April 18, 2020; at 105 hespitals in the United States, Europe,		549485		attol\$2.	CHEND		1008	
	and Asia. The date of final follow sprwas May 30, 2020.				day coar		2		
	Introvenences Patients were tandamized in a 11.4 ratio to receive a 10-day course of nendesive in a 1971, a 5-day course of nendesive in a 1980, or standard care/or a 2000.				-day on				
	Rendeskri masdasel intanencusty al 200 mgon day 1 followel by 100 mgbl.		Nausea 0					(Daaling	0.4
	NORM DUTCOMES AND MEASURES The primary and point was divical status on day if		Materi		Arm.	Events		Tetal	_
	on a 7-point ordinal scale-ranging/how dealty/builegory () to discharged libringery 7). Differences/between sendeduit tradment groups and standard care-were calculated using		~	0	arteolit		6		
	propertional odds models and expresent as adds ratios. An odds ratio greater than 1 indicates		4	5	day cour		19		
	difference in clinical status distribution toward category 7 for the rendesivir group vs the sizedant care group.		1	10	-day cau		10		
	RENULTI Among SHG patients who were tandomized. SH4 began the study and received		Length of ho	spital stay				Deseline	0.4
	rendes/vir ar continuent standard care/median age, 57 Britangaettile range, 46-661 prans.		Status	Arm	Median	IQR Lower	IQR Upper		N
	202 (1994) warren; 56% had cardinascular disease, 42% hypertension, and 42% diabetes), and 511 (0%%)-completed the truit itteduar length of treatment was 3-days/far patients in the			Cantral/St					
	5-day remderiving roup and 6-days for patients in the 10-day renderiving outp. On day 11,			S-day cour					
	patients in the 5-day remdealvir group/vad statistically significantly higher odds of a better			t0-day.cou					_
	clinical status distribution than these receiving standard care todds ratio, 1.05: 99% C, 1.09-2.48, P = 221. The dirical status distribution on day Tibehveen the TD-day remdering		Age Mean					Deteline	0,6
	and standard care groups was not significantly different (P = 38 by Wikows sark sum test).		95/5v6	Arm		fixan	90	N	4
	By day 28.9 patients had cled: 2 INC/initie 5-day rendesiving toop. 3 GNC/initie 10-day rendesiving toop, and 6 (216) in the standard care group. Raoses (XRN is INC), hypotiatienta			Cantrol(SL.					
	00% vs.2%), and beaclache 0% vs.2%) were more frequent among reindexive-tosated			5-day cour					

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).

The Extracted Data form contains means, medians, dichotomous rates, and categorical counts corresponding to baseline characteristics and outcomes for the study. Modify some of the data points, which will be auto-saved. If you enter incomplete or invalid data (e.g. a negative value for N), the leading Status column of the table will show a red X. Hover to view the error message.

## Synthesis

At this point, we've reviewed all the evidence gathered in AutoLit for the *COVID-19 Antivirals* Nest. Now let's navigate to Synthesis Home to draw some conclusions from our evidence, by clicking the Synthesis menu heading.

	COVID-19. We report of study size meant then compared to 9.5% for data reported and also	<b>COVID-19: Antivirals</b> This nest displays a network meta-analysis of all studies reporting patient outcomes from randomized controlled trials (RCB) for antivirals used to treat COVID-19. We report over 8,000 patients treated in 16 RCTs of 6 anti-virals compared against standard of care (SDC). 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 1.5% to 18.4% compared to 19.5% for SOC) and mortally (from 1.2% to 19.7%), though SOC had the highest mortality rate at 13.5%. The dataset had high heterogeneity of data reported and also in patient populations; most netably, rate of severe CDVID-19 infection at baseline ranged from 9.8% to 86.5%. Our findings indicate a prossing need for improved data harmenization in CDVID-19 research to enable more effective cress-trial comparisons of therapies.			
		Qualitative Synthesis	Most	Frequent Tags	
		Browse common concepts discussed in studies of interest. You can interact with the tag diagram to find studies that address your research goals.	Tag	Frequency	
		THE SAME AND BUILDED AND THE AND THE SECOND STREET	Control/Standard of Care	9	
			Martality	7	
			Diabetes Mellitus	16	
			Total Patient Population/Number of Patien	nts 14	
		Quantitative Synthesis	M	eta-Analysis	
		Examine summary data and statistical analysis. You can compare therapies across outcomes of interest or review evidence from the underlying studies.	Outcomes	Interventions	
	$\cdot \setminus \cdot$		Mechanical Vertilation	Control/Standard of Care	
			Supplemental Oxygen	Favipiravir	
	1.		Martality	Lapirumin/Ritornhir	
			Dianhea	Sefosbuviv/dadataswir	
PRISMA 15	Ĩ	Manuscript Road the authors' report of key findings and conclusions. You can also view updated methods, figures, and sources for this review.			

#### PRISMA

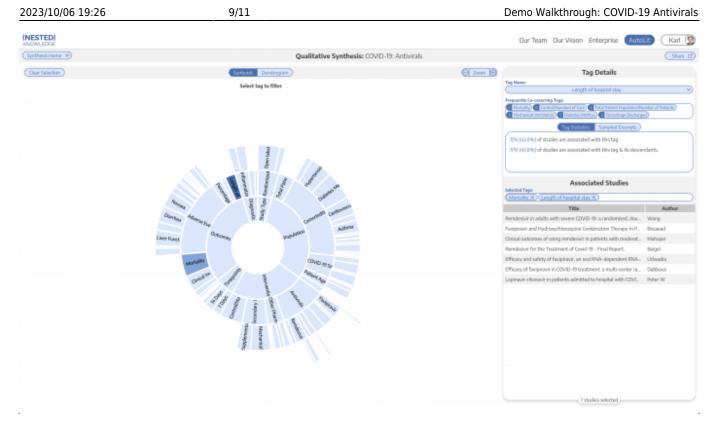
Click the PRISMA button in the bottom left of the page to view a PRISMA 2020 flow diagram. The diagram is auto-populated based on searches imported and studies screened in AutoLit.

esis Home (+)		PRISMA Diagram	COVID-19: Antivirals		
Show Searches		Choose Previous Publication Da	te (mm/dd/yyy		(Download)
	Identification of new studies via data	abases and registries	Identification of new studies via other	nathods	
	Records identified fram: Endoses (m25) PubMet (m91)	Records removed prior to acreening: Duplicate records removed (n=E) Records still awaiting acreening (n=E2)	Records identified via: Expert Recommendation (n=17)		
	Records Scherned (In-14)	Recards excluded (r+62)     Editorias, comment, or opinion     addite (r+62)     Hindler, or in     work, on a matching (r+6)     work an eXPT of a matching of     work on a matching (r+6)     work on a matching (r			
	Preports sought far retrieval (N=12)	Reports not retrieved (vm0)	Reports sought for retrieval (##11)	Reports not retrieved (x=0)	
	Proports assessed for alighting (n=12)	<ul> <li>Recentle excluded (r=5)</li> <li>Biased Subcopulation (r=1)</li> <li>Not an RCT of a drug pl interest (r=2)</li> <li>Not an enthrmit (r=1)</li> <li>Protocol or Methods article (r=1)</li> </ul>	Reports assessed for eligibility (e=11)	<ul> <li>Records excluded (n=2)</li> <li>Not an antivital (n=2)</li> </ul>	
	+ New studies included in review (n=10) Reports of new included studies (n=10)	•			

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 arbtirary 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 hierearchy (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.

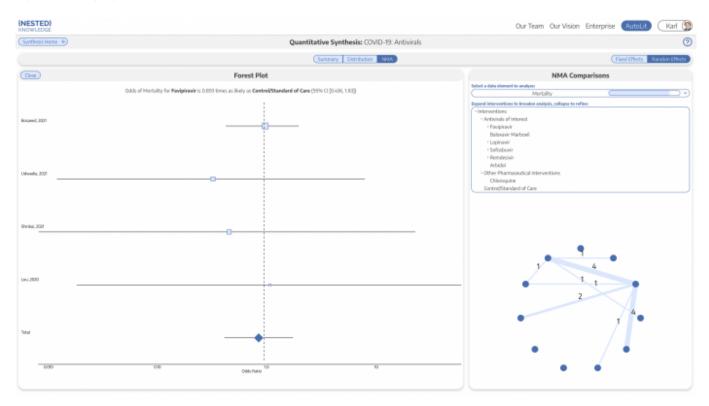
#### **Quantitative Synthesis**

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.

(ESTED) (OWLEDGE						Our Te	eam Our Vision	Enterprise 🗛	utoLit) 🤇 Karl 🕻
iynthesis Hone 🔹		Q	uantitative Synthesis:	COVID-19: Antivir	rals				(
			Summary Diritica	ton NVA				Fiedd	Random Effects
		Outcome			Outcome			Outcome	
Intervention	Morta	ity (		Diam	hea 🤇		Mechanical V	entilation (	
	(n/N)		[0]	(n/N)	75	[0]	(n/N)		[0]
interventions	1423/8297	9.8%	[7.7%, 12.3%]	105/1725	67%	[4.4%, 10.1%]	852/7991	8.4%	[6.0%, 11.7%]
VAntivirals of Interest	514/3595	7.3%	[4.8%, 11.0%]	86/1143	8.5%	[5.2%, 13.4%]	370(34(3	7.2%	[4.9%, 11.8%]
D Pasipinasir	15,1476	2.9%	[0.5%, 8.6%]	23/294	2.5%	[33%, 26.0%]	42/234	75.3%	[9.4%, Z3.8%]
D Balaxavir Marbedi	0/10	4.5%	[0.3%, 44.8%]	1/10	10.0%	[14%, 46.7%]	1/10	1D.D%	[14%, 46.7%]
D-Lopinavir	393/015	22.9%	[21.0%, 25.0%]	19/198	11.2%	[1.5%, 50.8%]	190,1215	9.3%	[8.0%, 10.8%]
D Ritesovir									
D Atazaravir									
þ Sofesbavir	15/153	10.4%	[5.4%, 15.6%]				6/153	5.2%	[2.5%, 10:9%]
D Daclatosvir									
D-Randosivir	94/1121	6.6%	[3.2%, 13.7%]	27/951	5.0%	[3.5%, 7.2%]	134/1121	17%	[0.2%, 15.4%]
D-Ribavinin									
• Arbidal	D/12D	0.4%	[0.0%, 6.3%]	18/155	11.7%	[7.5%, 17.8%]	23/120	22.5%	[15.9%, 30.8%]
Li et al.				3/95	8.6%	[2.8%, 23.4%]			
Chen et al.	0/120	0.4%	[2.0%, 6.3%]	15/12/0	12.5%	[7.2%, 19.2%]	23/120	22.5%	[15.9%, 30.8%]
D Novaferon									
D Azvadine									
D Other Pharmaceutical Interventions	2/4.8	4.2%	[1.0%, 15.2%]	2348	4.2%	[1.0%, 15.2%]	4/48	8.3%	[3.2%, 20.2%]
> Secondary Interventions									
Control/Standard of Care	9004654	1.5%	(7.9%, 16.6%)	10534	1.3%	[1.9%, 8.2%]	478/4530	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 evergrowing 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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