Demo Walkthrough: ACE Inhibitors & ARBs for Heart Failure

Welcome to the walkthrough of the *Heart Failure: ACE Inhibitors & ARBs* 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 a comparison of patient outcomes from treatment of Heart Failure with Angiotensin-converting enzyme (ACE) Inhibitors and Angiotensin II Receptor Blockers (ARBs) that were reported in randomized controlled trials (RCTs).

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| est Home | Show Table of Contents | Protocol Descrip | tice Hatariah) | Comments | |
| Interature Search Interature Search Interature Search Interature Search Interation Review Interation Review Interation | converting enzyme (ACE) In this rest, yee can exam- practizing addings and num- included studies. To fullow If you have any questions: Research question: Hour do the existing plant serious adverse events, of Background: Hourt failum is one of the physicans a waker range. | evicesh-completed review presenting a comparison of partient o initiations and Anglotman II Receptor Blockins (ARBI) that were ine the search, screening, Tapping, and entraction completed in this may assoche, including and enclosing meach, editing the tappin a guided solid-through of this demo, please with aux document screening assoches, including and well and the tapping of the screening of the search of the search of the search of the screening of the search of the search of the search of the screening of the search of the search of the search of the screening of the search of the search of the search of the screening of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the search of the search of the search of the screening of the search of the screening of the search of the screening of the search o | reported in randomized cavirolled trials (RCTU). This review, as well as editing the protocol (below) and phenetiky, and collecting tags and data based on underlying abor. Intel support. Happy next building! Lice compare with respect to safety outcomes: mortality, and approval of angiotemin Il receptor blockers (AHIb) gives | | 3/20/21, 4-39 al to this read 4 3/20/21, 10-42, sh associate complete a in more contral(devisus fro 3/20/21, 11-28 protocol be written? Befere |
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Nest Home

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 demo nest **intentionally has no searches** in order to focus on demonstrating how to add records manually. So if you navigate to the "Literature Search" menu heading, it will show an empty table.

This is typically **not standard practice for a review**, and the original completed nest did include several searches. For the purposes of this demo, all 16 studies were manually imported into screening allowing you to follow the records all the way through the workflow.

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. 16 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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| | Dual angistensin receptor and neprilysin inhibition as an alternativ | John J V McMurray | Eur.) Hisart Fail | 7/13/2021 | Averi Barrett | × | Flacaholder |
| | Angiotemin-reprilysin inhibition versus enalopei in heart failure. | John V McMurray | N Engl.] Med | 6(24)(2021 | Kevin Kallmes | × | |
| | | | | | | | |

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: Heart Failure: ACE I | hibitors & ARBs | 15/16 | | |
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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, 15 studies have been screened and 9 included. Try including the last remaining reference by clicking the include button. You may exclude references 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.

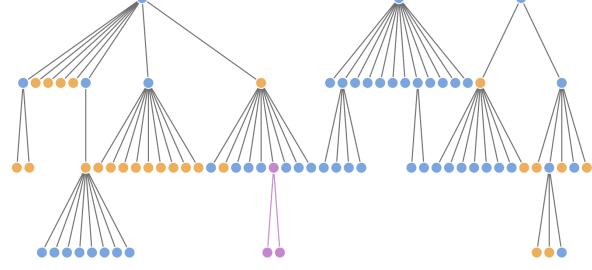
Abstract text may also be underlined with User Keywords, which are configured under the Settings menu item.

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 3 "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, "Serious Adverse Event" is a "Outcome", "Acute Kidney Injury" is a "Serious Adverse Event". Hover around the hierarchy to explore tags and read off the "is a" relationships a you go. Last update: 2023/06/27 21:52 wiki:start:demo:heart https://wiki.nested-knowledge.com/doku.php?id=wiki:start:demo:heart
Edit Mode: Click on a tag to view and edit.
Create New Tag
Import Hierarchy
Search by Name
Patient Characteristics
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Outcomes



Tagging Module

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

| Tagging: Heart Failure: ACE In | hibitors & ARBs | | (819 | |
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| | J.P. Teeflink, R. Diaz, G.M. Feller, J.J.Y. McMurray, M. Metra, S.D. Solomon, K.F. Adama, I. Anand, A. Asian-Mendeza, T. Biering-Seranaen, M. Böhm, D. Bonderman, J.G.F. Cleland, R. Cottalan, M.G. Crespe-Leira, | Placebo | We randomly assigned 8256 patient | ts (inpatients and outpatients |
| tady tespector | U. Dahlatzém, L.E. Echeverria, J.C. Fang, G. Filippatos, C. Fonseca, E. Goncalvesova, A.R. Goudev, J.G. Hawlett, D.E. Lanfear, J. Li, M. Land, P. Macdonald, V. Maneev, S. Momomana, E. O'Meana, A. Parhhomanko, P. Ponikowski, | All causes death | Table 1 | |
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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 included studies. Try out the title/abstract (TIAB) filter by typing "diabetes" into the search bar.

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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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The Study Design form specifies intervention arms in the study (Placebo and Omecamtiv Mecarbil, in this case) as well as outcome measurement timepoints in the study (0 and 663 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 *Heart Failure: ACE Inhibitors* & *ARBs* Nest. Now let's navigate to Synthesis Home to draw some conclusions from our evidence, by clicking the Synthesis menu heading.

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| {NESTED} | | | Our Team O | ur Vision Enterprise AutoLit (Karl 🕻 |
|-------------------------|--|--|--|--|
| Contributors | existing and emerging AutoLit living review HFrEF against one an Network (SIGN) oritor outcomes included th studies in our system (ACEI) (5 trials) or sod | Heart Failure: ACE Inhibitors & ARBs takes with reduced ejection fraction (PFEE) have an overall poor prognosis and high mortality. This sture pharmacological HFEE therapies using data from recently published randomized controlled trials (RCTs) platform was used to identify and scores RCTs published between 2010 and 2021 that compore the use of their and against platebox. Risk of bias and levels of evidence for each study were scored using the Scuti ta for RCTs. Primary outcomes included cardiovascular doath, al-cause mortality, and event ratis for first. a downer events of hypotension, symptomatic hypotension, hypotension, hypotension, and cause in advection, and the intel is compared all events. Most of these trials compared angiotension involved-involves and systematic reviews periority of SCLT2 inhibitors over placebo. Our systematic review suggests that ARNI and SCLT2 inhibitors | The Nested Knowledge f pharmacological therapies for shi Intercological therapies hospitalization. Secondary (injury. We included 12 rolevant -converting enzyme inhibitors sugent the superiority of ARNI | AutoLit Construct or edit your living systematic review. You can also invite collaborators, share your work, or write a report. |
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| | | 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 |
| | \therefore \vee : | | All causes death | Placebo |
| | · X | | Serious Adverse Events | Enalapril |
| | 1. | | First Hospitalization | Sacubtril/valuartan |
| | | | Cardiovascalar Death | Eplerenane |
| | | | | |
| FRISMA To Redefine P | X | Manuscript Road the authors' report of lowy 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.



In this case, PRISMA is not particularly relevant to the type of searching performed, as only our 16 expert recommendations were considered for screening. Regardless, 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.

| (NESTED) KNOWLEDGE | | | Our Team Our Vision Enterprise Auto | Rarl 🐧 |
|-----------------------|---|------------|-------------------------------------|-----------|
| Synthesis Home | Qualitative Synthesis: Heart Failure: ACE Inhibitors & ARBs | | | Share (2) |
| (Gear Selection) | Sizbart Deedrogram) | Q 2000 (D) | Tag Details | |
| | Select tag to filter | | Tag Name: ACE Inhibitors | v) |
| | And | | | darts. |
| | | | 4 studies selected | |

In this tag selection, we see that Hyperkalaemia was reported as an outcome in 4 studies that included a patient population that was on an Ace Inhibitor at Baseline. 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 17.6% mortality rate for Placebo against generally lower rates for other medications; Omecamtiv m ecarbil carries a 25.9% mortality rate, but the estimate is only built on a single, albeit large, study.

| nthesisHone +) | | Quantita | tive Synthesis: Heart | Failure: ACE Inhibit | ors & ARBs | | | | | |
|---------------------------------|-------------|----------|-----------------------|----------------------|--|--------------|-------------|----------------------|---------------------|--|
| | | | Summary Dim | Butice NVM | | | | Field | Texts Fandon Effect | |
| | | Outcome | | | Baseline | | | Outcome | | |
| Intervention | Alcases | |) • | | Left ventricular ejection fraction (%) | | | Cardiovascular Death | | |
| | (4,14) | % | [0] | Mean | N | 101 | (n/h) | % | [0] | |
| terventions | 7286,440001 | 15.9% | [13.7%, 18.3%] | 291 | 40001 | [18.3, 29.9] | 5875/38/297 | 13.5% | [12.3%, 15.6%] | |
| Placebo | 2959/155H | 17.6% | [14.0%, 21.9%] | 281 | 1551 | [26.3, 29.5] | 2390/15511 | 36.6% | [11.9%, 37.3%] | |
| Sacubtrill/valsartan | 70/4488 | 2.1% | [0.1%, 30.7%] | 34.5 | 4488 | [28.5, 34.5] | 558/4197 | 13.3% | [12.3%, 14.4%] | |
| > Empaglifizzin | 246(1863 | 13.4%b | [71.9%, 15.0%] | 27.7 | 1863 | [27.4, 28.0] | 187/1863 | 10.0% | [8.8%, 11.5%] | |
| • Enalspril | 833/4615 | 2.0% | [0.2%, 32.4%] | 31.0 | 4515 | [28.5, 33.4] | 620/4212 | 36.5% | [75.496, 17.696] | |
| Khondwalla et al. | 1/70 | 1.496 | [0.2%, 9.4%] | 30.6 | 70 | [28.8, 32.4] | | | | |
| McMurray et al. | 835/42/2 | 19.8% | [18.6%, 21.1%] | 29.4 | 4212 | [29.2, 29.6] | 693/4212 | 16.5% | [15.4%, 17.9%] | |
| Denal et al. | 1/233 | 0.4% | [0.7%, 3.0%] | 35.D | 233 | [31.7, 34.3] | | | | |
| Epierenarie | 171/1364 | 12.5% | [10.9%, 14.4%] | 26.2 | 1364 | [26.0, 26.4] | 142/1364 | 10.8% | [9.2%, 12.5%] | |
| ♥ Dapagii flozin | 276(2373 | 11.6% | [10.4%, 13.0%] | 312 | 2373 | [30.9, 31.5] | 227/2373 | 9.6% | [8.4%, 10.8%] | |
| McMurray et al. | 276(2373 | 11.6% | [10.4%, 13.0%] | 31.2 | 2373 | [30.9, 31.5] | 227/2373 | 9.6% | [8.4%, 10.8%] | |
| > Sataglificatin | | | | | | | | | | |
| D Valsartan | | | | | | | | | | |
| Omecanitiv mecantil | 1057/4/20 | 25.9% | [24.6%, 27.3%] | 26.6 | 4/20 | [26.4, 26.8] | 806/420 | 19.6% | [18.4%.20.9%] | |
| Teerlink et al. | 1057/4120 | 25.9% | [24.6%, 27.9%] | 26.6 | 4120 | [26.4, 26.8] | 806/420 | T3.5% | [18.4%, 20.9%] | |
| Vericipant | \$10/2526 | 20.3% | [18.2%, 21.9%] | 29.0 | 2526 | [28.3, 29.3] | 444/2526 | 35.4% | [15.0%, 17.9%] | |
| > Nabradine | 503/324 | 15.5% | [14.3%, 16.8%] | 29.0 | 3241 | [28.8, 29.2] | 448/324 | 18.9% | [12,7%, 15,1%] | |
| > rh8NP (recombinant human BNP) | | | | | | | | | | |

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.

| Synthesis Horne 🕤 | Quantitative Synthesis: Heart Failure: ACE Inhibito | ors & ARBs |
|-------------------|--|--|
| | Summary Distribution NW | (Field Effects Aardon Effe |
| (ase) | Forest Plot | NMA Comparisons |
| | Odds of All causes death for Enalogefi is 1.23 times as likely as Sacabbril/valuartae (15% C [1.08, 1.32]) | Select a data element to analyze: Mit canves death |
| andwala, 305 | - | Transferrentians to lossafile analysis, collipse to ordina |
| +64,229 | | |
| tal | 4.0 13 Odds Lafer 10 10 | |

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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Last update: 2023/06/27 21:52